

Cost-Sharing and Initiation of Disease-Modifying Therapy for Multiple Sclerosis

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Objectives: To assess the effects of patient cost-sharing on initiation of disease-modifying therapies (DMTs) in multiple sclerosis (MS).

Study Design: Retrospective claims database study of privately insured patients newly diagnosed with MS between 2004 and 2008 from 33 large employers.

Methods: We assessed the effects of plan-level cost-sharing on DMT initiation during a 2-year follow-up period after diagnosis. Incident cases were identified by 2 or more claims with ICD-9 codes for MS within a year, subsequent to a year with no such claims. Covariates for adjustment included age, gender, relationship to primary beneficiary, comorbid conditions, and calendar year, as well as unobserved factors that did not vary within plans over time.

Results: Out of a sample of 3460 patients meeting criteria for inclusion, only 17% initiated a DMT within 2 years of diagnosis. An increase in the cost-sharing rate from zero to the 95th percentile (17.8%) was predicted to decrease initiation within 2 years of diagnosis by 2.9 percentage points, or 12.7% ($P = .019$).

Conclusions: High cost-sharing is associated with delayed initiation of effective MS therapies.

(*Am J Manag Care. 2012;18(8)460-464*)

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Healthcare costs in the United States have been growing faster than the overall rate of inflation.¹ As policy makers and insurers search for ways to control cost growth, they have frequently turned toward cost-sharing. In particular, increasing cost-sharing for prescription drugs is often proposed as a cost-containment mechanism.²⁻⁴

The rationale for this approach is 2-fold: First, the health plan may offset a portion of its drug acquisition costs through copayment or co-insurance revenue collected from patients. Second, when patients are directly affected economically by their treatment choices, they will be more discriminating consumers.⁵

However, cost-sharing can negatively impact therapy utilization, particularly among those with chronic conditions. Reduced initiation of pharmaceutical treatments with proven health benefits could result in worse long-term health outcomes.⁶⁻⁸

Multiple sclerosis (MS) is an autoimmune disorder characterized by inflammation of the central nervous system.^{9,10} Its most common symptoms are fatigue, reduced mobility, bowel and bladder disturbances, diminished cognitive function, pain, sensory loss, and depression. Currently, there are approximately 400,000 people living with MS in the United States.¹¹

Disease-modifying therapies (DMTs) have become the standard for MS treatment. Randomized clinical trials and long-term follow-up studies have found that DMTs are effective in reducing relapse rates, slowing the progression of disability, and reducing MS disease activity.¹²⁻¹⁵

The costs of DMTs make them attractive targets for high cost-sharing by health plans seeking to contain pharmacy costs.¹⁶ The existing evidence on the link between cost-sharing and MS DMT utilization is limited and does not control for the selection of individuals into benefit plans.¹⁷

The objective of this study was to evaluate the association between health plan cost-sharing for DMT drugs and initiation of these therapies among US commercial health plan beneficiaries with MS.

METHODS

This was a retrospective longitudinal cohort study, which used a data set of deidentified administrative, claims, and benefit information

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from 33 Fortune 500 employers. The data provided information on enrollment, medical, and pharmacy records for the years 2003 through 2009. The data included detail on age of beneficiaries, gender, diagnoses, and relationship of beneficiary to the primary beneficiary. The data included total and beneficiary-level spending for all outpatient pharmaceutical purchases, as well as all inpatient and outpatient medical services. National drug code and dosage were reported in drug claims; each medical claim reported up to 9 diagnoses and 6 procedures.

Inclusion and Exclusion Criteria

The study sample consisted of beneficiaries 18 years or older with 2 or more inpatient or outpatient diagnoses of MS (*International Classification of Diseases, Ninth Revision, Clinical Modification* code of 340) within 1 year. The index date was the date of the first MS diagnosis during the patient identification period between January 1, 2004, and March 31, 2008. Patients had to have at least 2 years of continuous enrollment after (and inclusive of) the index quarter and at least 1 year of continuous enrollment prior to the index quarter, with no MS diagnosis or DMT use in the pre-index period.

Key Variables and Outcomes

For all analyses, DMTs were identified by National Drug Codes in pharmacy claims or Healthcare Common Procedure Coding System codes in medical claims. DMTs included interferon beta-1a (subcutaneous and intramuscular), interferon beta-1b, glatiramer acetate, natalizumab, and mitoxantrone.

In measuring cost-sharing, our goal was to quantify how DMT utilization responds to cost-sharing. Plans have disparate benefit designs, differing with respect to multi-tier formularies, out-of-pocket discounts for mail order or in-network retail pharmacies, and deductibles, maximums, and caps. A cost-sharing measure that characterizes plan design in a consistent, comprehensive, and economically meaningful way was needed. Hence, we took the ratio of total out-of-pocket payments for DMTs to total payments for DMTs, among all MS patients in a given plan by year. This approach has been used in other studies in the literature.¹⁸ Treatment initiation was defined as any fill of a DMT prescription during the 2-year follow-up period after diagnosis.

Statistical Analysis

Multivariate regression analyses estimated linear relationships between health plan cost-sharing and DMT initiation

Take-Away Points

While cost-sharing for pharmaceuticals has been proposed as a means of controlling health spending, it can reduce the use of therapy by patients. This study examines the association between cost-sharing and initiation of disease-modifying therapies (DMTs) among privately insured patients with multiple sclerosis (MS).

- Higher cost-sharing is associated with less frequent initiation of DMTs among recently diagnosed MS patients.
- This finding, together with evidence that DMTs are effective in slowing the progression of MS, suggests that increased cost-sharing as a means of controlling spending could lead to unintended consequences for MS patients.

controlling for patient age, gender, and whether the patient was the primary beneficiary. To measure health status, the Charlson Comorbidity Index was computed from inpatient and outpatient claims in each calendar year, and included in the analysis.^{19,20}

Each incident MS patient was tracked for 8 calendar quarters (including the diagnosis quarter). The cost-sharing rate in each quarter was the rate for the plan in the corresponding calendar year. In order to measure the cumulative initiation rate, patients who initiated remained in the analysis sample in subsequent quarters. We included the number of quarters since diagnosis in the regressions to allow for increases in the cumulative initiation rate. The cost-sharing rate was interacted with quarter since diagnosis, so the effect of cost-sharing could vary with time since diagnosis.

To control for any overall trends in initiation (due to, for example, factors such as disease management), indicator variables for each year were used. In addition, indicator variables for each plan (plan “fixed effects”) were used to help control for unobserved determinants of initiation which did not vary over time (for example, a tendency for MS patients with a strong unobserved preference for DMTs to enroll in plans with low DMT cost-sharing). This empirical approach was facilitated by the use of linear regression models.

RESULTS

The data included 4.76 million unique beneficiaries over 2004-2008. A total of 9513 beneficiaries had 2 or more claims with an MS diagnosis in at least 1 of these calendar years, with 9351 having an initial diagnosis prior to March 31, 2008. Of these, 5244 were enrolled throughout the prior year, and did not have an MS diagnosis or DMT use in that year. A total of 3460 incident MS cases were continuously enrolled for 2 years after initial diagnosis. This sample of patients was analyzed. The average age of the patients was 42.2 years (SD +/- 22 years), and the majority were females (66.6%). These and other summary statistics are shown in **Table 1**.

For patients using DMTs, total DMT spending averaged \$16,742 (2009 dollars) per year over 2004-2009. Mean out-

■ **Table 1.** Descriptive Statistics for Study Sample

| Variable | Mean (Standard Deviation) |
|----------------------------|--|
| DMT cost-sharing rate (%) | 4.3% (7.5%) |
| Quarters since diagnosis | 4.5 (2.3) |
| Age (years) | 42.2 (22.0) |
| Male (%) | 33.4% (47.2%) |
| Primary beneficiary (%) | 43.4% (49.6%) |
| Charlson Comorbidity Index | 0.84 (1.48) |
| Observations | 27,033 patient quarters (3460 patients) |

DMT indicates disease-modifying therapy

of-pocket expenditures on DMTs were \$691 per year. For half of MS patients, cost-sharing was 1.6% or less of DMT costs (Table 2). On average, the cost-sharing rate was 4.3%. Ten percent of patients faced a rate of at least 12.0%, 5 percent faced a rate of 17.8% or more, and 1 percent faced an extreme rate of 39.5% or higher. In terms of out-of-pocket spending, half of DMT users spent less than \$251 per year, while 5 percent of users spent more than \$2625 (all in 2009 dollars).

Only 17% of incident MS cases (586 patients) initiated DMTs over the 8 quarters after the initial diagnosis. In the regression results, the coefficient estimate for the interaction between the cost-sharing rate and quarters since diagnosis was negative in sign and statistically significant ($P = .019$). Thus the negative effect of cost-sharing on the proportion of MS patients who initiated DMTs increased with time since diagnosis. Complete results are reported in the eAppendix (available at www.ajmc.com). The preferred specification excluded the cost-sharing rate on its own (that is, the level effect). In an alternative specification, the coefficient estimate for the cost-sharing rate on its own was positive, but

■ **Table 2.** DMT Cost-Sharing Rate and Annual Out-of-Pocket Expenses

| Statistic | Cost-Sharing Rate |
|----------------------|-------------------|
| Mean | 4.3% |
| Median | 1.6% |
| 25th Percentile | 1.2% |
| 75th Percentile | 3.4% |
| 90th Percentile | 12.0% |
| 95th Percentile | 17.8% |
| 99th Percentile | 39.5% |
| Patient quarters (n) | 27,033 |

DMT indicates disease-modifying therapy. DMTs include interferon beta-1a, interferon beta-1b, glatiramer acetate, natalizumab, and mitoxantrone. Estimates correspond to plan-level DMT cost-sharing among multiple sclerosis patients in the first 8 quarters since diagnosis over the period 2004 through 2009.

was not statistically distinguishable from zero.

To interpret the regression results, the Figure shows cumulative initiation rates at various cost-sharing levels, by time since diagnosis. In the quarter of diagnosis, we predict that 4.2% of patients would have initiated if there were no cost-sharing. The predicted initiation rate decreases to 4.1% at the 75th percentile of cost-sharing (3.4%, as shown in Table 2), and to 3.9% at the 95th percentile (17.8%). The effect of cost-sharing increased in magnitude with

time since diagnosis, and was largest at 2 years post-diagnosis: The cumulative initiation rate is 22.6% without cost-sharing, but 19.7% at the 95th percentile ($P = .019$ for the difference). This 2.9 percentage point reduction in the initiation rate is a 12.7% reduction in relative terms.

DISCUSSION

This study contributes to the literature regarding the impact of cost-sharing on drug utilization, focusing on initiation of DMTs among incident MS cases commercially insured by large companies over 2004-2009.

Cost-sharing rates for DMT therapy tended to be modest (4.3% on average). Mean out-of-pocket costs among DMT users were \$691 per year (2009 dollars), due to the high cost of the treatments (\$16,742 per year on average). Within the same commercially insured population, persons with type 2 diabetes who used antidiabetic drugs experienced a mean cost-sharing rate of 32.3%, and average out-of-pocket spending of \$219. Considering the specialty cancer drugs studied in Goldman et al,²¹ mean cost-sharing rates for the oral therapies imatinib mesylate and erlotinib were comparable to the DMT rate (3.7% and 4.8%, respectively, vs 4.3% for DMTs). Mean out-of-pocket spending was also similar (\$857 and \$449 per year, vs \$691). For the injectable agents bevacizumab, rituximab, and trastuzumab, mean cost-sharing rates were much higher than for DMTs (24.1%, 16.8%, and 11.7%, vs 4.3%). Mean out-of-pocket spending by users of these agents was also higher than for DMT use in MS (\$3542, \$5610, and \$5602, vs \$691).

This study also found that high cost-sharing for DMTs was associated with a reduced likelihood of initiating therapy in the 2 years after an initial MS diagnosis, most commonly relapsing-remitting MS.²² A negative effect of cost-sharing has been found in numerous prior studies of drug utilization.³ For 8 therapeutic classes used by the chronically ill, a doubling of copayments was associated with anywhere from a 25% to a 45% reduction in utilization, with a smaller reduction for

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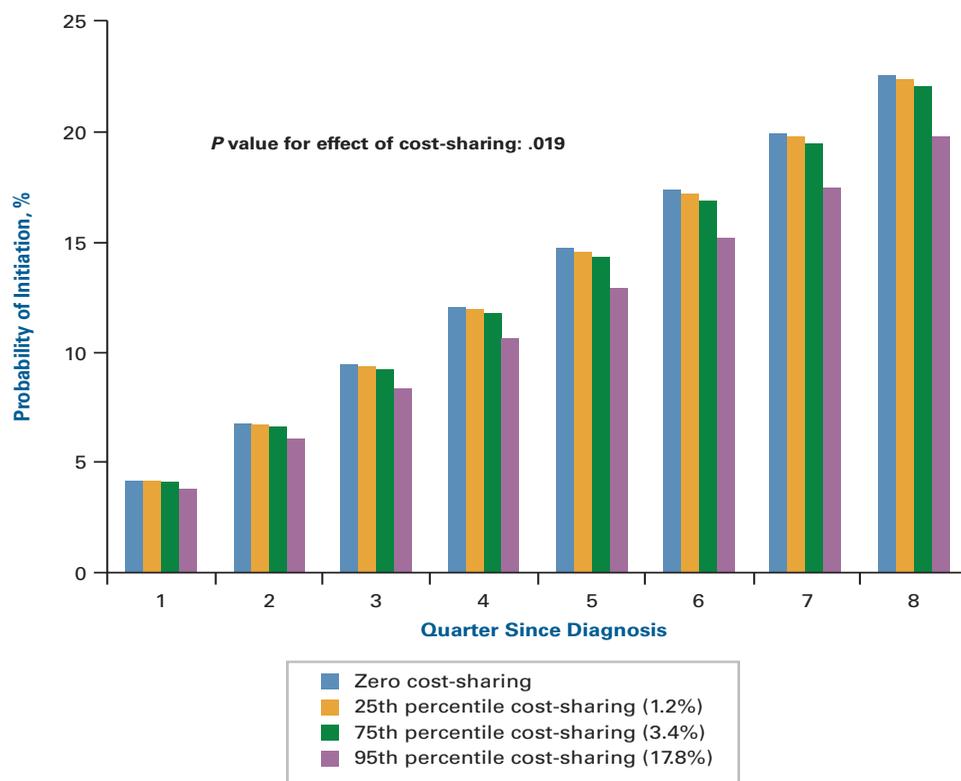
essential classes.¹⁸ In the present context, a doubling of the cost-sharing rate from its mean level (4.3%) is predicted to decrease initiation of DMTs by 4% within 2 years of initial MS diagnosis. Cost-sharing has a larger effect at the extremes. An increase in the DMT cost-sharing rate from zero to its 95th percentile (17.8%) is associated with a 13% reduction in initiation within 2 years.

Although cost-sharing may be a method for reducing health plan costs, it may have unintended consequences. This study showed that only 17% of patients initiated DMT treatment within 2 years of an initial diagnosis of MS. There is growing evidence that earlier initiation of DMTs

may prevent relapses and disability progression.^{23,24} A recent study also demonstrated that treatment with DMTs prior to a confirmed MS diagnosis was associated with fewer hospitalizations and lower expenditures compared with DMT treatment after a confirmed diagnosis.²⁵ In the present context, additional regression analysis showed no association between DMT cost-sharing rates and hospitalization with a primary diagnosis of MS (patients who never initiated DMTs within 2 years of diagnosis were less likely to have been hospitalized for MS, 6.1% vs 11.8%, $P < .001$). For patients with a confirmed diagnosis, the effect of DMT use on disease progression and healthcare utilization may manifest itself beyond the 2-year post-diagnosis window analyzed here.¹⁵ Altogether, this study and the related literature suggest that high cost-sharing for DMTs discourages initiation, which in turn may lead to negative clinical outcomes.

There are several limitations of our study that are reflective of administrative claims data studies. First, DMT initiation is based on filled prescription claims and therefore does not capture utilization based on samples provided by physicians. However, physicians are unlikely to provide 2 years of samples, the time frame after diagnosis over which we analyze initiation. In addition, the plan fixed effects in our analysis control only for confounders that do not change over time.

■ **Figure.** Cost-Sharing and Probability of Initiating a DMT, by Quarter Since Diagnosis



DMT indicates disease-modifying therapy.

They do not control for unobserved factors which vary over time. Given the high cost of DMTs, it is possible that enrollees with a strong preference for these drugs switched to plans with low cost-sharing when confronted with an increase in cost-sharing in their current plan. If so, our analysis may underestimate the degree to which high cost-sharing actually discourages utilization.

Copayment assistance programs are available for many drugs, and 6.2 million patients were reportedly enrolled in a program in 2003.²⁶ These programs are designed to reduce copayment burden and its effects on patient consumption. There are copayment assistance programs for DMTs,²⁷ but our analysis could not measure, and did not capture, their effects on patient costs and initiation. For this reason, our analysis may again underestimate the true effect of cost-sharing on DMT utilization.

Despite our study's limitations, high cost-sharing for DMTs appears to significantly reduce utilization of highly effective MS therapies in the 2 years after initial diagnosis, with the potential effect of increasing risk of relapses and disability progression. While the costs of DMTs are substantial and may not be fully offset by reductions in medical costs,²⁸ employer costs with respect to lost productivity and short- and long-term disability may be considerable. These potential unintended

effects of drug benefit design should be considered in the context of how under-treatment of disease may affect patients, payers, and employers.

In conclusion, high cost-sharing significantly reduces utilization of DMTs among MS patients insured by large private employers. In particular, patients in high cost-sharing plans are less likely to initiate DMTs, and this effect grows in magnitude over the 2 years after initial MS diagnosis.

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Funding Source: This study was funded by the Novartis Pharmaceuticals Corporation.

Author Disclosures: Dr Romley reports receiving consultancies from Novartis Pharmaceuticals Corporation, the funder of the study. Dr Goldman reports receiving consultancies from Novartis Pharmaceuticals Corporation, Bristol-Myers Squibb, and Amgen, as well as pending grants from the National Institutes of Health. Mr Eber reports employment with Precision Health Economics, which provides consulting services to Novartis Pharmaceuticals Corporation. Drs Dastani and Kim report employment with Novartis Pharmaceuticals Corporation, as well as stock ownership in the company. Ms Raparla reports no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this article.

Authorship Information: Concept and design (JR, DG, HD, EK); acquisition of data (DG); analysis and interpretation of data (JR, DG, ME, HD, EK, SR); drafting of the manuscript (JR, HD, EK); critical revision of the manuscript for important intellectual content (JR, DG, ME, HD, EK); statistical analysis (JR, DG, ME); obtaining funding (DG); administrative, technical, or logistic support (DG, SR); and supervision (JR, DG, EK, SR).

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