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RESEARCH ARTICLE

Utilization and Costs

Cost Sharing, Family Health Care Burden, and the Use of Specialty Drugs for Rheumatoid Arthritis

Pinar Karaca-Mandic, Geoffrey F. Joyce, Dana P. Goldman, and Marianne Laouri

Objectives. To examine the impact of benefit generosity and household health care financial burden on the demand for specialty drugs in the treatment of rheumatoid arthritis (RA).

Data Sources/Study Setting. Enrollment, claims, and benefit design information for 35 large private employers during 2000–2005.

Study Design. We estimated multivariate models of the effects of benefit generosity and household financial burden on initiation and continuation of biologic therapies.

Data Extraction Methods. We defined initiation of biologic therapy as first-time use of etanercept, adalimumab, or infliximab, and we constructed an index of plan generosity based on coverage of biologic therapies in each plan. We estimated the household's burden by summing up the annual out-of-pocket (OOP) expenses of other family members.

Principal Findings. Benefit generosity affected both the likelihood of initiating a biologic and continuing drug therapy, although the effects were stronger for initiation. Initiation of a biologic was lower in households where other family members incurred high OOP expenses.

Conclusions. The use of biologic therapy for RA is sensitive to benefit generosity and household financial burden. The increasing use of coinsurance rates for specialty drugs (as under Medicare Part D) raises concern about adverse health consequences.

Key Words. Specialty drugs, pharmacy benefit design, household burden

High-cost drugs and biotechnology-derived agents used to treat complex chronic conditions such as cancer, anemia, and autoimmune disorders are often referred to as "specialty drugs." Many of these agents provide highly sophisticated treatment for which there are few other viable treatment options, but at prices that can be substantially higher than traditional medications.

Spending on biotechnology products is increasing twice as fast as traditional pharmaceuticals and is expected to account for one-quarter of total drug spending by 2010. A major part of the cost lies in the development and manufacturing of these products, and a lack of generics or "bio-similars."

Given this rapid spending growth, many insurers have adopted strategies to control their use and costs. An increasing number of insurers are covering biologics under the pharmacy benefit rather than the medical benefit and applying traditional cost containment measures and utilization management (Goldman et al. 2006a). The effects of these changes are unknown.

According to economic theory, individuals consume less health care services when insurance covers a smaller portion of the costs (Pauly 1968). A large body of research focusing on traditional oral pharmaceuticals links increased patient cost sharing with reduced use of prescription drugs (e.g., Motheral and Fairman 2001; Joyce et al. 2002; Huskamp et al. 2003; Goldman et al. 2004; Goldman, Joyce, and Zheng 2007). A similar strand of research also documents that utilization management effectively reduces demand for traditional prescription drugs (Smalley et al. 1995; Phillips and Larson 1997; Cunningham 2005). However, it is not well known how responsiveness differs for high-cost biologics and other specialty drugs costing as much as ten times as traditional medications. If high cost sharing forces people away from preferred therapies, it may end up producing more complications and higher overall health care costs (Rizzo and Simons 1997; Groban et al. 1998; Thompson et al. 1998; McCulloch 2000; Wei et al. 2002; Sokol et al. 2005; Goldman, Joyce, and Karaca-Mandic 2006b; Gaynor, Li, and Vogt 2007).

In this paper, we examine how the generosity of insurance coverage affects the demand for specialty drugs in the treatment of rheumatoid arthritis (RA). RA provides a good test case because biologics have been widely used in treating the disease over the past decade and they are expensive in both absolute terms (about U.S.$15,000 annually) and relative to alternative

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Address correspondence to Pinar Karaca-Mandic, Ph.D., Assistant Professor, Division of Health Policy and Management, School of Public Health, University of Minnesota, 420 Deleware Street SE, MMC729, Minneapolis, MN 55455; e-mail: pkmandic@umn.edu. Geoffrey F. Joyce, Ph.D., Associate Professor, is with the Clinical Pharmacy and Pharmaceutical Economics & Policy, School of Pharmacy, University of Southern California, Los Angeles, CA. Dana P. Goldman, Ph.D., Professor, is with Norman Topping/National Medical Enterprises, University of Southern California, Los Angeles, CA. Dana P. Goldman, Ph.D., Chair, is also with Medicine and Public Policy, University of Southern California, Los Angeles, CA. Dana P. Goldman, Ph.D., Director, is also with Leonard D. Schaeffer Center for Health Policy and Economics, University of Southern California, Los Angeles, CA. Marianne Laouri, Ph.D., Director, Health Economics & Outcomes, is with Quorum Consulting, San Francisco, CA.

treatments. In addition, there is considerable variation in how generously these drugs are covered both within and across health plans.

We also explore the impact of household out-of-pocket (OOP) health care expenses on the decision of RA patients to initiate and continue use of biologics. Few studies have examined the family's financial constraints and their impact on the demand for high-cost medical treatments.

METHODS

Data

We assembled an extensive data set of deidentified administrative, claims, and benefit information for 35 private employers and 176 health plans from 2000 to 2005. Data include all claims and encounters, including prescription drugs, inpatient, emergency, and ambulatory services. Expenditures reflect 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). Because employers enter and exit the data over time, we did not have a complete panel on all individuals.

RA Treatments

Historically, treatment options for RA included analgesics, corticosteroids, and nonsteroidal antiinflammatory drugs to treat pain and inflammation, as well as disease-modifying antirheumatic drugs (DMARDs) that can promote disease remission and prevent progressive joint destruction. While effective for many patients, DMARDs can have serious side effects and are less effective as the disease progresses or 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 antiinflammatory 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 more rapid onset of action and can have powerful effects on stopping progressive joint damage. While only about one in four RA patients takes a biologic, recent studies show that two-thirds respond favorably, with most of them achieving remission (Maini et al. 1999; Moreland et al. 1999; Weinblatt et al. 1999; Kavanaugh et al. 2000; Lipsky et al. 2000; Furst et al. 2001; Rau 2002; Hochberg et al. 2003; Mpofu, Fatima, and Moots 2005).

Six BRMs are approved for the treatment of RA, but the market is dominated by three drugs that constitute the class of tumor necrosis factor α (TNF-α) blockers: etanercept (Enbrel), adalimumab (Humira), and infliximab (Remicade). The earliest drug, etanercept, was approved by the FDA in November 1998, infliximab in November 1999, and adalimumab in December 2002. The drugs differ in terms of their target mechanism and how they are administered (infused intravenously versus self-administered), but they all aim to stimulate or restore the ability of the immune system to fight disease or infection. Nonetheless, these agents usually work more quickly than traditional DMARDs to stop progressive joint damage and relieve the symptoms associated with RA. The most significant side effect of these drugs is an increased risk for all types of infection.

Coverage of Biologics

Tracking utilization and spending for specialty drugs is more complex than for traditional medications. Claims may enter the system through multiple points: pharmacy submissions, billings from physicians' offices, home-care agencies, and outpatient facilities such as outpatient hospital clinics. Injectable drugs administered by physicians or other health care providers are commonly termed office-administered injectables (OAIs). Most payers cover these products under the medical benefit. In contrast, self-administered injectables (SAIs) are increasingly covered under the pharmacy benefit, where insurers can exert greater control on their utilization and cost.

Plans differ in how they cover these products (medical or pharmacy benefit), where they are purchased (by physicians or at specialty pharmacies), and whether these costs apply to annual OOP maximums. Thus, it is often difficult to translate the plan's stated medical and pharmacy benefits into actual prices that consumers face for these drugs. As a result, we followed the approach of Goldman et al. (2004) and computed indices of plan generosity for RA-related biologics. The general idea is to estimate how much an average beneficiary would pay under each plan for a fixed basket of drugs.

For each drug, we first computed the average OOP expenses per script in each plan. We then multiplied each average by the average annual number of scripts in the overall sample representing a proxy for the annual cost of the drug in the plan for an average user.[1] In our sample, infliximab, an OAI drug, is covered under the medical benefit while etanercept and adalimumab, which are SAI drugs, are covered under the pharmacy benefit. Therefore, we constructed separate plan indexes for the medical and pharmacy benefits. The

medical benefit generosity index represents the annual OOP cost for infliximab in the plan for an average user in the overall sample. To compute the pharmacy benefit generosity index, we took a weighted average of the corresponding average annual OOP costs of etanercept and adalimumab in the plan where the weights represented each drug's market share among the two in the overall sample.[2] Benefit generosity indexes were calculated separately for each year, and all prices were inflated to 2005 dollars using the medical services consumer price index.

Study Sample

We created two distinct study samples to examine the decisions to both initiate and continue biologic drug therapy. We identified patients with RA based on the existence of two or more inpatient or outpatient claims with the International Classification of Diseases (ICD-9) for RA (714.XX). The first sample consisted of patients newly diagnosed with the disease. Patients were considered "newly diagnosed" if they had at least 2 years of data before the index date (date of first ICD-9 code) without a claim for the condition. For example, an individual with two ICD-9 codes for RA in 2002 would be considered newly diagnosed if he or she was in the data in 2000 and 2001 and had no other ICD-9 codes for the condition in those years. We assumed that individuals diagnosed with the disease had it in all subsequent years. Restricting the initiation sample to the newly diagnosed reduced the heterogeneity of disease severity across individuals, yielding a sample of 8,557 unique individuals and 19,342 person-years. The continuation sample included all RA patients (not just the newly diagnosed) who initiated a biologic for RA, based on the absence of any biologic use in prior years since the RA diagnosis date.[3] Accordingly, the continuation sample included both the newly diagnosed initiators and those who are not. This resulted in a sample of 2,066 unique biologic users and 4,609 person-years post biologic initiation.

Statistical Analysis

Our goal was to assess the impact of plan generosity on the initiation and use of biologic treatments for RA. First, we estimated models that relate initiation of biologic therapies to the level of plan generosity (average OOP costs for BRMs) under medical and pharmacy benefits separately.

We defined initiation of biologic therapy as first-time use of etanercept, adalimumab, or infliximab during the study period. As such, our models represent initiating BRM therapy in the TNF-α blockers class without

distinguishing by drug type. Once a patient used a BRM, s/he was dropped from the initiation sample in subsequent years. We estimated the model using a probit specification while clustering standard errors at the individual level to account for the correlation of unobserved individual-level factors over time. Therefore, the econometric framework has a discrete-time hazard model interpretation (with censoring), which is used in previous consumer adoption studies (Allison 1982; Van den Bulte and Lilien 2001).

We ran similar models on continuation of biologic use, conditional on having initiated therapy. We estimated the probability of biologic use in each subsequent year for the sample of users with a probit specification, clustering at the individual level.

In addition to the key independent variables, the plan generosity of biologic coverage under the medical and pharmacy benefits, the models included a set of demographic variables including indicators for age groups (25–44; 45–64, 65+), gender, work status (retiree/active), enrollment eligibility status (primary beneficiary/dependent), marital status, residential status (urban/rural), and median household income measured in the three-digit zip code. We also included a set of binary indicators for the presence of comorbid conditions (such as asthma, hypertension, diabetes, lipid disorder, heart disease, depression, and osteoarthritis), use of other RA drugs, and year fixed-effects. Initiation models included time since diagnosis, while the continuation models included time since BRM initiation.

Household OOP Burden

To examine the effect of household constraints on the use of biologic therapies, we controlled for the OOP expenses of other family members. For families with two or more members enrolled in the same plan, we defined household OOP burden as the sum of all health care expenses incurred by all other family members without RA.

There are two main concerns with including this measure as an additional covariate. First, the generosity of coverage for biologics is likely to be correlated with overall plan generosity, and hence with the other family OOP expenses. Second, unobserved characteristics of the family, such as the proclivity to use medical services, could affect both the demand for biologics and non-RA-related medical services. To account for the first issue, we constructed quartiles of household OOP expenses (for those without RA) for each plan and constructed an indicator variable for whether household OOP burden of the non-RA members fell in the top quartile in the plan-year. This measure

compares families with high versus low household OOP expenses within a plan, who all face the same overall coverage generosity. To account for the second issue, we used the number of chronic conditions of other family members as an instrument. This is a plausible instrument that it is correlated with the OOP expenses of other family members, but it is unlikely to affect biologic use other than through household OOP burden.

RESULTS

Descriptive Statistics

Our data exhibit considerable variation in biologic generosity across the 176 plans as well as across benefit types within the same plan. Some plans are more generous under the medical benefit and less generous under the pharmacy benefit, and vice versa. Average biologic OOP cost of an average plan is U.S.$1,518 (standard deviation [SD] U.S.$2,117) under the medical benefit, and U.S.$426 (SD U.S.$674) under the pharmacy benefit.[4]

Table 1 classifies new RA patients by the biologic generosity of their plan where nongenerous plans are characterized as those with average OOP costs in the top quartile of the corresponding distribution. The first column represents those in generous plans both under medical and pharmacy benefits; the second and third columns represent those in generous plans under only pharmacy or medical benefit; and the fourth column represents those in nongenerous plans under both the pharmacy and medical benefits. As the Table suggests, in nongenerous plans under the medical benefit, an average biologic user faces more than U.S.$4,300 in biologic OOP annually. Corresponding average OOP cost in nongenerous plans under the pharmacy benefit is U.S.$1,100.

There are demographic differences between patients in the most generous plans and the least generous plans (columns 1 and 4). Those in the most generous plans are slightly younger, more likely to be women, and more likely to be actively working. Interestingly, no major differences exist in the prevalence of comorbid conditions with the exception of depression (more likely among those in the most generous plans). Relative to patients in these two groups of plans, those in plans that are generous under only medical or pharmacy benefit (columns 2 and 3) are younger, more likely to be active workers, and are healthier.

Table 2 presents selected summary statistics of RA patients and their family members. The first two columns distinguish between those who never

Table 1: Summary Statistics for Newly Diagnosed RA Patients by Plan Generosity, 2000–2005

Average plan biologic OOP costs in top quartile under medical benefits	No	Yes	No	Yes
Average plan biologic OOP costs under medical benefits (mean/SD)	436 (535)	4,364 (1,911)	722 (626)	4,961 (2,451)
Average plan biologic OOP costs in top quartile under pharmacy benefits	No	No	Yes	Yes
Average plan biologic OOP costs under pharmacy benefits (mean/SD)	133 (92)	176 (108)	1,177 (767)	1,456 (1,127)
Number of plans in the group	104	28	28	16
	Mean (SD)			
Demographics				
Age	64 (15)	59 (14)	52 (15)	70 (12)
Age 65 or older (%)	48	33	16	80
Male (%)	28	32	28	39
Socioeconomic status				
Currently working (%)	27	35	74	12
Median HH income (U.S.$1,000)	41 (9)	45 (11)	44 (10)	46 (12)
Urban residence (%)	99	99	99	99
Household composition				
One or more family members (in plan) (%)	61	71	79	77
Family size	1.87 (0.96)	2.08 1.04)	2.48 (1.23)	1.88 (0.68)
Comorbid conditions (RA patient) (%)				
Asthma	5	5	3	4
Hypertension	35	26	18	34
Diabetes	12	10	8	11
Hyperlipidemia	12	10	6	14
Heart disease	21	13	8	21
Depression	7	7	10	3
Osteoarthritis	24	17	15	24
Number of person-years	13,194	3,302	549	2,297

HH, household; OOP, out of pocket; RA, rheumatoid arthritis; SD, standard deviation.

Table 2: Summary Statistics for Patients with RA Diagnosis, 2000–2005

	All Newly Diagnosed RA Patients		*Biologic Users among RA Patients*	
	Patients Who Never Initiated Biologic Therapy Mean (SD)	*Patients Who Initiated Biologic Therapy Mean (SD)*	*Patients Who Do Not Continue Biologic Use Every Year Post Initiation Mean (SD)*	*Patients Who Continue Biologic Use Every Year Post Initiation Mean (SD)*
Demographics				
Age	64 (15)	59 (13)	62(14)	59 (13)
Age 65 or older (%)	50	33	47	35
Male (%)	30	32	22	26
Socioeconomic status				
Currently working (%)	27	36	23	32
Median HH income (U.S.$)	42,505 (10,051)	43,132 (10,491)	41,758 (9,852)	42,260 (9,982)
Urban residence (%)	99	99	99	99
Household composition				
One or more family members (in plan) (%)	65	75	66	71
Family size	1.91 (0.96)	2.09 (0.98)	1.89 (0.90)	2.01 (0.95)
Family size given at least one additional family member	2.4 (0.85)	2.46 (0.86)	2.36 (0.78)	2.42 (0.83)
Comorbid conditions (RA patient) (%)				
Asthma	5	4	7	4
Hypertension	34	23	26	22
Diabetes	12	8	11	9
Hyperlipidemia	12	8	6	7
Heart disease	20	12	18	13
Depression	6	6	6	4
Osteoarthritis	23	15	21	13

continued

Table 2. *Continued*

	All Newly Diagnosed RA Patients		*Biologic Users among RA Patients*	
	Patients Who Never Initiated Biologic Therapy Mean (SD)	*Patients Who Initiated Biologic Therapy Mean (SD)*	*Patients Who Do Not Continue Biologic Use Every Year Post Initiation Mean (SD)*	*Patients Who Continue Biologic Use Every Year Post Initiation Mean (SD)*
Use of RA drugs (RA patient) (%)				
NSAID or analgesics	57	67	64	63
Corticosteroids	41	65	68	60
Nonbiologic DMARDS	24	71	66	64
Comorbid conditions (non-RA patients in the family) (%)				
Asthma	4	3	3	4
Hypertension	25	20	22	19
Diabetes	10	8	8	8
Hyperlipidemia	34	22	26	26
Heart disease	28	19	22	22
Depression	4	5	5	5
Osteoarthritis	8	5	8	6
OOP spending (RA patient)				
Medical services	3,291 (11,413)	3,149 (14,894)	3,352 (10,732)	2,304 (11,698)
Pharmacy	642 (1,849)	1,293 (2,399)	1,084 (2,823)	1,378 (2,741)
RA drugs	80 (312)	694 (2,034)	298 (877)	805 (2,169)
OOP spending (non-RA patients in the family)				
Medical services	2,207 (8,710)	1,863 (7,391)	1,610 (6,091)	1,453 (6,061)
Pharmacy	474 (1,352)	521 (1,566)	423 (765)	437 (1,115)
Number of person-years	17,713	1,629	1,352	3,257

DMARDS, disease-modifying antirheumatic drugs; HH, household; NSAID, nonsteroidal antiinflammatory drugs; OOP, out of pocket; RA, rheumatoid arthritis; SD, standard deviation.

use biologics and those who initiate biologics during the study period. Columns 3 and 4 focus on biologic users but distinguish between those who have at least a 1-year gap in their therapy and those who continue every year since initiation. Biologic initiators are typically younger, have lower prevalence of non-RA comorbid conditions, and are heavier users of nonbiologic RA drugs. Among biologic users, those who continue therapy are slightly younger, more likely to be active workers, and have a slightly lower prevalence of non-RA comorbid conditions.

Given the high cost of specialty drugs, it is worth considering to what extent the financial risk for these conditions is generated by drug spending. Table 2 reports that the mean annual OOP spending is substantial for RA patients (U.S.$3,291 for medical services and U.S.$642 for pharmaceuticals for noninitiators; U.S.$3,149 for medical services and U.S.$1,293 for pharmaceuticals for initiators). Naturally, mean pharmaceutical OOP spending is significantly higher among biologic users, and the RA drugs make up about half of that spending. The families of RA patients also incur substantial OOP expenses.

In addition, a subset of patients and their families face substantial financial risk. For example, more than 10 percent of RA patients have annual OOP expenses in excess of U.S.$6,500 for medical services and U.S.$1,404 for pharmaceuticals. Five percent pay more than U.S.$15,000 for medical services and U.S.$2,200 for pharmaceuticals per year.

Use of Drug Therapies

Only one in seven RA patients was taking a biologic in 2005, although the fraction doubled from 7 percent in 2000 to 14 percent in 2005. Among biologic users, 56 percent used etanercept, 26 percent received infliximab, and 23 percent used adalimumab. Nearly seven out of 10 biologic users were also taking an oral DMARD, most commonly methotrexate. Biologic use was also highly persistent. Among those who initiated in 2001, 78 percent used a biologic in 2002, and 69 percent in 2004 and 2005. These results are consistent with prior work who found continuation rates of 75–79 percent up to 20 months after initiating therapy (Geborek et al. 2002).

Multivariate Models of Initiation and Continuation

Table 3 summarizes the findings from our multivariate models of initiation (columns 1–3) and continuation (columns 4–6) of biologic therapies. Columns 1 and 4 report estimates for the full sample, while others are restricted to the

Table 3: Probit Models of Biologic Initiation and Continuation

	Use Biologic Conditional on Not Having Used It before			*Use Biologic Conditional on Initiation*		
	All Newly Diagnosed (1) Probit	*Newly Diagnosed with Other Family (2) Probit*	*Newly Diagnosed with Other Family (3) IV Probit*	*All Biologic Initiators (4) Probit*	*Biologic Initiators with Other Family (5) Probit*	*Biologic Initiators with Other Family (6) IV Probit*
Average plan biologic OOP costs under medical benefits (in U.S.$100)	0.0017	0.0017	0.0010	− 3.5e-05	− 4e-04	− 2.5e-04
	(0.0012)	(0.0014)	(0.0010)	(0.001)	(0.002)	(0.002)
Average plan biologic OOP costs under pharmacy benefits (in U.S.$100)	− 0.012***	0.010**	− 0.011**	− 0.01*	− 0.02***	− 0.02***
	(0.004)	(0.005)	(0.005)	(0.006)	(0.006)	(0.006)
Other family OOP in top quartile within the plan		0.047	− 0.494***		− 0.070	0.045
		(0.047)	(0.178)		(0.067)	(0.299)
Used an analgesic or NSAID previous year	0.070*	0.051	0.075	0.056	0.100	0.099
	(0.041)	(0.047)	(0.046)	(0.058)	(0.069)	(0.069)
Used a corticosteroid previous year	0.217***	0.221***	0.212***	− 0.099*	− 0.091	− 0.095
	(0.041)	(0.047)	(0.046)	(0.055)	(0.066)	(0.067)
Used a nonbiologic DMARD previous year	0.622***	0.618***	0.607***	0.018	0.024	0.024
	(0.044)	(0.052)	(0.052)	(0.058)	(0.069)	(0.069)
No. of years from first RA diagnosis	− 0.157***	− 0.159***	− 0.144***			
	(0.020)	(0.024)	(0.023)			
No. of years from first biologic				− 0.131***	− 0.117***	− 0.116***
				(0.022)	(0.027)	(0.027)

Age 25–44	0.145	0.130	− 0.057	0.260	0.352	0.404
	(0.167)	(0.214)	(0.216)	(0.265)	(0.353)	(0.374)
Age 45–64	0.177	0.186	− 0.021	0.446*	0.579	0.633*
	(0.159)	(0.209)	(0.215)	(0.259)	(0.354)	(0.376)
Age 65+	− 0.063	− 0.027	− 0.174	0.257	0.467	0.511
	(0.165)	(0.217)	(0.215)	(0.266)	(0.364)	(0.377)
Currently working	0.024	0.030	− 0.009	0.109	0.195**	0.205**
	(0.055)	(0.063)	(0.062)	(0.086)	(0.098)	(0.101)
Median HH income (in U.S.$1,000)	1.786	1.482	2.050	2.030	1.885	2.016
	(1.840)	(2.066)	(2.025)	(3.163)	(3.578)	(3.583)
Married	0.058	0.021	0.114	0.056	− 0.089	− 0.112
	(0.056)	(0.152)	(0.149)	(0.083)	(0.249)	(0.256)
Male	0.048	− 0.026	− 0.008	0.100	0.090	0.081
	(0.047)	(0.056)	(0.055)	(0.080)	(0.091)	(0.093)
Urban	0.107	0.359	0.369	− 0.178	− 0.231	− 0.231
	(0.214)	(0.284)	(0.277)	(0.430)	(0.420)	(0.423)
Primary beneficiary	− 0.043	− 0.001	− 0.030	0.032	0.002	0.011
	(0.051)	(0.052)	(0.052)	(0.080)	(0.083)	(0.084)
Asthma	− 0.066	− 0.064	− 0.033	− 0.270*	− 0.278	− 0.278
	(0.096)	(0.112)	(0.110)	(0.142)	(0.172)	(0.171)
Hypertension	− 0.126***	− 0.077	− 0.060	− 0.100	− 0.134	− 0.134
	(0.047)	(0.056)	(0.055)	(0.073)	(0.088)	(0.088)
Diabetes	− 0.099	− 0.118	− 0.113	− 0.132	− 0.135	− 0.136
	(0.071)	(0.087)	(0.085)	(0.107)	(0.130)	(0.130)
Hyperlipidemia	− 0.155**	− 0.208**	− 0.194**	0.003	0.097	0.098
	(0.069)	(0.085)	(0.083)	(0.112)	(0.138)	(0.139)
Heart disease	− 0.090	− 0.032	− 0.020	− 0.168**	− 0.072	− 0.079
	(0.061)	(0.074)	(0.071)	(0.085)	(0.106)	(0.107)
Depression	− 0.026	− 0.061	− 0.049	0.068	− 0.070	− 0.075
	(0.081)	(0.100)	(0.098)	(0.135)	(0.170)	(0.170)

Table 3. *Continued*

	Use Biologic Conditional on Not Having Used It before			*Use Biologic Conditional on Initiation*		
	All Newly Diagnosed (1) Probit	*Newly Diagnosed with Other Family (2) Probit*	*Newly Diagnosed with Other Family (3) IV Probit*	*All Biologic Initiators (4) Probit*	*Biologic Initiators with Other Family (5) Probit*	*Biologic Initiators with Other Family (6) IV Probit*
Osteoarthritis	−0.113**	−0.051	−0.029	−0.263***	−0.214**	−0.214**
	(0.053)	(0.063)	(0.061)	(0.084)	(0.104)	(0.104)
Year fixed effects	Included	Included	Included	Included	Included	Included
Observations	18,697	12,183	12,183	4,608	3,207	3,207

Notes. Standard errors (clustered at the individual level) in parentheses.

*Significant at 10%;

**Significant at 5%;

***Significant at 1%.

BRM, biologic response modifiers; DMARDS, disease-modifying antirheumatic drugs; HH, household; IV, instrumental variables; NSAID, nonsteroidal antiinflammatory drugs; RA, rheumatoid arthritis.

subsample of RA patients with other family members enrolled in the plan and include a binary indicator for whether the family faces substantial OOP burden (i.e., other family members' OOP expenses are in the top quartile within the plan). In columns 3 and 6, we instrument for the family's OOP burden.

The results in columns 1 and 2 of Table 3 suggest that initiation is sensitive primarily to the generosity under the pharmacy benefit, not the generosity under the medical benefit, perhaps due to smaller between-plan variation in generosity under medical benefit. Prior use of corticosteroids and a nonbiologic DMARD and time since RA diagnosis are also strong predictors of biologic initiation.

To assess the potential endogeneity of family OOP expenses, we used an instrumental variables (IV) approach. We verified that the instrument is highly correlated with the endogenous variable,[5] and we rejected the exogeneity of other family household OOP burden ($p = .01$). As such, model 3 is our preferred specification for modeling initiation. The IV results presented in column 3 suggest that RA patients in high OOP households are less likely to initiate a biologic, controlling for the overall generosity of coverage within the plan, and this effect is significant at 1 percent level of significance.

Using the estimates in column 3, we find that doubling the average OOP costs under the pharmacy benefit from U.S.$400 (approximately the mean value) to U.S.$800 (approximately the standard deviation) reduces the predicted probability of initiating a biologic by 9.3 percent from .043 to .039. Further increasing the OOP costs to U.S.$1,200 reduces initiation probability to .036. In a given plan, RA patients in families with high OOP costs are much less likely to initiate biologics (2 percent annually) compared with those in less-constrained families (5.6 percent).

Given the high level of persistency in biologic use, factors affecting initiation of therapy may be quite distinct from those affecting the decision to continue therapy. Columns 4–6 of Table 3 present models on the decision to continue therapy. All three specifications indicate that the generosity of biologic coverage under pharmacy benefits is positively correlated with continuation of biologics, although the coefficient is not statistically significant in the first specification.

Predictions from the IV estimates (column 6) suggest that doubling the average OOP costs under the pharmacy benefit from U.S.$400 to U.S.$800 reduces the predicted probability of continuation by 3.8 percent from .80 to .77. Further increasing the OOP costs to U.S.$1,200 reduces the probability of continuation to .75.[6] Family OOP burden is uncorrelated with rates of continuation.

Sensitivity Analyses

Table 4 presents several robustness assessments of our findings. First, we estimated models characterizing plan generosity using two indicator variables for less generous coverage (top quartile biologic OOP costs across all plans) under pharmacy and medical benefits. This change had no substantive effect on the probability of initiating (column 2) or continuing (column 6) a biologic. As before, we found that initiation was sensitive primarily to the generosity under the pharmacy benefit, not to the generosity under the medical benefit. In an additional specification, we defined the least generous plans as those in the top quartile of OOP costs under both the medical and pharmacy benefits. This specification also resulted in similar findings on initiation (column 3) and continuation (column 7). The annual predicted probability of initiating a biologic was .046 for RA patients in generous plans and .026 for those in the least generous plans.

Second, we focused on average per-person OOP expenses of family members without RA instead of a cumulative sum to characterize high OOP burden families. This modification did not substantially affect our findings (columns 4 and 8).

DISCUSSION

Greater cost sharing and less pharmaceutical use could come about through reduced initiation of therapies, worse compliance among existing users, or more frequent discontinuation of therapy (although the latter could be interpreted as an extreme example of poor compliance among users). Distinguishing between these hypotheses is important because it affects the advice and monitoring that physicians and plans should use to counteract any adverse consequences of plan design changes.

We found that RA patients enrolled in plans with less generous coverage of biologic therapies were less likely to initiate a biologic and more likely to discontinue use, although the effects on initiation were larger (and statistically significant across specifications). The results were primarily driven by the generosity under the pharmacy benefit, rather than generosity under the medical benefit, most likely due to much smaller between-plan variation in generosity under medical benefit. We also found that individuals in households with high OOP burden are also less likely to initiate a biologic, pointing to the importance of considering demand in a family context in the case of these expensive pharmaceuticals. Nevertheless, the magnitudes of our

Table 4: Sensitivity Analyses on Initiation and Continuation Models

	Use Biologic Conditional on Not Having Used It Before Newly Diagnosed with Other Family IV Probit Estimation Original Specification in Table 3				*Use Biologic Conditional on Initiation Newly Diagnosed with Other Family IV Probit Estimation Original Specification in Table 3*			
	(1)	*(2)*	*(3)*	*(4)*	*(5)*	*(6)*	*(7)*	*(8)*
Measures of plan biologic generosity								
Average plan biologic OOP costs under medical benefits (in U.S.$100)	0.001			0.0016	– 2.5e-04			– 3.02 e-04
	(0.001)			(0.0013)	(0.002)			(0.002)
Average plan biologic OOP costs under pharmacy benefits (in U.S.$100)	– 0.011**			– 0.01**	– 0.02***			– 0.019***
	(0.005)			(0.005)	(0.006)			(0.006)
Average plan biologic OOP costs in top quartile under medical benefits (1/0)		0.05				– 0.02		
		(0.05)				(0.08)		
Average plan biologic OOP costs in top quartile under pharmacy benefits (1/0)		– 0.24***				– 0.18**		
		(0.07)				(0.09)		
Average plan biologic OOP costs in top quartile under medical and pharmacy benefits (1/0)			– 0.29***				– 0.20**	
			(0.08)				(0.10)	
Measures of family OOP burden								
Other family OOP in top quartile within the plan	– 0.494***	– 0.50***	– 0.52***		0.045	0.04	0.04	
	(0.178)	(0.18)	(0.17)		(0.299)	(0.30)	(0.30)	
Other family OOP per capita in top quartile within the plan				– 0.65***				0.06
				(0.23)				(0.39)
All control variables listed in Table 3	Included	Included	Included	Included	Included	Included	Included	Included
Observations	12,183	12,183	12,183	12,183	3,207	3,207	3,207	3,207

Notes. Standard errors (clustered at the individual level) in parentheses.

*Significant at 10%;

**Significant at 5%;

***Significant at 1%.

IV, instrumental variables; OOP, out of pocket.

estimates are small. Doubling the average OOP costs under the pharmacy benefit reduces the predicted probability of initiating a biologic by 9.3 percent. Solomon et al. (2009) show that doubling copayments results in larger reductions in the predicted probability of initiating traditional oral pharmaceuticals for hypertension (27 percent from .55 to .40), hypercholesterolemia (23 percent from .40 to .31), and diabetes (13 percent from .46 to .40). This suggests that these new biologic drugs are highly demand inelastic, perhaps reflecting the fact that they can be very effective for patients for whom other more traditional therapies have failed to treat this symptomatic condition.

As spending on specialty drugs increases, benefit managers' interest in monitoring and containing their utilization has intensified. Plans that cover physician-administered injectibles under their medical benefit are starting to move them to their pharmacy benefit, where they can be more easily subjected to the same utilization management as traditional drugs. Furthermore, health plans that cover these drugs under their pharmacy plan are increasingly requiring consumers to share the costs of high-cost drugs via coinsurance rather than copayments.

Research by Hoadley et al. (2009) reports that under Medicare Part D, the proportion of Medicare Advantage Drug Plan enrollees facing a specialty tier increased from 69 percent in 2006 to 98 percent in 2009. More than half the Part D plans had coinsurance rates exceeding 33 percent in the specialty tier. While such high coinsurance rates for the expensive specialty drugs curb plan liability, it also increases OOP costs for the enrollees before they reach the catastrophic coverage threshold. As Part D claims data become available, future research could examine how cost sharing influences biologic demand and subsequent patient outcomes for this population.

Our findings generalize to most biologics and high-cost drugs. As in prior work looking at high-cost treatments for cancer, multiple sclerosis, and kidney disease (Goldman et al. 2006a), the "average patient" is well insured under most private plans. However, a minority of patients face considerable cost sharing that affects their access to these medications. Restricting access is often more consequential for high-cost specialty drugs for there are few alternative treatments and, as of now, no biosimilars. Given their high costs, management of these drugs should focus on making sure only patients who will most benefit receive them. However, once such patients are identified, it makes little sense to limit coverage.

Our paper has several limitations. First, we cannot assess the severity of condition. However, we restricted the initiation sample to the newly diagnosed to reduce the heterogeneity of disease severity across individuals. In

addition, we control for time since diagnosis and use of nonbiologics to proxy disease severity.

Second, we cannot assess clinical effectiveness and side effects of biologics. Such factors may influence discontinuation of therapy. Presumably such clinical reasons for discontinuation are equally likely under the generous and nongenerous plans. However, we conducted a sensitivity analysis by including in the continuation model only those who have been on a biologic for at least 2 years. Our assumption is that if the biologic therapy is not clinically effective, or if it involves important side effects, the patient would discontinue after the first year. Our results were robust under this restriction.

Third, as this research is based on claims data, it is sensitive to potential diagnosis coding errors. Singh, Holmgren, and Noorbaloochi (2004) documented that diagnosis of RA with ICD-9 code 714.XX has 100 percent sensitivity but 55 percent specificity for the Veterans Administration databases. Studies using Medicare claims reported sensitivity of 65–90 percent and a high positive predictive value around 86 percent for RA (Katz et al. 1997; Losina et al. 2003). In the context of our study, if coding errors are uniform across health plans of differing generosity, this should not bias our findings.

Finally, we cannot fully rule out selection into plans based on unobserved factors, which is always a concern in observational studies. Although we find an association between the generosity of plan coverage and the use of biologics in the treatment of RA, it is possible that individuals with more aggressive forms of RA or those who have failed lower cost therapies are more likely to enroll in plans offering generous coverage of biologics. Although biologic therapies are just one component of care, our results would be biased if plan choice was correlated with unobserved health status or individuals' proclivity to use high-cost treatments.

To test whether individuals select plans based on their biologic use, we focused on a narrow definition of plan generosity: whether the average biologic OOP costs fell in the top quartile of the distribution, both under the medical and pharmacy benefits. Based on this characterization, we identified individuals who had a choice of generous and nongenerous plans, that is, firms offering multiple plans, with one or more plans defined as generous and nongenerous in terms of biologic coverage (12 percent of the sample).

Interestingly, of all the plan changes among those with a choice, almost all (99 percent) involved switching from a more generous plan to a less generous plan. Nevertheless, this finding does not rule out the possibility that those in an already generous plan select to stay in it if they anticipate biologic use in the near future, or if they already initiated biologics. To test this, we

further constrained the sample to those who initiated therapy during the study period. We hypothesized that if plan selection based on the need for biologics is substantial, the tendency to stay in the generous plan (i.e., not switch) would be more likely just before and after the initiation of biologics relative to other years. Accordingly, we estimated a probit model with a binary-dependent variable that took on value "1" if the individual stayed in the generous plan, and "0" if s/he switched from the generous plan. The key regressor was an indicator of whether the observation fell in a 2-year window around the biologic initiation (2 years before, the year of, and 2 years after). We did not find a statistically significant relationship between plan switching and this key time period before and after initiation (p-value .14). The same model with an indicator of 1-year window around the initiation date also yielded insignificant point estimates (p-value .25). In additional specifications, we extended the key indicator variable to include all time periods post initiation, and again we did not find evidence that plan switching is significantly different just before or after initiation. Thus, the extent of selection bias is likely to be small.

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NOTES

1. We chose not to multiply with average number of annual scripts in the plan as such a measure may be endogenous to plan generosity. In less generous plans, individuals may suboptimally use the drug resulting in lower scripts per year relative to more generous plans.

2. An alternative index could use the unweighted average OOP in each plan. The concern with that approach is that it reflects choices made by patients, who may switch to lower-cost medications because of high costs for some medications. These choices can distort comparisons of benefit generosity. As an example, consider a situation with two drugs. Plan A may charge U.S.$X for either drug, whereas Plan B charges U.S.$X for one drug and significantly more for the other one. If virtually all patients take the cheaper drug in Plan B, there is little difference observed in the prices consumers pay in the two plans. However, a comparison of the benefits suggests otherwise.
3. We have enrollment and claims data dating back to 1997 for most of the sample, so we can track the RA diagnosis date back to 1997 for those individuals.
4. Coefficient of variation is higher under the pharmacy benefit, suggesting more dispersion of generosity under pharmacy benefit across plans.
5. In first-stage estimation, the instrumental variable had a positive coefficient estimate that is statistically significant with *t*-statistic of 24.29. This large *t*-statistic lessens the concern of a weak instrument.
6. In continuation models for those with other family members, we also reject the exogeneity of the family OOP burden measure, and we verify the correlation between the instrument and the endogenous variable (*t*-statistic of 13).

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