

Cost Sharing and the Initiation of Drug Therapy for the Chronically Ill

Matthew D. Solomon, MD, PhD; Dana P. Goldman, PhD; Geoffrey F. Joyce, PhD; José J. Escarce, MD, PhD

Background: Increased cost sharing reduces utilization of prescription drugs, but little evidence demonstrates how this reduction occurs or the factors associated with price sensitivity.

Methods: We conducted a retrospective cohort study of older adults with employer-provided drug coverage from 1997 to 2002 from 31 different health plans. We measured the time until initiation of medical therapy for 17 183 patients with newly diagnosed hypertension, diabetes, or hypercholesterolemia.

Results: For all study conditions, higher copayments were associated with delayed initiation of therapy. In survival models, doubling copayments resulted in large reductions in the predicted proportion of patients initiating pharmacotherapy at 1 and 5 years after diagnosis: for hypertension, 54.8% vs 39.9% at 1 year and 81.6% vs 66.2% at 5 years ($P < .001$); for hypercholesterolemia, 40.2% vs 31.1% at 1 year and 64.3% vs 53.8% at 5 years ($P < .002$); and for diabetes, 45.8% vs 40.0% at 1 year and 69.3% vs

62.9% at 5 years ($P < .04$). However, patients' rate of initiation and sensitivity to copayments strongly depended on their prior experience with prescription drugs. Those without prior drug use (26.1%, 10.4%, and 12.9%) initiated later (833, >1170, and >1402 days later in median time until initiation) and were far more price sensitive (increase of 34.5%, 20.1%, and 27.2% remaining untreated after 5 years when copayments doubled) than those with a history of drug use among patients with newly diagnosed hypertension, hypercholesterolemia, and diabetes, respectively. These results were robust to a wide range of sensitivity analyses.

Conclusions: High cost sharing delays the initiation of drug therapy for patients newly diagnosed with chronic disease. This effect is greater among patients who lack experience with prescription drugs. Policy makers and physicians should consider the effects of benefits design on patient behavior to encourage the adoption of necessary care.

Arch Intern Med. 2009;169(8):740-748

IN THE PAST DECADE, HEALTH PLANS have responded to rising prescription drug costs by implementing more restrictive insurance benefits, the hallmark of which has been increased cost sharing (ie, "copayments"), multi-tier formularies, and mandatory generic substitution.¹ Several studies have demonstrated that these new arrangements reduce overall drug utilization and expenditures²⁻⁴ and that the chronically ill are sensitive to out-of-pocket (OOP) costs.^{5,6} However, detailed mechanisms outlining how these reductions occur are lacking.

*See also pages 737,
750, and 757*

The interruption of drug therapy can have negative health consequences for the chronically ill,⁷⁻¹¹ particularly for elderly patients, who have the highest rates of chronic disease and prescription drug use.¹²⁻¹⁵ Studies measuring the effect of pharmacy benefit's design on drug treatment for the chronically ill are inconsistent,^{3,5,6,16-21} but

surveys find cost to be the leading reason why elderly patients do not fill prescriptions, skip doses, or take smaller doses, followed by other causes, such as medication adverse effects and beliefs about whether drugs improve health.²² Most empirical studies of cost sharing have examined aggregate measures of utilization, such as total expenditures or days supplied, without explanations of how patients adjust their regimens. Although several studies suggest that price sensitivity depends on a drug's therapeutic class,^{5,21,23,24} and that increased cost sharing may decrease "nonessential" drug use more than "essential" drug use,^{5,20,25-29} few studies have dissected the multiple mechanisms by which patients reduce their utilization in the face of higher cost sharing.

*See Invited Commentary
at end of article*

To fill this gap, this study examines whether cost sharing affects the initiation of drug treatment for patients newly diagnosed with chronic disease. A sophis-

Author Affiliations: Department of Medicine, Stanford University School of Medicine, Stanford, California (Dr Solomon); RAND Corporation, Santa Monica, California (Drs Solomon, Goldman, Joyce, and Escarce); and Department of Medicine, David Geffen School of Medicine at University of California, Los Angeles (Dr Escarce).

ticated understanding of the effects of drug benefits is crucial for policy makers, who, rather than applying blunt tools to control utilization, need to target those most at risk for the potentially harmful effects of utilization reductions.

METHODS

The RAND Human Subjects Protection Committee ruled that this research was exempt from institutional review board approval.

DATA

We linked enrollment files, pharmacy claims, medical claims, and the salient features of health plan benefits for retirees of 15 large employers from 1997 to 2002. Each employer offered 1 or more health plans to its elderly retirees for a total of 59 health plans covering 399 034 retirees. All but 2 employers that offered multiple health plans provided a single drug benefit to their retirees, such that retirees had no choice of drug benefits. The content of the claims files have been described elsewhere.^{3,5} The eText, eFigure 1, eFigure 2, and eTable provide more details on the construction of our longitudinal data sets from the raw claims (<http://www.archinternmed.com>). Resulting data sets included 31 health plans (plan-year combinations) covering 272 474 unique persons.

STUDY SAMPLE

Our algorithms to identify patients with newly diagnosed hypertension (HTN), hypercholesterolemia (CHOL), and diabetes (DIAB) from *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes were designed to ensure that “rule-out” diagnoses were excluded from the sample. We required patients to be observed for at least their first year in the data without any outpatient or inpatient physician visits with an *ICD-9-CM* code for the chronic disease (hereafter *diagnosis*) and without filling any disease-specific medications. Subsequent to this washout period, we required that they have the diagnosis of interest recorded during a physician visit on at least 2 occasions, the first of which must have occurred prior to or the same day as their first disease-specific medication. The first diagnosis was the *index date* on which the patient was considered newly diagnosed with the condition (eText, eFigure 1, eFigure 2, and eTable). Studies that examine the validity of using claims data to identify patients with chronic disease suggest our algorithm would yield specificity levels of 0.85 to 0.90.^{30,31}

Disease-specific medications were identified by matching the pharmaceutical claims to the Redbook Database. Manual verifications and edits were completed by the authors with clinical experience (M.D.S. and J.J.E.). Medications for HTN included angiotensin receptor blockers, angiotensin-converting enzyme inhibitors, β -blockers, calcium channel blockers, thiazide diuretics, potassium-sparing diuretics, α 1-inhibitors, α 2-agonists, and vasodilators. Medications for DIAB included insulins, sulfonylureas, metformin, thiazolidinediones, and α -glucosidase blockers. Medications for CHOL included statins, bile acid sequestrants, nicotinic acid, and fibric acid derivatives.

OUTCOME VARIABLE

The primary outcome measure was the *time until initiation of prescription drug therapy*, defined as the number of days between a patient's first diagnosis and the filling of the first disease-

specific prescription. Because patients were observed from 2 to 6 years and may have been diagnosed at any time after their first year in the data, the outcome is right-censored (ie, it was possible that patients who were not observed initiating drug therapy may have begun therapy after we ceased to observe them).

EXPLANATORY VARIABLES

The main explanatory variable in our analysis was an index that measured the generosity of a plan's prescription drug benefits. Multi-tier cost-sharing structures, in which drugs are separated into different groups with different copayments, are now the standard for most prescription drug plans. For example, patients might pay \$5 for a 30-day supply for all drugs (1-tier plan), or \$5 for generics and \$10 for brand-name drugs (2-tier), or \$5 for generics, \$10 for preferred brand-name drugs, and \$25 for nonpreferred brand-name drugs (3-tier). Many plans also offer discounts for purchases made through mail-order or in-network pharmacies. These complexities, in addition to mandatory generic substitution rules and restrictive formularies, mean that the price a consumer will pay for a given drug depends not only on its tier but also on where it is dispensed. To capture these features, we developed a single index that summarized the average annual OOP expense that members of a standard sample would have paid for their prescription drugs had they faced the copayments and restrictions of each plan. This OOP index is similar to what would be calculated for the medical consumer price index, but it is specific to each plan. Details on calculating the OOP index have been described elsewhere⁵ and are included in eFigure 2. The OOP index ranked plans by their cost-sharing structure in a manner consistent with their absolute and relative copayment levels. We also calculated separate OOP indices for disease-specific medications to measure the OOP burden for specific drug classes, but these indices were highly correlated with the overall OOP index value and yielded the same results.

Covariates in the models included indicators for age categories; an indicator for sex; median household income in the zip code of residence; a categorical variable for urban residence; indicators for the year of the index date to control for secular time trends; selected outpatient medical benefits to include an exogenous measure of outpatient medical utilization; and indicators for 15 comorbid conditions as health status controls, identified by *ICD-9-CM* codes from physician visits in the year prior to a patient's index date. Finally, we included an indicator variable for any prescription medication use in the year prior to the index date and, in some models, the interaction of this indicator and the OOP index, to assess whether prior use of prescription drugs affected time until initiation of drug therapy and price responsiveness.

STATISTICAL ANALYSIS

Because the data were structured in a time-to-event framework, we used survival analysis techniques. For unadjusted analyses, we used Kaplan-Meier methods and log-rank tests to compare survival functions. For adjusted analyses, we estimated 6 multivariate Cox proportional hazards models. For each of the 3 study conditions, we estimated a main effects and interacted model. The main effects models included the variables described, and the interacted models included the interaction between the OOP index and indicator prior drug use. To make the results easier to understand, we used the multivariate models to predict the effect of doubling copayments on the time to initiation for each study condition. For the predictions, we chose to double an OOP index value near the 25th percentile for the plans in our sample (OOP index = 205), which corresponded to a 1-tier \$5/\$10 retail/mail-order copayment plan. This ensured that both the baseline and doubled copayment val-

Table 1. Characteristics of Persons With Newly Identified Chronic Disease, 1997-2002^a

Characteristic	HTN	CHOL	DIAB
Sample size	7879	6450	4486
Overlap between study samples			
Single newly diagnosed study condition	6657	5277	3679
Newly diagnosed HTN and CHOL	763	763	NA
Newly diagnosed HTN and DIAB	397	NA	397
Newly diagnosed DIAB and CHOL	NA	348	348
New diagnoses of all 3 study conditions	62	62	62
Age, mean (SD), y	75.8 (6.6)	74.5 (5.8)	75.5 (6.2)
Men, %	38.9	40.6	48.8
Median income in zip code, \$	29 145	29 049	28 943
Number of unique medications in prior year, %			
0	26.1	10.4	12.9
1-3	26.1	21.6	14.1
4-6	21.1	24.7	19.0
≥7	26.6	43.3	54.0
Year of first diagnosis, %			
1998	23.5	25.3	19.8
1999	27.7	28.3	26.7
2000	18.0	17.3	17.4
2001	15.4	15.0	17.5
2002	15.4	14.1	18.6
Plan type, %			
1-Tier	3.2	1.6	3.3
2-Tier	11.0	9.0	10.5
3-Tier	81.7	86.4	82.9
Coinsurance	4.0	2.9	3.2
Comorbidities, % ^b			
Conditions contributing to cardiovascular risk			
HTN	NA	54.2	55.4
CHOL	20.3	NA	26.4
DIAB	11.8	16.4	NA
Congestive heart failure	4.5	5.6	13.1
Vascular disease	3.5	4.1	5.7
Coronary artery disease	2.9	6.1	7.8
Conditions not contributing to cardiovascular risk			
Osteoarthritis	17.0	17.2	17.0
Gastric acid disorder	9.4	9.7	10.3
Thyroid disorder	8.2	9.5	7.5
Depression	7.1	5.3	7.1
Glaucoma	6.8	7.8	7.9
Asthma and/or COPD	5.3	5.6	8.7
Allergic rhinitis	4.7	5.5	4.8
Chronic sinusitis	2.2	2.8	2.8
Inflammatory bowel disease	2.0	1.8	1.8
Ulcer	1.2	1.1	1.9

Abbreviations: CHOL, hypercholesterolemia; COPD, chronic obstructive pulmonary disease; DIAB, diabetes; HTN, hypertension; *ICD-9-CM*, *International Classification of Diseases, Ninth Revision, Clinical Modification*; NA, not applicable.

^aUnless otherwise indicated, data are reported as number of subjects.

^bComorbidities identified as 1 or more physician visits with an *ICD-9-CM* code for the comorbid condition in the year prior to the new diagnosis of the study condition (ie, the index date).

ues for the predictions corresponded to OOP index values that were within sample (OOP index values of 205 and 410).

We conducted multiple sensitivity analyses to assess the robustness of our results. First, to ensure that rule-out diagnoses were not affecting our findings, we tested the models using restrictive inclusion criteria designed to produce samples with more homogeneous and severe disease, including samples that required patients to have at least 3 outpatient physician visits for the disease condition after diagnosis, and required that the second and third visits be at least 30 days apart. Second, we examined whether the type of drug used prior to initial diagnosis changed our model outcomes. Specifically, we separated the effect of prior medications used to treat conditions that contributed additional cardiovascular risk (defined as drugs for HTN, CHOL, DIAB, coronary artery disease, congestive heart failure, and vascular disease) from remaining medications. Third, we examined patients who used a small supply of medications in the prior year—as little as 30 days worth of medications—as well as those patients who used only antibiotics in the prior year. Finally, we estimated models that included controls for physician visits; examined alternative definitions for comorbid conditions; excluded the oldest subjects (age >80 years); and excluded plans requiring coinsurance, the least generous plans in our sample.

RESULTS

DESCRIPTIVE RESULTS

Table 1 summarizes the characteristics of our 3 study samples, which included 7879, 6450, and 4486 patients with newly diagnosed HTN, CHOL, and DIAB, respectively. Little overlap existed between the 3 samples; together, the analyses included 17 183 unique patients (**Table 1**). Within each sample, however, the study conditions were the most frequent comorbid conditions in each others' sample among preexisting conditions that contributed additional cardiovascular risk. The mean (SD) duration of observation after diagnosis was 877 (540) days for HTN, 930 (544) days for CHOL, and 799 (533) days for DIAB. Age was similar across samples; for all conditions, nearly half of patients were between ages 65 and 74 years (46.3% for HTN, 54.1% for CHOL, 47.5% for DIAB). The samples included more women than men; as age increased, the proportion of men decreased. Most patients used at least 1 other medication in the year prior to the index date, but a substantial proportion from each group had no prior prescription drug use (26.1% for HTN, 10.4% for CHOL, and 12.9% for DIAB). Cardiovascular drugs, central nervous system drugs, and hormone and/or synthetic treatments were the most commonly used drugs in the year prior to diagnosis, accounting for 52% of prescriptions.

Overall, the mean (SD) OOP index value at the plan level was 305 (118), with an interquartile range of 220 to 370. Three-tier plans were the most prevalent in the sample and included the largest share of each sample's patients (**Table 2**). In addition, 3-tier plans were, on average, the most generous plans, as measured by the OOP index. This was due to two factors. First, 3-tier plans had lower co-payments for generic drugs (vs 1- and 2-tier plans) and preferred brand drugs (vs 2-tier plans) at retail pharmacies and

Table 2. Mean Prescription Drug Benefits by Type of Plan^a

Category	Copayment, Mean (SD), \$			Coinsurance Coverage, Mean (SD), % (n=5)
	1-Tier (n=5)	2-Tier (n=7)	3-Tier (n=14)	
Retail				
Generics	6.6 (0.9)	5.3 (0.8)	4.5 (0.2)	28 (6.7)
Preferred brands	6.6 (0.9)	12.7 (1.8)	9.5 (1.6)	43 (17.5)
Nonpreferred brands	6.6 (0.9)	12.7 (1.8)	13.6 (2.9)	43 (17.5)
Mail order				
Generics	14 (2.2)	7.7 (3.5)	3.6 (3.3)	28 (6.7)
Preferred brands	14 (2.2)	17.1 (6.9)	8.7 (5.8)	43 (17.5)
Nonpreferred brands	14 (2.2)	17.1 (6.9)	13.5 (6.5)	43 (17.5)

Abbreviations: CHOL, hypercholesterolemia; DIAB, diabetes; HTN, hypertension.

^aAll copayment and coinsurance means were computed at the plan level. The HTN, CHOL, and DIAB samples included 253 (3.2%), 103 (1.6%), and 149 (3.3%) patients in 1-tier plans; 870 (11.0%), 584 (9.0%), and 471 (10.5%) in 2-tier plans; 6439 (81.7%), 5577 (86.4%), and 3719 (82.9%) in 3-tier copayment plans; and 317 (4.0%), 186 (2.9%), and 147 (3.2%) in coinsurance plans. The mean (SD) out-of-pocket indexes for the 1-, 2-, and 3-tier plans and coinsurance plans were 259 (30), 323 (71), 238 (67), and 516 (78). The mean (SD) percentage of prescriptions filled through mail order in the respective plans were 5% (0.3%), 39% (0.1%), 36% (0.1%), and 51% (0.1%). Mail-order copayments are generally higher than retail because they cover up to a 90-day supply, whereas retail covers a 30-day supply. Several 3-tier plans in our sample offered mail-order copayments that were equal to or less than their retail equivalents.

Table 3. Mapping the OOP Index and Pharmacy Benefits Design

OOP Index	Plan Type	Copayments, \$		Coinsurance, % ^a
		Retail	Mail Order	
15th-25th Percentile				
179	2-tier	5-10	1-5	NA
207	1-tier	5	10	NA
220	3-tier	4.50-9-12	4.50-9-12	NA
50th Percentile				
272	1-tier	7	15	NA
75th-85th Percentile				
370	2-tier	5-12	10-24	NA
393	2-tier	NA	NA	20-45
426	3-tier	5-15-20	10-20-30	NA

Abbreviations: NA, not applicable; OOP, out-of-pocket.

^aCoinurance plans in our sample did not differ in their retail and mail-order cost-sharing levels.

lower copayments at mail-order pharmacies across all tiers (vs 1- and 2-tier plans). Second, mail-order copayments were higher in 1- and 2-tier plans than in 3-tier plans. The 5 coinsurance plans were the least generous plans and had flat coinsurance rates of 25% (n=2), or 2-tier rates of 20% and 45% (n=1) or 35% and 60% (n=2).

Table 3 lists examples of pharmacy benefits and OOP index values for plans in the lower, median, and upper percentiles of the OOP index in our sample. Several formulations of plans, including 1-, 2-, and 3-tier plans, yielded OOP index values near those used for our predictions (OOP indexes of 205 and 410). As noted, the OOP index depended on the magnitude of both retail pharmacy and mail-order cost-sharing arrangements.

Figure 1 displays the Kaplan-Meier survival estimates for the number of days until a patient's first prescription for their newly diagnosed HTN, CHOL, or DIAB. The figure separates survival functions for patients in plans above and below the median OOP index. For all conditions, the rate of initiation was high in the first several months after diagnosis; subsequently, the rate of initiation slowed. Log-rank tests showed that

for each condition, survival functions for patients in high- and low-OOP index groups were significantly different: $P < .001$ for HTN; $P < .001$ for CHOL; and $P = .04$ for DIAB. Thus, in the unadjusted data, higher cost sharing was associated with delayed initiation of drug therapy. At 5 years after diagnosis, the percentage (95% confidence interval) of patients remaining untreated with medications in our sample was 21.5% (19.9%-23.1%) for HTN, 36.0% (34.3%-37.8%) for CHOL, and 32.5% (30.1%-34.9%) for DIAB.

MULTIVARIATE RESULTS

Figure 2 shows that doubling copayments resulted in large differences in the predicted time until initiation for all study conditions. When copayments doubled, the predicted percentage of patients with newly diagnosed HTN initiating pharmacotherapy fell from 54.8% to 39.9% at 1 year and from 81.6% to 66.2% at 5 years ($P < .001$). For patients with newly diagnosed CHOL, the proportion initiating pharmacotherapy fell from 40.2% to 31.1% at 1 year and from 64.3% to 53.8% at 5 years ($P < .002$). For patients with newly diagnosed

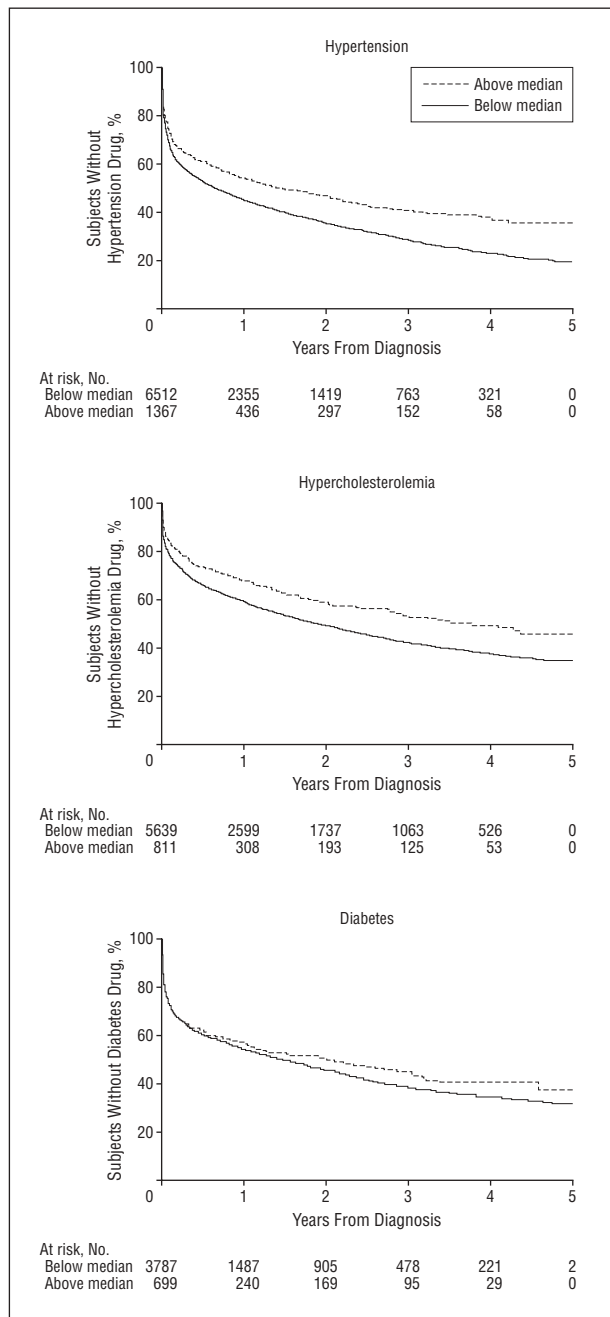


Figure 1. Unadjusted Kaplan-Meier estimates of time until first medication for patients with newly diagnosed chronic disease, above and below the median out-of-pocket (OOP) index, 1997 to 2002. The median OOP index was 272. Below median includes patients in plans with an OOP index lower than 272. Above median includes patients in plans with an OOP index of 272 or higher.

DIAB, initiation fell from 45.8% to 40.0% at 1 year and 69.3% to 62.9% at 5 years ($P=.04$). The difference in the median number of days until pharmacotherapy that resulted from doubling copayments was substantial for all study conditions (244 vs 776 days for HTN; 766 vs 1382 days for CHOL; and 527 vs 813 days for DIAB).

Figure 3 demonstrates that the rate of initiation of drug therapy and the effect of doubling copayments depended on a patient's history of prescription drug use. Compared with patients with no drug use in the year prior to the in-

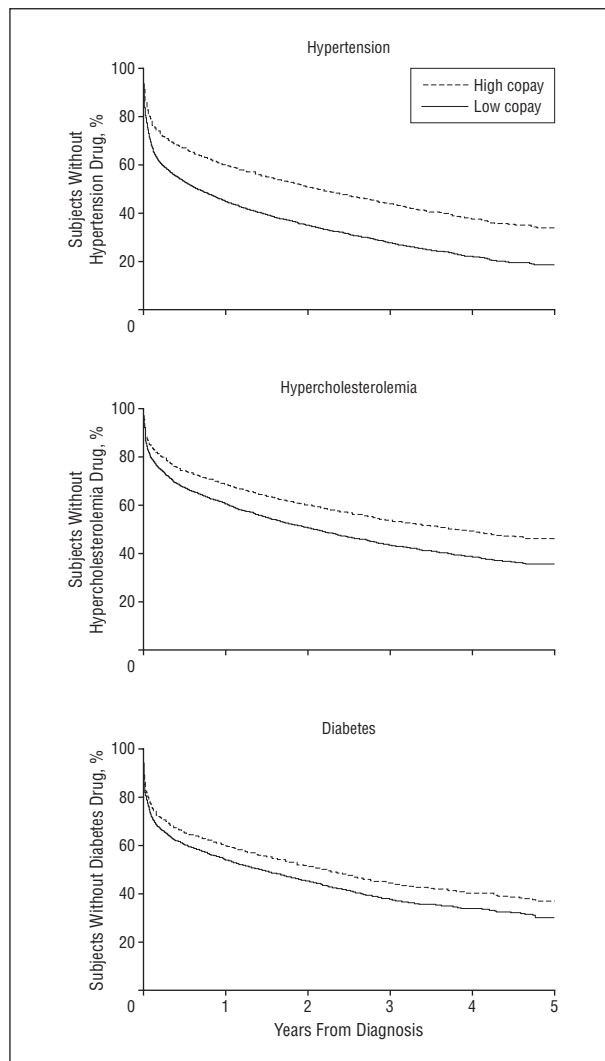


Figure 2. Effect of doubling copayments on the initiation of drug therapy for patients with newly diagnosed chronic disease. An out-of-pocket cost (OOP) index of 205 roughly corresponded to a 1-tier \$5/\$10 retail/mail-order copayment plan (actual OOP index, 206.7). An OOP index of 410 roughly corresponded to a 3-tier \$5-\$15-\$20/\$10-\$20-\$30 retail/mail-order copayment plan (actual OOP index, 425.7). Both values were well within the range observed in the sample.

dex date, patients with any drug use in that period initiated pharmacotherapy earlier and were much less price sensitive. For example, holding cost-sharing levels constant at the lower of our 2 predicted levels (OOP index, 205), the percentage of patients initiating drug therapy by 1 year after diagnosis was much larger among patients with a history of prior drug use for all study conditions: 60.7% vs 40.3% for HTN ($P<.001$); 41.9% vs 21.0% for CHOL ($P<.001$); and 48.4% vs 30.4% for DIAB ($P<.001$).

Doubling copayments among patients with a history of drug use resulted in small differences in the rate of initiation, and the model yielded statistically significant differences only for patients with newly diagnosed HTN or CHOL: 60.7% vs 54.4% at 1 year for HTN ($P=.02$); 42.0% vs 36.3% at 1 year for CHOL ($P=.03$); and 48.5% vs 48.0% at 1 year for DIAB ($P=.85$). By contrast, among patients without a history of drug use, the effect of doubling copayments resulted in large, statistically significant dif-

ferences in survival functions for all study conditions: 40.3% vs 16.6% at 1 year for HTN ($P < .001$); 21.1% vs 9.5% at 1 year for CHOL ($P < .002$); and 30.5% vs 12.9% at 1 year for DIAB ($P < .001$).

SENSITIVITY ANALYSES

We tested more homogeneous samples of higher disease severity; different types and quantities of drugs used in the prior year; various definitions of comorbid conditions; added controls for physician visits; exclusions of the oldest patients; and coinsurance plans (data not shown). None of these sensitivity analyses appreciably changed our model results.

COMMENT

Previous work has established that the chronically ill are sensitive to the cost of prescription drugs. Our study looked at 1 component of utilization: the initiation of drug therapy after diagnosis. We found that increased cost sharing delays the initiation of medications to treat newly diagnosed chronic disease, suggesting that OOP costs may prevent patients from initiating medically necessary care.

In addition, we found that the initiation of drug therapy and sensitivity to prices depends on a patient's experience with prescription drug use. Relative to those without experience, patients with experience using prescription drugs were less price-sensitive and adopted therapy earlier, suggesting that patients differ in their willingness to initiate prescription drug therapy. For some patients, an initial resistance against treatment may be reduced once experience using prescription drugs is established. We found no threshold effect for the number of prior or concurrent medications at which the results of our models changed. Thus, our data suggest that OOP costs may prevent patients from initiating treatment—which could negatively impact health outcomes—but that patient sensitivity to prices strongly depends on whether patients have experience using prescription drugs.

Most prescription drug initiation occurred soon after diagnosis, with a subsequent slowing in the rate of initiation. Also, the effect of cost sharing on the rate of initiation was largest soon after diagnosis, but declined over time. However, the price sensitivity of patients without prescription drug experience declined less rapidly than for those with drug experience, indicating the persistent effect that increased copayments had in this population—a potential indication of a preference against drug therapy.

Our survival estimates were consistent with epidemiologic studies from the National Health and Nutrition Examination Survey (NHANES) III¹⁰ and other sources that estimate the proportion of patients who are aware they have a medical condition but remain untreated.^{12,13,32-44}

In our study, the proportion of newly diagnosed patients who had not initiated anti-HTN, anti-CHOL, or anti-DIAB drug therapy by 5 years was 21.5%, 36.0%, and 32.5%, respectively. Consistent with our data, a variety

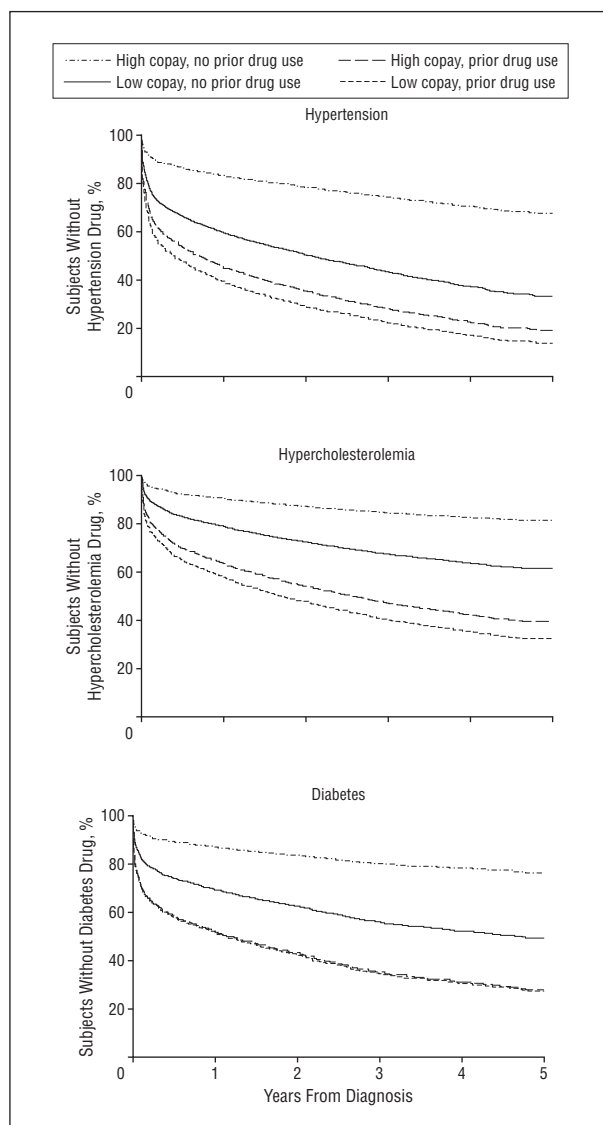


Figure 3. Effect of doubling copayments on the initiation of drug therapy for patients with newly diagnosed chronic disease with and without prior drug use. An out-of-pocket cost (OOP) index of 205 roughly corresponded to a 1-tier \$5/\$10 retail/mail-order copayment plan (actual OOP index, 206.7). An OOP index of 410 roughly corresponded to a 3-tier \$5-\$15-\$20/\$10-\$20-\$30 retail/mail-order copayment plan (actual OOP index, 425.7). Both values were well within the range observed in the sample. For patients with newly diagnosed hypertension, hypercholesterolemia, and diabetes, 26.1%, 10.4%, and 12.9% of each respective sample had no prescription drug use in the year prior to diagnosis.

of studies indicate that the proportion of patients aware of their hypertension but without drug treatment ranges from 8% to 68%.^{32-39,43} In the Framingham Heart Study,⁴³ 68.3% of patients with newly diagnosed HTN had not initiated antihypertensive therapy by 4 years, including 53.9% of those with stage 2 hypertension at baseline,⁴³ and recent estimates range from 8% in a Veterans Affairs institution population³⁴ to 38% to 55% in a community population.³⁵

Untreated CHOL among those aware of their condition is a well-documented and chronic problem. Our estimate of the proportion diagnosed but untreated by 5 years is at the lower end of most population-based estimates, which range from 25% to 66%.^{32,36,41,42,45,46}

Among patients diagnosed with DIAB, estimates of the proportion without drug treatment range from 8% to 47%⁴⁷⁻⁴⁹; recent analyses of NHANES data yield estimates ranging from 19% to 28.6%.^{32,36,50-52} In fact, 23.2% of patients with DIAB who survived a myocardial infarction or stroke, a group likely to be hypervigilant about controlling cardiovascular risk factors, did not use anti-diabetic medications.⁵⁰ Although our estimate of the proportion of patients newly diagnosed with DIAB who remained untreated after 5 years was slightly higher than NHANES estimates, NHANES subjects carried their diagnoses for 2 to 3 times longer than our 5-year follow-up period,³² and the proportion of untreated patients with DIAB increases with age.^{47,49}

There are several limitations to our study. First, our sample may not be generalizable to a younger population. However, Medicare Part D has increased the proportion of elderly retirees who have prescription drug insurance. Thus, our results are particularly relevant for federal policy makers setting standards for Medicare Part D insurance packages.

Second, we could not completely control for selection of drug benefits. However, for all but 2 employers in the sample, employees had no choice of drug benefits, minimizing the possibility that employees selected plans suited to their anticipated needs, and patients with these 2 employers accounted for less than 2.5% of the sample. Excluding these patients did not change our results. Third, despite controls for comorbidities, disease severity may differ between patients with and without prior drug experience.

Although administrative data do not contain detailed clinical information contained in medical charts, our sensitivity analyses examining more homogeneous and severe disease did not change our findings. One initial treatment option for patients newly diagnosed with less severe disease is to initiate nonpharmaceutical therapy such as diet modification and exercise. However, there was no a priori reason that disease severity was correlated with benefit generosity, since almost no patients in our study had a choice of drug benefits plans. Furthermore, analysis of the NHANES data has shown that patients diagnosed with hypertension without pharmacologic treatment have, for example, disease severe enough to warrant treatment (systolic blood pressure >140 mm Hg).¹⁰

Finally, although the data are a few years old, the phenomena studied here are likely to be generalizable and enduring ones. Our results suggest a novel distinction between groups of patients, some of whom are price-sensitive to prescription drugs and others who are not. Although most patients in our sample had experience using prescription drugs, the large impact of cost sharing on those without experience make this population a prime target for interventions to encourage the adoption of appropriate treatment, particularly for patients newly diagnosed with diseases that contribute cardiovascular risk. Future research should explore the mechanisms underlying our results, such as the factors that may influence the effect of cost sharing within specific patient populations, and should examine the health outcomes of varying times to initiation of drug therapy for chronic disease.

Our findings have implications for policy makers designing insurance benefits and for physicians treating patients with chronic disease. First, these results raise concerns about high cost-sharing levels for elderly, insured patients without experience using prescription drugs. Based on our findings, high cost-sharing levels could be a barrier to treatment for this population and possibly result in poor health outcomes. Physicians should also heed these findings when treating patients with newly diagnosed HTN, CHOL, or DIAB; those without experience with pharmacologic therapy may be less likely to initiate prescribed treatments and may be very sensitive to cost-sharing levels.

More broadly, these results add to the growing consensus that our reliance on blunt instruments to influence utilization, such as formularies and tiered copayments, which are primarily used to manage cost, need to be updated with more sophisticated tools that take into account therapeutic need as well as patients' complex responses to insurance benefits.^{53,54} For example, recent evidence indicates that among patients who initiated new medications for treatment of chronic disease, adherence is poorer for those who begin with high copayments than for those who begin with lower copayments that gradually increase.⁵⁵ This suggests that new users are likely to be more price sensitive than continuing users and is congruent with our finding that patients with prescription drug experience are less price-sensitive. Lessons such as these need to be incorporated into benefits design to ensure that patients who require medical therapy are not discouraged from initiating treatment.

Accepted for Publication: November 3, 2008.

Correspondence: Matthew D. Solomon, MD, PhD, Stanford University School of Medicine, Department of Medicine, S101 (m/c 5109), 300 Pasteur Dr, Stanford, CA 94305 (msolomon@stanford.edu).

Author Contributions: Dr Solomon had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Solomon, Goldman, Joyce, and Escarce. *Acquisition of data:* Solomon, Goldman, Joyce, and Escarce. *Analysis and interpretation of data:* Solomon, Goldman, Joyce, and Escarce. *Drafting of the manuscript:* Solomon. *Critical revision of the manuscript for important intellectual content:* Solomon, Goldman, Joyce, and Escarce. *Statistical analysis:* Solomon, Goldman, Joyce, and Escarce. *Obtained funding:* Solomon. *Administrative, technical, and material support:* Solomon. *Study supervision:* Solomon, Goldman, Joyce, and Escarce.

Financial Disclosure: Dr Goldman has received honoraria and consulting income from Amgen, Genentech, and UnitedHealth.

Funding/Support: This research was supported by grant R03 HS013869-01 from the Agency for Healthcare Research and Quality, Rockville, Maryland, with additional funding from the California HealthCare Foundation, Oakland. Data were provided by Ingenix Inc, Eden Prairie, Minnesota.

Role of the Sponsor: Neither the Agency for Healthcare Research and Quality nor California HealthCare Found-

dition had any authority over the design or conduct of this study; the collection, analysis, preparation, or interpretation of the data; or the preparation of the manuscript.

Additional Information: The RAND Corporation is solely responsible for this article's content. The eText, eFigure 1, eFigure 2 and, eTable are available at <http://www.archinternmed.com>.

REFERENCES

1. Smith C, Cowan C, Heffler S, Caitlin A. National health spending in 2004: recent slowdown led by prescription drug spending. *Health Aff (Millwood)*. 2006; 25(1):186-196.
2. Mothral B, Fairman KA. Effect of a three-tier prescription copay on pharmaceutical and other medical utilization. *Med Care*. 2001;39(12):1293-1304.
3. Joyce GF, Escarce JJ, Solomon MD, Goldman DP. Employer drug benefit plans and spending on prescription drugs. *JAMA*. 2002;288(14):1733-1739.
4. Huskamp HA, Deverka PA, Epstein AM, Epstein RS, McGuigan KA, Frank RG. The effect of incentive-based formularies on prescription drug utilization and spending. *N Engl J Med*. 2003;349(23):2224-2232.
5. 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.
6. Hsu J, Price M, Huang J, et al. Unintended consequences of caps on Medicare drug benefits. *N Engl J Med*. 2006;354(22):2349-2359.
7. Mueller C, Schur C, O'Connell J. Prescription drug spending: the impact of age and chronic disease status. *Am J Public Health*. 1997;87(10):1626-1629.
8. McCombs JS, Nichol MB, Newman CM, Sclar DA. The costs of interrupting antihypertensive drug therapy in a Medicaid population. *Med Care*. 1994;32(3): 214-226.
9. Andersson F, Cline C, Ryden-Bergsten T, Erhardt L. Angiotensin converting enzyme (ACE) inhibitors and heart failure: the consequences of underprescribing. *Pharmacoeconomics*. 1999;15(6):535-550.
10. Franklin SS, Jacobs MJ, Wong ND, Italiani GJ, Lapuerta P. Predominance of isolated systolic hypertension among middle-aged and elderly US hypertensives: analysis based on National Health and Nutrition Examination Survey (NHANES) III. *Hypertension*. 2001;37(3):869-874.
11. Grant RW, Cagliero E, Murphy-Sheehy P, Singer DE, Nathan DM, Meigs JB. Comparison of hyperglycemia, hypertension, and hypercholesterolemia management in patients with type 2 diabetes. *Am J Med*. 2002;112(8):603-609.
12. Burt VL, Whelton P, Roccella EJ, et al. Prevalence of hypertension in the US adults population: results from the Third National Health and Nutrition Examination Survey, 1988-1991. *Hypertension*. 1995;25(3):305-313.
13. Burt VL, Cutler JA, Higgins M, et al. Trends in the prevalence, awareness, treatment, and control of hypertension in the adult US population: data from the health examination surveys, 1960 to 1991. *Hypertension*. 1995;26(1):60-69.
14. Harris MI, Flegal KM, Cowie CC, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in US adults: the Third National Health and Nutrition Examination Survey, 1988-1994. *Diabetes Care*. 1998;21(4): 518-524.
15. Hwang W, Weller W, Ireys H, Anderson G. Out-of-pocket medical spending for care of chronic conditions. *Health Aff (Millwood)*. 2001;20(6):267-276.
16. Kane NM. Pharmaceutical cost containment and innovation in the United States. *Health Policy*. 1997;41(suppl):S71-S89.
17. Lipton HL, Gross DJ, Stebbins MR, Syed LH. Managing the pharmacy benefit in Medicare HMOs: what do we really know? *Health Aff (Millwood)*. 2000;19(2): 42-58.
18. Hong SH, Shepherd MD. Outpatient prescription drug use by children enrolled in five drug benefit plans. *Clin Ther*. 1996;18(3):528-545.
19. Smith DG, Kirking DM. Impact of consumer fees on drug utilization. *Pharmacoeconomics*. 1992;2(4):335-342.
20. Harris BL, Stergachis A, Reid LD. The effect of drug co-payments on utilization and cost of pharmaceuticals in a health maintenance organization. *Med Care*. 1990;28(10):907-917.
21. Johnson RE, Goodman MJ, Hornbrook MC, Eldredge MB. The impact of increasing patient prescription drug cost sharing on therapeutic classes of drugs received and on the health status of elderly HMO members. *Health Serv Res*. 1997; 32(1):103-122.
22. Safran DG, Neuman P, Schoen C, Kitchman MS, Wilson IB, Cooper B, Li A, Chang H, Rogers WH. Prescription drug coverage and seniors: findings from a 2003 national survey [published online April 19, 2005]. *Health Aff (Millwood)*. doi:10.1377/hlthaff.w5.152.
23. Reeder CE, Nelson AA. The differential impact of copayment on drug use in a Medicaid population. *Inquiry*. 1985;22(4):396-403.
24. Federman AD, Adams AS, Ross-Degnan D, Soumerai SB, Ayanian JZ. Supplemental insurance and use of effective cardiovascular drugs among elderly Medicare beneficiaries with coronary heart disease. *JAMA*. 2001;286(14):1732-1739.
25. Lohr KN, Brook RH, Kamberg CJ, et al. Use of medical care in the Rand Health Insurance Experiment: diagnosis- and service-specific analyses in a randomized controlled trial. *Med Care*. 1986;24(9)(suppl):S1-S87.
26. 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.
27. Soumerai SB, McLaughlin TJ, Ross-Degnan D, Casteris CS, Bollini P. Effects of limiting Medicaid drug reimbursement benefits on the use of psychotropic agents and acute mental health services by patients with schizophrenia. *N Engl J Med*. 1994;331(10):650-655.
28. Martin BC, McMillan JA. The impact of implementing a more restrictive prescription limit on Medicaid recipients: effects on cost, therapy, and out-of-pocket expenditures. *Med Care*. 1996;34(7):686-701.
29. Fortess EE, Soumerai SB, McLaughlin TJ, Ross-Degnan D. Utilization of essential medications by vulnerable older people after a drug benefit cap: importance of mental disorders, chronic pain, and practice setting. *J Am Geriatr Soc*. 2001; 49(6):793-797.
30. Quam L, Ellis LB, Venus P, Clouse J, Taylor CG, Leatherman S. Using claims data for epidemiological research: the concordance of claims-based criteria with the medical record and patient survey for identifying a hypertensive population. *Med Care*. 1993;31(6):498-507.
31. Rector TS, Wickstrom SL, Shah M, et al. Specificity and sensitivity of claims-based algorithms for identifying members of Medicare+choice health plans that have chronic medical conditions. *Health Serv Res*. 2004;39(6, pt 1):1839-1857.
32. Saydah SH, Fradkin J, Cowie CC. Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. *JAMA*. 2004;291(3): 335-342.
33. Hajjar I, Kotchen T. Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988-2000. *JAMA*. 2003;290(2):199-206.
34. Berlowitz DR, Ash AS, Hickey EC, et al. Inadequate management of blood pressure in a hypertensive population. *N Engl J Med*. 1998;339(27):1957-1963.
35. Raji MA, Kuo YF, Salazar JA, Satish S, Goodwin JS. Ethnic differences in antihypertensive medication use in the elderly. *Ann Pharmacother*. 2004;38(2): 209-214.
36. Hertz RP, Unger AN, Ferrario CM. Diabetes, hypertension, and dyslipidemia in Mexican Americans and non-Hispanic whites. *Am J Prev Med*. 2006;30(2): 103-110.
37. Ong KL, Cheung BM, Man YB, Lau CP, Lam KS. Prevalence, awareness, treatment, and control of hypertension among United States adults 1999-2004. *Hypertension*. 2007;49(1):69-75.
38. Psaty BM, Manolio TA, Smith NL, et al; Cardiovascular Health Study. Time trends in high blood pressure control and the use of antihypertensive medications in older adults: the Cardiovascular Health Study. *Arch Intern Med*. 2002;162(20): 2325-2332.
39. Natarajan S, Nietert PJ. National trends in screening, prevalence, and treatment of cardiovascular risk factors. *Prev Med*. 2003;36(4):389-397.
40. Barker WH, Mullooly JP, Linton KL. Trends in hypertension prevalence, treatment, and control in a well-defined older population. *Hypertension*. 1998;31 (1, pt 2):552-559.
41. Ford ES, Mokdad AH, Giles WH, Mensah GA. Serum total cholesterol concentrations and awareness, treatment, and control of hypercholesterolemia among US adults: findings from the National Health and Nutrition Examination Survey, 1999 to 2000. *Circulation*. 2003;107(17):2185-2189.
42. Arnett DK, Jacobs DR Jr, Luepker RV, Blackburn H, Armstrong C, Claas SA. Twenty-year trends in serum cholesterol, hypercholesterolemia, and cholesterol medication use: the Minnesota Heart Survey, 1980-1982 to 2000-2002. *Circulation*. 2005;112(25):3884-3891.
43. Lloyd-Jones DM, Evans JC, Larson MG, Levy D. Treatment and control of hypertension in the community: a prospective analysis. *Hypertension*. 2002;40 (5):640-646.
44. Glynn RJ, Monane M, Gurwitz JH, Choodnovskiy I, Avorn J. Aging, comorbidity, and reduced rates of drug treatment for diabetes mellitus. *J Clin Epidemiol*. 1999; 52(8):781-790.

45. Jacobs MJ, Kleisli T, Pio JR, et al. Prevalence and control of dyslipidemia among persons with diabetes in the United States. *Diabetes Res Clin Pract.* 2005;70(3):263-269.
46. Nelson K, Norris K, Mangione CM. Disparities in the diagnosis and pharmacologic treatment of high serum cholesterol by race and ethnicity: data from the Third National Health and Nutrition Examination Survey. *Arch Intern Med.* 2002;162(8):929-935.
47. Spooner JJ, Lapane KL, Hume AL, Mor V, Gambassi G. Pharmacologic treatment of diabetes in long-term care. *J Clin Epidemiol.* 2001;54(5):525-530.
48. Grant RW, Buse JB, Meigs JB; University HealthSystem Consortium (UHC) Diabetes Benchmarking Project Team. Quality of diabetes care in U.S. academic medical centers: low rates of medical regimen change. *Diabetes Care.* 2005;28(2):337-442.
49. 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.
50. Qureshi AI, Suri FK, Guterman LR, Hopkins LN. Ineffective secondary prevention in survivors of cardiovascular events in the US population: report from the Third National Health and Nutrition Examination Survey. *Arch Intern Med.* 2001;161(13):1621-1628.
51. Harris MI. Health care and health status and outcomes for patients with type 2 diabetes. *Diabetes Care.* 2000;23(6):754-758.
52. Harris MI. Racial and ethnic differences in health care access and health outcomes for adults with type 2 diabetes. *Diabetes Care.* 2001;24(3):454-459.
53. Fendrick AM, Smith DG, Chernew ME, Shah SNA. 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.
54. Goldman DP, Joyce GF, Karaca-Mandic P. Varying pharmacy benefits with clinical status: the case of cholesterol-lowering therapy. *Am J Manag Care.* 2006;12(1):21-28.
55. Gibson TB, Mark TL, McGuigan KA, Axelsen K, Wang S. The effects of prescription drug copayments on statin adherence. *Am J Manag Care.* 2006;12(9):509-517.

INVITED COMMENTARY

Cost-related nonadherence (CRN) is common, and one-third of older adults take less medication than prescribed to reduce out-of-pocket costs.¹ Common strategies to reduce out-of-pocket costs include splitting pills, skipping doses, or delaying refills, all secondary forms of nonadherence.¹ Less attention has been paid to “primary” nonadherence, ie, not even filling the prescription. This strategy is the most effective way to reduce out-of-pocket costs, and primary nonadherence is practiced by 10% to 20% of patients.²

Short of a randomized trial, the best way to understand the effect of out-of-pocket costs on primary or secondary nonadherence would be to undertake a large longitudinal study of older insured patients who are “exposed” to drug benefit plans of differing generosity and who go on to develop an incident diagnosis of a chronic condition that requires new treatment and then to measure the receipt of a prescription (under control of physicians), the actual filling and refilling of the prescription (under control of patients), and the outcomes related to therapeutic targets and clinical events. This is a tall order, but Solomon et al report a statistically sophisticated study that comes fairly close and, to my knowledge, is the first study to convincingly examine CRN in the context of a new medication regimen for 3 newly diagnosed and common conditions (ie, incident hypertension, dyslipidemia, and diabetes) that require life-long treatment.

There are 2 key findings from their study that adhere to Newton’s laws:

1. *Every action has an equal and opposite reaction.* For all 3 conditions, higher out-of-pocket costs led to long delays in the initiation of drug treatment, and doubling copayments was associated with substan-

tially higher rates of nontreatment 1 and 5 years after the initial diagnosis. Attempts at nonpharmacologic control and use of samples should be exhausted within 6 months, so demonstrating price sensitivity strongly suggests some degree of primary nonadherence. Unfortunately, the investigators’ database was unable to assess this directly because they measured dispensing rather than prescribing records.

2. *Objects at rest tend to stay at rest.* For all 3 conditions, patients who had never before used prescription medications were far more price sensitive and delayed starting treatment far longer than those who had experience with prescription drugs. “Inexperienced” patients did, however, constitute a sizable and easily identified minority of the population (ie, 26% of those with new hypertension, 10% with dyslipidemia, and 13% with diabetes). This subgroup analysis suggests that starting a prescription medication for the first time for an asymptomatic condition and then having to pay out-of-pocket for the opportunity is too bitter a pill to swallow for many patients.

What do these provocative findings mean? For policymakers, it means that blunt instruments such as cost sharing lead to blunt effects, both intended (drug cost savings) and unintended (delays in the initiation of treatment and other forms of CRN that lead to suboptimal health and perhaps to increased total costs).³ More evidence-informed and patient-centered strategies to minimize the unintended consequences of cost sharing need to be developed and then tested in randomized trials or quasi-experimental studies.³

For physicians, it means acknowledging that 10% to 20% of patients never fill our prescriptions and that we need to pay more attention to out-of-pocket costs and discuss them at every opportunity. Unfortunately,