Health Resource Utilization and Associated Health Care Costs of Biologic Disease-Modifying Antirheumatic Drugs in German Patients With Psoriatic Arthritis

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Objective. To investigate health care costs associated with biologic disease-modifying antirheumatic drugs (bDMARDs) in a German real-world cohort of adult biologics-naive patients with psoriatic arthritis (PsA).

Methods. Claims data from the Institute for Applied Health Research Berlin (InGef) research database for patients with a PsA diagnosis and bDMARD claims record (index date) between January 1, 2014, and December 31, 2017, and no bDMARD prescriptions for 365 days before the index date were retrospectively analyzed. Primary outcomes were determination of health care resource utilization and associated annual health care costs for overall and individual bDMARDs in the 12-month pre-index and post-index periods. These outcomes were compared between persistent and nonpersistent groups. Nonpersistence was defined as treatment gap or switch to a bDMARD other than the index therapy.

Results. Among 10,954 patients with a PsA diagnosis, 348 were eligible. Although mean ± SD post-index costs were significantly higher in the persistent group than the nonpersistent group (€27,869 ± 8,001 versus €21,897 ± 10,600, P < 0.001) due to higher bDMARD acquisition costs (€23,996 ± 4,818 versus €16,427 ± 9,033, P < 0.001), persistence reduced inpatient treatment costs (−€760), outpatient treatment costs (−€192), other drug costs (−€724), and sick leave costs (−€601).

Conclusion. Although initiation of bDMARDs increased the total health care costs irrespective of persistence status, partial cost offsets were observed in the persistent patient population.

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory rheumatic disease presenting mostly along with psoriasis as a concomitant condition. Its major characteristics include pain, stiffness, swollen joints, and joint erosion and bone formation (1,2). In Germany, the age-standardized prevalence of PsA was reported to be 1.8–2.1 per 100,000 in men and 2.1–2.5 per 100,000 in women from 2009 to 2012, resulting in an estimated 200,000 patients with PsA living in Germany in 2018 (3). Impairment in daily function and capability to work, fatigue, and reduced social participation due to PsA has been associated with a negative impact on health-related quality of life (HRQoL) (4,5). The economic burden associated with PsA has also been reported. Analysis of German claims data (2010–2013) revealed average health care costs in treated prevalent patients with PsA to be €5,557 and €5,761 in the first and second year after diagnosis, respectively (6). Moreover, another German claims data study (2010–2014) reported the average cost of disease-modifying antirheumatic drugs (DMARDs) and biologic DMARDs (bDMARDs) to be €322 per patient/year and €15,304 per patient/year, respectively (7).
Treatment options for PsA include conventional symptomatic therapies (glucocorticoids and nonsteroidal antiinflammatory drugs [NSAIDs]), DMARDs (methotrexate, leflunomide, and cyclosporine), bDMARDs (tumor necrosis factor inhibitors, interleukin-12/23, interleukin-17 inhibitors, or soluble fusion proteins against CTLA-4), and targeted synthetic DMARDs (tsDMARDs) such as phosphodiesterase 4 or JAK inhibitors (8–10). Treatment with bDMARDs or tsDMARDs is recommended for patients with active PsA refractory to conventional DMARDs (csDMARDs)/NSAIDs ± local glucocorticoid injections depending on the predominant affected domain (9,10). Many German patients with PsA undergo systemic treatment (53.7%), and the majority of these patients are treated with DMARDs (72.1%), with the remaining 20.9% being treated with a combination of DMARDs and bDMARDs (7). As of today, 9 bDMARDs (certolizumab pegol, etanercept, abatacept, adalimumab, infliximab, golimumab, secukinumab, ustekinumab, and ixekizumab) and 2 tsDMARDs (apremilast and tofacitinib) are approved in Germany for the treatment of PsA. Apremilast has been available since 2015, while abatacept, ixekizumab, and tofacitinib were launched in 2018.

Studies from Brazil (11), Sweden (12,13), and the US (14,15) have reported that persistence, i.e., the duration from initiation to discontinuation of treatment (16), influences health care resource utilization (HRU) and associated costs. While the expenditure on bDMARDs is greater in persistent patients compared with nonpersistent patients, other costs such as inpatient and outpatient treatment costs were greater in nonpersistent patients. The persistence rate in German patients with PsA who were treated with bDMARDs was 57.9% after 1 year (17) and 33.2% after 5 years (18). However, data on the economic aspects of treatment before and after bDMARD initiation as well as with respect to persistence are unavailable. Therefore, we evaluated the real-world HRU and related health care costs associated with bDMARDs prescribed to patients with PsA using data from a large German claims database.

**MATERIALS AND METHODS**

**Data source.** This retrospective study analyzed anonymized patient data from the Institute for Applied Health Research Berlin (InGef) research database. This database contains longitudinal patient-level electronic records of health insurance claim information such as inpatient and outpatient treatments, prescription drugs, and other health-related claims data for ~4 million members of the German statutory health insurance (SHI), which covers ~90% of the German population. The data are structured to represent the German population in terms of age and sex according to the Federal Office of Statistics (Destatis) (19). External validation regarding the representativeness of this database in terms of morbidity, mortality, and drug usage with the general German population has been performed (20). The InGef research database has been extensively utilized for health services research (21–24).

**Study population.** The study period spanned from January 1, 2013, to December 31, 2018. The first observed bDMARD prescription (i.e., dispense date) was defined as the index date. The inclusion criteria were as follows: a PsA diagnosis as per International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, German Modification (ICD-10-GM) code L40.5 in combination with M07.0/07.1/07.2/07.3 (see Supplementary Table 1, available on the Arthritis Care & Research website at http://onlinelibrary.wiley.com/doi/10.1002/acr.24598) in the inpatient (primary or secondary diagnosis) or outpatient setting (verified diagnosis) and a claims record of biologic treatment licensed for PsA as per Anatomical Therapeutic Chemical (ATC) classification codes (see Supplementary Table 2, available on the Arthritis Care & Research website at http://onlinelibrary.wiley.com/doi/10.1002/acr.24598) between January 1, 2014, and December 31, 2017; age ≥18 years in the index quarter; a diagnosis of PsA and biologic claim in the same quarter of the index date; biologics-naïve status at the index date; and presence of at least 365 days of continuous enrollment prior to and after the index date. Patients without a prescription record for any PsA-licensed biologic at any strength in the 365 days before the index date were defined as biologics-naïve patients. Patients identified with rheumatoid arthritis (ICD-10-GM codes M05–M07), ankylosing spondylitis (ICD-10-GM code M45), Crohn’s disease (ICD-10-GM code K50), and ulcerative colitis (ICD-10-GM code K51) and patients with 2 different bDMARD index prescriptions on the same day were excluded (Figure 1).

**Sample size and study power.** A previously performed feasibility analysis revealed that between January 1, 2014, and December 31, 2017, ~1,900 patients with an ICD-10-GM diagnosis code for PsA (excluding juvenile PsA) (see Supplementary Table 1, available at http://onlinelibrary.wiley.com/doi/10.1002/acr.24598) and with an ATC code for biologic treatment (see Supplementary Table 2, available at http://onlinelibrary.wiley.com/doi/10.1002/acr.24598) were available in the InGef research database.
Covariates. The baseline covariates of interest included age, sex, insurance status, degree of polypharmacy, use of glucocorticoids, diagnosis of psoriasis in the individual quarter of the index event, and the updated Charlson comorbidity index (CCI) (25). Polypharmacy and glucocorticoid prescriptions were assessed based on ATC codes for specific comediations used in the 12-month pre-index period (see Supplementary Table 3, available on the Arthritis Care & Research website at http://onlinelibrary.wiley.com/doi/10.1002/acr.24598). ICD-10-GM codes L40.0–L40.4, L40.8, and L40.9 were used to diagnose psoriasis. The updated CCI included 19 comorbidities as given in Supplementary Tables 4 and 5, available on the Arthritis Care & Research website at http://onlinelibrary.wiley.com/doi/10.1002/acr.24598, and assigned a weight between 1 and 6 to each comorbidity. A higher CCI score indicates a greater morbidity of the patient.

Outcomes. The primary outcomes were determination of HRU and associated health care costs for 12 months in the pre- and post-index periods for the overall biologics-naive population as well as for each individual bDMARD. HRU comprised the number of all-cause hospitalizations, all-cause outpatient visits (identified using Uniform Assessment Standard codes), sick leave cases, and length of stay for hospitalizations and sick leave. Difference in the number of days from admission to discharge was considered as the length of stay, and difference in the number of days from start to end of sick leave +1 was considered as the length of the sick leave.

Health care costs were stratified as inpatient costs, outpatient costs, medication costs (further stratified into bDMARD and other drug costs), medical remedies, devices, and aid-related costs, and sick leave costs. Sick leave costs refer to the costs...
covered by the SHI. In Germany, during an employee’s illness, the agreed salary wage continues to be paid for a period of 42 days by the employer. After that timeframe, the health insurance covers sick pay for up to 546 days. Patients obtain up to 90% of their net salary, with a cap of €103.25 per day.

The outcomes were also evaluated based on persistence. Patients were assigned to a persistent group if they continued bDMARD usage in the 12-month post-index period and to a nonpersistent group if they discontinued or switched their index bDMARD in the 12-month post-index period. The persistence period was defined as the time from treatment initiation (index date) until discontinuation of the index biologic or switch to another biologic during follow-up, whichever came first. Non-persistence occurred if 1) a gap exceeding 60 days (grace period) after the end of supply of the index bDMARD was found, or 2) the patient switched from the index bDMARD to a non-index treatment(s). This definition of drug survival is consistent with that in earlier studies (26–28). Days of supply were calculated based on the daily defined doses as reported by the World Health Organization for each bDMARD (see Supplementary Table 2, available at http://onlinelibrary.wiley.com/doi/10.1002/acr.24598) (29).

Statistical analysis. Means and SDs for continuous variables and counts and percentages for categorical variables were calculated. Due to the skewed nature of cost data, \( P \) values for comparisons of mean ± SD HRU and health care costs were calculated using the bootstrapping \( t \)-test. For comparing proportions of persistent versus nonpersistent patients with health care costs, the chi-square test was used or, in case of small sample sizes or groups with 0 patients, Fisher’s test was applied. \( P \) values less than 0.05 were considered significant. All analyses were undertaken using R software, version 3.5.0.

RESULTS

Population characteristics. Among the 10,954 patients diagnosed with PsA, 348 were eligible for the study (Figure 1) (adalimumab \( n = 105 \), certolizumab pegol \( n = 29 \), etanercept \( n = 100 \), golimumab \( n = 20 \), infliximab \( n = 9 \), secukinumab \( n = 53 \), and ustekinumab \( n = 32 \)). Baseline characteristics are reported in Table 1. The majority of the patients were ≤60 years old (80.2%), and the mean ± SD patient age was 50.4 ± 12.4 years. The majority of the patients were full members (73.3%). Most of the patients had a CCI score of ≤2 (89.1%), and the mean ± SD CCI score was 0.99 ± 1.24. The mean ± SD number of medications for specific comedications prescribed was 1.7 ± 1.03, and most of the patients were prescribed 1–2 medications (68.7%).

| Parameter | Total (n = 348) | Men (n = 184) | Women (n = 164) |
|-----------|----------------|--------------|-----------------|
| Age, mean ± SD years | 50.4 ± 12.4 | 50.5 ± 11.7 | 50.4 ± 13.2 |
| Age groups, years | | | |
| ≤60 | 279 (80.2) | 149 (81.0) | 130 (79.3) |
| 61–70 | 49 (14.1) | 25 (13.6) | 24 (14.6) |
| >70 | 20 (5.8) | 10 (5.4) | 10 (6.1) |
| Insurance status | | | |
| Full member | 255 (73.3) | 149 (81.0) | 106 (64.6) |
| Family insured | 21 (6.0) | <5 (-) | 20 (12.2) |
| Pensioner | 72 (20.7) | 34 (18.5) | 38 (23.2) |
| CCI score, mean ± SD | 0.99 ± 1.24 | - | - |
| CCI score | | | |
| ≤2 | 310 (89.1) | 162 (88.0) | 148 (90.2) |
| 3–5 | 36 (10.3) | 22 (12.0) | 14 (8.5) |
| >5 | <5 (-) | 0 | <5 (-) |
| Degree of polypharmacy, mean ± SD | 1.7 ± 1.03 | - | - |
| Degree of polypharmacy | | | |
| 0 | 46 (13.2) | 24 (13.0) | 22 (13.4) |
| 1–2 | 239 (68.7) | 132 (71.7) | 107 (65.2) |
| 3–5 | 63 (18.1) | 28 (15.2) | 35 (21.3) |
| Glucocorticoid prescriptions/patient, mean ± SD | 1.3 ± 1.9 | - | - |
| Glucocorticoids prescribed | | | |
| No | 184 (52.9) | 103 (56.0) | 81 (49.4) |
| Yes | 164 (47.1) | 81 (44.0) | 83 (50.6) |
| Psoriasis diagnosis in the individual quarter of the index event | | | |
| No | 62 (17.8) | 26 (14.1) | 36 (22.0) |
| Yes | 286 (82.2) | 158 (85.9) | 128 (78.0) |

* Values are the number (%) unless indicated otherwise. Patient counts <5 are reported as <5 due to data protection regulations. CCI = Charlson comorbidity index.
| Parameter | Total (n = 348) | Persistent (n = 200) | Nonpersistent (n = 148) | P (Z, bootstrap t-test) | P (Fisher's test) |
|-----------|----------------|----------------------|-------------------------|-------------------------|-------------------|
|           | Pre-index | Post-index | Pre-index | Post-index | Pre-index | Post-index | Pre-index | Post-index | Pre-index | Post-index |
| Health care resource utilization |          |           |           |           |           |           |           |           |           |           |
| Hospitalizations |          |           |           |           |           |           |           |           |           |           |
| No. of patients, no. (%) | 170 (48.8) | 158 (45.4) | 99 (49.5) | 77 (38.5) | 71 (48.0) | 81 (54.7) | 0.778 | 0.003 | 0.828 | 0.003 |
| No. of hospitalizations | 1.21 ± 1.77 | 1.34 ± 1.98 | 1.12 ± 1.53 | 1.05 ± 1.67 | 1.34 ± 2.06 | 1.73 ± 2.29 | 0.289 | 0.002 | – | – |
| LOS in days | 10.88 ± 28.74 | 13.93 ± 37.69 | 10.82 ± 29.44 | 11.68 ± 30.78 | 10.96 ± 27.87 | 16.99 ± 45.32 | 0.965 | 0.227 | – | – |
| Outpatient visits |          |           |           |           |           |           |           |           |           |           |
| No. of patients, no. (%) | 348 (100) | 348 (100) | 200 (100) | 200 (100) | 148 (100) | 148 (100) | – | – | 1.000 | 1.000 |
| No. of outpatient visits | 20.63 ± 8.26 | 18.95 ± 7.95 | 20.80 ± 8.29 | 18.38 ± 7.59 | 20.41 ± 8.23 | 19.71 ± 8.37 | 0.670 | 0.129 | – | – |
| Sick leave |          |           |           |           |           |           |           |           |           |           |
| No. of patients, no. (%) | 162 (46.9) | 149 (42.8) | 95 (47.5) | 85 (42.5) | 67 (45.3) | 64 (43.2) | 0.680 | 0.890 | 0.745 | 0.913 |
| No. of sick leaves | 1.30 ± 1.80 | 1.21 ± 1.90 | 1.22 ± 1.69 | 1.13 ± 1.89 | 1.41 ± 1.94 | 1.32 ± 1.91 | 0.352 | 0.346 | – | – |
| Duration in days | 24.34 ± 52.78 | 15.53 ± 34.54 | 25.53 ± 53.43 | 13.11 ± 28.11 | 22.74 ± 52.02 | 18.80 ± 41.56 | 0.629 | 0.157 | – | – |
| Health care costs, € |          |           |           |           |           |           |           |           |           |           |
| Inpatient treatment |          |           |           |           |           |           |           |           |           |           |
| No. of patients, no. (%) | 170 (48.8) | 158 (45.4) | 99 (49.5) | 77 (38.5) | 71 (48.0) | 81 (54.7) | 0.778 | 0.003 | 0.828 | 0.003 |
| Costs | 1,818 ± 3,558 | 1,450 ± 3,698 | 2,030 ± 3,861 | 1,270 ± 3,961 | 1,532 ± 3,090 | 1,693 ± 3,308 | 0.182 | 0.286 | – | – |
| Outpatient treatment |          |           |           |           |           |           |           |           |           |           |
| No. of patients, no. (%) | 348 (100) | 348 (100) | 200 (100) | 200 (100) | 148 (100) | 148 (100) | – | – | 1.000 | 1.000 |
| Costs | 1,339 ± 1,630 | 1,253 ± 1,826 | 1,371 ± 2,023 | 1,179 ± 2,095 | 1,296 ± 857 | 1,352 ± 1,383 | 0.672 | 0.385 | – | – |
| Drug costs (all bDMARDs) |          |           |           |           |           |           |           |           |           |           |
| No. of patients, no. (%) | 0 | 348 (100) | 0 | 200 (100) | 0 | 148 (100) | – | – | 1.000 | 1.000 |
| Costs | 0 | 20,777 ± 7,869 | 0 | 23,996 ± 4,818 | 0 | 16,427 ± 9,033 | – | <0.001 | – | – |
| Drug costs (PsA bDMARDs) |          |           |           |           |           |           |           |           |           |           |
| No. of patients, no. (%) | 0 | 348 (100) | 0 | 200 (100) | 0 | 148 (100) | – | – | 1.000 | 1.000 |
| Costs | 0 | 20,772 ± 7,869 | 0 | 23,996 ± 4,818 | 0 | 16,415 ± 9,033 | – | <0.001 | – | – |
| Other drug costs |          |           |           |           |           |           |           |           |           |           |
| No. of patients, no. (%) | 344 (98.8) | 339 (97.4) | 198 (99.0) | 191 (95.5) | 146 (98.6) | 148 (100) | 0.761 | – | 1.000 | 0.012 |
| Costs | 1,626 ± 2,679 | 1,179 ± 2,663 | 1,664 ± 2,907 | 940 ± 2,121 | 1,573 ± 2,345 | 1,503 ± 2,326 | 0.751 | 0.077 | – | – |
| Sick leave |          |           |           |           |           |           |           |           |           |           |
| No. of patients, no. (%) | 30 (8.6) | 21 (6.0) | 17 (8.5) | 5 (2.5) | 13 (8.8) | 16 (10.8) | 0.926 | 0.001 | 1.000 | 0.002 |
| Costs | 649 ± 3,298 | 303 ± 1,948 | 739 ± 3,689 | 138 ± 1,198 | 527 ± 2,689 | 526 ± 2,632 | 0.553 | 0.145 | – | – |
| Medical remedies, devices, and aid costs |          |           |           |           |           |           |           |           |           |           |
| No. of patients, no. (%) | 196 (56.3) | 197 (56.6) | 115 (57.5) | 110 (55.0) | 81 (54.7) | 87 (58.8) | 0.606 | 0.481 | 0.662 | 0.513 |
| Costs | 337 ± 853 | 368 ± 918 | 361 ± 817 | 347 ± 848 | 304 ± 901 | 396 ± 1,006 | 0.563 | 0.652 | – | – |
| Total costs |          |           |           |           |           |           |           |           |           |           |
| No. of patients, no. (%) | 348 (100) | 348 (100) | 200 (100) | 200 (100) | 148 (100) | 148 (100) | – | – | 1.000 | 1.000 |
| Costs | 5,769 ± 6,365 | 25,330 ± 9,646 | 6,165 ± 7,128 | 27,899 ± 8,001 | 5,232 ± 5,133 | 21,897 ± 10,600 | 0.156 | <0.001 | – | – |

* Values are the mean ± SD unless indicated otherwise. P values are reported for persistent versus nonpersistent group comparisons for the pre- and post-index periods. bDMARDs = biologic disease-modifying antirheumatic drugs; LOS = length of stay; PsA = psoriatic arthritis.
HRU and health care costs. Table 2 reports the HRU, while Figure 2 reports the associated health care costs before and after initiation of bDMARDs. Mean ± SD total annual health care costs per patient for the overall study population increased from €5,769 ± 6,365 to €25,330 ± 9,646 after bDMARD initiation, with prescription of bDMARDs comprising a major proportion of the total health care costs (82.0%). The proportion of patients requiring hospitalization in the pre- and post-index periods decreased from 49.5% to 38.5% in the persistent group but increased from 48.0% to 54.7% in the nonpersistent group. Similarly, mean ± SD number of hospitalizations in the pre- and post-index periods decreased from 1.1 ± 1.5 to 1.0 ± 1.7 in the persistent group and increased from 1.3 ± 2.1 to 1.7 ± 2.3 in the nonpersistent group. In line with these results, mean ± SD annual inpatient costs per patient reduced by €760 in the persistent group but increased by €161 in the nonpersistent group after bDMARD initiation. Reduction in mean ± SD sick leave duration from pre- to post-index periods was larger in the persistent group (25.5 ± 53.4 to 13.1 ± 28.1) compared with the nonpersistent group (22.7 ± 52.0 to 18.8 ± 41.6). Therefore, mean ± SD number of hospitalizations in the pre- and post-index periods decreased from 49.5% to 38.5% in the persistent group but increased by 86.1% and 75.0% in the nonpersistent group (P < 0.001, and €27,869 ± 8,001 versus €21,897 ± 10,600, P < 0.001, respectively).

Supplementary Table 3, available at http://onlinelibrary.wiley.com/doi/10.1002/acr.24598, reports the health care cost analysis for individual bDMARDs stratified by persistent and nonpersistent patients as well as by pre- and post-index period. Mean ± SD annual post-index total health care costs per patient in the overall study population were €25,579 ± 10,174 for adalimumab, €24,961 ± 6,328 for certolizumab pegol, €22,510 ± 9,897 for etanercept, €27,302 ± 8,982 for golimumab, €33,516 ± 9,998 for infliximab, €26,768 ± 8,680 for secukinumab, and €27,737 ± 9,289 for ustekinumab. Post-index mean ± SD annual bDMARD costs and total health care costs per patient were significantly higher in the persistent group than the nonpersistent group for adalimumab (€23,664 ± 2,551 versus €17,434 ± 9,023, P < 0.001) and secukinumab (€33,516 ± 9,998 versus €21,425 ± 7,805, P < 0.001). Other bDMARDs did not have any significant differences in health care costs.

**DISCUSSION**

Initiation of bDMARDs in German patients with PsA increased the mean annual total health care costs from €5,769 to €25,330. The majority of the health care costs (€20,777; 82.0%) were due to the prescription of bDMARDs, across all groups. These results are consistent with a previous study by Sondermann et al (7), wherein analysis of data from the Rhine- land/Hamburg SHI database (2010–2014) revealed higher gross total annual costs of bDMARDs (€28,082,663) compared with csDMARDs (€3,591,172). In terms of costs per patient-year, it translated to €322 and €15,304 for csDMARDs and bDMARDs,
respectively. A systematic review also reported that direct medical costs of PsA in Europe ranged from $3,693 to $8,871 per patient-year, with bDMARDs comprising a major proportion of the direct costs (30).

Comparing differences in total health care costs between persistent and nonpersistent patients shows a higher annual cost increase for persistent patients compared with nonpersistent patients ($Δ 5,039 per patient) primarily due to higher bDMARD acquisition costs. A similar difference was reported in a Brazilian study (average Δ of all bDMARDs $4,022) (11). However, in a study on patients with psoriasis and/or PsA, Lee et al (15) analyzed claims data from the US Department of Defense (2010–2015) and reported a difference of only $1,201 among persistent ($22,678) and nonpersistent ($21,477). The lower difference in costs compared with the current study could have occurred due to the differing databases used and the patient population, as well as higher costs for hospitalization in the US. In the current study, fewer hospitalizations and outpatient visits were observed in the persistent group in the post-index period, resulting in lower inpatient and outpatient treatment costs compared with the nonpersistent group. These findings are in line with the results of a study of Lee et al (15) from the US.

We observed a decrease in the duration of sick leave in the overall cohort (36.2%), with a greater reduction in the persistent group than the nonpersistent group (48.6% versus 17.3%). This observation is consistent with a clinical trial of patients with psoriasis that reported a 47% reduction in sick days after 12 weeks of treatment with etanercept (31), as well as with a Swedish population-based cohort study that reported a significant reduction in sickness leave (41.5% on biologic initiation versus 20.2% after 3 years of treatment; \(P < 0.001\)) in patients with PsA (32). Although we observed a similar reduction in overall sick days in a previous claims data analysis on German patients with psoriasis (28), unlike the current study, the nonpersistent group showed a greater reduction probably due to higher pre-index disease activity in nonpersistent patients or greater treatment efficacy and likelihood of discontinuation due to remission. Additional research on savings in indirect costs due to fewer sick leaves could provide insights into the cost-related aspects of bDMARDs.

Similar to the overall results, a cost analysis for individual bDMARDs showed higher annual total medical costs per patient in the persistent group due to increased utilization of the respective bDMARDs. Although we did not consider the benefits of persistence such as better clinical outcomes in this economic evaluation, Gandjour et al (33) recently performed a cost-utility analysis for bDMARDs in German patients with PsA and reported secukinumab to be cost effective compared with other bDMARDs for the treatment of active PsA in bDMARD-naive and bDMARD-experienced patients.

The burden of illness in PsA is high due to progressive joint damage, deterioration of physical function and HRQoL, as well as reduction in the ability to work and work productivity (4,5,34,35). A recent Danish study reported a comprehensive picture of the burden imparted by PsA on patients. Kristensen et al (36) compared patients with PsA to the general population and reported that patients with PsA had greater comorbidities, higher total health care costs, lower annual income, greater risk of unemployment, and greater risk of being on disability pension compared to the general population both before and after PsA diagnosis. Apart from the imported burden, patients may require therapy for a long period due to the chronic nature of the disease. Therefore, therapies that are effective, safe, and economically viable are required to increase the probability of faster recovery and benefit patients not only with respect to HRQoL but also employment. Although csDMARDs are currently recommended as first-line therapy for PsA, recent recommendations suggest initiating treatment with bDMARDs if required (8).

Current evidence also supports prescribing bDMARDs or tsDMARDs as first-line agents in treatment-naive patients due to similar or greater treatment efficacy as well as cost savings (37–40). Additionally, bDMARDs and tsDMARDs have been reported to help patients regain normal physical function and improve work productivity (41–45), which could generate additional active and productive hours, resulting in a positive impact on the German economy, as shown by Himmler et al (46). However, as existing health care systems do not provide adequate coverage for advanced medications in every instance, rheumatologists may not yet prefer them as first-line therapy. Use of biosimilars in patients with PsA may result in lower overall costs while maintaining efficacy and safety (47–49); however, off-patent drugs have been reported to be less cost effective compared to new agents (33). Therefore, revision of health care coverage to keep up with current developments in therapy may increase the uptake of new therapies for PsA.

This study has a few limitations due to the nature of claims data. Misclassification or coding error could have resulted in a false diagnosis of PsA in the health claims data. Although we only included patients who did not receive bDMARDs for 365 days prior to the index date, a possibility of some patients receiving bDMARDs before the 365 days washout period cannot be excluded. Claims data also insufficiently reflects disease severity and other influencing circumstances. We identified bDMARD use using claims data; however, it can only be presumed that the medication was administered, as the data only support receipt and payment. Additionally, bDMARD prescriptions were evaluated only for the outpatient setting. Another common bias in database analysis is the channeling bias, which is defined as “a form of allocation bias, where drugs with similar therapeutic indications are prescribed to groups of patients with prognostic differences” (50). Here, clinicians may prescribe a new drug to patients with a preexisting comorbidity or those who are refractory to existing treatments due to its claimed advantages. However, if any resultant adverse event or outcomes are correlated to treatment discontinuation, then the recently introduced new drug could be
subject to a negative selection bias. Finally, new agents such as ixekizumab, brodalumab, guselkumab, tildrakizumab, risankizumab, and tofacitinib were excluded from the analysis, as data were unavailable for these agents in the study period. Further research can provide insights into these bDMARDs and tsDMARDs.

In conclusion, initiation of bDMARDs increased the total health care costs irrespective of persistence status. Although better persistence decreased costs associated with inpatient and outpatient treatment, high unit costs and increased utilization of bDMARDs resulted in higher total health care costs in the persistent population. We observed a reduction in hospitalizations and sick leaves after initiation of bDMARDs. Future research into the indirect costs associated with PsA treatment is required to understand the effect of persistence.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Sewerin had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Sewerin, Borchert, Meise, Schneider, Mahlich.

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ROLE OF THE STUDY SPONSOR

Janssen-Cilag had no role in the study design or in the collection, analysis, or interpretation of the data, the writing of the manuscript, or the decision to submit the manuscript for publication. Publication of this article was not contingent upon approval by Janssen-Cilag.

ADDITIONAL DISCLOSURES

Authors Borchert and Meise are employees of Xcenda.

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