Copayment Level and Compliance With Antihypertensive Medication: Analysis and Policy Implications for Managed Care

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Objective: To measure the impact of medication copayment level and other predictors on compliance with antihypertensive medications, as measured by the medication possession ratio.

Study Design: Retrospective observational analysis.

Methods: We used claims data from a large managed care organization. The identification of subjects was based on a diagnosis of hypertension and a filled prescription for antihypertensive medication between January 1999 and June 2004. Multivariate logistic regression models were used to evaluate copayment level and patient characteristics as predictors of medication compliance.

Results: Analysis of data for 114 232 patients filling prescriptions for antihypertensive medications revealed that compliance was lower for drugs in less preferred tiers. Relative to medications with a $5 copayment, the odds ratio (95% confidence interval) for compliance with drugs having a $20 copayment was 0.76 (0.75, 0.78); for drugs requiring a $20 to $165 copayment, the odds ratio for compliance was 0.48 (0.47, 0.49). Medication compliance also differed by patient age, morbidity level, and ethnicity, as well as by medication therapeutic class—with the best compliance observed for angiotensin receptor blockers, followed by calcium channel blockers, β-adrenergic receptor antagonists (β-blockers), angiotensin-converting enzyme inhibitors, and last, thiazide diuretics.

Conclusion: Copayment level, independent of other determinants, was found to be a strong predictor of compliance with antihypertensive medications, with greater compliance seen among patients filing pharmacy claims for drugs that required lower copayments. This finding suggests that patient use is sensitive to price. The potential impact on compliance should be considered when making pricing and policy decisions.

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Poor blood pressure control raises the risk of stroke, myocardial infarction, and heart failure for the 65 million Americans with hypertension.[1] Efforts to control hypertension through the use of antihypertensive medications are considered to be among the most efficacious. Because hypertension often is asymptomatic, however, poor patient compliance with pharmacologic treatment has consistently limited the effectiveness of these interventions.[2] Other factors, including patient forgetfulness, the number of daily doses, side effects, and/or class of agent, also affect patient compliance.[3-6] Substantial economic costs are associated with noncompliance.[7,8]

In previous studies, increasing levels of patient cost-sharing have been associated with lower medication compliance and persistency.[8-14] However, our study is the first comprehensive analysis of the effect of copayment level on medication compliance for all classes of antihypertensive drugs. Our analysis also links data from medical claims to derive an estimate of patient morbidity level, from surveys to include a measure of self-reported ethnicity for a subset of members, and from enrollment files for information on age and sex and type of coverage.

METHODS

Study Population

The study sample was drawn from members of a managed care organization covering approximately 650 000 members. Study eligibility required participants (1) to have received a medical diagnosis of hypertension on any type of claim, professional or facility, and (2) to have filled at least 1 antihypertensive medication prescription with at least a 15-day supply between January 1999 and June 2004. We did not require continuous enrollment; instead, we excluded days without coverage from the compliance calculation.

Data Sources and Variable Definitions

Patient information such as age, sex, and type of coverage (HMO, preferred provider organization [PPO], Medicare cost contract) was obtained from administrative data. The diagnosis of hypertension and the data to determine comorbidity level were obtained from medical claims databases. Patient morbidity level was determined by using *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes

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according to the Johns Hopkins Adjusted Clinical Group methodology; levels of 4 or 5 on the 5-point scale were considered high morbidity.[15]

Prescription data on medication names, fills, and number of days supply were obtained from pharmacy claims databases. Compliance was assessed for each specific therapeutic class. Hence, if a patient switched drugs within a therapeutic class, the number of days supply for the 2 drugs would be added together. If they switched to a new therapeutic class, the days supply would be counted toward the new class. From these data, we calculated a medication possession ratio for each prescription based on the number of days supply from the index prescription fill, divided by the number of days to the last prescription fill (calculated as the fill date of the last prescription claim minus the fill date of the first prescription claim).[10] This approach, in which a medication possession ratio of 0.8 was deemed compliant, has been used in other compliance studies.[10,16,17] The overall medication possession ratio was obtained by summing the total days of compliance per year across all prescriptions and dividing by the number of days of drug coverage within the year.

Formulary tier was used as an indicator of copayment level. Three copayment levels were possible: $5 for tier 1, generic agents; $20 for tier 2, preferred branded agents; and a variable copayment for nonpreferred branded agents (tier 3) that reflected the difference between the price of the nonpreferred brand and the preferred brand, ranging from $20 to $165.

Ethnicity and education data were drawn from self-reported satisfaction surveys available for 33% of the study population. These mail surveys, which used the 17 ethnic categories developed by the Hawaii Department of Health's Hawaii Health Surveillance Program, asked health plan members to indicate each of the categories that applied to them. Data from these respondents were analyzed to determine medication compliance for the following 6 main ethnic groups: Japanese, Chinese, Caucasians, Hawaiians (this group includes all those who claim Hawaiian ethnicity regardless of other ethnicity selections, because of the small number of pure Hawaiians), Filipinos, and Koreans. Those who claimed membership in more than one of these groups, except Hawaiian, were categorized as "Mixed" ethnicity. Those who indicated membership in any other ethnic group were categorized as "Other."

Statistical Methods

Patient characteristics were analyzed according to copayment level; if members switched drugs over time, they could appear in several categories. The likelihood of compliance with antihypertensive medications was estimated as a logistic function of copayment level, patient age, sex, race/ethnicity, morbidity level (low/high), type of insurance coverage, and therapeutic class of medication. All analyses were conducted using Stata, version 8 (StataCorp, College Station, Tex). Results were considered significant at the $P < .05$ level.

RESULTS

Descriptive Analysis of the Study Population

A total of 114 232 patients met study inclusion criteria. The mean age of the study sample was 64 years (SD = 14 years; range, 18 to 107 years). Approximately 50% of all patients were female, and 25% had a high morbidity level. Approximately 70% of all patients were enrolled in the PPO, 28% in the HMO, and 2% in the Medicare cost contract plan. Of the 37 697 patients for whom ethnicity data were available, 42% were Japanese, 14% Hawaiian, 13% Caucasian, 12% Filipino, 8% Chinese, 4% Mixed, and 5% Other. A summary of patient characteristics, broken out by copayment level, is shown in **Table 1**.

The number of patients submitting pharmacy claims for antihypertensive medications was as follows: 58 809 (31.6%) for medications with a $5 copayment (tier 1); 66 486 (35.8%) for medications with a $20 copayment (tier 2); and 60 553 (32.6%) for medications with a $20 to $165 copayment (tier 3).

Characteristics of patients at each copayment level differed significantly ($P < .05$); however, the magnitude of these differences was small. Patients with pharmacy claims for tier 1 medications were slightly older (64.5 years vs 63.6 and 64.0 years for tiers 2 and 3, respectively), more likely to be female (51.3% vs <50% for the other 2 tiers), and more likely to have a high morbidity level (26.4% vs 25.6% and 21.1% for tiers 2 and 3, respectively). Patients filling prescriptions at the 3 copayment levels varied slightly by ethnic group. The percentage of Caucasian patients receiving tier 1 medications was slightly higher than the percentage of Caucasian patients in the overall study population (15.3% vs 13%). Filipino patients were more likely than other ethnic groups to have received tier 3 medications (13.4% vs 12%).

Analytical Results

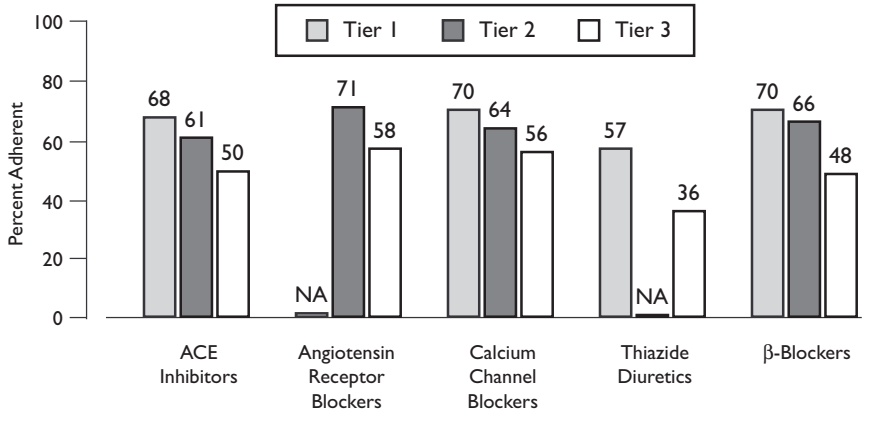
Unadjusted Medication Compliance. Overall compliance for antihypertensive agents was 66.8% in tier 1, 66.1% in tier 2, and 54.6% in tier 3. Compliance by therapeutic class of agent is shown in **Figure 1**. The therapeutic class with the highest compliance was the angiotensin receptor blockers, whereas thiazide diuretics had the lowest compliance. Therapeutic classes with the greatest disparities in compliance between the least ($5) and greatest ($20 to $165) copayment levels were β-

Table 1. Sociodemographic and Descriptive Characteristics by Copayment Level

Characteristics*	Copayment Level, $ 5	20	20-165
No. of patients submitting pharmacy claims for antihypertensive medications†	58 809	66 486	60 553
Age, %			
<40 y	3.4	3.1	3.3
40-64 y	48.3	51.5	50.3
65+ y	48.3	45.4	46.4
Female, %	51.3	48.2	49.5
High morbidity, %	26.4	25.6	21.1
Type of coverage, %			
Preferred provider organization	70.0	69.5	69.5
HMO	27.7	28.6	28.2
Medicare cost contract	2.3	1.9	2.2
Ethnicity, %‡			
Japanese	41.9	41.9	42.2
Caucasian	15.3	12.5	12.1
Hawaiian	13.6	14.8	13.8
Filipino	11.0	12.5	13.4
Chinese	7.5	8.1	8.1
Mixed	4.1	4.1	4.0
Other	5.3	4.6	4.8

*All group differences were statistically significant at $P < .05$.
†Patients may have been receiving antihypertensive drugs in more than 1 class at a time.
‡Ethnicity data were available for approximately 33% of all patients.

Figure 1. Medication Compliance by Therapeutic Class and Copayment Level



NA indicates that the tier is not available for the therapeutic class; β-blocker, β-adrenergic receptor antagonist; ACE, angiotensin-converting enzyme. Tier 1, $5 copayment for generic agents; tier 2, $20 copayment for preferred branded agents; tier 3, $20 to $165 copayment for nonpreferred branded agents.

adrenergic receptor antagonists (β-blockers) (70% vs 48%) and thiazide diuretics (57% vs 36%).

Compliance was also significantly associated with all patient characteristics examined, including age, sex, morbidity level, type of coverage, and ethnicity (**Table 2**). Groups that may need to be targeted because of low compliance include members under age 40 years (42.5% compliance), members with Filipino ethnicity (58.7% compliance), and members with HMO coverage (59.7% compliance).

Adjusted Odds Ratios for Medication Compliance. Adjusted odds ratios and 95% confidence intervals (CIs) for medication compliance by copayment level with respect to studied variables are summarized in **Table 3**. These odds ratios were adjusted to account for differences in tier, therapeutic class, and patient characteristics.

Relative to medications in tier 1, the adjusted odds ratio for compliance with medications in tier 2 was 0.76 (95% CI = 0.75, 0.78), and for medications in tier 3 it was 0.48 (95% CI = 0.47, 0.49) (**Figure 2**).

The adjusted odds ratio and 95% CIs for medication compliance were shown to increase with age, male sex, presence of low morbidity, and PPO enrollment; and compliance varied by ethnic group. Patients aged 40 to 64 years were nearly twice as likely to be compliant with medications as those age <40 years; patients aged 65 years or older were the most likely to remain compliant. Relatively little difference in compliance was observed by sex. Lower medication compliance was seen in those patients with high morbidity (ie, indicating the presence of other comorbid conditions) compared with patients with low comorbidity. Compared with whites, patients

of Japanese ethnicity were more likely to comply with treatment, whereas patients of Filipino and part Hawaiian ethnicity were less likely to comply.

Members of HMOs had lower compliance than members of PPOs. Relative to thiazide diuretics, the adjusted odds ratio for medication compliance was considerably higher for all other therapeutic classes.

DISCUSSION

This retrospective analysis demonstrated that compliance with antihypertensive drugs decreased significantly with increasing copayment levels. Better understanding of variable determinants of medication compliance may lead to better therapeutic management and improvements in the economic efficiency of healthcare provision. In our study, copayment level, as set by the pharmacy benefit design, was a strong predictor of compliance. We found that compliance decreased with increasing copayment level, even after adjustment for age, sex, morbidity level, ethnicity, type of medical care coverage, and therapeutic class of agent. There was no possibility for plan-selection bias (ie, patients favoring a particular plan with a lower copayment because they anticipated heavy medication usage and/or better medication compliance), because all members of the study population utilized the same drug formulary.

This study evaluated copayment level and medication compliance. It is possible that other drug benefit features (eg, use of a mail order pharmacy) could influence medication compliance independently of copayment level. To assess the potential for mail order pharmacy use to bias our results, we calculated the percentage of scripts purchased by mail order pharmacy for each formulary tier, as follows: 16.7% generic, 17.4% preferred, and 17.8% nonpreferred. These results did not differ significantly by tier, and we therefore concluded that use of a mail order pharmacy would not bias our analyses of the impact of copayment development level on medication compliance.

The impact of formulary placement on drug use has been documented before. Shrank and colleagues studied patients enrolled in 3-tier pharmacy benefit plans who received generic, preferred, and nonpreferred brand drugs when initiating chronic therapy for various conditions, including hypertension, to determine their level of adherence.[10] With a 1-year follow-up, this study concluded that patients who initiated therapy with generic and preferred drugs had 62% and 30% greater odds, respectively, of achieving adequate adherence compared with those who received nonpreferred drugs. Although we did not limit our study to patients receiving an initial prescription and we focused on the impact of antihypertensive medications, our study results support their findings that there is a steady decrease in compliance with increasing tier level. Our findings suggest that this difference is due to copayment level and not a difference between brand and generic drugs.

Table 2. Patient Characteristics Related to Compliance

Characteristic*	Percent Compliant
Age, y	
<40	42.5
40-64	61.0
65+	66.8
Sex	
Male	62.8
Female	63.2
Morbidity level	
Low	63.9
High	60.8
Type of coverage	
Preferred provider organization	64.2
HMO	59.7
Medicare cost contract	68.6
Ethnicity†	
Japanese	71.4
Caucasian	66.0
Hawaiian	62.4
Filipino	58.7
Chinese	67.4
Mixed	63.4
Other	63.0

*All group differences were statistically significant at $P < .05$.
†Ethnicity data were available for approximately 33% of all patients.

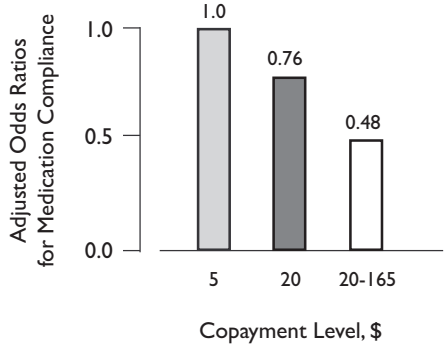
In another study, Huskamp et al recognized that changes in formulary administration may have dramatically different effects on utilization and spending, and in some instances may lead enrollees to discontinue therapy.[11] They compared utilization and spending on several classes of drugs in 2 employer-sponsored health plans and showed high discontinuation rates of drugs in a given class after the 2-tier formulary system was changed to a 3-tier system (ie, with a change in copayment levels). Landsman et al compared a reference drug benefit program (ie, one that undertook no changes) with plans that changed drug copayment levels as a result of changing from a 2-tier to a 3-tier formulary design.[12] A decline in the use of retail prescription medications within specific therapeutic classes was found when copayment levels were increased. Monthly prescription fills per person decreased by 10% to 16% for angiotensin-converting enzyme inhibitors, calcium channel blockers, and

Table 3. Logistic Regression Results: Adjusted Odds Ratios for Medication Compliance

Characteristic	Adjusted Odds Ratio	95% CI
Medication copayment level, $		
5	1.00	…
20	0.76	0.75, 0.78
20-165	0.48	0.47, 0.49
Medication therapeutic class		
Thiazide diuretics	1.00	…
Angiotensin receptor blockers	2.50	2.41, 2.58
Calcium channel blockers	1.85	1.79, 1.90
β-Blockers	1.82	1.77, 1.87
ACE inhibitors	1.63	1.58, 1.68
Patient age, y		
<40	1.00	…
40-64	1.97	1.89, 2.04
65+	2.43	2.33, 2.53
Sex		
Male	1.00	…
Female	0.98	0.96, 0.99
Morbidity		
Low	1.00	…
High	0.82	0.81, 0.84
Type of coverage		
PPO	1.00	…
HMO	0.91	0.89, 0.92
Medicare cost contract	1.04	0.99, 1.09
Ethnicity		
Caucasian	1.00	…
Japanese	1.21	1.16, 1.25
Chinese	0.98	0.93, 1.04
Part Hawaiian	0.87	0.84, 0.92
Filipino	0.74	0.70, 0.78
Mixed	0.96	0.89, 1.03
Other	0.89	0.84, 0.95
Race missing	0.86	0.83, 0.88

CI indicates confidence interval; β-blocker, β-adrenergic receptor antagonist; ACE, angiotensin-converting enzyme; PPO, preferred provider organization.

Figure 2. Adjusted Odds Ratios for Medication Compliance by Copayment Level



angiotensin receptor blockers as copayments increased by 66% to 100%. Sokol et al evaluated the impact of medication compliance on healthcare utilization and cost in the treatment of hypertension and 3 other chronic conditions, but drug copayment issues were not analyzed and all hypertensive agents were evaluated in aggregate.[8] Chapman et al analyzed various predictors, including copayment, of adherence with antihypertensive agents collectively, but provided no information on drug classes.[9]

Our research makes several unique contributions to the literature on patient drug copayment level and compliance with antihypertensive therapy. We examined all specific therapeutic classes of antihypertensive medications. We analyzed compliance with respect to copayment level adjusted for a number of important patient characteristics, including comorbidity level and ethnicity.

Poor medication compliance has been associated with higher healthcare costs. Sokol et al conducted a retrospective cohort study and documented cost offsets for all-cause medical costs at high levels of medication adherence in patients with hypertension, hypercholesterolemia, and diabetes.[8] Mojtabai and Olfson evaluated the association of prescription drug coverage with adherence to medications for various chronic conditions and the association of cost-related poor adherence with health outcomes in community-dwelling older Americans.[18] Patients with cost-related poor adherence were more likely than those without it to perceive their overall health as poor (23% vs 10%, respectively) and to have been hospitalized (43% vs 33%, respectively). Increasing medication compliance may improve patient outcomes.

There are several limitations to our study. First, the study population was selected from a single health plan in Hawaii, and results may not generalize to other populations. Second, medication compliance was determined indirectly from pharmacy claims; the actual consumption of medication was not assessed and the provision of free drug samples (if any) would not be captured by the pharmacy claims system. Provision of these samples likely would result in underestimation of compliance for drugs on the second and third tier. (Free drug samples are rarely given for tier 1 generic medications.) In addition, we did not have pharmacy claims on

medications prescribed while patients were hospitalized. If a patient's medication supply overlapped his or her hospitalization days, those days would be counted as compliant. However, it is possible that a patient with a long hospitalization would have been labeled noncompliant even if the patient had received his or her medication during the hospital stay.

Third, information on blood pressure levels was not available from claims data. Hence, important outcomes, such as achievement of goal blood pressure, were not evaluated. Fourth, we did not control for all potential confounders, such as patient-physician relations, patient knowledge about hypertension, and patient health beliefs.

Last, because of the observational design of this study, there may be unobserved characteristics related to tier choice that also are associated with adherence level. Patients across tiers are taking different medications and patients are not randomly assigned to tiers. If unobserved traits of the patients or drugs in tier 3 were correlated with adherence, there would be a bias. For instance, if income were positively associated with adherence and patients receiving tier 3 medications were more likely to have higher incomes than patients receiving medications in lower tiers, income would be a confounding factor. In this particular case, we may have underestimated the impact of tier on adherence.

Despite the potential limitations of this research, we believe the results are valid, informative, and generalizable with respect to the central issue of the impact of copayment level on medication compliance.

In summary, we found that copayment level is a strong and independent predictor of medication compliance after adjusting for other model explanatory variables. Poor compliance may result in an increased risk for adverse events, decreased health-related quality of life, and higher long-term healthcare costs. This finding argues that for managed care decision makers, the copayment price-setting decision represents a powerful tool that can be used to influence medication compliance of plan members, as well as the associated clinical and economic consequences for the healthcare plan. Moreover, because compliance drops significantly even within therapeutic class as copayment level increases (Figure 1), it is important that patients be informed of their full range of options and the copayment levels associated with each so they can make cost-effective decisions that may lead to improved compliance and health outcomes.

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