

Cost-Sharing and Adherence to Antihypertensives for Low and High Adherers

Jean Yoon, PhD, MHS; and Susan L. Ettner, PhD

As a result of the growing prevalence of chronic diseases due to the aging population and better detection and identification of individuals with such diseases, and the development of new drugs that are highly effective, the healthcare system relies heavily on prescription drugs to manage chronic conditions and reduce morbidity and mortality. Adherence to some drugs can be low, and concerns exist over whether patients are receiving the full benefit from their drugs. Among factors influencing patients' adherence to drugs, one of the strongest relationships exists between higher out-of-pocket payments for drugs and less drug utilization, including lower adherence to drug prescriptions¹⁻⁵ with modest price effects for drugs to treat asymptomatic conditions including hypertension.^{6,7}

It is unknown, however, whether patients with low drug utilization are more likely to be responsive to drug prices compared with patients with higher utilization of drugs. Demand for prescription drugs may have heterogeneity in price responsiveness; for example, patients who experience adverse effects or do not feel the drug is working well for them may have more price-elastic demand for the drug than other patients.

Using claims data from employer-sponsored health plans for a large sample of working-age adults diagnosed with hypertension, we applied an innovative quantile regression approach to examine how drug cost-sharing and other patient and health plan characteristics affect adherence to antihypertensive drugs across the distribution of adherence rather than looking at mean adherence, which provides a more limited picture. We focused on hypertension because it is one of the most prevalent chronic conditions in the United States, can be treated effectively with prescription drugs, and is similar to other asymptomatic conditions for which long-term management is critical to reduce the risk of morbidity and mortality. Moreover, when comorbid with other conditions such as diabetes, hypertension leads to development of diseases and complications including renal and diabetic eye disease.⁸ The direct costs of care attributable to hypertension are estimated to be \$569 per year per capita, and the total costs (including the cost of comorbid conditions) are estimated to be \$4073 per year per capita, or \$110.3 billion per year for the United States.⁹ Therefore, adherence to drugs and overall management of hypertension have significant cost implications.

In this article
Take-Away Points / p834
www.ajmc.com
Full text and PDF

Objective: To examine how the influence of cost-sharing on adherence to antihypertensive drugs varies across adherence levels.

Study Design: Cross-sectional study using medical and pharmacy claims and benefits data on 83,893 commercially insured patients with hypertension from the 2000-2001 Medstat MarketScan Database.

Methods: We measured drug adherence using the medication possession ratio (MPR) for antihypertensive drugs over 9 months. Drug cost-sharing was measured as either copayments or coinsurance. Other patient characteristics included age, sex, comorbidity, health plan type, and county-level sociodemographics. We compared adherence for different cost-sharing categories with a bivariate test of equal medians and simultaneous quantile regressions predicting different percentiles of drug adherence.

Results: Median MPR was high (>80%) across all cost-sharing categories. Among the poorest adherers, the regression-adjusted MPR was 8 to 9 points lower among patients with the highest drug cost-sharing compared with patients with the lowest cost-sharing (copayment \$5 or less). The effects of cost-sharing were smaller at the median (2-3 points lower) and nonsignificant at higher levels of adherence. Other significant factors influencing adherence at low adherence levels were drug class and comorbidity.

Conclusion: Cost-sharing had a substantial negative association with adherence among low adherers and little association at higher adherence levels. At a clinical level, physicians should closely monitor adherence to antihypertensive drugs, particularly for patients with multiple comorbidities and those taking multiple drugs. At a health system level, current benefit designs should encourage adherence while limiting the cost burden of drugs for patients with multiple chronic conditions taking multiple drugs.

(*Am J Manag Care.* 2009;15(11):833-840)

For author information and disclosures, see end of text.

Take-Away Points

A cross-sectional study of a large sample of working-age adults was done to examine how cost-sharing affects adherence to antihypertensive drugs.

- Cost-sharing had the most significant and negative relationship with adherence for low adherers; it did not have a significant relationship with adherence for high adherers.
- Other predictors of worse adherence for low adherers were drug class and greater comorbidity.
- Rising costs for prescription drugs are a particular concern for poor adherers.

truncated for 2% of patients with an MPR above 120%.

A single MPR was calculated if patients switched from one drug class to another during the study period. If patients filled prescriptions for drugs in multiple classes simultaneously, then a separate MPR was calculated for each drug class, and the mean of all classes was calculated.

METHODS

Sample

This study used data from the 2000-2001 Medstat MarketScan Database. Claims data were analyzed for 83,893 patients age 18 to 64 years who were diagnosed with hypertension (*International Classification of Diseases, Ninth Revision [ICD-9] codes 401-405*) on any medical claim during 2000, were continuously enrolled in their health plan for the entire 2-year study period, and had at least 1 drug claim for an antihypertensive drug during an index period (January 2000-June 2000). Benefits information was available only from large firms, covering approximately 59% of patients.

Patient-level variables were measured in 2000 and obtained from enrollment and benefits information linked to medical and pharmacy claims data. County of residence was used to link to US Census data on household income, race, and education. This study was approved by the UCLA Institutional Review Board (approval #G06-09-089-02).

Adherence

Antihypertensive drugs included all drugs identified in 7 classes of drugs: angiotensin-converting enzyme (ACE) inhibitors, beta blockers, angiotensin II receptor blockers, thiazide diuretics, calcium channel blockers, alpha-1 blockers, and sympathetic blockers. Users of antihypertensive drugs were identified by any prescription for an antihypertensive drug occurring within a 6-month period at the beginning of 2000, which was considered to be the index prescription. Immediately following the last days supply of the index prescription, refill information was used to calculate the medication possession ratio (MPR) over a 9-month period by drug class. (An earlier study using administrative data measured adherence to antihypertensive drugs over 250 days and concluded that this measure of adherence was valid as it correlated well with drug effects.¹⁰) The days supplied for all refills within a given class was summed and divided by 270 days to calculate the MPR, prorating the last refill when necessary. The MPR represents the amount of time for which a patient had his/her drug supply, and it could vary from 0% to more than 100% if patients had overlapping prescriptions. The MPR values were

Covariates

Patient cost-sharing for drugs was categorized as \leq \$5 copayment per prescription (the reference group), \$6 to \$12 copayment, \geq \$15 copayment, 10% coinsurance, or 20% coinsurance. Separate groups were created for copayment and coinsurance groups because the amount paid under coinsurance depends on the type of drug filled, and patients are more price responsive under coinsurance than under copayments.¹¹ As 64% of study patients filled prescriptions for brand-name rather than generic drugs, and cost-sharing between brand-name and generic drugs was highly correlated (Pearson correlation coefficient = 0.44), only cost-sharing for brand-name drugs was used in analyses. Analyses originally included separate indicators of cost-sharing for generic and brand-name drugs and number of drug plan tiers, but a high degree of collinearity was found among these measures, so generic cost-sharing and number of drug plan tiers were dropped from analyses.

Comorbidity was measured using morbidity groupings from ICD-9 codes in medical claims called aggregated diagnosis groups (ADGs)¹² using dummy codes for 32 ADGs (not mutually exclusive), count of major ADGs (conditions with greater severity) ranging from 0 to 8, and dummy variables for congestive heart failure, diabetes, ischemic heart disease, hyperlipidemia, and depression—comorbidities associated with cardiovascular disease.

Dummy categories were created for each of the 7 classes of antihypertensive drugs with thiazide diuretics as the reference category.

Additional covariates included patient cost-sharing for outpatient visits, type of health plan, receipt of preventive care, age, sex, employee working status, county-level median household income, percentage of nonwhite residents, and percentage of residents with less than a high school education.

Statistical Analyses

A nonparametric test of equal medians was used to test for bivariate differences in the median MPR by patient and health plan characteristics. Simultaneous quantile regression then was used to estimate MPR. Quantile regression allows

for differential effects of cost-sharing on the conditional median and other conditional quantiles of adherence. In quantile regression we regressed specific quantiles (or percentiles) of the dependent variable on patient characteristics.¹³ Predicting the *conditional* quantile in quantile regression is different from taking the *unconditional* distribution and dividing up the dependent variable to run separate regressions; the latter procedure is problematic because it artificially reduces the variation in the dependent variable.

For the regression model $d_i = \beta_0 + \beta_1 x_{1i} + \beta_2 x_{2i} + \dots + \beta_k x_{ki} + e_i$, where d = drug adherence, to model the q th quantile, we defined the function

$$h_i = \begin{cases} q & \text{if } e_i > 0 \\ (1 - q) & \text{otherwise} \end{cases}$$

where q is any quantile ranging between 0 and 1.0.

The regression coefficients were chosen to minimize the function:

$$\sum_{i=1}^n |e_i| h_i$$

The estimated quantile of the distribution of d , conditional on the values of the predictor variables, was:

$$Q[d_i | x_{1i}, x_{2i}, \dots, x_{ki}] = \beta_0 + \beta_1 x_{1i} + \beta_2 x_{2i} + \dots + \beta_k x_{ki}$$

where $Q(\cdot)$ denotes the predicted quantile.

Five simultaneous quantile regression models were estimated setting q equal to 0.1, 0.25, 0.5, 0.75, and 0.9 (representing the 10th, 25th, 50th or median, 75th, and 90th percentiles of adherence). Coefficients are presented along with standard errors bootstrapped using the normal method with 500 repetitions. The coefficient in quantile regression represents how the specific quantile (q) changes with a unit change in the predictor, so the coefficients represent the difference in points of the MPR. Wald tests of the differences between coefficients in the median regression model versus the 0.10 and 0.90 quantile model estimates were conducted. A conservative significance level of $<.01$ was used in all analyses because of the large number of significance tests conducted. All analyses were conducted with Stata version 9.2 (Stata-Corp LP, College Station, TX).

RESULTS

Discussion of the bivariate and regression results presented below focus on the impact of the main covariates of interest (cost-sharing, drug class, comorbidity) on adherence.

Sample

Characteristics of the sample are shown in **Table 1**. Most

of the patients were older than 45 years of age and fairly diverse in terms of their sociodemographic characteristics and health plan type. Drug copayments were more common than coinsurance, and cost-sharing requirements were quite high. For example, only 13% of study patients had copayments of \$5 or less and 25% of patients had coinsurance rates of 20%. Comorbidities were common among this sample of patients with hypertension. More than one-third of patients had hyperlipidemia, and almost one-fifth had diabetes.

Bivariate Results

Higher drug cost-sharing in the form of higher copayments and coinsurance was associated with lower median adherence. Among patients with copayments, the lowest drug copayment group (\$5 or less) experienced the highest median adherence, and there was little difference between patients who paid \$6 to \$12 versus patients who paid \$15 or more. Patients with 10% or 20% drug coinsurance also had lower median adherence levels compared with patients who had copayments of \$5 or less. Similarly, medical cost-sharing had a negative relationship with median adherence.

By drug class, median adherence was highest for patients on ACE inhibitors and beta blockers, and lowest for patients taking sympathetic blockers and thiazide diuretics, 2 drug classes with the strongest side effects. Comorbidity appeared to be negatively associated with adherence.

Quantile Regression Results

In the quantile regression results (**Table 2**), the significant relationship between higher cost-sharing and lower adherence was observed in the median and lower percentiles of adherence, seen by comparing coefficients by cost-sharing category down the columns within each percentile of adherence. The coefficients represent the change in adherence compared with the lowest cost-sharing group (copayment of \$5 or less). The regression constants shown in the second-to-last row of the table (“Constant”) represent the percentile of adherence when all covariates are equal to zero, and the coefficients are additive in order to calculate the percentile for a particular group. For example, the 10th percentile of adherence for patients with a copayment of \$5 or less who were taking thiazide diuretics and had no comorbidities, with all other covariates set to zero, was 8.63%.

In column 2 (the 10th percentile of adherence), patients with higher drug cost-sharing (copayments greater than \$5 or drug coinsurance rates of 10% and 20%) had an adherence measure of 8 to 10 points less compared than that for patients with copayments of \$5 or less. At the median (the 50th percentile of adherence), the association with cost-sharing was more modest, with differences of 2 to 3 points in

Table 1. Patient Characteristics and Median Adherence to Antihypertensive Drugs (N = 83,893)

Characteristic	No. (%)	Median MPR ^a	P ^b
Brand-name drug cost-sharing			.000
Copayment ≤\$5	10,878 (13.0)	88.9	
Copayment \$6-\$12	24,831 (29.6)	85.2	
Copayment ≥\$15	19,112 (22.8)	85.7	
Coinsurance 10%	7823 (9.3)	85.4	
Coinsurance 20%	21,249 (25.3)	86.1	
Age, y			.000
18-44	13,286 (15.8)	80.0	
45-54	34,614 (41.3)	86.1	
55-64	35,993 (42.9)	88.0	
Sex			.717
Male	40,898 (48.8)	86.2	
Female	42,995 (51.3)	86.3	
Employee type			.000
Active worker	40,713 (48.5)	85.7	
Nonactive worker	16,429 (19.6)	87.3	
Spouse/dependent	26,751 (31.9)	86.5	
Median county income			.000
<\$43,000	45,467 (54.2)	85.4	
\$43,000-\$53,000	24,514 (29.2)	87.1	
>\$53,000	13,912 (16.6)	87.4	
Nonwhite residents in county			.000
<9%	14,313 (17.1)	87.6	
9%-42%	53,229 (63.5)	86.9	
≥43%	16,351 (19.5)	82.3	
Residents with less than high school education in county			.000
<20%	53,281 (63.5)	87.2	
≥20%	30,612 (36.5)	84.6	
Drug class			.000
ACE inhibitors	32,852 (39.2)	87.6	
Beta blockers	27,286 (32.5)	87.6	
Alpha blockers	5292 (6.3)	85.7	
Calcium channel blockers	26,952 (32.1)	86.5	
ARBs	7930 (9.5)	85.7	
Thiazide diuretics	15,417 (18.4)	83.3	
Sympathetic blockers	2138 (2.5)	82.3	
Type of health plan			.000
Fee-for-service	19,888 (23.7)	87.8	
Capitated	23,768 (28.3)	84.6	
Preferred provider organization	29,029 (34.6)	86.5	
Point-of-service/other	11,208 (13.4)	85.7	

(Continued)

MPR across the higher cost-sharing groups. At the 90th percentile of adherence, higher drug copayments and drug coinsurance no longer had a significant negative association with adherence, and the \$6 to \$12 copayment group actually had a significantly higher MPR than the group with the lowest copayment. Overall, the relationship with cost-sharing appeared to be consistently reduced between the 10th percentile and the higher percentiles, which is apparent when comparing coefficients across the rows for each cost-sharing category.

Although there were significant differences in adherence between the lowest cost-sharing group and higher cost-sharing groups, there did not appear to be much of a gradient in adherence between higher cost-sharing groups.

Patients taking ACE inhibitors had a 10-point higher MPR than patients taking thiazide diuretics at the 10th percentile, and all the other drug classes except for sympathetic blockers had a positive impact on adherence compared with thiazide diuretics. Across the drug classes, drug class coefficients at the lowest percentile significantly differed from the median, whereas differences between the highest percentile and the median were less significant.

Comorbidity, as measured by number of major ADGs, negatively impacted adherence, and this negative effect was significantly reduced

Cost-Sharing and Antihypertensive Adherence

between the median and the 90th percentile. Patients with congestive heart failure had lower adherence, whereas the presence of hyperlipidemia had a strong, positive impact on adherence. Ischemic heart disease, diabetes, and depression were not associated with adherence to antihypertensive drugs.

DISCUSSION

Cost-sharing through copayments and coinsurance for drugs is a policy lever to improve adherence to drugs that has particular implications for low adherers. These results demonstrate that cost-sharing had a substantial negative association with adherence for low adherers and little association for high adherers.

One reason why patients with poor adherence may be more responsive to out-of-pocket drug prices is because they are more apt to experience worse side effects from the drugs¹⁴ and may have greater difficulty keeping their hypertension under control with antihypertensive drugs; therefore, they are unwilling to pay higher prices for the drugs.

Comorbidity also had a negative effect on adherence, and patients with more comorbid conditions or ADGs, in particular, were at risk for low adherence. This finding is supported by earlier research associating greater patient nonadherence with more chronic conditions and worse health status.^{15,16} Patients with hyperlipidemia, in contrast, had higher adherence to their drugs, most likely because of their increased cardiovascular risk. The strong negative effect of comorbidity on adherence is a concern as control of hypertension is critical for patients with multiple risk factors to prevent greater morbidity. Increasing adherence for these patients is made more difficult by complex drug regimens and possible adverse drug interactions.

Limitations

Although a few drug plans in the study had 3-tiered plans with differential cost-sharing between preferred and non-

Table 1. Patient Characteristics and Median Adherence to Antihypertensive Drugs (N = 83,893) (Continued)

Characteristic	No. (%)	Median MPR ^a	P ^b
Medical benefit			.000
Coinurance, no copay	28,786 (34.3)	88.0	
No coinsurance, copay ≤\$10	13,272 (15.8)	86.5	
Coinurance plus copay ≤\$10	4788 (5.7)	85.4	
No coinsurance, copay \$15-\$20	21,787 (26.0)	85.0	
Coinurance plus copay \$15-\$20	15,260 (18.2)	84.5	
Recent preventive care			.000
Yes	43,454 (51.8)	87.6	.000
No	40,439 (48.2)	84.8	
Comorbidity			
Congestive heart failure	1683 (2.0)	79.4	.000
Diabetes	14,551 (17.3)	85.7	.030
Hyperlipidemia	30,465 (36.3)	87.7	.000
Ischemic heart disease	8811 (10.5)	85.6	.013
Depression	3413 (4.1)	84.3	.000
Major ADG count (0-8)			.000
0	38,224 (45.6)	86.7	
1	26,981 (32.2)	86.5	
≥2	18,688 (22.3)	85.0	

ACE indicates angiotensin-converting enzyme; ADG, aggregated diagnosis group; ARB, angiotensin II receptor blocker; MPR, medication possession ratio.

^aAdherence was measured using the MPR.

^bP value was for nonparametric test of equal medians across category groups.

preferred brand-name drugs, we were unable to examine the separate relationship of each type of cost-sharing in our analysis.

There did not appear to be a significant dose response or large differences in adherence between patients in the middle and high drug cost-sharing groups. The modest differences in drug cost-sharing between categories may partly explain these results; for example, most of the patients in the \$6 to \$12 copayment group had a copay of \$12, whereas most of the patients in the ≥\$15 copay group had a copayment of \$15 or \$16. We would expect to see a more significant gradient effect with larger cost-sharing differentials between groups, so it is a limitation of our dataset that we cannot determine whether there is a gradient effect when cost-sharing increases substantially.

As our study design was cross-sectional, we were unable to draw conclusions about cause and effect. Patients had a choice of drug plans, and self-selection into plans with differing levels of cost-sharing could bias the estimated association between drug cost-sharing and adherence if interpreted as a causal effect. For example, individuals with a higher propen-

■ **Table 2.** Regressions Predicting Medication Possession Ratio for Antihypertensive Drugs (N = 83,893)^a

Patient Characteristics	Percentile of Adherence ^b				
	10th	25th	50th	75th	90th
Drug cost-sharing					
Copayment ≤\$5	Reference	Reference	Reference	Reference	Reference
Copayment \$6-\$12	-7.96 (1.33) ^{c,d}	-5.96 (1.04) ^c	-2.92 (0.59) ^c	0.29 (0.28)	3.13 (0.57) ^{c,d}
Copayment ≥\$15	-9.13 (1.40) ^{c,d}	-5.88 (1.03) ^c	-2.21 (0.61) ^c	-0.10 (0.31)	1.28 (0.59) ^d
Coinsurance 10%	-9.61 (0.99) ^{c,d}	-7.64 (0.71) ^c	-2.55 (0.34) ^c	-0.44 (0.19)	-0.60 (0.25) ^d
Coinsurance 20%	-8.21 (1.80) ^{c,d}	-4.07 (1.28) ^c	-2.20 (0.71) ^c	-0.81 (0.42)	0.17 (0.68) ^d
Drug class					
Thiazide diuretics	Reference	Reference	Reference	Reference	Reference
ACE inhibitors	9.53 (0.47) ^{c,d}	4.51 (0.34) ^c	0.91 (0.19) ^c	0.15 (0.11)	0.42 (0.16) ^c
Beta blockers	8.84 (0.47) ^{c,d}	3.67 (0.34) ^c	0.97 (0.19) ^c	0.25 (0.11)	0.21 (0.16) ^d
Alpha blockers	5.25 (0.66) ^{c,d}	0.70 (0.50)	-1.62 (0.32) ^c	-1.12 (0.20) ^c	-1.12 (0.25) ^c
Calcium channel blockers	8.47 (0.43) ^{c,d}	3.26 (0.30) ^c	0.14 (0.19)	-0.48 (0.10) ^c	-0.63 (0.14) ^{c,d}
ARBs	6.99 (0.64) ^{c,d}	2.14 (0.50) ^c	-0.19 (0.29)	-0.20 (0.17)	-0.22 (0.24)
Sympathetic blockers	3.35 (1.54) ^d	-0.29 (0.84)	-2.33 (0.69) ^c	-0.64 (0.30)	-0.06 (0.41) ^d
Comorbidity					
Congestive heart failure	-6.16 (1.28) ^c	-7.09 (1.06) ^c	-4.33 (0.81) ^c	-1.37 (0.51) ^c	0.34 (0.67) ^d
Diabetes	0.12 (0.60)	-0.97 (0.41)	-0.44 (0.22)	0.09 (0.14)	0.44 (0.19) ^d
Hyperlipidemia	3.72 (0.46) ^{c,d}	2.63 (0.30) ^c	1.40 (0.17) ^c	0.50 (0.10) ^c	0.30 (0.14) ^d
Ischemic heart disease	-0.72 (0.74)	0.13 (0.56)	-0.52 (0.31)	-0.55 (0.19) ^c	-0.47 (0.30)
Depression	2.49 (1.45)	1.79 (1.08)	1.34 (0.73)	-0.18 (0.34)	-0.04 (0.56)
Major ADG count (0-8)	-6.00 (1.57) ^c	-5.64 (1.15) ^c	-3.39 (0.93) ^c	-0.65 (0.43)	-0.18 (0.55) ^d
Constant	8.63	42.02	70.96	87.80	93.02
Pseudo R²	0.06	0.04	0.02	0.01	0.02

ACE indicates angiotensin-converting enzyme; ADG, aggregated diagnosis group; ARB, angiotensin II receptor blocker.

^aModels also were adjusted for age, sex, employment status, county sociodemographic characteristics, health plan characteristics, use of preventive care, and 32 aggregated diagnosis groups.

^bCoefficients are points of the medication possession ratio and are shown with bootstrapped standard errors in parentheses.

^cCoefficient significant at $P < .01$.

^dCoefficient significantly different from 50th percentile at $P < .01$.

sity for risk prevention/healthy lifestyles may simultaneously choose drug plans with lower cost-sharing and have better drug adherence, so the effect of cost-sharing on adherence could be overestimated because of adverse selection. It is unclear whether this bias would differ across quantiles. On the other hand, greater comorbidity was associated with lower adherence, so unmeasured health status may lead to choosing lower cost-sharing and lower adherence, and the effect of cost-sharing on adherence could be underestimated.

Although the MPR is considered comparable in accuracy to other adherence measures, it is possible that there was some measurement error in determining adherence level. This would have led to an underestimate of the effect of cost-sharing if the MPR was a poor measure of whether a patient was truly a high adherer versus a low adherer, because we

would expect the difference in cost-sharing effects across percentiles to be biased toward zero.

The high rate of adherence to antihypertensive drugs in this sample of patients may limit the generalizability of the findings, as these patients had more generous health insurance and were healthier than patients without employer-based insurance. For instance, patients with disabling chronic conditions who are unable to work were not represented in this sample. Also, populations such as low-income patients and Medicaid recipients have been shown to be sensitive to increased out-of-pocket costs for drugs^{17,18} and are likely to experience a greater cost-sharing impact than people in commercial plans.

Although hypertension was the only condition analyzed in this study, these results may have greater generalizability,

as responsiveness to cost-sharing for drugs to treat other asymptomatic conditions is lower compared with that for drugs to treat acute conditions.^{6,19}

CONCLUSION

These results add to the literature on drug adherence by examining the association between cost-sharing and patient characteristics at different levels of adherence. Given that the mean adherence level to antihypertensive drugs in this population of patients was more than 80%, using quantile regression provided additional information about the factors influencing drug adherence for low and high adherers. In this sample, higher adherence levels did not vary much in response to drug cost-sharing. However, patients with poor adherence were the most responsive to modest differences in cost-sharing. These patients also were at greater risk for poor control of hypertension, leading to serious adverse outcomes such as myocardial infarction and stroke, so the trend toward rising healthcare costs being shifted onto patients by employers suggests that costs will continue to be a burden for patients with poor adherence.

At a clinical level, physicians should closely monitor adherence to antihypertensive drugs, particularly for patients who have multiple comorbidities and for those taking multiple drugs. Communication between patients and physicians about drug affordability, complexity of drug regimens, and drug interactions is infrequent.^{20,21} Physician-initiated discussions regarding patients' out-of-pocket costs can enable switching prescriptions to lower-cost, generic, or higher-dose drugs to reduce frequency of drug refills and lessen the cost burden for patients, especially those with the poorest adherence. Physicians also should raise questions with their patients about side effect profiles and effectiveness of antihypertensive drugs so that simplified drug regimens or alternative classes can be prescribed for patients experiencing problems taking their drugs. Additionally, more pharmacy counseling when drugs are dispensed can educate patients about cost-sharing and the importance of adhering to their drugs. The role of health literacy in improving adherence to drugs also suggests that interventions aimed at improving patients' basic health knowledge may be critical for improving adherence to drugs and health status for low-literacy patients.²²

At a health system level, current benefit designs do not encourage adherence, nor do they limit the cost burden of drugs for patients with multiple chronic conditions taking multiple drugs. In particular, reducing the risk for cardiovascular morbidity and mortality depends on long-term maintenance therapy for hypertension as well as hyperlipidemia and diabetes, conditions that also rely heavily on prescription drugs for management. Alternative benefit designs have been proposed

(eg, value-based insurance design) that involve reduced cost-sharing for drugs to treat certain conditions like hypertension either for all patients or for patients with high-risk characteristics determined by age and comorbidities.^{23,24} These types of benefit designs provide incentives for long-term adherence to essential drugs. Drugs are a cost-effective means to treat chronic conditions, and employers and policymakers should continue to search for better mechanisms to protect the sickest patients and prevent high costs to the healthcare system.

Acknowledgments

We gratefully acknowledge valuable comments from Todd Wagner and 3 anonymous reviewers.

Author Affiliations: From the Health Economics Resource Center (JY), Palo Alto VA Healthcare System, Menlo Park, CA; and the Division of General Internal Medicine (SLE), UCLA David Geffen School of Medicine, Los Angeles, CA.

Funding Source: Funding for this study was provided by Agency for Healthcare Research and Quality Dissertation Award 1R36HS016815-01 and by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Health Services Research and Development.

Author Disclosures: The authors (JY, SLE) report no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this article.

Authorship Information: Concept and design (JY, SLE); acquisition of data (JY); analysis and interpretation of data (JY, SLE); drafting of the manuscript (JY); critical revision of the manuscript for important intellectual content (SLE); statistical analysis (JY); and obtaining funding (JY).

Address correspondence to: Jean Yoon, PhD, MHS, Health Economics Resource Ctr, Palo Alto VA Healthcare System, 795 Willow Rd (152 MPD), Menlo Park, CA 94025. E-mail: jean.yoon@va.gov.

REFERENCES

1. Gibson TB, Ozminkowski RJ, Goetzel RZ. The effects of prescription drug cost sharing: a review of the evidence. *Am J Manag Care*. 2005;11(11):730-740.
2. Piette JD, Heisler M, Wagner TH. Cost-related medication underuse among chronically ill adults: the treatments people forgo, how often, and who is at risk. *Am J Public Health*. 2004;94(10):1782-1787.
3. Roblin DW, Platt R, Goodman MJ, et al. Effect of increased cost-sharing on oral hypoglycemic use in five managed care organizations: how much is too much? *Med Care*. 2005;43(10):951-959.
4. Ellis JJ, Erickson SR, Stevenson JG, Bernstein SJ, Stiles RA, Fendrick AM. Suboptimal statin adherence and discontinuation in primary and secondary prevention populations. *J Gen Intern Med*. 2004;19(6):638-645.
5. Kamal-Bahl S, Briesacher B. How do incentive-based formularies influence drug selection and spending for hypertension? *Health Aff (Millwood)*. 2004;23(1):227-236.
6. Landsman PB, Yu W, Liu X, Teutsch SM, Berger ML. Impact of 3-tier pharmacy benefit design and increased consumer cost-sharing on drug utilization. *Am J Manag Care*. 2005;11(10):621-628.
7. Gibson TB, Mark TL, Axelsen K, Baser O, Rublee DA, McGuigan KA. Impact of statin copayments on adherence and medical care utilization and expenditures. *Am J Manag Care*. 2006;12(spec no):SP11-SP19.
8. Patel A; ADVANCE Collaborative Group, MacMahon S, Chalmers J, Neal B, et al. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial): a randomised controlled trial. *Lancet*. 2007;370(9590):829-840.
9. Druss BG, Marcus SC, Olfson M, Tanielian T, Elinson L, Pincus HA. Comparing the national economic burden of five chronic conditions. *Health Aff (Millwood)*. 2001;20(6):233-241.
10. Steiner JF, Koepsell TD, Fihn SD, Inui TS. A general method of compliance assessment using centralized pharmacy records. Description and validation. *Med Care*. 1988;26(8):814-823.

- 11. Dor A, Encinosa W.** How does cost-sharing affect drug purchases? Insurance regimes in the private market for prescription drugs. Cambridge, MA: National Bureau of Economic Research; September 2004. Revised August 18, 2009. NBER Working Paper 10738. <http://www.nber.org/papers/w10738>. Accessed September 2, 2009.
- 12. The Johns Hopkins ACG Case Mix System [computer program].** Version 8.01. Baltimore, MD: Johns Hopkins Bloomberg School of Public Health; April 2007.
- 13. Koenker R, Bassett G.** Regression quantiles. *Econometrica*. 1978;46(1):33-50.
- 14. Elliott RA, Ross-Degnan D, Adams AS, Safran DG, Soumerai SB.** Strategies for coping in a complex world: adherence behavior among older adults with chronic illness. *J Gen Intern Med*. 2007;22(6):805-810.
- 15. Safran DG, Neuman P, Schoen C, et al.** Prescription drug coverage and seniors: findings from a 2003 national survey. *Health Aff (Millwood)*. 2005;Suppl Web Exclusives:W5:152-166.
- 16. Soumerai SB, Pierre-Jacques M, Zhang F, et al.** Cost-related medication nonadherence among elderly and disabled Medicare beneficiaries: a national survey 1 year before the Medicare drug benefit. *Arch Intern Med*. 2006;166(17):1829-1835.
- 17. Soumerai SB, Avorn J, Ross-Degnan D, Gortmaker S.** Payment restrictions for prescription drugs under Medicaid. Effects on therapy, cost, and equity. *N Engl J Med*. 1987;317(9):550-556.
- 18. Soumerai SB, Ross-Degnan D, Avorn J, McLaughlin T, Choodnovskiy I.** Effects of Medicaid drug-payment limits on admission to hospitals and nursing homes. *N Engl J Med*. 1991;325(15):1072-1077.
- 19. Goldman DP, Joyce GF, Escarce JJ, et al.** Pharmacy benefits and the use of drugs by the chronically ill. *JAMA*. 2004;291(19):2344-2350.
- 20. Alexander GC, Casalino LP, Meltzer DO.** Patient-physician communication about out-of-pocket costs. *JAMA*. 2003;290(7):953-958.
- 21. Shrank W, Fox S, Kirk A, et al.** The effect of pharmacy benefit design on patient-physician communication about costs. *J Gen Intern Med*. 2006;21(4):334-339.
- 22. Kalichman SC, Ramachandran B, Catz S.** Adherence to combination antiretroviral therapies in HIV patients of low health literacy. *J Gen Intern Med*. 1999;14(5):267-273.
- 23. Cherner M, Rosen A, Fendrick A.** Value-based insurance design. *Health Aff (Millwood)*. 2007;26(2):w195-w203.
- 24. Fendrick AM, Smith DG, Cherner ME, Shah SN.** A benefit-based copay for prescription drugs: patient contribution based on total benefits, not drug acquisition cost. *Am J Manag Care*. 2001;7(9):861-867. ■