

# Two-Year Adherence and Costs for Biologic Therapy for Rheumatoid Arthritis

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**R**heumatoid arthritis (RA) is a chronic disease that requires long-term therapy. The goal of treatment is to achieve low disease activity or remission and to inhibit the progression of joint damage and other complications from RA.<sup>1</sup> American College of Rheumatology guidelines suggest multiple options to assess disease activity, including the Disease Activity Score based on 28 joints (DAS 28).<sup>2</sup> An algorithm to determine effective treatment based on DAS 28 outcomes from claims databases has been developed and validated.<sup>3</sup> A key component of the algorithm is adherence (ie, taking medication in accordance with prescribed timing and dose), and this approach is intended to ensure that the patient's disease activity is attributable to the initial medication rather than to subsequent therapies.<sup>3</sup>

Currently available therapies for moderate to severe RA include conventional synthetic disease-modifying antirheumatic drugs (csDMARDs; eg, methotrexate) and biologic DMARDs (bDMARDs).<sup>1</sup> The most commonly used bDMARDs include the selective T-cell costimulation modulator abatacept and the tumor necrosis factor inhibitors adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab.

Understanding medication use, particularly adherence and persistence (ie, medication use without significant gaps in therapy), is important in achieving clinical goals. In particular, although the short-term and long-term utilization patterns for bDMARDs directly influence treatment effectiveness, utilization over the longer term is not well understood. In general, real-world adherence to bDMARDs, as evaluated by medication utilization in claims data in patients with RA, is suboptimal, although most studies have not examined periods longer than 12 months.<sup>4</sup> Poor adherence to all RA medications has been associated with disease progression or flares<sup>5,6</sup> and increased healthcare resource utilization.<sup>7-9</sup>

These findings of studies on adherence and outcomes reflect the experience of heterogeneous RA populations, which suggests that maintaining adherence is likely important even for patients with low disease activity who have met criteria for being effectively treated. Treatment adherence following periods when patients were

## ABSTRACT

**OBJECTIVES:** To evaluate adherence to newly initiated biologic disease-modifying antirheumatic drugs (bDMARDs) in effectively treated patients with rheumatoid arthritis (RA).

**STUDY DESIGN:** Retrospective cohort study of administrative claims data (IMS PharMetrics Plus) for services incurred from July 1, 2008, to December 31, 2014.

**METHODS:** Data from patients with RA aged 18 to 64 years with continuous enrollment for at least 30 months and initiating abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, or infliximab were analyzed. Treatment effectiveness was determined using a validated algorithm. Outcomes included adherence rates (proportion of days covered  $\geq 80\%$ ) for 1 year and 2 years, year 2 adherence among patients effectively and noneffectively treated in year 1, year 2 adherence predictors, and year 2 costs and cost predictors.

**RESULTS:** Across 10,374 patients, adherence rates were 46% for year 1 and 34% for 2 years; rates were lowest for golimumab and highest for infliximab. In year 1, 3076 (29.7%) patients were considered effectively treated. Year 2 adherence was 59% in effectively treated patients, 32% in patients who failed any effectiveness criteria, and 12% in patients who failed only the adherence criterion. Intravenous bDMARDs, older age, male sex, Northeast region, commercial payer, prior DMARD use, index year 2010 or later, and lower preindex all-cause costs each predicted better adherence. Adjusted year 2 all-cause and RA-related costs were \$39,425 and \$22,123, respectively, for effectively treated patients and \$25,313 and \$9250 for noneffectively treated patients. Cost predictors included effective treatment, region, payer, and index year.

**CONCLUSIONS:** Adherence to the first bDMARD was suboptimal even in effectively treated patients, suggesting opportunities to improve adherence in patients with RA initiating biologics.

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## TAKEAWAY POINTS

- ▶ Compared with noneffectively treated patients, patients who were effectively treated in the first year of biologic therapy for rheumatoid arthritis (RA) were more likely to be adherent in the second year of therapy.
- ▶ Adherence was suboptimal in both effectively and noneffectively treated patients, indicating a need for better strategies to improve adherence in patients with RA initiating biologic therapy.

effectively or noneffectively treated have not yet been described for patients in the routine care setting. Therefore, in this study, we assessed adherence and persistence in the first 2 years after initiating a bDMARD in a cohort of patients with RA. In addition, we classified patients as either effectively or noneffectively treated in their first year on bDMARD therapy and measured their adherence in their second year on therapy. Additional objectives explored other aspects of medication use across the first 2 years on therapy, including examination of predictors of adherence and costs.

## METHODS

## Study Design

Claims used in this retrospective cohort study were incurred from July 1, 2008, through December 31, 2014. The index date was defined as the date of the first bDMARD claim. The preindex (baseline) period comprised the 6 months immediately preceding the index date. The postindex (follow-up) period was the 24 months immediately following the index date.

The primary objective of the study was to measure adherence to bDMARD therapies for 1 year and 2 years among patients with RA newly initiating bDMARD treatment. For this analysis, “year 1” refers to the first 12 months of treatment, “year 2” refers to months 13 to 24 of treatment, and “24 months” refers to months 1 to 24 of treatment. Adherence in the second year of therapy was assessed among patients who were effectively or noneffectively treated in the first year on therapy and among patients who were persistent or nonpersistent in the first year of therapy. The secondary objective was to explore predictors of adherence to bDMARD therapies for patients with RA newly initiating biologic treatment. Exploratory objectives included describing all-cause and RA-related costs and predictors of costs in the study population.

## Data Source

This analysis was based on data obtained from the aggregated IMS PharMetrics Plus database, which comprises adjudicated claims for more than 100 million unique enrollees across the United States. Enrollees with both medical and pharmacy coverage throughout the study period represented approximately 40 million active lives on an annual basis. PharMetrics Plus provides detailed information on inpatient and outpatient diagnoses and procedures, retail and

mail order prescription records, pharmacy and medical benefits (co-payment, deductible), and inpatient stays (admission type and source, discharge status).

## Patient Selection and Categorization

To be eligible, patients were 18 years or older at index date; had a diagnosis of RA (*International Classification of Diseases, Ninth Revision, Clinical Modification* code 714.0x) during the 6-month preindex period; were bDMARD-naïve; had continuous enrollment in the same health plan for at least 30 months (6 months preindex and 24 months post index); and had a pharmacy or medical claim for abatacept; a pharmacy claim for adalimumab, certolizumab pegol, etanercept, or golimumab; or a medical claim for infliximab between January 1, 2009, and December 31, 2012. Exclusion criteria included being 65 years or older and having no coverage by a Medicare Risk plan (to ensure patients 65 years or older were enrolled in a Medicare Risk plan that provides complete data capture); having a claim for any bDMARD indicated for first- or second-line treatment for RA, or for tofacitinib, during the preindex period (to identify bDMARD-naïve patients); having a claim for 2 or more bDMARDs on the index date (patients could only be assigned to a single exposure cohort); having a diagnosis of a non-RA bDMARD indication (plaque psoriasis, psoriatic arthritis, ankylosing spondylitis, juvenile idiopathic arthritis, Crohn disease, ulcerative colitis) during the preindex period or on the index date (to include only patients with RA); administration of any bDMARD indicated for RA before its FDA approval date (only FDA-approved and commercially available bDMARDs were evaluated); having a Healthcare Common Procedure Coding System procedure code for bDMARDs administered subcutaneously (SC) (ie, the use of a procedure code for a self-administered medication that should be captured under a prescription claim); or having a National Drug Code prescription code for bDMARDs administered intravenously (IV) (ie, the use of a prescription code that should be billed as a medical procedure).

Patients were assigned to a treatment cohort based on the index bDMARD claim. Patients remained in the assigned treatment cohort throughout the study, even if the treatment regimen changed. Patients were categorized as effectively or noneffectively treated in year 1 based on a validated claims-based algorithm.<sup>3</sup> To be considered effectively treated with a bDMARD, patients had to fulfill all of the following: high adherence (proportion of days covered [PDC] >80%), no switch to a different bDMARD or addition of a different bDMARD to the current regimen, no addition of a new csDMARD, no increase in bDMARD dose or dosing frequency, no more than 1 glucocorticoid injection, and no increase in oral glucocorticoid dose over the first year. Patients were also categorized as being persistent (no gaps ≥90 days during 6 months following index date, in accordance with other claims-based analyses<sup>10,11</sup>) or nonpersistent with the index bDMARD.

## Study Outcomes

Study outcomes included rates of adherence and persistence in all patients for 1 year and for 2 years after treatment initiation. Additionally, using data from year 1, patients were classified as effectively or noneffectively treated and as persistent or nonpersistent; year 2 adherence rates were assessed for each of these groups. Predictors of adherence, all-cause and RA-specific direct costs, and predictors of cost were also evaluated.

Index bDMARDs were SC-administered adalimumab, certolizumab pegol, etanercept, and golimumab, and IV-administered abatacept and infliximab. Labeled SC dosing regimens were: 40 mg every other week (EOW) for adalimumab, 400 mg at weeks 2 and 4 followed by 200 mg EOW for certolizumab pegol, 50 mg weekly for etanercept, and 50 mg monthly for golimumab. Labeled IV dosing regimens were: 500 mg for patients weighing less than 60 kg, 750 mg for patients 60 to 100 kg, and 1000 mg for patients greater than 100 kg at weeks 0, 2, and 4 followed by the same dose every 4 weeks for abatacept, and 3 mg/kg at 0, 2, and 6 weeks followed by dosing every 8 weeks for infliximab.

Adherence was computed using PDC over year 1 of therapy, year 2 of therapy, and the fixed 24-month postindex period, and it was capped at 100%. PDC was calculated as the total number of days supplied for a patient's prescriptions for the index biologic divided by the total number of days in the associated follow-up period (365 days or 730 days). Claims extending beyond the associated follow-up period were prorated to include only the days' supply during the follow-up period. Patients were considered adherent if their PDC was 80% or higher. Year 2 adherence was reported separately for patients who were effectively or noneffectively treated and for patients who were persistent or nonpersistent in the first year of therapy. Potential predictors of adherence included demographic (age, sex, geographic region, health plan type, payer type) and clinical (comorbidities, prior and concomitant csDMARD utilization, baseline and concomitant glucocorticoid utilization, healthcare costs during the preindex period) characteristics.

Total all-cause and RA-related direct healthcare costs were assessed for year 2. Total postindex all-cause healthcare costs included health plan- and patient-paid amounts for all inpatient and outpatient costs reported on medical and pharmacy claims. Costs were attributable to RA if the claim had an RA diagnosis or was an outpatient pharmacy claim for a csDMARD or bDMARD. Costs were inflated to 2014 US\$ based on the medical care component of the Consumer Price Index.

## Statistical Considerations

Medication use was assessed using descriptive statistics. Number of observations and percentages are provided for dichotomous and continuous variables, and number of observations, means, and SDs are provided for continuous variables. Adherence to, and persistence with, the index bDMARD were assessed by treatment

cohort and follow-up period (year 1, year 2, and 24-month follow-up). Patients were stratified into 2 subgroups based on results from year 1 (effectively treated or persistent) and evaluated for adherence in year 2. For the analysis, 2 groups of noneffectively treated patients were defined: patients who failed any of the effectiveness criteria and those who failed only the adherence criterion. Chi-square tests were used to evaluate statistical significance of differences for categorical variables, *t* tests and analysis of variance were used for normally distributed continuous variables, and nonparametric Wilcoxon and Kruskal-Wallis tests were used for continuous variables that were not normally distributed. Statistical significance was set at  $P < .05$  with no adjustment for multiplicity.

Logistic regression models were used for adjusted assessments of demographic and clinical characteristics that predict adherence (years 1 and 2 separately), with statistically significant ( $P < .05$ ) variables from univariate analysis selected for inclusion in the multivariable analysis. Characteristics included index bDMARD (compared with etanercept), age group (compared with patients aged 18-34 years), sex, region (compared with Northeast), payer type (compared with commercial), prior DMARD use, index year (compared with 2009), and preindex all-cause healthcare costs. Odds ratios (ORs) with 95% CIs were calculated for adherence during year 1 and year 2.

Inverse probability of treatment-weighted structural models were used to estimate adjusted all-cause and RA-related healthcare costs in year 2 for effectively and noneffectively treated patients, based on a generalized linear model with log link and gamma distribution. To balance the groups, propensity scores were calculated from demographic and baseline measures for all patients in the effectively and noneffectively treated populations. After creating the propensity scores, an evaluation of the distributions was used to check for sizeable overlap between the groups, demonstrating that the groups were comparable. Next, the propensity score weight was calculated as the inverse of the propensity score, using  $1/p$  for effectively and  $1/(1-p)$  for noneffectively treated patients. Finally, the propensity score-weighted regression model was fit to compare treatment outcomes. Potential predictors of costs included effective treatment in year 1, index bDMARD (compared with etanercept), age, sex, preindex glucocorticoid use, Charlson Comorbidity Index score (compared with score of 1 or 2), region (compared with Northeast), payer type (compared with commercial), preindex DMARD use, index year (compared with 2009), and preindex costs.

## RESULTS

### Patients

A total of 10,374 patients with RA were eligible for inclusion in the analysis. The mean (SD) age was 49.6 (9.7) years, and most patients were female (76.1%) (Table 1). The most commonly used bDMARDs

**TABLE 1.** Baseline Demographic and Clinical Characteristics

Characteristic	All Patients (N = 10,374)
Age, years, mean (SD)	49.6 (9.7)
Female sex, n (%)	7898 (76.1)
Geographic region, n (%)	
Northeast	2221 (21.4)
Midwest	3329 (32.1)
South	4062 (39.2)
West	762 (7.3)
Payer type, n (%)	
Commercial plan	6585 (63.5)
Medicaid	62 (0.6)
Medicare risk	10 (0.1)
Self-insured	3675 (35.4)
Unknown	42 (0.4)
Plan type, n (%)	
Consumer-directed healthcare product	56 (0.5)
Health maintenance organization	925 (8.9)
Indemnity plan	368 (3.5)
Point of service	513 (4.9)
Preferred provider organization	8484 (81.8)
Unknown	28 (0.3)
Index year, n (%)	
2009	3129 (30.2)
2010	2587 (24.9)
2011	2458 (23.7)
2012	2200 (21.2)
CCI score, n (%)	
0	0 (0)
1-2	9482 (91.4)
3-4	802 (7.7)
≥5	90 (0.9)
Prior csDMARD use, n (%)	8082 (77.9)
Prior oral or injectable glucocorticoid use, n (%)	6768 (65.2)
Concomitant <sup>a</sup> csDMARD use, n (%)	6835 (65.9)
Concomitant <sup>a</sup> glucocorticoid use, n (%)	4398 (42.4)
Index bDMARD, n (%)	
Abatacept	487 (4.7)
Adalimumab	3926 (37.8)
Certolizumab pegol	255 (2.5)
Etanercept	4426 (42.7)
Golimumab	369 (3.6)
Infliximab	911 (8.8)

bDMARD indicates biologic disease-modifying antirheumatic drug; CCI, Charlson Comorbidity Index; csDMARD, conventional synthetic disease-modifying antirheumatic drug.

<sup>a</sup>Concomitant medications were used within 90 days of the index date, including on the index date.

were etanercept (42.7%) and adalimumab (37.8%). Overall, 3076 patients (29.7%) fulfilled all criteria for being effectively treated during year 1. A total of 6251 patients were eligible to be included in adherence analysis for year 2, which required patients to remain on index therapy in year 2. Of these, 2934 were categorized as effectively treated and 3317 were noneffectively treated in year 1. Of the noneffectively treated patients, 1354 failed only the adherence criterion and 1963 failed any of the other effectiveness criteria (**eAppendix Figure** [eAppendix available at [ajmc.com](http://ajmc.com)]). A total of 4931 patients (47.5%) were persistent on index therapy for 6 months following index date.

### Adherence and Predictors of Adherence

Across all patients, 46.0% were adherent with their index bDMARD (PDC ≥80%) for 1 year and 33.6% were adherent for 2 years (**Figure, part A**). In year 2, 44.4% of eligible patients (those who remained on index biologic through year 2; n = 6251) were adherent, including 59.0% (n = 1731) of effectively treated patients and 31.5% (n = 1731) of noneffectively treated patients. Rates of adherence were similar among patients using the bDMARDs administered SC: abatacept, adalimumab, certolizumab, and etanercept. Adherence rates were numerically lowest among patients using golimumab and highest among patients using infliximab. The noneffectively treated patients who failed only the adherence criterion had a very low adherence rate in year 2 (12%) (**Figure, part B**). Patients who were persistent with index medication for 6 months post index had higher adherence during year 2 (60.6%) compared with patients who were not persistent (10.6%;  $P < .0001$ ) (**Figure, part C**).

Statistically significant predictors of higher adherence included index biologic (abatacept and infliximab for year 1 adherence, compared with etanercept, and infliximab for year 2 adherence), age group (45-54 years, 55-64 years), sex (male), prior DMARD use, and index year (2010, 2011 for year 1 adherence) (**Table 2**). Predictors of lower adherence included index biologic (golimumab), region (South), payer type (other/unknown), and lower preindex total healthcare costs.

### Costs and Predictors of Costs

All patients were assessed for year 2 costs. The average total healthcare cost in year 2 was \$32,270, ranging from \$29,356 for golimumab to \$43,008 for abatacept (**Table 3**). Mean total RA-related costs in year 2 ranged from \$17,425 (golimumab) to \$23,959 (infliximab). Adjusted total all-cause healthcare costs for year 2 were \$39,425 (95% CI, \$34,873-\$44,570) for effectively treated patients and \$25,313 (95% CI, \$22,235-\$28,818) for noneffectively treated patients. Adjusted total RA-related costs for year 2 were \$22,123 (95% CI, \$20,468-\$23,911) for effectively treated patients and \$9250 (95% CI, \$8499-\$10,067) for noneffectively treated patients.

Predictors of higher total healthcare costs included effective treatment in year 1, abatacept as the index bDMARD, older

age, preindex glucocorticoid use, Charlson Comorbidity Index (score of 3), and preindex healthcare costs (Table 4). Predictors of higher RA-related costs included effective treatment in year 1 and index year (2012). Predictors of lower RA-related costs included region (South) and payer type (self-pay or other/unknown).

## DISCUSSION

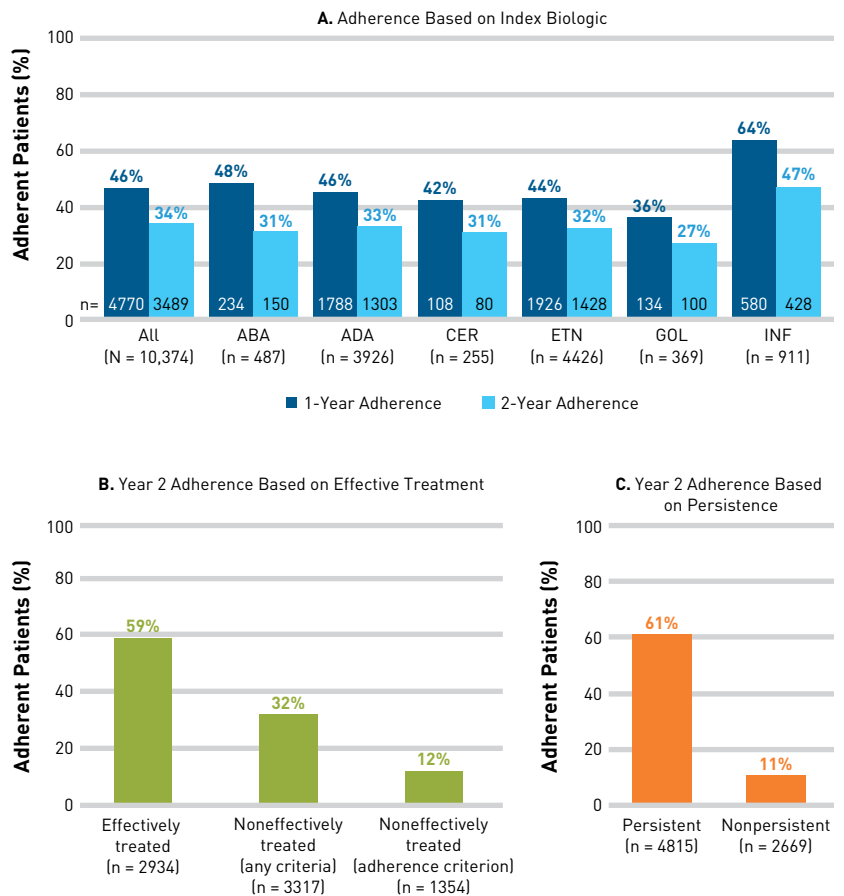
In this analysis of patients with RA initiating bDMARD therapy, adherence (PDC  $\geq 80\%$ ) in patients considered effectively treated in their first year of treatment was only 59% in year 2. Many patients were excluded from the year 2 adherence assessment because they did not remain on their index biologic through year 2. For those patients who did remain on index therapy and were considered ineffectively treated, only 32% of those who failed any effectiveness criteria and 12% of those who failed the adherence criterion were adherent to their index biologic in year 2. It is important to note that most patients who were considered to be noneffectively treated during year 1 did not fail the adherence criterion of the effectiveness algorithm. Similarly, 61% of patients who were persistent in the first 6 months of initiating therapy and 11% of those who were nonpersistent in that interval were adherent in year 2. Across all patients, adherence was only 34% at 2 years after bDMARD initiation. This finding was within the wide range of published medication adherence rates in patients with RA, which range from 30% to 90% in studies spanning 6 months to 3 years.<sup>4,12,13</sup>

In large part, the predictors of nonadherence identified in this study are not clinically modifiable characteristics (eg, geographic region, payer type). Despite that, these results do suggest that older patients and those with prior DMARD experience are more likely to be adherent compared with younger patients and those without prior DMARD use. Agents administered IV might be expected to be associated with a better adherence compared with agents administered SC, because infusions are administered in the clinic and interactions with the clinician or staff may encourage patients to remain adherent. Although this expectation was met by both abatacept and infliximab in year 1, only infliximab continued to be associated with increased likelihood of adherence in year 2. Among agents administered SC, although the likelihood of being adherent did not differ between etanercept and certolizumab or

adalimumab, golimumab users had a lower likelihood of adherence compared with etanercept users in both year 1 and year 2. These findings suggest that choice of agent may play an important role in adherence and that younger or less experienced patients may benefit from additional monitoring and support.

In this analysis, only 30% of patients were considered to have been effectively treated in their first year of treatment according to the claims-based algorithm for effective treatment. This result is consistent with those of other studies using this algorithm to examine effectiveness of bDMARDs for RA with data from other commercial databases (including IMS, Optum, and MarketScan databases), the Veterans Health Administration, and a Medicaid database.<sup>3,14-18</sup> Our results indicate that establishing effective treatment in year 1 may improve subsequent medication adherence and suggest that early medication-taking behaviors and treatment effectiveness may have lasting impact.

**FIGURE.** Adherence to Index bDMARD in Patients With RA



ABA indicates abatacept; ADA, adalimumab; bDMARD, biologic disease-modifying antirheumatic drug; CER, certolizumab; ETN, etanercept; GOL, golimumab; INF, infliximab; RA, rheumatoid arthritis.

**A.** The percentages of adherent patients for 1 year and 2 years are shown. Adherence based on **B.** effective or noneffective treatment and **C.** persistence and nonpersistence are shown.



## ORIGINAL RESEARCH

**TABLE 2.** Predictors of Year 1 and 24-Month Adherence (PDC  $\geq$ 80%) With bDMARD Therapy<sup>a</sup>

Independent Variable	Year 1 Adherence OR (95% CI) (N = 10,374)	24-Month Adherence OR (95% CI) (N = 10,374)
Index biologic (vs etanercept)		
Abatacept	1.3 (1.1-1.6)**	1.0 (0.8-1.2)
Adalimumab	1.1 (1.0-1.2)	1.0 (0.9-1.1)
Certolizumab	0.9 (0.7-1.2)	1.0 (0.7-1.3)
Golimumab	0.7 (0.6-0.9)**	0.8 (0.6-1.0)*
Infliximab	2.4 (2.0-2.7)***	1.9 (1.6-2.2)***
Age group, years (vs 18-34)		
35-44	1.1 (0.9-1.3)	1.1 (1.0-1.4)
45-54	1.3 (1.1-1.5)***	1.6 (1.3-1.9)***
55-64	1.6 (1.4-1.9)***	2.0 (1.7-2.3)***
Male sex (vs female)		
	1.3 (1.2-1.5)***	1.4 (1.2-1.5)***
Region (vs Northeast)		
Midwest	1.0 (0.9-1.1)	1.0 (0.9-1.1)
South	0.8 (0.7-0.8)***	0.8 (0.7-0.9)***
West	0.9 (0.7-1.0)	0.9 (0.7-1.1)
Payer type (vs commercial)		
Self-insured	0.9 (0.9-1.0)	0.9 (0.9-1.0)
Other/unknown	0.5 (0.4-0.8)**	0.5 (0.3-0.8)**
Prior csDMARD use (vs no use)		
	1.5 (1.4-1.7)***	1.5 (1.3-1.6)***
Index year (vs 2009) <sup>b</sup>		
2010	1.2 (1.1-1.3)**	–
2011	1.1 (1.0-1.3)*	–
2012	1.1 (1.0-1.2)	–
Log (preindex total healthcare costs)		
	0.9 (0.9-1.0)***	0.9 (0.9-1.0)***

bDMARD indicates biologic disease-modifying antirheumatic drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; OR, odds ratio; PDC, proportion of days covered.

\* $P < .05$ ; \*\* $P < .01$ ; \*\*\* $P < .001$ .

<sup>a</sup> $P$  values are nominal, not adjusted for multiplicity.

<sup>b</sup>Index year did not meet selection criteria for inclusion in year 2 model.

We also assessed costs during the second year of treatment with a bDMARD. In general, studies have found that patients who are effectively treated<sup>18</sup> are adherent to therapy<sup>7</sup> or persistent with therapy<sup>9</sup> and have lower healthcare utilization and nonpharmacy costs than patients who are noneffectively treated, nonadherent,

or nonpersistent. In our study, adjusted all-cause costs and RA-related costs were higher among effectively treated patients than among noneffectively treated patients. We cannot directly compare our results with those of prior studies because we did not separate pharmacy and nonpharmacy costs. Differences in how costs were quantified in other published studies (eg, total or only nonpharmacy costs, paid vs submitted charges) and any differences in how effective treatment was defined in each study may also account for the differences between our findings and those of previous reports. More adherent patients would be expected to have higher pharmacy costs, and it is possible that effectively treated patients may have additional nonpharmacy utilization if additional encounters and monitoring play a role in their better adherence.

### Limitations

Claims-based studies have inherent limitations. Claims data are subject to coding errors. Adherence measures are based on prescription fill information and may not represent true medication usage. Disease severity and treatment response were not captured in the database, and effectiveness was therefore estimated using the claims-based algorithm. These results obtained from commercially insured patients may not be generalizable to underinsured or uninsured patients.

## CONCLUSIONS

This study showed that effective treatment in the first year of initiating bDMARD therapy for RA was associated with higher rates of adherence in the second year after therapy initiation compared with noneffective treatment. Strategies to promote adherence in this population remain elusive, but they are clearly warranted. ■

**TABLE 3.** Unadjusted Healthcare Costs and RA-Related Costs During Year 2 Only (2014 US\$)

	All Patients (N = 10,374)	Abatacept (n = 487)	Adalimumab (n = 3926)	Certolizumab (n = 255)	Etanercept (n = 4426)	Golimumab (n = 369)	Infliximab (n = 911)
Mean (SD) total healthcare costs	32,270 (35,961)	43,008 (79,510)	31,592 (32,891)	32,507 (27,132)	30,557 (28,241)	29,356 (32,930)	38,892 (45,292)
Mean (SD) total RA-related costs	19,126 (14,028)	19,894 (15,475)	18,821 (13,806)	18,388 (13,086)	18,501 (12,864)	17,425 (12,900)	23,959 (18,607)

RA indicates rheumatoid arthritis.

**TABLE 4.** Predictors of Total Healthcare Costs and RA-Related Costs in Year 2 Only

Independent Variable	Year 2 Cost β Estimate (95% CI)
Total healthcare costs	
Effectively treated in year 1 (vs noneffectively treated)	0.44 (0.39-0.50)***
Index bDMARD (vs etanercept)	
Abatacept	0.20 (0.04-0.36)*
Adalimumab	-0.03 (-0.08 to 0.03)
Certolizumab	0.07 (-0.07 to 0.22)
Golimumab	0.01 (-0.12 to 0.14)
Infliximab	0.0 (-0.13 to 0.12)
Age	0.01 (0.01-0.01)***
Male sex (vs female)	-0.02 (-0.08 to 0.03)
Preindex glucocorticoid use	0.05 (0.00-0.10)*
CCI score (vs 1 or 2)	
3	0.26 (0.13-0.39)***
4	0.32 (-0.01 to 0.64)
Log (preindex cost)	0.14 (0.11-0.17)***
Total RA-related costs	
Effectively treated in year 1 (vs noneffectively treated)	0.87 (0.82-0.92)***
Age	0.00 (0.00-0.00)
Male sex (vs female)	0.01 (-0.04 to 0.06)
Region (vs Northeast)	
Midwest	0.00 (-0.08 to 0.07)
South	-0.13 (-0.19 to -0.06)***
West	-0.01 (-0.12 to 0.09)
Payer (vs commercial type)	
Self-pay	-0.06 (-0.10 to -0.01)*
Other/unknown	-0.26 (-0.48 to -0.04)*
Preindex csDMARD use (vs no use)	0.04 (-0.02 to 0.09)
Index year (vs 2009)	
2010	0.02 (-0.04 to 0.08)
2011	0.06 (-0.01 to 0.12)
2012	0.13 (0.07 to 0.19)**

bDMARD indicates biologic disease-modifying antirheumatic drug; CCI, Charlson Comorbidity Index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; RA, rheumatoid arthritis.

\* $P < .05$ ; \*\* $P < .01$ ; \*\*\* $P < .001$ .

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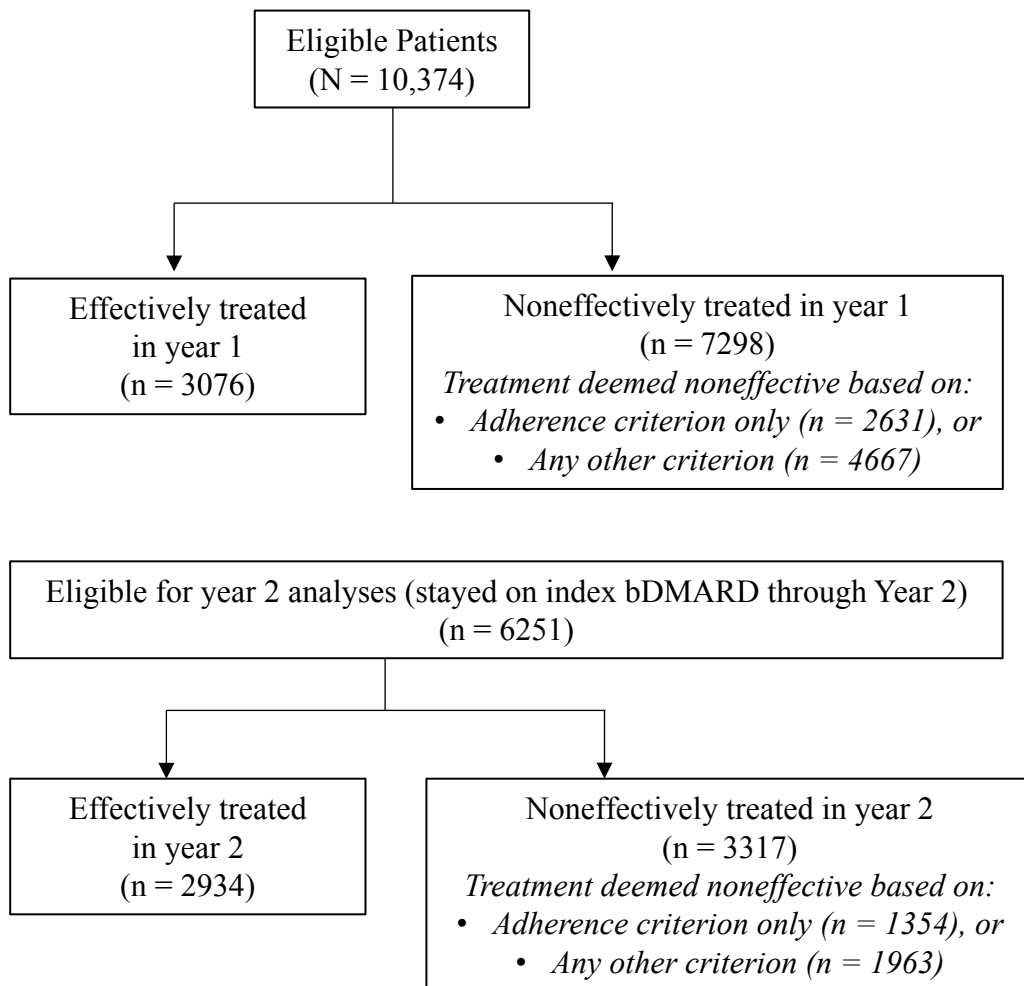
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**eAppendix Figure. Patient Flow**



bDMARD indicates biologic disease-modifying antirheumatic drug.