ORIGINAL ARTICLE

Biologic therapy adherence, discontinuation, switching, and restarting among patients with psoriasis in the US Medicare population

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Background: Studies indicate adherence to biologics among patients with psoriasis is low, yet little is known about their use in the Medicare population.

Objective: We sought to investigate real-world utilization patterns in a national sample of Medicare beneficiaries with psoriasis initiating infliximab, etanercept, adalimumab, or ustekinumab.

Methods: We conducted a retrospective claims analysis using 2009 through 2012 100% Medicare Chronic Condition Data Warehouse Part A, B, and D files, with 12-month follow-up after index prescription. Descriptive and multivariate analyses were used to examine rates of and factors associated with biologic adherence, discontinuation, switching, and restarting.

Results: We examined 2707 patients initiating adalimumab (40.0%), etanercept (37.9%), infliximab (11.7%), and ustekinumab (10.3%); during 12-month follow-up, 38% were adherent and 46% discontinued treatment, with 8% switching to another biologic and 9% later restarting biologic treatment. Being female and being ineligible for low-income subsidies were associated with increased odds of decreased adherence. Outcomes varied by index biologic.

Limitations: Patient-reported reasons for nonadherence or gaps in treatment are unavailable in claims data.

Conclusion: Medicare patients initiating biologics for psoriasis had low adherence and high discontinuation rates. Further investigation into reasons for inconsistent utilization, including exploration of patient and provider decision-making and barriers to more consistent treatment, is needed. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2016.01.048.)

Key words: adalimumab; adherence; biologic; discontinuation; etanercept; infliximab; Medicare; psoriasis; specialty drug; ustekinumab.

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Psoriasis is a chronic, multisystem, inflammatory disease that affects as many as 7.5 million people in the United States.[1] It is associated with significant physical,[2] psychosocial,[3] and economic[4] burden. Biologics represent an important treatment option for moderate to severe disease, which affects approximately 20% of all patients with psoriasis.[5] Five biologics are currently approved in the US to treat moderate to severe plaque psoriasis, yet numerous studies indicate that adherence to biologics in the real-world setting is low.[6-9]

Existing research on biologic treatment patterns among patients with psoriasis in the US has largely focused on privately insured populations.[6-9] Little is known about treatment patterns among US elderly and disabled individuals, the majority of whom are covered by Medicare, a nationwide health insurance program administered by the US federal government.[10] Lack of data on the treatment of psoriasis in the elderly has been identified as a major research gap,[11] especially because they are often underrepresented in clinical trials and may have unique treatment concerns.[10,12] To address this gap, we examined national claims data for Medicare patients with psoriasis who were initiating biologics to investigate adherence, discontinuation, switching, and restarting of biologic treatment.

CAPSULE SUMMARY

- Previous US-based studies of biologic utilization patterns for psoriasis have focused on privately insured patients.
- We studied Medicare patients with psoriasis, finding low adherence and high discontinuation rates with minimal switching or restarts within 12 months of biologic initiation.
- Reasons for such real-world utilization patterns warrant further investigation.

METHODS

Data

We performed a retrospective claims analysis using the 2009 through 2012 100% Medicare Chronic Condition Data Warehouse files, including the Medicare inpatient (Part A), outpatient (Part B), and prescription drug (Part D) data files linked with beneficiary summary files and Part D prescription drug plan characteristics files.

Sample

Patients were included if they: (1) had a claim for a biologic approved for treatment of plaque psoriasis (ie, infliximab, etanercept, adalimumab, or ustekinumab) between January 1, 2010, and December 31, 2011 (representing the index date); (2) had continuous enrollment in fee-for-service Medicare and a stand-alone Part D prescription plan in the 12 months before and after the index date; (3) had no claims for a biologic approved for psoriasis in the 12 months before the index date, thus identifying a new biologic treatment episode; and (4) had at least 1 claim for psoriasis (*International Classification of Diseases, Ninth Revision, Clinical Modification* code 696.1) in the 12 months before their index date (Appendix Figure 1; available at http://www.jaad.org). Patients were excluded if they: (1) had other indications for which the study biologics are approved (ie, rheumatoid arthritis, ankylosing spondylitis, or inflammatory bowel disease) in the pre-index period; (2) were using multiple biologics for psoriasis on the index date; or (3) were using alefacept, which was withdrawn from the market in November 2012, as the index biologic. Secukinumab was not approved during the study period and thus not included. Because patients were required to have a diagnosis of plaque psoriasis, individuals with psoriatic arthritis in the absence of skin disease were not included. Patients were followed up for 12 months after their index date.

Although Medicare is primarily a program for elderly and disabled adults, children are eligible beneficiaries under some restricted circumstances. We did not impose an age restriction on our sample, but application of other study criteria resulted in a sample with a minimum age of 21 years.

Outcomes

Primary outcomes included adherence to, discontinuation of, switching from, and restarting of the index biologic. Adherence was captured using the proportion of days covered (PDC), measured as the number of days covered with the index biologic divided by a fixed time interval (ie, 365 days) from the date of index biologic therapy initiation.[13] For example, a patient with biologic coverage available for 292 days during the 365 day post-index date period would have a PDC of 292/365 = 0.80.[14] Patients with PDC greater than or equal to 0.80 were classified as adherent.[15,16]

Number of days covered with each biologic was captured based on its mode of administration. Etanercept and adalimumab, self-administered biologics dispensed via the pharmacy, were identified from the Part D prescription records using National Drug Codes (NDC codes). Prescription fill date and days' supply information were used to

calculate the number of days covered by each biologic fill. Infliximab, which requires infusion under supervision of a medical professional, was identified from Part B medical claims using the Healthcare Common Procedure Coding System (HCPCS codes). Because Part B claims do not include days' supply information, we assigned days' supply after each administration using infliximab's recommended dosage regimen and then used the assigned days' supply and administration date to calculate covered days (Appendix Table I; available at http://www.jaad.org). Ustekinumab, administered by subcutaneous injection and approved only for administration by a medical professional during our study period (under Part B), was nonetheless found in both Part D prescription records and Part B medical claims among the study sample. Thus, we calculated ustekinumab-covered days using the prescription fill or administration dates and assigned days' supply.

Discontinuation, generally operationalized as a continuous gap in availability of treatment for a prespecified period of time,[6,8] was our primary outcome and captured via a dichotomous measure indicating the presence of a period of 90 consecutive days or more without the index biologic during the 12-month follow-up period.[14] That is, if another prescription fill (or administration) for the index biologic did not occur at least 90 consecutive days after the final day covered by the previous days' supply (or assigned days' supply) of a fill (or administration) of the biologic, then this was coded as discontinuation.

Finally, we measured whether patients who discontinued their index biologic switched to another biologic, defined as the first occurrence of a prescription fill for or administration of a different (substitute) biologic (Part B or Part D) within 90 days after the last day of supply of the index biologic; or restarted biologic treatment, defined as a prescription fill for or administration of the index biologic or another biologic after the continuous gap of 90 days or more but within 1 year after the index date. Patients who had neither switched nor restarted biologic treatment before the end of the follow-up period were categorized as other discontinuers.

Statistical analyses

Descriptive outcomes were calculated overall and by type of index biologic. Logistic regressions were used to examine adherence and discontinuation. Multinomial logistic regressions were used to examine factors associated with being switchers, restarters, and other discontinuers compared with continuous biologic users. The regressions included a series of covariates including patient age, sex, race, census region, Part D low-income subsidy (LIS) status, county-level per capita income, county-level availability of dermatologists (as a general proxy for treatment accessibility), and Part D plan type. We also controlled for relevant comorbidities,[2,17-20] number of other nonpsoriasis medications, and the prescription drug hierarchical condition category score,[21] which has been used to adjust for potential selection biases in drug use studies among Medicare patients.[22-25] In addition, we included indicators for index date year to capture any temporal trends and for each index biologic; ustekinumab, the newest biologic on the market at the time of the study, was used as the reference.

Analyses were repeated in 3 subgroups: (1) disabled (ie, age <65 years), (2) elderly (ie, age ≥65 years), and (3) those without medical claims for psoriatic arthritis. All analyses were conducted in SAS, Version 9.4 (SAS Institute, Cary, NC) and STATA, Version 12 (StataCorp LP, College Station, TX).

RESULTS

Our sample included 2707 patients, of which 1084 (40.0%) initiated adalimumab, 1025 (37.9%) initiated etanercept, 318 (11.7%) initiated infliximab, and 280 (10.3%) initiated ustekinumab. Table I presents sample characteristics by index biologic cohort. Nearly half of the sample (48.9%) was younger than 65 years (ie, eligible for Medicare based on disability), and 43.9% were male. Age and sex were generally similar across index drug cohorts, although a smaller percentage of patients receiving infliximab were younger than 65 years. Fewer patients receiving infliximab were eligible for full LIS (27.8%, vs more than half of all other biologic groups). Cardiometabolic disorders were the most prevalent comorbidities. Overall prevalence of psoriatic arthritis was 28.9%; however, it was substantially higher among patients on infliximab (70.8%) and lowest among patients on ustekinumab (15.7%), which had not yet been approved for psoriatic arthritis during our study period. As indicators of overall comorbidity, the average number of nonpsoriasis medications among the overall sample was 4.89 (SD 3.63), and the mean prescription drug hierarchical condition category score was 1.13 (SD 0.65).

Descriptive outcomes, both overall and by type of index biologic, are summarized in Table II. Overall, 37.7% of patients were adherent, average PDC was 0.61 (SD 0.31), and 45.5% of all patients discontinued their biologic during the 12-month follow-up period. In all, 8% of the sample switched to another biologic for psoriasis, and 9.2% restarted treatment after a

Table I. Sample characteristics

Characteristic	All, N = 2707	Adalimumab, n = 1084	Etanercept, n = 1025	Infliximab, n = 318	Ustekinumab, n = 280
Age, mean (SD), y	60.7 (14.5)	59.4 (14.4)	60.3 (14.9)	65.5 (12.0)	61.6 (15.1)
Age category, y					
<65	48.9%	54.7%	50.6%	28.0%	44.3%
65-69	19.5%	16.9%	19.1%	31.1%	17.5%
70-74	16.3%	14.7%	14.3%	24.5%	20.0%
75-79	8.0%	7.7%	7.9%	8.2%	9.6%
≥80	7.3%	6.0%	8.1%	8.2%	8.6%
Sex, male	43.9%	43.7%	42.0%	48.7%	46.1%
Race					
White	84.6%	83.9%	84.0%	91.2%	82.8%
Black	6.5%	7.2%	6.7%	3.5%	6.1%
Hispanic	3.5%	2.6%	4.1%	3.1%	5.0%
Other/unknown	5.4%	6.3%	5.2%	2.2%	6.1%
Census region					
Northeast	15.6%	14.8%	15.6%	14.4%	19.9%
Midwest	22.4%	22.5%	23.8%	23.3%	16.1%
South	43.2%	43.0%	41.3%	48.1%	45.4%
West	18.8%	19.7%	19.3%	14.2%	18.6%
County-level characteristics					
Income, per capita, $10,000s, mean (SD)	3.8 (1.1)	3.8 (1.0)	3.8 (1.0)	3.8 (1.0)	4.1 (1.4)
Dermatologists/10,000 residents, mean (SD)	0.3 (0.3)	0.3 (0.3)	0.3 (0.3)	0.3 (0.3)	0.4 (0.4)
Part D low-income subsidy status					
Full	60.6%	69.5%	62.5%	27.8%	55.7%
Partial	1.6%	1.4%	2.0%	0.9%	1.8%
None	36.6%	28.2%	33.9%	70.4%	41.1%
Mixed (switched status)	1.2%	0.9%	1.6%	0.9%	1.4%
Drug benefit type					
Basic alternative	30.5%	25.3%	32.7%	40.3%	31.8%
Defined standard benefit	9.7%	9.9%	10.8%	6.9%	8.2%
Actuarially equivalent standard	38.6%	45.9%	38.0%	18.9%	35.4%
Unknown	3.8%	3.8%	3.7%	3.8%	3.9%
Comorbid conditions					
Rheumatologic disease	1.8%	1.6%	1.5%	4.1%	1.4%
Congestive heart failure	8.1%	7.0%	7.1%	8.5%	15.4%
Diabetes	35.1%	35.8%	33.9%	32.7%	39.6%
Dyslipidemia	53.1%	51.3%	52.4%	60.4%	54.6%
Hypertension	61.4%	59.8%	60.0%	67.0%	66.1%
Obesity	11.9%	12.5%	11.0%	11.9%	12.9%
Atherosclerotic conditions	16.2%	14.9%	16.3%	18.6%	18.2%
Liver disease	7.3%	6.9%	7.8%	7.2%	6.8%
Dementia	1.0%	0.6%	1.3%	1.9%	1.1%
Depression	19.8%	21.6%	19.6%	16.7%	17.5%
Psoriatic arthritis	28.9%	25.5%	23.2%	70.8%	15.7%
Renal disease	8.2%	7.8%	8.5%	6.0%	11.4%
Immunosuppressive conditions	5.5%	5.3%	5.8%	4.7%	6.8%
No. of 30-d supply equivalent prescriptions for nonpsoriasis medications, mean (SD)	4.89 (3.63)	4.95 (3.78)	4.79 (3.50)	4.72 (3.36)	5.21 (3.75)
RxHCC score, mean (SD)	1.13 (0.65)	1.15 (0.66)	1.13 (0.67)	1.09 (0.58)	1.12 (0.59)
Index year					
2010	46.4%	47.6%	51.3%	42.1%	46.4%
2011	53.6%	52.4%	48.7%	57.9%	53.6%

Rheumatologic disease category excludes rheumatoid arthritis. Atherosclerotic conditions category includes cerebrovascular disease, myocardial infarction, and peripheral vascular disease. Immunosuppressive conditions include HIV/AIDS, cancer, and metastatic solid tumor.
RxHCC, Prescription drug hierarchical condition category.

Table II. Adherence, discontinuation, switch, and restart outcomes*

Outcome	All	Adalimumab	Etanercept	Infliximab	Ustekinumab
Overall					
N	2707	1084	1025	318	280
PDC, mean (SD)	0.61 (0.31)	0.63 (0.31)	0.56 (0.31)	0.66 (0.32)	0.70 (0.28)
Adherent (PDC ≥0.80)	37.7%	40.7%	29.4%	49.4%	43.2%
Discontinued	45.5%	43.4%	51.7%	42.5%	35.0%
Switched	8.0%	9.0%	9.5%	5.0%	1.8%
Restarted	9.2%	6.6%	9.9%	10.4%	15.0%
With index biologic	7.6%	5.1%	8.4%	6.9%	15.0%
With different biologic	1.6%	1.5%	1.5%	3.5%	0.0%
Other discontinuer	28.4%	27.8%	32.4%	27.0%	18.2%
Age <65 y					
N	1325	593	519	89	124
PDC, mean (SD)	0.62 (0.30)	0.65 (0.30)	0.57 (0.34)	0.59 (0.34)	0.73 (0.27)
Adherent (PDC ≥0.80)	37.7%	43.3%	29.1%	40.4%	45.2%
Discontinued	44.1%	40.6%	50.3%	49.4%	30.6%
Switched	9.5%	9.1%	11.8%	7.9%	3.2%
Restarted	9.8%	7.3%	10.4%	14.6%	15.3%
With index biologic	7.8%	5.1%	8.7%	10.1%	15.3%
With different biologic	2.0%	2.2%	1.7%	4.5%	0.0%
Other discontinuer	24.8%	24.3%	28.1%	27.0%	12.1%
Age ≥65 y					
N	1382	491	506	229	156
PDC, mean (SD)	0.61 (0.32)	0.60 (0.32)	0.55 (0.32)	0.69 (0.31)	0.68 (0.28)
Adherent (PDC ≥0.80)	37.6%	37.5%	29.6%	52.8%	41.7%
Discontinued	47.0%	46.6%	53.2%	39.7%	38.5%
Switched	6.5%	9.0%	7.1%	3.9%	0.6%
Restarted	8.6%	5.7%	9.3%	8.8%	14.7%
With index biologic	7.4%	5.1%	8.1%	5.7%	14.7%
With different biologic	1.2%	0.6%	1.2%	3.1%	0.0%
Other discontinuer	31.9%	32.0%	36.8%	27.1%	23.1%
No medical claims for psoriatic arthritis					
N	1720	719	715	72	214
PDC, mean (SD)	0.60 (0.31)	0.63 (0.31)	0.55 (0.30)	0.61 (0.32)	0.69 (0.29)
Adherent (PDC ≥0.80)	35.6%	42.0%	26.2%	41.7%	43.9%
Discontinued	46.6%	42.3%	54.0%	47.2%	36.0%
Switched	8.4%	9.6%	9.5%	4.2%	2.3%
Restarted	9.2%	6.4%	9.9%	13.9%	14.0%
With index biologic	7.7%	4.7%	8.5%	9.7%	14.0%
With different biologic	1.5%	1.7%	1.4%	4.2%	0.0%
Other discontinuer	29.0%	26.3%	34.5%	29.2%	19.6%

PDC, Proportion of days covered.

*Discontinuation defined as continuous gap of 90 d. Switch indicates beginning treatment with a new biologic within 90 d of discontinuing the index biologic. Restart indicates resuming treatment with the index biologic or a new biologic after 90 d of discontinuing the index biologic. Other indicates no resumption of treatment before the end of the follow-up period.

90-day gap. Restarting the initial biologic was more common than restarting with a different biologic.

Mean PDC varied and was lowest for etanercept (mean PDC 0.56, SD 0.31) and highest for ustekinumab (mean PDC 0.70, SD 0.28). The percentage of adherent patients also varied, from 29.4% for etanercept to 49.4% for infliximab. Rates of discontinuation ranged from 35.0% for ustekinumab to 51.7% for etanercept. Discontinuing the index biologic and switching to another occurred in a small proportion of patients, from 1.8% of ustekinumab users to 9.5% of etanercept users. Discontinuation of the index biologic and subsequent restart of a biologic was less common among adalimumab users (6.6%) and more common among ustekinumab users (15%). Subgroup analyses among elderly, disabled, and those without a concomitant diagnosis of psoriatic arthritis were generally consistent with the main analysis, with the exception of lower

adherence and higher discontinuation rates for infliximab in the disabled and psoriasis only subgroups.

Factors associated with lower odds of being adherent included age younger than 65 years or older than 75 years (compared with beneficiaries aged 65-74 years); being female; and being ineligible for full LIS (Table III). With the exception of atherosclerotic conditions, comorbidities and other markers of pharmacologic complexity were not significantly associated with adherence. Compared with patients on index ustekinumab, use of index etanercept was associated with lower odds of adherence.

Factors associated with discontinuation largely mirrored those associated with adherence (Table IV). In addition, residence in the Northeast (compared with the Midwest) and use of fewer nonpsoriasis medications at baseline were associated with higher odds of discontinuing the index biologic. Those on etanercept and adalimumab as their index biologic had significantly higher odds of discontinuation compared with ustekinumab users.

The odds of switching to a new biologic within 90 days of discontinuing the index biologic were higher among disabled beneficiaries, females, and those who switched LIS status during the study period (compared with those with full LIS coverage) (Appendix Table II; available at http://www.jaad.org). Compared with index users of ustekinumab, index users of all 3 remaining biologics had higher odds of switching. After a gap of at least 90 days, odds of restarting biologic therapy were lower among beneficiaries living in the Midwest, South, and West (compared with those in the Northeast); patients with full LIS (compared with non-LIS status); and index users of adalimumab (compared with index users of ustekinumab).

DISCUSSION

This study adds to the literature by examining biologic treatment patterns among a national sample of fee-for-service Medicare beneficiaries with psoriasis. Overall, slightly over one third of the patients were adherent to their index biologic and almost half discontinued within 12 months of initiation. Only 8% of patients switched to another biologic, and 9% restarted biologic treatment (with either the index biologic or an alternate).

Our estimates of the adherence and discontinuation rates for biologics among Medicare beneficiaries with psoriasis exhibit some similarities and differences from what has been reported in the literature. However, it is difficult to directly compare estimates because differences in study populations may explain some observed variation. Compared with younger privately insured populations that have been the focus of prior research in the United States, Medicare beneficiaries are more likely to have had psoriasis for a longer period of time and/or be disabled, to have more comorbidities and competing health priorities, and to have different drug cost-sharing arrangements. Methodological differences among studies, particularly regarding definitions of discontinuation (eg, gaps ranging from 45-130 days), also contribute to differences in findings.[6-8,26] Examination of factors associated with adherence and discontinuation revealed both expected and novel findings. Similar to other studies,[26,27] we found that being female was associated with less persistent treatment. It is unclear whether this is the result of an underlying biological cause, a health care delivery issue (eg, differences in patient-provider interaction), or other factors. Our finding that adherence was lower and discontinuation was higher in individuals who were not eligible for LIS (and thus faced substantial cost sharing under Medicare Part D) is consistent with prior studies that have found similar treatment patterns in privately insured individuals who face higher out-of-pocket costs for specialty drugs indicated for various chronic conditions.[28-31] The associations we observed between atherosclerotic conditions and census region and adherence and/or discontinuation rates suggests a need for future research to identify the reasons for these variations.

Finally, we found substantial variation in both adherence and discontinuation rates by index biologic. Interestingly, our results suggest that patients using etanercept were less likely to be adherent and patients using etanercept and adalimumab, both self-administered biologics, were more likely to discontinue compared with those on ustekinumab, which during our study period was administered under the supervision of a physician. This may partly reflect greater awareness of adherence problems (ie, missed appointments indicate missed doses) and thus greater opportunity for intervention when patients are receiving treatment in the office. On the other hand, patients on ustekinumab, the newest treatment option on the market at the time of study, were likely to have been on and failed other biologic therapies in the past (beyond the 12-month preindex period observed in our study); thus a lack of alternative therapeutic options may have driven treatment persistence. Although the reasons for these differences across biologics deserve further investigation, it is notable that all biologic agents including ustekinumab had high levels of nonadherence and discontinuation in our study.

Table III. Odds of adherence (proportion of days covered ≥0.80) among Medicare beneficiaries with psoriasis

	Odds ratio	95% CI	*P* value
Age category, y			
<65	0.74	0.57-0.95	.019
65-69	Ref		
70-74	0.80	0.62-1.05	.110
75-79	0.66	0.47-0.94	.020
≥80	0.67	0.47-0.97	.032
Sex, male	1.28	1.08-1.51	.004
Race			
White	Ref		
Black	0.88	0.62-1.24	.456
Hispanic	1.21	0.78-1.88	.395
Other/unknown	0.96	0.66-1.39	.837
Census region			
Northeast	Ref		
Midwest	1.26	0.95-1.66	.113
South	1.11	0.85-1.45	.435
West	1.26	0.94-1.67	.121
County-level characteristics			
Income, per capita, $10,000s	1.05	0.94-1.17	.393
Dermatologists/10,000 residents	0.88	0.62-1.26	.490
Low-income subsidy status			
Full	Ref		
Partial	0.86	0.45-1.65	.647
None	0.67	0.51-0.88	.004
Mixed (switched status)	0.34	0.14-0.83	.018
Drug benefit type			
Enhanced alternative	Ref		
Basic alternative	1.19	0.92-1.52	.183
Defined standard benefit	1.34	0.93-1.92	.118
Actuarially equivalent standard	0.94	0.71-1.25	.669
Unknown	1.04	0.65-1.66	.872
Comorbidities			
Rheumatologic disease	1.27	0.70-2.28	.434
Congestive heart failure	1.06	0.77-1.45	.738
Diabetes	0.88	0.73-1.07	.215
Dyslipidemia	1.14	0.95-1.36	.164
Hypertension	1.03	0.85-1.25	.733
Obesity	1.03	0.80-1.33	.829
Atherosclerotic conditions	0.71	0.56-0.90	.005
Liver disease	0.95	0.69-1.30	.737
Dementia	0.54	0.21-1.38	.196
Depression	0.83	0.67-1.04	.111
Psoriatic arthritis	1.16	0.95-1.42	.148
Renal disease	0.83	0.60-1.13	.231
Immunosuppressive conditions	1.05	0.74-1.51	.774
No. of 30-d supply equivalent prescriptions for nonpsoriasis medications	1.03	1.00-1.05	.074
RxHCC score, mean	0.94	0.78-1.13	.496
Index year			
2010	Ref		
2011	0.95	0.81-1.11	.515
Index biologic			
Etanercept	0.51	0.39-0.68	<.001
Infliximab	1.20	0.85-1.71	.303
Ustekinumab	Ref		
Adalimumab	0.85	0.65-1.12	.260

Rheumatologic disease category excludes rheumatoid arthritis. Atherosclerotic conditions category includes cerebrovascular disease, myocardial infarction, and peripheral vascular disease. Immunosuppressive conditions include HIV/AIDS, cancer, and metastatic solid tumor.

CI, Confidence interval; *Ref*, reference group; *RxHCC*, prescription drug hierarchical condition category.

Several limitations should be noted. As a retrospective insurance claims-based study, details on treatment response, side effects, and reasons for nonadherence or gaps in treatment were unavailable. As such, we were unable to determine if treatment discontinuation was deliberate and appropriate, for example as a result of adverse effect or loss of efficacy.[32] In addition, unobserved covariates (eg, patient preferences) may have confounded the relationship between measured variables and biologic use patterns. Although rigorous, our measures are also subject to some limitations. First, we used several proxies of comorbidity status but did not have access to primary measures of psoriasis severity beyond the fact that biologics are indicated for moderate to severe disease. Second, although PDC reflects availability of medication supply, it does not capture whether patients use their medication supply as directed and has the potential to overestimate actual adherence to self-administered medications. Similarly, if prescribers increased the dosing frequency for clinician-administered biologics to overcome loss of response, which has been shown previously for infliximab dosing,[33] our calculation of assigned days' supply using the standard dosing schedule would have overestimated adherence if patients missed an interim dose. Third, we were unable to determine whether those who discontinued treatment eventually restarted after our study period ended. Finally, as with all claims analyses, data may be subject to coding errors.

Despite these limitations, our findings indicate low biologic adherence and high discontinuation rates in Medicare patients treated for psoriasis. Prior data suggest that interruption of biologic treatment

Table IV. Odds of discontinuation in Medicare beneficiaries receiving biologics for psoriasis

	Discontinuation (90 d)		
	Odds ratio	95% CI	*P* value
Age category, y			
<65	1.37	1.06-1.77	.015
65-69	Ref		
70-74	1.23	0.95-1.60	.120
75-79	1.52	1.09-2.11	.013
≥80	1.49	1.05-2.10	.024
Sex, male	0.73	0.62-0.86	<.001
Race			
White	Ref		
Black	1.11	0.80-1.55	.525
Hispanic	0.80	0.51-1.25	.326
Other/unknown	1.02	0.71-1.47	.911
Census region			
Northeast	Ref		
Midwest	0.66	0.50-0.86	.002
South	0.89	0.69-1.14	.353
West	0.79	0.59-1.04	.088
County-level characteristics			
Income, per capita, $10,000s	0.95	0.85-1.06	.333
Dermatologists/10,000 residents	1.15	0.81-1.62	.437
Low-income subsidy status			
Full	Ref		
Partial	2.09	1.11-3.93	.023
None	1.96	1.51-2.55	<.001
Mixed (switched status)	4.29	1.94-9.48	<.001
Drug benefit type			
Enhanced alternative	Ref		
Basic alternative	0.98	0.77-1.24	.839
Defined standard benefit	0.86	0.60-1.23	.402
Actuarially equivalent standard	1.12	0.85-1.47	.436
Unknown	0.93	0.59-1.44	.733
Comorbidities			
Rheumatologic disease	1.06	0.59-1.90	.859
Congestive heart failure	1.00	0.74-1.37	.990
Diabetes	1.06	0.88-1.28	.572
Dyslipidemia	0.93	0.78-1.10	.384
Hypertension	0.98	0.82-1.18	.851
Obesity	1.08	0.84-1.38	.570
Atherosclerotic conditions	1.28	1.02-1.61	.033
Liver disease	1.27	0.94-1.72	.120
Dementia	1.56	0.70-3.48	.276
Depression	1.20	0.97-1.49	.100
Psoriatic arthritis	0.83	0.68-1.01	.066
Renal disease	0.93	0.69-1.25	.610
Immunosuppressive conditions	1.15	0.81-1.63	.430
No. of 30-d supply equivalent prescriptions for nonpsoriasis medications	0.97	0.94-1.00	.020
RxHCC score, mean	1.14	0.95-1.37	.159
Index year			
2010	Ref		
2011	1.10	0.94-1.28	.258
Index biologic			
Etanercept	2.18	1.64-2.90	<.001
Infliximab	1.41	0.99-2.02	.060
Ustekinumab	Ref		
Adalimumab	1.60	1.20-2.13	.001

Rheumatologic disease category excludes rheumatoid arthritis. Atherosclerotic conditions category includes cerebrovascular disease, myocardial infarction, and peripheral vascular disease. Immunosuppressive conditions include HIV/AIDS, cancer, and metastatic solid tumor.

CI, Confidence interval; *Ref*, reference group; *RxHCC*, prescription drug hierarchical condition category.

for psoriasis is associated with poorer outcomes compared with continuous therapy,[34] so understanding the reasons for treatment discontinuation will be important. Future patient- and provider-centered research examining treatment decision-making is essential to more deeply explore factors that may be contributing to the utilization patterns we observed, and to inform interventions to promote adherence and persistence to biologic therapies for psoriasis.

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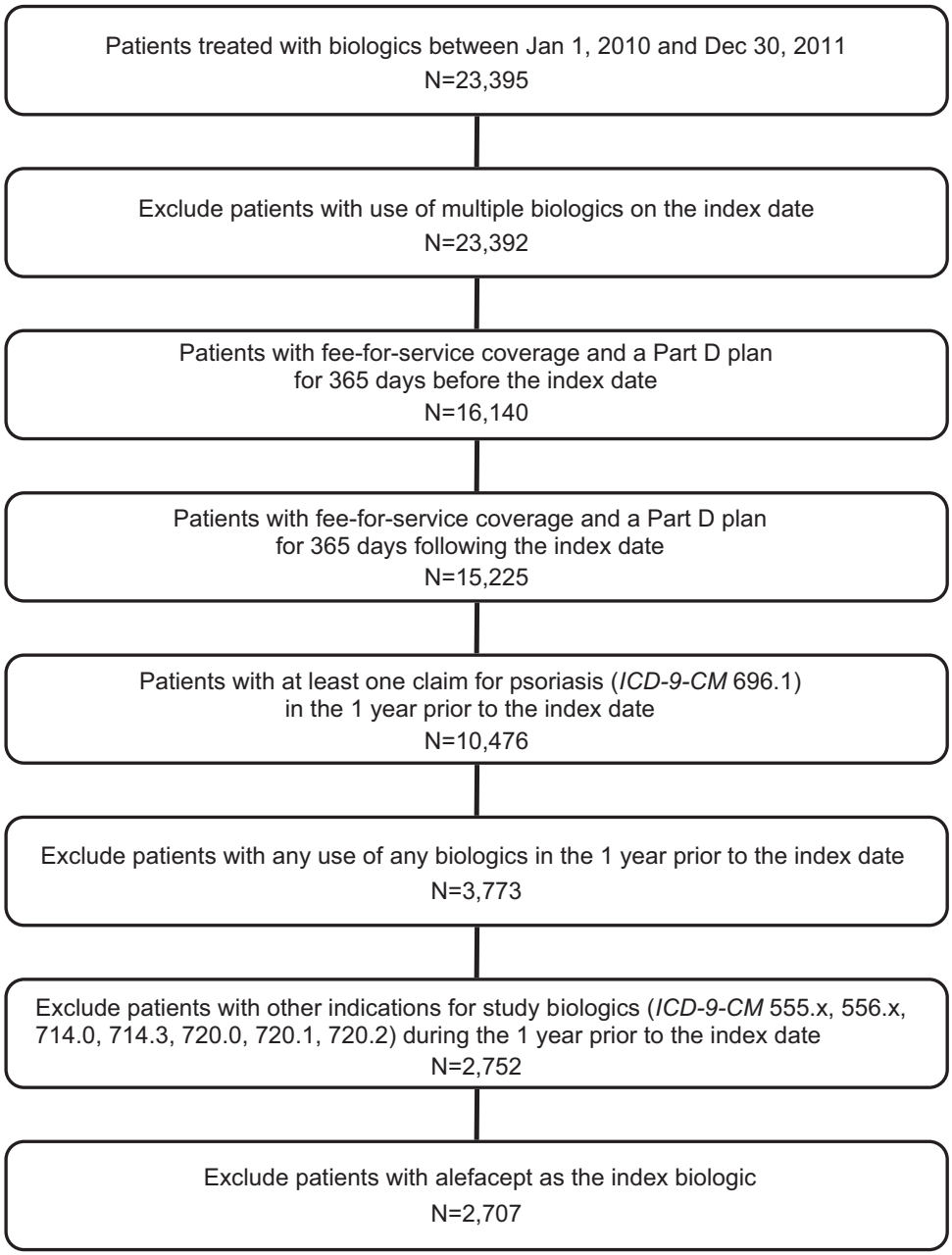

Appendix Fig 1. Sample selection diagram. *ICD-9-CM*, *International Classification of Diseases, Ninth Revision, Clinical Modification*.

Appendix Table I. Identification of biologic agents and assignment of days' supply

Biologic agent	Biologic identified from Part B or D claims	Recommended dosage schedule	Days' supply as reported or assigned	Rules for assigning days' supply
Enbrel (etanercept)	Part D	50 mg 2×/wk for 12 wk, then 50 mg 1×/wk	As reported	NA
Humira (adalimumab)	Part D	80 mg once on wk 0, then 40 mg once every 2 wk starting on wk 1	As reported	NA
Remicade (infliximab)	Part B	5 mg/kg on wk 0, 2, and 6, then every 8 wk	Assigned	First administration: 14 d; second administration: 28 d; ≥third administration: 56 d
Stelara (ustekinumab)	Part B and D*	45 mg (≤100 kg) or 90 mg (>100 kg) once on wk 0 and wk 4, then every 12 wk	Assigned†	First administration or fill: 28 d; ≥second administration or fill: 84 d

Manufacturers: Enbrel, Amgen Inc, Thousand Oaks, CA; Humira, AbbVie Inc, North Chicago, IL; Remicade, Janssen Biotech, Inc, Horsham, PA; Stelara, Janssen Biotech, Inc, Horsham, PA.

*Ustekinumab is administered by subcutaneous injection and was only approved for administration by a medical professional during our study period (ie, covered under Part B). Ustekinumab use under Part D may reflect some clinicians requiring patients to pick up prescriptions from the pharmacy and bring them to office visits for administration.

†Our assessment of the days' supply field for Part D ustekinumab claims revealed a large proportion of the ≥second fills being consistently coded as 28-d or 30-d supply despite their fill dates being approximately 12 wk (ie, 84 d) apart. Hence, we assigned days' supply to both Part D and B ustekinumab claims based on the dosage schedule.

Appendix Table II. Multinomial logistic regression results for switchers, restarters, and other discontinuers of index biologic (compared with continuing users of index biologic)

	Switcher			Restarter			Other discontinuer		
	OR	95% CI	*P* value	OR	95% CI	*P* value	OR	95% CI	*P* value
Age category, y									
<65	1.84	1.13-3.00	.014	1.50	0.95-2.35	.079	1.21	0.90-1.62	.207
65-69	Ref						Ref		
70-74	1.52	0.92-2.51	.106	0.96	0.59-1.56	.863	1.26	0.93-1.70	.130
75-79	0.79	0.36-1.72	.547	1.42	0.79-2.54	.240	1.71	1.19-2.46	.004
≥80	0.77	0.35-1.70	.513	1.34	0.73-2.47	.341	1.70	1.16-2.49	.006
Sex, male	0.64	0.47-0.88	.005	0.96	0.72-1.27	.764	0.70	0.58-0.84	<.001
Race									
White	Ref						Ref		
Black	1.27	0.71-2.29	.417	1.05	0.59-1.88	.860	1.10	0.75-1.60	.639
Hispanic	1.03	0.45-2.37	.944	0.79	0.36-1.72	.549	0.74	0.42-1.28	.275
Other/unknown	0.60	0.27-1.35	.216	1.42	0.79-2.53	.239	1.03	0.68-1.57	.887
Census region									
Northeast	Ref						Ref		
Midwest	0.67	0.41-1.10	.113	0.52	0.33-0.81	.004	0.72	0.52-0.99	.045
South	0.78	0.49-1.25	.307	0.59	0.39-0.89	.012	1.08	0.80-1.45	.634
West	0.89	0.54-1.46	.637	0.52	0.32-0.82	.006	0.89	0.64-1.23	.485
County-level characteristics									
Income, per capita, $10,000s	1.02	0.83-1.25	.850	0.91	0.76-1.09	.300	0.94	0.83-1.07	.357
Dermatologists/10,000 residents	1.04	0.54-1.99	.916	1.42	0.80-2.53	.234	1.08	0.73-1.61	.704
Low-income subsidy status									
Full	Ref						Ref		
Partial	0.77	0.17-3.42	.726	1.88	0.67-5.29	.233	2.68	1.35-5.35	.005
None	1.50	0.92-2.45	.109	1.72	1.08-2.75	.022	2.25	1.66-3.05	<.001
Mixed (switched status)	3.83	1.12-13.13	.033	3.04	0.89-10.33	.075	5.05	2.15-11.83	<.001
Drug benefit type									
Enhanced alternative	Ref						Ref		
Basic alternative	0.84	0.54-1.30	.431	1.24	0.80-1.93	.329	0.95	0.72-1.24	.685
Defined standard benefit	0.51	0.26-1.00	.051	1.09	0.58-2.08	.785	0.94	0.62-1.44	.775
Actuarially equivalent standard	0.71	0.43-1.17	.179	1.34	0.82-2.20	.248	1.22	0.89-1.67	.219
Unknown	0.77	0.33-1.79	.544	1.10	0.49-2.47	.818	0.93	0.57-1.52	.764
Comorbidities									
Rheumatologic disease	1.37	0.50-3.73	.541	0.95	0.32-2.79	.919	1.00	0.51-1.98	.997
Congestive heart failure	0.70	0.35-1.41	.313	1.01	0.61-1.69	.959	1.07	0.75-1.52	.711
Diabetes	0.82	0.57-1.17	.273	1.24	0.89-1.73	.196	1.06	0.86-1.32	.574
Dyslipidemia	0.90	0.65-1.26	.543	0.83	0.61-1.13	.224	0.97	0.79-1.19	.756
Hypertension	0.90	0.64-1.27	.537	1.07	0.77-1.49	.695	0.99	0.79-1.22	.896
Obesity	1.13	0.71-1.78	.616	1.09	0.71-1.66	.695	1.06	0.79-1.42	.714
Atherosclerotic conditions	1.29	0.83-2.00	.258	1.66	1.14-2.41	.008	1.16	0.90-1.51	.257
Liver disease	1.43	0.84-2.43	.187	1.00	0.58-1.72	.999	1.33	0.94-1.88	.109
Dementia	0.88	0.11-7.20	.908	1.38	0.41-4.68	.603	1.71	0.71-4.10	.229
Depression	1.17	0.80-1.73	.422	1.48	1.03-2.12	.033	1.12	0.87-1.44	.390
Psoriatic arthritis	0.92	0.64-1.33	.656	0.94	0.67-1.33	.743	0.77	0.62-0.97	.027
Renal disease	1.13	0.63-2.01	.692	1.07	0.65-1.76	.792	0.83	0.59-1.18	.310
Immunosuppressive conditions	0.97	0.47-1.97	.925	1.09	0.59-2.02	.785	1.23	0.83-1.81	.306
No. of 30-d supply equivalent prescriptions for nonpsoriasis medications	1.00	0.95-1.05	.933	0.97	0.92-1.01	.136	0.96	0.93-0.99	.011
Mean RxHCC score	0.96	0.68-1.35	.792	1.07	0.78-1.46	.694	1.23	1.00-1.52	.056
Index year									
2010	Ref						Ref		
2011	1.10	0.82-1.48	.533	1.13	0.86-1.50	.385	1.08	0.90-1.30	.406

Continued

Appendix Table II. Cont'd

	Switcher			Restarter			Other discontinuer		
	OR	95% CI	*P* value	OR	95% CI	*P* value	OR	95% CI	*P* value
Index biologic									
Etanercept	7.48	2.97-18.82	<.001	0.94	0.62-1.42	.769	2.69	1.89-3.82	<.001
Infliximab	3.20	1.11-9.19	.031	0.83	0.48-1.44	.509	1.72	1.12-2.66	.014
Ustekinumab	Ref						Ref		
Adalimumab	6.20	2.46-15.60	<.001	0.54	0.35-0.82	.004	2.04	1.43-2.90	<.001

Switcher indicates patients beginning treatment with a new biologic within 90 d of discontinuing the index biologic. Restarter indicates patients resuming treatment with the index biologic or a new biologic after 90 d of discontinuing the index biologic. Other discontinuer indicates patients with discontinuation of index biologic and no resumption of treatment before the end of the follow-up period. Rheumatologic disease category excludes rheumatoid arthritis. Atherosclerotic conditions category includes cerebrovascular disease, myocardial infarction, and peripheral vascular disease. Immunosuppressive conditions include HIV/AIDS, cancer, and metastatic solid tumor. *CI*, Confidence interval; *Ref*, reference group; *RxHCC*, prescription drug hierarchical condition category.