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Author: William H. Crown, Ernst R. Berndt, Onur
Baser, Stan N. Finkelstein, Whitney P. Witt, Jonathan
Maguire, Kenan E. Haver

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Benefit Plan Design and Prescription Drug Utilization Among Asthmatics: Do Patient Copayments Matter?

William H. Crown, *Medstat*

Ernst R. Berndt, *MIT Sloan School and NBER*

Onur Baser, *Medstat*

Stan N. Finkelstein, *MIT Sloan School*

Whitney P. Witt, *Northwestern University*

Jonathan Maguire, *Medstat*

Kenan E. Haver, *Massachusetts General Hospital*

Executive Summary

The ratio of controller-to-reliever medication use has been proposed as a measure of treatment quality for asthma patients. In this study we examine the effects of plan-level mean out-of-pocket asthma medication patient copayments and other features of benefit plan design on the use of controller medications alone, controller and reliever medications (combination therapy), and reliever medications alone. The 1995–2000 MarketScan™ claims data were used to construct plan-level out-of-pocket copayment and physician/practice prescriber preference variables for asthma medications. Separate multinomial logit models were estimated for patients in fee-for-service (FFS) and non-FFS plans relating benefit plan design features, physician/practice prescribing preferences, patient demographics, patient comorbidities, and county-level income variables to patient-level asthma treatment patterns. We find that the controller-to-reliever ratio rose steadily over 1995–2000, along with out-of-pocket payments for asthma medications, which rose more for controllers than for relievers. After controlling for other variables, however, plan-level mean out-of-pocket copayments were not found to have a statistically significant influence on patient-level asthma treatment patterns. On the other hand, physician/practice prescribing patterns strongly influenced patient-level treatment patterns. There is no strong statistical evidence that higher levels of out-of-pocket copayments for prescription drugs influence asthma treatment patterns. However, physician/practice prescribing preferences influence patient treatment.

I. Introduction

It has long been known that trade-offs exist between the gains from pooling across individuals to insure against catastrophic medical

expenditures and the efficiency losses from the moral hazard effects that arise because of the implicit marginal subsidies to health services utilization occurring under conventional medical insurance plans.¹ The existence of this trade-off suggests that, given preferences and costs, there may be an optimal amount of coinsurance. Using data from the RAND Health Insurance Experiment in the 1980s, Manning and Marquis (1996) have estimated that, with an \$8,000 cap on total expenditures, the optimal coinsurance rate would have been about 50 percent.²

Although coinsurance rates for office visits, emergency room visits, inpatient hospitalization, and prescription drug services were set equal in the design of the RAND Health Insurance Experiment, current practice in the United States means that coinsurance and, more commonly, patient copayment amounts differ considerably among the different categories of health care services.³

Within the last decade, considerable controversy has arisen involving the design of prescription drug benefits in health insurance plans. This controversy partly reflects the fact that prescription drugs have become an increasingly important component of health care costs, rising sharply from 5.6 percent in 1980 to 9.7 percent in 2000.⁴ Continuing a recent pattern, in 2001 total prescription drug expenditures in the United States increased by about 17 percent to \$154.5 billion.⁵

Managed-care organizations and the employers with whom they contract have attempted to control rising prescription drug costs by changing cost-sharing provisions, seeking to steer use to preferred drugs on the insurer's list of approved medications (formularies).⁶ Already in the early and mid-1990s, plans began experimenting with two-tier copayment schemes in which a low patient copay (say, \$5) was assessed for a generic (first-tier) drug, and a somewhat higher but still modest copay (say, \$10) was assessed for branded (second-tier) drugs; in some rare cases, physicians needed prior authorization from the payer before being granted permission to prescribe particularly costly medications.

After continued increases in prescription drug costs, in the mid- and late 1990s some plans began implementing less generous three-tier copay schemes. A typical three-tier plan design of several years ago consisted of a \$5 copay for a first-tier generic drug, a \$10 copay for a preferred branded drug within a given therapeutic class (the second tier); and a heftier \$25 copay for the nonpreferred branded (third-tier) drugs within the therapeutic class. Many plans also had a second, more generous three-tier system for mail-order pharmacy prescriptions.

Use of the three-tier copayment designs created incentives not only for insureds to shift toward increased use of the less costly medications, but it also gave insurance plans and payers increased bargaining power with pharmaceutical companies by allowing them to threaten to banish their branded products to the third tier unless drug manufacturers offered the payer substantial discounts or rebates.⁷

Frustrated again by continued increases in prescription drug spending, many plans have recently increased the levels of prescription drug copayments at all three tiers, with the third-tier copayment as high as \$40 or \$50 per prescription; other plans have turned to the use of coinsurance rather than copayment designs. According to one source, in 2000 the average patient retail copayment for a generic first-tier drug was \$7.17; for preferred brands in the second tier, it was \$14.14; and for all other nonpreferred brands on the third tier, it was \$27.35.⁸

The increased use of multi-tier copayment design mechanisms for prescription drugs raises at least two sets of important issues. (1) Do variations in copay structures alter the level and composition of prescription drug utilization? Are they effective instruments in controlling prescription drug costs?⁹ Or do persistent physician prescribing patterns dominate, with copayment variations having only a negligible impact? (2) To the extent three-tier copays affect the level and composition of drug utilization, what are the associated health outcomes? Can copayment design mechanisms be used not only to control costs but also to steer utilization to more medically appropriate uses of prescription drugs?¹⁰

In this paper, we examine the first set of questions in detail; although we discuss possibilities concerning the second set, we leave it largely for future research. We also examine variation over time and among plans involving copayments for other medical services, such as physician office visits, emergency room treatments, and inpatient hospitalizations.

We address these issues using the therapeutic class of asthma medications as a case study. As described in detail below, asthma drugs can be envisioned as being primarily reliever medications (used to relieve symptoms in an acute asthmatic exacerbation—an asthma attack) or as being primarily controller medications (used to control pulmonary inflammation and prevent an attack). For some time now, health care officials have argued that the appropriate use of controller medications can result in reduced outpatient office visits, emergency room treatments, and inpatient hospitalizations.¹¹ While the optimal ratio of asthma controller to reliever drug utilization is difficult to quantify

precisely (and likely is patient idiosyncratic), it is widely believed that in most cases increases in the controller-to-reliever ratio are beneficial in terms of both economic and medical considerations.¹² A recent historical overview of trends in asthma pharmacotherapy between 1978 and 2002 by Stafford et al. (2002) suggests that, particularly in the last decade, the controller-to-reliever ratio has increased while the number of asthma-related office visits has stabilized or declined.

Before proceeding with a discussion of hypotheses to be tested, underlying data, and econometric methods, we first digress and provide some medical background on asthma and its treatment.

II. Background on Asthma and Its Treatment

Asthma is a chronic disease characterized by inflammation of the airways and constricted bronchial tubes. Asthma affects about 6 percent of the population and is the third most common chronic condition among children. Although death from asthma is fairly unusual, morbidity from the condition is common. Since 1991, when consensus guidelines on the treatment of asthma were first released by the National Asthma Education Program (1991), clinicians have encouraged the use of maintenance therapy, typically using inhaled corticosteroids to control inflammation and to reverse chronic airway obstruction and hyperreactivity. Other medications, particularly the short-acting beta-two agonist class of bronchodilators, are recommended as reserves for relief of acute episodes of bronchospasm.¹³

Several published articles have examined the benefits that have accrued as the preference of controller over reliever medications for asthma maintenance therapy has gained acceptance.¹⁴ Some of these articles have attempted to correlate a particular metric, commonly called the C/B ratio (the ratio of inhaled corticosteroids to bronchodilators) with populationwide changes in survival and medical services utilization.¹⁵ Greater use of inhaled corticosteroids relative to bronchodilators has been reported to be associated with lower mortality rates and less frequent use of emergency room, inpatient, and outpatient services in the care of patients with asthma.¹⁶

III. Hypothesis to Be Tested/Assessed Empirically

We empirically assess the effects of several benefit plan design features on asthma treatment patterns. In particular, we test the hypothesis that

higher controller/reliever copay ratios will be associated with reduced use of controller medications, other factors being equal, and whether any effects differ by plan type: fee-for-service (FFS) versus non-FFS plans. Finally, we examine whether physician/practice prescribing patterns influence patient-level asthma treatment patterns and, if so, whether these effects differ between FFS and non-FFS plans.

IV. Data Sources and Construction of Variables

The MarketScan™ private insurance database for 1995–2000 was used in this study. MarketScan™ is the largest database of its kind and contains detailed descriptions of inpatient, outpatient medical, and outpatient prescription drug services for approximately 3 million persons in 2000 who were covered by corporate-sponsored health care plans. These individuals' health care was provided under various fee-for-service (FFS), fully capitated, and partially capitated health plans, including exclusive provider organizations, preferred provider organizations, point-of-service plans, indemnity plans, and health maintenance organizations.

Race, ethnicity, and income information were extracted from a different data set: the Bureau of Health Professions Area Resource File (ARF), a compendium of county-level information produced annually. The ARF data were then merged with the Medstat analytic file by county.

Identification of Asthma Patients

Patients with evidence of asthma were selected from the intersection of the medical claims and encounter records, enrollment files, and pharmaceutical data files. Evidence of asthma was provided by searching the claims data during 1995–2000 for individuals meeting at least one of the following criteria:

- At least two outpatient claims with primary or secondary diagnoses of asthma.
- At least one emergency room claim with primary diagnosis of asthma, and a drug transaction for an asthma drug ninety days prior or seven days following the emergency room claim.
- At least one inpatient claim with a primary diagnosis of asthma.
- A secondary diagnosis of asthma and a primary diagnosis of respiratory infection in an outpatient or inpatient claim.

- At least one drug transaction for a(n) anti-inflammatory agent, oral anti-leukotrienes, long-acting bronchodilators, or inhaled or oral short-acting beta-agonists.

Patients with a diagnosis of chronic obstructive pulmonary disease (COPD) and who had one or more diagnosis or procedure codes indicating pregnancy or delivery or who were not continuously enrolled for twenty-four months were excluded from our study group.

Measures

Sociodemographic Characteristics. The sociodemographic characteristics included the age of the head of the household, percentage of patients who were female, geographic region (Northeast, North Central, South, West, and unknown), member type, and year of entry into the study. In addition, several sociodemographic variables defined at the county level were merged with the patient-level data. These variables included racial composition (percentage of white, black, and other) and income strata.

Plan Type. Fee-for-service plans were defined as plans that did not have an incentive for patients to use a particular list of providers and included basic, major medical, and comprehensive health insurance coverage. The remaining plans, called non-FFS, were defined as plans that either required patients to choose from a list of providers or provided financial incentives to use a specific list of providers. Non-FFS plans included exclusive provider organizations, health maintenance organizations, noncapitated point-of-service plans, preferred provider organizations, or capitated or partially capitated point-of-service plans.

Copayments. Copayments for outpatient pharmaceuticals were calculated by first stratifying all prescription drug claims by year, then by plan within year. Next, we calculated the average out-of-pocket patient copayments for asthma drugs by therapeutic class for each plan, as well as the ratio of mean controller copayments to mean reliever copayments. These plan-level ratios were then attached to each patient's record within a given plan.

We also constructed variables for the average out-of-pocket copayments paid for outpatient physician visits, emergency room visits, and hospital stays. The average copayment captured the actual dollar

amount that the patients paid out-of-pocket. Note that we use the term *copayment* to refer to any out-of-pocket payment by individuals for health care. This includes both traditional copayments (e.g., \$5 per office visit) as well as coinsurance (e.g., patient pays 20 percent of the bill).

Comorbidities. Several asthma-related comorbidities, including allergic rhinitis, anxiety, depression, gastroesophageal reflux disease (GERD), and migraine, were examined. The number of unique three-digit ICD-9 codes (International Classification of Diseases, Ninth Revision) was used as a proxy for the extent of overall medical and mental health comorbidities.

Charlson Index scores were generated to capture the level and burden of comorbidity. This index draws on diagnostic information from ICD-9 codes and procedure codes, resulting in nineteen conditions that are weighted based on the adjusted risk of one-year mortality. The index score is the sum of the weights for all of a patient's conditions and ranges from one to six, with higher numbers indicating increased levels of comorbidity.¹⁷ The Charlson Index has been highly effective in predicting clinical outcomes and costs.¹⁸ A recent study by Sin and Tu (2001) found that high levels of comorbidity, as measured by the Charlson Index, were strongly associated with the underuse of inhaled steroid therapy in elderly patients with asthma, a finding that is of particular importance for our research.

Utilization. Utilization of health care services or prescription drugs was captured through claims and encounters over the study period. For individuals, we examined the mean annualized number of emergency room visits, hospitalizations, hospital days, outpatient visits, and allergy/asthma specialist visits. Prescription drugs for the treatment of persons with asthma were categorized as either controller or reliever medications. Controllers included inhaled anti-inflammatory agents, oral corticosteroids, oral anti-leukotrienes, and long-acting bronchodilators; relievers were defined as drugs categorized as anticholinergics or inhaled short-acting beta-agonists. Based on this dichotomy, a ratio of controller to relievers was constructed and interpreted as a measure of adequate management of asthma.

Costs. The analytic file contains patients with fee-for-service health plans and those with partially or fully capitated plans. Data on costs

were not available, however, for the capitated plans. Therefore, the value of patients' service utilization under the capitated plan was priced and imputed using average payments from the MarketScan™ FFS inpatient and outpatient services by region, year, and procedure.

V. Econometric Methods

Our econometric analysis proceeds in two steps, using a variant of the Lee (1983) multinomial logit selection model, as proposed by Bourguignon, Fournier, and Gurgand (2001). First we model choice among three alternative drug treatments: controller only, reliever only, and a combination of controller and reliever, all on an annual basis. We employ as identifying instruments (variables affecting choice of drug treatment but not total expenditures) plan copayment variables, and physician/provider prescribing composition. Then we employ least squares regressions of log total expenditures for each treatment arm, in addition to a usual set of covariates, the three lambda selection terms (conditional expectations of residuals from the three arms of the treatment selection model).

More specifically, to reduce the potential for endogeneity between plan-level copayment variables and plan-level controller-to-reliever ratios in the multivariate analyses, we utilize a discrete counterpart to the plan-level controller-to-reliever ratio examined in the descriptive analyses. In particular, we construct an annual patient-level dependent variable with three mutually exclusive categories: a controller drug alone ($n = 3,903$), a combination of a controller drug and a reliever drug ($n = 11,427$), and a reliever drug alone ($n = 11,049$). A likelihood ratio test was carried out to examine whether separate models were required for the FFS and non-FFS samples. Based on the results of this test, we estimated separate multinomial logit models for the FFS and non-FFS subsamples. County-level income variables were appended to patient records to augment the medical claims. Robust standard errors were used to adjust for potential intracounty covariance among patients living in the same counties that may have been introduced by these variables. Hausman tests were then conducted to compare selectivity-corrected models with standard ordinary least squares (OLS) models.

In terms of instruments, we construct two sets of identifying variables. Our first set is plan copayments. For each year and plan, we calculate mean copayment values for each class of drug and then take the ratio of controller mean to reliever mean copayment. This plan-specific

variable is utilized as a regressor in the multinomial drug treatment choice equations for each person year. A second set involves calculating, for each physician/provider tax identification number in the claims data, the proportion of patients obtaining controller-only, reliever-only, and combination treatment. In many cases this taxation identification number covers a multiphysician medical practice, but in some cases it is unique to one physician. Because the sum of these three percentages is 100 percent for each physician/provider practice, we delete one of the three percentages but include two of them as regressors in the multinomial drug treatment model. We recognize that this approach still leaves room for some selectivity in the form of patients' choice of physician and choice of plan, but we believe nonetheless that this method provides a reasonable first step in mitigating the effects of such selectivity. We also note that, in this paper, we do not examine the implications of treatment patterns on components of subsequent health care utilization, although we do model total health care expenditures.

VI. Descriptive Results

Based on the definitions of asthma episodes discussed above, we obtained a sample that included 44,926 patients in FFS plans and 18,305 in non-FFS plans (63,231 patients total).

Controller-to-Reliever Ratio

As shown in figure 4.1, the controller-to-reliever ratio has been rising over time. Between 1995 and 1999, it increased by approximately 40 percent, with more rapid increases in the two most recent years. The ratio is consistently higher for patients in FFS plans than for those in non-FFS plans and, since 1997, the rate of increase appears to be higher for the FFS plan beneficiaries than for those in non-FFS plans. Irrespective of plan type, however, almost all plans had average controller-to-reliever ratios greater than 1 (plan-specific data not shown).

Patient Demographics

Table 4.1 reports the demographic characteristics of the sample, stratified by FFS and non-FFS plans. Patients in FFS plans had a mean age of 34 years compared to 27 years for non-FFS plans ($p < .001$) and were more likely to be female (57 percent versus 52 percent, $p < .001$). Patients in FFS plans were also more likely than patients in non-FFS plans to be located in the North Central region (67 percent versus 9 percent,

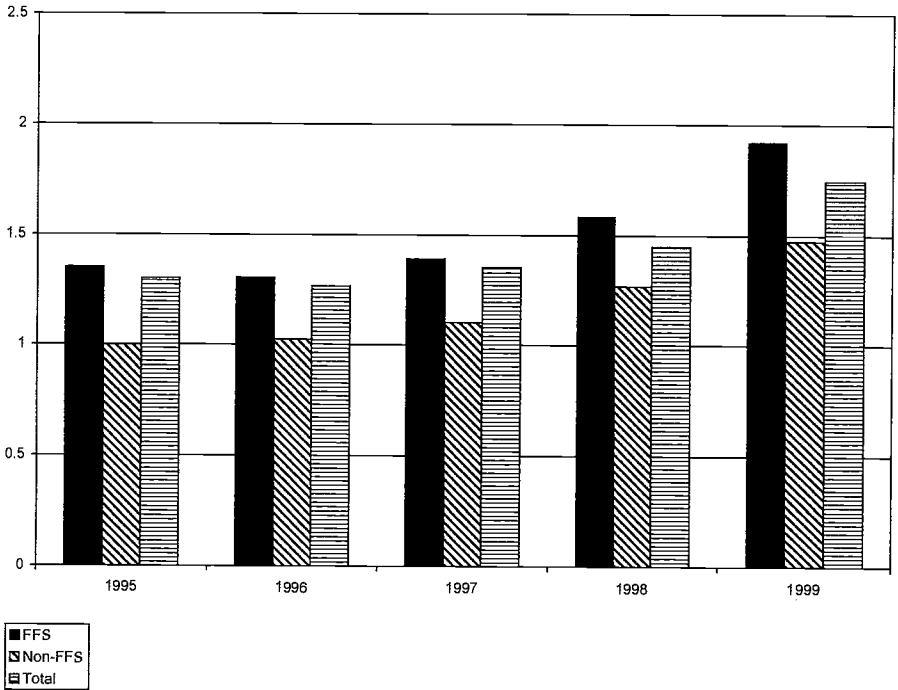


Figure 4.1
Controller/reliever medication ratios by plan type and year

Table 4.1
Summary of asthma patient characteristics by insurance plan type, 1995–2000

	FFS	Non-FFS	Total	<i>p</i>
<i>N</i>	44,926	18,305	63,231	NA
Trigger type				
(1) 2 OP asthma claims	37.05%	36.91%	37.01%	0.74
(2) Asthuna ER + asthuna RX	0.69%	0.82%	0.73%	0.06
(3) IP resp. inf. + asthuna	0.04%	0.08%	0.05%	0.12
(4) IP asthma	0.26%	0.32%	0.28%	0.15
(5) 2 asthuna RX	61.97%	61.87%	61.94%	0.82
Mean age	34.09	27.19	32.09	<.01
% females	57.41%	52.09%	55.87%	<.01

Table 4.1
(continued)

	FFS	Non-FFS	Total	<i>p</i>
<i>N</i>	44,926	18,305	63,231	NA
Geographic region				
Northeast	15.63%	47.56%	24.88%	<.01
North central	67.01%	8.76%	50.15%	<.01
South	12.05%	32.76%	18.04%	<.01
West	5.31%	10.92%	6.93%	<.01
Year of trigger				
1996	34.67%	13.13%	28.43%	<.01
1997	20.21%	13.55%	18.28%	<.01
1998	21.99%	14.62%	19.86%	<.01
1999	23.13%	58.71%	33.43%	<.01
Member type				
Employee	40.76%	38.68%	40.16%	<.01
Spouse	22.02%	17.55%	20.73%	<.01
Dependents	37.21%	43.77%	39.11%	<.01
4–11 years	15.76%	27.97%	19.30%	<.01
12–18 years	15.94%	14.24%	15.45%	<.01
Other	5.51%	1.57%	4.37%	<.01
County race/ethnicity				
White				
0–25%	0.49%	0.84%	0.59%	<.01
26–50%	1.44%	7.00%	3.05%	<.01
51–75%	21.25%	35.73%	25.44%	<.01
76–100%	76.82%	56.43%	70.92%	<.01
Black				<.01
0–25%	91.70%	76.30%	87.24%	<.01
26–50%	8.02%	22.85%	12.31%	<.01
51–75%	0.26%	0.85%	0.43%	<.01
76–100%	0.01%	0.00%	0.01%	0.15
Hispanic				
0–25%	96.76%	93.35%	95.77%	<.01
26–50%	2.67%	5.52%	3.49%	<.01
51–75%	0.52%	1.13%	0.69%	<.01
76–100%	0.06%	0.01%	0.04%	<.01
Other				<.01
0–25%	99.94%	99.83%	99.91%	<.01
26–50%	0.02%	0.15%	0.06%	<.01
51–75%	0.04%	0.02%	0.03%	0.21
76–100%	0.01%	0.00%	0.01%	0.20
County mean household income	27,001	31,223	28,269	<.01

$p < .001$) and were more likely to receive their health care coverage as the employee rather than as the spouse or dependent (41 percent versus 37 percent, $p < .001$).

County Race and Income

Substantial differences in racial distribution and mean income between FFS and non-FFS plans were evident from county-level U.S. census data linked to the claims data. The mean household county income of patients covered by FFS plans (\$27,001) was significantly lower than that for patients covered by non-FFS plans (\$31,223) ($p < .001$). The racial distribution in counties for patients covered by FFS plans was less likely to be white than that of non-FFS plans.

Health Status

As expected given possibilities for adverse selection, patients in FFS plans appear to be sicker than those in non-FFS plans. Table 4.2 documents that patients in FFS plans have higher numbers of major diagnostic categories; higher Charlson comorbidity scores; and higher rates of comorbidities of allergic rhinitis, depression, gastrointestinal disorders, and migraine ($p < .001$ for all comparisons). The rate of comorbid anxiety was not statistically different between FFS and non-FFS plans ($p = 0.78$). Qualitatively similar patterns were evident both for patients age 4 to 11 and those age 12 to 64, although differences were typically larger for adults than for children.

Copayments

Table 4.3 indicates that prescription drug copayments are significantly higher in non-FFS plans than in FFS plans for both asthma medications and nonasthma medications. Across all drugs and all years (1995–2000), the average out-of-pocket copayment made by patients in non-FFS plans was \$8.64 compared to \$5.20 in FFS plans ($p < .001$). As shown in figure 4.2, however, average controller/reliever copayment ratios were higher in FFS plans than in non-FFS plans, even as FFS plan beneficiaries had greater controller/reliever medication utilization ratios (see figure 4.1). In both types of plans, the controller/reliever copayment ratio has been rising over time along with the increased use of controller medications.

The mean copayments reported in table 4.3 mask considerable variation in copayments over time and across plans. Figure 4.3 illustrates that out-of-pocket copayments for asthma medications have

Table 4.2
Comorbidities among asthma patients by insurance plan type, 1995–2000

	FFS	Non-FFS	Total	<i>p</i>
All patients, <i>N</i>	44,926	18,305	63,231	NA
Number of major diagnostic categories	6.26	5.35	6.00	<.01
Charlson comorbidity index	0.79	0.62	0.74	<.01
Asthma-specific comorbidities				
Allergic rhinitis	23.27%	18.67%	21.94%	<.01
Anxiety	2.39%	2.35%	2.38%	0.78
Depression	10.31%	8.17%	9.69%	<.01
GI disorders	24.55%	20.73%	23.45%	<.01
Migraine	6.02%	5.05%	5.74%	<.01
Patients age 4–11, <i>N</i>	7,084	5,123	12,207	NA
Number of major diagnostic categories	5.19	4.85	5.05	<.01
Charlson comorbidity index	0.55	0.51	0.53	<.01
Asthma-specific comorbidities				
Allergic rhinitis	25.72%	20.69%	23.61%	<.01
Anxiety	0.78%	0.49%	0.66%	0.05
Depression	4.29%	2.81%	3.67%	<.01
GI disorders	15.30%	14.50%	14.97%	0.22
Migraine	3.08%	3.10%	3.09%	0.93
Patients Age 12–64, <i>N</i>	37,842	13,182	51,024	NA
Number of major diagnostic categories	6.46	5.55	6.22	<.01
Charlson comorbidity index	0.84	0.66	0.79	<.01
Asthma-specific comorbidities				
Allergic rhinitis	22.81%	17.88%	21.53%	<.01
Anxiety	2.69%	3.07%	2.79%	0.02
Depression	11.44%	10.26%	11.13%	<.01
GI disorders	26.28%	23.15%	25.47%	<.01
Migraine	6.57%	5.81%	6.38%	<.01

been consistently higher for patients in non-FFS plans compared to patients in FFS plans. Although patients in both types of plans experienced significant jumps in out-of-pocket copayments beginning in 1998, the gap between FFS and non-FFS plans appears to have narrowed. In addition to these time trends, there is high variation in copayment levels for specific drugs within a year. For example, 1999 copayments for fluticasone, an inhaled corticosteroid (a controller medication), varied from \$2 in one plan to \$28 in another. Similarly, 1999 copayments for albuterol, a short-acting beta-agonist (a reliever

Table 4.3
Plan-level average copayments by insurance plan type, 1995–2000

	FFS	Non-FFS	Total	<i>p</i>
N ^a	33,828	18,214	52,042	NA
Prescription copayment	5.20	8.64	6.20	<.01
For asthma-related drugs	5.06	8.04	5.92	<.01
For non-asthma-related drugs	5.24	8.83	6.28	<.01
Outpatient visit copayment	7.71	8.10	7.84	<.01
For asthma-related visits	7.83	8.25	7.97	<.01
For non-asthma-related visits	7.69	8.09	7.83	<.01
Emergency room visit copayment	10.24	13.03	11.22	<.01
For asthma-related visits	15.25	13.92	14.79	<.01
For non-asthma-related visits	9.89	12.94	10.96	<.01
Inpatient visit copayment	16.12	2.78	11.45	<.01
For asthma-related visits	18.07	1.79	12.37	<.01
For non-asthma-related visits	15.92	2.94	11.38	<.01

^aAverage copayment was not available for all plans.

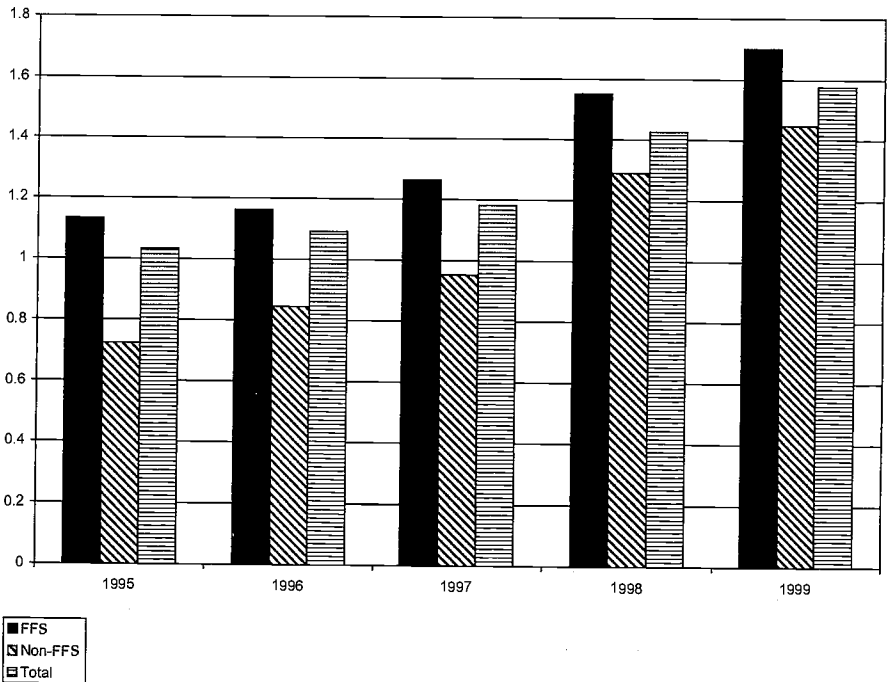


Figure 4.2
Controller/reliever copayment ratios by plan type and year

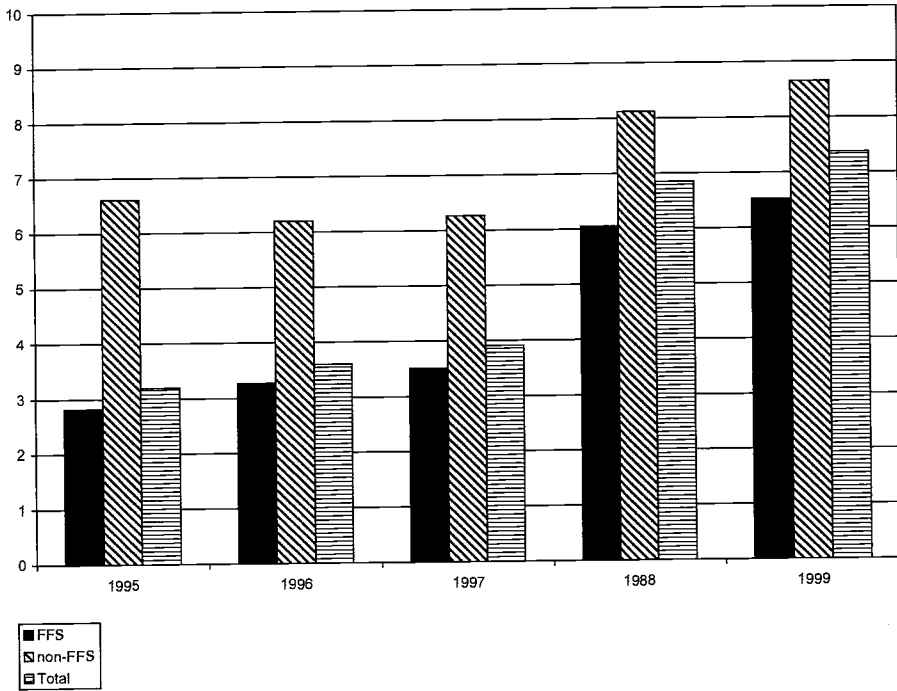


Figure 4.3
Trends in asthma medication copayments by plan type

medication typically sold as a generic), ranged from \$2 to \$12 across plans.

Figure 4.4 reports the trend in the ratio of total payments (third-party payer plus patient copayment) for controller versus reliever prescription drug claims alongside the trend in the ratio of patient out-of-pocket copayments for controller versus reliever medications. Both ratios show an upward trend, largely reflecting the increased use of controller medications. Figure 4.4 clearly indicates, however, that between 1995 and 1999, the total payment ratio rose at a steeper rate than the copayment ratio. This trend suggests that, although large employers and health plans were using copayments to help manage rising prescription drug costs, at least between 1995 and 1999 they appeared to be absorbing proportionately more of the cost increase than they transferred to beneficiaries in the form of higher copayments. Put another way, the practice of medicine improved in the sense of both FFS and non-FFS beneficiaries increasing the controller/reliever

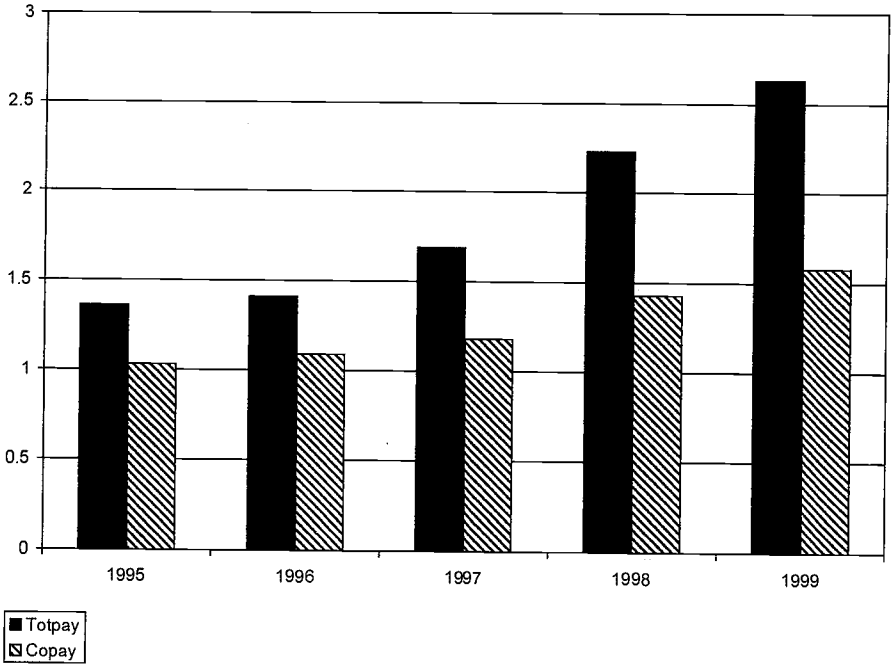


Figure 4.4
Trends in total payment versus copayment ratios

utilization ratio, and while beneficiaries experienced increases in controller/reliever copayment ratios, third-party payers bore an even larger increase in controller/reliever payments.

Average copayments for outpatient visits, emergency room visits, and inpatient visits also differed between non-FFS and FFS plans (table 4.3). Although statistically significant, copayments for outpatient visits and emergency room visits were fairly similar across non-FFS and FFS plans. By contrast, copayments for inpatient stays were significantly and materially higher among patients covered by FFS plans than were those covered by non-FFS plans (\$16.12 versus \$2.78, respectively, $p < .001$). Hence, while non-FFS plans had significantly higher copayment rates for prescription drugs relative to FFS plans, the opposite took place in terms of inpatient copayments.

Medication Use

Table 4.4 summarizes the medication use of asthma patients covered by non-FFS and FFS health plans. Patients covered by FFS plans have a

Table 4.4

Annualized asthma medication claims by insurance plan type, 1995–2000

	FFS	Non-FFS	Total	<i>p</i>
<i>N</i>	44,926	18,305	63,231	NA
Ratio of controller to reliever	1.49	1.17	1.40	<.01
Number of asthma prescriptions	4.89	4.17	4.68	<.01
Bronchodilators	0.71	0.37	0.61	<.01
Oral steroids	0.45	0.45	0.45	0.69
SABAs	2.14	2.11	2.13	0.20
Inhaled steroids	1.22	0.90	1.13	<.01
Luekotriene modifiers	0.24	0.28	0.25	<.01
Anticholinergics	0.12	0.05	0.10	<.01
Estimated days of therapy				
Bronchodilators	21.99	10.43	18.64	<.01
Oral steroids	5.91	4.59	5.53	<.01
SABAs	46.44	41.75	45.09	<.01
Inhaled steroids	30.19	20.96	27.51	<.01
Luekotriene modifiers	8.89	9.09	8.94	0.61
Anticholinergics	2.89	1.07	2.36	<.01
Units dispensed				
Bronchodilators	34.05	14.86	28.50	<.01
Oral steroids	18.65	18.16	18.51	0.44
SABAs	78.01	79.50	78.44	0.37
Inhaled steroids	31.33	21.46	28.47	<.01
Luekotriene modifiers	12.73	12.44	12.65	0.63
Anticholinergics	5.26	2.36	4.42	<.01
Selection of asthma medication				
Bronchodilators	15.94%	9.66%	14.12%	<.01
Oral steroids	23.71%	26.42%	24.50%	<.01
SABAs	76.57%	80.63%	77.75%	<.01
Inhaled steroids	35.00%	31.95%	34.11%	<.01
Luekotriene modifiers	5.88%	6.62%	6.09%	<.01
Anticholinergics	4.14%	2.13%	3.56%	<.01

higher ratio of controller-to-reliever medications than patients in non-FFS plans (1.49 versus 1.17, $p < .001$), as well as a higher number of annualized asthma prescriptions (4.89 versus 4.17, $p < .001$). With the exception of leukotriene modifiers (the most recent new therapeutic agents), patients in FFS plans have more days of therapy and higher units dispensed for each therapeutic class of asthma medication than do patients in non-FFS plans ($p < .001$ for all comparisons). For leukotriene modifiers, days of therapy and units dispensed were higher for asthma patients covered by non-FFS plans ($p < .001$).

The most commonly prescribed asthma medications were the short-acting beta-agonists (SABAs). Patients in non-FFS plans were somewhat more likely than patients in FFS plans to be prescribed SABAs, oral steroids, and leukotriene modifiers; they were less likely to be prescribed bronchodilators, inhaled steroids, and anticholinergics ($p < .001$ for all comparisons).

Health Care Utilization

Table 4.5 reports the nonprescription drug health care utilization of patients in non-FFS and FFS plans. For each measure—emergency room visits, hospitalizations, hospital days, and outpatient visits—annualized utilization was higher in FFS plans than it was in non-FFS plans ($p = 0.09$ for emergency room visits). Thus, despite higher controller/reliever medication ratios, health care utilization was higher in FFS plans than it was in non-FFS plans. This association is likely to be confounded, however, by the greater average age and level of disease severity of patients covered by FFS plans (table 4.2).

VII. Econometric Findings

FFS Model

Table 4.6 reports the results of a multinomial logit model of the log odds of a patient receiving controller medication alone, or a controller and a reliever (combination therapy), relative to a reliever alone. Residents of the North Central region are significantly less likely to be treated with controllers alone or a combination of controllers and relievers than with relievers alone ($p < 0.01$). Females were significantly less likely to receive a combination treatment rather than a reliever-only treatment.

Table 4.5

Annualized per-beneficiary, asthma-related health care utilization by insurance plan type, 1995–2000

	FFS	Non-FFS	Total	<i>p</i>
<i>N</i>	44,926	18,305	63,231	NA
Measures of health care use				
Emergency room visits	0.38	0.37	0.38	0.09
Hospitalizations	0.08	0.05	0.07	<.01
Hospital days	0.36	0.23	0.32	<.01
Outpatient visits	5.46	1.40	4.29	<.01

Table 4.6Multinomial logit model of medication selection: patients in FFS plans^a

	Controller Alone		Controller + reliever	
	Parameter estimate	Pr > t	Parameter estimate	Pr > t
Intercept	-3.4707	<0.001	-2.2667	<0.001
Demographics				
Region North central	-0.3932	<0.001	-0.1591	0.0020
Region Northeast	-0.0290	0.8430	-0.0014	0.9900
Region West	-0.1649	0.1410	-0.0199	0.8070
Female	-0.0119	0.7700	-0.1062	<0.001
Adult	0.8893	<0.001	0.2170	<0.001
Clinical characteristics				
Allergic rhinitis	0.5128	<0.001	0.6086	<0.001
Migraine	-0.0270	0.7380	-0.0390	0.5220
Depression	-0.1795	0.0060	-0.0067	0.8850
GI disorders	-0.0537	0.2740	-0.1022	0.0050
Sinusitis	-0.0655	0.1520	0.0110	0.7400
Anxiety disorders	-0.1843	0.1320	-0.2209	0.0150
3-digit ICD-9 codes	0.0483	<0.001	0.0481	<0.001
County characteristics				
County average income \$15–20K	0.2960	0.3290	-0.0804	0.6810
County average income \$20–25K	0.4274	0.1550	0.0241	0.9010
County average income \$25–35K	0.3661	0.2240	0.0713	0.7140
County average income >\$35K	0.8503	0.0050	0.1602	0.4170
Coplay variables				
Ratio of controller/reliever copayment	-0.0667	0.5030	0.0308	0.6820
Tax provider ID controller, %	6.4705	<0.001	1.1769	0.1840
Tax provider ID combination, %	1.0605	0.0320	4.1513	<0.001
Chi2(3) ^b	60.3200	<0.001	164.5700	<0.001
LR chi2(38)	1816.3600	<0.001		
Psuedo-R2	0.0341			
Number of observations	26,379			

^aReference category is reliever alone.^bChi-square test for significance of coplay variables.

Adults were more likely to receive a controller alone or a combination treatment (with the former being particularly large) than a reliever-only treatment.

We also included county-level variables from the census as proxies for the income of patients—variables not available directly from the claims. Living in a county with the highest category of average income (> \$35,000) significantly increased the odds of receiving a controller-only treatment but had no significant effect on combination treatment relative to reliever-only treatments. None of the other county characteristic income variables was statistically significant.

The presence of allergic rhinitis increased the odds of getting a controller alone or a combination therapy relative to reliever-only therapy. Comorbidities of migraine or sinusitis had no significant impact on choice of drug therapy. Depression reduced the odds of getting controller-only therapy relative to reliever alone but had no significant impact on combination therapy. The presence of an anxiety disorder increased the odds of getting a combination therapy ($p < 0.02$) but had no significant impact on the odds of receiving a controller alone. The number of unique three-digit ICD-9 codes was positively associated with the odds of getting a controller alone or a controller plus reliever relative to reliever-only therapy.

The ratio of plan mean controller to mean reliever copay had no significant impact on drug treatment choice ($p > 0.50$). In results not shown in a table or figure, this lack of significance persisted when mean copays were entered separately in levels or in various other forms. On the other hand, the medication ratios measuring physician/provider prescribing preferences for controller alone ($p < 0.01$) or for combination treatment ($p < 0.01$) were positive, large, and highly significant determinants for the probability of the patient receiving that therapy relative to reliever-only therapy. In terms of cross-effects, only physician/provider prescribing preferences for combination therapy positively and significantly affected the probability of a patient receiving controller-only therapy; physician/provider preferences for controller-only therapy had no significant impact on the patient's probability of receiving combination treatment ($p = 0.184$). The chi-square test statistic for the null hypothesis that coefficient estimates on the copay and physician/provider prescribing preference variables are simultaneously equal to zero indicate decisive rejection in both equations ($p < 0.01$).

Non-FFS Model

Table 4.7 reports the results of the corresponding multinomial logit model for patients in non-FFS plans. Living in the West reduced the odds of receiving either controller-only or combination treatment relative to reliever-only therapy. Residents of the North Central region were more likely to receive combination treatment but not controller-only therapy, relative to reliever alone treatment. As in the FFS case, females were significantly less likely to receive combination therapy, relative to reliever-only therapy, and adults were more likely to receive a controller alone or a combination therapy (with the former being particularly large), relative to reliever-only treatment. None of the county-level income variables from the census was statistically significant.

The presence of allergic rhinitis significantly increased the odds of getting controller-only or combination therapy relative to reliever-only treatment; the effects of other comorbidities were similar in this non-FFS regression to those in the FFS analysis. Higher numbers of unique three-digit ICD-9 codes significantly increased the odds of getting a controller-only or combination therapy relative to reliever-only treatment.

As with the FFS model, the ratio of plan mean controller to mean reliever copayment had no significant impact on the probability of receiving controller-only therapy, although it did have a positive and significant impact on the odds of receiving combination treatment. On the other hand, both medication percentages measuring provider prescribing preferences were highly significant determinants of the probability of a patient receiving the corresponding therapy; while these own effects were positive and significant, both cross-effects were not statistically significant. The chi-square test statistics for the null hypothesis that coefficients on the copay and provider prescriber preference variables simultaneously equal zero indicate decisive rejection in both equations ($p < 0.01$).

Turning now to the log total expenditure regressions for FFS (table 4.8) and non-FFS (table 4.9) beneficiaries, we provide parameter estimates with and without the sample selectivity adjustments for each of the three treatment arms. In the FFS regressions of table 4.8, we note first that parameter estimates on the lambdas (conditional expected values of the residuals derived from each of multinomial logistic equations) are negative and statistically significant (all $p < 0.001$). Not surprisingly, differences between the selectivity-adjusted and unadjusted

parameter estimates are particularly large for those variables significantly affecting prescriber therapy in the first-stage multinomial logit equations. For example, coefficient estimates on the adult variable in all three equations are much smaller in the selectivity-adjusted than in the unadjusted regressions; this finding also holds for the allergic rhinitis variable, where sign changes occur.

However, when a Hausman test is conducted to test whether the coefficient estimates differ significantly in the selectivity-adjusted and unadjusted OLS regressions with the FFS sample, the null hypothesis of parameter equality is not rejected. Indeed, the test statistic is negative, a reflection of the fact that the difference in diagonal elements of the variance-covariance matrices can be negative in given samples, even though asymptotically they are positive in expectation.

In terms of the non-FFS sample (table 4.9), results are qualitatively similar to those in the FFS population. In particular, estimates of the three lambdas are negative and significant in all three treatment equations ($p < 0.001$), with the exception of the reliever-only equation, where the negative estimate is not statistically significant. Two of the three Hausman test statistics on parameter equality in the selectivity-adjusted and unadjusted OLS regressions are positive, but in all three cases the null hypothesis is not rejected.

VIII. Discussion and Limitations

This study describes the patterns of medication use among patients with asthma, factors affecting the type of drug therapy prescribed for these patients, and the effects on total health care expenditures using a data set containing medical claims and encounters for more than 63,000 asthma patients. The average controller-to-reliever ratios were found to be greater than 1 for members of non-FFS (1.17) and FFS (1.49) plans. The controller/reliever medication ratio has been consistently rising over time, suggesting that the clinical practices it embodies reflects a considerable degree of acceptance of the consensus guidelines and the supporting research literature.

Holding other factors equal, one would theoretically expect higher relative prices for controller-to-reliever medicines to be associated with a lower controller-to-reliever ratio. However, teasing this conclusion out of the data statistically is complex. Shifts in the composition of drugs in the controller and reliever classes over time and changes in plan design could cause the ratio of controller-to-reliever copays either

Table 4.7
Multinomial logit model of medication selection: patients in non-FFS plans^a

	Controller alone		Controller + reliever	
	Parameter estimate	Pr > t	Parameter estimate	Pr > t
Intercept	-6.1203	<0.001	-5.2240	<0.001
Demographics				
Region: North Central	-0.2239	0.0880	-0.1658	0.0440
Region: Northeast	-0.2124	0.0960	-0.0735	0.3350
Region: West	-0.2940	0.0170	-0.3179	<0.001
Female	-0.0941	0.2870	-0.1897	<0.001
Adult	1.1020	<0.001	0.2973	<0.001
Clinical characteristics				
Allergic rhinitis	0.8721	<0.001	0.7965	<0.001
Migraine	-0.0033	0.9870	0.1745	0.2130
Depression	0.0975	0.5540	-0.1856	0.1160
GI disorders	-0.0568	0.6290	-0.1773	0.0230
Sinusitis	0.0685	0.5400	0.0651	0.3690
Anxiety disorders	-0.6812	0.0450	-0.3315	0.1250
3-digit ICD-9 codes	0.0667	<0.001	0.0632	<0.001
County characteristics				
County average income \$15–20K	-0.2739	0.5990	-0.2224	0.5050
County average income \$20–25K	-0.1448	0.7660	-0.1310	0.6770
County average income \$25–35K	-0.1357	0.7770	-0.2558	0.4080
County average income >\$35K	-0.3545	0.4770	-0.3857	0.2280
Copay variables				
Ratio of controller/reliever copayments	0.0816	0.7120	0.6444	<0.001
Tax ID prescriber controller, %	11.4306	0.0030	1.0697	0.6640
Tax ID prescriber combination, %	6.6881	0.0650	11.1009	<0.001
Chi2(3)	16.1400	0.0011	53.6800	<0.001
LR chi2(38)	598.6700	<0.001		
Psuedo-R2	0.0463			
Number of observations	6,768			

^aReference category is reliever alone.

Table 4.8
 Log-linear regression results: patients in FFS plans [dependent variable: $\log(\text{total payments})$]^a

	Controller alone			Controller + reliever			Reliever alone					
	Selectivity adjusted		Not adjusted	Selectivity adjusted		Not adjusted	Selectivity adjusted		Not adjusted			
	Parameter estimate	Pr > t	Parameter estimate	Pr > t	Parameter estimate	Pr > t	Parameter estimate	Pr > t	Parameter estimate	Pr > t		
Intercept	1.9666	0.1070	6.0066	<0.001	5.1129	<0.001	6.1208	<0.001	2.1427	<0.001	5.0938	<0.001
Demographics												
Region: North Central	0.2803	<0.001	0.0633	0.1480	0.2251	<0.001	0.0277	0.2860	0.2460	<0.001	-0.0547	0.1360
Region: Northeast	0.1217	0.3370	0.0510	0.6300	0.0421	0.5890	-0.0277	0.6590	-0.0985	0.3030	-0.1831	0.0160
Region: West	0.0961	0.2430	-0.0021	0.9790	0.0357	0.6270	-0.0488	0.2720	-0.0528	0.5290	-0.1999	<0.001
Female	-0.0138	0.6880	-0.0282	0.3620	0.0364	0.1000	0.0018	0.9160	0.0295	0.4590	0.0208	0.2720
Adult	0.0208	0.8410	0.6823	<0.001	0.2500	0.0010	0.6550	<0.001	0.1375	0.0510	0.6722	<0.001
Clinical characteristics												
Allergic rhinitis	-0.1254	0.0030	0.1099	0.0010	-0.1567	<0.001	0.1311	<0.001	-0.0451	0.0180	0.1312	<0.001
Migraine	-0.0165	0.7140	-0.0320	0.5810	0.0102	0.8330	-0.0150	0.6480	-0.0002	0.9950	-0.0284	0.5050
Depression	0.3995	<0.001	0.3139	<0.001	0.3262	<0.001	0.2709	<0.001	0.4994	<0.001	0.4013	<0.001
GI disorders	0.0789	0.0090	0.0648	0.0710	0.1248	<0.001	0.0992	<0.001	0.0661	0.1720	0.0460	0.0640
Sinusitis	0.0539	0.0510	0.0222	0.5120	-0.0033	0.8630	-0.0139	0.4530	0.0220	0.3810	-0.0107	0.6360
Anxiety disorders	0.1709	0.1370	0.0651	0.4730	0.2036	0.0100	0.0827	0.1090	0.3699	<0.001	0.2874	<0.001
3-digit ICD-9 codes	0.0877	<0.001	0.1055	<0.001	0.0763	<0.001	0.0986	<0.001	0.1119	<0.001	0.1324	<0.001
County characteristics												
County average												
income \$15-20 K	-0.1565	0.6690	-0.0311	0.8940	0.0583	0.6350	0.0944	0.3860	0.0111	0.9420	0.1220	0.3730
County average												
income \$20-25 K	-0.2616	0.4660	-0.0493	0.8310	-0.0396	0.7390	0.0696	0.5190	-0.0803	0.5820	0.1146	0.4000
County average												
income \$25-35 K	-0.1384	0.6950	0.0375	0.8710	-0.0055	0.9670	0.0906	0.4010	-0.0379	0.8140	0.1104	0.4190
County average												
income >\$35 K	-0.4295	0.2400	-0.0510	0.8270	-0.2139	0.1420	0.0553	0.6140	-0.3223	0.0290	0.0816	0.5560

Correlations									
Lambda (1)	-3.1896	<0.001	-7.0098	<0.001	-8.9698	<0.001			
Lambda (2)	-10.5181	<0.001	-4.1839	<0.001	-8.2394	<0.001			
Lambda (3)	-7.8338	<0.001	-5.4709	<0.001	-3.1968	<0.001			
R-square		0.4597		0.4791					
Hausman test									
statistic		-13.9200		<0.001		<0.001		62.0700	<0.001
Number of									
observations		3,903		11,427				11,049	

^a Lambda is the conditional expected values of the residuals derived from the multinomial logit model of controller alone or controller + reliever, relative to reliever alone. P-values are derived from bootstrapped standard errors.

Correlations								
Lambda (1)	-2.3181	0.0000	-3.4653	0.0010	-1.1454	0.4450		
Lambda (2)	-5.6860	0.0000	-2.1676	<0.001	-3.9541	<0.001		
Lambda (3)	-7.3977	0.0000	-5.0881	<0.001	-1.9950	<0.001		
R-square		0.4563			0.3806		0.3872	
Hausman test		16.2200			-4.8800		3.3300	0.9997
statistic			0.4381					
Number of observations		711			2.881			3.176

^aLambda is the conditional expected values of the residuals derived from the multinomial logit model of controller alone or controller + reliever, relative to reliever alone. P-values are derived from bootstrapped standard errors.

to rise or to fall over time. After controlling for other variables, we do not find a statistically significant relationship between out-of-pocket copayments and asthma treatment patterns. Figure 4.4 indicates that total payments (third-party payer plus patient copay) have been rising more rapidly than copayments only, suggesting that health plans and large employers are reluctant to increase copayments for covered beneficiaries at the same rate that total payments have increased. In this sense and over this 1995–1999 period, health plans and payers have contributed to greater diffusion of guideline-compatible treatments that favor increases in the controller-to-reliever ratio.

The observation that the prescribing of all classes of asthma medications (except leukotriene modifiers) was greater among members of FFS plans is generally consistent with the findings that these patients are sicker than their counterparts in non-FFS plans, as measured by the number of comorbid conditions and higher levels of health care utilization. Asthma patients covered by FFS health plans made more extensive use of all other types of health services that we examined, including inpatient hospitalizations, use of emergency services, and ambulatory visits.

The principal objective of this study has been to examine whether and how the characteristics of health plan coverage as part of the employee benefits program affects the therapy selection decision among patients with asthma. Most of the clinical literature now suggests that patients with asthma experience more favorable clinical courses when they make regular use, often several times daily, of inhaled corticosteroids, leukotriene modifiers, and other medications that control inflammation and reversible airway disease. In the descriptive analysis, we found that the controller-to-reliever ratio continued to rise (and its increase even accelerated in recent years) despite rising medication copays. However, this apparent association between mean copayments at the plan level and plan-level controller-to-reliever ratios is potentially endogenous. For example, if mean copayments are higher for controller medications than they are for reliever medications, growing use of controllers would result in a rising mean copayment ratio for controller-to-reliever medications. That is, at the plan level, the direction of influence between the controller-to-reliever copayments and the controller-to-reliever ratio could go in either direction, or even both ways.

To reduce the endogeneity problem, we examined the effect of plan-level copayment variables on individual treatment choices. When we

did so, no statistically significant association was found. It is possible that this lack of association resulted from an understatement of the size of out-of-pocket copayments. This understatement is due to the averaging of patient copays across asthma drugs and years at the plan level, an effort we undertook to reduce the number of degrees of freedom consumed by plan-, drug-, and year-specific copayments. Most of the large copayment increases have occurred since 1999. Plans that instituted large copayment increases for certain asthma drugs may indeed have shifted asthma treatment patterns. In our analysis, however, these more recent changes were aggregated with the earlier experience of patients where copayment changes were not as common nor as large. Thus, we expect that a downward bias exists in our estimate of the copayment effect and that it deserves further scrutiny. We have re-estimated our models using only 1998–2000 data, and while we obtained results on the copay variables that trended more toward becoming statistically significant, they were not significant at usual p values. We suspect that these copay variables will become more significant as additional years of post-2000 data are added to the sample.

On the other hand, we found that physician/provider prescribing patterns were strongly associated with patient treatment patterns, although the nature of this association differed somewhat for patients in FFS and non-FFS plans. We leave it for future research to assess whether (controlling for physician/practice prescribing preferences) differences in copayment benefit design across plans serviced by the same physician/practice result in statistically different treatment patterns. Of course, it is possible instead that physician/practice effects are dominant regardless of the variation in the copayment benefit designs of the plans covering the patients they treat. Resolution of this issue will have important implications for the effectiveness of plan design in controlling health care costs.

In addition to the specific statistical issues already discussed, the conclusions from our analysis should be viewed in light of the limitations common to most retrospective studies. In particular, although we have attempted to correct for selection bias associated with patients having higher versus lower controller-to-reliever ratios, other sources of selection bias may remain. For example, the MarketScan™ claims data used in the analysis lack clinical measures of symptom severity (e.g., results of spirometry tests). In addition, missing data on within-region location (e.g., rural, urban, suburban) could have introduced

bias because of geographical variations in asthma treatment practice patterns.

Although future work is unlikely to be able to control for all sources of selection bias in retrospective database studies of the type reported here, the physician/provider prescribing pattern variables appear to offer promise as identifying variables. For example, future work could use instrumental variables or parametric selection models to control for unobserved factors associated with both treatment selection and outcomes when examining the effects of asthma treatments on health care utilization. This general approach is also likely to have broad applicability to other medical conditions and treatments.

Notes

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1. See Zeckhauser (1970) for a seminal discussion. For more recent analyses, see the exchanges among Nyman (1999), Blomqvist (2001), and Manning and Marquis (1996, 2001).
2. For evidence from the RAND Health Insurance Experiment, see Newhouse and the Insurance Experiment Group (1993); Manning et al. (1986); Leibowitz, Manning, and Newhouse (1985); and Marquis (1985). More recent evidence for a more aged population is given in Feenberg and Skinner (1994).
3. The term *copayment* typically refers to fixed payments by the individual for service received (e.g., \$5 for each generic prescription); *coinsurance* typically refers to a fixed percentage payment by the individual (e.g., 20 percent of the retail price of the drug). In this paper, we use the term *copayment* to refer to any out-of-pocket payments by consumers for drugs or other services.
4. See Berndt (2002); see also Berndt (2001).
5. See National Institute for Health Care Management (2002).
6. For policies and the impact of changing prescription drug cost-sharing provisions in Canada, see Alan et al. (2002), Grootendorst (2002), Poirier et al. (1998), and Tamblyn et al. (2001).
7. For further discussion, see Berndt (2002) and the references cited therein.
8. See Pharmacy Benefit Management Institute (2001).
9. For related empirical evidence (much of it quite dated), see Harris et al. (1990); Johnson et al. (1997); Leibowitz, Manning, and Newhouse (1985); Marquis (1985); and Smith (1993).

10. For related empirical analyses, see Keeler et al. (1985), Leibowitz et al. (1985), and Newhouse and the Insurance Experiment Group (1993).
11. See, for example, Levine, Campen, Millares, and Barrueta (2000).
12. See Gottlieb, Belser, and O'Connor (1995); Frischer et al. (1999); and Shelley et al. (2000).
13. See Jain and Golish (1996); Majeed, Ferguson, and Field (1999); Nestor et al. (1998); and Suissa et al. (1994).
14. See Majeed, Ferguson, and Field (1999); Nestor et al. (1998); Suissa et al. (1994); Laumann and Bjornson (1998); and Donahue et al. (1997).
15. See Frischer et al. (1999) and Shelley et al. (2000).
16. See, for example, Gottlieb, Belser, and O'Connor (1995).
17. For further details, see D'Hoore, Bouckaert, and Tilquin (1996).
18. See, for example, D'Hoore, Bouckaert, and Tilquin (1996) and Beddhu et al. (2000).

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