ORIGINAL RESEARCH

It's Not Too Late to Improve Statin Adherence: Association Between Changes in Statin Adherence from Before to After Acute Myocardial Infarction and All-Cause Mortality

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Background—Many older patients have a change in statin adherence—either an increase or a decrease—from before to after an acute myocardial infarction (AMI), but its association with mortality is unknown.

Methods and Results—Using Medicare administrative claims, a cohort of patients ≥66 years old with an AMI hospitalization from 2008 to 2010 was assembled. Statin adherence was measured for 180 days pre-AMI and 180 days post-AMI and categorized as severely nonadherent, moderately nonadherent, or adherent. Categorical change in statin adherence from pre- to post-AMI was assessed. Patients were then followed for up to 18 months for all-cause mortality. A Cox proportional hazards model was applied to estimate the effects of statin adherence change on all-cause mortality, adjusted for patient baseline characteristics. Of 101 011 eligible patients, 20% had a categorical increase in adherence, 16% decreased, and 14% remained nonadherent both pre- and post-AMI. Compared with patients who were always severely nonadherent (both pre- and post-AMI), patients whose adherence increased from severely nonadherent to adherent (hazard ratio=0.83; 95% CI: 0.75–0.92) and patients who were always adherent (hazard ratio=0.88; 95% CI: 0.82–0.94) were less likely to die; patients whose adherence decreased from moderately nonadherent to severely nonadherent were more likely to die (hazard ratio=1.11; 95% CI: 1.01–1.22).

Conclusions—After an AMI, patients with decreased statin adherence had the worst mortality outcomes. However, patients with increased statin adherence had a similar risk of mortality compared with continuously adherent patients, suggesting that, even after an AMI, it is not too late to improve statin adherence. **(*J Am Heart Assoc*. 2019;8:e011378. DOI: 10.1161/JAHA.118.011378.)**

Key Words: behavior change • medication adherence • myocardial infarction • older adults • secondary prevention

Statin therapy is a major component of guideline-recommended secondary prevention after an acute myocardial infarction (AMI).[1] Clinical benefit from statins after an AMI requires adherence to this medication therapy,[2,3] and statin adherence after an AMI was previously shown to have a dose–response-type association with mortality.[4] Clinical trials and many observational studies often assess the effectiveness of statins for secondary prevention among patients who are naïve to statin therapy; however, many patients are already taking a statin when they are hospitalized for an AMI, especially among older adults.[5]

Among US Medicare beneficiaries who were already taking a statin before being hospitalized for an AMI, 20% had increased statin adherence, 16% had decreased adherence, and 14% were consistently nonadherent both pre- and post-AMI hospitalization.[5] Other studies have found similar patterns of statin adherence changes after an AMI.[6,7] An important clinical question remains unknown among patients who were already taking a statin before experiencing an AMI: Does improving statin adherence matter, or is it too late to improve statin adherence after an AMI? No studies have evaluated whether and to what extent these *changes* in statin adherence may impact clinical outcomes. Therefore, the objective of this study was to investigate whether *statin*

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Accompanying Tables S1 through S8 and Figures S1 through S3 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.011378

This article was handled independently by Kerry-Anne Rye, PhD, as a guest editor.

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Received November 12, 2018; accepted February 22, 2019.

Clinical Perspective

What Is New?

- This is the first study to investigate the association between changes in statin adherence from before to after an acute myocardial infarction (AMI) hospitalization and all-cause mortality.
- Patients who increased their statin adherence—even if they only increased from severely nonadherent to moderately nonadherent—had a similar risk of all-cause mortality compared to patients who were always adherent.
- Patients who decreased their statin adherence had a similar or an even higher risk of all-cause mortality than patients who were always severely nonadherent.

What Are the Clinical Implications?

- Many patients who increase their statin adherence after an AMI can experience similar benefits from statin therapy as patients who were always adherent, suggesting that, even after an AMI, it is not too late to improve statin adherence.
- Among patients who were previously adherent to statin therapy, continued adherence is important after an AMI because decreasing statin adherence may lead to a higher risk of mortality compared to patients who were essentially never adherent to their statin.
- After a patient experiences an AMI, counseling about the need for statin therapy that is tailored to the patient's previous experience with the medication may increase the likelihood of positive adherence changes and better clinical outcomes.

adherence change from before to after an AMI hospitalization is associated with all-cause mortality in a large cohort of US Medicare beneficiaries.

Methods

The authors cannot make the Centers for Medicare and Medicaid Services (CMS) research data used for this study available to other researchers per the terms of the data use agreement. However, investigators can request access to Medicare administrative claims data through application with CMS.

Data Sources and Study Cohort

US Medicare 2007–2011 data including enrollment summaries, medical service claims (inpatient, outpatient, carrier, and skilled-nursing facility), and prescription Part D claims from the CMS Chronic Conditions Data Warehouse were used to create a cohort of patients hospitalized for an AMI between 2008 and 2010. This cohort has previously been described,[5] but this study additionally required patients to survive at least 180 days after hospital discharge. The eligibility criteria were (1) index AMI hospitalization between January 1, 2008, and December 31, 2010; (2) ≥66 years old; (3) continuous enrollment in Medicare Parts A, B, and D for ≥360 days prehospital admission, through the AMI hospitalization, and ≥180 days posthospital discharge; (4) discharged to home/self-care and survived >180 days prehospital admission discharge; (5) filled ≥1 statin prescription between 360 and 14 days prehospital admission; and (6) no pre-AMI end-stage renal disease. Details on patient selection and attrition can be seen in Figure 1. AMI hospitalizations were identified using an *International Classification of Diseases, Ninth Revision* (*ICD-9*) code of 410.x1 in the primary or secondary discharge field. If a patient had multiple AMIs during the index year, their index event was defined as their first observed AMI.

The institutional review board of the University of North Carolina at Chapel Hill approved this study. The need for informed consent was waived because this was a secondary analysis of deidentified administrative claims data.

Assessment of Statin Adherence and Change in Statin Adherence

Our measurements of statin adherence and statin adherence change were previously described.[5] Prescription claims for statins were identified in Part D event files. Adherence was measured using the proportion of days covered (PDC; 0–100%), adjusting for hospital stays and oversupply from previous prescription fills. Adherence was measured separately in both the 180 days pre- and 180 days post-AMI hospitalization and then categorized as severely nonadherent (PDC <40%), moderately nonadherent (PDC 40–79.9%), or adherent (PDC ≥80%).[4,5]

The primary exposure of interest was the *categorical change in statin adherence from pre- to post-AMI* (9 categories for all combinations of pre- and post-AMI adherence), with patients who were always severely nonadherent serving as the reference group. To simplify the display and description of results, statin adherence change was also categorized into the following groups (previously described as 5-level adherence change[5]): a "major decrease" if patients were adherent pre-AMI and severely nonadherent post-AMI, a "moderate decrease" for all other adherence *decreases*, "no change," a "major increase" if patients were severely nonadherent pre-AMI and adherent post-AMI, and a "moderate increase" for all other adherence *increases*.

Assessment of Outcome

The study design was similar to our previous work,[5] but after assessing statin adherence change, we followed patients up for mortality outcomes (Figure 2). All-cause mortality was measured with the verified date of death found in the

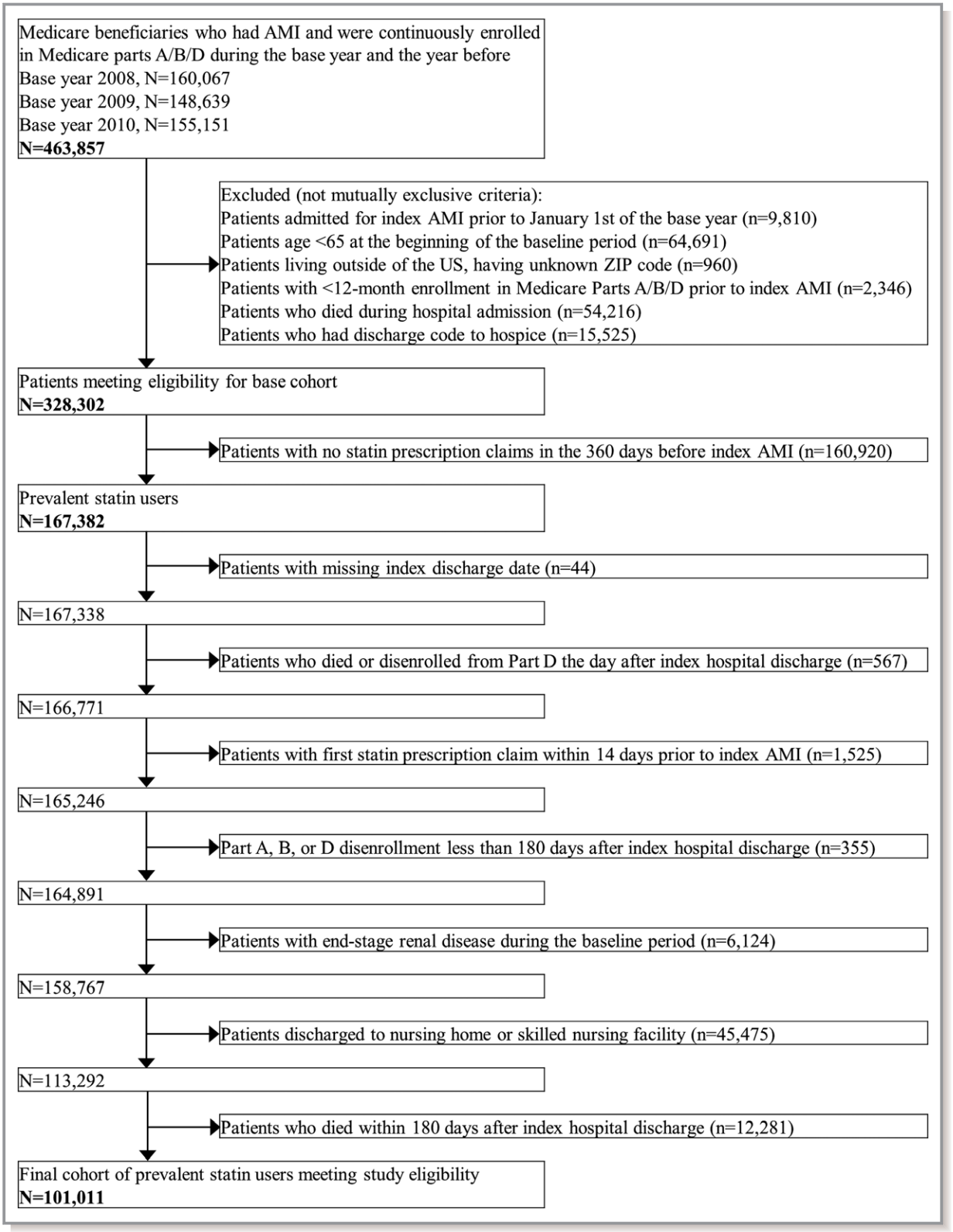


Figure 1. Patient eligibility and attrition. AMI indicates acute myocardial infarction; US, United States.

Medicare enrollment file. Patients were followed up from the end of the 180-day post-AMI adherence measurement period until whichever of the following occurred first: death, loss of continuous enrollment in Medicare Parts A/B/D, or end of available data for the patient (maximum of 18 months follow-up). In other words, survival was measured starting at

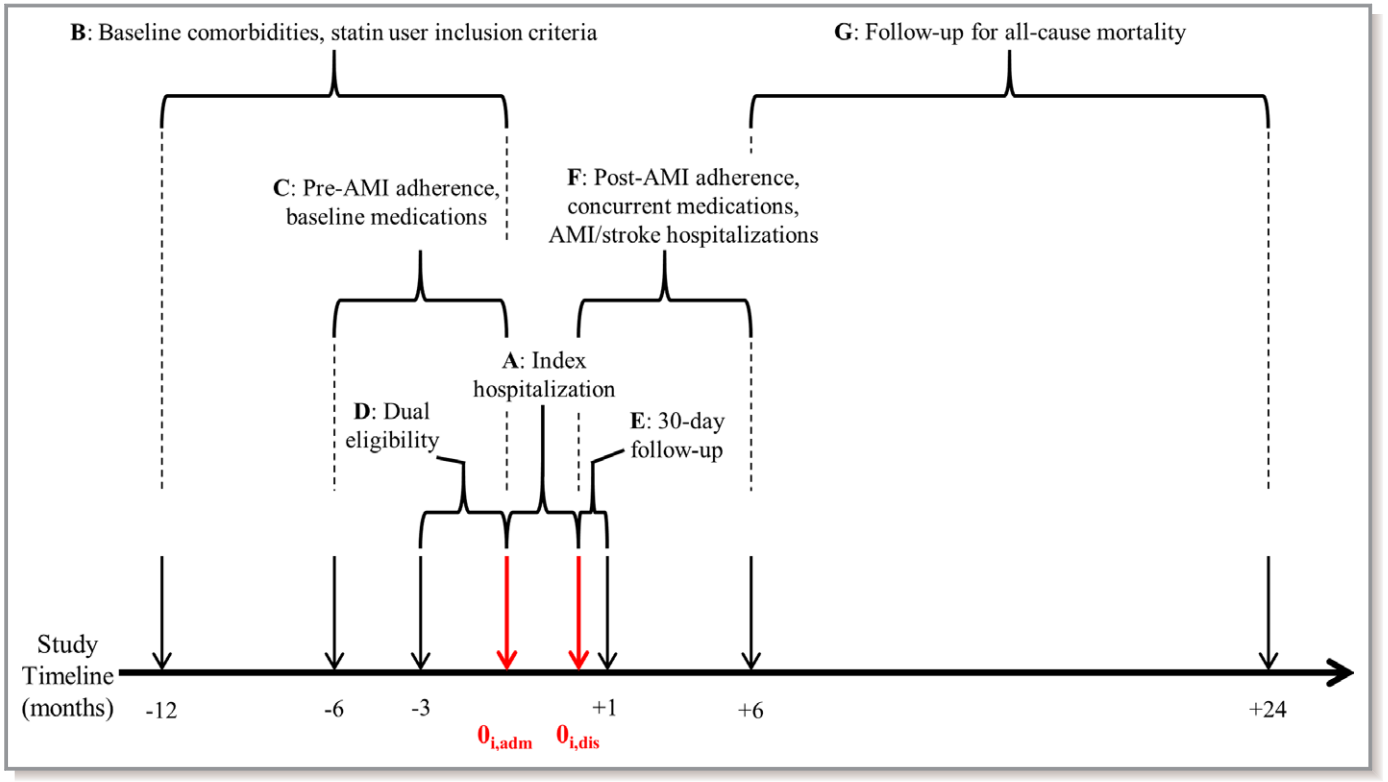


Figure 2. Study timeline in months, relative to index hospital admission. **A**: Length of stay for the index AMI hospitalization goes from admission date ($0_{i,adm}$) to discharge date ($0_{i,dis}$). **B**: 12-month period used to measure baseline comorbidities and identify prevalent statin users for study inclusion. **C**: 6-month period used to measure *pre-AMI statin adherence*. If a patient's first prescription claim for a statin was identified during this period (i.e. they were a "new user" according to our study definitions), pre-AMI adherence was measured from that date until the index hospital admission date. Concurrent use of other cardiovascular medications also measured during this period. **D**: 3-month period used to identify patients with dual Medicare and Medicaid eligibility. If a patient was dually enrolled during any of these 3 months, they were considered dual eligible for the entire study. **E**: 30-day period after index hospital discharge date to measure whether patient followed up with a primary care provider and/or cardiologist. **F**: 6-month period used to measure **post-AMI statin adherence**. Concurrent use of other cardiovascular medications and hospitalizations for a stroke or a recurrent AMI were also measured during this period. Patients had to survive until the end of this period for study inclusion. **G**: Patients were followed up for all-cause mortality from 6-months after the index hospital discharge date until whichever occurred first: death, loss of continuous enrollment in Medicare Parts A/B/D, or end of available data for the patient (maximum of 18 months follow-up). AMI indicates acute myocardial infarction.

181 days after index AMI hospital discharge up to a maximum of 24 months after the discharge date.

Patient Characteristics

Other patient characteristics of interest that were measured fell into the following categories: (1) sociodemographic characteristics, (2) baseline clinical conditions and medication use, (3) characteristics of the index AMI hospitalization, and (4) postdischarge events and medication use.

Sociodemographic characteristics were measured from enrollment summary files and included age at index AMI admission, sex, race/ethnicity, dual eligibility in Medicare and Medicaid, and median household income. Dual eligibility was measured in the 3 months pre-AMI. Median household income was calculated for individuals ≥65 years old at the US Census block group level.

Baseline comorbidities and recent cardiovascular procedures were measured in the 12 months before the index AMI admission from inpatient and outpatient medical claims. Comorbidities included previous AMI, dementia/Alzheimer's disease, depression, ischemic heart disease, unstable angina, lipid abnormalities, and rhabdomyolysis/myopathy. A modified Charlson Comorbidity Index was calculated that excluded AMI and dementia.[5] Recent cardiovascular procedures included coronary artery bypass surgery and stent/percutaneous transluminal coronary angioplasty. Baseline use of secondary prevention medications was measured in the 6 months pre-AMI from prescription claims (having at least 1 prescription claim for the medication class in the 180 days pre-index AMI admission). Medications of interest included angiotensin-converting enzyme (ACE) inhibitors/angiotensin II receptor blockers, β-blockers, $P2Y_{12}$ inhibitors, calcium channel blockers, and aldosterone receptor antagonists. Finally, we identified

whether patients were "new users" of statins, defined as having their first prescription claim for a statin within 6 months before the index AMI.

Characteristics of the index AMI included type of AMI (subendocardial or transmural), procedures (coronary artery bypass surgery, percutaneous transluminal coronary angioplasty/stent, cardiac catheterization, angiocardiography, and infusion of platelet inhibitors), and complications (cardiogenic shock, cardiac dysrhythmias, hypotension, acute renal failure, and heart failure). Additionally, length of the index hospitalization, admission to an intensive care unit and/or coronary care unit, and consultation from a cardiologist were measured.

Outpatient follow-up with a cardiologist and/or primary care provider was measured in the 30 days after hospital discharge.[5] Hospitalizations for AMI and stroke were also measured from the index discharge date for 6 months. Use of secondary prevention medications during this same 6-month period was also assessed, including measures for ACE inhibitors/angiotensin II receptor blockers, β-blockers, $P2Y_{12}$ inhibitors, calcium channel blockers, and aldosterone receptor antagonists (having at least 1 prescription claim for the medication class during the index AMI hospital stay or within 180 days after discharge). Finally, change in the simvastatin-equivalent average daily dose was calculated (6-month post-AMI average daily dose minus 6-month pre-AMI average daily dose).[5]

Statistical Analyses

Distributions of patient characteristics were described. Additionally, the distribution of changes in statin adherence—stratified by pre-AMI statin adherence—was described. All multivariable analyses (survival curves and Cox proportional hazards models) assessing the association between *change* in statin adherence and all-cause mortality were adjusted for all variables described in the Patient Characteristics section above; multivariable analyses assessing the association between *post-AMI* statin adherence and all-cause mortality were adjusted for these same variables, as well as *pre-AMI* statin adherence.

To visualize the association of statin adherence and all-cause mortality after an AMI hospitalization in a familiar way, direct adjusted survival curves[8] for the outcome of all-cause mortality were plotted, stratified by *post-AMI* statin adherence (3 curves). To show the importance of *changes in statin adherence* on this association, another set of direct adjusted survival curves was plotted, stratified by *change* in statin adherence from pre- to post-AMI (9 curves). The adjusted survival probabilities with 95% CIs at 1-year of follow-up were also estimated for both sets of survival curves.

We then used a multivariable Cox proportional hazards model to estimate hazard ratios (HRs) and 95% CIs for the association between statin adherence and all-cause mortality. The first model estimated the association between *post-AMI* statin adherence and all-cause mortality (patients who were severely nonadherent post-AMI were the reference group). The final model, highlighting the importance of the change in statin adherence, estimated the association between *changes in statin adherence* and all-cause mortality (patients who were severely nonadherent both pre- and post-AMI were the reference group). Schoenfeld residuals for statin adherence change categories were plotted against survival time to assess the proportional hazards assumption.

Several sensitivity analyses were conducted to assess the robustness and consistency of the estimates for the association between all-cause mortality and *statin adherence change*. First, because some covariates were measured during the same period when the exposure of interest (statin adherence change) was measured, we iteratively added covariates to the Cox model based upon when they were measured to see how estimates were affected: crude estimates only followed by iterative adjustment for (1) sociodemographics, (2) pre-AMI variables, (3) index AMI hospitalization variables, and (4) post-AMI variables (this is the full model). Second, using the full study sample, 3 sensitivity analyses were conducted: (1) requiring a 10% absolute change in PDC from pre- to post-AMI to officially be defined as an adherence change (to minimize the influence of small changes in adherence);[5,7] (2) adjusting for pre- and post-AMI statin intensity[1,5] instead of change in simvastatin-equivalent average daily dose; and (3) adding a liver disease variable to the model. Third, study eligibility was altered in 6 models by excluding (1) patients who were "new users," (2) patients with pre-AMI PDC of 0%, (3) "new users" and patients with pre-AMI PDC of 0%, (4) patients with only 1 pre-AMI statin prescription fill, (5) "new users" and patients with only 1 pre-AMI statin fill, and (6) patients with an AMI or stroke hospitalization within 6 months after the index AMI discharge date. Finally, a sensitivity analysis was conducted among the subgroup of patients who were also taking an ACE inhibitor or an angiotensin II receptor blocker as well as a β-blocker pre-AMI; the association between statin adherence change and all-cause mortality was adjusted for (1) changes in ACE inhibitor/angiotensin II receptor blocker and β-blocker adherence, followed by iterative adjustment for (2) sociodemographics, (3) pre-AMI variables, (4) index AMI hospitalization variables, and (5) post-AMI variables.

All analyses were conducted with SAS 9.4 (SAS Institute Inc).

Results

Our final study sample included 101 011 Medicare beneficiaries who were already taking a statin before the index AMI

Table. Distribution of Patient Characteristics

Patient Characteristics	Full Cohort: N=101 011, n (%)
Sociodemographics	
Age (y)	
66–75	47 128 (46.7)
76–85	39 698 (39.3)
86+	14 185 (14.0)
Female	54 886 (54.3)
Race/ethnicity	
White	85 318 (84.5)
Black	8495 (8.4)
Hispanic	3001 (3.0)
Asian	2227 (2.2)
Other	1970 (2.0)
Pre-AMI comorbidities and cardiovascular procedures*	
Adjusted Charlson comorbidity index†	
0	21 946 (21.7)
1–2	40 745 (40.3)
3–5	29 876 (29.6)
6–8	7102 (7.0)
9+	1342 (1.3)
Baseline comorbidities and procedures	
Prior AMI‡	4288 (4.2)
Dementia/Alzheimer's disease§	9396 (9.3)
Depression	15 207 (15.1)
CABG	1064 (1.1)
PTCA/stent	6748 (6.7)
Pre-AMI medications	
New user of statin‖	10 220 (10.1)
Concurrent medications¶	
ACE inhibitor/ARB	65 524 (64.9)
β-Blocker	63 437 (62.8)
$P2Y_{12}$ inhibitor	31 546 (31.2)
Characteristics of index AMI hospitalization	
Procedures	
CABG	6778 (6.7)
PTCA/stent	39 479 (39.1)
Duration of hospitalization (d)	
1–3	46 047 (45.6)
4–6	30 966 (30.7)
7–11	16 714 (16.5)
12+	7284 (7.2)
30-d post-AMI follow-up	
None	14 873 (14.7)
Primary care provider# only	29 301 (29.0)
Cardiologist only	19 161 (19.0)
Both	37 676 (37.3)
Post-AMI medications	
Concurrent medications**	
ACE inhibitor/ARB	72 011 (71.3)
β-Blocker	87 887 (87.0)
$P2Y_{12}$ inhibitor	66 607 (65.9)
Post-AMI clinical events	
Hospitalization for recurrent AMI††	6386 (6.3)
Hospitalization for stroke‡‡	972 (1.0)

ACE indicates angiotensin-converting enzyme; AMI, acute myocardial infarction; ARB, angiotensin II receptor blocker; CABG, coronary artery bypass surgery; *ICD-9, International Classification of Diseases, Ninth Revision*; PTCA, percutaneous transluminal coronary angioplasty.
*Measured in the 12 months before the index AMI hospital admission date.
†Charlson comorbidity index does not include counts for AMI and dementia.
‡Charlson comorbidity index definition.
§Medicare Chronic Conditions Data Warehouse definition.
‖First prescription claim for a statin was identified during the 6 months before the index AMI hospital admission date.
¶At least 1 prescription fill within medication class during the 6 months before the index AMI hospital admission date.
#Primary care physician, physician assistant, or nurse practitioner.
**At least 1 prescription fill within medication class during the index AMI hospitalization period or within 6 months after index AMI discharge date.
††Inpatient *ICD-9* diagnosis code of 410.x1 in the primary or secondary discharge field within 6 months after index AMI discharge date.
‡‡Inpatient *ICD-9* diagnosis code of 430, 431, 433.x1, 434.x1, or 436 in the primary discharge field within 6 months after index AMI discharge date.

hospitalization and survived at least 6 months after hospital discharge. Characteristics of the study sample can be seen in the Table. The distribution of changes in statin adherence from pre- to post-AMI can be seen in Figure 3. Out of the entire study sample, the distribution of categorical changes in statin adherence was 3622 (3.6%) patients with a major decrease, 12 443 (12.3%) patients with a moderate decrease, 64 736 (64.1%) patients with no change (including 6892 [6.8%] patients who were always severely nonadherent and 6926 [6.9%] patients who were always moderately nonadherent), 15 022 (14.9%) patients with a moderate increase, and 5188 (5.1%) patients with a major increase. A total of 50 093 (49.6%) patients were nonadherent (PDC <80%) in the pre-AMI and/or post-AMI periods. The distribution of patient characteristics across statin adherence change groups has been previously described in this cohort[5] (see Table S1 for results specific to this study).

Starting at 181 days post-AMI hospital discharge, patients were followed for a median of 346 days (interquartile range 244–447 days). During follow-up, 13 274 (13.1%) patients died, 941 (0.9%) were censored from losing Part D continuous enrollment, and 27 (<0.1%) were censored from losing Part A/B continuous enrollment.

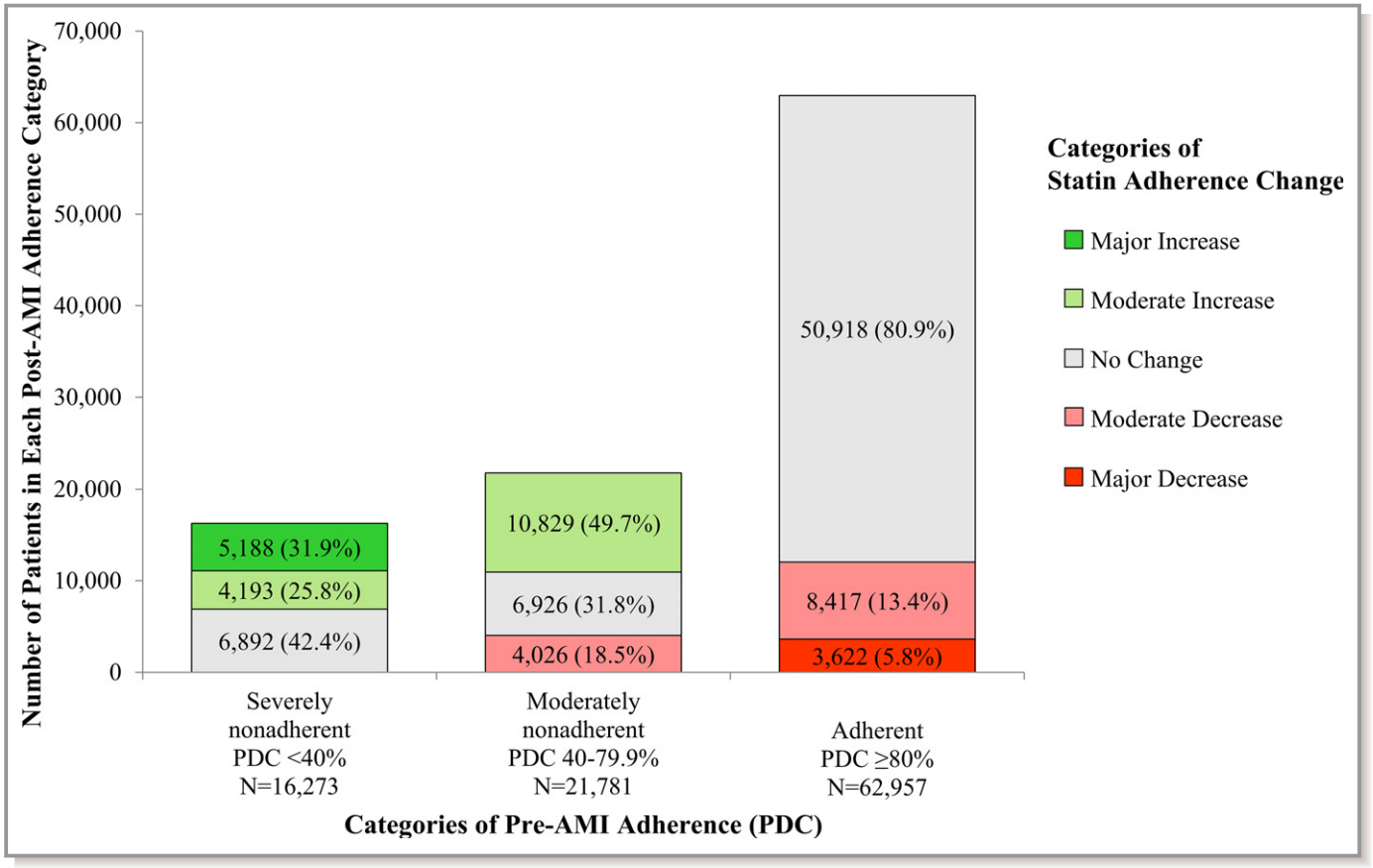


Figure 3. Distribution of categorical statin adherence change stratified by pre-AMI statin adherence. Percentages were calculated for each pre-AMI statin adherence category separately. AMI indicates acute myocardial infarction; PDC, proportion of days covered.

Survival Curves by Post-AMI Statin Adherence

The direct adjusted survival curves for all-cause mortality stratified by *post-AMI* statin adherence (Figure 4A) showed a dose–response-type relationship; patients who were severely nonadherent to statin therapy had the lowest probability of survival (12-month survival 0.853 [95% CI: 0.847–0.859]), while patients who were adherent had the highest probability of survival (12-month survival 0.879 [0.876–0.882]).

Survival Curves by Statin Adherence Change

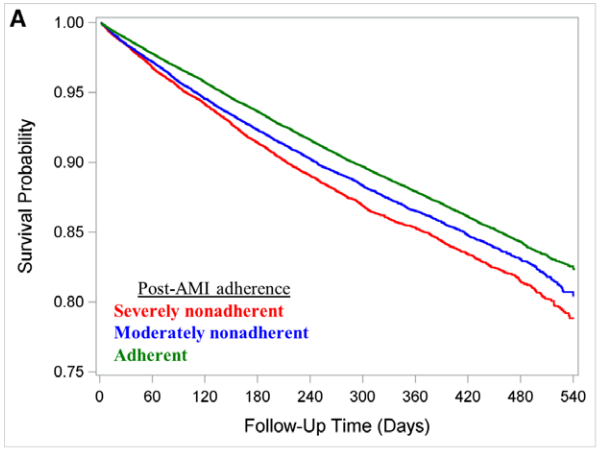
In Figure 4B, direct adjusted survival curves were further stratified by pre-AMI adherence to give 9 strata representing all categorical *changes in statin adherence*. Compared with patients who were always severely nonadherent (dotted red line; 12-month survival 0.864 [95% CI: 0.856–0.872]), patients with *decreases in statin adherence* (solid red, dashed red, and solid blue lines) tended to have similar or lower survival probabilities (12-month estimates ranged from 0.852 [95% CI: 0.841–0.862] to 0.857 [95% CI: 0.849–0.864]). Compared with patients who were always adherent (solid green line; 12-month survival 0.876 [95% CI: 0.873–0.879]), patients with *increases in statin adherence* (dotted green, dashed green, and dotted blue lines) tended to have similar or slightly higher survival probabilities (12-month estimates ranged from 0.876 [95% CI: 0.865–0.872] to 0.884 [95% CI: 0.874–0.894]). See Figure S1 for the unadjusted survival curves.

Association Between Post-AMI Statin Adherence and All-Cause Mortality

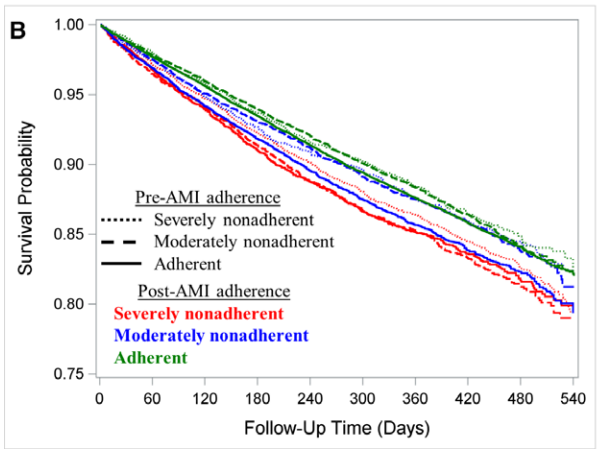
When assessing the association between *post-AMI statin adherence* and all-cause mortality, patients who were adherent *post-AMI* were less likely to die compared with patients who were severely nonadherent (hazard ratio [HR] 0.79; 95% CI: 0.74–0.83). Patients who were moderately nonadherent *post-AMI* were also less likely to die compared with patients who were severely nonadherent but to a lesser degree (HR 0.89; 95% CI: 0.84–0.95), consistent with a dose–response-type relationship. See Table S2 for full model results.

Association Between Statin Adherence Change and All-Cause Mortality

In the final multivariable model, the association between statin adherence *change* (9 groups) and all-cause mortality



Post-AMI statin adherence	12-month* survival probability (95% confidence interval)
Severely nonadherent	0.853 (0.847-0.859)
Moderately nonadherent	0.865 (0.860-0.870)
Adherent	0.879 (0.876-0.882)



Pre-AMI statin adherence	Post-AMI statin adherence	12-month* survival probability (95% confidence interval)
Severely nonadherent	Severely nonadherent	0.864 (0.856-0.872)
Moderately nonadherent		0.852 (0.842-0.862)
Adherent		0.852 (0.841-0.862)
Severely nonadherent	Moderately nonadherent	0.876 (0.865-0.886)
Moderately nonadherent		0.875 (0.867-0.883)
Adherent		0.857 (0.849-0.864)
Severely nonadherent	Adherent	0.884 (0.874-0.894)
Moderately nonadherent		0.883 (0.877-0.890)
Adherent		0.876 (0.873-0.879)

Figure 4. Direct adjusted survival curves for all-cause mortality after AMI, stratified by statin adherence. Adjusted for sociodemographics, baseline clinical conditions and medication use, whether the patient was a new user of statins (initiated statin within the 180 days pre-index AMI), index hospitalization events, postdischarge clinical events and medication use, and changes in statin doses. Adjustment for medication use was accomplished by including a binary indicator variable for each of the following medication classes: (1) ACE inhibitor/ARB, (2) β-blocker, (3) $P2Y_{12}$ inhibitor, (4) calcium channel blocker, and (5) aldosterone receptor antagonist; a patient was classified as using a medication in the pre-AMI period if they had at least 1 prescription claim in the 180 days before the index AMI and were classified as using a medication in the post-AMI period if they had at least 1 prescription claim for the medication during the index AMI or within 180 days after discharge. Follow-up begins 6 months after index AMI discharge (ie, Day 0 is 180 days after index AMI discharge). **A**, Stratified by *post-AMI* statin adherence. **B**, Stratified by *change* in statin adherence from pre- to post-AMI. *12-month estimate calculated from 6 months post-AMI discharge through 18 months post-AMI discharge. ACE indicates angiotensin-converting enzyme; AMI, acute myocardial infarction; ARB, angiotensin II receptor blocker.

was estimated (Figure 5). Compared with patients who were severely nonadherent both *pre-* and *post-AMI*, patients with decreases in statin adherence tended to have a higher risk of all-cause mortality: a HR of 1.11 (95% CI: 1.01–1.22) for patients with a *moderate decrease* in statin adherence from moderately nonadherent to severely nonadherent and a HR of 1.09 (95% CI: 0.99–1.20) for patients with a *major decrease* in statin adherence. Patients with a *moderate decrease* from adherent to moderately nonadherent had a similar risk of all-cause mortality compared with patients who were always severely nonadherent (HR 1.04; 95% CI: 0.96–1.13). Patients with *moderate* or *major increases* in statin adherence (HRs ranging from 0.83 [95% CI: 0.75–0.92] to 0.89 [95% CI: 0.80–0.99]) had similar risks of all-cause mortality as patients who were consistently adherent both *pre-* and *post-AMI* (HR 0.88; 95% CI: 0.82–0.94). See Table S3 for full model results. Schoenfeld residuals for statin adherence change were consistent with the proportional hazards assumption (Figure S2).

Sensitivity Analyses

When iteratively adding covariates to the model based on the timing of covariate measurement (Table S4), some estimates differed from the fully adjusted model but were still on the same side of the null; most crude estimates were further from

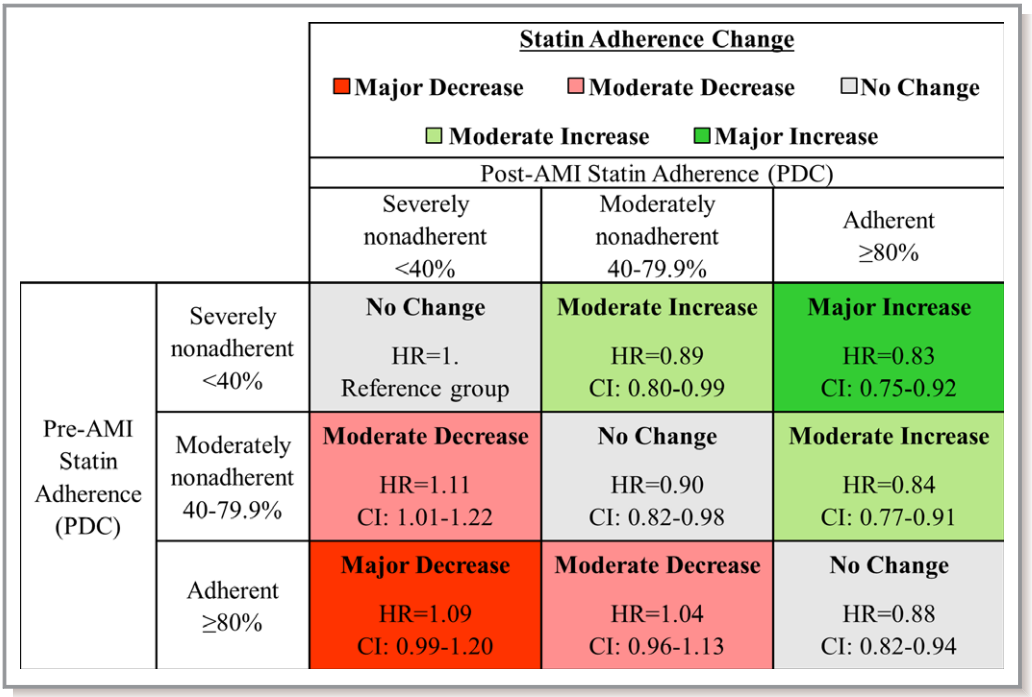


Figure 5. All-cause mortality adjusted hazard ratios (HRs) and 95% CIs by changes in statin adherence. Multivariable Cox proportional hazards model adjusted for sociodemographics, baseline clinical conditions and medication use, whether the patient was a new user of statins (initiated statin within the 180 days pre-index AMI), index hospitalization events, postdischarge follow-up, changes in statin doses, use of other secondary prevention medications, and AMI and stroke events that occurred within 180 days after index hospital discharge. Adjustment for medication use was accomplished by including a binary indicator variable for each of the following medication classes: (1) ACE inhibitor/ARB, (2) β-blocker, (3) $P2Y_{12}$ inhibitor, (4) calcium channel blocker, and (5) aldosterone receptor antagonist; a patient was classified as using a medication in the pre-AMI period if they had at least 1 prescription claim in the 180 days before the index AMI and were classified as using a medication in the post-AMI period if they had at least 1 prescription claim for the medication during the index AMI or within 180 days after discharge. The coloring scheme is only used to illustrate direction of adherence change, not for interpreting HRs. See Table S3 for a full list of and description of adjustment variables, as well as results from the full model. AMI indicates acute myocardial infarction; HR, hazard ratio; PDC, proportion of days covered.

the null than the fully adjusted model, and adjusting for additional variables brought estimates closer to the null. Most other sensitivity analyses (Tables S5 and S6) were consistent with findings from the final model (Figure 5). Among the subgroup of patients who were also taking an ACE inhibitor or angiotensin II receptor blocker and a β-blocker pre-AMI (N=48 580), the association between statin adherence change and all-cause mortality, while adjusting for the change in adherence to these other medications, was mostly consistent with findings from the primary analysis (Table S7; the full model results for this sensitivity analysis can be seen in Table S8). The point estimate for statin adherence change from severely nonadherent to adherent was outside of the range from the primary analysis CIs; the 3 adherence change measures in this model were highly correlated and only 4% of the population was in this category of statin adherence change. All other findings from the "Fully adjusted model" sensitivity analysis in Table S7 were consistent with the final model (Figure 5).

Discussion

In our cohort of 101 011 older Medicare beneficiaries who were already taking a statin when hospitalized for an AMI, 20% had increased statin adherence, 16% had decreased adherence, and 14% were either severely or moderately nonadherent *pre-AMI* and did not change their adherence category *post-AMI*. Our study sheds light on the mortality risk associated with *changes in statin adherence* from before to after an AMI among older patients who were taking a statin before their AMI hospitalization. We found that patients with a categorical decrease in statin adherence had the greatest risk of all-cause mortality between 6 and 24 months after hospital discharge. The results from our study also show that patients

with increased statin adherence had a lower risk of all-cause mortality compared with patients who were always severely nonadherent; indeed, the most intriguing and important finding from our study suggests the risk of death among patients with increased statin adherence was comparable to the risk among patients who were continuously adherent during the study period, even if they only increased from severely nonadherent to moderately nonadherent.

While statin adherence change after an AMI has been previously studied,[5–7,9,10] to our best knowledge this is the first study that has investigated mortality outcomes associated with changes in statin adherence from pre- to post-AMI among patients who were already taking a statin. Our findings for the association between *post-AMI* adherence and mortality were consistent with a previous study, both in terms of magnitude and a dose–response-type relationship;[4] this 2007 study evaluating *post-AMI* medication adherence found that—compared with patients who were adherent to statin therapy—patients who were severely nonadherent or moderately nonadherent had a 25% or 12% increased risk of mortality, respectively.[4]

A possible reason why patients may become less adherent to statin therapy post-AMI aligns with the Sentinel Event Effect: a patient may believe that statin therapy is ineffective in preventing future events since an AMI occurred while taking a statin.[5,7,11,12] Also, many patients who were nonadherent to statins before their AMI did not improve their adherence after their AMI hospitalization; these patients may not understand the importance of improving their statin adherence. Contrary to these beliefs, our study found that patients with decreased statin adherence—even if they were adherent to statin therapy before their index AMI hospitalization—often had a higher risk of all-cause mortality compared with patients who were always severely nonadherent. Additionally, while patients with decreased adherence from adherent to severely nonadherent had a similar risk of mortality compared with patients who were always severely nonadherent, their risk of mortality was considerably higher than that of patients who remained adherent both pre- and post-AMI.

Therefore, our study provides evidence that (1) it is not too late to improve statin adherence *after an AMI* for patients who were taking a statin but were nonadherent to therapy *before their AMI*, and (2) continued adherence after an AMI is important among those patients who were previously adherent. Hospitalization for an AMI and clinician counseling about the need for adherence may act as a "wake-up call" to improve statin adherence to prevent further coronary events.[7,11–13] Given the significant number of patients without an improvement in statin adherence after an AMI, cardiologists and other providers should emphasize that *it is not too late to improve statin adherence* among patients who were nonadherent to statin therapy pre-AMI. Also, the consequence of decreasing statin adherence may be a clinically significant increase in the risk for post-AMI mortality: an important message for patients who were adherent to statin therapy pre-AMI. Statin therapy for both primary and secondary prevention has been shown to reduce the risk of future coronary events.[14–16] Therefore, experiencing an AMI despite being adherent should not necessarily be viewed as a failure of statin therapy. If patients classified as adherent pre-AMI had instead not taken their statin, they may have experienced an AMI even sooner. Our study also adjusted for within-patient changes in simvastatin-equivalent dosing, implying the importance of continued adherence or addressing nonadherence—independent of statin dose—even in patients who cannot tolerate high-intensity statins. Importantly, clinicians may need to probe and address patient perceptions of statin effectiveness after an AMI, even among patients who were previously adherent to statin therapy.

Furthermore, our study results suggest that—among patients who were taking a statin before an AMI—measuring statin adherence as a *change in adherence* may give us a better understanding of the association between statin adherence and mortality after an AMI. Clinical interventions addressing the need for *post-AMI statin adherence* among prevalent statin users that are tailored to patients after assessing their *pre-AMI statin adherence* may lead to better clinical outcomes after AMI hospitalizations. While an AMI hospitalization may serve as a teachable moment regarding the need for statin therapy (and patients are already interacting with providers), such an intervention may be more impactful if delivered during follow-up after hospital discharge.[7,17,18] Future research could investigate how to best deliver these interventions.

Our observation that patients with decreased statin adherence had a higher risk of mortality compared with patients who were always severely nonadherent may reflect residual confounding. For example, sicker patients who have previously experienced a coronary event, or with high-risk comorbidities such as diabetes mellitus, may have been more adherent to statins in the pre-AMI period. Another potential reason that some patients experience an AMI despite being adherent is less responsiveness to the therapeutic effect of statins. A third potential reason is that *statin adherence change* may be a proxy for other health behavior changes (including changes in adherence to other secondary prevention medications, eg, ACE inhibitors/angiotensin II receptor blockers, and β-blockers) that may also be associated with outcomes after an AMI. For example, factors associated with greater AMI severity (eg, requiring a coronary stent or coronary artery bypass surgery) have been previously associated with both increases in statin adherence and smoking cessation,[5,19] both of which may affect mortality outcomes. Future research could investigate these hypotheses further.

Limitations

Our study has some limitations. First, residual confounding bias from unmeasured confounders and covariate misclassification error are possible in this quasi-experimental observational study. We analyzed the change in medication adherence before and after an AMI, which may serve as a self-control to mitigate this limitation. As previously mentioned, statin adherence change may also be a proxy for other health behavior changes that are unmeasured in administrative claims data; therefore, our results may be partially explained by other behavior changes, including adherence changes to other secondary prevention medications that were correlated with statin adherence change. This may bias the association between statin adherence change and mortality away from the null. However, patients who were always severely nonadherent or always adherent could not have decreases or increases in adherence, respectively, even though they may have changed other health behaviors. Additionally, the high correlation between statin adherence change and other health behavior changes increased the likelihood of multicollinearity; this would reduce our ability to interpret point estimates independent of these other behavior change variables if they were included in a regression model. The direction and magnitude of these biases is therefore difficult to assess, but our results were consistent across several sensitivity analyses.

Second, using administrative prescription claims data may lead to an overestimation of medication adherence because there is no information available about whether the patient actually took the medication. However, prescription claims records have good validity and correlation with other adherence measures[20–22] and clinical outcomes.[4] We applied standard algorithms in using prescription claims to measure adherence to mitigate this limitation. Prescription claims data may also underestimate adherence if prescriptions are paid for outside of a patient's Medicare Part D plan. However, this is not common for Medicare beneficiaries, and these claims are often adjudicated through Part D when they do occur.[23–25] Medicare patients are also less likely than privately insured patients to use medication samples.[26] Our results were consistent with a dose–response-type association with *post-AMI* statin adherence[4] and robust to a more conservative measure of categorical adherence change.[5,7]

Finally, our study includes both patients who were recently initiated on statin therapy before their index AMI and patients who had been taking statins for at least a year. Therefore, our study may be susceptible to a healthy user selection bias and time-varying hazards.[27,28] However, in our sensitivity analyses, the findings were consistent when excluding "new users" and when excluding patients who may have discontinued statin therapy before their index AMI. Patients with primary nonadherence to statins[29] and patients who discontinued statin therapy more than 1 year before experiencing an AMI were not included in this study. However, a body of work has already explored discontinuing statin therapy because of intolerance and re-initiation of statin therapy.[13,30–33]

Conclusions

Even after an AMI, it is not too late to improve statin adherence. Patients who increased their statin adherence from before to after an AMI had a similar risk of all-cause mortality as patients who were consistently adherent. However, continued adherence is also important because patients who decreased their statin adherence tended to have worse outcomes than patients who were always nonadherent. Among patients who were already taking a statin, counseling about the need for statin therapy after an AMI that is tailored to the patient's previous experience with the medication may increase the likelihood of positive adherence change and better clinical outcomes.

Sources of Funding

This research was supported in part by the US NIH National Institute on Aging grants 1R01AG046267-01A1 & 1R21AG043668-01A1 (principal investigator: Fang). Dr Hickson was supported by the US NIH National Heart, Lung, and Blood Institute through a National Research Service Award (NRSA) training grant (4T32HL007055-41) as a postdoctoral research fellow with the Cardiovascular Disease Epidemiology Program at The University of North Carolina at Chapel Hill. Dr Hickson was also supported by the American Foundation for Pharmaceutical Education (AFPE) as the 2018 Pre-Doctoral Fellow in Health Outcome Disparities.

Disclosures

Dr Robinson worked on grants from Acasti, Amarin, Amgen, Astra-Zeneca, Esai, Esperion, Merck, Novo-Nordisk, Regeneron, Sanofi, and Takeda. Dr Robinson was a consultant for Amgen, Merck, Novartis, Novo-Nordisk, Pfizer, Regeneron, and Sanofi. The authors have no other disclosures.

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SUPPLEMENTAL MATERIAL

Supplemental Tables

Table S1. Patient characteristics for the full cohort and stratified by change in statin adherence after AMI.

Table S2. Full model results for the association between all-cause mortality and **post-AMI** statin adherence, while adjusting for *pre-AMI* statin adherence.

Table S3. Full model results for the association between all-cause mortality and change in statin adherence after acute myocardial infarction (AMI).

Table S4. Crude estimates and models adjusted iteratively based on the timing of covariate measurement for the association between all-cause mortality and change in statin adherence after acute myocardial infarction (AMI).

Table S5. Sensitivity analyses involving changing variable definitions or adding new variables to the model estimating the association between all-cause mortality and change in statin adherence after acute myocardial infarction (AMI).

Table S6. Sensitivity analyses with restricted study eligibility estimating the association between all-cause mortality and change in statin adherence after acute myocardial infarction (AMI).

Table S7. Association between all-cause mortality and change in statin adherence, adjusted for changes in ACE/ARB and beta-blocker adherence, among the subgroup of prevalent users for all 3 medication classes: models adjusted iteratively based on the timing of covariate measurement and comparison to final model from manuscript.

Table S8. Full model results for the association between all-cause mortality and change in statin adherence after acute myocardial infarction, adjusted for changes in ACE/ARB and beta-blocker adherence, among the subgroup of prevalent users for all 3 medication classes (N=48,580).

Supplemental Figures

Figure S1. Unadjusted survival curves and 95% confidence bands for all-cause mortality after acute myocardial infarction, stratified by statin adherence.

Figure S2. Schoenfeld residuals (dots) with smooth fitted spline (line) for statin adherence change.

Table S1. Patient characteristics for the full cohort and stratified by change in statin adherence after AMI.

		Pre-AMI statin adherence								
		Severely nonadherent			Moderately nonadherent			Adherent		
		Post-AMI statin adherence			**Post-AMI statin adherence**			**Post-AMI statin adherence**		
	Full cohort	Sev NA	Mod NA	Adh	Sev NA	Mod NA	Adh	Sev NA	Mod NA	Adh
	N=101,011	n=6,892	n=4,193	n=5,188	n=4,026	n=6,926	n=10,829	n=3,622	n=8,417	n=50,918
Patient characteristics	n (%)	%	%	%	%	%	%	%	%	%
Sociodemographics										
Age										
66-75	47,128 (46.7)	48.1	52.7	51.8	45.7	49.9	49.3	43.7	44.3	45.1
76-85	39,698 (39.3)	37.7	36.6	37.1	40.1	38.1	38.6	39.8	40.2	40.0
86+	14,185 (14.0)	14.1	10.7*	11.1	14.3	12.1	12.1	16.5	15.5	14.9
Female	54,886 (54.3)	55.8	55.1	56.1	54.6	55.6	56.1	56.2	54.7	53.1
Race/ethnicity										
White	85,318 (84.5)	81.6	78.3	79.7	81.4	80.7	82.1	84.5	84.9	87.0*
Black	8,495 (8.4)	11.8	13.0	11.4	11.2	11.8	9.6	8.5*	7.9*	6.4*
Hispanic	3,001 (3.0)	3.3	4.2	4.2	3.5	3.5	3.8	3.1	3.2	2.4
Asian	2,227 (2.2)	1.7	2.4	2.5	1.7	1.8	2.4	1.9	2.0	2.3
Other	1,970 (2.0)	1.6	2.1	2.2	2.2	2.3	2.0	2.0	2.1	1.8
Dual eligibility[†]	24,723 (24.5)	22.5	25.8	28.3*	22.0	23.1	26.2	24.9	22.7	24.5
Household income[‡]										
≤$30,000	47,442 (47.0)	49.1	50.2	49.2	48.8	47.2	47.2	48.1	46.7	45.9
$30,001-60,000	41,801 (41.4)	40.9	39.0	39.7	40.4	41.2	40.9	40.6	41.3	42.1
$60,001-100,000	9,467 (9.4)	8.2	9.0	9.0	8.9	9.5	9.4	9.2	9.5	9.6
$100,001-150,000	1,760 (1.7)	1.4	1.3	1.6	1.5	1.6	1.8	1.7	2.0	1.8
>$150,000	541 (0.5)	0.5	0.4	0.5	0.4	0.5	0.7	0.5	0.5	0.6
Pre-AMI comorbidities and cardiovascular procedures[§]										
Adjusted Charlson comorbidity index[‖]										
0	21,946 (21.7)	18.0	22.9*	26.7*	18.6	21.2	23.8*	18.8	19.6	22.1*
1-2	40,745 (40.3)	39.4	39.6	42.3	38.9	41.0	40.9	38.2	39.0	40.6
3-5	29,876 (29.6)	32.3	29.9	24.2*	31.7	29.2	27.9	32.4	32.2	29.3
6-8	7,102 (7.0)	8.4	6.4	5.8*	9.1	7.3	6.1	9.0	7.7	6.8
9+	1,342 (1.3)	1.9	1.2	1.1	1.8	1.2	1.3	1.6	1.6	1.2

Patient characteristics	Full cohort N=101,011 n (%)	*Pre-AMI statin adherence* Severely nonadherent Post-AMI statin adherence Sev NA n=6,892 %	Mod NA n=4,193 %	Adh n=5,188 %	Moderately nonadherent Post-AMI statin adherence Sev NA n=4,026 %	Mod NA n=6,926 %	Adh n=10,829 %	Adherent Post-AMI statin adherence Sev NA n=3,622 %	Mod NA n=8,417 %	Adh n=50,918 %
Baseline comorbidities and procedures										
Prior AMI[#]	4,288 (4.2)	6.0	4.6	3.3*	5.4	4.1	3.6*	5.7	4.5	4.0
Dementia/Alzheimer's**	9,396 (9.3)	10.6	8.7	8.1	10.3	9.3	9.3	13.2	10.4	8.8
Depression	15,207 (15.1)	16.2	15.0	14.6	17.2	15.8	14.9	17.9	16.4	14.3
CABG	1,064 (1.1)	1.0	0.9	0.9	1.2	0.9	1.2	1.4	1.2	1.0
PTCA/stent	6,748 (6.7)	8.6	6.4	5.2*	8.2	7.3	5.9*	7.7	7.0	6.4
Ischemic heart disease	60,303 (59.7)	65.3	58.4*	47.1*	65.9	61.4	56.3*	62.7	62.6	59.6*
Unstable angina	5,401 (5.3)	6.6	5.1	4.3	6.6	5.8	4.5	5.6	5.7	5.2
Lipid abnormalities****	90,639 (89.7)	88.5	87.9	87.0	90.0	90.4	90.1	88.9	90.7	90.1
Rhabdomyolysis/myopathy	6,570 (6.5)	8.8	7.8	6.7	8.3	6.6	6.5	7.0	7.2	5.7*
Pre-AMI medications										
New user of statin[††]	10,220 (10.1)	9.8	7.1	7.5	20.8*	11.4	9.6	24.4*	14.9*	8.0
Concurrent medications[‡‡]										
ACE inhibitor/ARB	65,524 (64.9)	55.8	57.9	57.3	63.1*	64.8*	64.6*	64.5*	66.7*	67.4*
Beta-blocker	63,437 (62.8)	57.2	54.8	50.8*	62.2*	62.9*	60.1	62.9*	64.1*	65.8*
$P2Y_{12}$ inhibitor	31,546 (31.2)	31.8	27.7	22.5*	35.2	32.7	29.1	33.4	33.1	31.8
Calcium channel blocker	35,730 (35.4)	31.3	31.5	32.4	34.1	34.1	36.1*	35.1	36.2*	36.5*
Aldosterone antagonist	5,002 (5.0)	4.9	4.3	3.9	5.8	4.8	4.6	5.2	5.3	5.1
Characteristics of index AMI hospitalization										
Clinical diagnoses and procedures										
Subendocardial infarction[§§]	79,978 (79.2)	81.3	77.7	72.2*	80.8	79.2	76.6*	80.5	81.0	79.7
CABG	6,778 (6.7)	4.5	7.8*	9.5*	5.2	6.4	7.6*	6.2	6.1	6.7
PTCA/stent	39,479 (39.1)	35.1	42.2*	50.2*	32.2	39.0	43.9*	30.7	34.2	39.2
Antiplatelet use	4,627 (4.6)	4.6	5.0	5.5	4.0	4.7	5.0	3.5	3.9	4.6
Cardiac catheterization	61,062 (60.5)	57.2	65.2*	70.5*	54.8	61.2	64.9*	52.4	56.5	60.1
Angiocardiography	61,122 (60.5)	57.3	64.6*	68.4*	55.1	61.3	64.7*	52.0*	56.2	60.5
Cardiogenic shock	2,150 (2.1)	1.4	1.9	2.8	2.1	2.0	2.6	2.0	2.2	2.1
Cardiac dysrhythmia	31,326 (31.0)	31.3	29.5	29.0	30.4	29.6	29.4	31.8	32.0	31.7

		Pre-AMI statin adherence								
		Severely nonadherent			Moderately nonadherent			Adherent		
		Post-AMI statin adherence			**Post-AMI statin adherence**			**Post-AMI statin adherence**		
	Full cohort	Sev NA	Mod NA	Adh	Sev NA	Mod NA	Adh	Sev NA	Mod NA	Adh
	N=101,011	n=6,892	n=4,193	n=5,188	n=4,026	n=6,926	n=10,829	n=3,622	n=8,417	n=50,918
Patient characteristics	n (%)	%	%	%	%	%	%	%	%	%
Hypotension	4,999 (4.9)	4.7	4.5	5.0	5.1	4.7	5.3	4.8	5.0	5.0
Acute renal failure	14,774 (14.6)	14.3	13.7	13.3	15.7	14.4	13.9	17.4	16.5	14.5
Heart failure	38,222 (37.8)	38.8	35.3	33.7*	40.6	36.6	36.5	43.5	39.8	37.9
Duration of hospitalization (days)										
1-3	46,047 (45.6)	45.6	46.4	45.8	43.0	47.4	46.5	38.4*	43.4	46.1
4-6	30,966 (30.7)	31.9	30.3	29.8	31.5	30.1	30.2	31.2	31.0	30.6
7-11	16,714 (16.5)	15.7	16.1	16.6	17.6	15.6	15.8	19.9*	17.7	16.5
12+	7,284 (7.2)	6.8	7.2	7.8	7.9	6.9	7.5	10.5*	8.0	6.8
Admission to intensive care										
None	25,146 (24.9)	26.1	23.6	20.6*	26.4	25.2	23.9	24.2	24.8	25.4
Coronary care unit only	23,706 (23.5)	23.4	24.7	25.9	22.1	23.5	24.3	22.1	23.0	23.2
Intensive care unit only	41,551 (41.1)	41.0	40.7	41.0	41.1	40.8	40.4	43.1	42.0	41.1
Both	10,608 (10.5)	9.4	11.0	12.5	10.4	10.6	11.4	10.5	10.2	10.3
Cardiologist consultation	87,858 (87.0)	85.7	87.2	89.3*	85.2	87.7	87.6	85.9	86.4	87.0
30-day post-AMI follow-up										
None	14,873 (14.7)	18.4	16.0	14.1*	17.9	16.2	13.9*	14.6*	14.4*	14.0*
Primary care provider[‖‖] only	29,301 (29.0)	31.3	28.9	26.0*	30.2	29.6	28.1	32.4	29.3	28.7
Cardiologist only	19,161 (19.0)	17.4	19.9	19.7	18.0	19.4	19.8	15.6	17.9	19.3
Both	37,676 (37.3)	32.9	35.2	40.2*	33.9	34.9	38.2*	37.3	38.4*	38.0*
Post-AMI medications										
Change in simvastatin-equivalent ADD[##] (mean ± std)	4.4 ± 33.2	-20.1 ± 42.4	7.5 ± 37.4*	13.2 ± 40.5*	-16.5 ± 40.1	4.4 ± 28.6*	10.8 ± 33.0*	-17.7 ± 38.8	3.2 ± 28.2*	8.6 ± 27.7*
Concurrent medications***										
ACE inhibitor/ARB	72,011 (71.3)	61.4	71.9*	75.7*	63.2	70.7*	73.9*	61.8	69.1*	73.3*
Beta-blocker	87,887 (87.0)	77.1	86.5*	90.1*	78.7	85.9*	89.5*	80.1	85.6*	89.1*
$P2Y_{12}$ inhibitor	66,607 (65.9)	58.2	68.4*	74.0*	57.3	66.1*	69.8*	55.7	63.0	67.0*
Calcium channel blocker	32,162 (31.8)	30.5	31.6	29.6	29.8	31.5	31.6	28.6	32.5	32.6
Aldosterone antagonist	8,689 (8.6)	8.5	8.0	8.6	9.0	8.5	8.3	9.4	9.4	8.5

		Pre-AMI statin adherence								
		Severely nonadherent			Moderately nonadherent			Adherent		
		Post-AMI statin adherence			**Post-AMI statin adherence**			**Post-AMI statin adherence**		
	Full cohort	Sev NA	Mod NA	Adh	Sev NA	Mod NA	Adh	Sev NA	Mod NA	Adh
	N=101,011	n=6,892	n=4,193	n=5,188	n=4,026	n=6,926	n=10,829	n=3,622	n=8,417	n=50,918
Patient characteristics	n (%)	%	%	%	%	%	%	%	%	%
Post-AMI clinical events										
Recurrent AMI†††	6,386 (6.3)	7.1	6.9	5.8	6.5	6.7	5.9	6.5	7.8	6.0
Stroke‡‡‡	972 (1.0)	1.2	1.1	1.0	1.3	1.0	0.7	1.3	1.5	0.8
Statin intensity§§§										
Pre-AMIǁǁǁ										
Low intensity	10,851 (10.7)	12.3	8.7*	12.7	10.0	7.7*	10.8	11.6	10.0	11.0
Moderate intensity	68,527 (67.8)	66.3	65.1	69.1	66.3	64.8	68.6	68.3	67.2	68.6
High intensity	21,633 (21.4)	21.4	26.2*	18.2	23.7	27.5*	20.6	20.0	22.8	20.4
Post-AMI###										
Low intensity	8,256 (8.2)	10.8	6.2*	7.2*	9.7	6.3*	7.4*	10.4	8.6	8.1
Moderate intensity	64,773 (64.1)	65.5	60.7*	63.9	65.0	61.9	62.5	67.3	64.5	64.5
High intensity	27,982 (27.7)	23.7	33.1*	28.9*	25.3	31.8*	30.0*	22.3	26.9	27.3

Percentages are column percents. Statin adherence was measured separately in the 6 months pre-AMI and the 6 months post-AMI. Adherence was categorized as follows: severely nonadherent (PDC <40%), moderately nonadherent (PDC 40-79.9%), and adherent (PDC ≥80%). For absolute standardized difference calculations, all statin adherence change groups are compared to the group who was severely nonadherent both pre- and post-AMI.

* Absolute standardized difference ≥10% compared to the reference group (severely nonadherent both pre- and post-AMI).

† Enrolled in Medicare and Medicaid.

‡ Median household income of US Census block groups for individuals aged 65 and older.

§ Measured in the 12 months prior to the index AMI hospital admission date.

ǁ CCI score does not include counts for AMI and dementia.

CCI definition.

** Medicare Chronic Conditions Data Warehouse definition.

†† First prescription claim for a statin was identified during the 6 months prior to the index AMI hospital admission date.

‡‡ At least one prescription fill within medication class during the 6 months prior to the index AMI hospital admission date.

§§ Index AMI had diagnosis code for subendocardial infarction, compared to transmural infarction.

ǁǁ Primary care physician, physician assistant, or nurse practitioner.

		Pre-AMI statin adherence								
		Severely nonadherent			Moderately nonadherent			Adherent		
		Post-AMI statin adherence			**Post-AMI statin adherence**			**Post-AMI statin adherence**		
	Full cohort	Sev NA	Mod NA	Adh	Sev NA	Mod NA	Adh	Sev NA	Mod NA	Adh
	N=101,011	n=6,892	n=4,193	n=5,188	n=4,026	n=6,926	n=10,829	n=3,622	n=8,417	n=50,918
Patient characteristics	n (%)	%	%	%	%	%	%	%	%	%

Continuous weighted average of the simvastatin-equivalent average daily dose in the post-AMI period minus the weighted average in the pre-AMI period. Dose equivalency calculations were made as follows: fluvastatin, pravastatin, and lovastatin doses in mg were divided by 4, 2, and 2, respectively; atorvastatin, rosuvastatin, and pitavastatin doses were multiplied by 2, 4, and 10, respectively.

*** At least one prescription fill within medication class during the index AMI hospitalization period or within 6 months after index AMI discharge date.

††† Inpatient ICD-9 diagnosis code of 410.x1 in the primary or secondary discharge field within 6 months after index AMI discharge date.

‡‡‡ Inpatient ICD-9 diagnosis code of 430, 431, 433.x1, 434.x1, or 436 in the primary discharge field within 6 months after index AMI discharge date.

§§§ According to the 2013 American College of Cardiology/ American Heart Association guidelines on the reduction of atherosclerotic cardiovascular risk.

‖‖‖ Intensity of the last statin prescription fill before the index AMI.

Intensity of the first statin prescription fill after the index AMI.

**** Inpatient or outpatient ICD-9 diagnosis code of 272.xx in any position.

Abbreviations: ACE, angiotensin-converting enzyme; ADD, average daily dose; Adh, Adherent; AMI, acute myocardial infarction; ARB, angiotensin II receptor blocker; CABG, coronary artery bypass surgery; CCI, Charlson comorbidity index; ICD-9, International Classification of Diseases, Ninth Revision; Mod NA, moderately nonadherent; PDC, proportion of days covered; PTCA, percutaneous transluminal coronary angioplasty; Sev NA, severely nonadherent; std, standard deviation.

Table S2. Full model results for the association between all-cause mortality and **post-AMI** statin adherence, while adjusting for *pre-AMI* statin adherence.

Patient characteristics	**HR (95% CI)**
Post-AMI statin adherence*	
Severely nonadherent	1.
Moderately nonadherent	0.89 (0.84, 0.95)
Adherent	0.79 (0.74, 0.83)
*Pre-AMI statin adherence**	
Severely nonadherent	1.
Moderately nonadherent	1.05 (0.99, 1.11)
Adherent	1.11 (1.05, 1.17)
Sociodemographics	
Age	
66-75	1.
76-85	1.34 (1.28, 1.39)
86+	1.94 (1.85, 2.04)
Female	0.83 (0.80, 0.86)
Race/ethnicity	
White	1.
Black	0.90 (0.85, 0.96)
Hispanic	0.86 (0.78, 0.95)
Asian	0.83 (0.73, 0.93)
Other	0.85 (0.75, 0.97)
Dual eligibility[†]	1.12 (1.08, 1.17)
Household income[‡]	
≤$30,000	1.
$30,001-60,000	1.01 (0.98, 1.05)
$60,001-100,000	0.97 (0.91, 1.04)
$100,001-150,000	1.02 (0.89, 1.16)
>$150,000	0.95 (0.75, 1.20)
Pre-AMI comorbidities and cardiovascular procedures[§]	
Adjusted Charlson comorbidity index[‖]	
0	1.
1-2	1.48 (1.39, 1.58)
3-5	2.18 (2.05, 2.33)
6-8	2.79 (2.58, 3.02)
9+	5.04 (4.54, 5.60)
Baseline comorbidities and procedures	
Prior AMI[#]	1.14 (1.07, 1.22)
Dementia/Alzheimer's disease**	1.32 (1.25, 1.38)
Depression	1.07 (1.03, 1.12)
CABG	0.51 (0.41, 0.64)
PTCA/stent	0.81 (0.74, 0.87)
Ischemic heart disease	1.05 (1.01, 1.10)
Unstable angina	1.05 (0.98, 1.13)
Lipid abnormalities[§§§]	0.78 (0.74, 0.83)

Patient characteristics	HR (95% CI)
Rhabdomyolysis/myopathy	0.94 (0.88, 1.00)
Pre-AMI medications	
New user of statin[††]	0.90 (0.85, 0.95)
Concurrent medications[‡‡]	
ACE inhibitor/ARB	0.96 (0.92, 0.99)
Beta-blocker	1.07 (1.03, 1.12)
$P2Y_{12}$ inhibitor	1.08 (1.03, 1.12)
Calcium channel blocker	1.07 (1.03, 1.12)
Aldosterone receptor antagonist	1.04 (0.97, 1.12)
Characteristics of index AMI hospitalization	
Clinical diagnoses and procedures	
Subendocardial infarction[§§]	1.10 (1.04, 1.15)
CABG	0.33 (0.29, 0.38)
PTCA/stent	0.78 (0.74, 0.83)
Antiplatelet use	0.89 (0.80, 0.99)
Cardiac catheterization	0.85 (0.79, 0.91)
Angiocardiography	0.81 (0.75, 0.87)
Cardiogenic shock	1.01 (0.89, 1.16)
Cardiac dysrhythmia	1.09 (1.05, 1.13)
Hypotension	0.98 (0.90, 1.06)
Acute renal failure	1.13 (1.08, 1.18)
Heart failure	1.50 (1.44, 1.55)
Duration of hospitalization (days)	
1-3	1.
4-6	1.14 (1.10, 1.19)
7-11	1.23 (1.17, 1.29)
12+	1.36 (1.27, 1.46)
Admission to intensive care	
None	1.
Coronary care unit only	0.97 (0.92, 1.02)
Intensive care unit only	0.99 (0.95, 1.03)
Both	0.93 (0.87, 1.00)
Cardiologist consultation	1.00 (0.95, 1.05)
30-day post-AMI follow-up	
None	1.
Primary care provider[‖‖] only	0.87 (0.83, 0.92)
Cardiologist only	0.75 (0.70, 0.80)
Both	0.81 (0.77, 0.86)
Post-AMI medications	
Change in simvastatin-equivalent average daily dose[##]	1.00 (1.00, 1.00)
Concurrent medications***	
ACE inhibitor/ARB	0.87 (0.83, 0.90)
Beta-blocker	0.92 (0.88, 0.97)
$P2Y_{12}$ inhibitor	0.93 (0.89, 0.97)
Calcium channel blocker	0.89 (0.85, 0.93)
Aldosterone receptor antagonist	1.26 (1.19, 1.33)

Patient characteristics	**HR (95% CI)**
Post-AMI clinical events	
Hospitalization for recurrent AMI†††	1.96 (1.86, 2.06)
Hospitalization for stroke‡‡‡	1.82 (1.61, 2.06)

These are the results for the fully adjusted Cox proportional hazards model to estimate the association between all-cause mortality and **post-AMI** statin adherence, while adjusting for *pre-AMI* statin adherence.

* Statin adherence was measured separately in the 6 months pre-AMI and the 6 months post-AMI. Adherence was categorized as follows: severely nonadherent (PDC <40%), moderately nonadherent (PDC 40-79.9%), and adherent (PDC ≥80%).

† Enrolled in Medicare and Medicaid.

‡ Median household income of US Census block groups for individuals aged 65 and older.

§ Measured in the 12 months prior to the index AMI hospital admission date.

‖ CCI score does not include counts for AMI and dementia.

CCI definition.

** Medicare Chronic Conditions Data Warehouse definition.

†† First prescription claim for a statin was identified during the 6 months prior to the index AMI hospital admission date.

‡‡ At least one prescription fill within medication class during the 6 months prior to the index AMI hospital admission date.

§§ Index AMI had diagnosis code for subendocardial infarction, compared to transmural infarction.

‖‖ Primary care physician, physician assistant, or nurse practitioner.

Continuous weighted average of the simvastatin-equivalent average daily dose in the post-AMI period minus the weighted average in the pre-AMI period. Dose equivalency calculations were made as follows: fluvastatin, pravastatin, and lovastatin doses in mg were divided by 4, 2, and 2, respectively; atorvastatin, rosuvastatin, and pitavastatin doses were multiplied by 2, 4, and 10, respectively.

*** At least one prescription fill within medication class during the index AMI hospitalization period or within 6 months after index AMI discharge date.

††† Inpatient ICD-9 diagnosis code of 410.x1 in the primary or secondary discharge field within 6 months after index AMI discharge date.

‡‡‡ Inpatient ICD-9 diagnosis code of 430, 431, 433.x1, 434.x1, or 436 in the primary discharge field within 6 months after index AMI discharge date.

§§§ Inpatient or outpatient ICD-9 diagnosis code of 272.xx in any position.

Abbreviations: ACE, angiotensin-converting enzyme; AMI, acute myocardial infarction; ARB, angiotensin II receptor blocker; CABG, coronary artery bypass surgery; CCI, Charlson comorbidity index; CI, confidence interval; HR, hazard ratio; ICD-9, International Classification of Diseases, Ninth Revision; PDC, proportion of days covered; PTCA, percutaneous transluminal coronary angioplasty.

Table S3. Full model results for the association between all-cause mortality and change in statin adherence after acute myocardial infarction (AMI).

Patient characteristics		**HR (95% CI)**
Statin adherence change*		
Pre-AMI adherence	**Post-AMI adherence**	
Severely nonadherent	Severely nonadherent	1.
	Moderately nonadherent	0.89 (0.80, 0.99)
	Adherent	0.83 (0.75, 0.92)
Moderately nonadherent	Severely nonadherent	1.11 (1.01, 1.22)
	Moderately nonadherent	0.90 (0.82, 0.98)
	Adherent	0.84 (0.77, 0.91)
Adherent	Severely nonadherent	1.09 (0.99, 1.20)
	Moderately nonadherent	1.04 (0.96, 1.13)
	Adherent	0.88 (0.82, 0.94)
Sociodemographics		
Age		
66-75		1.
76-85		1.34 (1.28, 1.39)
86+		1.94 (1.84, 2.03)
Female		0.83 (0.80, 0.86)
Race/ethnicity		
White		1.
Black		0.90 (0.85, 0.96)
Hispanic		0.86 (0.78, 0.95)
Asian		0.83 (0.73, 0.93)
Other		0.85 (0.75, 0.97)
Dual eligibility†		1.12 (1.08, 1.17)
Household income‡		
≤$30,000		1.
$30,001-60,000		1.01 (0.98, 1.05)
$60,001-100,000		0.97 (0.91, 1.04)
$100,001-150,000		1.02 (0.89, 1.16)
>$150,000		0.95 (0.75, 1.20)
Pre-AMI comorbidities and cardiovascular procedures§		
Adjusted Charlson comorbidity indexǁ		
0		1.
1-2		1.48 (1.39, 1.58)
3-5		2.18 (2.05, 2.33)
6-8		2.79 (2.58, 3.02)
9+		5.04 (4.53, 5.59)
Baseline comorbidities and procedures		
Prior AMI#		1.14 (1.07, 1.22)
Dementia/Alzheimer's disease**		1.32 (1.25, 1.38)
Depression		1.07 (1.03, 1.12)
CABG		0.51 (0.41, 0.64)
PTCA/stent		0.81 (0.74, 0.87)
Ischemic heart disease		1.05 (1.01, 1.10)

Patient characteristics	HR (95% CI)
Unstable angina	1.05 (0.97, 1.13)
Lipid abnormalities§§§	0.78 (0.74, 0.83)
Rhabdomyolysis/myopathy	0.94 (0.88, 1.00)
Pre-AMI medications	
New user of statin††	0.90 (0.84, 0.95)
Concurrent medications‡‡	
ACE inhibitor/ARB	0.96 (0.92, 0.99)
Beta-blocker	1.07 (1.03, 1.12)
$P2Y_{12}$ inhibitor	1.08 (1.03, 1.12)
Calcium channel blocker	1.07 (1.03, 1.12)
Aldosterone receptor antagonist	1.04 (0.97, 1.12)
Characteristics of index AMI hospitalization	
Clinical diagnoses and procedures	
Subendocardial infarction§§	1.10 (1.04, 1.15)
CABG	0.33 (0.29, 0.38)
PTCA/stent	0.79 (0.74, 0.83)
Antiplatelet use	0.89 (0.80, 0.99)
Cardiac catheterization	0.85 (0.78, 0.91)
Angiocardiography	0.81 (0.75, 0.87)
Cardiogenic shock	1.01 (0.88, 1.16)
Cardiac dysrhythmia	1.09 (1.05, 1.13)
Hypotension	0.98 (0.90, 1.06)
Acute renal failure	1.13 (1.08, 1.18)
Heart failure	1.50 (1.44, 1.55)
Duration of hospitalization (days)	
1-3	1.
4-6	1.14 (1.10, 1.19)
7-11	1.23 (1.17, 1.29)
12+	1.36 (1.27, 1.46)
Admission to intensive care	
None	1.
Coronary care unit only	0.97 (0.92, 1.02)
Intensive care unit only	0.99 (0.95, 1.03)
Both	0.93 (0.87, 1.00)
Cardiologist consultation	1.00 (0.95, 1.05)
30-day post-AMI follow-up	
None	1.
Primary care providerǁǁ only	0.87 (0.83, 0.92)
Cardiologist only	0.75 (0.70, 0.80)
Both	0.81 (0.77, 0.86)
Post-AMI medications	
Change in simvastatin-equivalent average daily dose##	1.00 (1.00, 1.00)
Concurrent medications***	
ACE inhibitor/ARB	0.87 (0.83, 0.91)
Beta-blocker	0.92 (0.88, 0.97)
$P2Y_{12}$ inhibitor	0.93 (0.89, 0.97)
Calcium channel blocker	0.89 (0.85, 0.93)

Patient characteristics	HR (95% CI)
Aldosterone receptor antagonist	1.26 (1.19, 1.33)
Post-AMI clinical events	
Hospitalization for recurrent AMI†††	1.95 (1.86, 2.06)
Hospitalization for stroke‡‡‡	1.82 (1.61, 2.06)

These are the results for the fully adjusted Cox proportional hazards model also presented in Figure 5 within the manuscript. The purpose of this model was to estimate the association between all-cause mortality and change in statin adherence.

* Statin adherence was measured separately in the 6 months pre-AMI and the 6 months post-AMI. Adherence was categorized as follows: severely nonadherent (PDC <40%), moderately nonadherent (PDC 40-79.9%), and adherent (PDC ≥80%). Change in statin adherence was defined as a categorical change in statin adherence.

† Enrolled in Medicare and Medicaid.

‡ Median household income of US Census block groups for individuals aged 65 and older.

§ Measured in the 12 months prior to the index AMI hospital admission date.

‖ CCI score does not include counts for AMI and dementia.

CCI definition.

** Medicare Chronic Conditions Data Warehouse definition.

†† First prescription claim for a statin was identified during the 6 months prior to the index AMI hospital admission date.

‡‡ At least one prescription fill within medication class during the 6 months prior to the index AMI hospital admission date.

§§ Index AMI had diagnosis code for subendocardial infarction, compared to transmural infarction.

‖‖ Primary care physician, physician assistant, or nurse practitioner.

Continuous weighted average of the simvastatin-equivalent average daily dose in the post-AMI period minus the weighted average in the pre-AMI period. Dose equivalency calculations were made as follows: fluvastatin, pravastatin, and lovastatin doses in mg were divided by 4, 2, and 2, respectively; atorvastatin, rosuvastatin, and pitavastatin doses were multiplied by 2, 4, and 10, respectively.

*** At least one prescription fill within medication class during the index AMI hospitalization period or within 6 months after index AMI discharge date.

††† Inpatient ICD-9 diagnosis code of 410.x1 in the primary or secondary discharge field within 6 months after index AMI discharge date.

‡‡‡ Inpatient ICD-9 diagnosis code of 430, 431, 433.x1, 434.x1, or 436 in the primary discharge field within 6 months after index AMI discharge date.

§§§ Inpatient or outpatient ICD-9 diagnosis code of 272.xx in any position.

Abbreviations: ACE, angiotensin-converting enzyme; AMI, acute myocardial infarction; ARB, angiotensin II receptor blocker; CABG, coronary artery bypass surgery; CCI, Charlson comorbidity index; CI, confidence interval; HR, hazard ratio; ICD-9, International Classification of Diseases, Ninth Revision; PDC, proportion of days covered; PTCA, percutaneous transluminal coronary angioplasty.

Table S4. Crude estimates and models adjusted iteratively based on the timing of covariate measurement for the association between all-cause mortality and change in statin adherence after acute myocardial infarction (AMI).

Statin adherence change after AMI		Crude estimates	Model adjusted for			
			Sociodem	Sociodem + Pre	Sociodem + Pre + Hosp	Fully adjusted model†
Pre-AMI adherence	**Post-AMI adherence**	HR (95% CI)				
Severely nonadherent	Severely nonadherent	1.	1.	1.	1.	1.
	Moderately nonadherent	0.69 (0.62, 0.77)*	0.72 (0.64, 0.80)*	0.77 (0.69, 0.85)*	0.82 (0.74, 0.91)	0.89 (0.80, 0.99)
	Adherent	0.58 (0.52, 0.64)*	0.59 (0.53, 0.66)*	0.67 (0.61, 0.75)*	0.75 (0.68, 0.84)	0.83 (0.75, 0.92)
Moderately nonadherent	Severely nonadherent	1.10 (1.00, 1.21)	1.10 (1.00, 1.21)	1.11 (1.01, 1.22)	1.09 (0.99, 1.20)	1.11 (1.01, 1.22)
	Moderately nonadherent	0.75 (0.69, 0.82)*	0.77 (0.71, 0.85)*	0.81 (0.74, 0.89)*	0.84 (0.77, 0.92)	0.90 (0.82, 0.98)
	Adherent	0.65 (0.60, 0.70)*	0.66 (0.61, 0.71)*	0.72 (0.66, 0.78)*	0.76 (0.70, 0.83)*	0.84 (0.77, 0.91)
Adherent	Severely nonadherent	1.18 (1.07, 1.30)	1.14 (1.03, 1.25)	1.14 (1.04, 1.25)	1.07 (0.97, 1.18)	1.09 (0.99, 1.20)
	Moderately nonadherent	1.00 (0.92, 1.08)	0.98 (0.90, 1.06)	1.00 (0.92, 1.08)	0.99 (0.92, 1.07)	1.04 (0.96, 1.13)
	Adherent	0.75 (0.71, 0.80)*	0.73 (0.69, 0.78)*	0.78 (0.73, 0.83)*	0.80 (0.75, 0.85)*	0.88 (0.82, 0.94)

Cox proportional hazards models. The first model on the left ("Crude estimates") is unadjusted for other covariates. Each model is then adjusted for an additional set of covariates based on when the variables were measured (sociodemographics, pre-AMI comorbidities/medications, characteristics of the index AMI hospitalization, and post-AMI follow-up/medications/stroke/recurrent AMI).

* Point estimate does not fall within the 95% confidence interval for the fully adjusted model.

† Fully adjusted model also presented in Figure 5 within the manuscript.

Abbreviations: AMI, acute myocardial infarction; CI, confidence interval; Hosp, measures from the index AMI hospitalization; HR, hazard ratio; Pre, pre-AMI measures; Sociodem, sociodemographic measures.

Table S5. Sensitivity analyses involving changing variable definitions or adding new variables to the model estimating the association between all-cause mortality and change in statin adherence after acute myocardial infarction (AMI).

Statin adherence change after AMI		Fully adjusted model*	Conservative adherence change measure†	Add statin intensity variable‡	Add liver disease variable§
Pre-AMI adherence	**Post-AMI adherence**	HR (95% CI)			
Severely nonadherent	Severely nonadherent	1.	1.	1.	1.
	Moderately nonadherent	0.89 (0.80, 0.99)	0.88 (0.79, 0.98)	0.85 (0.77, 0.95)	0.89 (0.80, 0.99)
	Adherent	0.83 (0.75, 0.92)	0.83 (0.74, 0.92)	0.79 (0.71, 0.88)	0.83 (0.75, 0.92)
Moderately nonadherent	Severely nonadherent	1.11 (1.01, 1.22)	1.10 (1.00, 1.21)	1.10 (1.00, 1.21)	1.11 (1.01, 1.22)
	Moderately nonadherent	0.90 (0.82, 0.98)	0.89 (0.82, 0.98)	0.86 (0.79, 0.94)	0.90 (0.82, 0.98)
	Adherent	0.84 (0.77, 0.91)	0.84 (0.77, 0.91)	0.80 (0.74, 0.87)	0.84 (0.77, 0.91)
Adherent	Severely nonadherent	1.09 (0.99, 1.20)	1.09 (0.99, 1.20)	1.09 (0.99, 1.20)	1.09 (0.99, 1.20)
	Moderately nonadherent	1.04 (0.96, 1.13)	1.06 (0.97, 1.15)	1.00 (0.92, 1.08)	1.04 (0.96, 1.13)
	Adherent	0.88 (0.82, 0.94)	0.88 (0.82, 0.94)	0.84 (0.79, 0.89)	0.88 (0.82, 0.94)

All four models are estimating the association between all-cause mortality and change in statin adherence using Cox proportional hazards models. No point estimates from sensitivity analyses fell outside of the 95% confidence intervals from the fully adjusted model.

* Fully adjusted model also presented in Figure 5 within the manuscript.

† This model changed the definition of the statin adherence change measure to make it more conservative, attempting to eliminate the influence of small changes in adherence near the category cutoffs. This measure required a categorical change in statin adherence to also be at least a 10% absolute difference from pre- to post-AMI PDC (e.g. a change from pre-AMI PDC of 78% to post-AMI PDC of 84% would not be considered an increase in adherence from "moderately nonadherent" to "adherent"; instead, it would be defined as no change in adherence from "moderately nonadherent" to "moderately nonadherent". Changing the definition of this measure resulted in 571 patients being reclassified from a decrease in adherence to no change and 624 patients being reclassified from an increase in adherence to no change.

‡ Statin intensity was measured using the LAST statin prescription claim filled BEFORE the index AMI hospitalization and using the FIRST claim filled AFTER the index hospitalization discharge. Statin intensity was measured using the 2013 American College of Cardiology/ American Heart Association Guideline on Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults. Both of these variables were added to the model and the variable for simvastatin-equivalent change in average daily dose was removed from the model.

§ CCI measures of liver disease were added as separate variables to the model. The CCI score variable was further adjusted by not including mild and moderate/severe liver disease (as previously described, CCI measures of previous AMI and dementia were not included in the CCI score variable).

Abbreviations: AMI, acute myocardial infarction; CCI, Charlson comorbidity index; CI, confidence interval; HR, hazard ratio; PDC, proportion of days covered.

Table S6. Sensitivity analyses with restricted study eligibility estimating the association between all-cause mortality and change in statin adherence after acute myocardial infarction (AMI).

Statin adherence change after AMI		Fully adjusted model*	Prevalent statin users†,‡	Persistent statin users§	Prevalent & persistent users‖,‡	Multiple pre-AMI statin fills#	Prevalent users with multiple pre-AMI fills**,‡	No AMI or stroke 6-month post-AMI††
Pre-AMI adherence	**Post-AMI adherence**	N=101,011	N=90,791	N=95,228	N=85,008	N=92,674	N=86,452	N=93,770
		HR (95% CI)						
Sev NA	Sev NA	1.	1.	1.	1.	1.	1.	1.
	Mod NA	0.89 (0.80, 0.99)	0.88 (0.79, 0.99)	0.86 (0.75, 0.99)	0.85 (0.74, 0.98)	0.85 (0.74, 0.97)	0.84 (0.73, 0.95)	0.88 (0.78, 0.99)
	Adherent	0.83 (0.75, 0.92)	0.81 (0.72, 0.90)	0.86 (0.76, 0.98)	0.84 (0.73, 0.96)	0.88 (0.78, 0.99)	0.86 (0.76, 0.97)	0.83 (0.74, 0.93)
Mod NA	Sev NA	1.11 (1.01, 1.22)	1.09 (0.99, 1.21)	1.13 (1.02, 1.26)	1.12 (0.99, 1.26)	1.12 (1.00, 1.24)	1.10 (0.98, 1.23)	1.09 (0.98, 1.21)
	Mod NA	0.90 (0.82, 0.98)	0.88 (0.80, 0.97)	0.92 (0.83, 1.02)	0.91 (0.81, 1.01)	0.89 (0.81, 0.99)	0.88 (0.79, 0.98)	0.89 (0.81, 0.99)
	Adherent	0.84 (0.77, 0.91)	0.82 (0.75, 0.89)	0.86 (0.78, 0.95)	0.84 (0.76, 0.94)	0.84 (0.77, 0.93)	0.82 (0.74, 0.91)	0.85 (0.77, 0.93)
Adherent	Sev NA	1.09 (0.99, 1.20)	1.13 (1.02, 1.25)	1.12 (1.00, 1.25)	1.15 (1.02, 1.30)	1.12 (1.01, 1.25)	1.13 (1.01, 1.27)	1.07 (0.97, 1.19)
	Mod NA	1.04 (0.96, 1.13)	1.06 (0.98, 1.16)	1.07 (0.97, 1.18)	1.09 (0.98, 1.21)	1.07 (0.97, 1.17)	1.07 (0.97, 1.18)	1.04 (0.95, 1.14)
	Adherent	0.88 (0.82, 0.94)	0.88 (0.82, 0.94)	0.90 (0.83, 0.98)	0.90 (0.82, 0.99)	0.89 (0.82, 0.96)	0.88 (0.81, 0.95)	0.87 (0.81, 0.94)

All seven models are estimating the association between all-cause mortality and change in statin adherence using Cox proportional hazards models. No point estimates from sensitivity analyses fell outside of the 95% confidence intervals from the fully adjusted model.

* Fully adjusted model also presented in Figure 5 within the manuscript.

† Excluded "new users" of statins who had first statin prescription fill within 6 months pre-AMI.

‡ Model not adjusted for the "new user" variable (every patient had the same value for this variable).

§ Excluded patients who had a PDC of 0% during the 6-month pre-AMI period (i.e. had no statin available during pre-AMI adherence measurement period).

‖ Excluded "new users" of statin and patients with a pre-AMI PDC of 0%

Excluded patients with only one statin prescription fill in the 12-month pre-AMI period.

** Excluded "new users" and patients with only one statin prescription fill in the 12-month pre-AMI period.

†† Excluded patients who experienced a recurrent AMI or stroke hospitalization within 6 months after index AMI hospitalization discharge. These hospitalizations were therefore not included in model for this sensitivity analysis.

Abbreviations: AMI, acute myocardial infarction; CI, confidence interval; HR, hazard ratio; Mod NA, moderately nonadherent; PDC, proportion of days covered; Sev NA, severely nonadherent.

Table S7. Association between all-cause mortality and change in statin adherence, adjusted for changes in ACE/ARB and beta-blocker adherence, among the subgroup of prevalent users for all 3 medication classes: models adjusted iteratively based on the timing of covariate measurement and comparison to final model from manuscript.

			Subgroup of prevalent ACE/ARB & beta-blocker users (N=48,580) Model adjusted for				
Statin adherence change after AMI		Original fully adjusted model† (N=101,011)	Only ACE/ARB & beta-blocker adherence change	+ Sociodem	+ Sociodem + Pre	+ Sociodem + Pre + Hosp	Fully adjusted model
Pre-AMI adherence	**Post-AMI adherence**	HR (95% CI)					
Severely nonadherent	Severely nonadherent	1.	1.	1.	1.	1.	1.
	Moderately nonadherent	0.89 (0.80, 0.99)	0.76 (0.65, 0.89)*	0.77 (0.66, 0.89)*	0.80 (0.69, 0.93)	0.85 (0.73, 0.99)	0.91 (0.78, 1.06)
	Adherent	0.83 (0.75, 0.92)	0.80 (0.69, 0.93)	0.79 (0.68, 0.92)	0.85 (0.73, 0.98)	0.90 (0.78, 1.05)	0.98 (0.84, 1.13)*
Moderately nonadherent	Severely nonadherent	1.11 (1.01, 1.22)	1.15 (1.01, 1.31)	1.14 (1.00, 1.30)	1.17 (1.03, 1.34)	1.14 (1.00, 1.31)	1.16 (1.02, 1.33)
	Moderately nonadherent	0.90 (0.82, 0.98)	0.79 (0.70, 0.90)*	0.80 (0.70, 0.90)*	0.82 (0.72, 0.93)	0.84 (0.74, 0.95)	0.88 (0.77, 1.00)
	Adherent	0.84 (0.77, 0.91)	0.78 (0.69, 0.88)	0.77 (0.69, 0.86)	0.80 (0.71, 0.90)	0.83 (0.74, 0.93)	0.89 (0.79, 1.01)
Adherent	Severely nonadherent	1.09 (0.99, 1.20)	1.22 (1.07, 1.39)*	1.17 (1.03, 1.34)	1.16 (1.02, 1.33)	1.11 (0.97, 1.27)	1.12 (0.98, 1.28)
	Moderately nonadherent	1.04 (0.96, 1.13)	1.06 (0.95, 1.19)	1.03 (0.92, 1.16)	1.04 (0.93, 1.17)	1.04 (0.93, 1.16)	1.07 (0.96, 1.21)
	Adherent	0.88 (0.82, 0.94)	0.86 (0.78, 0.94)	0.83 (0.75, 0.91)	0.85 (0.77, 0.93)	0.86 (0.78, 0.94)	0.92 (0.84, 1.02)

Cox proportional hazards models for the subgroup of patients (N=48,580) who were already taking the following medications before the index AMI: (1) a statin, (2) an ACE inhibitor or ARB, and (3) a beta-blocker. The first model on the left ("Original fully adjusted model") is the primary model found in Figure 5 within the manuscript (N=101,011). The second model ("Only ACE/ARB & beta-blocker adherence change") is only adjusted for these adherence change measures (N=48,580). Each model is then adjusted for an additional set of covariates based on when the variables were measured (sociodemographics, pre-AMI comorbidities/medications, characteristics of the index AMI hospitalization, and post-AMI follow-up/medications/stroke/recurrent AMI in the "Fully adjusted model" on the right).

* Point estimate does not fall within the 95% confidence interval for the original fully adjusted model.

† Original fully adjusted model also presented in Figure 5 within the manuscript.

Abbreviations: ACE inhibitor, angiotensin-converting enzyme inhibitor; AMI, acute myocardial infarction; ARB, angiotensin II receptor blocker; CI, confidence interval; Hosp, measures from the index AMI hospitalization; HR, hazard ratio; Pre, pre-AMI measures; Sociodem, sociodemographic measures.

Table S8. Full model results for the association between all-cause mortality and change in statin adherence after acute myocardial infarction, adjusted for changes in ACE/ARB and beta-blocker adherence, among the subgroup of prevalent users for all 3 medication classes (N=48,580).

Patient characteristics		**HR (95% CI)**
Statin adherence change*		
Pre-AMI adherence	**Post-AMI adherence**	
Severely nonadherent	Severely nonadherent	1.
	Moderately nonadherent	0.91 (0.78, 1.06)
	Adherent	0.98 (0.84, 1.13)
Moderately nonadherent	Severely nonadherent	1.16 (1.02, 1.33)
	Moderately nonadherent	0.88 (0.77, 1.00)
	Adherent	0.89 (0.79, 1.01)
Adherent	Severely nonadherent	1.12 (0.98, 1.28)
	Moderately nonadherent	1.07 (0.96, 1.21)
	Adherent	0.92 (0.84, 1.02)
ACE inhibitor/ARB adherence change*		
Pre-AMI adherence	**Post-AMI adherence**	
Severely nonadherent	Severely nonadherent	1.
	Moderately nonadherent	0.82 (0.70, 0.96)
	Adherent	0.84 (0.72, 0.98)
Moderately nonadherent	Severely nonadherent	0.92 (0.82, 1.04)
	Moderately nonadherent	0.92 (0.81, 1.04)
	Adherent	0.77 (0.68, 0.86)
Adherent	Severely nonadherent	1.02 (0.92, 1.14)
	Moderately nonadherent	0.92 (0.83, 1.02)
	Adherent	0.80 (0.73, 0.87)
Beta-blocker adherence change*		
Pre-AMI adherence	**Post-AMI adherence**	
Severely nonadherent	Severely nonadherent	1.
	Moderately nonadherent	0.87 (0.72, 1.04)
	Adherent	0.85 (0.72, 1.01)
Moderately nonadherent	Severely nonadherent	1.02 (0.86, 1.21)
	Moderately nonadherent	0.95 (0.82, 1.10)
	Adherent	0.95 (0.83, 1.10)
Adherent	Severely nonadherent	1.03 (0.88, 1.22)
	Moderately nonadherent	1.11 (0.97, 1.28)
	Adherent	0.97 (0.86, 1.10)
Sociodemographics		
Age		
66-75		1.
76-85		1.31 (1.24, 1.39)
86+		1.87 (1.75, 2.00)
Female		0.83 (0.79, 0.88)
Race/ethnicity		

Patient characteristics	HR (95% CI)
White	1.
Black	0.91 (0.84, 0.99)
Hispanic	0.84 (0.73, 0.95)
Asian	0.80 (0.68, 0.95)
Other	0.89 (0.75, 1.06)
Dual eligibility[†]	1.10 (1.04, 1.16)
Household income[‡]	
≤$30,000	1.
$30,001-60,000	1.02 (0.97, 1.07)
$60,001-100,000	0.97 (0.89, 1.06)
$100,001-150,000	1.03 (0.85, 1.25)
>$150,000	1.01 (0.73, 1.40)
Pre-AMI comorbidities and cardiovascular procedures[§]	
Adjusted Charlson comorbidity index[‖]	
0	1.
1-2	1.37 (1.24, 1.51)
3-5	1.99 (1.81, 2.20)
6-8	2.64 (2.36, 2.95)
9+	4.22 (3.64, 4.89)
Baseline comorbidities and procedures	
Prior AMI[#]	1.15 (1.06, 1.24)
Dementia/Alzheimer's disease**	1.24 (1.16, 1.33)
Depression	1.05 (0.99, 1.12)
CABG	0.51 (0.39, 0.66)
PTCA/stent	0.82 (0.75, 0.90)
Ischemic heart disease	1.02 (0.96, 1.08)
Unstable angina	1.10 (1.01, 1.20)
Lipid abnormalities[§§§]	0.80 (0.74, 0.87)
Rhabdomyolysis/myopathy	0.91 (0.83, 0.99)
Pre-AMI medications	
New user of statin[††]	0.95 (0.87, 1.03)
New user of ACE inhibitor/ARB[††]	1.01 (0.92, 1.10)
New user of beta-blocker[††]	0.98 (0.90, 1.07)
Concurrent medications[‡‡]	
P2Y12 inhibitor	1.04 (0.99, 1.10)
Calcium channel blocker	1.05 (0.99, 1.12)
Aldosterone receptor antagonist	1.07 (0.98, 1.17)
Characteristics of index AMI hospitalization	
Clinical diagnoses and procedures	
Subendocardial infarction[§§]	1.08 (1.00, 1.16)
CABG	0.35 (0.29, 0.42)
PTCA/stent	0.80 (0.74, 0.86)
Antiplatelet use	0.83 (0.71, 0.97)
Cardiac catheterization	0.82 (0.74, 0.91)
Angiocardiography	0.84 (0.76, 0.93)
Cardiogenic shock	0.89 (0.73, 1.09)

Patient characteristics	HR (95% CI)
Cardiac dysrhythmia	1.10 (1.04, 1.15)
Hypotension	0.96 (0.86, 1.08)
Acute renal failure	1.13 (1.07, 1.20)
Heart failure	1.48 (1.41, 1.56)
Duration of hospitalization	
1-3	1.
4-6	1.11 (1.05, 1.17)
7-11	1.24 (1.16, 1.33)
12+	1.33 (1.21, 1.47)
Admission to intensive care	
None	1.
Coronary care unit only	0.96 (0.90, 1.03)
Intensive care unit only	0.97 (0.92, 1.03)
Both	0.95 (0.87, 1.04)
Cardiologist consultation	1.02 (0.95, 1.09)
30-day post-AMI follow-up	
None	1.
Primary care provider‖‖ only	0.91 (0.84, 0.98)
Cardiologist only	0.81 (0.75, 0.89)
Both	0.87 (0.81, 0.93)
Post-AMI medications	
Change in simvastatin-equivalent average daily dose##	1.00 (1.00, 1.00)
Concurrent medications***	
P2Y12 inhibitor	0.96 (0.90, 1.02)
Calcium channel blocker	0.86 (0.81, 0.91)
Aldosterone receptor antagonist	1.23 (1.14, 1.32)
Post-AMI clinical events	
Hospitalization for recurrent AMI†††	1.94 (1.81, 2.07)
Hospitalization for stroke‡‡‡	1.71 (1.44, 2.03)

These are the results for the fully adjusted Cox proportional hazards model for the subgroup of patients (N=48,580) who were already taking the following medications before the index AMI: (1) a statin, (2) an ACE inhibitor or ARB, and (3) a beta-blocker (results for this model were also presented in the far right column ["Fully adjusted model"] of Supplemental Table S7). The purpose of this model was to estimate the association between all-cause mortality and change in statin adherence, while also adjusting for the change in ACE inhibitor/ARB adherence and the change in beta-blocker adherence.

* The HRs for the association between adherence change and mortality in this model should be interpreted with caution given the high level of correlation between adherence change for all 3 medications: statins, ACE/ARBs, and beta-blockers. Adherence was measured separately in the 6 months pre-AMI and the 6 months post-AMI. Adherence was categorized as follows: severely nonadherent (PDC <40%), moderately nonadherent (PDC 40-79.9%), and adherent (PDC ≥80%). Change in adherence was defined as a categorical change in adherence.

† Enrolled in Medicare and Medicaid.

‡ Median household income of US Census block groups for individuals aged 65 and older.

§ Measured in the 12 months prior to the index AMI hospital admission date.

‖ CCI score does not include counts for AMI and dementia.

CCI definition.

Patient characteristics	HR (95% CI)

** Medicare Chronic Conditions Data Warehouse definition.

†† First prescription claim for medication was identified during the 6 months prior to the index AMI hospital admission date.

‡‡ At least one prescription fill within medication class during the 6 months prior to the index AMI hospital admission date.

§§ Index AMI had diagnosis code for subendocardial infarction, compared to transmural infarction.

‖‖ Primary care physician, physician assistant, or nurse practitioner.

Continuous weighted average of the simvastatin-equivalent average daily dose in the post-AMI period minus the weighted average in the pre-AMI period. Dose equivalency calculations were made as follows: fluvastatin, pravastatin, and lovastatin doses in mg were divided by 4, 2, and 2, respectively; atorvastatin, rosuvastatin, and pitavastatin doses were multiplied by 2, 4, and 10, respectively.

*** At least one prescription fill within medication class during the index AMI hospitalization period or within 6 months after index AMI discharge date.

††† Inpatient ICD-9 diagnosis code of 410.x1 in the primary or secondary discharge field within 6 months after index AMI discharge date.

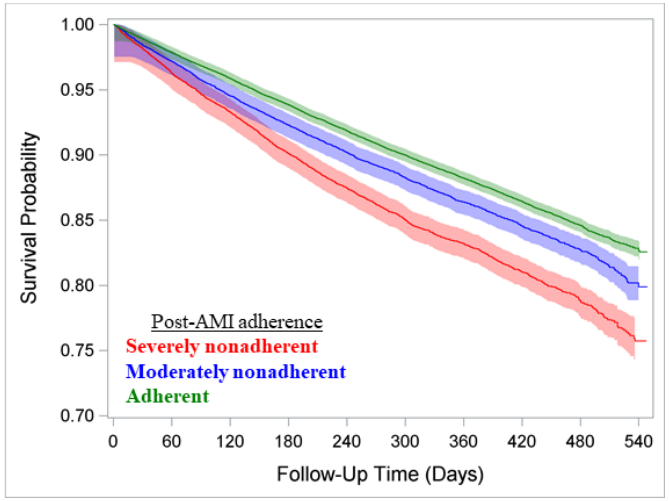
‡‡‡ Inpatient ICD-9 diagnosis code of 430, 431, 433.x1, 434.x1, or 436 in the primary discharge field within 6 months after index AMI discharge date.

§§§ Inpatient or outpatient ICD-9 diagnosis code of 272.xx in any position.

Abbreviations: ACE, angiotensin-converting enzyme; AMI, acute myocardial infarction; ARB, angiotensin II receptor blocker; CABG, coronary artery bypass surgery; CCI, Charlson comorbidity index; CI, confidence interval; HR, hazard ratio; ICD-9, International Classification of Diseases, Ninth Revision; PDC, proportion of days covered; PTCA, percutaneous transluminal coronary angioplasty.

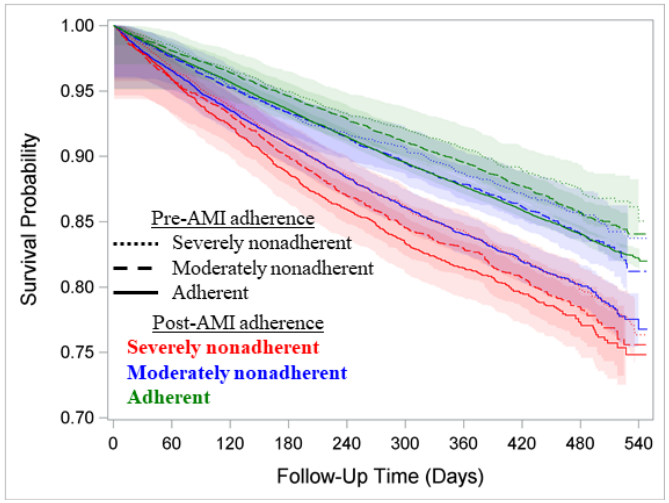
Figure S1. Unadjusted survival curves and 95% confidence bands for all-cause mortality after acute myocardial infarction, stratified by statin adherence.

A



Post-AMI statin adherence	12-month* survival probability (95% confidence interval)
Severely nonadherent	0.832 (0.825-0.838)
Moderately nonadherent	0.864 (0.859-0.869)
Adherent	0.882 (0.879-0.885)

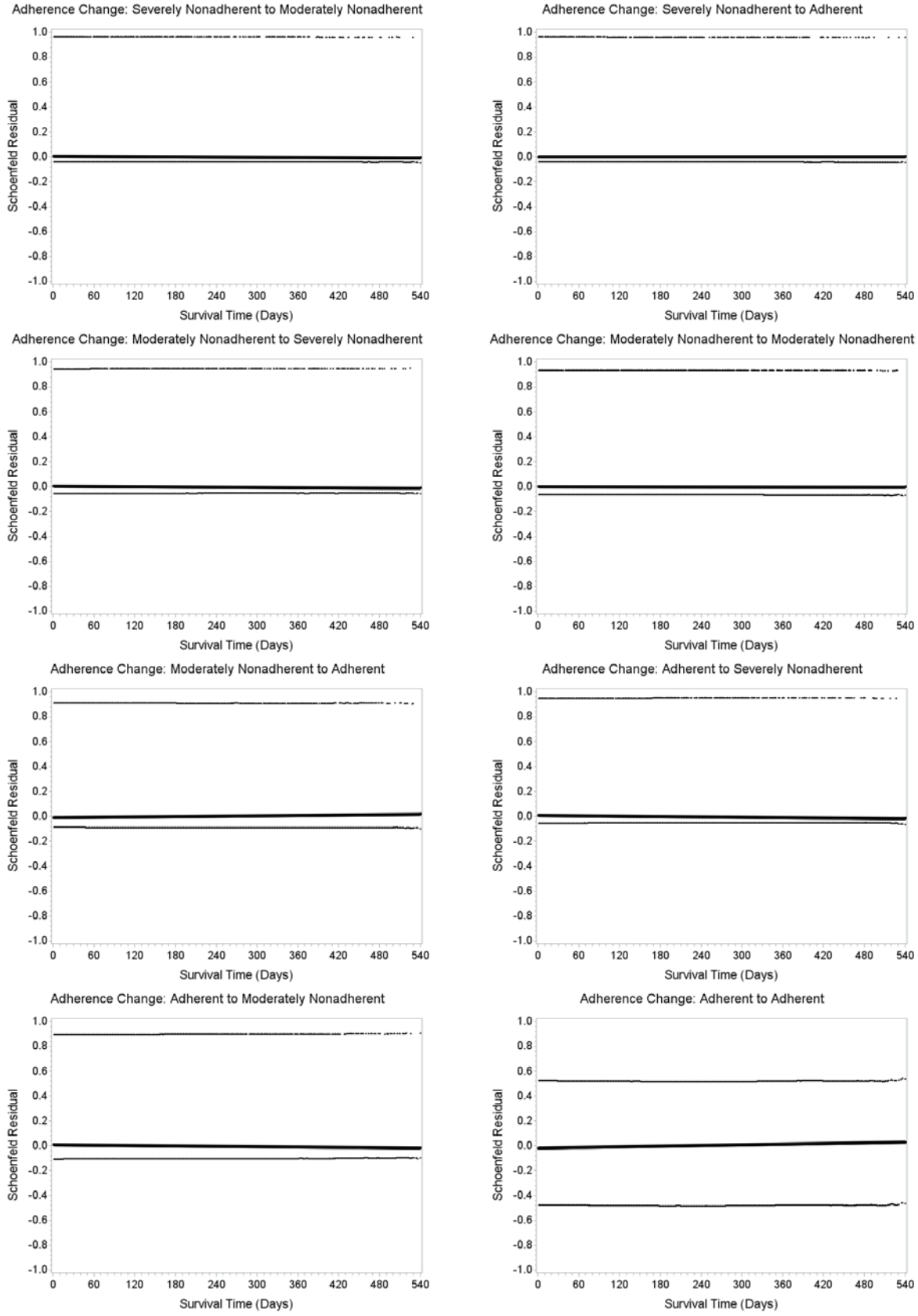
B



Pre-AMI statin adherence	Post-AMI statin adherence	12-month* survival probability (95% confidence interval)
Severely nonadherent	Severely nonadherent	0.843 (0.833-0.852)
Moderately nonadherent		0.829 (0.816-0.841)
Adherent		0.815 (0.801-0.828)
Severely nonadherent	Moderately nonadherent	0.887 (0.876-0.897)
Moderately nonadherent		0.879 (0.870-0.887)
Adherent		0.840 (0.832-0.848)
Severely nonadherent	Adherent	0.906 (0.897-0.914)
Moderately nonadherent		0.895 (0.889-0.901)
Adherent		0.877 (0.874-0.880)

Follow-up begins 6 months after index AMI discharge (i.e. Day 0 is 180 days after index AMI discharge). A: Stratified by **post-AMI** statin adherence. B: Stratified by change in statin adherence from pre- to post-AMI.
* 12-month estimate calculated from 6 months post-AMI discharge through 18 months post-AMI discharge.
Abbreviations: AMI, acute myocardial infarction.

Figure S2. Schoenfeld residuals (dots) with smooth fitted spline (line) for statin adherence change.



SUPPLEMENTAL MATERIAL

Supplemental Tables

Table S1. Patient characteristics for the full cohort and stratified by change in statin adherence after AMI.

Table S2. Full model results for the association between all-cause mortality and **post-AMI** statin adherence, while adjusting for *pre-AMI* statin adherence.

Table S3. Full model results for the association between all-cause mortality and change in statin adherence after acute myocardial infarction (AMI).

Table S4. Crude estimates and models adjusted iteratively based on the timing of covariate measurement for the association between all-cause mortality and change in statin adherence after acute myocardial infarction (AMI).

Table S5. Sensitivity analyses involving changing variable definitions or adding new variables to the model estimating the association between all-cause mortality and change in statin adherence after acute myocardial infarction (AMI).

Table S6. Sensitivity analyses with restricted study eligibility estimating the association between all-cause mortality and change in statin adherence after acute myocardial infarction (AMI).

Table S7. Association between all-cause mortality and change in statin adherence, adjusted for changes in ACE/ARB and beta-blocker adherence, among the subgroup of prevalent users for all 3 medication classes: models adjusted iteratively based on the timing of covariate measurement and comparison to final model from manuscript.

Table S8. Full model results for the association between all-cause mortality and change in statin adherence after acute myocardial infarction, adjusted for changes in ACE/ARB and beta-blocker adherence, among the subgroup of prevalent users for all 3 medication classes (N=48,580).

Supplemental Figures

Figure S1. Unadjusted survival curves and 95% confidence bands for all-cause mortality after acute myocardial infarction, stratified by statin adherence.

Figure S2. Schoenfeld residuals (dots) with smooth fitted spline (line) for statin adherence change.

Table S1. Patient characteristics for the full cohort and stratified by change in statin adherence after AMI.

		Pre-AMI statin adherence								
		Severely nonadherent			Moderately nonadherent			Adherent		
		Post-AMI statin adherence			**Post-AMI statin adherence**			**Post-AMI statin adherence**		
	Full cohort	Sev NA	Mod NA	Adh	Sev NA	Mod NA	Adh	Sev NA	Mod NA	Adh
	N=101,011	n=6,892	n=4,193	n=5,188	n=4,026	n=6,926	n=10,829	n=3,622	n=8,417	n=50,918
Patient characteristics	n (%)	%	%	%	%	%	%	%	%	%
Sociodemographics										
Age										
66-75	47,128 (46.7)	48.1	52.7	51.8	45.7	49.9	49.3	43.7	44.3	45.1
76-85	39,698 (39.3)	37.7	36.6	37.1	40.1	38.1	38.6	39.8	40.2	40.0
86+	14,185 (14.0)	14.1	10.7*	11.1	14.3	12.1	12.1	16.5	15.5	14.9
Female	54,886 (54.3)	55.8	55.1	56.1	54.6	55.6	56.1	56.2	54.7	53.1
Race/ethnicity										
White	85,318 (84.5)	81.6	78.3	79.7	81.4	80.7	82.1	84.5	84.9	87.0*
Black	8,495 (8.4)	11.8	13.0	11.4	11.2	11.8	9.6	8.5*	7.9*	6.4*
Hispanic	3,001 (3.0)	3.3	4.2	4.2	3.5	3.5	3.8	3.1	3.2	2.4
Asian	2,227 (2.2)	1.7	2.4	2.5	1.7	1.8	2.4	1.9	2.0	2.3
Other	1,970 (2.0)	1.6	2.1	2.2	2.2	2.3	2.0	2.0	2.1	1.8
Dual eligibility[†]	24,723 (24.5)	22.5	25.8	28.3*	22.0	23.1	26.2	24.9	22.7	24.5
Household income[‡]										
≤$30,000	47,442 (47.0)	49.1	50.2	49.2	48.8	47.2	47.2	48.1	46.7	45.9
$30,001-60,000	41,801 (41.4)	40.9	39.0	39.7	40.4	41.2	40.9	40.6	41.3	42.1
$60,001-100,000	9,467 (9.4)	8.2	9.0	9.0	8.9	9.5	9.4	9.2	9.5	9.6
$100,001-150,000	1,760 (1.7)	1.4	1.3	1.6	1.5	1.6	1.8	1.7	2.0	1.8
>$150,000	541 (0.5)	0.5	0.4	0.5	0.4	0.5	0.7	0.5	0.5	0.6
Pre-AMI comorbidities and cardiovascular procedures[§]										
Adjusted Charlson comorbidity index[‖]										
0	21,946 (21.7)	18.0	22.9*	26.7*	18.6	21.2	23.8*	18.8	19.6	22.1*
1-2	40,745 (40.3)	39.4	39.6	42.3	38.9	41.0	40.9	38.2	39.0	40.6
3-5	29,876 (29.6)	32.3	29.9	24.2*	31.7	29.2	27.9	32.4	32.2	29.3
6-8	7,102 (7.0)	8.4	6.4	5.8*	9.1	7.3	6.1	9.0	7.7	6.8
9+	1,342 (1.3)	1.9	1.2	1.1	1.8	1.2	1.3	1.6	1.6	1.2

Patient characteristics	Full cohort N=101,011 n (%)	*Pre-AMI statin adherence* Severely nonadherent Post-AMI statin adherence Sev NA n=6,892 %	Mod NA n=4,193 %	Adh n=5,188 %	Moderately nonadherent Post-AMI statin adherence Sev NA n=4,026 %	Mod NA n=6,926 %	Adh n=10,829 %	Adherent Post-AMI statin adherence Sev NA n=3,622 %	Mod NA n=8,417 %	Adh n=50,918 %
Baseline comorbidities and procedures										
Prior AMI[#]	4,288 (4.2)	6.0	4.6	3.3*	5.4	4.1	3.6*	5.7	4.5	4.0
Dementia/Alzheimer's**	9,396 (9.3)	10.6	8.7	8.1	10.3	9.3	9.3	13.2	10.4	8.8
Depression	15,207 (15.1)	16.2	15.0	14.6	17.2	15.8	14.9	17.9	16.4	14.3
CABG	1,064 (1.1)	1.0	0.9	0.9	1.2	0.9	1.2	1.4	1.2	1.0
PTCA/stent	6,748 (6.7)	8.6	6.4	5.2*	8.2	7.3	5.9*	7.7	7.0	6.4
Ischemic heart disease	60,303 (59.7)	65.3	58.4*	47.1*	65.9	61.4	56.3*	62.7	62.6	59.6*
Unstable angina	5,401 (5.3)	6.6	5.1	4.3	6.6	5.8	4.5	5.6	5.7	5.2
Lipid abnormalities****	90,639 (89.7)	88.5	87.9	87.0	90.0	90.4	90.1	88.9	90.7	90.1
Rhabdomyolysis/myopathy	6,570 (6.5)	8.8	7.8	6.7	8.3	6.6	6.5	7.0	7.2	5.7*
Pre-AMI medications										
New user of statin[††]	10,220 (10.1)	9.8	7.1	7.5	20.8*	11.4	9.6	24.4*	14.9*	8.0
Concurrent medications[‡‡]										
ACE inhibitor/ARB	65,524 (64.9)	55.8	57.9	57.3	63.1*	64.8*	64.6*	64.5*	66.7*	67.4*
Beta-blocker	63,437 (62.8)	57.2	54.8	50.8*	62.2*	62.9*	60.1	62.9*	64.1*	65.8*
$P2Y_{12}$ inhibitor	31,546 (31.2)	31.8	27.7	22.5*	35.2	32.7	29.1	33.4	33.1	31.8
Calcium channel blocker	35,730 (35.4)	31.3	31.5	32.4	34.1	34.1	36.1*	35.1	36.2*	36.5*
Aldosterone antagonist	5,002 (5.0)	4.9	4.3	3.9	5.8	4.8	4.6	5.2	5.3	5.1
Characteristics of index AMI hospitalization										
Clinical diagnoses and procedures										
Subendocardial infarction[§§]	79,978 (79.2)	81.3	77.7	72.2*	80.8	79.2	76.6*	80.5	81.0	79.7
CABG	6,778 (6.7)	4.5	7.8*	9.5*	5.2	6.4	7.6*	6.2	6.1	6.7
PTCA/stent	39,479 (39.1)	35.1	42.2*	50.2*	32.2	39.0	43.9*	30.7	34.2	39.2
Antiplatelet use	4,627 (4.6)	4.6	5.0	5.5	4.0	4.7	5.0	3.5	3.9	4.6
Cardiac catheterization	61,062 (60.5)	57.2	65.2*	70.5*	54.8	61.2	64.9*	52.4	56.5	60.1
Angiocardiography	61,122 (60.5)	57.3	64.6*	68.4*	55.1	61.3	64.7*	52.0*	56.2	60.5
Cardiogenic shock	2,150 (2.1)	1.4	1.9	2.8	2.1	2.0	2.6	2.0	2.2	2.1
Cardiac dysrhythmia	31,326 (31.0)	31.3	29.5	29.0	30.4	29.6	29.4	31.8	32.0	31.7

		Pre-AMI statin adherence								
		Severely nonadherent			Moderately nonadherent			Adherent		
		Post-AMI statin adherence			**Post-AMI statin adherence**			**Post-AMI statin adherence**		
	Full cohort	Sev NA	Mod NA	Adh	Sev NA	Mod NA	Adh	Sev NA	Mod NA	Adh
	N=101,011	n=6,892	n=4,193	n=5,188	n=4,026	n=6,926	n=10,829	n=3,622	n=8,417	n=50,918
Patient characteristics	n (%)	%	%	%	%	%	%	%	%	%
Hypotension	4,999 (4.9)	4.7	4.5	5.0	5.1	4.7	5.3	4.8	5.0	5.0
Acute renal failure	14,774 (14.6)	14.3	13.7	13.3	15.7	14.4	13.9	17.4	16.5	14.5
Heart failure	38,222 (37.8)	38.8	35.3	33.7*	40.6	36.6	36.5	43.5	39.8	37.9
Duration of hospitalization (days)										
1-3	46,047 (45.6)	45.6	46.4	45.8	43.0	47.4	46.5	38.4*	43.4	46.1
4-6	30,966 (30.7)	31.9	30.3	29.8	31.5	30.1	30.2	31.2	31.0	30.6
7-11	16,714 (16.5)	15.7	16.1	16.6	17.6	15.6	15.8	19.9*	17.7	16.5
12+	7,284 (7.2)	6.8	7.2	7.8	7.9	6.9	7.5	10.5*	8.0	6.8
Admission to intensive care										
None	25,146 (24.9)	26.1	23.6	20.6*	26.4	25.2	23.9	24.2	24.8	25.4
Coronary care unit only	23,706 (23.5)	23.4	24.7	25.9	22.1	23.5	24.3	22.1	23.0	23.2
Intensive care unit only	41,551 (41.1)	41.0	40.7	41.0	41.1	40.8	40.4	43.1	42.0	41.1
Both	10,608 (10.5)	9.4	11.0	12.5	10.4	10.6	11.4	10.5	10.2	10.3
Cardiologist consultation	87,858 (87.0)	85.7	87.2	89.3*	85.2	87.7	87.6	85.9	86.4	87.0
30-day post-AMI follow-up										
None	14,873 (14.7)	18.4	16.0	14.1*	17.9	16.2	13.9*	14.6*	14.4*	14.0*
Primary care provider[‖‖] only	29,301 (29.0)	31.3	28.9	26.0*	30.2	29.6	28.1	32.4	29.3	28.7
Cardiologist only	19,161 (19.0)	17.4	19.9	19.7	18.0	19.4	19.8	15.6	17.9	19.3
Both	37,676 (37.3)	32.9	35.2	40.2*	33.9	34.9	38.2*	37.3	38.4*	38.0*
Post-AMI medications										
Change in simvastatin-equivalent ADD[##] (mean ± std)	4.4 ± 33.2	-20.1 ± 42.4	7.5 ± 37.4*	13.2 ± 40.5*	-16.5 ± 40.1	4.4 ± 28.6*	10.8 ± 33.0*	-17.7 ± 38.8	3.2 ± 28.2*	8.6 ± 27.7*
Concurrent medications***										
ACE inhibitor/ARB	72,011 (71.3)	61.4	71.9*	75.7*	63.2	70.7*	73.9*	61.8	69.1*	73.3*
Beta-blocker	87,887 (87.0)	77.1	86.5*	90.1*	78.7	85.9*	89.5*	80.1	85.6*	89.1*
$P2Y_{12}$ inhibitor	66,607 (65.9)	58.2	68.4*	74.0*	57.3	66.1*	69.8*	55.7	63.0	67.0*
Calcium channel blocker	32,162 (31.8)	30.5	31.6	29.6	29.8	31.5	31.6	28.6	32.5	32.6
Aldosterone antagonist	8,689 (8.6)	8.5	8.0	8.6	9.0	8.5	8.3	9.4	9.4	8.5

		Pre-AMI statin adherence								
		Severely nonadherent			Moderately nonadherent			Adherent		
		Post-AMI statin adherence			**Post-AMI statin adherence**			**Post-AMI statin adherence**		
	Full cohort	Sev NA	Mod NA	Adh	Sev NA	Mod NA	Adh	Sev NA	Mod NA	Adh
	N=101,011	n=6,892	n=4,193	n=5,188	n=4,026	n=6,926	n=10,829	n=3,622	n=8,417	n=50,918
Patient characteristics	n (%)	%	%	%	%	%	%	%	%	%
Post-AMI clinical events										
Recurrent AMI†††	6,386 (6.3)	7.1	6.9	5.8	6.5	6.7	5.9	6.5	7.8	6.0
Stroke‡‡‡	972 (1.0)	1.2	1.1	1.0	1.3	1.0	0.7	1.3	1.5	0.8
Statin intensity§§§										
Pre-AMIǁǁǁ										
Low intensity	10,851 (10.7)	12.3	8.7*	12.7	10.0	7.7*	10.8	11.6	10.0	11.0
Moderate intensity	68,527 (67.8)	66.3	65.1	69.1	66.3	64.8	68.6	68.3	67.2	68.6
High intensity	21,633 (21.4)	21.4	26.2*	18.2	23.7	27.5*	20.6	20.0	22.8	20.4
Post-AMI###										
Low intensity	8,256 (8.2)	10.8	6.2*	7.2*	9.7	6.3*	7.4*	10.4	8.6	8.1
Moderate intensity	64,773 (64.1)	65.5	60.7*	63.9	65.0	61.9	62.5	67.3	64.5	64.5
High intensity	27,982 (27.7)	23.7	33.1*	28.9*	25.3	31.8*	30.0*	22.3	26.9	27.3

Percentages are column percents. Statin adherence was measured separately in the 6 months pre-AMI and the 6 months post-AMI. Adherence was categorized as follows: severely nonadherent (PDC <40%), moderately nonadherent (PDC 40-79.9%), and adherent (PDC ≥80%). For absolute standardized difference calculations, all statin adherence change groups are compared to the group who was severely nonadherent both pre- and post-AMI.

* Absolute standardized difference ≥10% compared to the reference group (severely nonadherent both pre- and post-AMI).

† Enrolled in Medicare and Medicaid.

‡ Median household income of US Census block groups for individuals aged 65 and older.

§ Measured in the 12 months prior to the index AMI hospital admission date.

ǁ CCI score does not include counts for AMI and dementia.

CCI definition.

** Medicare Chronic Conditions Data Warehouse definition.

†† First prescription claim for a statin was identified during the 6 months prior to the index AMI hospital admission date.

‡‡ At least one prescription fill within medication class during the 6 months prior to the index AMI hospital admission date.

§§ Index AMI had diagnosis code for subendocardial infarction, compared to transmural infarction.

ǁǁ Primary care physician, physician assistant, or nurse practitioner.

		Pre-AMI statin adherence								
		Severely nonadherent			Moderately nonadherent			Adherent		
		Post-AMI statin adherence			**Post-AMI statin adherence**			**Post-AMI statin adherence**		
	Full cohort	Sev NA	Mod NA	Adh	Sev NA	Mod NA	Adh	Sev NA	Mod NA	Adh
	N=101,011	n=6,892	n=4,193	n=5,188	n=4,026	n=6,926	n=10,829	n=3,622	n=8,417	n=50,918
Patient characteristics	n (%)	%	%	%	%	%	%	%	%	%

Continuous weighted average of the simvastatin-equivalent average daily dose in the post-AMI period minus the weighted average in the pre-AMI period. Dose equivalency calculations were made as follows: fluvastatin, pravastatin, and lovastatin doses in mg were divided by 4, 2, and 2, respectively; atorvastatin, rosuvastatin, and pitavastatin doses were multiplied by 2, 4, and 10, respectively.

*** At least one prescription fill within medication class during the index AMI hospitalization period or within 6 months after index AMI discharge date.

††† Inpatient ICD-9 diagnosis code of 410.x1 in the primary or secondary discharge field within 6 months after index AMI discharge date.

‡‡‡ Inpatient ICD-9 diagnosis code of 430, 431, 433.x1, 434.x1, or 436 in the primary discharge field within 6 months after index AMI discharge date.

§§§ According to the 2013 American College of Cardiology/ American Heart Association guidelines on the reduction of atherosclerotic cardiovascular risk.

‖‖‖ Intensity of the last statin prescription fill before the index AMI.

Intensity of the first statin prescription fill after the index AMI.

**** Inpatient or outpatient ICD-9 diagnosis code of 272.xx in any position.

Abbreviations: ACE, angiotensin-converting enzyme; ADD, average daily dose; Adh, Adherent; AMI, acute myocardial infarction; ARB, angiotensin II receptor blocker; CABG, coronary artery bypass surgery; CCI, Charlson comorbidity index; ICD-9, International Classification of Diseases, Ninth Revision; Mod NA, moderately nonadherent; PDC, proportion of days covered; PTCA, percutaneous transluminal coronary angioplasty; Sev NA, severely nonadherent; std, standard deviation.

Table S2. Full model results for the association between all-cause mortality and **post-AMI** statin adherence, while adjusting for *pre-AMI* statin adherence.

Patient characteristics	**HR (95% CI)**
Post-AMI statin adherence*	
Severely nonadherent	1.
Moderately nonadherent	0.89 (0.84, 0.95)
Adherent	0.79 (0.74, 0.83)
*Pre-AMI statin adherence**	
Severely nonadherent	1.
Moderately nonadherent	1.05 (0.99, 1.11)
Adherent	1.11 (1.05, 1.17)
Sociodemographics	
Age	
66-75	1.
76-85	1.34 (1.28, 1.39)
86+	1.94 (1.85, 2.04)
Female	0.83 (0.80, 0.86)
Race/ethnicity	
White	1.
Black	0.90 (0.85, 0.96)
Hispanic	0.86 (0.78, 0.95)
Asian	0.83 (0.73, 0.93)
Other	0.85 (0.75, 0.97)
Dual eligibility[†]	1.12 (1.08, 1.17)
Household income[‡]	
≤$30,000	1.
$30,001-60,000	1.01 (0.98, 1.05)
$60,001-100,000	0.97 (0.91, 1.04)
$100,001-150,000	1.02 (0.89, 1.16)
>$150,000	0.95 (0.75, 1.20)
Pre-AMI comorbidities and cardiovascular procedures[§]	
Adjusted Charlson comorbidity index[‖]	
0	1.
1-2	1.48 (1.39, 1.58)
3-5	2.18 (2.05, 2.33)
6-8	2.79 (2.58, 3.02)
9+	5.04 (4.54, 5.60)
Baseline comorbidities and procedures	
Prior AMI[#]	1.14 (1.07, 1.22)
Dementia/Alzheimer's disease**	1.32 (1.25, 1.38)
Depression	1.07 (1.03, 1.12)
CABG	0.51 (0.41, 0.64)
PTCA/stent	0.81 (0.74, 0.87)
Ischemic heart disease	1.05 (1.01, 1.10)
Unstable angina	1.05 (0.98, 1.13)
Lipid abnormalities[§§§]	0.78 (0.74, 0.83)

Patient characteristics	HR (95% CI)
Rhabdomyolysis/myopathy	0.94 (0.88, 1.00)
Pre-AMI medications	
New user of statin[††]	0.90 (0.85, 0.95)
Concurrent medications[‡‡]	
ACE inhibitor/ARB	0.96 (0.92, 0.99)
Beta-blocker	1.07 (1.03, 1.12)
$P2Y_{12}$ inhibitor	1.08 (1.03, 1.12)
Calcium channel blocker	1.07 (1.03, 1.12)
Aldosterone receptor antagonist	1.04 (0.97, 1.12)
Characteristics of index AMI hospitalization	
Clinical diagnoses and procedures	
Subendocardial infarction[§§]	1.10 (1.04, 1.15)
CABG	0.33 (0.29, 0.38)
PTCA/stent	0.78 (0.74, 0.83)
Antiplatelet use	0.89 (0.80, 0.99)
Cardiac catheterization	0.85 (0.79, 0.91)
Angiocardiography	0.81 (0.75, 0.87)
Cardiogenic shock	1.01 (0.89, 1.16)
Cardiac dysrhythmia	1.09 (1.05, 1.13)
Hypotension	0.98 (0.90, 1.06)
Acute renal failure	1.13 (1.08, 1.18)
Heart failure	1.50 (1.44, 1.55)
Duration of hospitalization (days)	
1-3	1.
4-6	1.14 (1.10, 1.19)
7-11	1.23 (1.17, 1.29)
12+	1.36 (1.27, 1.46)
Admission to intensive care	
None	1.
Coronary care unit only	0.97 (0.92, 1.02)
Intensive care unit only	0.99 (0.95, 1.03)
Both	0.93 (0.87, 1.00)
Cardiologist consultation	1.00 (0.95, 1.05)
30-day post-AMI follow-up	
None	1.
Primary care provider[‖‖] only	0.87 (0.83, 0.92)
Cardiologist only	0.75 (0.70, 0.80)
Both	0.81 (0.77, 0.86)
Post-AMI medications	
Change in simvastatin-equivalent average daily dose[##]	1.00 (1.00, 1.00)
Concurrent medications***	
ACE inhibitor/ARB	0.87 (0.83, 0.90)
Beta-blocker	0.92 (0.88, 0.97)
$P2Y_{12}$ inhibitor	0.93 (0.89, 0.97)
Calcium channel blocker	0.89 (0.85, 0.93)
Aldosterone receptor antagonist	1.26 (1.19, 1.33)

Patient characteristics	**HR (95% CI)**
Post-AMI clinical events	
Hospitalization for recurrent AMI†††	1.96 (1.86, 2.06)
Hospitalization for stroke‡‡‡	1.82 (1.61, 2.06)

These are the results for the fully adjusted Cox proportional hazards model to estimate the association between all-cause mortality and **post-AMI** statin adherence, while adjusting for *pre-AMI* statin adherence.

* Statin adherence was measured separately in the 6 months pre-AMI and the 6 months post-AMI. Adherence was categorized as follows: severely nonadherent (PDC <40%), moderately nonadherent (PDC 40-79.9%), and adherent (PDC ≥80%).

† Enrolled in Medicare and Medicaid.

‡ Median household income of US Census block groups for individuals aged 65 and older.

§ Measured in the 12 months prior to the index AMI hospital admission date.

‖ CCI score does not include counts for AMI and dementia.

CCI definition.

** Medicare Chronic Conditions Data Warehouse definition.

†† First prescription claim for a statin was identified during the 6 months prior to the index AMI hospital admission date.

‡‡ At least one prescription fill within medication class during the 6 months prior to the index AMI hospital admission date.

§§ Index AMI had diagnosis code for subendocardial infarction, compared to transmural infarction.

‖‖ Primary care physician, physician assistant, or nurse practitioner.

Continuous weighted average of the simvastatin-equivalent average daily dose in the post-AMI period minus the weighted average in the pre-AMI period. Dose equivalency calculations were made as follows: fluvastatin, pravastatin, and lovastatin doses in mg were divided by 4, 2, and 2, respectively; atorvastatin, rosuvastatin, and pitavastatin doses were multiplied by 2, 4, and 10, respectively.

*** At least one prescription fill within medication class during the index AMI hospitalization period or within 6 months after index AMI discharge date.

††† Inpatient ICD-9 diagnosis code of 410.x1 in the primary or secondary discharge field within 6 months after index AMI discharge date.

‡‡‡ Inpatient ICD-9 diagnosis code of 430, 431, 433.x1, 434.x1, or 436 in the primary discharge field within 6 months after index AMI discharge date.

§§§ Inpatient or outpatient ICD-9 diagnosis code of 272.xx in any position.

Abbreviations: ACE, angiotensin-converting enzyme; AMI, acute myocardial infarction; ARB, angiotensin II receptor blocker; CABG, coronary artery bypass surgery; CCI, Charlson comorbidity index; CI, confidence interval; HR, hazard ratio; ICD-9, International Classification of Diseases, Ninth Revision; PDC, proportion of days covered; PTCA, percutaneous transluminal coronary angioplasty.

Table S3. Full model results for the association between all-cause mortality and change in statin adherence after acute myocardial infarction (AMI).

Patient characteristics		**HR (95% CI)**
Statin adherence change*		
Pre-AMI adherence	**Post-AMI adherence**	
Severely nonadherent	Severely nonadherent	1.
	Moderately nonadherent	0.89 (0.80, 0.99)
	Adherent	0.83 (0.75, 0.92)
Moderately nonadherent	Severely nonadherent	1.11 (1.01, 1.22)
	Moderately nonadherent	0.90 (0.82, 0.98)
	Adherent	0.84 (0.77, 0.91)
Adherent	Severely nonadherent	1.09 (0.99, 1.20)
	Moderately nonadherent	1.04 (0.96, 1.13)
	Adherent	0.88 (0.82, 0.94)
Sociodemographics		
Age		
66-75		1.
76-85		1.34 (1.28, 1.39)
86+		1.94 (1.84, 2.03)
Female		0.83 (0.80, 0.86)
Race/ethnicity		
White		1.
Black		0.90 (0.85, 0.96)
Hispanic		0.86 (0.78, 0.95)
Asian		0.83 (0.73, 0.93)
Other		0.85 (0.75, 0.97)
Dual eligibility†		1.12 (1.08, 1.17)
Household income‡		
≤$30,000		1.
$30,001-60,000		1.01 (0.98, 1.05)
$60,001-100,000		0.97 (0.91, 1.04)
$100,001-150,000		1.02 (0.89, 1.16)
>$150,000		0.95 (0.75, 1.20)
Pre-AMI comorbidities and cardiovascular procedures§		
Adjusted Charlson comorbidity indexǁ		
0		1.
1-2		1.48 (1.39, 1.58)
3-5		2.18 (2.05, 2.33)
6-8		2.79 (2.58, 3.02)
9+		5.04 (4.53, 5.59)
Baseline comorbidities and procedures		
Prior AMI#		1.14 (1.07, 1.22)
Dementia/Alzheimer's disease**		1.32 (1.25, 1.38)
Depression		1.07 (1.03, 1.12)
CABG		0.51 (0.41, 0.64)
PTCA/stent		0.81 (0.74, 0.87)
Ischemic heart disease		1.05 (1.01, 1.10)

Patient characteristics	HR (95% CI)
Unstable angina	1.05 (0.97, 1.13)
Lipid abnormalities§§§	0.78 (0.74, 0.83)
Rhabdomyolysis/myopathy	0.94 (0.88, 1.00)
Pre-AMI medications	
New user of statin††	0.90 (0.84, 0.95)
Concurrent medications‡‡	
ACE inhibitor/ARB	0.96 (0.92, 0.99)
Beta-blocker	1.07 (1.03, 1.12)
$P2Y_{12}$ inhibitor	1.08 (1.03, 1.12)
Calcium channel blocker	1.07 (1.03, 1.12)
Aldosterone receptor antagonist	1.04 (0.97, 1.12)
Characteristics of index AMI hospitalization	
Clinical diagnoses and procedures	
Subendocardial infarction§§	1.10 (1.04, 1.15)
CABG	0.33 (0.29, 0.38)
PTCA/stent	0.79 (0.74, 0.83)
Antiplatelet use	0.89 (0.80, 0.99)
Cardiac catheterization	0.85 (0.78, 0.91)
Angiocardiography	0.81 (0.75, 0.87)
Cardiogenic shock	1.01 (0.88, 1.16)
Cardiac dysrhythmia	1.09 (1.05, 1.13)
Hypotension	0.98 (0.90, 1.06)
Acute renal failure	1.13 (1.08, 1.18)
Heart failure	1.50 (1.44, 1.55)
Duration of hospitalization (days)	
1-3	1.
4-6	1.14 (1.10, 1.19)
7-11	1.23 (1.17, 1.29)
12+	1.36 (1.27, 1.46)
Admission to intensive care	
None	1.
Coronary care unit only	0.97 (0.92, 1.02)
Intensive care unit only	0.99 (0.95, 1.03)
Both	0.93 (0.87, 1.00)
Cardiologist consultation	1.00 (0.95, 1.05)
30-day post-AMI follow-up	
None	1.
Primary care providerǁǁ only	0.87 (0.83, 0.92)
Cardiologist only	0.75 (0.70, 0.80)
Both	0.81 (0.77, 0.86)
Post-AMI medications	
Change in simvastatin-equivalent average daily dose##	1.00 (1.00, 1.00)
Concurrent medications***	
ACE inhibitor/ARB	0.87 (0.83, 0.91)
Beta-blocker	0.92 (0.88, 0.97)
$P2Y_{12}$ inhibitor	0.93 (0.89, 0.97)
Calcium channel blocker	0.89 (0.85, 0.93)

Patient characteristics	HR (95% CI)
Aldosterone receptor antagonist	1.26 (1.19, 1.33)
Post-AMI clinical events	
Hospitalization for recurrent AMI†††	1.95 (1.86, 2.06)
Hospitalization for stroke‡‡‡	1.82 (1.61, 2.06)

These are the results for the fully adjusted Cox proportional hazards model also presented in Figure 5 within the manuscript. The purpose of this model was to estimate the association between all-cause mortality and change in statin adherence.

* Statin adherence was measured separately in the 6 months pre-AMI and the 6 months post-AMI. Adherence was categorized as follows: severely nonadherent (PDC <40%), moderately nonadherent (PDC 40-79.9%), and adherent (PDC ≥80%). Change in statin adherence was defined as a categorical change in statin adherence.

† Enrolled in Medicare and Medicaid.

‡ Median household income of US Census block groups for individuals aged 65 and older.

§ Measured in the 12 months prior to the index AMI hospital admission date.

‖ CCI score does not include counts for AMI and dementia.

CCI definition.

** Medicare Chronic Conditions Data Warehouse definition.

†† First prescription claim for a statin was identified during the 6 months prior to the index AMI hospital admission date.

‡‡ At least one prescription fill within medication class during the 6 months prior to the index AMI hospital admission date.

§§ Index AMI had diagnosis code for subendocardial infarction, compared to transmural infarction.

‖‖ Primary care physician, physician assistant, or nurse practitioner.

Continuous weighted average of the simvastatin-equivalent average daily dose in the post-AMI period minus the weighted average in the pre-AMI period. Dose equivalency calculations were made as follows: fluvastatin, pravastatin, and lovastatin doses in mg were divided by 4, 2, and 2, respectively; atorvastatin, rosuvastatin, and pitavastatin doses were multiplied by 2, 4, and 10, respectively.

*** At least one prescription fill within medication class during the index AMI hospitalization period or within 6 months after index AMI discharge date.

††† Inpatient ICD-9 diagnosis code of 410.x1 in the primary or secondary discharge field within 6 months after index AMI discharge date.

‡‡‡ Inpatient ICD-9 diagnosis code of 430, 431, 433.x1, 434.x1, or 436 in the primary discharge field within 6 months after index AMI discharge date.

§§§ Inpatient or outpatient ICD-9 diagnosis code of 272.xx in any position.

Abbreviations: ACE, angiotensin-converting enzyme; AMI, acute myocardial infarction; ARB, angiotensin II receptor blocker; CABG, coronary artery bypass surgery; CCI, Charlson comorbidity index; CI, confidence interval; HR, hazard ratio; ICD-9, International Classification of Diseases, Ninth Revision; PDC, proportion of days covered; PTCA, percutaneous transluminal coronary angioplasty.

Table S4. Crude estimates and models adjusted iteratively based on the timing of covariate measurement for the association between all-cause mortality and change in statin adherence after acute myocardial infarction (AMI).

Statin adherence change after AMI		Crude estimates	Model adjusted for			
			Sociodem	Sociodem + Pre	Sociodem + Pre + Hosp	Fully adjusted model†
Pre-AMI adherence	**Post-AMI adherence**	HR (95% CI)				
Severely nonadherent	Severely nonadherent	1.	1.	1.	1.	1.
	Moderately nonadherent	0.69 (0.62, 0.77)*	0.72 (0.64, 0.80)*	0.77 (0.69, 0.85)*	0.82 (0.74, 0.91)	0.89 (0.80, 0.99)
	Adherent	0.58 (0.52, 0.64)*	0.59 (0.53, 0.66)*	0.67 (0.61, 0.75)*	0.75 (0.68, 0.84)	0.83 (0.75, 0.92)
Moderately nonadherent	Severely nonadherent	1.10 (1.00, 1.21)	1.10 (1.00, 1.21)	1.11 (1.01, 1.22)	1.09 (0.99, 1.20)	1.11 (1.01, 1.22)
	Moderately nonadherent	0.75 (0.69, 0.82)*	0.77 (0.71, 0.85)*	0.81 (0.74, 0.89)*	0.84 (0.77, 0.92)	0.90 (0.82, 0.98)
	Adherent	0.65 (0.60, 0.70)*	0.66 (0.61, 0.71)*	0.72 (0.66, 0.78)*	0.76 (0.70, 0.83)*	0.84 (0.77, 0.91)
Adherent	Severely nonadherent	1.18 (1.07, 1.30)	1.14 (1.03, 1.25)	1.14 (1.04, 1.25)	1.07 (0.97, 1.18)	1.09 (0.99, 1.20)
	Moderately nonadherent	1.00 (0.92, 1.08)	0.98 (0.90, 1.06)	1.00 (0.92, 1.08)	0.99 (0.92, 1.07)	1.04 (0.96, 1.13)
	Adherent	0.75 (0.71, 0.80)*	0.73 (0.69, 0.78)*	0.78 (0.73, 0.83)*	0.80 (0.75, 0.85)*	0.88 (0.82, 0.94)

Cox proportional hazards models. The first model on the left ("Crude estimates") is unadjusted for other covariates. Each model is then adjusted for an additional set of covariates based on when the variables were measured (sociodemographics, pre-AMI comorbidities/medications, characteristics of the index AMI hospitalization, and post-AMI follow-up/medications/stroke/recurrent AMI).

* Point estimate does not fall within the 95% confidence interval for the fully adjusted model.

† Fully adjusted model also presented in Figure 5 within the manuscript.

Abbreviations: AMI, acute myocardial infarction; CI, confidence interval; Hosp, measures from the index AMI hospitalization; HR, hazard ratio; Pre, pre-AMI measures; Sociodem, sociodemographic measures.

Table S5. Sensitivity analyses involving changing variable definitions or adding new variables to the model estimating the association between all-cause mortality and change in statin adherence after acute myocardial infarction (AMI).

Statin adherence change after AMI		Fully adjusted model*	Conservative adherence change measure†	Add statin intensity variable‡	Add liver disease variable§
Pre-AMI adherence	**Post-AMI adherence**	HR (95% CI)			
Severely nonadherent	Severely nonadherent	1.	1.	1.	1.
	Moderately nonadherent	0.89 (0.80, 0.99)	0.88 (0.79, 0.98)	0.85 (0.77, 0.95)	0.89 (0.80, 0.99)
	Adherent	0.83 (0.75, 0.92)	0.83 (0.74, 0.92)	0.79 (0.71, 0.88)	0.83 (0.75, 0.92)
Moderately nonadherent	Severely nonadherent	1.11 (1.01, 1.22)	1.10 (1.00, 1.21)	1.10 (1.00, 1.21)	1.11 (1.01, 1.22)
	Moderately nonadherent	0.90 (0.82, 0.98)	0.89 (0.82, 0.98)	0.86 (0.79, 0.94)	0.90 (0.82, 0.98)
	Adherent	0.84 (0.77, 0.91)	0.84 (0.77, 0.91)	0.80 (0.74, 0.87)	0.84 (0.77, 0.91)
Adherent	Severely nonadherent	1.09 (0.99, 1.20)	1.09 (0.99, 1.20)	1.09 (0.99, 1.20)	1.09 (0.99, 1.20)
	Moderately nonadherent	1.04 (0.96, 1.13)	1.06 (0.97, 1.15)	1.00 (0.92, 1.08)	1.04 (0.96, 1.13)
	Adherent	0.88 (0.82, 0.94)	0.88 (0.82, 0.94)	0.84 (0.79, 0.89)	0.88 (0.82, 0.94)

All four models are estimating the association between all-cause mortality and change in statin adherence using Cox proportional hazards models. No point estimates from sensitivity analyses fell outside of the 95% confidence intervals from the fully adjusted model.

* Fully adjusted model also presented in Figure 5 within the manuscript.

† This model changed the definition of the statin adherence change measure to make it more conservative, attempting to eliminate the influence of small changes in adherence near the category cutoffs. This measure required a categorical change in statin adherence to also be at least a 10% absolute difference from pre- to post-AMI PDC (e.g. a change from pre-AMI PDC of 78% to post-AMI PDC of 84% would not be considered an increase in adherence from "moderately nonadherent" to "adherent"; instead, it would be defined as no change in adherence from "moderately nonadherent" to "moderately nonadherent". Changing the definition of this measure resulted in 571 patients being reclassified from a decrease in adherence to no change and 624 patients being reclassified from an increase in adherence to no change.

‡ Statin intensity was measured using the LAST statin prescription claim filled BEFORE the index AMI hospitalization and using the FIRST claim filled AFTER the index hospitalization discharge. Statin intensity was measured using the 2013 American College of Cardiology/ American Heart Association Guideline on Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults. Both of these variables were added to the model and the variable for simvastatin-equivalent change in average daily dose was removed from the model.

§ CCI measures of liver disease were added as separate variables to the model. The CCI score variable was further adjusted by not including mild and moderate/severe liver disease (as previously described, CCI measures of previous AMI and dementia were not included in the CCI score variable).

Abbreviations: AMI, acute myocardial infarction; CCI, Charlson comorbidity index; CI, confidence interval; HR, hazard ratio; PDC, proportion of days covered.

Table S6. Sensitivity analyses with restricted study eligibility estimating the association between all-cause mortality and change in statin adherence after acute myocardial infarction (AMI).

Statin adherence change after AMI		Fully adjusted model*	Prevalent statin users†,‡	Persistent statin users§	Prevalent & persistent users‖,‡	Multiple pre-AMI statin fills#	Prevalent users with multiple pre-AMI fills**,‡	No AMI or stroke 6-month post-AMI††
Pre-AMI adherence	**Post-AMI adherence**	N=101,011	N=90,791	N=95,228	N=85,008	N=92,674	N=86,452	N=93,770
		HR (95% CI)						
Sev NA	Sev NA	1.	1.	1.	1.	1.	1.	1.
	Mod NA	0.89 (0.80, 0.99)	0.88 (0.79, 0.99)	0.86 (0.75, 0.99)	0.85 (0.74, 0.98)	0.85 (0.74, 0.97)	0.84 (0.73, 0.95)	0.88 (0.78, 0.99)
	Adherent	0.83 (0.75, 0.92)	0.81 (0.72, 0.90)	0.86 (0.76, 0.98)	0.84 (0.73, 0.96)	0.88 (0.78, 0.99)	0.86 (0.76, 0.97)	0.83 (0.74, 0.93)
Mod NA	Sev NA	1.11 (1.01, 1.22)	1.09 (0.99, 1.21)	1.13 (1.02, 1.26)	1.12 (0.99, 1.26)	1.12 (1.00, 1.24)	1.10 (0.98, 1.23)	1.09 (0.98, 1.21)
	Mod NA	0.90 (0.82, 0.98)	0.88 (0.80, 0.97)	0.92 (0.83, 1.02)	0.91 (0.81, 1.01)	0.89 (0.81, 0.99)	0.88 (0.79, 0.98)	0.89 (0.81, 0.99)
	Adherent	0.84 (0.77, 0.91)	0.82 (0.75, 0.89)	0.86 (0.78, 0.95)	0.84 (0.76, 0.94)	0.84 (0.77, 0.93)	0.82 (0.74, 0.91)	0.85 (0.77, 0.93)
Adherent	Sev NA	1.09 (0.99, 1.20)	1.13 (1.02, 1.25)	1.12 (1.00, 1.25)	1.15 (1.02, 1.30)	1.12 (1.01, 1.25)	1.13 (1.01, 1.27)	1.07 (0.97, 1.19)
	Mod NA	1.04 (0.96, 1.13)	1.06 (0.98, 1.16)	1.07 (0.97, 1.18)	1.09 (0.98, 1.21)	1.07 (0.97, 1.17)	1.07 (0.97, 1.18)	1.04 (0.95, 1.14)
	Adherent	0.88 (0.82, 0.94)	0.88 (0.82, 0.94)	0.90 (0.83, 0.98)	0.90 (0.82, 0.99)	0.89 (0.82, 0.96)	0.88 (0.81, 0.95)	0.87 (0.81, 0.94)

All seven models are estimating the association between all-cause mortality and change in statin adherence using Cox proportional hazards models. No point estimates from sensitivity analyses fell outside of the 95% confidence intervals from the fully adjusted model.

* Fully adjusted model also presented in Figure 5 within the manuscript.

† Excluded "new users" of statins who had first statin prescription fill within 6 months pre-AMI.

‡ Model not adjusted for the "new user" variable (every patient had the same value for this variable).

§ Excluded patients who had a PDC of 0% during the 6-month pre-AMI period (i.e. had no statin available during pre-AMI adherence measurement period).

‖ Excluded "new users" of statin and patients with a pre-AMI PDC of 0%

Excluded patients with only one statin prescription fill in the 12-month pre-AMI period.

** Excluded "new users" and patients with only one statin prescription fill in the 12-month pre-AMI period.

†† Excluded patients who experienced a recurrent AMI or stroke hospitalization within 6 months after index AMI hospitalization discharge. These hospitalizations were therefore not included in model for this sensitivity analysis.

Abbreviations: AMI, acute myocardial infarction; CI, confidence interval; HR, hazard ratio; Mod NA, moderately nonadherent; PDC, proportion of days covered; Sev NA, severely nonadherent.

Table S7. Association between all-cause mortality and change in statin adherence, adjusted for changes in ACE/ARB and beta-blocker adherence, among the subgroup of prevalent users for all 3 medication classes: models adjusted iteratively based on the timing of covariate measurement and comparison to final model from manuscript.

			Subgroup of prevalent ACE/ARB & beta-blocker users (N=48,580) Model adjusted for				
Statin adherence change after AMI		Original fully adjusted model† (N=101,011)	Only ACE/ARB & beta-blocker adherence change	+ Sociodem	+ Sociodem + Pre	+ Sociodem + Pre + Hosp	Fully adjusted model
Pre-AMI adherence	**Post-AMI adherence**	HR (95% CI)					
Severely nonadherent	Severely nonadherent	1.	1.	1.	1.	1.	1.
	Moderately nonadherent	0.89 (0.80, 0.99)	0.76 (0.65, 0.89)*	0.77 (0.66, 0.89)*	0.80 (0.69, 0.93)	0.85 (0.73, 0.99)	0.91 (0.78, 1.06)
	Adherent	0.83 (0.75, 0.92)	0.80 (0.69, 0.93)	0.79 (0.68, 0.92)	0.85 (0.73, 0.98)	0.90 (0.78, 1.05)	0.98 (0.84, 1.13)*
Moderately nonadherent	Severely nonadherent	1.11 (1.01, 1.22)	1.15 (1.01, 1.31)	1.14 (1.00, 1.30)	1.17 (1.03, 1.34)	1.14 (1.00, 1.31)	1.16 (1.02, 1.33)
	Moderately nonadherent	0.90 (0.82, 0.98)	0.79 (0.70, 0.90)*	0.80 (0.70, 0.90)*	0.82 (0.72, 0.93)	0.84 (0.74, 0.95)	0.88 (0.77, 1.00)
	Adherent	0.84 (0.77, 0.91)	0.78 (0.69, 0.88)	0.77 (0.69, 0.86)	0.80 (0.71, 0.90)	0.83 (0.74, 0.93)	0.89 (0.79, 1.01)
Adherent	Severely nonadherent	1.09 (0.99, 1.20)	1.22 (1.07, 1.39)*	1.17 (1.03, 1.34)	1.16 (1.02, 1.33)	1.11 (0.97, 1.27)	1.12 (0.98, 1.28)
	Moderately nonadherent	1.04 (0.96, 1.13)	1.06 (0.95, 1.19)	1.03 (0.92, 1.16)	1.04 (0.93, 1.17)	1.04 (0.93, 1.16)	1.07 (0.96, 1.21)
	Adherent	0.88 (0.82, 0.94)	0.86 (0.78, 0.94)	0.83 (0.75, 0.91)	0.85 (0.77, 0.93)	0.86 (0.78, 0.94)	0.92 (0.84, 1.02)

Cox proportional hazards models for the subgroup of patients (N=48,580) who were already taking the following medications before the index AMI: (1) a statin, (2) an ACE inhibitor or ARB, and (3) a beta-blocker. The first model on the left ("Original fully adjusted model") is the primary model found in Figure 5 within the manuscript (N=101,011). The second model ("Only ACE/ARB & beta-blocker adherence change") is only adjusted for these adherence change measures (N=48,580). Each model is then adjusted for an additional set of covariates based on when the variables were measured (sociodemographics, pre-AMI comorbidities/medications, characteristics of the index AMI hospitalization, and post-AMI follow-up/medications/stroke/recurrent AMI in the "Fully adjusted model" on the right).

* Point estimate does not fall within the 95% confidence interval for the original fully adjusted model.

† Original fully adjusted model also presented in Figure 5 within the manuscript.

Abbreviations: ACE inhibitor, angiotensin-converting enzyme inhibitor; AMI, acute myocardial infarction; ARB, angiotensin II receptor blocker; CI, confidence interval; Hosp, measures from the index AMI hospitalization; HR, hazard ratio; Pre, pre-AMI measures; Sociodem, sociodemographic measures.

Table S8. Full model results for the association between all-cause mortality and change in statin adherence after acute myocardial infarction, adjusted for changes in ACE/ARB and beta-blocker adherence, among the subgroup of prevalent users for all 3 medication classes (N=48,580).

Patient characteristics		**HR (95% CI)**
Statin adherence change*		
Pre-AMI adherence	**Post-AMI adherence**	
Severely nonadherent	Severely nonadherent	1.
	Moderately nonadherent	0.91 (0.78, 1.06)
	Adherent	0.98 (0.84, 1.13)
Moderately nonadherent	Severely nonadherent	1.16 (1.02, 1.33)
	Moderately nonadherent	0.88 (0.77, 1.00)
	Adherent	0.89 (0.79, 1.01)
Adherent	Severely nonadherent	1.12 (0.98, 1.28)
	Moderately nonadherent	1.07 (0.96, 1.21)
	Adherent	0.92 (0.84, 1.02)
ACE inhibitor/ARB adherence change*		
Pre-AMI adherence	**Post-AMI adherence**	
Severely nonadherent	Severely nonadherent	1.
	Moderately nonadherent	0.82 (0.70, 0.96)
	Adherent	0.84 (0.72, 0.98)
Moderately nonadherent	Severely nonadherent	0.92 (0.82, 1.04)
	Moderately nonadherent	0.92 (0.81, 1.04)
	Adherent	0.77 (0.68, 0.86)
Adherent	Severely nonadherent	1.02 (0.92, 1.14)
	Moderately nonadherent	0.92 (0.83, 1.02)
	Adherent	0.80 (0.73, 0.87)
Beta-blocker adherence change*		
Pre-AMI adherence	**Post-AMI adherence**	
Severely nonadherent	Severely nonadherent	1.
	Moderately nonadherent	0.87 (0.72, 1.04)
	Adherent	0.85 (0.72, 1.01)
Moderately nonadherent	Severely nonadherent	1.02 (0.86, 1.21)
	Moderately nonadherent	0.95 (0.82, 1.10)
	Adherent	0.95 (0.83, 1.10)
Adherent	Severely nonadherent	1.03 (0.88, 1.22)
	Moderately nonadherent	1.11 (0.97, 1.28)
	Adherent	0.97 (0.86, 1.10)
Sociodemographics		
Age		
66-75		1.
76-85		1.31 (1.24, 1.39)
86+		1.87 (1.75, 2.00)
Female		0.83 (0.79, 0.88)
Race/ethnicity		

Patient characteristics	HR (95% CI)
White	1.
Black	0.91 (0.84, 0.99)
Hispanic	0.84 (0.73, 0.95)
Asian	0.80 (0.68, 0.95)
Other	0.89 (0.75, 1.06)
Dual eligibility[†]	1.10 (1.04, 1.16)
Household income[‡]	
≤$30,000	1.
$30,001-60,000	1.02 (0.97, 1.07)
$60,001-100,000	0.97 (0.89, 1.06)
$100,001-150,000	1.03 (0.85, 1.25)
>$150,000	1.01 (0.73, 1.40)
Pre-AMI comorbidities and cardiovascular procedures[§]	
Adjusted Charlson comorbidity index[‖]	
0	1.
1-2	1.37 (1.24, 1.51)
3-5	1.99 (1.81, 2.20)
6-8	2.64 (2.36, 2.95)
9+	4.22 (3.64, 4.89)
Baseline comorbidities and procedures	
Prior AMI[#]	1.15 (1.06, 1.24)
Dementia/Alzheimer's disease**	1.24 (1.16, 1.33)
Depression	1.05 (0.99, 1.12)
CABG	0.51 (0.39, 0.66)
PTCA/stent	0.82 (0.75, 0.90)
Ischemic heart disease	1.02 (0.96, 1.08)
Unstable angina	1.10 (1.01, 1.20)
Lipid abnormalities[§§§]	0.80 (0.74, 0.87)
Rhabdomyolysis/myopathy	0.91 (0.83, 0.99)
Pre-AMI medications	
New user of statin[††]	0.95 (0.87, 1.03)
New user of ACE inhibitor/ARB[††]	1.01 (0.92, 1.10)
New user of beta-blocker[††]	0.98 (0.90, 1.07)
Concurrent medications[‡‡]	
P2Y12 inhibitor	1.04 (0.99, 1.10)
Calcium channel blocker	1.05 (0.99, 1.12)
Aldosterone receptor antagonist	1.07 (0.98, 1.17)
Characteristics of index AMI hospitalization	
Clinical diagnoses and procedures	
Subendocardial infarction[§§]	1.08 (1.00, 1.16)
CABG	0.35 (0.29, 0.42)
PTCA/stent	0.80 (0.74, 0.86)
Antiplatelet use	0.83 (0.71, 0.97)
Cardiac catheterization	0.82 (0.74, 0.91)
Angiocardiography	0.84 (0.76, 0.93)
Cardiogenic shock	0.89 (0.73, 1.09)

Patient characteristics	HR (95% CI)
Cardiac dysrhythmia	1.10 (1.04, 1.15)
Hypotension	0.96 (0.86, 1.08)
Acute renal failure	1.13 (1.07, 1.20)
Heart failure	1.48 (1.41, 1.56)
Duration of hospitalization	
1-3	1.
4-6	1.11 (1.05, 1.17)
7-11	1.24 (1.16, 1.33)
12+	1.33 (1.21, 1.47)
Admission to intensive care	
None	1.
Coronary care unit only	0.96 (0.90, 1.03)
Intensive care unit only	0.97 (0.92, 1.03)
Both	0.95 (0.87, 1.04)
Cardiologist consultation	1.02 (0.95, 1.09)
30-day post-AMI follow-up	
None	1.
Primary care provider‖‖ only	0.91 (0.84, 0.98)
Cardiologist only	0.81 (0.75, 0.89)
Both	0.87 (0.81, 0.93)
Post-AMI medications	
Change in simvastatin-equivalent average daily dose##	1.00 (1.00, 1.00)
Concurrent medications***	
P2Y12 inhibitor	0.96 (0.90, 1.02)
Calcium channel blocker	0.86 (0.81, 0.91)
Aldosterone receptor antagonist	1.23 (1.14, 1.32)
Post-AMI clinical events	
Hospitalization for recurrent AMI†††	1.94 (1.81, 2.07)
Hospitalization for stroke‡‡‡	1.71 (1.44, 2.03)

These are the results for the fully adjusted Cox proportional hazards model for the subgroup of patients (N=48,580) who were already taking the following medications before the index AMI: (1) a statin, (2) an ACE inhibitor or ARB, and (3) a beta-blocker (results for this model were also presented in the far right column ["Fully adjusted model"] of Supplemental Table S7). The purpose of this model was to estimate the association between all-cause mortality and change in statin adherence, while also adjusting for the change in ACE inhibitor/ARB adherence and the change in beta-blocker adherence.

* The HRs for the association between adherence change and mortality in this model should be interpreted with caution given the high level of correlation between adherence change for all 3 medications: statins, ACE/ARBs, and beta-blockers. Adherence was measured separately in the 6 months pre-AMI and the 6 months post-AMI. Adherence was categorized as follows: severely nonadherent (PDC <40%), moderately nonadherent (PDC 40-79.9%), and adherent (PDC ≥80%). Change in adherence was defined as a categorical change in adherence.

† Enrolled in Medicare and Medicaid.

‡ Median household income of US Census block groups for individuals aged 65 and older.

§ Measured in the 12 months prior to the index AMI hospital admission date.

‖ CCI score does not include counts for AMI and dementia.

CCI definition.

Patient characteristics	HR (95% CI)

** Medicare Chronic Conditions Data Warehouse definition.

†† First prescription claim for medication was identified during the 6 months prior to the index AMI hospital admission date.

‡‡ At least one prescription fill within medication class during the 6 months prior to the index AMI hospital admission date.

§§ Index AMI had diagnosis code for subendocardial infarction, compared to transmural infarction.

‖‖ Primary care physician, physician assistant, or nurse practitioner.

Continuous weighted average of the simvastatin-equivalent average daily dose in the post-AMI period minus the weighted average in the pre-AMI period. Dose equivalency calculations were made as follows: fluvastatin, pravastatin, and lovastatin doses in mg were divided by 4, 2, and 2, respectively; atorvastatin, rosuvastatin, and pitavastatin doses were multiplied by 2, 4, and 10, respectively.

*** At least one prescription fill within medication class during the index AMI hospitalization period or within 6 months after index AMI discharge date.

††† Inpatient ICD-9 diagnosis code of 410.x1 in the primary or secondary discharge field within 6 months after index AMI discharge date.

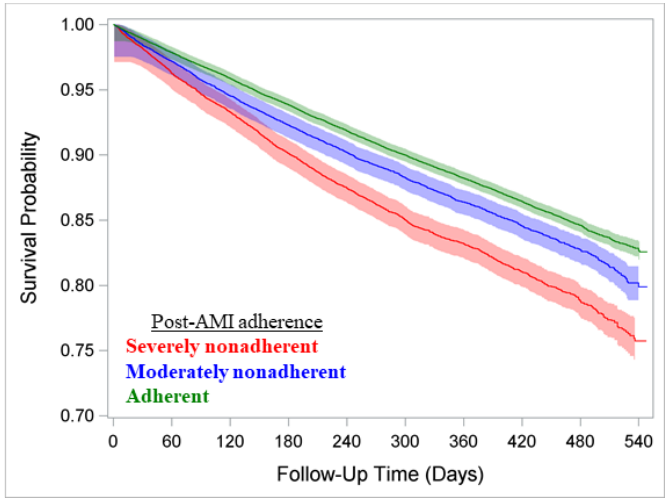
‡‡‡ Inpatient ICD-9 diagnosis code of 430, 431, 433.x1, 434.x1, or 436 in the primary discharge field within 6 months after index AMI discharge date.

§§§ Inpatient or outpatient ICD-9 diagnosis code of 272.xx in any position.

Abbreviations: ACE, angiotensin-converting enzyme; AMI, acute myocardial infarction; ARB, angiotensin II receptor blocker; CABG, coronary artery bypass surgery; CCI, Charlson comorbidity index; CI, confidence interval; HR, hazard ratio; ICD-9, International Classification of Diseases, Ninth Revision; PDC, proportion of days covered; PTCA, percutaneous transluminal coronary angioplasty.

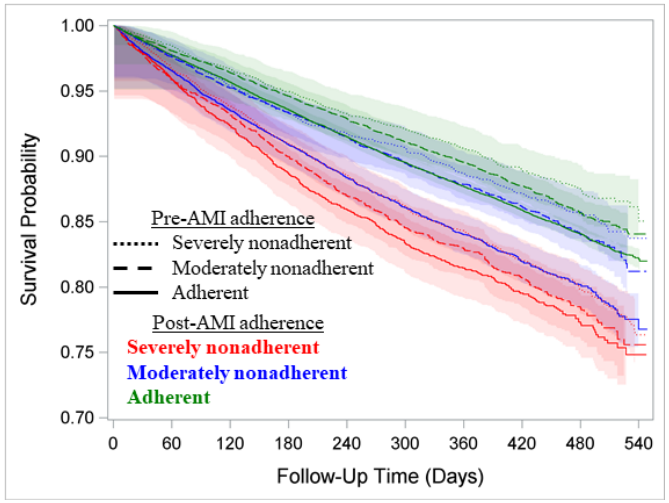
Figure S1. Unadjusted survival curves and 95% confidence bands for all-cause mortality after acute myocardial infarction, stratified by statin adherence.

A



Post-AMI statin adherence	12-month* survival probability (95% confidence interval)
Severely nonadherent	0.832 (0.825-0.838)
Moderately nonadherent	0.864 (0.859-0.869)
Adherent	0.882 (0.879-0.885)

B



Pre-AMI statin adherence	Post-AMI statin adherence	12-month* survival probability (95% confidence interval)
Severely nonadherent	Severely nonadherent	0.843 (0.833-0.852)
Moderately nonadherent		0.829 (0.816-0.841)
Adherent		0.815 (0.801-0.828)
Severely nonadherent	Moderately nonadherent	0.887 (0.876-0.897)
Moderately nonadherent		0.879 (0.870-0.887)
Adherent		0.840 (0.832-0.848)
Severely nonadherent	Adherent	0.906 (0.897-0.914)
Moderately nonadherent		0.895 (0.889-0.901)
Adherent		0.877 (0.874-0.880)

Follow-up begins 6 months after index AMI discharge (i.e. Day 0 is 180 days after index AMI discharge). A: Stratified by **post-AMI** statin adherence. B: Stratified by change in statin adherence from pre- to post-AMI.
* 12-month estimate calculated from 6 months post-AMI discharge through 18 months post-AMI discharge.
Abbreviations: AMI, acute myocardial infarction.

Figure S2. Schoenfeld residuals (dots) with smooth fitted spline (line) for statin adherence change.