RESEARCH

Initiation of Statins After Hospitalization for Coronary Heart Disease

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ABSTRACT

BACKGROUND: Coronary heart disease (CHD) is a major public health problem in the United States. It has been well recognized that patients with prior CHD are at very high risk for recurrent CHD. Statins have been recommended as an effective treatment in the secondary prevention of CHD.

OBJECTIVE: To (1) determine the proportion of patients who received outpatient statin therapy after CHD hospitalization and (2) identify factors associated with initiation of outpatient statin use.

METHODS: Using MedStat MarketScan 1999-2003 databases, CHD hospitalizations (ICD-9-CM codes 410.xx-414.xx, 429.2) between January 1, 2000, and June 30, 2003, were identified, with each patient's first such hospitalization defined as the index hospitalization. The study sample consisted of patients who had had no statin use during the year preceding the index hospitalization and had at least 6 months of follow-up after discharge. Initiation of any statin prescription during follow-up was the outcome of interest. Demographic and clinical predictors were selected with the guidance of Andersen's health services utilization model and past studies. Effects of these independent variables on statin initiation were examined using logistic regression models.

RESULTS: Of 17,631 subjects who met the inclusion criteria, only 8,424 (7.8%) had received statin therapy within 6 months after discharge. The following characteristics were inversely related to the likelihood of receiving an outpatient statin: baseline Charlson comorbidity score (6+ vs. 1-2, odds ratio [OR] 0.35; 95% confidence interval [CI], 0.25-0.51), nonacute myocardial infarction CHD hospitalization (OR 0.55; 95% CI, 0.51-0.58), baseline psychoses (OR 0.61; 95% CI, 0.50-0.75), use of lipid-modifying drugs other than statins at baseline (OR 0.61; 95% CI, 0.53-0.71), and patient age (continuous) (OR 0.97; 95% CI, 0.97-0.98). The following characteristics were associated with a higher likelihood of receiving an outpatient statin prescription: hospitalization for CHD in a recent year (2003 vs. 2000, OR 1.77; 95% CI, 1.61-1.94), baseline dyslipidemia (OR 1.54; 95% CI, 1.41-1.68), care by a cardiologist (OR 1.26; 95% CI, 1.18-1.34), and male gender (OR 1.18; 95% CI, 1.10-1.26). In a separate analysis of subjects with complete copayment information (N = 13,765), amount of copayment for the first outpatient statin prescription was inversely related to the likelihood of receiving an outpatient statin (≥$20 vs. <$10; OR 0.62; 95% CI, 0.56-0.68). In that equation, hospitalization for CHD in 2003 instead of in 2000 multiplied the odds of receiving statin therapy after discharge by 3.31 (95% CI, 2.95-3.71).

CONCLUSION: Less than 50% of patients with a CHD hospitalization during the 4-year study period from 2000 through 2003 received outpatient statin therapy within 6 months after discharge, but the proportion increased each year to 56% of patients with a CHD hospitalization in 2003. For CHD patients admitted in 2003, the odds of receiving statin therapy after discharge were approximately 80% to 230% higher than for patients admitted in 2000. Higher statin copayment amount and female gender were associated with lower likelihood of receiving a statin prescription after a CHD hospitalization.

KEYWORDS: Coronary heart disease, Copayment, Statins

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What is already known about this subject

- Previous research has shown that as much as 60% of patients with a diagnosis of CHD do not receive lipid-modifying therapy in the ambulatory care setting.
- In previous studies, relevant factors associated with the use of lipid-modifying drugs included younger age, history of myocardial infarction or coronary artery bypass graft, hypertension, diagnostic testing for lipids, and treatment by cardiology specialists.

What this study adds

- Although the data used in this study represent dates of service that are not recent, this is one of the first studies that documents the use of statins in patients who had a CHD hospitalization.
- Imputing average copayment amounts for nonstatin users revealed that a higher copayment amount was associated with absence of statin therapy after hospitalization for a primary diagnosis of CHD.
- Unlike previous studies, female gender was found to be associated with nonuse of statins after a hospitalization with a primary diagnosis of CHD.

Coronary heart disease (CHD) is a major public health problem in the United States and in the world. It is the leading cause of death in the United States and accounted for 1 of every 5 deaths in the United States in 2004.[1] About 16 million Americans currently suffer from CHD, and the direct and indirect costs of CHD are estimated to be $152 billion in 2007.

Results from major secondary prevention clinical trials and numerous observational studies clearly demonstrate that use of statins can decrease CHD recurrence and reduce total mortality, myocardial infarction (MI), stroke, peripheral vascular disease, and the need for revascularization procedures in patients with preexisting CHD.[2-7]

On the basis of the preponderance of evidence confirming the importance of aggressive lipid reduction in patients at risk for CHD, the National Cholesterol Education Program (NCEP) published updated guidelines, endorsed by the American College of Cardiology (ACC) and the American Heart Association (AHA), for treating high blood cholesterol and identified additional high-risk groups, including patients with established CHD. The guidelines recommend intensive low-density lipoprotein cholesterol (LDL-C)-lowering therapy for patients with established CHD, with a goal of reducing LDL-C to <100 mg/dL or further lowering it to

<70 mg/dL when the risk is very high.[8,9] The NCEP Adult Treatment Panel (ATP) III guideline (May 2001) states specifically, "In persons admitted to the hospital for a major coronary event, LDL cholesterol should be measured on admission or within 24 hours. In general, persons hospitalized for a coronary event or procedure should be discharged on drug therapy if the LDL cholesterol is ≥130 mg per dL."

In spite of the popularity and widespread use of statins, research reports have documented that many patients with CHD, in whom the greatest benefit of statin treatment has been shown, still do not receive it.[10-15] For instance, one observational study using 2001 medical and drug claims data from a managed care organization revealed that only 15,984 of 40,179 (39.8%) of CHD patients were receiving statin therapy (including "risk equivalent" CHD patients, such as persons with diabetes, aortic aneurysm, and peripheral arterial disease).[14] In previous studies, relevant factors associated with lipid-modifying drugs included diagnostic testing for lipids, younger age, history of MI or coronary artery bypass grafting, hypertension, and treatment by cardiology specialists.[13,15]

Although an informative body of research has examined the use of lipid-modifying drugs and has explored factors that might affect their use, few studies have focused on patients discharged from a CHD hospitalization or examined financial concerns such as patients' medication copayment requirements. Therefore, the primary objectives of this study were to estimate the proportion of patients who receive statin therapy after being discharged from CHD hospitalization and to identify the factors that affect the initiation of statin therapy among these patients. This research was reviewed and approved by the University of Minnesota Institutional Review Board.

Methods

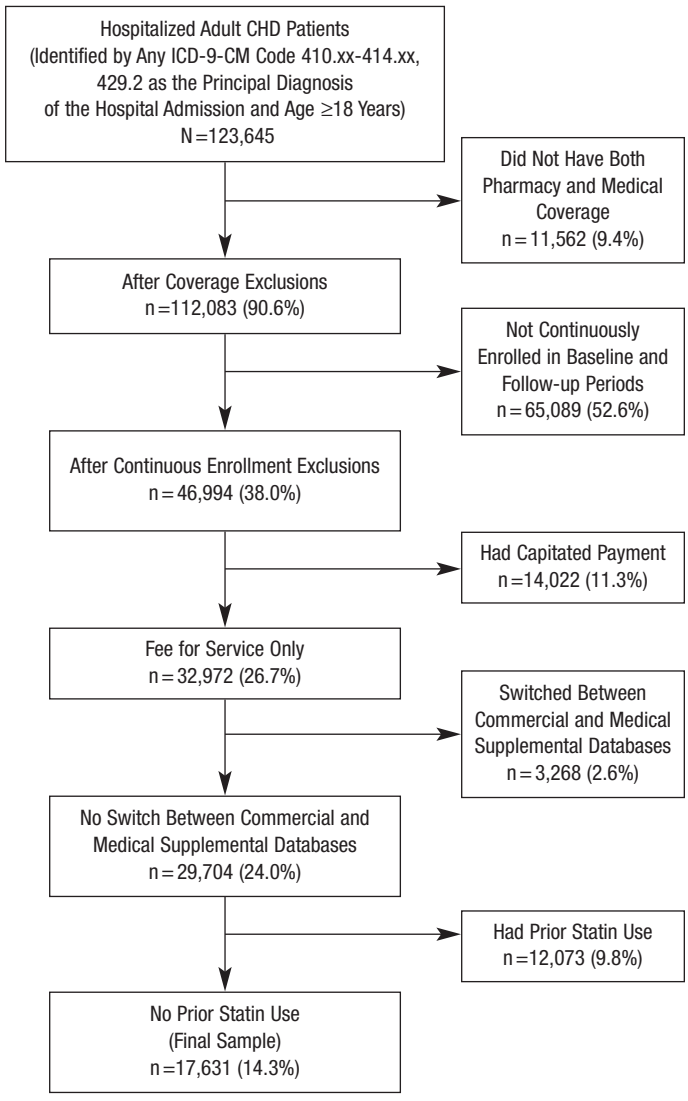
Data Sources

This study employed a longitudinal retrospective cohort study design using pharmacy, outpatient, inpatient, and enrollment claims data from the 1999-2003 MedStat MarketScan Commercial Claims and Encounters Database and the Medicare Supplemental and Coordination of Benefit Database (Medstat Group, Inc., Ann Arbor, MI). These databases represent the health care experience of approximately 15 million enrollees who are covered by employer-sponsored commercial health insurance or are Medicare-eligible retirees with employer-sponsored supplemental benefit plans. Information includes person-specific medical and pharmacy claims expenditures (including gross and net payments to providers from health plans and patients, including patient copayment amounts for prescriptions), and enrollment across inpatient, outpatient, prescription drug, and carve-out services from more than 100 large employers, health plans, and government and public organizations. The MarketScan database links paid claims and encounter data over time to detailed patient information across sites and types of providers. For the purpose of this study, the MarketScan Commercial Claims and Medicare Supplemental databases were combined for analysis.

Study Patients

The sample for this study consisted of patients hospitalized with a principal diagnosis (identified from the standard field in the UB-92 form) of CHD *(International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] codes 410.xx-414.xx, 429.2) between January 1, 2000, and June 30, 2003 (see Figure 1). These patients were identified directly from the Inpatient Admission

FIGURE 1 Flowchart of Patient Selection



CHD=coronary heart disease; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

Table included in the MarketScan database. The first such hospitalization was identified as the index hospitalization. The 12-month time period before the admission date of the index hospitalization was examined for baseline patient characteristics, and patients were followed for 6 months after the discharge date of the index hospitalization. Patients who met the following criteria were included in the final study sample: (1) aged 18 years or older at the index hospitalization admission date, (2) had continuous enrollment throughout the baseline and follow-up periods with both pharmacy and medical coverage, (3) did not switch between the Commercial Claims and Medicare Supplemental databases, (4) did not take any statins during the baseline period, and (5) had no capitated payments.

Measures

The outcome of interest of this study was the initiation of statin therapy during the follow-up period since it is recommended that patients with established CHD receive intensive LDL-C-lowering therapy.[8] On the basis of results from recent clinical trials, the ACC/AHA consensus statement (2004) encourages early initiation of statins for patients hospitalized because of CHD.[9] In this study, initiation of statins was defined as receiving any statin prescription within the 6-month follow-up period after discharge from the index CHD hospitalization.[11] Statins available during the study period included lovastatin, pravastatin, simvastatin, fluvastatin, cerivastatin, atorvastatin, and rosuvastatin. To identify these pharmacy claims in the database, we first used brand and generic names to search for National Drug Code (NDC) codes for statins from a separate drug database *(Red Book)* provided by MedStat and then used these NDC codes to identify statin claims in the database of pharmacy claims. To ensure that all NDC codes for statins were identified, we also randomly selected 10% of pharmacy claims not classified as statins and verified that those claims were not misclassified.

Nonstatin lipid-modifying therapy, such as niacin, gemfibrozil, fenofibrate, or bile-sequestering agents such as cholestyramine, were not included in this study, as none of these drugs are considered first-line therapy for LDL-C lowering in this situation.

To identify predictors of statin therapy initiation, we examined a set of demographic and clinical characteristics selected with the guidance of Andersen's health services utilization model.[16] This model suggests that use of health services, including prescription medications, is a function of patients' predisposition to use health care services, their need for care, and factors that enable or impede use. Predisposing variables describe the propensity of individuals to seek care and include demographics, social structure, and health beliefs. Need variables refer to health status or illness and can be based on individual or provider judgments regarding the presence and severity of conditions requiring treatment. Enabling variables describe the means available to individuals to use services, including personal factors (poverty level, employment status) and factors related to medical care resources (insurance coverage, usual source of care).[17,18] The Andersen model has been applied to predict use of prescription and nonprescription drugs in several studies.[19-23]

In this study, a series of predisposing, need, and enabling factors were hypothesized to explain patients' initial use of statins. Specifically, predisposing variables included age and gender. Need variables included length of hospital stay, type of CHD (see Table 1), overall comorbidities as measured by the Charlson index, total number of baseline medication therapeutic classes, baseline use of nonstatin lipid-modifying drugs and baseline history of dyslipidemia, hypertension, diabetes, psychoses, depression, renal disease, and liver disease (see Table 2 for codes). Enabling variables included copayment for statins, type of health plan (comprehensive, preferred provider organization, etc.), enrollee type (commercial, Medicare Supplemental), seeing a cardiologist, and year of CHD hospitalization.

For patients who received an outpatient statin within the 6-month follow-up period after discharge from the index CHD hospitalization, the copayment was measured as the amount that the patient paid for the first outpatient statin prescription. For

TABLE 1 ICD-9-CM Codes Used to Identify CHD Hospitalization

Acute Myocardial Infarction (AMI)	
410.0	Of anterolateral wall
410.1	Of other anterior wall
410.2	Of inferolateral wall
410.3	Of inferoposterior wall
410.4	Of other inferior wall
410.5	Of other lateral wall
410.6	True posterior wall infarction
410.7	Subendocardial infarction
Non-AMI CHD	
411	Other acute and subacute forms of ischemic heart disease
411.0	Postmyocardial infarction syndrome
411.1	Intermediate coronary syndrome
412	Old myocardial infarction
413	Angina pectoris
413.0	Angina decubitus
413.1	Prinzmetal angina
414	Other forms of chronic ischemic heart disease
414.0	Coronary atherosclerosis
414.1	Aneurysm and dissection of heart
414.8	Other specified forms of chronic ischemic heart disease
414.9	Chronic ischemic heart disease, unspecified
429.2	Cardiovascular disease, unspecified

CHD = coronary heart disease; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

patients who did not receive a statin during the follow-up period, the copayment was imputed using the average of copayments for all statin prescriptions filled by other members in the same benefit plan with the same pharmacy coverage, copayments, and deductible (either within or across employer groups) during the same year. The copayment for statins was further categorized as low (<$10), medium (≥$10 to <$20), and high (≥$20).[24]

Statistical Analysis

All study variables were analyzed descriptively. Counts and proportions were provided for dichotomous and polychotomous variables. Means, medians, standard deviations, and percentiles were calculated for continuous variables. These results were stratified by study groups. Bivariate comparisons of baseline characteristics and outcome measures between statin users and nonstatin users were conducted with t-tests for continuous variables and chi-square tests for categorical variables. Fisher's Exact Test was used when cell sizes contained too few cases for appropriate use of the chi-square test. All statistical tests were considered as significant at $P<0.05$.

Univariate logistic regression models were first used to examine the relationship between each predictor variable and the initiation of statin therapy. Significant factors identified by the univariate logistic regressions were then included in the multivariate logistic regression model, which examined the relationship between each independent and dependent variable controlling for all others.

The overall fit of the multivariate logistic model was assessed using the Max-rescaled pseudo-R2 and the Hosmer-Lemeshow statistic. The pseudo-R2 is a summary measure with an interpretation similar to the R2 measure in least-squares regression, indicating how much variance in the dependent variable could be explained by the independent variables in the model. The Hosmer-Lemeshow statistic follows a chi-square distribution under the null hypothesis that the model fits the data (i.e., a nonsignificant value represents "good").[25,26] In addition, as this data set encompassed several years, a subset of patients who had had an index CHD hospitalization in 2003 were examined separately in an ad hoc analysis to evaluate factors associated with statin use in the most current year. All statistical analyses were conducted using SAS (SAS version 8.2, Cary, NC).

TABLE 2 ICD-9-CM Codes Used to Identify Comorbidities

Comorbidity	ICD-9-CM Codes
Diabetes	250.xx, 648.00-648.04, 775.1x
Hypertension	401.xx- 405.xx, 642.00-642.04, 642.10-642.14, 642.20-642.24, 642.70-642.74, 642.90-642.94
Renal disease	582.xx, 583.0x-583.7x, 585.xx-586.xx, V42.0x, V45.1x, V56.xx
Liver disease	571. xx, 572.2x -572.8x ,456.0x -456.2x
Dyslipidemia	272.0x-272.4x, 272.9x
	272.0 Pure hypercholesterolemia
	272.4 Hyperlipidemia nec/nos
	272.9 Lipoid metabol dis nos
Psychoses	295.xx-298.xx, 299.10, 299.11
Depression	300.4x, 301.12, 309.0x, 309.1x, 311.xx

ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

Results

A total of 17,631 patients met study criteria and were included in the analysis. Among those patients, only 8,424 (47.78%) received statin therapy within 6 months after they were discharged from the CHD hospitalization. Table 3 displays patients' demographic and baseline characteristics, stratified by the initiation of statin therapy. The average age of the study patients was 65.67 + 13.12 (mean + SD). Most study patients were men. Compared with nonstatin users, those who initiated statin therapy were significantly younger than nonstatin users ($t = 28.69$, $P <0.001$) and a significantly higher percentage were male (chi-square = 121.11, $P <0.001$).

Approximately 38% patients were hospitalized for acute myocardial infarction (AMI), with a significantly higher percentage in statin users than in nonstatin users (44.2% vs. 31.9%, respectively). Hypertension was the most common comorbid condition among the study patients in the baseline period (40.11%), followed by diabetes (20.41%) and dyslipidemia (16.11%). Renal disease, liver disease, psychoses, and depression were less common (<5%) during the baseline period. Chi-square tests suggested that prevalence of hypertension, diabetes, renal disease, psychoses, and depression was significantly higher among nonstatin users than among statin users. However, the percentage of patients with dyslipidemia in the baseline period was significantly higher among statin users.

Most study patients (80.30%) had a Charlson comorbidity score of 1 or 2. Compared with nonstatin users, proportionally more statin users had low Charlson scores. This disparity reflected a higher prevalence of overall comorbidity among nonstatin users.

On average, statin users paid a copayment of $16.50 for their index prescription. The average copayment for nonstatin users would have been $18.00 if they had received a statin prescription. Compared with the copayment for nonstatin users, the copayment for statin users was significantly lower, on average ($P <0.001$). Consistently, the percentage of patients with a low copayment (<$10) was significantly higher among statin users ($P <0.001$). However, because of missing information, membership in specific benefit plans could not be determined for 3,865 (42%) nonstatin users, and therefore the copayment for statins among those

TABLE 3 Study Subjects Characteristics

Variable	Nonstatin Users (n = 9,207) n (%)	Statin Users (n = 8,424) n (%)	*P* Value
Predisposing factors			
Age	Mean [SD] 68.32 [13.43]	Mean [SD] 62.78 [12.12]	<0.001
Female	3,739 (40.6)	2,747 (32.6)	<0.001
Need variables (measured during the 1-year baseline)			
Dyslipidemia	1,138 (12.4)	1,715 (20.4)	<0.001
Hypertension	3,819 (41.5)	3,252 (38.6)	<0.001
Diabetes	2,046 (22.2)	1,553 (18.4)	<0.001
Psychoses	303 (3.3)	164 (2.0)	<0.001
Depression	179 (1.9)	131 (1.6)	0.050
Renal disease	307 (3.3)	136 (1.6)	<0.001
Liver disease	11 (0.12)	4 (0.05)	0.101
Charlson comorbidity			<0.001
1-2	6,969 (75.7)	7,189 (85.3)	
3-4	1,765 (19.2)	1,020 (12.1)	
5-6	330 (3.6)	168 (2.0)	
6 +	143 (1.6)	47 (0.6)	
Nonstatin lipid-modifying drug use	552 (6.0)	345 (4.1)	<0.001
Number of medication therapeutic classes	Mean [SD] 4.30 [7.72]	Mean [SD] 3.94 [5.43]	
Type of CHD*			<0.001
AMI	2,936 (31.9)	3,724 (44.2)	
Non-AMI CHD	6,271 (68.1)	4,700 (55.8)	
Length of stay (days)	Mean [SD] 4.30 [7.72]	Mean [SD] 3.94 [5.43]	<0.001
Enabling variables			
Medicare Supplemental enrollee	5,484 (59.6)	3,384 (40.2)	<0.001
Health plan type			<0.001
Comprehensive	4,619 (50.2)	3,617 (42.9)	
EPO	31 (0.3)	50 (0.6)	
Noncap POS	802 (8.7)	932 (11.1)	
PPO	3,755 (40.8)	3,824 (45.4)	
Missing	0 (0%)	1 (0.01)	
Rx copayment†			<0.001
<$10	1,352 (14.7)	2,411 (28.6)	
≥$10 and <$20	1,402 (15.2)	2,253 (26.8)	
≥$20	2,588 (28.1)	3,760 (44.6)	
Missing	3,865 (42.0)	0 (0)	
Rx copayment (continuous)†			<0.001
Mean	$18.00	$16.50	
Median	$20.00	$15.70	
SD	$8.50	$14.20	
25th percentile	$10.00	$5.30	
75th percentile	$22.50	$20.00	
Index year			<0.001
2000	2,770 (30.1)	1,799 (21.4)	
2001	2,352 (25.6)	2,055 (24.4)	
2002	2,415 (26.2)	2,456 (29.2)	
2003	1,670 (18.1)	2,114 (25.1)	
Seeing cardiologist	3,453 (37.5)	3,877 (46.0)	

(continued above, right)

TABLE 3 Study Subjects Characteristics (continued)

** See Table 1 for specific ICD-9-CM codes.*

† For nonstatin users, only patients whose copayment could be imputed were included. 42% of the nonstatin users had missing group information that made it impossible to impute a copayment amount.

AMI = acute myocardial infarction; CHD = coronary heart disease; EPO = exclusive provider organization; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification; POS = point of service; PPO = preferred provider organization; Rx = prescription; SD = standard deviation.

patients could not be imputed.

All patients (N = 17,631) were included in univariate logistic regressions, except that only patients with no missing data were included to examine the effect of copayment (N = 13,766) and plan type (N = 17,630). Because of the relatively large number of patients with missing copayment information, multivariate logistic regression was conducted in patients with no missing data on other covariates in order to study the relationship between other covariates and initiation of statins (N = 17,630-multivariate Model 1). Another multivariate logistic regression that included copayment and other covariates was conducted using the subset of patients with no missing copayment (N = 13,765-multivariate Model 2).

Significant factors associated with initiation of statins identified from univariate logistic regression and the results from the multi-

variate logistic regression models that included these factors are displayed in Table 4. The odds ratios (ORs) associated with copayment were derived from multivariate Model 2. The ORs associated with other covariates were derived from both multivariate Models 1 and 2. However, only the results from multivariate Model 1 are described and discussed because this model includes all of the patients (except one with missing plan type), and because the results from both models, in general, are similar. The Max-rescaled R-squares of multivariate Models 1 and 2 were 0.13 and 0.14, respectively. The Hosmer and Lemeshow Goodness-of-Fit Test had a *P* value of 0.906 for multivariate Model 1 and 0.997 for multivariate Model 2, respectively. Therefore, the null hypotheses that the multivariate logistic models fit data well were not rejected. These results suggested the models can explain a significant portion of the variance in the initiation of statins among study patients.

It is apparent from these analyses that a large number of variables from Andersen's health services utilization model[16] are related to the initiation of statin therapy. The predisposing variables of age and gender were significantly associated with the

TABLE 4 *Logistic Regression Results (2000-2003)*

	Univariate (N = 17,631)*		Multivariate Model 1 (N = 17,630)†		Multivariate Model 2 (N = 13,765)‡	
Variable	**OR (95% CI)**	***P* Value**	**OR (95% CI)**	***P* Value**	**OR (95% CI)**	***P* Value**
Age	0.967 (0.965-0.969)	<0.001	0.972 (0.968-0.977)	<0.001	0.977 (0.971-0.982)	<0.001
Gender		<0.001		<0.001		<0.001
Male vs. female	1.42 (1.34-1.52)		1.18 (1.10-1.26)		1.18 (1.09-1.28)	
Baseline dyslipidemia		<0.001		<0.001		<0.001
Yes vs. no	1.82 (1.67-1.97)		1.54 (1.41-1.68)		1.51 (1.36-1.68)	
Baseline hypertension		<0.001		0.167		0.913
Yes vs. no	0.89 (0.84-0.94)		0.96 (0.90-1.02)		1.00 (0.93-1.08)	
Baseline diabetes		<0.001		0.801		0.857
Yes vs. no	0.79 (0.74-0.85)		0.99 (0.91-1.08)		0.99 (0.90-1.10)	
Baseline psychoses		<0.001		<0.001		<0.001
Yes vs. no	0.58 (0.48-0.71)		0.61 (0.50-0.75)		0.59 (0.47-0.74)	
Baseline renal disease		<0.001		0.053		0.113
Yes vs. no	0.48 (0.39-0.58)		0.79 (0.62-1.00)		0.81 (0.62-1.05)	
Baseline comorbidity index		<0.001		<0.001		<0.001
6+	0.32 (0.23-0.44)		0.35 (0.25-0.51)		0.38 (0.25-0.57)	
5-6	0.49 (0.41-0.60)		0.61 (0.49-0.76)		0.58 (0.45-0.75)	
3-4	0.56 (0.52-0.61)		0.69 (0.62-0.76)		0.68 (0.60-0.76)	
1-2 (reference)	–		–		–	
Count of medication therapeutic classes	0.96 (0.96-0.97)	<0.001	1.00 (0.99-1.01)	0.972	1.00 (0.99-1.00)	0.210
Baseline nonstatin lipid-modifying drug		<0.001		<0.001		<0.001
Yes vs. no	0.67 (0.58-0.77)		0.61 (0.53-0.71)		0.62 (0.53-0.74)	
CHD type		<0.001		<0.001		<0.001
Non-AMI CHD	0.59 (0.56-0.63)		0.55 (0.51-0.58)		0.55 (0.51-0.60)	
AMI (reference)	–		–		–	
Length of stay	0.99 (0.98-0.99)	<0.001	1.00 (0.99-1.00)	0.528	1.00 (1.00-1.01)	0.755
Enrollee type		<0.001		0.964		<0.001
Medicare Supplemental	0.46 (0.43-0.48)		1.00 (0.89-1.13)		1.30 (1.13-1.50)	
Commercial (reference)						
Plan type		<0.001		0.871		<0.001
PPO	1.30 (1.22-1.39)		1.03 (0.96-1.10)		0.87 (0.80-0.94)	
Noncap POS	1.48 (1.34-1.65)		1.01 (0.90-1.14)		1.36 (1.16-1.58)	
EPO	2.06 (1.31-3.23)		1.14 (0.71-1.81)		0.71 (0.44-1.14)	
Comprehensive (reference)	–		–		–	

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TABLE 4 *Logistic Regression Results (2000-2003) (continued)*

	Univariate (N = 17,631)*		Multivariate Model 1 (N = 17,630)†		Multivariate Model 2 (N = 13,765)‡	
Variable	**OR (95% CI)**	***P* Value**	**OR (95% CI)**	***P* Value**	**OR (95% CI)**	***P* Value**
Copayments		<0.001		NA		<0.001
≥$20	0.82 (0.75-0.88)		NA		0.62 (0.56-0.68)	
≥$10 and <$20	0.90 (0.82-0.99)		NA		1.06 (0.95-1.17)	
<$10 (reference)	–		–		–	
Cardiologist visit		<0.001		<0.001		<0.001
Yes vs. no	1.42 (1.34-1.51)		1.26 (1.18-1.34)		1.15 (1.06-1.24)	
Year of index CHD hospitalization		<0.001		<0.001		<0.001
2003	1.95 (1.79-2.13)		1.77 (1.61-1.94)		3.31 (2.95-3.71)	
2002	1.57 (1.44-1.70)		1.47 (1.34-1.60)		2.79 (2.50-3.11)	
2001	1.35 (1.24-1.46)		1.28 (1.17-1.40)		1.49 (1.35-1.64)	
2000 (reference)	–		–		–	

** Due to missing data, the Ns for univariate analysis plan type and copayment were 17,630 and 13,766, respectively.*
† One patient with plan type missing was not included.
‡ The N for multivariate analysis of copayment was 13,765 due to missing data.
§ For nonstatin users, only patients whose copayment could be imputed were included.
AMI = acute myocardial infarction; CHD = coronary heart disease; CI = confidence interval; EPO = exclusive provider organization; OR = odds ratio; POS = point of service; PPO = preferred provider organization.

initiation of statin therapy. On the basis of the results from multivariate analysis, older patients were significantly less likely to receive a statin prescription within 6 months after discharge from the CHD hospitalization. The OR associated with each 1-year increase in age was 0.97, with a 95% confidence interval (CI) from 0.968 to 0.977. Male patients were approximately 20% more likely to receive a statin prescription than were female patients (OR 1.18; 95% CI, 1.10-1.26).

Among need variables, a number of clinical characteristics were associated with the initiation of statin therapy. Univariate logistic regressions showed that patients with dyslipidemia in the baseline period were significantly more likely to receive a statin prescription after discharge from the CHD hospitalization. In contrast, baseline diabetes, hypertension, renal disease, psychoses, overall comorbidity, nonstatin lipid-modifying drug use, total number of baseline medication therapeutic classes, and length of hospital stay were inversely related to initiation of statin therapy. Also, patients hospitalized because of AMI were significantly more likely to start statin therapy than were patients with other types of CHD hospitalizations. In the multivariate analysis, baseline psychoses, overall comorbidity, nonstatin lipid-modifying drug use, and type of CHD were still significantly associated with initiation of statin therapy. However, baseline diabetes, hypertension, renal disease, total number of baseline medication therapeutic classes, and length of hospital stay were no longer significant after adjusting for other covariates. This lack of significance indicates that these factors were not independent and that the unadjusted significant association between these variables and initiation of statin therapy is mediated or confounded by other factors.

Enabling variables also played important roles in explaining the use of statins after discharge from CHD hospitalizations. In univariate logistic regression analysis, enrollee type, health plan type, cardiologist visit, amount of prescription copayment for statins, and year of CHD hospitalization were significantly associated with the initiation of statins. However, the significance of enrollee type and health plan type disappeared after adjustment for other variables in multivariate analysis.

The year of index hospitalization was significantly associated with statin use based on the results from the multivariate analysis. The use of statins after CHD hospitalization increased significantly over the 4-year study period, rising from 39.4% of CHD patients discharged in 2000 to 55.9% of CHD patients discharged in 2003 (Figure 2). In Model 1, which included all study patients and did not control for copayment, the odds of receiving statin therapy after discharge were approximately 80% higher for CHD patients admitted in 2003 than for patients admitted in 2000 (OR 1.77; 95% CI, 1.61-1.94). In Model 2, which included only the subset of patients for whom copayment information was available, the odds of receiving statin therapy after discharge were 231% higher for CHD patients admitted in 2003 than for patients admitted in 2000 (OR 3.31; 95% CI, 2.95-3.71). Seeing a cardiologist was also associated with higher odds of receiving a statin (OR 1.26; 95% CI, 1.18-1.34). Copayment amount was inversely associated with the likelihood of initiation of statin therapy. The OR associated with

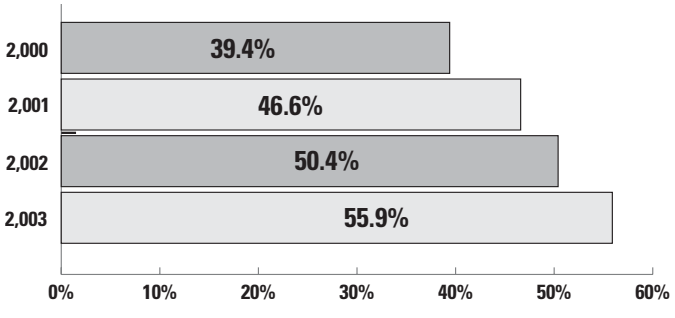
each dollar increase in copayment was 0.99 (95% CI, 0.98-0.99). Consistently, when patients were categorized as having a low (<$10), medium (≥$10 to <$20), or high (≥$20) copayment, the odds of receiving statin therapy after CHD hospitalization were approximately 40% lower for patients whose statin copayment was $20 or more than for those whose statin copayment was less than $10 (OR 0.62; 95% CI, 0.56-0.68).

A total of 3,784 patients who had an index CHD hospitalization in 2003 were included in the subgroup analysis. Of those, 2,114 (55.9%) had received statin therapy within 6 months after discharge from a CHD hospitalization. Significant factors associated with statin use among this subset of patients included age, gender, baseline dyslipidemia, baseline psychoses, baseline renal disease, baseline overall comorbidity, baseline nonstatin lipid-modifying drug use, CHD type, cardiologist visit, and statin copayment (Table 5).

Discussion

The clinical benefits and cost-effectiveness of statins in reducing recurrence of CHD events have been well established in patients with preexisting CHD,[27] and many experts recommend starting lipid-modifying therapy immediately after a significant coronary event.[8] However, recent data collected by the National Registry of Myocardial Infarction showed that only 31.7% of all patients who were hospitalized with AMI received lipid-modifying drugs at the time of discharge.[28] Animal, epidemiologic, and clinical trial data show that LDL-C is the primary target in preventing new and recurrent CHD events and statins are the most effective agents to lower LDL-C.[9] Our study evaluated statins and extended the observation period to 6 months after discharge from a CHD hospitalization. We found a higher percentage of patients taking statins, but still more than 50% of patients hospitalized because of CHD did not receive any statins. This finding adds to a growing body of literature demonstrating the suboptimal use of statins.

FIGURE 2 *Statin Use in Patients Discharged With a Primary Diagnosis of CHD*



CHD = coronary heart disease.

We adapted Andersen's health service utilization model as a conceptual framework in this study to examine the relationship between initiation of statin therapy and a variety of predictor variables. The results suggested that Andersen's utilization model is highly applicable for (1) guiding the selection of important predictor variables, and (2) explaining a significant portion of the variance in initiation of statin therapy.

The year of index hospitalization appeared to be one of the strongest predictors of initiation of statins based on the results from the multivariate analysis. The use of statins after CHD hospitalization has been consistently increasing over the study period from 2000 through 2003. This might reflect a lag in implementation of clinical trial results to regular practice. In addition, generic forms of lovastatin became available in the United States in 2002, and in the same year the NCEP guideline on cholesterol control was updated to recommend more aggressive LDL-C lowering among CHD patients.[8,29] Both of these factors might have contributed to the increased statin use in 2002 and more notably in 2003. Additionally, the magnitude of increased statin use in year 2003 was much greater in the subsample with available copayment information, which might be explained by higher homogeneity of the subsample.

Given the significant impact of the year of index hospitalization, we performed a separate analysis for the 2003 patients. Results from the subgroup analysis were quite consistent with results from the entire sample analysis, suggesting that the factors associated with statin use after CHD hospitalization and their impact remained relatively constant even though there was increased use of statins over the study timeframe.

We found a number of other factors associated with the initiation of statin therapy, including the new finding that the level of patient copayment was an independent predictor for receiving the first outpatient prescription for a statin after a CHD hospitalization. Compared with patients with a copayment of less than $10, patients who had a copayment of $20 or more were 40% less likely to initiate statin therapy after discharge from a CHD hospitalization. Copayments between $10 and $20 were not significantly associated with lower likelihood of initiation of statin therapy after adjustment for other factors. Although some other predictors were associated with more significant ORs, copayment is a potentially modifiable factor, which makes it interesting to examine for implications to improve health care.

Copayment is a longstanding component of pharmaceutical cost control in managed care organizations, which attempt to balance the demands for increased access to prescription drugs with the containment of escalating pharmaceutical costs. The rationale for cost sharing is to allow enrollees to express their preferences for selected pharmaceutical products by their willingness to pay, while ensuring that no prescription goes unfilled because of a high copayment.[24]

Recent findings have been mixed regarding the actual effects of copayment on prescription drug use. Some studies suggest that

TABLE 5 *Logistic Regression Results (2003 Subgroup Analysis)*

	Univariate Model (N = 3,784)*		Multivariate Model 1 (N = 3,782)†		Multivariate Model 2 (N = 2,864)‡†	
Variable	**OR (95% CI)**	***P* Value**	**OR (95% CI)**	***P* Value**	**OR (95% CI)**	***P* Value**
Age	0.97 (0.97-0.98)	<0.001	0.97 (0.96-0.98)	<0.001	0.99 (0.97-1.00)	0.029
Gender		<0.001		0.008		0.445
Male vs. female	1.47 (1.28-1.68)		1.22 (1.05-1.42)		1.08 (0.89-1.32)	
Baseline dyslipidemia		<0.001		<0.001		0.003
Yes vs. no	1.46 (1.25-1.71)		1.49 (1.25-1.77)		1.40 (1.12-1.75)	
Baseline hypertension		0.002		0.113		0.012
Yes vs. no	0.81 (0.72-0.92)		0.89 (0.77-1.03)		0.79 (0.66-0.95)	
Baseline diabetes		<0.001		0.392		0.242
Yes vs. no	0.73 (0.63-0.86)		0.92 (0.76-1.11)		0.87 (0.68-1.10)	
Baseline psychoses		<0.001		0.003		0.027
Yes vs. no	0.54 (0.36-0.80)		0.52 (0.34-0.80)		0.55 (0.32-0.93)	
Baseline renal disease		<0.001		0.029		0.390
Yes vs. no	0.47 (0.32-0.69)		0.60 (0.38-0.95)		0.77 (0.43-1.39)	
Baseline comorbidity index		<0.001		0.021		0.023
6+	0.40 (0.22-0.73)		0.49 (0.25-0.95)		0.65 (0.26-1.64)	
5-6	0.56 (0.39-0.81)		0.77 (0.50-1.18)		0.57 (0.33-0.98)	
3-4	0.61 (0.52-0.73)		0.76 (0.62-0.93)		0.68 (0.52-89)	
1-2 (reference)	–		–		–	
Count of medication therapeutic classes	0.97 (0.95-0.98)	<0.001	1.00 (0.99-1.02)	0.297	1.00 (0.99-1.02)	0.669
Baseline nonstatin lipid-modifying drug		<0.001		<0.001		<0.001
Yes vs. no	0.52 (0.41-0.67)		0.51 (0.38-0.67)		0.51 (0.36-0.73)	
CHD type		<0.001		<0.001		<0.001
Non-AMI CHD	0.49 (0.43-0.56)		0.44 (0.38-0.51)		0.45 (0.37-0.54)	
AMI (reference)	–		–			
Length of stay	0.99 (0.98-1.00)	0.181	1.00 (0.98-1.02)	0.944	1.01 (0.99-1.04)	0.312
Enrollee type	–	<0.001		0.998		<0.001
Medicare Supplemental	0.50 (0.44-0.57)		1.00 (0.77-1.31)		1.92 (1.34-2.74)	
Commercial (reference)	–		–		–	
Plan type		<0.001		0.355		0.079
PPO	1.18 (1.03-1.35)		0.93 (0.80-1.08)		0.89 (0.72-1.09)	
Noncap POS	1.18 (0.93-1.48)		0.85 (0.66-1.09)		1.26 (0.92-1.73)	
EPO	NA		NA		NA	
Comprehensive (reference)	–		–			
Copayment§		<0.001		NA		<0.001
≥$20	0.45 (0.38-0.54)		NA		0.34 (0.27-0.42)	
<$20 (reference)	–		–		–	
Cardiologist visit		<0.001		<0.001		<0.001
Yes vs. no	1.31 (1.15-1.49)		1.39 (1.20-1.61)		2.57 (2.08-3.17)	

* *Due to missing data, the Ns for univariate analysis plan type and copayment were 3,783 and 2,866, respectively.*

† *Only 1 patient had an EPO plan and another patient had plan type missing. These 2 patients were not included in the model.*

‡ *The N for multivariate analysis of copayment was 2,864, due to missing data.*

§ *For nonstatin users, only patients whose copayment could be imputed were included. Also, due to the small number of patients who had a copayment between $10 and $20 in the subgroup, copayment for statins was categorized as ≥$20 and <$20.*

AMI = acute myocardial infarction; CHD = coronary heart disease; CI = confidence interval; EPO = exclusive provider organization; OR = odds ratio; NA = not available; POS = point of service; PPO = preferred provider organization.

effective therapies are likely not to be used because of the high out-of-pocket expenditures.[30-33] For instance, one recent survey study among elderly patients with chronic obstructive pulmonary disease found that 40% of respondents chose to take less than the prescribed amount and 29% chose to stop taking medications altogether to reduce out-of-pocket prescription expenses.[33] On the other hand, other studies have found no difference in overall medication use or continuation rates before and after an increase in pharmacy copayment, following adjustments for relevant population differences.[34-37]

To our knowledge, however, no studies have examined the impact of copayment on the initiation of statins after discharge from CHD hospitalization. We found an inverse relationship between copayment and the initiation of statins, suggesting that high copayments may be a barrier to patient access to this cost-effective drug therapy. Additionally, Gibson et al. recently found that higher copayment was also associated with lower adherence to statin use.[38] Therefore, lowering the copayment amount for statins might decrease the economic burden for patients with CHD and potentially improve the use of statins in this high-risk population.

Both age and gender were significantly associated with the likelihood of initiation of statin therapy after discharge from CHD hospitalization, with older and female patients at a disadvantage. This finding regarding age is consistent with other research demonstrating that increasing age is inversely related to the receipt of lipid-modifying drugs despite high risk of CHD events in the elderly.[39,40] Secondary prevention of CHD in older patients might be viewed as a futile effort by some clinicians, in light of these patients' frailty and more limited life span.[41,42]

Regarding gender, previous studies have suggested that men are more likely to receive a statin than women, but the difference disappears once age differences and other factors are controlled.[15,41] In contrast, our findings show a gender bias regarding initiation of statin therapy after discharge from CHD hospitalization after adjustment for other factors. The discrepancy with previous literature might be because of the difference in study populations. Our study specifically focused on patients discharged from a CHD hospitalization. Men are at higher risk of CHD events than are women, but CHD is also the leading cause of death in women. Recent guidelines from the AHA and the ACC encourage a more aggressive approach to lipid lowering in women.[43] Therefore, recognizing and correcting gender bias in the secondary prevention of CHD with statins is important.

As expected and consistent with previous studies,[13,15,28] patients with dyslipidemia before CHD hospitalization and those hospitalized because of AMI were more likely to start statin therapy after discharge. Although the presence of baseline diabetes and hypertension was significantly associated with a lower likelihood of initiation of statins in univariate analysis, the significance disappeared after controlling for other factors, indicating that they were not independent factors and the lower observed rate of statin use in patients with diabetes and hypertension might be confounded by other factors.

We found that patients with higher comorbidity index scores, psychoses, and renal disease at baseline were less likely to receive a prescription for statins after discharge from a CHD hospitalization after adjustment for other factors. This finding supports the research hypothesis and confirms the treatment-risk paradox reported in previous research.[42] The relationship between high baseline risk and statin avoidance in the secondary prevention population implies suboptimal benefits of evidence-based therapies when they are applied to a real-world setting.

Several reasons might explain the treatment-risk paradox for statins, according to Ko et al.[42] First, the paradox might be explained by physicians' misconceptions about the benefit-harm tradeoffs when they consider generalizing clinical trial results to patients with complex comorbidities. Second, physicians may judge that patients with complex comorbidities might have low compliance with statins and therefore they might not even prescribe statin therapy. Third, physicians might be inattentive to the need for statin therapy when they are managing other concurrent conditions because of constraints on their time, expertise, and preferences. Fourth, some of these patients may have received a prescription from their physician, but chose not to have it filled.

Seeing a cardiologist was also associated with higher odds of receiving a first outpatient statin prescription. Patients who see cardiologists may have more severe CHD. However, it is unlikely to be the reason in this study, as all patients in the cohort had to have a CHD-related hospitalization and thus, by definition, had severe CHD. Cardiologists might be more familiar with lipid-modifying guidelines than would primary care or internal medicine practitioners. This discrepancy suggests continued need to provide education on lipid-modifying guidelines to nonspecialist physicians.

Limitations

First and foremost among the limitations of the present study is that we did not examine the use of other lipid-modifying drugs such as niacin, fibrates, or bile sequestrants. A portion of these patients who did not receive statin therapy may have received alternative lipid-modifying therapy, which was not measured in the present study. Therefore, our analysis would underestimate the proportion of patients with a CHD hospitalization who received lipid-modifying drug therapy after CHD discharge.

Second, we did not have data for serum cholesterol levels. Therefore, it was not possible to determine the type of dyslipidemia of these patients or determine with certainty that these patients with a hospital admission and primary diagnosis of CHD, in fact, required lipid-modifying therapy with a statin to attain therapeutic goals. The present analysis was completed under the assumption that all patients discharged from CHD hospitalization would benefit from statin therapy and would require statin therapy for life.

Although it is true that most CHD patients are candidates for statin therapy and will need continuous use of statins, a minority

of patients may have had cholesterol profiles that suggest no need for lipid-modifying therapy or the need for an alternative lipid-modifying therapy. Information on patient cholesterol levels would have facilitated understanding and reduced the confounding effects of nonstatin candidates in the study. Other variables, such as smoking status and race, also would have contributed to explaining differences in initiation of statins.

Third, we used a diagnosis of dyslipidemia as a need variable while focusing on statin therapy as the outcome of interest. The ICD-9-CM coding structure does not differentiate well among types of dyslipidemia (see Table 2). While we did exclude, for example, diagnosis codes 272.1 (pure hyperglyceridemia) and 272.2 (mixed hyperlipidemia), we did include 272.4 (hyperlipidemia not elsewhere classified). Had we had access to values for serum lipid panels or more specific types of dyslipidemia, we would have been able to determine the true clinical need.

Fourth, the dollar amount of the statin copayment had to be inferred for the nonstatin users from the average of copayment amounts for all statin prescriptions filled by other members in the same health benefit plan during the same year. For 42% of nonstatin users, the statin prescription copayment amount could not be imputed since the members could not be tied to a particular health benefit plan to determine an average copayment amount. Whether data loss of this magnitude affected our results depends on whether those with missing copayment information differed systematically (e.g., in terms of benefit design, industry, copayment amount, or other relevant factors) from those whose copayments were recorded in the database. Because we do not have access to this information, the effect of this limitation on our study results is unknown.

Fifth, while administrative records of pharmacy claims have been shown in other studies to be reliable sources of data for examining patient drug use, and patterns of ongoing prescription filling represent the most accurate way of estimating actual medication use in large populations,[44] we did not measure actual consumption of medications. Filling a statin prescription was used as the marker for actual medication use; however, we could not determine if patients actually took their medications once dispensed, and the present study did not assess what proportion of patients discontinued statin therapy after the first prescription. The difference between filling the prescription and actually consuming the drugs should be considered in interpreting our results.

Sixth, information on medication use during the hospitalization was not available in the MarketScan database. It is likely that some patients may have received a first statin prescription in the hospital but did not continue the therapy after discharge. Seventh, owing to the nature of observational data, this study cannot establish any causal relationships. In particular, as in any study employing a large database spanning multiple employers and health plans, numerous plan features, including disease management and adherence programs, flat copayment versus coinsurance designs, and deductibles versus first-dollar coverage, could have influenced study results but were unmeasured in this analysis.

Conclusions

Our study showed that statin use after CHD hospitalization in real-world practice seems to be suboptimal. However, the first year of the study period (2000) preceded the ATP III guidelines for cholesterol management, and we found that the proportion of patients receiving statin therapy increased significantly over the 4-year study period. Higher copayment and female gender were associated with not receiving a statin drug after hospitalization for CHD.

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