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RESEARCH

Association of Copayment with Likelihood and Level of Adherence in New Users of Statins: A Retrospective Cohort Study

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ABSTRACT

BACKGROUND: Statins remain a fundamental component of pharmacologic therapy for hyperlipidemia. Health benefits of statin therapy are jeopardized when adherence is reduced.

OBJECTIVES: To (a) assess the association between copayment and copayment type on statin adherence using 2 different thresholds of adherence and (b) identify the incremental change in statin adherence associated with presence of copayment and copayment type.

METHODS: We executed a retrospective cohort study of new users of statins with dyslipidemia from the Veterans Health Administration (VHA) within the Veterans Integrated Service Network 22 who initiated a statin between November 30, 2006, and December 2, 2007. We used exposure categories of Any Copayment versus No Copayment, indicating a patient had a copayment or had no copayment in order to obtain medications, respectively. As a separate analysis, we varied the exposures to the standard VHA copayment categories: (a) Service-Connected (SC) Copayment (patients with service-related injury), (b) Non-Service-Connected (NSC) Copayment (patients without a service-related injury), and (c) No Copayment. Using each set of exposures, we conducted separate multiple logistic regression analyses using 2 different adherence outcomes based on medication possession ratio (MPR) threshold: (1) adherence defined as MPR ≥ 0.8 and (2) adherence defined as MPR ≥ 0.9. We then proceeded with multiple linear regression models to determine the incremental change in MPR associated with the 2 sets of exposures. Subjects were required to be enrolled in VHA services for at least 2 years prior to index date and throughout the 1-year study period.

RESULTS: A total of 4,886 subjects were identified for analysis based on the inclusion and exclusion criteria. Patients who did not pay a copayment for their statin medications were more likely to have adherence rates of ≥ 0.8 MPR and ≥ 0.9 MPR relative to the No Copayment Group with odds ratios (OR) of 1.19 (95% CI = 1.03-1.37) and 1.28 (95% CI = 1.11-1.48), respectively. The second analysis applied the VHA exposure categories of SC Copayment, NSC Copayment, and No Copayment. Using the 0.8 MPR or greater adherence threshold, the No Copayment group was associated with an increased likelihood of adherence versus the SC Copayment category as reference group with an OR of 1.31 (95% CI = 1.10-1.58). The NSC Copayment was associated with a nonsignificant increase in odds of adherence at the 0.8 MPR level or greater with OR of 1.12 (95% CI = 0.98-1.39). Using the 0.9 MPR level or greater, adherence threshold findings were similar. The No Copayment group produced an OR of 1.42 (95% CI = 1.17-1.71) compared with the SC Copayment group. The NSC Copayment group was associated with a nonsignificant increase in odds of adherence at the 0.9 MPR level or greater with an OR of 1.12 (95% CI = 0.97-1.38).

The No Copayment group was associated with an increase in MPR of 0.02 (95% CI = 0.002-0.035) versus the Any Copayment category. Using the VHA copayment categories, we observed an increase in MPR for the No Copayment group versus the SC Copayment group of 0.03 (95% CI = 0.01-0.05). The NSC Copayment group was associated with a nonsignificant increase in MPR versus the SC Copayment group of 0.02 (95% CI = -0.003-0.036).

CONCLUSIONS: Patients without out-of-pocket payments for their statins were more likely to adhere to therapy. Patients who pay a copayment for their statin medications were also compared with each other based on whether they (a) received any of their nonstatin prescriptions without a copayment or (b) paid a copayment on all of their prescriptions including statins. Our findings suggest that, among those that pay for their statins, patients are less adherent to their statins if other medications they are prescribed are copayment free. Thus, patient consumption behavior may be influenced by the relative cost of medications in patient prescription lists. Additional counseling on the necessity of adherence should be given to patients paying a copayment for their statin prescriptions.

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What is already known about this subject

- A retrospective cohort of 171,535 health maintenance organization patients found that patients adherent to statin therapy experienced a decreased risk approaching one half that of nonadherent patients for myocardial infarction or performance of a cardiac revascularization procedure with a hazard ratio of 0.58 (95% CI = 0.55-0.62).
- Meta-analysis of publicly insured patients observed an increase in odds of nonadherence for patients with a copayment for their prescriptions of 1.11 (95% CI = 1.09-1.14).

What this study adds

- Previous studies have examined the influence on adherence of using a single threshold of adherence, typically an MPR ≥ 0.8. We have enhanced this standard by applying this traditional threshold as well as a more stringent adherence threshold of MPR ≥ 0.9.
- We observed that patients who did not pay a copayment for their statin medications were more likely to have adherence rates of 0.8 MPR or greater with odds ratio (OR) of 1.19 (95% CI = 1.03-1.37) favoring the No Copayment group. Using a threshold of 0.9 MPR or greater produced similar findings with OR of 1.28 (95% CI = 1.11-1.48).
- We also applied the VHA exposure categories of Service-Connected (SC) Copayment, Non-Service-Connected (NSC) Copayment, and No Copayment. Using the 0.8 MPR or greater adherence threshold, the No Copayment group was associated with an increased likelihood of adherence versus the SC Copayment category as reference group with an OR of 1.31 (95% CI = 1.10-1.58). NSC Copayment was associated with a nonsignificant increase in odds of adherence at the 0.8 MPR level or greater with OR of 1.12 (95% CI = 0.98-1.39).

Statin therapy remains the primary choice for pharmacotherapy-based treatment of hyperlipidemia if therapeutic lifestyle changes have not reached the desirable depth of lipid lowering.[1] Results from the most recent Cochrane Collaboration review of 18 randomized control trials (56,934 participants) demonstrated reductions in all-cause mortality, combined fatal and nonfatal cardiovascular disease, combined fatal and nonfatal coronary heart disease events, combined fatal and nonfatal stroke, and reduction of revascularization rates with reductions in low-density lipoprotein and total cholesterol levels.[2] The suite of possible cardiovascular benefits from statins continues to extend with an increasing body of evidence, demonstrating reduction in incidence and recurrence of atrial fibrillation for patients treated with statins.[3-5] However, suboptimal adherence has been demonstrated in follow-up studies of statin consumption.[6,7] This diminished adherence has been correlated extensively with worse cardiovascular outcomes. A retrospective cohort of 171,535 health maintenance organization patients found that patients with statin adherence levels at or exceeding 80% experienced a decreased risk approaching one half that of less adherent patients for myocardial infarction or performance of a cardiac revascularization procedure with a hazard ratio of 0.58 (95% confidence interval [CI] = 0.55-0.62).[8] Adherent patients have also been associated with reduced health services utilization. Gibson et al. (2006) observed that statin adherent patients experienced fewer visits to the emergency department, hospitalizations, and coronary heart disease-related hospitalizations.[9] Health services-related costs should be reduced for the adherent, benefiting from their diminished frequency of medical encounters compared with nonadherent patients. A 2013 systematic review of studies assessing adherence to coronary artery disease (CAD) medications and costs found that adherent patients have been associated with reductions in costs of secondary prevention of CAD between $294 and $868 per patient.[10] Diabetic patients who were adherent to statins were found to have statistically significant reductions in all-cause medical costs of 15% and a decrease in hyperlipidemia-related costs of 12%.[11]

Prior studies have examined the influence of copayment category on the change in adherence.[9,12-14] We have attempted to bolster previous approaches by determining the increase in likelihood of adherence based on copayment using 2 distinct adherence thresholds and also by determining the incremental change in adherence caused by copayment in a retrospective cohort of new users of statins in the Veterans Health Administration (VHA).

Methods

Design Overview

We executed a retrospective cohort study of new users of statins from the VHA to examine the influence of the 2 standard VHA copayment categories versus the No Copayment category. We also collapsed the 2 copayment groups and compared adherence in those with and without a copayment via multiple regression. This comparison allows a characterization of the increase in odds of adherence for the designated copayment groups of the VHA as well as a comparison of patients facing any copayment versus those patients who have none for receiving their statin prescriptions. We also executed multiple linear regressions to characterize the incremental effect of copayment categories on adherence. This use of multiple regressions provided for a robust analysis characterizing the influence of copayment on the odds of adherence as well as the unit change in adherence adjusted for confounders.

Sample Selection

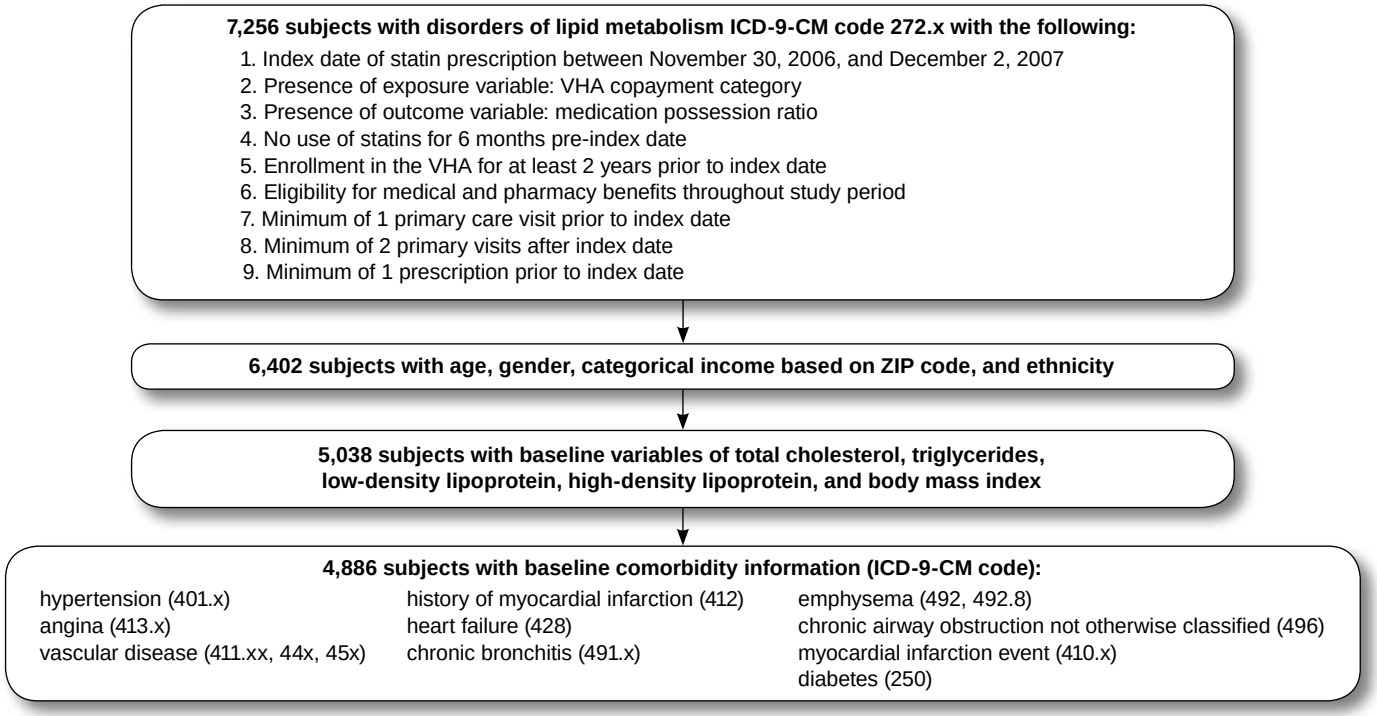
Study subjects were identified from the VHA Veterans Integrated System Network 22, a region that includes sites in Southern California (Loma Linda, Long Beach, Los Angeles, San Diego) and Nevada (Las Vegas), with a system enrollment of approximately 1.4 million members. "New statin users" were defined as patients with no active statin prescription in the 6 months prior to index date.

Included study subjects had a diagnosis of disorders of lipid metabolism, *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) code 272. Included patients had begun a statin between November 30, 2006, and December 2, 2007, and each subject was then followed for a 1-year period. Subjects were required to be enrolled in VHA services for at least 2 years prior to index date and throughout the 1-year study period. They were required to have medical and pharmacy benefits throughout the study period. Study subjects were required to have at least 1 primary care visit prior to index date, at least 2 primary care visits after index date, and at least 1 prescription prior to index date. Patients included in the analysis were required to have complete data for exposure, outcome, and regression adjustment variables (Figure 1).

Cohort Definitions

We used exposure categories of Any Copayment versus No Copayment, indicating a patient had a copayment in order to obtain statin medications or paid no copayment for statin medications, respectively. Then, as a separate analysis, we varied the exposures to the standard VHA copayment categories: (a) Service-Connected (SC) Copayment, (b) Non-Service-Connected (NSC) Copayment, and (c) No Copayment. A patient is deemed as SC status if the disease process under treatment is related to the enrollee's active military service. Service-Connected status influences the copayment requirements for veterans in the following fashion: SC copayment patients pay a copayment on their statin prescriptions but do not pay a copayment on their medications that are for Service-Connected conditions. NSC copayment patients pay a copayment for all of their prescriptions, including their statins, since the patient is not Service-Connected for any conditions.[15] Patients in the No Copayment category did not pay a copayment for statin therapy

FIGURE 1 Cohort Selection Diagram



ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification; VHA = Veterans Health Administration.

in the VA system because the patient qualified for 1 or more of the following reasons: (a) catastrophically disabled; (b) Service-Connected condition for dyslipidemia or a hyperlipidemia-related disorder; (c) household income below predetermined VA income thresholds (which varies based on family size and geographic location); (d) ex-prisoner of war; or (e) exposed to Agent Orange or ionizing radiation.

Outcomes Measurements

For the odds ratio assessments via logistic regression, the outcome of interest was the patient being "adherent" during the study period, determined via the medication possession ratio (MPR), which was defined as number of days supplied with prescription medication divided by days of observation.[16] MPR is the number of days supply of prescription medication actually received divided by days of observation with 1.0 MPR indicating 100% adherence.[17] MPR was calculated based on days supply over the 1-year period from index statin prescription. Days supply beyond the 1-year period from index date was not included in the MPR calculation. To prevent mean estimates of MPR that were inflated because of consistent early refills, the MPR was capped at 1.0. For each set of exposures, we used 2 different dichotomized "Adherent yes/no" outcomes by varying the adherence MPR threshold. Using the exposure categories of Any Copayment versus No Copayment in the first logistic regression analysis, patients were deemed "adherent" if their MPR was 0.8 or greater for the new statin. In the second logistic regression analysis for the primary and secondary aims, patients were "adherent" if their MPR was 0.9 or greater for the new statin. The logistic regressions were then repeated using the 3 standard VHA copayment categories as exposures. The varying adherent outcomes reflect the current absence of consensus regarding the required level of adherence for elevated patient clinical benefit.[16,18] To determine the incremental effect of copayment categories on adherence, the outcome of interest was MPR itself. Patients were followed for a 1-year observation period from index date, counting the medication supply filled from the new statin prescription and its refills. To reduce measurement error for MPR, patients were excluded if they switched statins or experienced an admission for more than 30 consecutive days.

Statistical Analysis

We used multiple logistic regression to ascertain whether the odds of being adherent were differentially associated with Any Copayment versus No Copayment categories. The Any Copayment category was set as the reference category for the regression. Cheetham et al. (2013) recently demonstrated that

TABLE 1 Summary Statistics of VHA Dataset by Copayment Category (N = 4,886)

Characteristic	Any Copayment (n = 3,246)		No Copayment (n = 1,640)		*P* Value
Age, mean (SD), years	64.4	(11.0)	61.1	(10.9)	< 0.01
Body mass index at baseline, mean (SD)	30.2	(5.7)	30.5	(5.9)	0.06
Number of medications at baseline, mean (SD)	6.9	(4.0)	8.7	(4.7)	< 0.01
Lipids					
Total cholesterol at baseline, mean (SD), mg/dL	212.7	(48.3)	214.6	(46.0)	0.19
High-density lipoprotein at baseline, mean (SD), mg/dL	42.5	(12.2)	42.3	(12.1)	0.61
Low-density lipoprotein at baseline, mean (SD), mg/dL	136.6	(40.0)	138.7	(38.6)	0.08
Nonhigh-density lipoprotein at baseline, mean (SD), mg/dL	170.2	(46.3)	172.3	(43.8)	0.13
Triglycerides at baseline, mean (SD), mg/dL	171.0	(161.5)	171.6	(126.7)	0.90
Male, n (%)	3,123	(96.2)	1,531	(93.4)	< 0.01
Race, n (%)					
White	1,588	(48.9)	742	(45.2)	< 0.01
Unspecified	755	(23.3)	290	(17.7)	
Black	420	(12.9)	302	(18.4)	
Hispanic	351	(10.8)	197	(12.0)	
Asian	90	(2.8)	91	(5.6)	
American Indian or Native	42	(1.3)	18	(1.1)	
New statin consumed, n (%)					
Simvastatin	2,744	(84.5)	1,387	(84.6)	0.15
Lovastatin	222	(6.8)	115	(7.0)	
Rosuvastatin	185	(5.7)	103	(6.3)	
Fluvastatin	36	(1.1)	21	(1.3)	
Pravastatin	40	(1.2)	8	(0.5)	
Atorvastatin	19	(0.6)	6	(0.4)	
Comorbidities, n (%)					
Hypertension	2,420	(74.6)	1,183	(72.1)	0.07
Diabetes mellitus	1,216	(37.5)	669	(40.8)	0.02
Peripheral vascular disease	1,076	(33.2)	510	(31.1)	0.15
Chronic obstructive pulmonary disease	318	(9.8)	181	(11.0)	0.18
Congestive heart failure	156	(4.8)	85	(5.2)	0.57
History of myocardial infarction	108	(3.3)	42	(2.6)	0.14
Angina	70	(2.2)	45	(2.7)	0.20
Mood disorder	44	(1.4)	42	(2.6)	< 0.01
Income category (dollars), n (%)					
Under 1,000	11	(0.3)	7	(0.4)	0.02
15,000-24,999	10	(0.3)	6	(0.4)	
25,000-34,999	260	(8.0)	175	(10.7)	
35,000-49,999	1,004	(30.9)	533	(32.5)	
50,000-74,999	1,384	(42.6)	636	(38.8)	
75,000-99,999	489	(15.1)	246	(15.0)	
≥ 100,000	88	(2.7)	37	(2.3)	

mg/dL = milligrams per deciliter; SD = standard deviation; VHA = Veterans Health Administration.

adherence may be influenced by patient characteristics such as age and health status.[19] With this influence in mind, our model incorporated the adjustment variables of age, gender, race, median income category based on ZIP code,[20-24] statin consumed, baseline medication count, baseline body mass index, and baseline lipid levels: total cholesterol, triglycerides, high-density lipoproteins (HDL), low-density lipoproteins and non-HDL lipoproteins. We also adjusted for the presence of the following comorbidities at baseline: hypertension (401.x), angina (413.x), vascular disease (411.xx, 44x, 45x), history of myocardial infarction (412), heart failure (428), chronic bronchitis (491.x), emphysema (492, 492.8), chronic airway obstruction not otherwise classified (496), myocardial infarction event (410.x), and diabetes (250).

In addition, we executed a model using the standard VHA copayment categories of SC Copayment, NSC Copayment, and No Copayment as exposures in the second set of regression models. For these analyses, SC Copayment was used as the

TABLE 2 Odds Ratios for Adherence Comparing No Copayment to Any Copayment Categories[a]

Medication Possession Ratio Adherence Threshold	Odds Ratio for Adherence with No Copayment
≥ 0.8	1.19 (95% CI = 1.03-1.37)
≥ 0.9	1.28 (95% CI = 1.11-1.48)

[a]Multiple logistic regression model adjustment variables included age, gender, race, median income category based on ZIP code, statin consumed, baseline medication count, baseline body mass index, and baseline lipid levels: total cholesterol, triglycerides, high-density lipoproteins, low-density lipoproteins and nonhigh-density lipoproteins. We also adjusted for the presence of the following comorbidities at baseline: hypertension, angina, vascular disease, history of myocardial infarction, heart failure, chronic bronchitis, emphysema, chronic airway obstruction not otherwise classified, myocardial infarction event, and diabetes.

CI = confidence interval.

TABLE 3 Condensed Summary by VHA Copayment Category

	Non-Service-Connected Copayment	Service-Connected Copayment
Age, years	65.2	62.3
Medication count at baseline	6.9	6.9
Total cholesterol, mg/dL	212.2	213.8
Female, %	3.5	4.5
White ethnicity, %	50.8	44.7
Simvastatin use, %	83.5	87.0
Diabetic, %	37.5	37.3
Median income at $35,000 to $49,999, %	31.9	28.7

mg/dL = milligrams per deciliter; VHA = Veterans Health Administration.

reference category for the regression models. As previously described, we proceeded with 2 separate logistic regression models based on setting the adherence threshold at 2 separate levels—MPR ≥ 0.8 and MPR ≥ 0.9—for each set of exposure categories. Summary statistics for baseline characteristics comparing Any Copayment versus No Copayment groups were determined via t-test for continuous variables and chi-squared test for categorical variables.

A significance level of 0.05 was set for all hypothesis tests used. Statistical analyses were executed using SAS 9.3 (Cary, NC). This retrospective study was approved by the San Diego VHA Institutional Review Board and met all criteria for protection of human subjects.

Results

A total of 4,886 patients met inclusion criteria. Study subjects who paid a copayment for their statin medications (n = 3,246) were more likely to be older, with a mean age of 64.4 years compared with 61.1 years for the No Copayment group (n = 1,640). Subjects with Any Copayment for statins took fewer medications at baseline with a mean of 6.9 medications compared with 8.7 medications for the No Copayment group. The Copayment groups were similar in terms of their baseline lipid parameters. The most common comorbidity reported was hypertension for both groups. Simvastatin was the most common statin consumed by both groups. The distribution of incomes and races was statistically different for the Any Copayment group compared with the No Copayment group (Table 1).

Patients who did not pay a copayment for their statin medications were more likely to have adherence rates of 0.8 MPR or greater with odds ratio (OR) of 1.19 (95% CI = 1.03-137) favoring the No Copayment group. Using a threshold of 0.9 MPR or greater produced similar findings with OR of 1.28 (95% CI = 1.11-1.48; Table 2).

The second analysis applied the VHA exposure categories of SC Copayment, NSC Copayment, and No Copayment. NSC patients were slightly older than SC patients (65.2 years vs. 62.3 years, respectively). A larger proportion of NSC patients were of white ethnicity compared with SC patients (50.8% vs. 44.7%, respectively). A smaller proportion of NSC patients were female versus SC patients (3.5% vs. 4.5%, respectively; Table 3). Using the 0.8 MPR or greater adherence threshold, the No Copayment group was associated with an increased likelihood of adherence versus the SC Copayment category as reference group with an OR of 1.31 (95% CI = 1.10-1.58). NSC Copayment was associated with a nonsignificant increase in odds of adherence at the 0.8 MPR level or greater with OR of 1.12 (95% CI = 0.98-1.39). Using the 0.9 MPR or greater adherence threshold, findings were similar. The No Copayment group produced an OR of 1.42 (95% CI = 1.17-1.71) compared with the SC Copayment group. NSC Copayment group was associated with a nonsignificant increase in odds of adherence at the 0.9 MPR level or greater with an OR of 1.12 (95% CI = 0.97-1.38; Table 4).

The linear regression results demonstrated that patients who did not have a copayment for their statin medication (No Copayment category) were associated with an increase in MPR of 0.02 (95% CI = 0.002-0.035) compared with patients who paid any copayment for their statin prescriptions (the Any Copayment category). Using the VHA copayment categories, we observed an increase in MPR for the No Copayment group versus the SC Copayment group of 0.03 (95% CI = 0.01-0.05). The NSC Copayment group was associated with a nonsignificant increase in MPR versus the SC Copayment group of 0.02 (95% CI = -0.003-0.036; Table 4).

Discussion

Absence of copayment for statin prescriptions was associated with an increase in likelihood of adherence based on either a 0.8 or the more stringent 0.9 MPR adherence threshold for new use of statins. Absence of copayment was also associated with

TABLE 4 Odds Ratios of Adherence and Changes in MPR Because of VHA Copayment Category[a]

VHA Copayment Category	Odds Ratio of Adherence MPR ≥ 0.8 (95% CI)	Odds Ratio of Adherence MPR ≥ 0.9 (95% CI)	Increase in MPR (95% CI)
Service-Connected	Reference	Reference	Reference
No Copayment	1.31 (1.10-1.58)	1.42 (1.17-1.71)	0.03 (0.01-0.05)
Non-Service-Connected	1.12 (0.98-1.39)	1.12 (0.97-1.38)	0.02 (-0.003-0.036)

[a]*Multiple regression model adjustment variables included age, gender, race, median income category based on ZIP code, statin consumed, baseline medication count, baseline body mass index, and baseline lipid levels: total cholesterol, triglycerides, high-density lipoproteins, low-density lipoproteins and nonhigh-density lipoproteins. We also adjusted for the presence of the following comorbidities at baseline: hypertension, angina, vascular disease, history of myocardial infarction, heart failure, chronic bronchitis, emphysema, chronic airway obstruction not otherwise classified, myocardial infarction event, and diabetes.*

CI = confidence interval; MPR = medication possession ratio; VHA = Veterans Health Administration.

a statistically significant increase in MPR when compared with patients who paid a copayment for their statins.

The analyses of VHA copayment categories of No Copayment, Non-Service-Connected, and Service-Connected association with adherence demonstrated once again the improvement in probability of adherence for patients without a copayment. However, these analyses also allowed us to discern a distinction, albeit nonstatistically significant, in adherence depending on the type of copayment category for the new statin user. Copayment-paying patients who were Non-Service-Connected were found to have an increase in probability of adherence at either 0.8 or 0.9 MPR threshold with ORs of 1.12 for both categories, although both CIs crossed null. Non-Service-Connected Copayment patients were correlated with a nonsignificant 0.02 improvement in MPR based on the linear regressions.

The improvement in MPR increase when No Copayment is compared with Service-Connected Copayment instead of Any Copayment indicates that Non-Service-Connected Copayment patients are dampening the adherence differences because of Service-Connected Copayments when the 2 copayment groups are collapsed into a single Any Copayment group. One possible explanation for the difference in follow-up adherence levels for the 2 copayment groups may relate to willingness to pay. Since Service-Connected veterans are granted medications for their Service-Connected comorbidity with no copayment, they may be less likely to obtain their statins, since a copayment is required. On the other hand, Non-Service-Connected veterans pay a copayment for all of their medications. For the Non-Service-Connected, the incurred cost for their statins is equal to that of any other medication provided by the VHA. This similarity of cost would result in improved consumption of their statin medications compared with the Service-Connected veterans. The findings from the VHA copayment category comparison may represent the same phenomenon as the No Copayment patients demonstrated: elevated adherence for medications when copayment is not required.

Although we witnessed a reduction in adherence for patients paying for their statin prescriptions, the policy implication is less clear. Reduction in copayments for statin prescriptions would cost the VHA system millions of dollars at a time when the federal government is contending with historic budget deficits and an aging veteran population. This increased pharmacy cost to the system would need to be justified in terms of enhanced mortality and a reduction in health services use. Future steps for investigators will involve cost-effectiveness analyses to determine whether the improvement in health outcomes would be justified by the price. These analyses will require longer studies where adherence and mortality outcomes can be robustly correlated.

It is important that patients with a copayment are counseled appropriately on the necessity of taking their medications according to the directions of their providers. Previous work in adherence has highlighted the critical importance of the patients' perceptions of the necessity of their medications.[25] Billups et al. (2000) postulated that an improvement in compliance for patients taking more medications could be related to the Health Belief Model in which patients are more likely to commit to a medical care regimen when they are convinced they are truly ill.[26] This belief model particularly applies to such silent diseases as hyperlipidemia, where the patient fails to experience day-to-day symptomatic worsening or improvement based on appropriate consumption. The burden rests on the clinicians and the health system to convince patients of the importance of taking their statin medications as instructed and to refill prescriptions continuously without gaps in consumption.

Limitations

This analysis was conducted with patients from the VHA. Results may vary in nonveteran populations. The copayment amount during the study period per prescription was a single amount of $8 per 30-day supply. Commercial populations often apply a tiered schedule with multiple copayment levels that may alter the influence on adherence because of copayment. Our study population was 95% male. Although this gender imbalance may influence the generalizability of our study findings, we are not aware of research demonstrating modification of copayment effect on health services utilization because of gender. MPR is based on medication fill frequency and does not measure physical consumption of the medication by the patient. However, published evidence has demonstrated that MPR is correlated with primary adherence and that improved MPR is associated with augmented health

outcomes.[18,27,28] We did not add additional days at the end of fill for early refills. A possibility remains that patients who were late at one point in the year filled early later that year and thus "repaired" their MPR. For this reason, our MPR estimate may be an overestimate of actual adherence. This overestimation is not expected to promote systematic bias, since this fill behavior does not vary depending on general adherence level as far as we are aware. The income variable used in the regression analysis was estimated based on the median income of the ZIP codes of the study subjects. Fills for 90 days could artificially bolster MPR. However, such artificial increase would introduce biased regression estimates only if 90-day fills were associated with copayment category in the VHA. This phenomenon has not been observed in the VHA. A priori, we did not include patients who switched statins to remove residual confounding for patients who used different statins for varying amounts of time and to allow for adjustment based on individual statin consumed by the subject. However, this switching does affect the generalizability of our study findings, since switching of statins for new users is not uncommon in real-world settings.

Conclusions

Patients without out-of-pocket costs for their statins are more likely to adhere to therapy. Moreover, our findings suggest that among those that pay a copayment, the patients are less adherent to their statins if other medications they are prescribed are free from copayments. Future studies are needed to explore the cost-effectiveness of reducing copayments to improve cardiovascular outcomes. Pharmacists must continue to educate patients on the importance of adherence. Additional counseling on the necessity of adherence should be given to patients paying a copayment for their prescriptions.

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DISCLOSURES

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