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Hydroxymethylglutaryl-CoA Reductase Inhibitors in Older Persons with Acute Myocardial Infarction: Evidence for an Age–Statin Interaction

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Abstract

OBJECTIVES—To characterize the relationship between hydroxymethylglutaryl-CoA reductase inhibitors (statins) and outcomes in older persons with acute myocardial infarction (AMI).

DESIGN—Observational study.

SETTING—Acute care hospitals in the United States from April 1998 to June 2001.

PARTICIPANTS—Medicare patients aged 65 and older with a principal discharge diagnosis of AMI (N = 65,020) who did and did not receive a discharge prescription for statins.

MEASUREMENTS—The primary outcome of interest was all-cause mortality at 3 years after discharge.

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RESULTS—Of 23,013 patients with AMI assessed, 5,513 (24.0%) were receiving a statin at discharge. Nearly 40% of eligible patients ($n=8,452$) were aged 80 and older, of whom 1,310 (15.5%) were receiving a statin at discharge. In a multivariable model taking into account demographic, clinical, physician and hospital characteristics, and propensity score, discharge statin therapy was associated with significantly lower 3-year mortality (hazard ratio (HR) =0.89 (95% confidence interval (CI) =0.83–0.96)). In an analysis stratified by age, discharge statins were associated with lower mortality in patients younger than 80 (HR =0.84, 95% CI =0.76–0.92) but not in those aged 80 and older (HR =0.97, 95% CI =0.87–1.09).

CONCLUSION—Statin therapy is associated with lower mortality in older patients with AMI younger than 80 but not in those aged 80 and older, as a group. This finding questions whether statin efficacy data in younger patients can be broadly applied to the very old and indicates the need for further study of this group.

Keywords

lipids; myocardial infarction; elderly; treatment

Although recent studies have argued that “undertreatment” and “age bias” exist in the management of hyperlipidemia in patients aged 80 and older,¹ there is clinical uncertainty about the optimal approach in the very old. Although the lowering of low-density lipoprotein cholesterol (LDL-C) levels in younger patients with acute myocardial infarction (AMI) is known to reduce disease progression,² adverse events, and mortality,^{3–8} data are lacking regarding the effect of treating hypercholesterolemia in patients aged 80 and older after AMI.⁹ Few patients aged 80 and older have been enrolled in clinical trials, and those that have been enrolled may not be representative.¹⁰ Accordingly, national guidelines support the aggressive use of lipid lowering in a wide range of patients younger than 80, but for those aged 80 and older, there are often reservations,¹¹ and physician discretion is advised.¹² As a result, there is substantial variation in how lipids are managed in older persons.¹

The clinical significance of hyperlipidemia, including elevations in total cholesterol and LDL-C, in patients aged 80 and older has been the subject of debate. Although it is generally held that the relationship between coronary artery disease (CAD) and total cholesterol is continuous and graded, the results of several studies suggest that the strength of this relationship decreases markedly in patients aged 80 and older.^{9,13–16} It has been suggested that the inconsistency of results regarding cholesterol and adverse outcomes in older people may be because of comorbidity and vulnerability to competing risks from other illnesses.^{17,18} The complex interplay of biological and nonbiological factors, competing risks, and physiological changes of aging may alter the relationship between cholesterol and CAD in this group of patients such that statins may be less effective in modifying outcomes. CAD may have different underlying causes and manifestations in patients aged 80 and older and may therefore require a different disease and treatment paradigm.^{19,20} As such, the benefits of therapy may diminish with age.

The specific hypothesis was that the initiation of hydroxymethylglutaryl-CoA reductase inhibitor (statin) therapy after AMI would be associated with better outcomes but that this association would diminish with age. Data abstracted from the medical records of more than 65,000 hospitalizations of Medicare beneficiaries in the United States between 1998 and 2001 with a principal discharge diagnosis of AMI were analyzed as part of the National AMI Project, a Centers for Medicare and Medicaid Services initiative to improve the quality of care and outcomes for Medicare beneficiaries with AMI.

METHODS

Data Sources

The study sample was obtained from patients in two national cohorts of fee-for-service Medicare beneficiaries who had experienced an AMI, as previously described.²¹ In brief, it consisted of 65,020 hospitalizations nationwide with a principal discharge diagnosis of AMI (*International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) code 410) from April 1998 to March 1999 and July 2000 to June 2001. Trained personnel abstracted predefined demographic, clinical, and treatment variables from copies of hospital records using a computerized abstraction instrument with explicit criteria that were developed and tested for these measures. Of the more than 250 variables collected, more than half are intended expressly for risk adjustment and other research purposes. The reliability of variables included in the national AMI project has been extensively studied.

Using the National Claims History File, which consists of Medicare Part A claims, a systematic random sample of discharges with a principal diagnosis of ICD-9-CM 410.xx, excluding 410.x2, was identified. The data were linked using the American Medical Association Physician Masterfile using unique physician identification numbers of the attending physicians. Characteristics of the treating hospitals were ascertained through linkage with the American Hospital Association annual surveys. Dates of death were assessed through linkage with the Medicare Enrollment Database.

Analysis Cohort

The analysis cohort was restricted to patients who had an AMI confirmed according to clinical criteria. An AMI was defined as (1) a peak creatine kinase (CK)-myocardial band fraction greater than 5%; (2) lactate dehydrogenase (LDH)-2 than greater than 1.5 times the normal value and LDH-1 greater than LDH-2; (3) troponin I or T greater than the upper limit of normal; (4) or two of the following three criteria: chest pain, a CK level twice as high as normal, or new Q waves on the electrocardiogram. If patients had more than one admission during the study time period, only the first admission was included. Patients who transferred to another hospital; left against medical advice; had a terminal illness, comorbid condition limiting statin use (e.g., hepatic failure, hepatitis, or myopathy), a do-not-resuscitate order, or intolerance to statins; or resided outside the United States were also excluded from the analysis cohort. Because this study focused upon the importance of statin prescription at hospital discharge, patients who were taking statins before admission and those who died during their hospitalization or had an unknown date of death were also excluded. Finally, patients with no medication prescribed at discharge were also excluded. After the application of these criteria, a sample of 23,013 records was analyzed. Three-year all-cause mortality after discharge was examined. Patient-level data were linked with the Medicare Enrollment Database, a validated means of assessing long-term follow-up and vital status of Medicare beneficiaries using Social Security Administration data.²² All-cause mortality was used rather than cause-specific mortality rates, because it is an objective and unbiased endpoint.²³

Statistical Analysis

Descriptive statistics (medians, interquartile ratios, and percentages) were generated for baseline demographic and clinical characteristics, including lipid values, treatments and procedures, and hospital characteristics. Survival estimates were calculated using the Kaplan-Meier method. Cox proportional hazards modeling was used for unadjusted and adjusted survival analysis. Unadjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for discharge statin prescription versus no statin were determined.

Because external factors bias treatment assignments in observational studies, propensity analysis was used to minimize bias in the likelihood to prescribe lipid-lowering therapy at discharge. Propensity analysis aims to identify patients with similar probability of receiving statin therapy on the basis of observed clinical characteristics. With the use of a backward stepwise multivariable logistic regression model that included the basic risk parameters as the independent variables, the probability (propensity) of a patient receiving a statin at discharge was calculated. The goodness of fit of the propensity score model was evaluated using the c statistic and the Hosmer-Lemeshow test. The variables entered into the propensity score model included age, sex, race, history of hypertension, diabetes mellitus, congestive heart failure, myocardial infarction, percutaneous coronary intervention (PCI), coronary-artery bypass grafting (CABG), dementia, and smoking status. Additionally, heart rate, systolic blood pressure, rales, location of MI, type of electrocardiogram at presentation (STelevation, left bundle branch block, or no ST elevation), left ventricular systolic function, peak CK more than four times the upper limit of normal, atrial fibrillation, stroke, cardiac arrest, shock, angina pectoris, hyperlipidemia, white blood count, creatinine, and glucose were included. Physician specialty (cardiology) and type of hospital (CABG available) were also included in the model. Finally, medications used on discharge (aspirin, beta-blockers, and angiotensin-converting enzyme (ACE) inhibitors) were also included. Other in-hospital test/treatment variables included cardiac catheterization, stress test, CABG, and PCI during index hospitalization.

As previously suggested, the patients were sorted by propensity score and compared within deciles.^{22,24} Within each decile, patients were divided into those who did and those who did not receive a prescription for a statin at discharge. Selection of quintiles to use for propensity analyses were based on inspection of the propensity scores themselves in patients receiving and not receiving statins within each decile, the variances of those propensity scores, and the values and variances of covariates. Deciles containing patients whose demographics, clinical characteristics, and treatments were poorly matched were excluded from the final analyses. All these variables, together with individual propensity scores, and other predictive variables from previously derived models predicting mortality in this population were entered into the multiple covariate Cox regression analyses evaluating the association between statins at discharge and 3-year mortality. The same model was also used in secondary analyses stratifying based on age and LDL-C values.

In the secondary analyses, the existence of an interaction between age and statin therapy was formally evaluated using the Mantel-Haenszel test of the heterogeneity of the effects of statin therapy according to age and a Cox proportional hazards model incorporating terms for including the main effect of age, the main effect of statin therapy, and the interaction between age and statin therapy.²⁴ To quantify the magnitude of the interaction, the difference in the effects of statin therapy were determined by age strata. All statistical analyses were performed using SAS (version 8.2, SAS Institute, Inc., Cary, NC).

RESULTS

Of the 23,013 AMI patients considered eligible for statin initiation after MI, 5,513 (23.9%) were taking a statin upon discharge. Nearly 40% of eligible patients, (n = 8,452 (36.7%)) were aged 80 and older, of whom 1,310 (15.5%) received a discharge prescription for statins. Of all patients prescribed statins, 2,359 (42.6%) received atorvastatin, 2,061 (37.2%) simvastatin, 842 (15.2%) pravastatin 143 (2.6%) cerivastatin, 79 (1.4%) fluvastatin, and 59 (1.1%) lovastatin. Baseline characteristics of patients receiving statins and those not receiving them are displayed in Table 1. Patients with a higher propensity for receipt of statins were younger (74.6 ± 6.6 vs 77.7 ± 7.5 , $P < .001$) and more often male and had a higher rate of hypertension, prior MI, and CABG before arrival. They were also less likely to present with left bundle branch block, left ventricular systolic dysfunction, cardiac arrest or shock, congestive heart failure, or

renal disease on admission and stroke, atrial fibrillation, or shock during the stay. There were also higher rates of cardiac catheterization, stress testing, and PCI performed in this group, as well as higher rates of discharge prescription of concomitant aspirin, ACE inhibitors, and beta-blockers. Finally, patients admitted to hospitals with a CABG facility or those seen by a cardiologist were more likely to be in the group prescribed statins at discharge.

Patients aged 80 and older receiving statins at discharge were younger, less likely to have heart failure or dementia, and more likely to present with ST-elevation MI. Those who presented with an elevated white blood cell count, renal dysfunction (creatinine level >2.5 , blood urea nitrogen level >40 , or elevated glucose level) were less likely to receive statins. As anticipated, the higher the LDL-C value, the more likely older persons were to receive statins. Patients undergoing cardiac catheterization or PCI or receiving care from an attending cardiologist were more likely to receive a statin at discharge. Similarly, patients hospitalized in teaching hospitals or hospitals with cardiac surgery facilities were more likely to receive statins. Finally, patients who received other evidence-based therapies upon discharge were also more likely to receive statins upon discharge. Table 2 shows select patient, physician, and hospital characteristics by the prescription of statins at discharge in persons aged 80 and older.

Patients were then sorted by propensity score and compared within deciles. Within each decile, patients were divided into those who did and those who did not receive a prescription for a statin at discharge. Selection of quintiles to use for propensity analyses were based on inspection of the propensity scores themselves in patients receiving and not receiving statins within each decile, the variances of those propensity scores, and the values and variances of covariates. Deciles containing patients whose demographic characteristics, clinical characteristics, and treatments were poorly matched were excluded from the final analyses. All these variables, together with individual propensity scores and other predictive variables from previously derived models predicting mortality in this population,^{26,27} were entered into the multiple covariate. Table 3 shows patient, physician, and hospital characteristics by the prescription of statin at discharge stratified by propensity decile.

Unadjusted and adjusted HRs for 3-year mortality are shown in Table 4. In unadjusted analysis, 3-year mortality (Figure 1) was lower in patients receiving statins than in those who were not. After adjustment for propensity score and covariates, significant differences in 3-year mortality remained between patients prescribed statin and those who were not (HR = 0.89, 95% confidence interval (CI) = 0.83–0.96).

In an analysis of the influence of age on the association between discharge lipid lowering medications and clinical outcomes, there were significant differences in age of patients who were receiving statins and those who were not. The Mantel–Haenszel test of crude rates and a Cox proportional hazards analysis identified a significant interaction between age and statin therapy with respect to death from any cause. After adjustment, statin therapy was associated with a significant reduction in all-cause mortality in patients younger than 80 (HR = 0.84, 95% CI = 0.76–0.92, $P = .002$) but not in patients aged 80 and older (HR = 0.97, 95% CI = 0.87–1.09, $P = .62$ for interaction between age and statin). Figure 2 demonstrates an interaction between age and statin in this cohort, such that the mortality benefit associated with statins diminishes with age. To further discern the effects of statins in those aged 80 and older, the adjusted odds of 3-year mortality for patients prescribed statins at discharges versus patients not prescribed statins at discharge specifically in those aged 80 and older were assessed, fitting a trend line to the individual point estimates. As demonstrated in Figure 3, the trend line crosses 1 at approximately 84 years of age.

Of the 9,315 patients with LDL-C documented in their chart, 38.5% were receiving a statin at discharge, compared with 14.1% of the patients who did not have LDL-C documented in their

chart. Only small differences in baseline lipid levels were observed between the statin and no-statin groups. Table 5 shows covariate- and propensity-adjusted hazard ratios for 3-year mortality comparing patients receiving statins with those who were not as a function of LDL-C. Patients with LDL-C greater than 130 mg/dL were most likely to benefit from statin therapy at discharge, whereas those with LDL-C less than 100 mg/dL were least likely to benefit at 3 years.

DISCUSSION

In a cohort of Medicare beneficiaries discharged with AMI between 1998 and 2001, 23.9% of patients eligible for initiation of statins during hospitalization were taking a statin upon discharge. In patients younger than 80, discharge statin therapy was associated with a 16% reduction in mortality risk, although no significant difference in 3-year mortality was observed in patients aged 80 and older. This study is consistent with clinical trials demonstrating the importance of lipid lowering in elderly patients with AMI younger than 80 and suggests that, in clinical practice, these results are being realized. Nevertheless, the results of the current study raise questions regarding the current approach to treatment of hyperlipidemia in patients with AMI aged 80 and older.

Statins are among the most widely prescribed medications in the world with one of the best safety profiles on record. Nevertheless, the narrowed therapeutic window for most drugs in older persons, in conjunction with polypharmacy, makes safety an important concern in people aged 80 and older. Treatment in people aged 80 and older therefore has more potential for adverse events than treatment in younger populations, in whom the most common adverse effects are asymptomatic elevations in hepatic transaminases and myopathy.²⁸ Drug toxicity is a particular concern in people aged 80 and older, the majority of whom are women, have multiple comorbid conditions, have reduced renal and hepatic function, and are taking many medications. Pharmacokinetic drug interactions are an important consideration in patients taking multiple medications. Because all statins undergo metabolism by the cytochrome P450 isoenzyme system to varying degrees, the potential for drug interactions is increased, although side effects occurred in only 3% of patients concurrently taking medications that could potentially interact.²⁹ Given the potential side effects of therapy,^{30,31} decisions regarding lipid lowering in the very elderly should be individualized, and physician discretion is advised. Further clinical trials are required to clarify the role of lipid lowering in the very old.

Large-scale, randomized clinical trials, such as the Scandinavian Simvastatin Survival Study,³² the Cholesterol and Recurrent Events trial,³³ have demonstrated consistent mortality reductions in younger patients with stable CAD, and the recent Heart Protection Study,⁵ and the Pravastatin in elderly individuals at risk for or with vascular disease study,³⁵ have further strengthened the role of lipid lowering in trial-eligible older persons up to 82 years of age, yet none addressed the role of lipids in the post-MI patient or in the very elderly.

The role of lipid lowering in patients with acute coronary syndromes is evolving. The Pravastatin or Atorvastatin Evaluation and Infection Therapy—Thrombolysis in Myocardial Infarction 22⁸ demonstrated improved outcomes in younger patients receiving aggressive versus moderate lipid lowering after acute coronary syndrome, yet in patients aged 65 and older, a more-aggressive approach was not associated with better outcomes than a conservative approach. Adding more uncertainty, an approach using high doses of simvastatin in post-MI patients was associated with no improvement in outcomes and a greater risk of myopathy and rhabdomyolysis. Although some have proposed modifications of lipid-lowering guidelines based on these results, others have expressed concern regarding the broad application of statins in clinical practice, particularly in older persons.^{11,12}

What may account for the reduction in efficacy of statins seen in older persons with AMI? These results underscore the difficulty in applying data from the idealized trial setting to the bedside when patients may bear no resemblance to those included in the investigation.^{37,38} This is particularly problematic with elderly patients, a group that has been frequently excluded from clinical trials.³⁹ Consistent with these concerns, these data demonstrate diminishing mortality benefits for older patients prescribed statins after MI. Competing risks and comorbid conditions may alter the relationship between benefit and harm, may not allow for treatment, or may necessitate withdrawal of therapy in these older patients. Finally, the pathophysiology of coronary heart disease in the very old may differ from that in younger patients. Although plaque erosions and rupture may be more predominant in younger patients, in older patients, flow-limiting lesions and calcific coronary disease may predominate. Furthermore, clotting mechanisms may differ in older persons. Statins may provide less benefit in highly advanced disease seen in older patients. Finally, the oldest patients may not tolerate the medication or discontinue its use frequently.⁴⁰ Each of these hypotheses remains to be tested further.

Although this study represents the largest study to assess the effect of lipid lowering in older patients with MI, there are several issues to consider. Although robust adjustments were made for clinical, physician, and hospital factors, as well as the propensity to receive statins, unmeasured confounders may remain. Medication dose, adherence, and changing prescription patterns cannot be accounted for, although this methodology has accurately assessed mortality benefits of other medications including aspirin and beta-blockers in AMI and ACE inhibitors in heart failure. Statin therapy may be associated with unmeasured confounders, including improved access to care and that events may have been higher because of more-accurate medical information and documentation. Although all-cause mortality was used for this purpose and is less prone to this bias, this may bias the findings to the null. Although the similarity of the subcohorts examined in the propensity analysis may imply that residual confounding was accounted for through propensity analysis, it is not possible short of true randomization to account fully for variability in patient characteristics. Even propensity analysis cannot adjust for subtle differences between patients in the severity of various characteristics or combinations of characteristics and patient preferences that weigh in physician decision-making and affect patient outcome. Finally, it was decided to use the endpoint of all-cause mortality as a relatively unbiased endpoint, but it is prone to problems of competing mortality. It was not possible to assess CHD hospitalizations, CHD mortality, stroke, cardiovascular disease (CHD plus stroke), or cardiovascular disease mortality specifically—all of which may be more relevant endpoints regarding the effect of statins.

Despite these limitations, this study has several important strengths. It represents the most-comprehensive evaluation of the use of lipid management and outcomes in elderly survivors of MI. As part of a national initiative to improve care for elderly patients with MI, this study involved the chart abstraction of more than 60,000 records across the country with robust patient-level clinical data and included more than 5,500 patients aged 80 and older with 3 years of follow-up. When can observational studies such as this add to the understanding of interventions? When the results of observational studies and randomized trials are congruent in both direction and magnitude, as is true for these findings in patients younger than 80, the case for broader therapeutic effectiveness is strengthened. Nevertheless, observational studies can also indicate where practices shown to be efficacious in special populations may not be widely generalizable, such as heparin administration after acute MI, thrombolytic therapy for non-ST segment elevation acute coronary syndromes,^{41,42} or in the case of this study, discharge statin therapy in the very old patient with AMI.

These data demonstrate that lipid lowering is under-used and is associated with substantial mortality reductions in a national sample of older patients with MI up to 80 years of age. These results are consistent with a large body of evidence supporting these agents in appropriate older

patients younger than 80 and extend these findings to older patients with recent acute coronary syndrome. Nevertheless, this study raises questions regarding the utility of these agents in people aged 80 and older and highlights an urgent need for a clinical trial in patients with AMI beyond this age. Randomized clinical trials will be required to address the potential role of statins in the significant and growing proportion of patients aged 80 and older who remain at risk for cardiovascular events.

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Figure 1. Unadjusted Kaplan-Meier estimates of 3-year survival in patients prescribed statins at discharge versus patients not prescribed statins at discharge.

Figure 2.

Adjusted hazard ratio (HR) of 3-year mortality for patients prescribed statins at discharges versus patients not prescribed statins at discharge by 5-year age increments. HR >1 indicates excess risk of death for statin prescription compared with no statin prescription; HR <1 indicates lesser risk of death.

Figure 3.

Adjusted odds of 3-year mortality for patients prescribed statins at discharge versus patients not prescribed statins at discharge by age 80 and older. Odds ratio >1 indicates excess risk of death for statin prescription compared with no statin prescription; odds ratio <1 indicates lesser risk of death.

Table 1

Patient, Physician, and Hospital Characteristics Stratified by Prescription of Statins at Discharge

	Total (N =23,013)	No Statins at Discharge (n =17,500)	Statins at Discharge (n =5,513)	
Characteristic	n (%)			P-value
Demographics				
Aged ≥80	8,452 (36.7)	7,142 (40.8)	1,310 (23.8)	<.001
Female	10,985 (47.7)	8,490 (48.5)	2,495 (45.3)	<.001
White	20,814 (90.4)	15,780 (90.2)	5,034 (91.3)	.01
Medical history				
MI	7,322 (31.8)	5,821 (33.3)	1,501 (27.2)	<.001
Coronary artery bypass graft	3,086 (13.4)	2,410 (13.8)	676 (12.3)	.004
Percutaneous coronary intervention	2,522 (11.0)	1,893 (10.8)	629 (11.4)	.20
Tobacco use in prior year	4,076 (17.7)	3,001 (17.1)	1,075 (19.5)	<.001
Heart failure	5,404 (23.5)	4,638 (26.5)	766 (13.9)	<.001
Diabetes mellitus	6,793 (29.5)	5,376 (30.7)	1,417 (25.7)	<.001
Hypertension	15,643 (68.0)	12,026 (68.7)	3,617 (65.6)	<.001
Dementia	1,462 (6.4)	1,309 (7.5)	153 (2.8)	<.001
Admission characteristics				
Anterior MI location	1,393 (6.1)	1,187 (6.8)	206 (3.7)	<.001
ST elevation	5,170 (22.5)	3,792 (21.7)	1,378 (25.0)	<.001
Systolic blood pressure <100 mmHg	1,343 (5.8)	1,088 (6.2)	255 (4.6)	<.001
Pulse >100 beats per minute	5,235 (22.7)	4,372 (25.0)	863 (15.7)	<.001
Left ventricular ejection fraction <40%	5,744 (25.0)	4,546 (26.0)	1,198 (21.7)	<.001
Congestive heart failure/rales/gallop on admission	7,075 (30.7)	5,834 (33.3)	1,241 (22.5)	<.001
Initial laboratory results				
White blood count >12,000/mm ³	5,267 (22.9)	4,187 (23.9)	1,080 (19.6)	<.001
Creatinine >2.5 μmol/L or blood urea nitrogen >40 μmol/L	2,286 (9.9)	1,990 (11.4)	296 (5.4)	<.001
Glucose >190 mg/dL	5,244 (22.8)	4,209 (24.1)	1,035 (18.8)	<.001
Low-density lipoprotein cholesterol, mg/dL				<.001
<100	3,704 (16.1)	2,889 (16.5)	815 (14.8)	
100–129	3,081 (13.4)	1,866 (10.7)	1,215 (22.0)	
≥130	2,530 (11.0)	975 (5.6)	1,555 (28.2)	
In-hospital care				
Cardiac catheterization	12,915 (56.1)	8,699 (49.7)	4,216 (76.5)	<.001
Percutaneous coronary intervention	7,218 (31.4)	4,455 (25.5)	2,763 (50.1)	<.001
Attending cardiology care	10,074 (43.8)	6,991 (39.9)	3,083 (55.9)	<.001
Hospital characteristics				
Cardiac surgery capabilities	13,321 (57.9)	9,517 (54.4)	3,804 (69.0)	<.001

	Total (N =23,013)	No Statins at Discharge (n =17,500)	Statins at Discharge (n =5,513)	
Characteristic	n (%)			P-value
Teaching hospital	11,149 (48.4)	7,996 (45.7)	3,153 (57.2)	<.001
Discharge medications				
Aspirin	18,528 (80.5)	13,561 (77.5)	4,967 (90.1)	<.001
Beta-blockers	15,092 (65.6)	10,723 (61.3)	4,369 (79.2)	<.001
Angiotensin-converting enzyme inhibitor	11,094 (48.2)	8,058 (46.0)	3,036 (55.1)	<.001
Crude 3-year mortality from discharge	7,807 (33.9)	6,688 (38.2)	1,119 (20.3)	<.001

MI =myocardial infarction; statins =hydroxymethylglutaryl-CoA reductase inhibitors.

Table 2

Patient, Physician, and Hospital Characteristics Stratified by Prescription of Statins at Discharge (Aged ± 80)

Characteristic	Total (N =8,452)	No Statins at Discharge (n =7,142)	Statins at Discharge (n =1,310)	P-value
Demographics				
Age, mean $\pm$ standard deviation	85.0 (4.0)	85.2 (4.1)	83.9 (3.3)	<.001
Female, n (%)	4,915 (58.2)	4,144 (58.0)	771 (58.9)	.57
White, n (%)	7,746 (91.6)	6,551 (91.7)	1,195 (91.2)	.54
Medical history, n (%)				
MI	2,912 (34.5)	2,490 (34.9)	422 (32.2)	.06
Coronary artery bypass graft	996 (11.8)	839 (11.7)	157 (12.0)	.81
Percutaneous coronary intervention	706 (8.4)	586 (8.2)	120 (9.2)	.25
Tobacco use in prior year	672 (8.0)	571 (8.0)	101 (7.7)	.73
Heart failure	2,699 (31.9)	2,413 (33.8)	286 (21.8)	<.001
Diabetes mellitus	2,199 (26.0)	1,877 (26.3)	322 (24.6)	.20
Hypertension	6,012 (71.1)	5,058 (70.8)	954 (72.8)	.14
Dementia	993 (11.7)	905 (12.7)	88 (6.7)	<.001
Admission characteristics, n (%)				
Anterior MI location	2,912 (34.5)	2,432 (34.1)	480 (36.6)	.07
ST elevation	1,698 (20.1)	1,388 (19.4)	310 (23.7)	<.001
Systolic blood pressure<100 mmHg	476 (5.6)	418 (5.9)	58 (4.4)	.04
Pulse>100 beats per minute	2,253 (26.7)	2,006 (28.1)	247 (18.9)	<.001
Left ventricular ejection fraction<40%	2,271 (26.9)	1,936 (27.1)	335 (25.6)	.25
Congestive heart failure/rales/gallop on admission	3,313 (39.2)	2,919 (40.9)	394 (30.1)	<.001
Initial laboratory results, n (%)				
White blood count>12	1,899 (22.5)	1,672 (23.4)	227 (17.3)	<.001
Creatinine>2.5 μ mol/L or blood urea nitrogen>40 μ mol/L	1,090 (12.9)	985 (13.8)	105 (8.0)	<.001
Glucose>190 mg/dL	1,912 (22.6)	1,663 (23.3)	249 (19.0)	<.001
Low-density lipoprotein cholesterol, mg/dL				<.001
<100	1,163 (13.8)	950 (13.3)	213 (16.3)	
100–129	887 (10.5)	606 (8.5)	281 (21.5)	
≥ 130	683 (8.1)	316 (4.4)	367 (28.0)	
In-hospital care, n (%)				
Cardiac catheterization	2,812 (33.3)	2,062 (28.9)	750 (57.3)	<.001
Percutaneous coronary intervention	1,590 (18.8)	1,112 (15.6)	478 (36.5)	<.001
Attending cardiology care	2,995 (35.4)	2,348 (32.9)	647 (49.4)	<.001
Hospital characteristics, n (%)				
Cardiac surgery capabilities	4,051 (47.9)	3,233 (45.3)	818 (62.4)	<.001
Teaching hospital	3,593 (42.5)	2,909 (40.7)	684 (52.2)	<.001

Characteristic	Total (N =8,452)	No Statins at Discharge (n =7,142)	Statins at Discharge (n =1,310)	P-value
Discharge medications, n (%)				
Aspirin	6,541 (77.4)	5,388 (75.4)	1,153 (88.0)	<.001
Beta blocker	5,346 (63.3)	4,296 (60.2)	1,050 (80.2)	<.001
Angiotensin-converting enzyme inhibitor	4,200 (49.7)	3,414 (47.8)	786 (60.0)	<.001
Crude 3-year mortality from discharge, n (%)	4,150 (49.1)	3,690 (51.7)	460 (35.1)	<.001

MI =myocardial infarction; statins =hydroxymethylglutaryl-CoA reductase inhibitors.

Table 3
on of Statins at Discharge and Propensity Decile

Received Prescription for Statins n (%)														
3 (n =2,302)	Decile 4 (n =2,301)		Decile 5 (n =2,301)		Decile 6 (n =2,302)		Decile 7 (n =2,302)		Decile 8 (n =2,301)		Decile 9 (n =2,301)		Decile 10 (n =2,301)	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
65 (39.2)	853 (40.4)	97 (40.2)	705 (36.4)	116 (32.0)	540 (29.2)	143 (31.4)	365 (21.6)	152 (24.8)	222 (27.4)	343 (23.0)	204 (17.0)	212 (19.3)	112 (16.6)	228 (14.0)
87 (52.4)	998 (46.4)	115 (47.7)	877 (45.2)	162 (44.8)	783 (42.4)	218 (47.9)	676 (40.0)	248 (40.5)	364 (45.0)	641 (43.0)	541 (45.0)	482 (43.8)	293 (43.5)	741 (45.5)
152 (91.6)	1,856 (80.1)	216 (89.6)	1,755 (90.5)	329 (90.9)	1,672 (90.5)	418 (91.9)	1,549 (91.7)	559 (91.3)	737 (91.1)	1,351 (90.5)	1,088 (90.6)	1,012 (92.0)	624 (92.6)	1,487 (91.4)
61 (36.7)	745 (35.2)	94 (39.0)	668 (34.5)	132 (36.5)	570 (30.9)	152 (33.4)	482 (28.5)	174 (28.4)	232 (28.7)	422 (28.3)	318 (26.5)	268 (24.4)	166 (24.6)	329 (20.2)
31 (18.7)	319 (15.5)	42 (17.4)	279 (14.4)	50 (13.8)	271 (14.7)	63 (13.8)	214 (12.7)	78 (12.7)	101 (12.5)	189 (12.7)	153 (12.7)	145 (13.2)	72 (10.7)	142 (8.7)
15 (9.0)	242 (11.7)	23 (9.5)	231 (11.9)	46 (12.7)	242 (13.1)	70 (15.4)	204 (12.1)	84 (13.7)	109 (13.5)	203 (13.6)	167 (13.9)	113 (10.3)	66 (9.8)	154 (9.5)
29 (17.5)	333 (16.2)	47 (19.5)	341 (17.6)	73 (20.2)	355 (19.2)	83 (18.2)	343 (20.3)	132 (21.6)	154 (19.0)	301 (20.2)	247 (20.6)	215 (19.5)	137 (20.3)	327 (20.1)
51 (30.7)	587 (27.5)	68 (28.2)	428 (22.1)	74 (20.4)	309 (16.7)	75 (16.5)	231 (13.7)	86 (14.1)	116 (14.3)	184 (12.3)	130 (10.8)	105 (9.5)	56 (8.3)	128 (7.9)
46 (27.7)	652 (31.7)	77 (32.0)	586 (30.2)	114 (31.5)	545 (29.5)	138 (30.3)	494 (29.2)	173 (28.3)	228 (28.2)	419 (28.1)	320 (26.6)	244 (22.2)	165 (24.5)	336 (20.7)
112 (67.5)	1,466 (72.2)	175 (72.6)	1,330 (68.6)	252 (69.6)	1,274 (69.0)	327 (71.9)	1,151 (68.1)	393 (64.2)	548 (67.7)	980 (65.7)	793 (66.0)	706 (64.2)	445 (66.0)	1,005 (61.8)
12 (7.2)	116 (5.6)	10 (4.1)	84 (4.3)	16 (4.4)	50 (2.7)	19 (4.2)	33 (2.0)	22 (3.6)	18 (2.2)	30 (2.0)	20 (1.7)	18 (1.6)	13 (1.9)	22 (1.4)
54 (32.5)	727 (33.3)	81 (33.6)	629 (32.4)	138 (38.1)	640 (34.7)	153 (33.6)	620 (36.7)	231 (37.7)	274 (33.9)	545 (36.5)	444 (37.0)	382 (34.7)	256 (38.0)	585 (36.0)
30 (18.1)	429 (20.8)	54 (22.4)	421 (21.7)	86 (23.8)	450 (24.4)	115 (25.3)	437 (25.9)	149 (24.3)	205 (25.3)	376 (25.2)	296 (24.6)	278 (25.3)	182 (27.0)	432 (26.6)
8 (4.8)	134 (6.5)	12 (5.0)	115 (5.9)	17 (4.7)	88 (4.8)	35 (7.7)	104 (6.2)	31 (5.1)	39 (4.8)	103 (6.9)	63 (5.2)	44 (4.0)	21 (3.1)	62 (3.8)
53 (31.9)	501 (24.3)	55 (22.8)	402 (20.7)	83 (22.9)	337 (18.2)	72 (15.8)	287 (17.0)	86 (14.1)	117 (14.5)	218 (14.6)	173 (14.4)	136 (12.4)	70 (10.4)	188 (11.6)
57 (34.3)	597 (29.0)	68 (28.2)	510 (26.3)	96 (26.5)	436 (23.6)	106 (23.3)	405 (24.0)	147 (24.0)	184 (22.7)	323 (21.6)	258 (21.5)	210 (19.1)	132 (19.6)	279 (17.1)
57 (34.3)	700 (34.0)	76 (31.5)	566 (29.2)	115 (31.8)	488 (26.4)	114 (25.1)	428 (25.3)	123 (20.1)	199 (24.6)	312 (20.9)	230 (19.2)	205 (18.6)	116 (17.2)	282 (17.3)
43 (25.9)	470 (22.8)	40 (16.6)	457 (23.6)	81 (22.4)	379 (20.5)	94 (20.7)	374 (22.1)	124 (20.3)	162 (20.0)	271 (18.2)	253 (21.1)	193 (17.5)	118 (17.5)	307 (18.9)
26 (15.7)	226 (11.0)	31 (12.9)	183 (9.4)	29 (8.0)	136 (7.4)	37 (8.1)	109 (6.4)	28 (4.6)	41 (5.1)	83 (5.6)	50 (4.2)	33 (3.0)	28 (4.2)	46 (2.8)
44 (26.5)	507 (24.6)	59 (24.5)	453 (23.4)	78 (21.5)	405 (21.9)	98 (21.5)	358 (21.2)	116 (19.0)	149 (18.4)	280 (18.8)	225 (18.7)	180 (16.4)	118 (17.5)	262 (16.1)

Received Prescription for Statins n (%)														
	Decile 4 (n =2,301)		Decile 5 (n =2,301)		Decile 6 (n =2,302)		Decile 7 (n =2,302)		Decile 8 (n =2,301)		Decile 9 (n =2,301)		Decile 10 (n =2,301)	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
35 (21.1)	351 (17.0)	38 (15.8)	365 (18.8)	71 (19.6)	439 (23.8)	103 (22.6)	422 (25.0)	145 (23.7)	349 (23.4)	175 (21.6)	250 (20.8)	204 (18.5)	16 (2.4)	20 (1.2)
9 (5.4)	95 (4.6)	14 (5.8)	142 (7.3)	28 (7.7)	212 (11.5)	62 (13.6)	286 (16.9)	99 (16.2)	388 (26.0)	209 (25.8)	425 (35.4)	371 (33.7)	216 (32.0)	421 (25.9)
0 (0.0)	10 (0.5)	4 (1.7)	22 (1.1)	7 (1.9)	40 (2.2)	8 (1.8)	75 (4.4)	33 (5.4)	142 (9.5)	101 (12.5)	259 (21.6)	243 (22.1)	424 (62.9)	1,159 (71.2)
61 (36.7)	928 (45.0)	117 (48.5)	1,119 (57.7)	226 (62.4)	1,268 (68.7)	310 (68.1)	1,353 (80.1)	494 (80.7)	1,215 (81.4)	634 (78.4)	1,029 (85.7)	909 (82.6)	599 (88.9)	1,440 (88.5)
9 (5.4)	330 (15.0)	35 (14.5)	486 (25.1)	103 (28.5)	687 (37.2)	175 (38.5)	811 (48.0)	287 (46.9)	801 (53.7)	415 (51.3)	710 (59.1)	657 (59.7)	410 (60.8)	1,078 (66.3)
42 (25.3)	756 (35.7)	106 (44.0)	871 (44.9)	169 (46.7)	934 (50.6)	226 (49.7)	953 (56.4)	324 (52.9)	862 (57.8)	462 (57.1)	734 (61.1)	661 (60.1)	418 (62.0)	1,056 (64.9)
79 (47.6)	1,057 (50.3)	136 (56.4)	1,182 (61.0)	223 (61.6)	1,160 (62.8)	294 (64.6)	1,179 (69.8)	435 (71.1)	1,035 (69.4)	584 (72.2)	921 (76.7)	788 (71.6)	505 (74.9)	1,204 (74.0)
56 (33.7)	877 (40.6)	109 (45.2)	945 (48.7)	192 (53.0)	989 (53.5)	261 (57.4)	962 (56.9)	371 (60.6)	843 (56.5)	465 (57.5)	783 (65.2)	643 (58.5)	431 (63.9)	1,005 (61.8)
124 (74.7)	1,625 (75.9)	197 (81.7)	1,620 (83.5)	296 (81.8)	1,631 (88.3)	401 (88.1)	1,527 (90.4)	552 (90.2)	1,354 (90.8)	718 (88.8)	1,117 (93.0)	1,029 (93.5)	645 (95.7)	1,562 (96.0)
87 (52.4)	1,236 (60.0)	147 (61.0)	1,338 (69.0)	242 (66.9)	1,366 (74.0)	345 (75.8)	1,281 (75.8)	462 (75.5)	1,196 (80.2)	651 (80.5)	1,035 (86.2)	946 (86.0)	583 (86.5)	1,434 (88.1)
74 (44.6)	940 (43.6)	102 (42.3)	907 (46.8)	159 (43.9)	911 (49.3)	205 (45.1)	851 (50.4)	308 (50.3)	824 (55.2)	457 (56.5)	731 (60.9)	663 (60.3)	370 (54.9)	1,005 (61.8)

Table 4

Hazard Ratios for 3-Year Mortality by Subgroup

Model	Hazard Ratio (95% Confidence Interval)	P-value
Entire cohort		
Unadjusted	0.47 (0.44–0.50)	<.001
With covariates	0.86 (0.80–0.93)	<.001
With propensity score and covariates	0.89 (0.83–0.95)	.001
Propensity-matched cohort		
Unadjusted	0.54 (0.51–0.58)	<.001
With covariates	0.88 (0.82–0.94)	<.001
With propensity score and covariates	0.89 (0.83–0.96)	.002

Note: Hazard ratio comparing patients discharged with a prescription for statins with those discharged without.

Table 5

Hazard Ratios for 3-Year Mortality by Low-Density Lipoprotein Cholesterol (LDL-C)

LDL-C (mg/dL)	N	%	Hazard Ratio (95% Confidence Interval)	P-value
<100	3,704	16.1	0.95 (0.80–1.14)	.59
100–129	3,081	13.4	0.95 (0.74–1.21)	.27
≥130	3,530	11.0	0.76 (0.58–0.98)	.048

Note: Hazard ratio comparing patients discharged with a prescription for statins with those discharged without for deciles 2 through 10 after adjusting for covariates and propensity.