

# Impact of Specialty Drugs on the Use of Other Medical Services

Geoffrey F. Joyce, PhD; Dana P. Goldman, PhD; Pinar Karaca-Mandic, PhD;  
and Grant D. Lawless, MD

**T**he unprecedented progress in biomedical and clinical research over the last half century continues to drive a revolution in the practice of medicine. The result has been substantial improvements in both health and longevity. At the same time, technology is widely viewed as the principal driver of rising healthcare spending.<sup>1</sup> In response, both public and private payers are demanding more objective evidence of the value of new technologies before they decide whether and how generously to cover them. Specialty pharmaceuticals, which include most injectables and biologic agents, provide perhaps the clearest example of this issue. Biotechnology-derived agents often are used to treat complex chronic conditions such as cancer, anemia, and autoimmune disorders for which there are few other viable treatment options, but at prices that can be substantially higher than traditional medications. Because only a small percentage of health plan members are afflicted with these conditions, the total population of specialty drug users is quite small. However, spending on biologics is increasing rapidly as broader uses are found for existing drugs and new drugs enter the market to treat more prevalent conditions such as diabetes and obesity.

Some biologics offer lifesaving and quality-of-life benefits, whereas others offer more modest clinical benefits compared with current treatments. The principal challenge facing public and private payers is to balance patients' access to these technologies with the need to constrain healthcare expenditures. To do this effectively, payers need more information on the clinical efficacy, long-term safety, and overall value of specialty drugs.

In this article, we examine the "cost-offset" hypothesis in the use of specialty drugs for the treatment of 2 autoimmune disorders: rheumatoid arthritis (RA) and multiple sclerosis (MS). These conditions provide a good test case because biologic treatments for RA and MS have been widely used over the past decade and cost \$15,000 or more annually. Although these drugs can be highly efficacious for patients who have failed to respond to traditional therapies, not all patients need them, nor do all patients respond to them. We follow service use for RA and MS patients up to 3 years before and 3 years after initiation of a biologic to estimate the impact of these therapies on the use of other medical services.

**Objective:** To examine whether initiation of a biologic agent to treat 2 autoimmune disorders—rheumatoid arthritis (RA) and multiple sclerosis (MS)—affects use of other medical services.

**Study Design:** Longitudinal analysis from 1997 to 2005 examining linked pharmacy and medical claims from large, private employers.

**Methods:** The study sample included 30,761 individuals newly diagnosed with RA (92,660 person-years) and 8961 unique individuals with MS (25,100 person-years). Negative binomial models were used to estimate changes in inpatient, outpatient, and procedure use before and after initiating a biologic drug for each condition.

**Results:** Starting a biologic response modifier was associated with a reduction in physician visits and use of expensive procedures for patients with RA within 2 to 3 years of initiation. Use of immunomodulatory therapy for MS was associated with a reduced number of hospitalizations and expensive procedures within 2 years of initiation. Although biologics may reduce other types of service use, the savings do not come close to offsetting the full cost of these drugs.

**Conclusions:** Given the high cost of many specialty drugs, health plans may rightly focus on making sure only patients who will most benefit receive them. But once such patients are identified, it makes little sense to limit coverage.

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## Rheumatoid Arthritis

The onset of RA usually occurs between 30 and 50 years of age, and RA is more common among women.<sup>2</sup> For

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some people, it lasts only a few months or 1 to 2 years and goes away without causing any noticeable damage. Other people have mild or moderate forms of the disease, marked by periods of flares and remissions. Still others have a severe form of the disease that is active most of the time, lasts for many years or a lifetime, and leads to serious joint damage and disability.<sup>3</sup> Recent studies show that early treatment with more powerful drugs may be more effective in reducing or preventing joint damage, particularly for patients with severe, rapidly progressing RA.<sup>4,7</sup>

Treatment options for RA historically have included analgesics, corticosteroids, and nonsteroidal anti-inflammatory drugs to treat pain and inflammation, as well as disease-modifying antirheumatic drugs (DMARDs) that can promote disease remission and prevent progressive joint destruction. Although effective for many patients, these drugs can have serious side effects and are less effective as the disease progresses and with more aggressive forms of the condition. Because of their potentially serious side effects, immunosuppressive agents are used in low doses, usually in combination with anti-inflammatory agents.

Biologic response modifiers (BRMs) represent a newer subclass of DMARDs and have proven effective in achieving remission, even for patients for whom other therapies have failed. In comparison with traditional DMARDs, biologics have a more rapid onset of action and can have powerful effects on stopping progressive joint damage. Although only about 1 in 4 RA patients takes a biologic, recent studies show that two thirds respond favorably, with most of them achieving remission.<sup>2</sup>

### Multiple Sclerosis

Multiple sclerosis is an autoimmune disorder characterized by inflammation of the central nervous system. Common symptoms of MS include fatigue, reduced mobility, bowel/bladder disturbances, optic neuritis, changes in cognitive function, pain, sensory loss, and depression. Multiple sclerosis affects approximately 400,000 people in the United States, with incidence peaking between the ages of 30 and 35 years. Females are 2 to 3 times more likely to develop MS than males, and whites are more likely to develop MS than persons of Asian or African descent.

Like RA, treatment options for MS used to consist of physical therapy and pharmacologic treatment for symptom management. Corticosteroids (prednisone, dexamethasone) and the hormone corticotropin were given during flare-ups to help reduce inflammation and swelling, but they did not prevent new attacks. Symptomatic management has been supplemented in the past decade by 2 new classes of immunomodulatory therapies. Evidence from randomized clinical

and long-term follow-up studies has shown that these immunomodulatory therapies are effective in reducing relapse rates, slowing the progression of disability, and reducing MS disease activity.<sup>8-11</sup> However, these therapies are not without risk. They have potentially serious side effects, and their long-term tolerability has not been established.

## METHODS

### Data

We assembled an extensive dataset of de-identified administrative, claims, and benefit information for 453 commercial health plans from 1997 to 2005. The data included more than 3 million beneficiaries continuously enrolled in a plan for an entire year. For this study, we restricted our attention to patients with at least 2 primary diagnoses for RA or MS as indicated by *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes.

The claims captured all healthcare claims and encounters, including prescription drugs and inpatient, emergency, and ambulatory services. Healthcare expenditures reflected total annual payments made by the enrollee (copayments, deductibles, excluded expenses) and by all third-party payers (primary and secondary coverage, net of negotiated discounts). Traditional oral pharmaceuticals were identified in the pharmacy claims using National Drug Code codes. By contrast, many biologics are administered by a physician or nurse in a clinical setting and are covered under the medical benefit. We used the medical claims to identify use of specialty products from physicians' offices, home care agencies, and outpatient facilities such as outpatient hospital clinics.

### Study Sample

We created 2 distinct study samples for patients newly diagnosed with RA or MS. We identified patients with each condition based on the existence of 2 or more inpatient or outpatient claims for RA (ICD-9-CM code 714) or MS (ICD-9-CM code 340). Patients were considered "newly diagnosed" if they had at least 1 year of data before the index date (date of first ICD-9-CM code) without a claim for the condition. For example, an individual with 2 ICD-9-CM codes for RA in 2000 would be considered newly diagnosed if he or she had no other ICD-9-CM codes for the condition in prior years (ie, 1997-1999) if continuously enrolled. Similarly, we defined initiation of biologic therapy based on the absence of any use in prior years. The study sample included 30,761 individuals with RA (92,660 person-years) and 8961 unique individuals with MS (25,100 person-years). Because firms entered and exited the data over time, we did not have a complete panel on all individuals. The majority of members were observed for

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3 to 5 years, with fewer than 10% of the sample followed for all 9 years.

### Statistical Analysis

Our goal was to assess the impact of biologics on the use of other medical services, controlling for differences in patient demographics and comorbid conditions that can affect the demand for medical care. Because we did not have a complete panel on all individuals, we could not estimate a difference-in-differences analysis. Instead, we estimated medical service use before and after initiation of a biologic using random-effects models, controlling for patient characteristics, disease duration, and temporal patterns in service use.

The key independent variables in the models were 7 binary indicator variables for the years before and after initiation of a biologic. More specifically, we included 3 binary indicator variables for the 3 years preinitiation, 1 binary indicator for the year of initiation, and 3 indicator variables for the years postinitiation. The models also included controls for patient demographics (age, sex, employment status) and comorbid conditions, geographic and socioeconomic measures (urban residence, median household income in the zip code), time since diagnosis, and a set of annual time dummies.

Because the primary dependent variables were counts, we estimated negative binomial models for the number of physician visits, expensive procedures, and hospitalizations. We identified the most common procedures used in treating RA and MS patients and selected those procedures costing \$100 or more. This roughly corresponded to the top quartile of the 100 most common procedures for each condition. The negative binomial is a generalization of the Poisson model that is appropriate when there is overdispersion of the data (ie, when the conditional variance of the distribution exceeds the conditional mean). By allowing for overdispersion, the negative binomial helps to account for unobserved heterogeneity among the individuals in the study. We used the coefficient estimates from the negative binomial models to obtain the predicted annual number of visits, hospitalizations, and procedures per person for the 3 years preinitiation of a biologic, the year of initiation, and 3 years postinitiation.

## RESULTS

**Table 1** presents summary statistics for the sample of RA patients, separately for users and nonusers of biologic agents. Users of biologics were slightly younger than nonusers (58 vs

**Table 1.** Sample Characteristics of Patients With Rheumatoid Arthritis, 1997-2005<sup>a</sup>

Patient Demographics	Nonusers of Biologic Agents		Users of Biologic Agents	
	Mean	SD	Mean	SD
Age, y	62	16	58	13
Male	28	45	25	43
Married	63	48	69	46
Working	29	45	36	48
Primary beneficiary	63	48	60	49
Median household income, \$	42,327	9449	42,324	9699
<b>Comorbid conditions</b>				
Anemia	9	28	9	29
Asthma	3	17	4	19
Cancer	7	25	6	23
Depression	5	22	4	19
Diabetes	9	29	7	26
Heart disease	16	37	11	31
Hyperlipidemia	7	26	5	21
Hypertension	26	44	19	39
Kidney disease	10	31	10	30
Osteoarthritis	18	38	12	32
<b>Person-years</b>	79,793		12,867	

<sup>a</sup>Values are percentages unless otherwise indicated.

■ **Table 2.** Sample Characteristics of Patients With Multiple Sclerosis, 1997-2005<sup>a</sup>

Patient Demographics	Nonusers of Biologic Agents		Users of Biologic Agents	
	Mean	SD	Mean	SD
Age, y	46	22	48	10
Male	32	47	23	42
Married	54	50	69	46
Working	53	50	56	50
Primary beneficiary	46	50	60	46
Median household income, \$	45,546	11,343	44,162	10,395
<b>Comorbid conditions</b>				
Anemia	5	21	5	22
Asthma	3	18	2	14
Cancer	4	19	3	16
Depression	6	24	8	27
Diabetes	6	23	4	18
Heart disease	7	26	4	19
Hyperlipidemia	4	19	3	18
Hypertension	12	32	10	30
Kidney disease	6	23	6	23
Osteoarthritis	3	18	2	15
<b>Person-years</b>	15,294		9806	

<sup>a</sup>Values are percentages unless otherwise indicated.

62 years), and were more likely to be married and actively working. More than 70% of all RA patients were female. The prevalence of comorbid conditions varied across the 2 groups, with higher prevalence of hypertension, heart disease, and osteoarthritis among nonusers of biologics and higher rates of asthma among users.

**Table 2** presents similar statistics for the sample of MS patients. The average person with MS was young (mean age, 47 years), as one would expect given the prevalence profile. The MS patients who used a biologic were more likely to be female, married, and a primary beneficiary. Although MS patients taking a biologic tended to be at a more advanced stage of disease, they did not have higher rates of comorbid conditions. The prevalence of hypertension, diabetes, and heart disease was similar to or modestly higher than that among nonusers of biologics.

Regardless of their drug therapy, treating patients with these conditions was expensive. **Table 3** shows the distribution of total and out-of-pocket healthcare expenditures for RA and MS patients, by service type. Mean annual spending for RA patients exceeded \$18,000 per year, with 10% of patients incurring costs of \$45,000 or more. Average spending for MS patients was modestly lower (\$14,278).

Despite the high costs of treating these conditions, the financial burden faced by these patients was generally modest. Mean out-of-pocket spending ranged from about \$3000 per year for MS patients to \$4500 per year for persons with RA. All of the patients in our study sample were privately insured through large employers, so one would expect their drug coverage to be generous. Nonetheless, some individuals were still at risk for substantial out-of-pocket spending. For example, 10% of RA patients had out-of-pocket costs that exceeded \$9000 per year and 5% incurred costs of \$19,000 or more. Patients with MS were at less financial risk, with a 95th percentile of \$9250 in out-of-pocket costs.

The use of a biologic increased total expenditures and shifted the distribution of healthcare spending. Spending on pharmaceuticals represented just 20% to 30% of total healthcare expenditures in the years before using a biologic, but rose to 60% to 70% of total spending in the years after initiation (**Table 4**).

**Figure 1** and **Figure 2** summarize findings from the multivariate models that controlled for differences in demographic attributes, health risks, disease duration, and area characteristics between users and nonusers of biologic therapies. Rheumatoid arthritis patients averaged 10 to 11 physician visits per year before initiating a BRM and about

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**Table 3.** Annual Distribution of Total and Out-of-Pocket Spending for Rheumatoid Arthritis (RA) and Multiple Sclerosis (MS) Patients<sup>a</sup>

Condition	Total Spending, \$				Out-of-Pocket Spending, \$			
	Mean	SD	90th Percentile	95th Percentile	Mean	SD	90th Percentile	95th Percentile
<b>Rheumatoid arthritis</b>								
<b>Service type</b>								
Inpatient	5318	23,101	15,054	33,811	1672	9708	762	7610
Outpatient	6481	11,902	15,290	22,308	1741	5627	3891	7033
Prescription drugs								
Biologics	1757	5792	6887	13,816	109	910	52	272
Nonbiologics	674	1553	1674	2710	120	408	285	485
Non-RA drugs	4277	10,179	8842	14,516	877	3129	1727	2808
<b>Total</b>	<b>18,506</b>	<b>32,900</b>	<b>44,926</b>	<b>67,563</b>	<b>4518</b>	<b>13,222</b>	<b>9061</b>	<b>18,971</b>
<b>Multiple sclerosis</b>								
<b>Service type</b>								
Inpatient	3261	19,546	3816	15,891	1069	10,290	157	1366
Outpatient	4311	9655	10,970	16,357	1187	3704	2475	4506
Prescription drugs								
Biologics	3546	7487	13,773	17,100	125	1652	233	432
Nonbiologics	202	4768	32	155	48	2870	10	36
Non-MS drugs	2958	8442	7022	10,668	644	3803	1322	2100
<b>Total</b>	<b>14,278</b>	<b>29,692</b>	<b>33,482</b>	<b>48,704</b>	<b>3073</b>	<b>13,871</b>	<b>4859</b>	<b>9250</b>

<sup>a</sup>Annual spending in 2004-2005, in 2005 dollars.

**Table 4.** Distribution of Total Spending Before and After Initiation of a Biologic<sup>a</sup>

Service Type	Percentage of Total Spending for RA Patients		Percentage of Total Spending for MS Patients	
	Postinitiation	Preinitiation	Postinitiation	Preinitiation
Inpatient	29.5	17.0	29.6	11.3
Outpatient	40.2	23.0	42.4	21.2
Prescription drugs	30.3	59.9	27.9	67.6

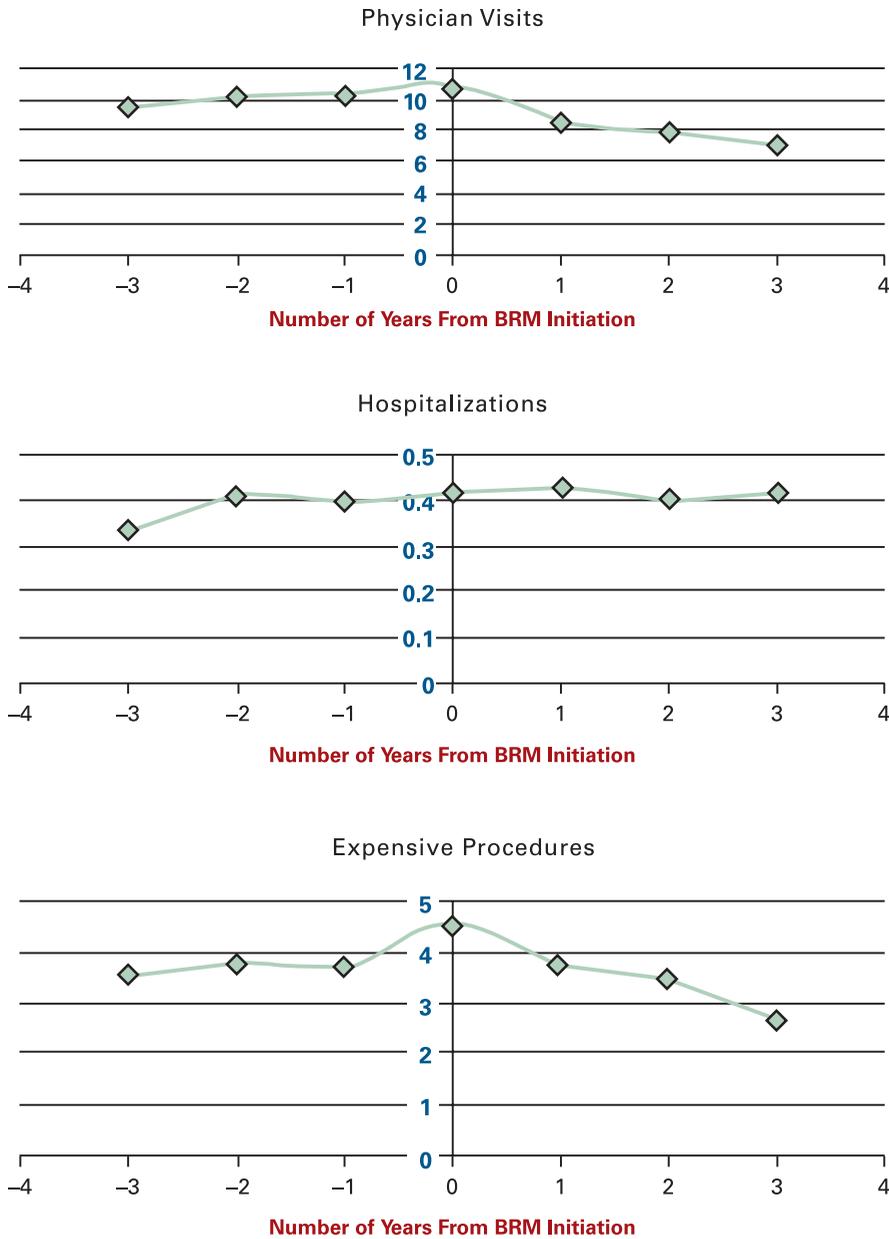
MS indicates multiple sclerosis; RA, rheumatoid arthritis.  
<sup>a</sup>Among patients who started a biologic for the treatment of RA or MS.

8 visits per year within 2 years after initiation (Figure 1). Use of expensive procedures increased markedly in the year of initiation, presumably due to a flare-up that often precipitates the use of a biologic. The number of procedures then declined postinitiation and remained slightly below preinitiation levels 3 years later. The use of a biologic did not alter the rate of hospitalizations for RA patients, but that was expected given the pathology of the disease. If untreated, RA can lead to progressive joint damage that may require surgery, but for the most part, the primary manifestations of the disease (inflammation, joint pain, disability)

are typically treated in ambulatory settings and borne by the patient.

By contrast, acute exacerbations of MS can lead to hospitalization. We found that use of a biologic in the treatment of MS was associated with a considerable decline in the number of hospitalizations and use of expensive procedures within 2 years of initiation. The mean number of hospitalizations fell from about 0.5 per patient per year before initiation to 0.3 within 3 years after initiation. Similarly, the number of expensive procedures declined by about one third within several years of starting a biologic. The use of immunomodula-

■ **Figure 1.** Predicted Use of Medical Services Before and After Use of a Biologic for Patients With Rheumatoid Arthritis<sup>a</sup>



BRM indicates biologic response modifier.

<sup>a</sup>For the sample of patients who started a biologic for the treatment of rheumatoid arthritis.

tory therapy was associated with an increase in the number of physician visits during the year of initiation, but returned to preinitiation levels in subsequent years (Figure 2).

### Sensitivity Analyses

Given the episodic nature of these conditions, one possible explanation for a reduction in service use postinitiation is “regression to the mean.” This is a particular concern for

MS, where recovery from a flare-up can be nearly complete in the early stages of disease. To test for this possibility, we reestimated the models for a subgroup of patients who were diagnosed with RA or MS at least 2 years before initiating a biologic. The longer baseline period should provide a more stable measure of resource use before starting a biologic. We also restricted the sample to individuals observed for at least 4 years to assess whether an unbalanced panel (ie, differential case mix) might be biasing our results.

For both RA and MS, the reductions in use were robust to these specification changes. For patients with RA, the number of physician visits and use of expensive procedures were stable before initiation and declined in the years after starting a BRM. For MS, the number of hospitalizations and expensive procedures were fairly constant in the 3 years before initiation and declined substantially after initiation (results available upon request).

Given that the decision to use a biologic is nonrandom, we instrumented for biologic use with the generosity of plan coverage for disease-specific specialty drugs. Although the parameter estimates were modestly reduced in the case of RA, the instrumental-variables results were unstable for MS. More importantly, the validity of the instrument is highly questionable given the

correlation between coverage of specialty drugs and overall plan generosity.

## DISCUSSION

We examined whether initiation of a biologic agent to treat 2 autoimmune disorders—RA and MS—affected the use of other medical services. Although biologic agents for

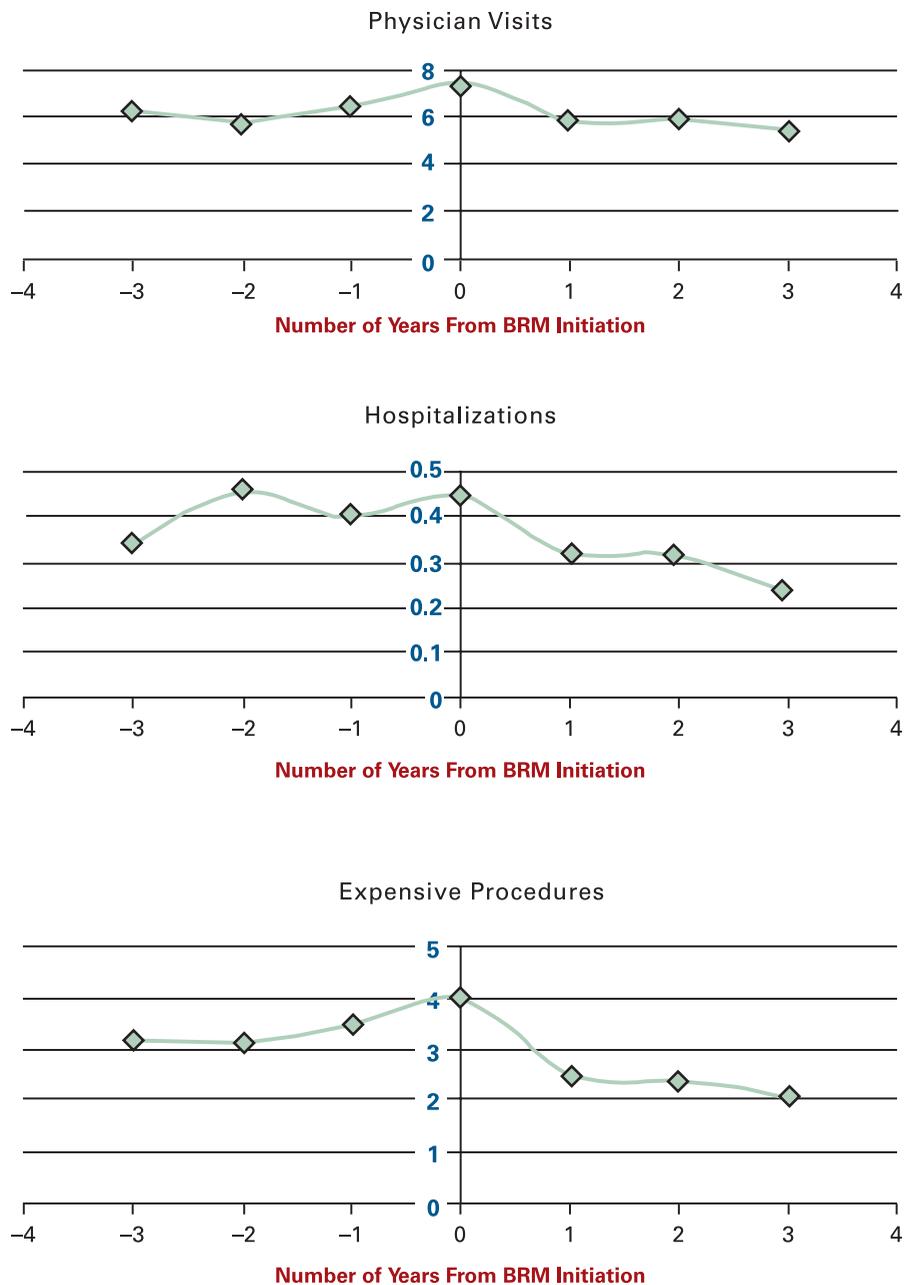
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RA and MS have been shown to slow the progression of the disease for some individuals, they are considerably more expensive than traditional therapies and are neither appropriate for nor well tolerated by all patients.

We found that starting a biologic for the treatment of RA or MS was associated with lower use of some types of medical services within 2 to 3 years of initiation. Starting a BRM was associated with a reduction in physician visits and use of expensive procedures for patients with RA, whereas use of immunomodulatory therapy for MS was associated with a reduced number of hospitalizations and expensive procedures. These results were robust to specification changes and alternative methods of estimation.

A full regimen of biologic agents for these conditions can easily cost \$15,000 or more per year. Thus, although use of these agents may reduce other types of service use, the savings do not come close to offsetting the full cost of these drugs. This raises an important policy debate that typically pits payers against patients and their doctors—to what extent should treatments pay for themselves? Requiring evidence that a treatment reduces costs somewhere else in the system (regardless of the clinical benefit) alters the fundamental rationale for medical care from improving health to reducing costs.<sup>12</sup> Because RA and MS (MS in particular) affect individuals during their prime earning years, the major costs of these illnesses are borne by the patients and their families through decrements in functionality and quality of life, lost income, and the need for informal care giving. For example, less than half of those with RA continue to work

■ **Figure 2.** Predicted Use of Medical Services Before and After Use of a Biologic for Patients With Multiple Sclerosis<sup>a</sup>



BRM indicates biologic response modifier.

<sup>a</sup>For the sample of patients who started a biologic for the treatment of multiple sclerosis.

after 10 years with the disease.<sup>13</sup> As such, making coverage decisions based solely on the extent of medical cost savings is shortsighted from a social perspective.

Nonetheless, healthcare resources are limited. Thus, inefficient use of one service often means insufficient access to another. Virtually all of the costs of caring for patients with these conditions are the result of relapses and often irreversible disease progression. Although use of biologics has been

### Take-away Points

Although newer biologic treatments for rheumatoid arthritis (RA) and multiple sclerosis (MS) can offer significant therapeutic benefits, payers are demanding more information on the overall value of these therapies in making coverage decisions.

- Starting a biologic for the treatment of RA or MS was associated with lower use of some types of medical services within 2 to 3 years of initiation.
- Although biologics may reduce other types of service use, the savings do not come close to offsetting the full cost of these drugs.
- Health plans may rightly focus on making sure only patients who will most benefit from biologics receive them. But once such patients are identified, it makes little sense to limit coverage.

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**Authorship Information:** Concept and design (GFJ, DPG, PK-M, GDL); acquisition of data (GFJ, DPG); analysis and interpretation of data (GFJ, DPG, PK-M, GDL); drafting of the manuscript (GFJ, DPG, PK-M, GDL); critical revision of the manuscript for important intellectual content (GFJ, DPG, PK-M, GDL); statistical analysis (GFJ, DPG); obtaining funding (DPG, PK-M, GDL); administrative, technical, or logistic support (GFJ); and supervision (GFJ, DPG).

**Address correspondence to:** Geoffrey F. Joyce, PhD, RAND Corporation, 1776 Main St, Santa Monica, CA 90401. E-mail: gjoyce@rand.org.

shown to delay disease progression and reduce disability, not all patients with RA or MS are at risk for joint damage and disability. Therefore, not all patients need to be treated aggressively. For example, only one quarter of RA patients in our sample ever used a BRM. Such heterogeneity creates an opportunity to reevaluate which patients are most likely to benefit from these therapies and to improve the response and long-term outcomes associated with treatment.<sup>14</sup>

Our analysis has several limitations. First, we could not estimate changes in disease-related service use because of the inherent limitations of claims data. Prior work has shown that many MS-related services cannot be reliably identified with ICD-9-CM codes.<sup>9</sup> Second, although we controlled for time since diagnosis, we could not measure the severity of disease using claims data. However, re-estimating the models for a subgroup of patients diagnosed at least 2 years before starting biologic therapy did not change our results.

Given the high cost of many specialty drugs, insurers would be better off finding ways to manage utilization so that only patients who would benefit would get access to them, rather than restricting access through high patient cost sharing or formulary requirements designed to deter use by all patients, regardless of clinical need. Management of these drugs may rightly focus on making sure that only those patients who will most benefit receive them and then monitoring the progress of these patients closely. But once such patients are identified, it makes little sense to limit coverage.

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**Author Affiliations:** From the RAND Corporation (GFJ, DPG), Santa Monica, CA; Division of Health Policy and Management, University of Minnesota (PK-M), Minneapolis; and Amgen Corporation (GDL), Thousand Oaks, CA.

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