Assessing the Association of Formulary Copayment Changes with Real-World Treatment Patterns in Patients with Rheumatoid Arthritis on Etanercept

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ABSTRACT

BACKGROUND: Rheumatoid arthritis (RA) is a chronic disease that requires long-term treatment to improve or maintain stable disease activity. Tumor necrosis factor inhibitors (TNFi), a class of biologic disease-modifying antirheumatic drugs (bDMARD), are effective at treating symptoms and inhibiting joint progression. Although treatment changes are not recommended in patients with stable disease, health plans have recently enacted formulary changes with higher copayments that could disrupt patient access to TNFis.

OBJECTIVE: To assess the association of formulary copayment changes with real-world treatment patterns, treatment effectiveness, and health care costs among bDMARD-naïve patients with RA receiving the TNFi etanercept.

METHODS: This retrospective observational cohort analysis used the IBM Watson Health MarketScan Commercial Claims and Encounters Database. Adult patients with RA with 6 months of stable etanercept use (no refill gap ≥ 45 days) from January 1, 2013, through December 31, 2015, were selected and the index date was set to the first fill date after the stable-use period. Average etanercept copayment was calculated at the drug-plan level. Copayment change was defined as a monthly increase of at least \$40 to account for copayment changes attributable to etanercept wholesale acquisition costs between 2014 and 2015. This amount also corresponded to the 90th percentile of average plan-level changes in etanercept copayments in the database, representing an average change in copayment by a payer. Patients were followed ≥ 12 months before and after the index date to track etanercept treatment changes and ≥ 12 months after a treatment change to track costs after etanercept copayment changes. Etanercept persistence, bDMARD switching, refill gaps, and treatment effectiveness (using a validated effectiveness algorithm) were described for patients with or without copayment change during the 12 months post-index or postchange. We also assessed the mean total of all-cause and RA-related expenditure during the 12-month post-index (or postchange) period.

RESULTS: 1,970 stable patients met study inclusion criteria (mean [standard deviation] age: 50.3 [9.5] years; 77.8% female) and were evaluated. Of these, 133 (6.8%) patients had a copayment change $\geq \$40$ during follow-up. Overall, most patients (60.3%) persisted on etanercept for the 12-month follow-up period, while 13.0% switched from etanercept, and 8.1% discontinued (refill gap of ≥ 45 days). Nearly half (48.0%) of all patients were considered effectively treated according to a validated algorithm. Compared with patients without a copayment change, those with a copayment change were more likely to switch biologics (19.5% vs. 12.6%; $P=0.021$). Although statistical significance was not reached, patients with a copayment change were less likely to be persistent (54.1% vs. 60.7%; $P=0.135$), and less likely to be effectively treated (42.1% vs. 48.4%; $P=0.161$) than patients without a copayment change. All-cause and RA-related expenditures at baseline and post-copayment change were similar between patients with and without a copayment change.

CONCLUSIONS: Changing formulary copayment of etanercept was associated with higher switching without difference in costs or health care utilization between copayment and no copayment change groups.

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What is already known about this subject

- Although treatment changes are not recommended in patients with stable disease, health plans have recently enacted formulary copayment changes with higher tier drugs having higher copayments, which could disrupt patient access to tumor necrosis factor inhibitors.
- Evidence suggests that copayment increases and the associated nonmedical biologic switching are detrimental to patient health and increase health care resource utilization and costs among patients with rheumatoid arthritis (RA).

What this study adds

- This study furthers our understanding of formulary copayment increases and real-world treatment patterns and treatment effectiveness among patients with RA who are naïve to biologic disease-modifying antirheumatic drugs and are receiving etanercept.
- Changing copayments of etanercept was associated with higher nonmedical switching to another RA medication. Validation in a larger study is recommended.

Rheumatoid arthritis (RA) is a chronic disease that requires long-term treatment to improve or maintain stable disease activity. Affecting approximately 1.3 million adults in the United States, RA is characterized by persistent inflammation in joints, which damages the surrounding cartilage and bone and negatively impacts physical health and patient functionality because of pain, swelling, and stiffness.¹ When unmanaged, RA leads to progressive joint damage resulting in physical impairment and long-term disability.

Effective treatment of RA symptoms with disease-modifying antirheumatic drugs (DMARDs) has been shown to increase

productivity at work and home and to improve health-related quality of life.^{2,3} Furthermore, the addition of a biologic DMARD (bDMARD) or a targeted synthetic DMARD to the treatment regimen is recommended for patients with RA who have moderate or high disease activity despite monotherapy with a conventional synthetic DMARD.⁴ Tumor necrosis factor inhibitors (TNFis), a class of targeted immune modulators, are effective at treating RA symptoms and inhibiting joint progression.⁵ TNFis are indicated for the treatment of moderate to severe RA, with etanercept being one of the most commonly prescribed.^{6,7}

Nonpersistence on biologic therapy may occur because of medical reasons (such as inadequate response or medication intolerance) or nonmedical reasons, defined as a reason unrelated to clinical efficacy or tolerability.⁸⁻¹⁰ Nonmedical reasons may include economic reasons, such as increased copay, change of insurance, job loss, or other economic factors that limit the affordability of a medication.¹¹ Although treatment changes are not recommended in patients with stable disease, formulary changes to health plans, such as increasing copayments or categorizing therapeutic agents in higher tiers, could disrupt patient access to TNFi therapy.⁴ Use of drugs in higher formulary tiers, often with higher copayment cost, may require prior approval from insurance providers and could drive patients to switch therapies for reasons unrelated to their RA management. Evidence suggests that formulary copayment changes and the associated nonmedical biologic switching are not only detrimental to patient health but also increase health care resource utilization and costs among patients with RA.¹²⁻¹⁵ Patients who switched for nonmedical reasons had increased disease flares, poorer disease control, had 14% more RA-related outpatient visits, and 29% more rheumatologist visits than patient persistent on their TNFi therapy.^{11,13,14} Furthermore, nonmedical switchers incurred significantly higher all-cause medical costs (\$4,557 vs. \$3,310; $P=0.0011$) and total costs (\$21,996 vs. \$17,379; $P<0.001$) than patients persistent on their TNFi therapy.¹²

This study sought to understand the effect of formulary copayment changes on real-world treatment patterns, treatment effectiveness, and health care costs among bDMARD-naïve patients with RA receiving etanercept.

Methods

Study Design

We performed a retrospective analysis of data from IBM Watson Health MarketScan Commercial Claims and Encounters Database, a large U.S. employer-based claims database that includes claims from approximately 137.6 million employees and their dependents. Data were from January 1, 2012, through December 31, 2016. This study used de-identified database records, which are fully compliant with the U.S. Health Insurance Portability and Accountability Act (HIPAA); this

compliance with HIPAA regulation meant that patient consent and institutional review board approval to conduct this study were not necessary.

Patients were grouped according to whether they were in a plan that experienced an etanercept copayment change or not. Copayment change was defined as a monthly increase of at least \$40 to account for copayment changes attributable to difference in etanercept wholesale acquisition costs between 2014 and 2015. The \$40 increase cutoff was derived by assessing copayments across 3- and 4-tiered formularies and calculating expected copayment changes based on etanercept wholesale acquisition cost changes. The cutoff also corresponds with the 90th percentile copayment amount among the eligible cohort.

The study design is outlined in Appendix A (available in online article). Study periods were defined as follows: Index date was the first fill date after a patient's 6-month stable etanercept use period (i.e., no refill gap ≥ 45 days). Baseline period was defined as the 12 months preceding the index date, which included 6 months of no TNFi use (to establish a bDMARD-naïve population), followed by the patient's 6-month stable use period. Demographic characteristics were captured on the index date. Clinical characteristics were determined from claims data during the 12-month baseline period. Post-index period was defined as the period following the index date (up to 12 months) and was used for assessment of etanercept treatment changes. Postchange period was defined as the 12 months after treatment changes for patients who were nonpersistent on etanercept (persistence was defined as having no refill gap ≥ 45 days and no switching therapy). Outcome measures were assessed post-index in the persistence group and postchange in the treatment change group. To ensure cost assessments were over a consistent duration, participants were required to have a continuous plan enrollment for ≥ 12 months post-index date or for ≥ 12 months postchange. Post-index periods were equal to the postchange period for persistent patients (Appendix A).

Study Population

Inclusion Criteria. Patient selection is described in Appendix B (available in online article). Adults (18-64 years) with RA who had at least 6 months of continuous etanercept use from January 1, 2013, through December 31, 2015, no pharmacy or medical claims for any TNFi during the 6 months before the 6-month stable etanercept use period were evaluated.

Exclusion Criteria. Patients were excluded if they had a non-diagnostic medical claim with an *International Classification of Diseases, Ninth/Tenth Revision, Clinical Modification* diagnosis code for juvenile idiopathic arthritis, psoriasis, psoriatic arthritis, ankylosing spondylitis, Crohn disease, or ulcerative colitis at any time during the study period.

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TABLE 1 Demographic and Clinical Characteristics for Patients with 6-Month Stable Etanercept Use

	No Copayment Change (n = 1,837)	Copayment Change (n = 133)	All (N = 1,970)
Mean (SD) age, years	50.4 (9.5)	50.0 (9.7)	50.3 (9.5)
Age category, % (n)			
18-34	7.8 (143)	8.3 (11)	7.8 (154)
35-44	17.0 (313)	16.5 (22)	17.0 (335)
45-54	35.4 (651)	37.6 (50)	35.6 (701)
55-64	39.7 (730)	37.6 (50)	39.6 (780)
Female, % (n)	77.5 (1,424)	82.0 (109)	77.8 (1,533)
Insurance plan type, % (n)			
Comprehensive/indemnity	4.7 (86)	0.0 (0)	4.4 (86)
EPO/PPO	59.0 (1,084)	66.9 (89)	59.5 (1,173)
POS/POS with capitation	5.9 (109)	10.5 (14)	6.2 (123)
HMO	11.2 (206)	9.8 (13)	11.1 (219)
CDHP/HDHP	17.9 (328)	12.8 (17)	17.5 (345)
Unknown	1.3 (24)	0.0 (0)	1.2 (24)
Index year, % (n)			
2013	26.6 (488)	47.4 (63)	28.0 (551)
2014	43.0 (789)	28.6 (38)	42.0 (827)
2015	30.4 (559)	24.1 (32)	30.0 (591)
2016	0.0 (1)	0.0 (0)	0.0 (1)
Deyo-Charlson Comorbidity Index, mean (SD)	1.4 (0.9)	1.5 (0.9)	1.4 (0.9)
Comorbid conditions, % (n)			
Chronic respiratory/pulmonary conditions			
Asthma	16.7 (307)	15.8 (21)	16.6 (328)
Chronic obstructive pulmonary disease	4.0 (74)	4.5 (6)	4.1 (80)
Bronchiolitis obliterans organizing pneumonia	0.2 (4)	0.0 (0)	0.2 (4)
Pulmonary fibrosis/interstitial lung disease	2.3 (43)	0.0 (0)	2.2 (43)
Pulmonary embolism	0.3 (6)	0.8 (1)	0.4 (7)
Cardiovascular disease			
Congestive heart failure	0.8 (14)	0.8 (1)	0.8 (15)
Coronary heart disease with or without old MI	4.6 (84)	6.8 (9)	4.7 (93)
Ischemic stroke/transient ischemic attack	0.8 (14)	0.0 (0)	0.7 (14)
Peripheral artery disease	2.1 (38)	1.5 (2)	2.0 (40)
Ventricular arrhythmia	0.5 (10)	0.8 (1)	0.6 (11)
Depression	12.0 (220)	5.3 (7)	11.5 (227)
Diabetes	10.2 (188)	13.5 (18)	10.5 (206)
Fibromyalgia	11.8 (217)	17.3 (23)	12.2 (240)
Hypertension	30.0 (551)	39.8 (53)	30.7 (604)
Serious infection ^a	5.7 (104)	3.0 (4)	5.5 (108)
Concomitant medication use, % (n)			
Conventional DMARDs	80.4 (1,477)	84.2 (112)	80.7 (1,589)
Glucocorticoids	73.8 (1,356)	77.4 (103)	74.1 (1,459)

^aIncludes inpatient infection or intravenous antibiotic use.

CDHP = consumer-driven health plan; DMARD = disease-modifying antirheumatic drug; EPO = exclusive provider organization; HDHP = high-deductible health plan; HMO = health maintenance organization; MI = myocardial infarction; POS = point of service; PPO = preferred provider organization; SD = standard deviation.

Outcomes

Etanercept treatment patterns within the post-index period were assessed. Treatment patterns were defined as follows: *persistence*, when no treatment modifications or refill gaps (≥ 45 days) occurred during the post-index period, and *nonpersistence*, when a refill gap ≥ 45 days or biologic switch from etanercept occurred during the post-index period. Nonpersistent patients

were further categorized into the following mutually exclusive categories: switch with a refill gap for etanercept, switch without a refill gap for etanercept, etanercept restart after a gap in treatment, and etanercept discontinuation.

A validated claims-based effectiveness algorithm that uses administrative data as a proxy for clinical response (as measured by the Disease Activity Score in 28 joints) was used to

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TABLE 2 Treatment Patterns After Copayment Change in Stable Etanercept Users (N = 1,970)

	No Copayment Change	Copayment Change	P Value
Stable etanercept use, % (n)	93.2 (1,837)	6.8 (133)	—
Persistence, % (n)	60.7 (1,115)	54.1 (72)	0.135
Nonpersistence, % (n)	39.3 (722)	45.9 (61)	—
Refill gap	26.7 (491)	26.3 (35)	0.917
Restart (those with gap)	70.3 (345)	60.0 (21)	0.202
Discontinuation ^a	7.9 (146)	10.5 (14)	0.293
Switch	12.6 (231)	19.5 (26)	0.021
Prior refill gap	3.4 (62)	3.8 (5)	0.813
No prior refill gap	9.2 (169)	15.8 (21)	0.013
Any refill gap (with or without switch)	30.1 (553)	30.1 (40)	0.995
Effectively treated	48.4 (889)	42.1 (56)	0.161

^aNo restart within 12 months. Persistence was defined as having no refill gap ≥ 45 days and no switching.

TABLE 3 Association Between Copayment Change and Treatment Patterns After Multivariable Adjustment

Outcome	Effect of Copayment Change		
	Odds Ratio	P Value	95% CI
Nonpersistence	1.255	0.231	(0.865-1.821)
Biologic switch	1.885	0.009	(1.170-3.039)
Not effectively treated	1.443	0.050	(1.000-2.082)

Note: Variables used for adjustment include effectively treated in stable period; baseline MTX use; baseline non-MTX conventional disease-modifying anti-rheumatic drug use; Deyo-Charlson Comorbidity Index; baseline number of emergency room visits; baseline number of rheumatologist office visits; health plan type; age; index year; geographical region (South, North East, North Central, and West); and baseline diagnoses of asthma, cardiovascular disease, fibromyalgia, hypertension, and malignancy. A claims-based effectiveness algorithm (Curtis et al. 2011) was used to assess rheumatoid arthritis control during the 12-month post-index (or postchange) period.¹⁶

CI = confidence interval; MTX = methotrexate.

describe effective or ineffective RA control during the 12-month post-index (or postchange) period.¹⁶ Patients who satisfied all 6 of the following algorithm criteria for the 12 months after the switch date were considered effectively treated:

1. Adherence (medication possession ratio of $\geq 80\%$)
2. No increase in dose or frequency once stable dose is achieved (post-index); no increase in dose or frequency after switching (postchange)
3. No switch or addition of new biologic
4. No addition of a new nonbiologic DMARD
5. No more than 1 intra-articular glucocorticoid injection
6. No new (or increased dose of) oral glucocorticoids

Additionally, we assessed the mean total all-cause and RA-related expenditures (outpatient and inpatient costs, and outpatient prescription costs) during the 12-month post-index (or postchange) period (patient and plan). Health care costs were attributable to RA if there was a nondiagnostic medical claim with RA in any position on an outpatient claim. The whole hospitalization cost was attributable to RA if RA was the primary discharge diagnosis of the hospitalization. All dollar estimates were inflated to 2016 dollars using the medical care component of the Consumer Price Index.

Statistical Considerations

Descriptive statistics were used to describe outcomes of patients grouped by having a formulary copayment change or not. Fisher's exact test was used for categorical comparisons. A chi-square test was used to test for differences in categorical variables. Multivariable regression analysis was used to assess the relationship between formulary copayment changes and treatment outcomes and health care costs, adjusting for baseline demographic and clinical characteristics (age, index year,

insurance plan type, geographical region, and baseline diagnosis [asthma, depression, diabetes, hypertension, infection, osteoarthritis, and osteoporosis]). The significance threshold was set at $P < 0.05$.

Results

Overall, 1,970 patients with 6 months stable etanercept use met the study inclusion and exclusion criteria and were evaluated (Table 1). The mean patient age was 50.3 years. Patients were grouped according to formulary copayment change: no copayment change group ($n = 1,837$) and copayment change group ($n = 133$). Except for the index year, demographics and clinical characteristics were similar between groups. Most were female (77.8%), ≥ 45 years (75.2%), and receiving conventional DMARD (80.7%) or glucocorticoid (74.1%) concomitant medication. Overall, the mean copayment increase was \$68.53 for patients in the copayment change group and a decrease of \$4.48 for patients in the no copayment change group.

Treatment Patterns

Across all patients, 60.3% (1,187/1,970) were categorized as persistent etanercept users during the 12-month post-index period (Table 2). Of the 783 nonpersistent patients, 32.8% switched from etanercept treatment and 46.7% had a refill gap but subsequently restarted etanercept treatment. Overall, one fifth of nonpersistent patients discontinued etanercept treatment without switching or restarting treatment.

A larger proportion of patients in the copayment change group switched treatments than those in the no copayment change group (19.5% vs. 12.6%; $P = 0.021$). Although statistical significance was not reached when compared with the no copayment change group, patients with copayment change tended to show higher rates of discontinuation (10.5% vs. 7.9%; $P = 0.293$) and lower rates of persistence (54.1% vs. 60.7%; $P = 0.135$).

FIGURE 1 Total All-Cause and RA-Related Costs at Baseline and Postformulary Change in Patients with and Without a Copayment Change

Note: Bar totals may be different due to rounding.
RA = rheumatoid arthritis.

Treatment Effectiveness

Across all patients, 65.7% (1,294/1,970) satisfied all 6 treatment effectiveness algorithm criteria during the 12-month post-index period. A larger proportion of persistent patients compared with nonpersistent patients were effectively treated (73.7% vs. 53.5%). Although statistical significance was not reached when compared with the no copayment change group, patients with copayment change tended to have lower rates of effective treatment (42.1% vs. 48.4%; $P=0.161$; Table 2).

Association Between the Formulary Copayment Change Group and Switching and Treatment Effectiveness

After controlling for baseline demographics and clinical characteristics, patients with a copayment change had 1.88 higher odds of switching biologic agents during the post-index period than patients without a copayment change ($P=0.009$). Additionally, patients with a copayment change had 1.44 higher odds of not being effectively treated during the post-index period, measured using a validated algorithm, than patients without a copayment change ($P=0.05$). The odds of

persistence with index therapy was similar regardless of copayment change status ($P=0.231$; Table 3).

Costs

The mean all-cause and RA-related expenditures at baseline and post-copayment change were similar between groups (Figure 1). Furthermore, after adjusting for potential confounders, multivariable analyses showed that total all-cause and total RA-related costs during the post-index period remained similar between patients regardless of copayment change (Table 4).

Discussion

Our data add to the growing evidence that formulary copayment changes are associated with nonmedical biologic switching, which may be detrimental to patient health among patients with RA.¹²⁻¹⁵ In summary, our analysis found that copayment changes were associated with higher rates of switching and lower rates of being effectively treated, without differences in costs. Consistent with previous findings that treatment persistence is associated with improvements in RA disease

TABLE 4 Multivariable Analyses Assessing the Association of Copayment Changes on Total and RA-Related Costs

	Predicted Value, Mean \$ (SD)		Beta Coefficient (95% CI)	P Value
	No Copayment Change	Copayment Change		
Total health care costs	42,953 (10,803)	43,454 (10,929)	−0.012 (−0.126-0.102)	0.842
Total RA-related costs	32,506 (5,228)	32,654 (5,252)	−0.005 (−0.083-0.073)	0.909

Note: Variables used for adjustment include effectively treated in stable period; baseline MTX use; baseline non-MTX conventional disease-modifying antirheumatic drug use; Deyo-Charlson Comorbidity Index; baseline number of emergency room visits; baseline number of rheumatologist office visits; health plan type; age; index year; geographical region (South, North East, North Central, and West); and baseline diagnoses of asthma, cardiovascular disease, fibromyalgia, hypertension, and malignancy. CI=confidence interval; MTX=methotrexate; RA=rheumatoid arthritis; SD=standard deviation.

activity and disability, multivariable analyses demonstrated that patients without copayment change were more likely to be effectively treated according to the validated effectiveness algorithm.¹²⁻¹⁵ Discontinuation of anti-TNF therapy for nonmedical reasons has been shown to result in significantly worse clinical outcomes and increased health care resource utilization.¹²⁻¹⁵ In contrast to our findings, previous studies have shown that patients who switched to another DMARD for no apparent medical reason other than to lower out-of-pocket costs used significantly more health care services as compared with those who remained on their index drug. Specifically, those who switched treatment incurred 42% more emergency department visits, 29% more rheumatologist visits, and 12% more outpatient visits as compared with those who remained on index therapy. Additionally, patients switching for nonmedical reasons were more likely to discontinue their new DMARD in the 6-month follow-up period.¹² Furthermore, patients who switched or discontinued TNFi treatment were at a significantly greater risk of flares than patients who continued TNFi treatment, as well as at an increased risk of emergency department visits and more repeat emergency department visits.¹³ Here, we demonstrated higher rates of switching without an increase in costs or health care utilization. This difference may reflect our cohort that was restricted to patients with 6 months stable etanercept use during the pre-index period and may represent a more homogenous population of stably treated patients than previous studies, ensuring our outcomes are not influenced by early nonpersistence.

Overall, rate of persistence observed in our study was higher than persistence rates in similar claims-based studies.^{17,18} The more homogenous and stable population may explain these differences, as TNFi switching usually occurs following 3 months of failed treatment.⁴ Previously, nonmedical switching of TNFi treatment has been shown to be associated with an increase in side effects and lack of efficacy that led to treatment adjustments and increased health care resource utilization.¹⁵ Furthermore, Liu et al. (2015) showed that patients who switched following a payer formulary change and for no apparent medical reason were found to incur significantly

higher all-cause medical costs and total costs during follow-up than those maintaining index therapy.¹² However, in contrast to these reports, and counterintuitively, we show that despite higher formulary copayments, total health care and RA-related costs remained similar, suggesting no increase in health care resource utilization. The small proportion of our cohort (6.8%) who had a formulary copayment change may indicate that the study was insufficiently powered to detect the difference. Alternatively, our analysis required that patients have 6 months of stable etanercept use as an inclusion criterion, which would exclude patients with shorter treatment durations after initiation; shorter treatment duration can be associated with lower costs, as therapy costs comprise the majority of health care costs in patients with RA.¹⁹

Strengths and Limitations

Our study had several strengths, including the use of a large, prescription coverage-based retrospective cohort. We determined new incident use of etanercept by identifying no previous use of bDMARD in the year before index. Furthermore, the requirement of 6-month stable etanercept use means our population was more stable and homogenous than similar claims-based studies without this criterion. However, further study is needed to determine if changes in coverage force more patients on a TNFi to switch treatment or have longer than expected refill gaps in therapy and if treatment changes are associated with changes in treatment effectiveness and health care costs.

Our study was subject to some limitations, including those inherent in the analysis of administrative claims data. The study was limited to individuals with 24-month continuous commercial health coverage between the ages of 18 and 64 years. As such, results of this analysis may not be generalizable to bDMARD-naïve patients with RA >65 years or those with other types of insurance, those with intermittent health care coverage, or those without health insurance coverage.

Our definition of copayment change was empirically derived based on a plan-level analysis of copayment changes from year to year. Despite the strength of the large population size and real-world data, only a small proportion of our cohort (6.8%)

had a copayment change of $\geq \$40$, which negatively impacts detectable differences for our comparisons. However, as the copayment cutoff corresponded with the 90th percentile copayment amount among the eligible cohort, it should be expected that less than 10% would have had a copayment change.

There is no single gold standard for adjusting health expenditures for inflation. Here, all dollar estimates were inflated to 2016 dollars using the medical care component of the Consumer Price Index, which may have led to overestimates of medical expenditures compared with adjusting with the Personal Health Care price or Personal Consumption Expenditures health component price index.²⁰ However, as there was no increase in health care resource utilization between those with and without copayment change, this finding is likely to stand regardless of index used.

Conclusions

This claims-based analysis of commercially insured patients in the United States showed that changing formulary status of etanercept was associated with higher switching that negatively impacted persistence and treatment effectiveness without differences in costs between no copayment change and copayment change groups. Further evaluation in a larger cohort of patients with a copayment change is recommended to validate these findings.

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DISCLOSURES

This study was sponsored by Amgen. Bonafede, Manjelievskaia, and Lopez-Gonzalez are employees of IBM Watson Health, which received funding from Amgen to conduct this study. Oko-osi, Collier, and Stolshek are employees and shareholders of Amgen. Gharaibeh was an employee of Amgen at the time of study execution and manuscript drafting. The authors have no other relationships that present a potential conflict of interest.

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APPENDIX A Study Design

A. Study Requirements

B. Study Requirements When Patient Had a Post-Index Treatment Change

bDMARD=biologic disease-modifying antirheumatic drug; ETN=etanercept; RA=rheumatoid arthritis; TNFi=tumor necrosis factor inhibitor.

Assessing the Association of Formulary Copayment Changes with Real-World Treatment Patterns in Patients with Rheumatoid Arthritis on Etanercept

APPENDIX B Patient Selection

ICD-9/10-CM=International Classification of Diseases, Ninth/Tenth Revision, Clinical Modification; TNF=tumor necrosis factor.