The Effects of Prescription Drug Copayments on Statin Adherence

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Background: High copayments may present a barrier to medication adherence among patients with chronic conditions such as hyperlipidemia.

Objective: To assess the effects of statin copayments on statin adherence among individuals with employer-based insurance.

Study Design: We used a cross-sectional time-series design, with patient as the cross section and month as the time unit.

Methods: Medical and pharmacy claims among continuously enrolled statin users were selected from the 2000-2003 Medstat MarketScan database. Generalized estimating equation models were used to estimate the effects of copayment changes on statin adherence. Adherence was derived from the medication possession ratio, which represents the percentage of days on therapy each month. Separate estimates were obtained for new statin users (n = 142 341) and for continuing statin users (n = 92 344).

Results: Higher copayments were associated with lower statin adherence rates. A 100% index copayment increase had a larger effect on monthly adherence (2.6 and 1.1 percentage point decreases in adherence among new users and continuing users, respectively [both $P < .01$]) than a 100% copayment increase over time (a 1.1 percentage point decrease among new users [$P < .01$] and a nonsignificant decrease among continuing users). In all models, new statin users were more price sensitive than continuing users.

Conclusions: High copayments are a financial barrier to statin adherence. The index copayment amount can affect compliance with statin use. Given the relationship between statin use and decreased frequency of cardiovascular events and procedures, the implications of high copayments should be considered by policy makers.

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Prescription drug spending continues to rise in the United States, with drug expenditures increasing at a double-digit annual rate for most of the past decade.[1] Prescription drug copayments have also increased as employers and other health plan managers attempt to contain prescription drug costs.[2] Patient cost sharing (ie, the price paid by the patient [eg, copayments]) is likely to continue to rise. Recent surveys reveal that many firms intend to continue to increase cost sharing in the near future.[2,3]

Higher prescription drug copayments are associated with lower consumption of prescription drugs and are of concern because they may also lead patients with chronic conditions to decrease utilization of maintenance drugs.[4,5] In practice, copayments may encourage nonadherent behaviors such as skipping doses or stopping a medication altogether.[6,7]

3-Hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (statin) therapy is a widely accepted treatment for patients with high cholesterol. Clinical trials (eg, the National Cholesterol Education Program Expert Panel,[8] Scandinavian Simvastatin Survival Study,[9] Air Force/Texas Coronary Atherosclerosis Prevention Study,[10] and West of Scotland Coronary Prevention Study[11]) demonstrate benefits such as decreases in mortality and morbidity associated with statin therapy. Moreover, the extent of risk reduction increases with the amount of time on statin therapy.[12] Retrospective studies show that higher statin adherence rates are associated with lower medical care costs,[13] fewer hospitalizations,[13,14] fewer emergency department visits,[14] and higher rates of low-density lipoprotein (LDL) cholesterol goal attainment[15] among patients with high cholesterol.

Previous studies[14-17] demonstrate that higher prescription drug copayments are associated with lower statin adherence. Schultz and colleagues[15] analyzed refill patterns among commercially insured patients from 23 independent practice association health plan affiliates of a single national managed care organization who were new users of statins. The authors found that a $1 statin copayment increase was associated with a 1% decrease in the odds of being adherent in the year following treatment initiation (with adherence defined as a daily dose of medication available for ≥80% of the days covered by a prescription). Among 216 patients in a Midwestern managed care organization with a history of acute myocardial infarction or other atherosclerotic event, Coombs and colleagues[16] observed that statin adherence (defined as the percentage of days covered)

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would increase from 0.80 to 0.88 if copayments were cut in half. Ellis and colleagues[17] found that statin adherence (defined as ≤10% of days without medication) decreased as copayments increased among commercially insured patients in a Midwestern managed care organization. For example, when copayments increased from less than $10 to at least $10 but less than $20, the percentage of patients who were compliant with statin use decreased by 10% from the first prescription fill until almost 4 years later (the maximum patient follow-up). Finally, in a study of patients enrolled in 88 health plans, Goldman and colleagues[14] reported that the percentage of fully compliant patients (ie, those with a medication possession ratio [MPR] ≥80%) in the year after statin initiation decreased between 6 and 10 percentage points when copayments for cholesterol-lowering drugs were doubled.

The objective of our study was to examine the effects of prescription drug copayments on statin adherence across a variety of health plans. We analyzed the healthcare experience of patients over time using a panel data framework, with patient as the cross section and month as the time unit. This allowed identification of longitudinal and cross-sectional price effects, as well as inclusion of a person-level effect that controlled for unobserved patient characteristics (heterogeneity) such as the propensity to be adherent to a treatment regimen. In addition, a panel data framework enabled us to delineate the price effects by examining the effects of the index copayment amount compared with the effects of the copayment changes over time. Because new users may respond differently to price changes than established users, we also estimate the magnitude of the price effects on new users of statins vs continuing users of statins.

METHODS

Data Source

The 2000-2003 Medstat MarketScan database was used for this study. More than 45 large firms and more than 100 benefit plan offerings were represented in the database. Patients 18 years and older who were continuously enrolled for 48 months from 2000 through 2003 and who had at least 1 statin prescription fill between 2001 and 2003 were selected for the analysis. Patients with an indication of pregnancy (which can affect adherence) during the study period were excluded from the analysis.

Patient Selection

We analyzed the adherence patterns of new users separately from those of continuing users of statins, because new users are more likely to go through a testing stage to establish treatment efficacy or presence of adverse effects. A total of 142 341 patients who had not filled a statin prescription in the year before the index date (the index date was the date of the first statin fill for new users and was assigned as January 1, 2001, for continuing users) were classified as new (or incident) statin users. There were 92 344 continuing (or prevalent) users.

Study Design

In this study, we followed up a cohort of patients from the index date through December 31, 2003. We used a cross-sectional time-series design, with patient as the cross section and month as the time unit for the adherence analysis. Each continuing user contributed 36 monthly adherence observations. On average, each new user contributed 19 monthly adherence observations.

Explanatory Variables

We developed a model of adherence using the following categories of explanatory variables: copayments, health plan type, comorbidities, time variables, sociodemographic characteristics, and coronary heart disease (CHD) prevalence.[17,18] The key explanatory variable was the statin copayment associated with the patient's health plan offering. For each month of the study, copayments were expressed as an amount per day supplied (in 2003 dollars) and were calculated based on the copayment on each pharmaceutical claim record.

Statin copayments were modeled in 2 ways. First, the mean statin copayment in effect during each month was included in the models. Second, to estimate the effects of the index copayment amount vs the effects of copayment amount changes, copayments were modeled as (1) the index copayment (ie, the copayment at the index date) or (2) the dollar amount of copayment change over time relative to the index copayment amount. Because higher physician office visit copayments are associated with lower prescription drug utilization,[19] health plan–level office visit copayments were included in the models.

Sociodemographic variables included sex, age, geographic region (Northeast, North Central, South, or West), urban residence (residence within a metropolitan statistical area), and an indicator of employee vs spouse/dependent status. Patient age was modeled using 2 linear spline variables to assess potential effects of aging and Medicare eligibility. The first variable was age in years up to and including 65 years old, and the second variable was age in years over 65. Information on patient race/ethnicity was unavailable. The median household annual income was assigned based on patient ZIP code according to the 2000 US Census.

Patients were grouped into high, medium, or low annual income levels by dividing the distribution of incomes among the study sample into thirds, with a low income representing less than $25 000, a medium income representing $25 000 to $49 930, and a high income representing greater than $49 930. The percentage of college graduates was available from the US Census information but was highly collinear with annual income and was not included in the models. Health plan type was classified as comprehensive, health maintenance organization, capitated point of service, noncapitated point of service, or preferred provider organization.

As a surrogate measure for CHD prevalence (and secondary prevention), we indicated the presence of the following cardiovascular diagnoses in a rolling 1-year lag before each month of the study: acute myocardial infarction, angina, coronary artery bypass graft, chronic ischemic heart disease, coronary atherosclerosis, other ischemic heart disease, and percutaneous transluminal angioplasty.[17,18] Comorbidities were measured using the Charlson Comorbidity Index (based on medical claims data and adapted from D'Hoore et al[20]) and using separate indicators for the common comorbid conditions of anxiety, dementia, depression, diabetes mellitus, and hypertension. CHD prevalence and comorbidities were also measured in a rolling 1-year lag. Physician-related variables included the number of different physicians seen by each patient and an indicator for a specialist visit to a cardiologist, endocrinologist, or nephrologist. The specialist visit indicator serves as a proxy for increased disease severity and complexity of comorbidities such as kidney disease. Medication-related variables included the number of different medications that were prescribed across all disease states, perhaps indicating the burden of managing prescriptions. An indicator for any prior mail-order use, which may represent a propensity to invest in health, was also included. An indicator was also included for the use of ezetimibe, a cholesterol-lowering drug approved by the Food and Drug Administration in October 2002, which can be used alone or in conjunction with statins. Physician and medication variables were also measured in a rolling 1-year lag.

Studies[15,17] indicate that the use of LDL cholesterol testing is associated with higher adherence levels. Given the rolling panel design of our study and the use of LDL cholesterol testing for monitoring during statin therapy, the use of LDL cholesterol testing was likely to be endogenous with adherence. Therefore, we chose to use other predictors of adherence.

Because statin adherence decreases over time,[18,21] the amount of time on statin therapy was measured as the number of months since the index date (0-3, 4-6, 7-9, 10-12, 13-18 months, or ≥19 months). For new users, the year of the index prescription was included to account for treatment pattern changes over time.

Outcome Measures

Adherence was derived from the MPR, calculated as the usable days supplied from among all statin refills in the month, divided by the number of days in the month. To calculate the monthly MPR, each day was evaluated as covered or as not covered by a prescription fill. Covered days comprised the time between the fill date and the end date of the prescription (ie, the fill date plus the days' supply of the prescription). If a refill for the same statin occurred before the end date of the previous prescription, the days' supply for the new prescription was appended to the end date of the previous prescription. If a refill for a statin occurred after the end date of the previous prescription, the days between the 2 prescriptions were considered uncovered days. If a patient received a prescription for a new statin drug while he or she had a usable supply of another statin on hand, no overlap occurred, and counting commenced from the fill date of the new statin. Few patients (approximately 10%) switched statin drugs during the study.

The MPR measures statin adherence and does not include switches to other cholesterol-lowering medications; therefore, the statin adherence rates reported herein are somewhat lower than the adherence rates associated with all cholesterol-lowering medications. We were unable to measure adherence behavior while patients were hospitalized, although hospitalization occurred infrequently (approximately 2% of patients each month).

The monthly MPR distribution was largely bimodal, so we expressed adherence as an MPR of 80% or higher.[15,21] Similar thresholds have been established as beneficial in clinical trials[11,22] and in the statin adherence literature.[14,15] By setting the adherence level at an MPR threshold of 80%, we allowed for some variation in use. However, we were unable to determine whether patients received drug samples or were splitting pills at the direction of a provider. In a well-insured population such as this, the use of samples is likely to be low. We did not see a large number of patients who had an MPR of 50% (which would indicate splitting pills in half), so the amount of pill splitting was also likely to be low.

Adherence was calculated among patients in each month following the index date through December 31, 2003. This allowed analysis of the actual adherence behavior of patients, including patients with inconsistent adherence patterns.

Modeling Approach

Adherence was modeled as a function of the following covariates: adherence_{it} = f (sociodemographic charac-

teristics$_{it}$, health plan type$_{it}$, physician variables$_{ip}$, medication variables$_{ip}$, CHD prevalence$_{ip}$, comorbidities$_{ip}$, copayment$_{it}$, and time variables$_{it}$), where i represents patient; t, month; and p, rolling 1-year lag.

Generalized Estimating Equation models were used to model adherence using a binomial outcome and a logit link.[23,24] Standard errors were adjusted for clustering by patient over time using robust standard errors to decrease the effects of unknown heteroscedasticity or specification errors.[25] Separate models were estimated for new users and for continuing users.

RESULTS

A total of 234 685 statin users were identified who met all inclusion criteria. Descriptive characteristics of the new users and the continuing users are given in **Table 1**. The patient cohort contained approximately 50% more new users (n = 142 341) than continuing users (92 344), with approximately one third of new users initiating statin therapy in each study year.

Among new users, 51.3% were men, and 48.7% were women (mean age, 57.0 years) (Table 1). New users were more likely to be employees (vs spouses/dependents), to reside in the South (vs other geographic regions), and to be enrolled in a preferred provider organization (vs other health plan types). Almost one fifth (18.1%) had a diagnosis of angina, and 12.5% had a diagnosis of coronary atherosclerosis in the year before the index prescription. Other CHD diagnoses (acute myocardial infarction, coronary artery bypass graft, chronic ischemic heart disease, and percutaneous transluminal angioplasty) were each present in fewer than 5% of patients. Comorbidities were prevalent among new users. Almost 44% of patients had a diagnosis of hypertension, and 19.6% had a diagnosis of diabetes mellitus in the year before the index prescription. New users filled a mean of 6.4 medications in the year before the index prescription, and 41.6% had used a mail-order pharmacy to fill a prescription in the previous year. The mean statin copayment was approximately $15 per prescription for a 30-day supply ($0.51 per day) (the models and the tables use a daily copayment rate; all copayments are reported elsewhere in the article as the amount per 30-day supply) at the time of the index prescription. The mean statin copayment increase was $1.50, including health plans that did and did not increase copayments, which aids identification of the effects of copayments on adherence. The maximum copayment increase was approximately $25.

Among continuing users, 55.4% were men, and 44.6% were women (mean age, 64.1 years) (Table 1). Continuing users were more likely to be employees (vs spouses/dependents), to reside in the South (vs other geographic regions), and to be enrolled in a capitated point-of-service health plan (vs other health plan types). Approximately one fifth (20.1%) had a diagnosis of coronary atherosclerosis, and 15.5% had a diagnosis of angina in the year before the index prescription. Almost 44% of patients had a diagnosis of hypertension, and 19.5% had a diagnosis of diabetes mellitus in the year before the index date. Continuing users filled a mean of 8.8 medications in the year before the index date, and 58.1% had used a mail-order pharmacy to fill a prescription in the year before the index date. The mean statin copayment was approximately $12 per prescription for a 30-day supply ($0.41 per day) at the index date. The mean statin copayment increase was $1.80, including health plans that did and did not increase copayments. The maximum copayment increase was approximately $39.

The mean monthly adherence, measured across all postindex months, was higher among continuing users, who had 71% of months with an MPR exceeding 80% (Table 1). New users had 48% of months with an MPR exceeding 80%.

Adherence Models

Results from the Generalized Estimating Equation models of adherence revealed that among new users higher copayments were associated with lower monthly adherence (**Table 2**). A $10 index copayment increase was associated with a 3% decrease ($P < .01$) in the odds of adherence. In percentage terms, a 100% index copayment increase was associated with a 1.2 percentage point decrease in the probability of monthly adherence.

Alternatively, the marginal effect of a $10 copayment increase over time was associated with a 0.76 percentage point ($P < .01$) decrease in the probability of monthly adherence. The marginal effect of a $20 copayment increase over time was associated with a 1.53 percentage point ($P < .01$) decrease in the probability of monthly adherence. By contrast, higher copayments were not associated with a significant decrease in the probability of monthly adherence among continuing users.

Previous studies also report decreased adherence associated with copayment increases among new users,[14,15] as well as among new users and continuing users combined.[16,17] To our knowledge, no studies other than the present study have analyzed effects on continuing users alone. Furthermore, our study measured monthly effects, while other studies[14-17] examined effects on an annual basis (or longer).

When copayments were modeled as index copayments vs amount of copayment change over time, index copayments had much larger effects on adherence than

Table 1. Patient Sociodemographic and Other Characteristics at the Index Date*

Characteristic	New Users (n = 142 341)	Continuing Users (n = 92 344)
Sex†		
Female	48.7	44.6
Male	51.3	55.4
Age, mean ± SD, y†	57.0 ± 11.9	64.1 ± 11.2
Geographic region†		
Northeast	19.4	25.3
North Central	24.2	33.6
South	51.8	35.6
West	4.5	5.4
Unknown	0.1	0.1
Urban residence†	74.9	81.4
Annual income, mean ± SD, $†	45 503 ± 18 550	48 236 ± 18 533
College graduate, mean ± SD†	23.9 ± 0.2	25.4 ± 0.2
Status indicator†		
Employee	68.6	71.4
Spouse/dependent	31.4	28.6
Health plan type†		
Comprehensive	27.7	29.0
Health maintenance organization	4.5	3.2
Capitated point of service	15.0	33.3
Noncapitated point of service/exclusive provider organization	16.7	6.4
Preferred provider organization	36.1	28.1
Physician variables, rolling 1-y lag		
Previous specialist visit†	19.8	13.6
No. of different physicians, mean ± SD†	3.9 ± 3.6	5.0 ± 3.8
Coronary heart disease prevalence, rolling 1-y lag		
Acute myocardial infarction†	3.7	2.1
Angina†	18.1	15.5
Coronary artery bypass graft†	1.8	1.1
Chronic ischemic heart disease†	2.3	4.3
Coronary atherosclerosis†	12.5	20.1
Other ischemic heart disease†	3.8	3.4
Percutaneous transluminal angioplasty†	1.6	2.0
No diagnosis of cardiovascular disease†	78.4	70.2
Comorbidities, rolling 1-y lag		
Charlson Comorbidity Index, mean ± SD†	1.0 ± 1.5	1.0 ± 1.5
Anxiety†	2.5	1.6
Dementia†	0.4	0.3
Depression†	5.5	3.8
Diabetes mellitus	19.6	19.5
Hypertension	43.7	43.7
Medication variables, rolling 1-y lag		
No. of different medications, mean ± SD†	6.4 ± 5.7	8.8 ± 5.4
Any prior mail-order use†	41.6	58.1
Time variables		
Index year 2001	30.8	100.0
Index year 2002	38.1	—‡
Index year 2003	31.1	—‡
Copayment per day, mean ± SD, $		
Statin†§	0.51 ± 0.19	0.41 ± 0.17
Index statin†§	0.49 ± 0.25	0.39 ± 0.21
Statin change†§‖	0.05 ± 0.19	0.06 ± 0.15
Outpatient physician visit†	8.38 ± 6.57	5.15 ± 4.05
Monthly adherence, mean of all months†	0.48 ± 0.50	0.71 ± 0.45

*Data are given as percentages unless otherwise indicated.
†$P < .1$.
‡For new users only, the year of the index prescription was included to account for treatment pattern changes over time.
§The models and tables use a daily copayment rate; all copayments are reported elsewhere in the article as the amount per 30-day supply.
‖This amount includes plans that did and did not increase copayments, which aids identification of the effects of copayments on adherence. The maximum copayment increase was $0.83 per day among new users and $1.29 per day among continuing users.

Table 2. Statin Adherence Models Among New Users and Continuing Users*

Variable	New Users (n = 142 341)		Continuing Users (n = 92 344)	
	Mean Copayment	Index Copayment + Copayment Change	Mean Copayment	Index Copayment + Copayment Change
Female sex	−0.148 (0.847-0.878)†	−0.147 (0.848-0.879)†	−0.105 (0.884-0.918)†	−0.104 (0.884-0.918)†
Age, y				
≥65	0.024 (1.023-1.025)†	0.023 (1.023-1.025)†	0.023 (1.022-1.025)†	0.023 (1.022-1.025)†
<65	−0.014 (0.984-0.988)†	−0.014 (0.984-0.988)†	−0.013 (0.985-0.989)†	−0.013 (0.985-0.989)†
Annual income				
Medium	0.228 (1.202-1.312)†	0.221 (1.194-1.303)†	0.187 (1.130-1.285)†	0.185 (1.129-1.283)†
High	0.241 (1.212-1.337)†	0.235 (1.204-1.328)†	0.220 (1.164-1.335)†	0.219 (1.162-1.332)†
College graduate	0.479 (1.493-1.745)†	0.484 (1.501-1.755)†	0.119 (1.042-1.218)†	0.124 (1.047-1.224)†
Physician variables, rolling 1-y lag				
Previous specialist visit	−0.023 (0.967-0.989)†	−0.023 (0.967-0.988)†	−0.007 (0.983-1.002)	−0.008 (0.983-1.002)
No. of different physicians	0.000 (0.998-1.001)	0.000 (0.998-1.001)	−0.008 (0.991-0.994)†	−0.008 (0.991-0.994)†
Coronary heart disease prevalence, rolling 1-y lag				
Acute myocardial infarction	0.073 (1.048-1.104)†	0.073 (1.048-1.104)†	−0.031 (0.943-0.996)‡	−0.031 (0.943-0.997)‡
Angina	−0.03 (0.96-0.98)†	−0.03 (0.96-0.98)†	−0.005 (0.987-1.004)	−0.004 (0.987-1.004)
Coronary artery bypass graft	0.058 (1.022-1.099)†	0.058 (1.022-1.099)†	−0.115 (0.859-0.925)	−0.115 (0.859-0.925)†
Chronic ischemic heart disease	0.010 (0.986-1.035)	0.010 (0.986-1.035)	0.002 (0.986-1.018)	0.002 (0.986-1.019)
Coronary atherosclerosis	0.032 (1.018-1.046)†	0.032 (1.018-1.046)†	0.016 (1.007-1.025)†	0.016 (1.007-1.025)†
Other ischemic heart disease	−0.006 (0.971-1.018)	−0.006 (0.971-1.018)	0.026 (1.006-1.047)†	0.026 (1.006-1.047)†
Percutaneous transluminal angioplasty	0.092 (1.058-1.135)†	0.091 (1.058-1.135)†	0.005 (0.973-1.039)	0.006 (0.973-1.039)
Comorbidities, rolling 1-y lag				
Charlson Comorbidity Index	−0.012 (0.985-0.992)†	−0.012 (0.985-0.992)†	−0.018 (0.980-0.985)†	−0.018 (0.980-0.985)†
Anxiety	−0.013 (0.962-1.012)	−0.013 (0.962-1.013)	−0.011 (0.965-1.013)	−0.011 (0.965-1.013)
Dementia	−0.097 (0.858-0.960)†	−0.098 (0.857-0.960)†	−0.136 (0.835-0.912)†	−0.136 (0.835-0.912)†
Depression	−0.009 (0.972-1.010)	−0.010 (0.971-1.010)	−0.055 (0.929-0.964)†	−0.055 (0.929-0.964)†
Diabetes mellitus	0.047 (1.031-1.066)†	0.048 (1.031-1.067)†	0.000 (1.016-1.046)†	0.030 (1.016-1.045)†
Hypertension	0.014 (1.006-1.022)†	0.014 (1.006-1.022)†	0.015 (1.009-1.022)†	0.015 (1.009-1.022)†
Medication variables, rolling 1-y lag				
No. of different medications	−0.023 (0.976-0.978)†	−0.023 (0.976-0.978)†	−0.005 (0.994-0.996)†	−0.005 (0.994-0.996)†
Any prior mail-order use	0.178 (1.184-1.205)†	0.178 (1.184-1.205)†	0.075 (1.069-1.087)†	0.075 (1.069-1.087)†
Ezetimibe	−0.498 (0.586-0.631)†	−0.499 (0.585-0.630)†	−0.306 (0.718-0.756)†	−0.306 (0.718-0.756)†
Time variables				
Index year 2002	0.342 (1.381-1.436)†	0.348 (1.388-1.444)†	—§ —§	—§ —§
Index year 2003	0.211 (1.207-1.265)†	0.222 (1.220-1.279)†	—§ —§	—§ —§
Months 4-6	−1.346 (0.258-0.263)†	−1.346 (0.258-0.263)†	−0.363 (0.688-0.703)†	−0.363 (0.688-0.703)†
Months 7-9	−1.766 (0.169-0.173)†	−1.766 (0.169-0.173)†	−0.726 (0.478-0.490)†	−0.726 (0.478-0.490)†
Months 10-12	−2.033 (0.129-0.132)†	−2.033 (0.129-0.132)†	−0.966 (0.376-0.385)†	−0.966 (0.376-0.386)†
Months 13-18	−2.292 (0.100-0.102)†	−2.294 (0.100-0.102)†	−1.200 (0.297-0.305)†	−1.200 (0.297-0.305)†
Months ≥19	−2.524 (0.079-0.081)†	−2.525 (0.079-0.081)†	−1.415 (0.240-0.246)†	−1.415 (0.240-0.246)†
Copayment per day				
Mean copayment‖	−0.093 (0.901-0.922)†	— —	−0.004 (0.987-1.006)	— —
Index copayment‖	— —	−0.206 (0.785-0.845)†	— —	−0.088 (0.874-0.960)†
Copayment change‖	— —	−0.085 (0.908-0.930)†	— —	−0.001 (0.989-1.008)
Outpatient physician visit	−0.007 (0.992-0.994)†	−0.007 (0.993-0.994)†	−0.008 (0.991-0.992)†	−0.008 (0.991-0.992)†
Monthly adherence, mean of all months	0.035 (0.957-1.121)	0.094 (1.014-1.191)‡	−0.248 (0.694-0.878)†	−0.232 (0.705-0.892)†

*Data are given as coefficient (95% confidence interval of adjusted odds ratio). Continuing users filled a statin prescription in the year before the study (ie, 2000). New users had at least 1 year before the index statin prescription without a previous statin fill. Models also included explanatory variables for geographic region, urban residence, health plan type, and employee vs spouse/dependent indicator.

†$P < .01$.

‡$P < .05$.

§For new users only, the year of the index prescription was included to account for treatment pattern changes over time.

‖The models and tables use a daily copayment rate; all copayments are reported elsewhere in the article as the amount per 30-day supply.

mean copayments or amount of copayment change. Increasing the index copayment by $10 led to a 6.6% decrease ($P < .01$) in the odds of being adherent among new users and a 2.9% decrease ($P < .01$) in the odds of being adherent among continuing users. The effect of a $10 copayment increase following the index date was a 2.8% decrease ($P < .01$) in the odds of being adherent among new users but the decrease was nonsignificant among continuing users.

In percentage terms, a 100% index copayment increase led to a 2.6 percentage point decrease in the probability of monthly adherence ($P < .01$) among new users and a 1.1 percentage point decrease in the probability of monthly adherence ($P < .01$) among continuing users. A 100% copayment increase over time led to a 1.1 percentage point decrease in the probability of monthly adherence among new users ($P < .01$) and a nonsignificant decrease among continuing users.

Figure 1. Index Copayment and Monthly Statin Adherence

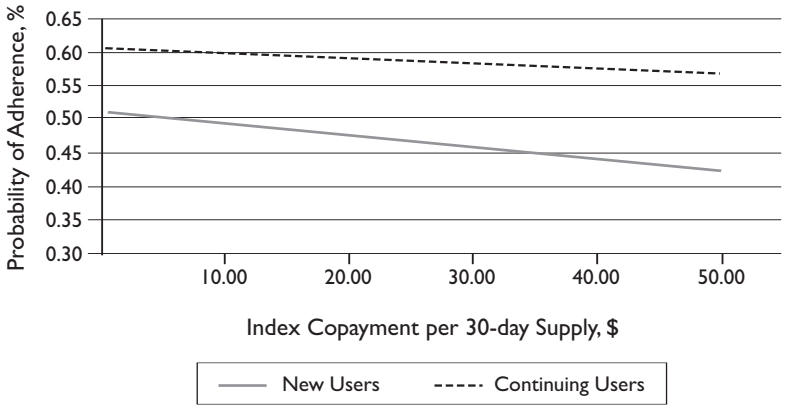


Figure 1 and **Figure 2** show the predicted percentage adherence at various copayment levels with all other variables held at their mean values. Continuing users had higher statin adherence rates and were less sensitive to copayment changes than new users. Statin adherence rates were more sensitive to index copayment changes than to copayment changes over time. For example, statin adherence rates were 2.5 percentage points lower among new users with a $20 index copayment (47.6% adherence) compared with new users with a $5 index copayment (50.1% adherence) (odds ratio [OR], 0.949; $P < .01$). When copayments remained the same over time (holding all other variables at the mean values), the predicted probability of monthly adherence was 48.8%, but a $10 copayment increase led to a 0.7 percentage point decrease in predicted adherence to 48.1% (OR, 0.984; $P < .01$), and a $20 copayment increase led to a 1.5 percentage point decrease in predicted adherence to 47.3% (OR, 0.971; $P < .01$).

Several sensitivity analyses were performed. First, the results were replicated using the index copayment amount and the percentage copayment increase over time (vs the dollar amount of copayment increase over time). Next, new users whose index date occurred in the final 3 months of the study (representing 7.9% of new users) were excluded to determine whether inclusion of short-term patients affected the results. We also repeated the analysis after excluding the mail-order use variable, in the event that mail-order use was correlated with price sensitivity. However, these models produced findings similar to those reported herein (data not shown).

We also added an employer fixed effect to the mean copayment model to identify the effects associated with copayment changes over time. Because the index copayment acts as a fixed effect, the results were similar to those reported herein.

The effect of time to first evidence of discontinuation (defined as a ≥30-day break in statin use) was analyzed using survival models. The results were similar to those reported herein (data not shown).

Effects of Explanatory Variables

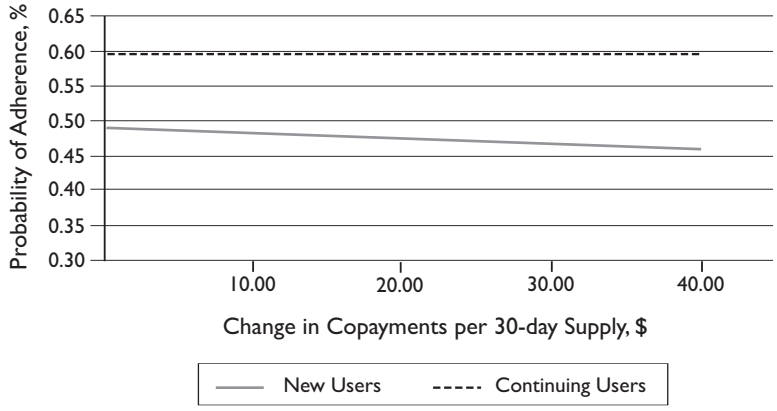
The effects of the explanatory variables on statin adherence were generally in the expected direction, and most of the explanatory variables had the same direction of effect on new users and on continuing users. Selected results are discussed herein. The effects of the other explanatory variables on adherence are given in Table 2.

Consistent with most previous studies,[15,17,21] women were less adherent to statin therapy than men. The effect of age on adherence was nonlinear. As age advanced toward 65 years, adherence increased; however, adherence decreased after age 65 years.

Among new users, statin adherence increased with the diagnosis of severe cardiovascular disease, which is consistent with the results of previous studies.[14,15] Among continuing users, statin adherence decreased with the diagnosis of acute myocardial infarction or coronary artery bypass graft in the previous 12 months, indicating a possible shift in the therapeutic regimen after these adverse events or a discontinuation of treatment because of perceived lack of efficacy.[18]

Increased numbers of different medications used were associated with decreased statin adherence, a result that is consistent with previous studies.[16,18] Not

Figure 2. Copayment Change Over Time and Monthly Statin Adherence



surprisingly, annual income played a role in statin adherence. Middle-income and high-income patients had higher adherence rates than low-income patients. One of the strongest negative predictors of adherence was the use of ezetimibe, a possible statin substitute. High physician copayments served as a barrier to statin adherence among new users and continuing users. A $1 increase in physician copayments led to less than a 1% decrease in the likelihood of adherence. Another predictor of low adherence was the amount of time since the index date. The odds of adherence decreased with the amount of time since the index date, and the largest decreases in adherence occurred within the first 9 months after the index date, which is consistent with previous findings.[18]

DISCUSSION

In this large cohort of statin users enrolled in employer-sponsored health plans, prescription drug copayments were a financial barrier to statin adherence. However, all statin users did not exhibit the same amount of price responsiveness to high copayments. Notably, new users of statins (who were less likely to have received care for a recent cardiovascular event) were more price responsive than continuing users in terms of adherence, which in our study is a measure of the supply of statins on hand.

When analyzed separately, the index copayment had a larger effect on adherence than copayment changes over time. Focusing on the index copayment amount may be a strategy to improve statin adherence. From an economic perspective, lowering the copayment would improve affordability of statins among consumers. Although economic loss of the high copayment may have an initial negative effect on health plan expenditures, the downstream cost savings associated with decreased frequency of cardiovascular events and procedures because of continued statin adherence, as supported by the clinical trial literature,[11,26] may more than offset the index copayment loss. Given the particular challenges faced by new users and the effects of index copayments on new users, temporary decreases in index copayments (through coupons, free samples, or other subsidies) may lessen financial barriers to initiation of statin therapy and to statin adherence.

The smaller longitudinal price effects of statin copayment increases that were observed among continuing users may be related to the paucity of good substitutes for statins. Patients may continue to consume statins after a price increase and may be less price responsive because they have few good alternatives.

There are several limitations to the findings in this study. Our study focuses on the effects in a continuously enrolled population with employer-sponsored insurance, among whom annual incomes tend to be high. Although the magnitude of effects is likely to apply to patients in employer-sponsored health plans, these results can provide a lower bound for estimates of the effects of copayments among patient populations in which the percentage of annual income spent on prescription drugs is high, such as among low-income or older patients and among patients with many chronic illnesses.

The copayment effects in our study more likely indicate the price effects on medication compliance among new users than among continuing users. Among continuing users, the amount of time on statin therapy before the index month varied and was not evaluated. The estimates likely represent the effects of copayments on subsequent adherence in an existing group of medication users, among whom adherence may have already been affected by copayments. In addition, it is possible that people select their drug plans based on drug copayments. If more adherent patients selected health plans with lower copayments, the results may be biased upward. We do not believe this to be substantial because the employers in the database typically offer little to no variation in the drug benefit plan to specific classes of enrollees (eg, hourly active or salaried retiree enrollees), although other aspects of the health plan may vary.

Many investigations focus on the effects of specific interventions in improving patient compliance. Our

study reveals that decreasing the patient's share of costs for a maintenance drug regimen may be an effective intervention. Given the effectiveness of long-term statin therapy on outcomes, additional research is needed to determine whether reduction of financial barriers by lowering copayments (with the expected expansion in prescription drug utilization and economic effects) is a clinically effective and cost-effective benefit plan option.

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