

Persisting sex differences in high-intensity statin use following myocardial infarction in the United States

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Abstract

Background: Historically, women have been less likely than men to receive guideline-recommended statin therapy for the secondary prevention of myocardial infarction (MI).

Objective: We examined contemporary sex differences in prescription fills for high-intensity statin therapy following a MI, overall and across population subgroups, and assessed whether sex differences were attenuated following recent efforts to reduce sex disparities in the use of cardiovascular disease preventive therapies.

Methods: We studied 16,898 (26% women) US adults <65 years of age with commercial health insurance in the MarketScan database, and 71,358 (49% women) US adults ≥ 66 years of age with government health insurance through Medicare who filled statin prescriptions within 30 days after hospital discharge for MI in 2014-2015. We calculated adjusted women-to-men risk ratios (RRs) and 95% confidence intervals for filling a high-intensity statin prescription (i.e., atorvastatin 40-80mg, and rosuvastatin 20-40mg) following hospital discharge for MI.

Results: In 2014-2015, 56% of men and 47% of women filled a high-intensity statin following hospital discharge for MI. Adjusted RRs (95% CI) for filling a high-intensity statin comparing women to men were 0.91 (0.90, 0.92) in the total population, 0.91 (0.89, 0.92) among those with no prior statin use, and 0.87 (0.85, 0.90) and 0.98 (0.97, 1.00) for those taking low/moderate and high-intensity statins prior to their MI, respectively. Women were less likely than men to fill high-intensity statins within all subgroups and the disparity was larger in the youngest and oldest adults and for those without prevalent comorbid conditions.

Conclusions: Despite recent efforts to reduce sex differences in guideline-recommended therapy, women continue to be less likely than men to fill a prescription for high-intensity statins following hospitalization for MI.

Condensed abstract

Historically, women were less likely than men to receive guideline-recommended statin therapy after myocardial infarction (MI). We assessed whether these sex differences still exist attenuated following recent efforts to reduce sex disparities in the use of preventive therapies in a contemporary US population. While the use of high-intensity statins increased in both sexes who filled any statin prescription following MI between 2007 and 2015, women continue to be less likely than men to fill a prescription for high-intensity statins. The underutilization of high-intensity statins in women can be expected to result in a substantial additional number of preventable vascular events.

Abbreviations

ACC/AHA, American College of Cardiology/American Heart Association

CHD, coronary heart disease

CI, confidence interval

CMS, Centers for Medicare and Medicaid Services

CVD, cardiovascular disease

MI, myocardial infarction

RCT, randomized controlled trial

RR, risk ratio

Introduction

The efficacy and safety of more-intensive versus less-intensive statin therapy for the secondary prevention of cardiovascular disease (CVD) has been established in several randomized controlled trials (RCTs).(1) The 2013 American College of Cardiology (ACC)/American Heart Association (AHA) guideline on the treatment of blood cholesterol to reduce atherosclerotic CVD risk in adults recommends the use of high-intensity statin therapy for patients ≤ 75 years of age with established CVD.(2) Moderate-intensity statin therapy is recommended for patients >75 years of age with established CVD. The 2013 ACC/AHA guideline on the treatment of blood cholesterol did not make sex-specific recommendations on statin dosage. This is supported by recent findings from a large meta-analysis of individual participant data of RCTs which demonstrated that the benefits of more-intensive versus less-intensive statin therapy among patients with a history of vascular disease were similar between men and women.(3)

Despite the similar efficacy of more- versus less-intensive statins for both sexes, analyses have consistently demonstrated that not only are women less likely than men to receive statin therapy for the secondary prevention of CVD,(4-10) but that, when prescribed a statin, the intensities are also lower in women than men.(5,6) Substantial efforts have been made to reduce sex differences in CVD and to recognize the importance of CVD in women, including the Go Red for Women initiative and the publication of three AHA evidence-based guidelines for the prevention of CVD in women.(11-15) However, it is unknown whether the 2013 ACC/AHA cholesterol treatment guideline and initiatives to raise awareness of CVD in women have reduced the gap between women and men in the use of high-intensity statin therapy for the secondary prevention of CVD. Moreover, while the overall uptake of high-intensity statins in secondary prevention has increased substantially in recent years, sex differences in the use of

high-intensity statin therapy following a hospital admission for myocardial infarction (MI) have not been assessed in detail.(16)

In this study, we used data from two large cohorts of US adults to assess the contemporary use of high-intensity statin therapy following an MI among women compared with men, and to identify factors associated with the underutilization of statin therapy among women. Moreover, we examined the sex-specific secular trends in the intensity of dosages of statin therapy from 2007 to 2015.

Methods

Data sources

We conducted a retrospective cohort study using administrative data from MarketScan and Medicare. The MarketScan database contains data for individuals in the US with commercial and Medicare supplemental health insurance and were obtained through the Truven Health MarketScan Research Database. Medicare is a government program that provides health insurance for US adults ≥ 65 years of age and younger adults with end-stage renal disease or who are disabled. Medicare data were obtained from the US Centers for Medicare and Medicaid Services (CMS) Chronic Conditions Warehouse. The current study was approved by the Institutional Review Board at the University of Alabama at Birmingham and the US CMS.

Study population

The primary study population was composed of adults in the MarketScan and Medicare databases with an overnight hospitalization for MI (defined by an International Classification of Diseases, ninth revision, clinical modification [ICD-9-CM] code of 410.x0 or 410.x1 in any

discharge diagnosis position) between January 1, 2014 and June 30, 2015 (**Supplemental Figure 1 and Supplemental Table 1**). To avoid overlap among beneficiaries with Medicare coverage, we excluded beneficiaries in the Marketscan database ≥ 65 years of age on their MI hospital admission date. Similarly, we excluded beneficiaries < 66 years of age on their MI hospital admission date in the Medicare database to allow a 1-year lookback period to identify baseline characteristics. Thus, no subjects in our combined database were aged 65 at their last birthday. Medicare beneficiaries were further required to be alive 30 days after their MI hospital discharge date resulting in the exclusion of 10% of men and 12% of women. Date of death is not available in Marketscan. We further restricted the analyses to patients who had continuous insurance coverage, including pharmacy benefits, and lived in the US, from 365 days prior to their MI hospital admission date through 30 days after their discharge date. We excluded beneficiaries who were admitted in an acute care facility, skilled nursing facility, or hospice within 30 days of their MI hospital discharge. We restricted the analysis to beneficiaries who had a statin fill for any dosage within 30 days of hospital discharge. In 2011, the US Food and Drug Administration recommended not prescribing simvastatin 80 mg to reduce the risk of muscle injuries associated with this medication.⁽¹⁷⁾ Beneficiaries whose initial statin fill following hospital discharge for MI was for simvastatin 80 mg were therefore excluded. For beneficiaries in Marketscan and Medicare who had multiple hospitalizations for MI meeting the inclusion criteria for the current analysis, only the first event was analyzed. To examine trends in sex differences in high-intensity statin use over time, we assembled a second study population which included beneficiaries with a MI hospitalization between January 1, 2007 and June 30, 2015, who met the inclusion criteria described above.

Statin use

Statin use was identified by pharmacy prescription fills using generic names, and included atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, and simvastatin. The intensity of each statin type was defined in accordance with the 2013 ACC/AHA cholesterol guideline,(2) as shown in **Supplemental Table 2**. For the main analysis, high-intensity statin use following hospital discharge for MI included atorvastatin 40 or 80mg and rosuvastatin 20 or 40mg.

Beneficiaries' characteristics

Age at the time of admission for the index MI and sex were obtained from the MarketScan Commercial Claims and Encounters database and the Medicare beneficiary summary file. Information on race/ethnicity is also available from the Medicare beneficiary summary file, but was not available for beneficiaries in MarketScan. Diabetes, coronary heart disease (CHD), stroke, heart failure, peripheral artery disease, chronic kidney disease, depression, Charlson comorbidity index, all-cause hospitalizations, cardiologist care, use of non-statin lipid-lowering therapy, and the total number of different prescription medications filled were identified using data in the 365 days prior to hospital admission for MI and previously published algorithms (**Supplemental Table 3**). Information on the use of cardiac rehabilitation and prescription fills for beta-blockers, antiplatelet agents, and non-statin lipid-lowering therapies within 30 days after hospital discharge for the index MI was also obtained.

Statistical analyses

Baseline characteristics and the percentage of patients filling a high-intensity statin following hospital discharge for MI were summarized for men and women separately, with the statistical significance of differences assessed using logistic regression for dichotomous variables and linear regression for continuous variables. Poisson regression models with sandwich estimators and progressive adjustment for potential confounders, selected a priori, were used to obtain risk ratios (RRs), 95% confidence intervals (CIs), and p-values for filling a high-intensity versus low/moderate-intensity statin following hospital discharge for MI among women compared to men. Model 1 adjusted for age, prior statin use and dosage, and ethnicity/race (only for Medicare beneficiaries). Model 2 adjusted for variables in Model 1 plus history of diabetes, CHD, stroke, peripheral artery disease, heart failure, and chronic kidney disease, depression, Charlson comorbidity index, all-cause hospitalization, cardiologist care, non-statin lipid lowering medication use, and total number of medications taken in the 365 days prior to the MI hospital admission date. Model 3 adjusted for variables in Model 2 plus the use of cardiac rehabilitation and prescription fills for beta-blockers, antiplatelet agents, and non-statin lipid-lowering therapies within 30 days after hospital discharge. Analyses were conducted overall and stratified by statin use and dosage (i.e., low/moderate and high-intensity) prior to the index MI. Subgroup analyses were conducted to assess the consistency of the associations across each of the demographic characteristics, comorbidities, and health care use covariables included in Model 3. Differences in RRs across subgroups were assessed by adding an interaction term to the models.

Sex-specific trends in high-intensity statin prescription fills following discharge for MI between 2007 and 2015 were assessed for the overall population and stratified by prior statin use and dosage. We also assessed the trends in RRs for high-intensity statin prescription fills among women versus men by calendar year between 2007 and 2015, after multivariable adjustment for

variables included in Model 3. As mentioned previously, patients filling simvastatin 80 mg following hospital discharge for MI were excluded from our primary analyses. We conducted a sensitivity analysis to determine whether the trend on sex differences in high-intensity statin use remained present when including those who had a prescription fill for simvastatin 80 mg within 30 days of hospital discharge following MI. The analyses described above were repeated among beneficiaries <65 years of age in the MarketScan database and Medicare beneficiaries ≥ 66 years of age, separately. All analyses were conducted using SAS version 9.4 software (SAS Institute Inc., Cary, NC). We considered a p-value <0.05 to denote statistical significance.

Results

In total, 16,898 (26% women) beneficiaries <65 years of age in MarketScan and 71,358 (49% women) Medicare beneficiaries ≥ 66 years of age filled statin prescriptions within 30 days after hospital discharge for MI in 2014-2015 (**Table 1 and Supplemental Table 4**).

Sex differences in the use of high-intensity statin therapy

High-intensity dosages were the first statin prescription fill following hospital discharge after MI for 56% of men and 47% of women; 68% of men and 60% of women in MarketScan and 53% of men and 45% of women in Medicare (**Table 2 and Supplemental Table 5**). The percentage of beneficiaries whose first statin prescription fill following hospital discharge for MI was for high-intensity dosages was 61% in men and 50% in women with no prior statin use, 39% in men and 30% in women with prior low/moderate-intensity statin use, and 92% in men and 90% in women with prior high-intensity statin use.

After adjustment for demographic characteristics, comorbidities, and health care use (Model 3), the women-to-men RRs (95% CI) for high-intensity statin use were 0.91 (0.90, 0.92) in the total population of statin users, 0.91 (0.89, 0.92) among those with no prior statin use, 0.87 (0.85, 0.90) among those with prior low/moderate-intensity statin use, and 0.98 (0.97, 1.00) among those with prior high-intensity statin use (p for interaction by prior statin use and dosages <0.001).

Sex differences in the use of high-intensity statins following MI were present in all subgroups, but differed in magnitude by age group, history of diabetes, history of CHD, history of heart failure, Charlson comorbidity index, and antiplatelet prescription fill 30-days after discharge (**Figure 1 and Supplemental Table 6**). There was a trend towards an attenuation, but not removal, of the sex difference in high-intensity statin use with higher age among those ≤ 75 years, but the difference increased in the 75 years and over age group.

Analyses stratified by prior statin use suggested that the sex differences in the use of high-intensity statins post-MI across patient characteristics were more pronounced among those without prior statin use and those with prior low/moderate intensity statin use (**Supplemental Tables 7-9**). Results were similar for MarketScan and Medicare beneficiaries when analyzed separately (**Supplemental Tables 10-13**).

Sex-specific trends in the use of high-intensity statin therapy

Between 2007 and 2015, the percentage of beneficiaries whose first statin prescription fill following hospital discharge after MI was for a high-intensity statin increased from 27% to 60% in men and from 22% to 50% in women (**Central illustration, Supplemental Figure 2, and Supplemental Tables 14-15**). The percentage of beneficiaries filling high-intensity statins

increased from 27% to 64% in men and 22% to 50% in women with no prior statin use, from 14% to 42% in men and from 10% to 33% in women with prior low/moderate intensity statin use, and from 81% to 93% in men and from 81% to 91% in women with prior high-intensity statin use. There was no evidence of a diminishing of the sex differential in the use of high-intensity statins post-MI following the 2013 ACC/AHA cholesterol guidelines. In the overall population, the women-to-men RR ranged from 0.94 (0.91, 0.97) in 2007 to 0.91 (0.89, 0.93) in 2015 (**Figure 2 and Supplemental Table 16**). No trends in the women to men RR were present when beneficiaries without prior statin use, with prior low/moderate-intensity statin use and with prior high-intensity statin use were analyzed separately. Sensitivity analysis including beneficiaries who had a prescription fill for simvastatin 80 mg within 30 days following hospital discharge for MI yielded similar findings (**Supplemental Tables 17-19**). Furthermore, additional adjustment for region of residence and socioeconomic status did minimally change the results (Supplemental Table 20).

Discussion

In this study of more than 88,000 US adults who filled a statin prescription following a hospitalization for MI in 2014-15, women were less likely than men to have filled a prescription for high-intensity dosage. The underutilization of high-intensity statins in women was not explained by sex differences in demographic characteristics, comorbidities, and health care utilization. The lower use of high-intensity statins among women compared with men was consistent across subgroups, but more pronounced among those without prior statin use or with prior low/moderate intensity statin, the youngest and oldest individuals, and those without

prevalent comorbid conditions. There was no evidence of a diminishing of the sex difference in the use of high-intensity statins post-MI between 2007 and 2015.

The findings of the present study are consistent with prior research showing an underutilization of statins, of any dosage, and other effective therapies for the secondary prevention of CVD among women compared to men.(4-9,16) The current study expands prior research by showing that, once prescribed a statin, the intensity of the dosage is lower in women than in men. Moreover, the sex differences were largest among those without prior statin use and those with prior low/moderate intensity statin use, suggesting that women are less likely than men to get up-titrated or less likely to initiate high-intensity statin therapy post-MI. The sex difference in the intensity of statin dosage was present despite unequivocal evidence on the effectiveness and safety of high-intensity statin therapy among men and women with clinical CVD. A recent meta-analysis of individual participant data of five RCTs demonstrated that more-intensive statins versus less-intensive statins reduces the risk of recurrent major vascular events by 29% in men and by 25% in women per 1mmol/L reduction in LDL cholesterol (p for heterogeneity = 0.57).(3) The 2013 ACC/AHA cholesterol guideline does not make a distinction by sex and recommends the use of high-intensity statin therapy among all patients with clinical CVD ≤ 75 years of age.(2) Hence, while the prescription of high-intensity statin therapy for the secondary is suboptimal in both sexes, the greater underutilization of high-intensity statins in women could result in a substantial additional excess vascular events among women,(18) preventable by adherence to guideline-recommended treatment strategies.

The reasons for sex differences in the use of high-intensity statin therapy are unclear. Previous studies have suggested that several patient characteristics, including older age and a higher prevalence of pre-existing comorbidities, and related polypharmacy, may explain the

lower statin treatment rates in women.(19,20) In this study, which was restricted to adults filling a statin prescription, we noted that the magnitude of the sex difference in the use of high-intensity statins after MI was larger among the youngest and oldest patients and, in contrast with other studies, among those *without* a history of diabetes, CHD, or heart failure. The finding of largest sex differences among those in the two extreme age groups is concerning because the oldest are at the highest risk, while young women have recently been shown to have the slowest rate of decline in CVD rates in the US.(10) Despite these age differences, women were consistently less intensively treated across a broad range of patient characteristics and the results were minimally affected by further multivariable adjustment suggesting that factors other than those analyzed in the current study may explain the lower use of high-intensity statins among women compared with men. Some studies have reported that women are more likely to experience side effects from statin therapy than men, which might explain why previous studies reported that statin discontinuation rates are higher in women than men.(21-23) The Understanding Statin Use in America and Gaps in Education (USAGE) survey reported that more women than men are likely to switch or discontinue statin therapy because of muscle-related symptoms.(22) Women typically weigh less than men and tend to have less muscle mass and higher percentages of body fat. Statin dosages are not based on body weight, which may lead to proportionally higher concentrations of statins in women, potentially leading to a higher risk of side effects associated with statins.(24) Most studies that have evaluated the safety of statins did not focus specifically on women.(25-27) However, analyses of six RCTs on statin therapy reported that rates of muscle-related symptoms were slightly higher in women than men in both the statin and placebo groups.(21) These data suggest that the risk for statin associated muscle symptoms should not be a barrier to prescribing high-intensity statins to women.

The sex difference in the use of high-intensity statins may also be explained by variation in the use of evidence-based therapies at the hospital or health care provider level. A recent report from the US Veterans Affairs health care system demonstrated that there was substantial facility-level variation in the use of high-intensity statins among female patients with CVD.(6) Facility-level variability among men was not reported. Moreover, health care providers may perceive women with MI to be at a lower risk of recurrent MI than their male counterparts. In a study of 500 physicians in the US, sex disparities in treatment were explained largely by the provider's lower perceived CVD risk in women, despite a similar calculated risk compared with men.(28) A sub-analysis of this study suggested that interventions aimed at promoting the use of CVD prevention guidelines in women should be directed towards solo practitioners and older physicians.(29) In 2004, the AHA launched the 'Go Red For Women' initiative and since that time has published three evidence-based guidelines for the prevention of CVD in women.(11-14) These guidelines may have contributed to the decline in CVD rates in women.(10,30) However, the results from the current study suggest that they have not led to elimination of the sex differences in high-intensity statin use after MI among individuals who filled any statin prescription. Whether there is a time lag between these efforts, the release of the 2013 ACC/AHA cholesterol guidelines and the elimination of sex differences in the use of high-intensity statins needs to be examined in future studies.

The strengths of this study include the analyses of two contemporary large real-world US healthcare data sources, MarketScan which includes younger patients with commercial health insurance and Medicare which includes older patients with government insurance. Therefore, we could assess temporal sex differences in the use of high-intensity statins across a broad age spectrum and within various other population subgroups. Since over 80% of US adults ≥ 65 years

receive health insurance through Medicare, the current findings have a high degree of generalizability. This study also has some limitations. First, pharmacy claims only identify prescription fills but do not enable assessment of whether beneficiaries took the medication. Moreover, we were unable to assess whether the lower prescription fills for high-intensity statins in women than men were appropriate based on more frequent drug interactions, intolerance to high-intensity statins, or other clinical characteristics. Finally, restricting the analyses to patients who survived 30 days after discharge could have introduced a bias if survival was sex-specific. However, this was not the case in this study.

In conclusion, among individuals who filled a statin prescription, women were less likely than men to fill high-intensity statin dosage following hospitalization for MI. This sex difference was present across a wide range of subpopulations defined by demographic and patient characteristics. While the uptake of high-intensity statins increased in both men and women who filled any statin prescription following MI between 2007 and 2015, there was no attenuation of the sex difference, even after publication of the 2013 ACC/AHA cholesterol guideline. The factors attributable to these sex differences need to be elucidated. Increased awareness of the benefits of high-intensity statins in women among health care providers are needed to reinforce the use of high-intensity statin among women with a prior MI.

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Conflicts of Interest

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Perspectives

Competency in patient care and procedural skills: Women continue to be less likely than men to fill a prescription for high-intensity statin dosage following hospitalization for MI, even after the 2013 ACC/AHA cholesterol guidelines which recommends the use of high-intensity statin therapy for patients ≤ 75 years of age with established CVD, regardless of sex.

Translational Outlook: Further efforts are needed to eliminate sex disparities in high-intensity statin use and to improve the use of high-intensity statin therapy following hospital discharge for MI for all patients.

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Figure legend

Central illustration Trends in the use of high-intensity statin therapy after hospital discharge for myocardial infarction between 2007 and 2015

Black diamonds are the percentage filling high intensity statin among those taking high-intensity statins prior to their myocardial infarction. Red squares are for low/moderate-intensity statin users prior to their myocardial infarction. Blue circles are for statin initiators. Solid lines are for men, dashed lines are for women.

Figure 1 Risk ratios (95% confidence intervals) for filling a high-intensity statin dosage among women versus men across patient characteristics in 2014-2015

CHD: coronary heart disease; CI: confidence interval; CKD: chronic kidney disease; PAD: peripheral artery disease; RR: risk ratio. Models include adjustment for age, race, prior statin use, history of diabetes, CHD, stroke, peripheral artery disease, heart failure, and chronic kidney disease, depression, Charlson comorbidity index, any hospitalization, cardiologist care, non-statin lipid lowering medication use, total number of medications taken and data from 30 days post-discharge (see Table 1).

Figure 2 Risk ratios (95% confidence intervals), for filling a high-intensity statin among women versus men, between 2007 and 2015

The line represents the risk ratio for filling a high-intensity statin comparing women to men and the shaded region shows the 95% confidence intervals. Models include adjustment for age, race, prior statin use, history of diabetes, CHD, stroke, peripheral artery disease, heart failure, and chronic kidney disease, depression, Charlson comorbidity index, any hospitalization, cardiologist care, non-statin lipid lowering medication use, total number of medications taken and data from 30 days post-discharge (see Table 1).

Table 1. Characteristics of adults filling a statin following hospital discharge for myocardial infarction in 2014-2015

Patient characteristics*	Men	Women	p-value‡
n	49,000	39,256	-
Marketscan, n (%)	12,462 (25.4)	4,436 (11.3)	-
Medicare, n (%)	36,538 (74.6)	34,820 (88.7)	-
Age, years, n (%)			
<50	2,630 (5.4)	877 (2.2)	<0.001
50-64	9,832 (20.1)	3,559 (9.1)	
66-75	20,330 (41.5)	15,089 (38.4)	
>75	16,208 (33.1)	19,731 (50.3)	
Race/ethnicity, n (%)†			
White	31,888 (65.1)	29,142 (74.2)	<0.001
African American	2,233 (4.6)	3,579 (9.1)	
Asian American	714 (1.5)	679 (1.7)	
Hispanic	630 (1.3)	734 (1.9)	
Other	1,073 (2.2)	686 (1.7)	
History of diabetes, n (%)	16,591 (33.9)	14,657 (37.3)	<0.001
History of CHD, n (%)	22,328 (45.6)	16,702 (42.5)	<0.001
History of stroke, n (%)	888 (1.8)	853 (2.2)	0.006
History of PAD, n (%)	1,578 (3.2)	1,400 (3.6)	0.515
History of heart failure, n (%)	5,601 (11.4)	6,223 (15.9)	<0.001
History of CKD, n (%)	9,484 (19.4)	8,609 (21.9)	0.454
Depression, n (%)	8,524 (17.4)	12,314 (31.4)	<0.001
Charlson comorbidity index, n (%)			
0	14,233 (29.0)	7,883 (20.1)	<0.001
1-3	16,394 (33.5)	13,205 (33.6)	
≥4	18,373 (37.5)	18,168 (46.3)	
Any hospitalization, n (%)	10,598 (21.6)	11,150 (28.4)	<0.001
Cardiologist care, n (%)	17,779 (36.3)	14,018 (35.7)	<0.001
Non-statin LLM use, n (%)	5,258 (10.7)	3,610 (9.2)	<0.001
Prior statin use, n (%)			
No statin use	22,816 (46.6)	17,962 (45.8)	<0.001
Low/moderate-intensity	19,346 (39.5)	16,599 (42.3)	
High-intensity	6,838 (14.0)	4,695 (12.0)	
Total number of medications taken, n (%)			
<5	13,185 (26.9)	5,834 (14.9)	<0.001
5-9	14,911 (30.4)	10,725 (27.3)	
≥10	20,904 (42.7)	22,697 (57.8)	
Data from 30 days post-discharge, n (%)			
Beta-blocker fill	39,765 (81.2)	31,223 (79.5)	0.019
Antiplatelet agent fill	30,214 (61.7)	21,383 (54.5)	<0.001
Non-statin LLM fill	2,388 (4.9)	1,659 (4.2)	<0.001
Cardiac rehabilitation	7,139 (14.6)	3,762 (9.6)	<0.001

CHD: coronary heart disease; CKD: chronic kidney disease; LLM: lipid-lowering medication; PAD: peripheral artery disease. * Definitions for patient characteristics are provided in **Supplemental Table 3**. † Restricted to beneficiaries in Medicare. ‡ P-values were calculated adjusting for the data source (i.e., MarketScan or Medicare), excepting for age and race. For age, Charlson comorbidity index and number of medications, the tests for differences and trends both had p<0.001.

Table 2. Risk ratios (95% confidence intervals) for filling a high-intensity statin dosage following hospital discharge for myocardial infarction, comparing women versus men in 2014-2015 among US adults in MarketScan and Medicare combined

	Total population (n= 88,256)	
	Men (n= 49,000)	Women (n= 39,256)
Overall population		
High-intensity statin fill, n (%)	27,635 (56.4)	18,270 (46.5)
	Risk ratio (95% CI)	
Model 1	1 (ref)	0.89 (0.88, 0.90)
Model 2	1 (ref)	0.90 (0.89, 0.91)
Model 3	1 (ref)	0.91 (0.90, 0.92)
No prior statin use		
High-intensity statin fill, n (%)	13,838 (60.7)	9,049 (50.4)
	Risk ratio (95% CI)	
Model 1	1 (ref)	0.88 (0.87, 0.90)
Model 2	1 (ref)	0.90 (0.88, 0.91)
Model 3	1 (ref)	0.91 (0.89, 0.92)
Prior low/moderate-intensity statin use		
High-intensity statin fill, n (%)	7,519 (38.9)	5,013 (30.2)
	Risk ratio (95% CI)	
Model 1	1 (ref)	0.84 (0.81, 0.86)
Model 2	1 (ref)	0.85 (0.83, 0.88)
Model 3	1 (ref)	0.87 (0.85, 0.90)
Prior high-intensity statin use		
High-intensity statin fill, n (%)	6,278 (91.8)	4,208 (89.6)
	Risk ratio (95% CI)	
Model 1	1 (ref)	0.98 (0.97, 0.99)
Model 2	1 (ref)	0.98 (0.97, 1.00)*
Model 3	1 (ref)	0.98 (0.97, 1.00)**

Model 1 includes adjustment for age, race, and prior statin use (overall population).

Model 2 includes adjustment for variables in Model 1 plus history of diabetes, CHD, stroke, peripheral artery disease, heart failure, and chronic kidney disease, depression, Charlson comorbidity index, any hospitalization, cardiologist care, non-statin lipid lowering medication use, and total number of medications taken.

Model 3 includes adjustment for variables in Model 2 plus data from 30 days post-discharge (see **Table 1**).

* P-value 0.008, ** P-value 0.011

Central illustration

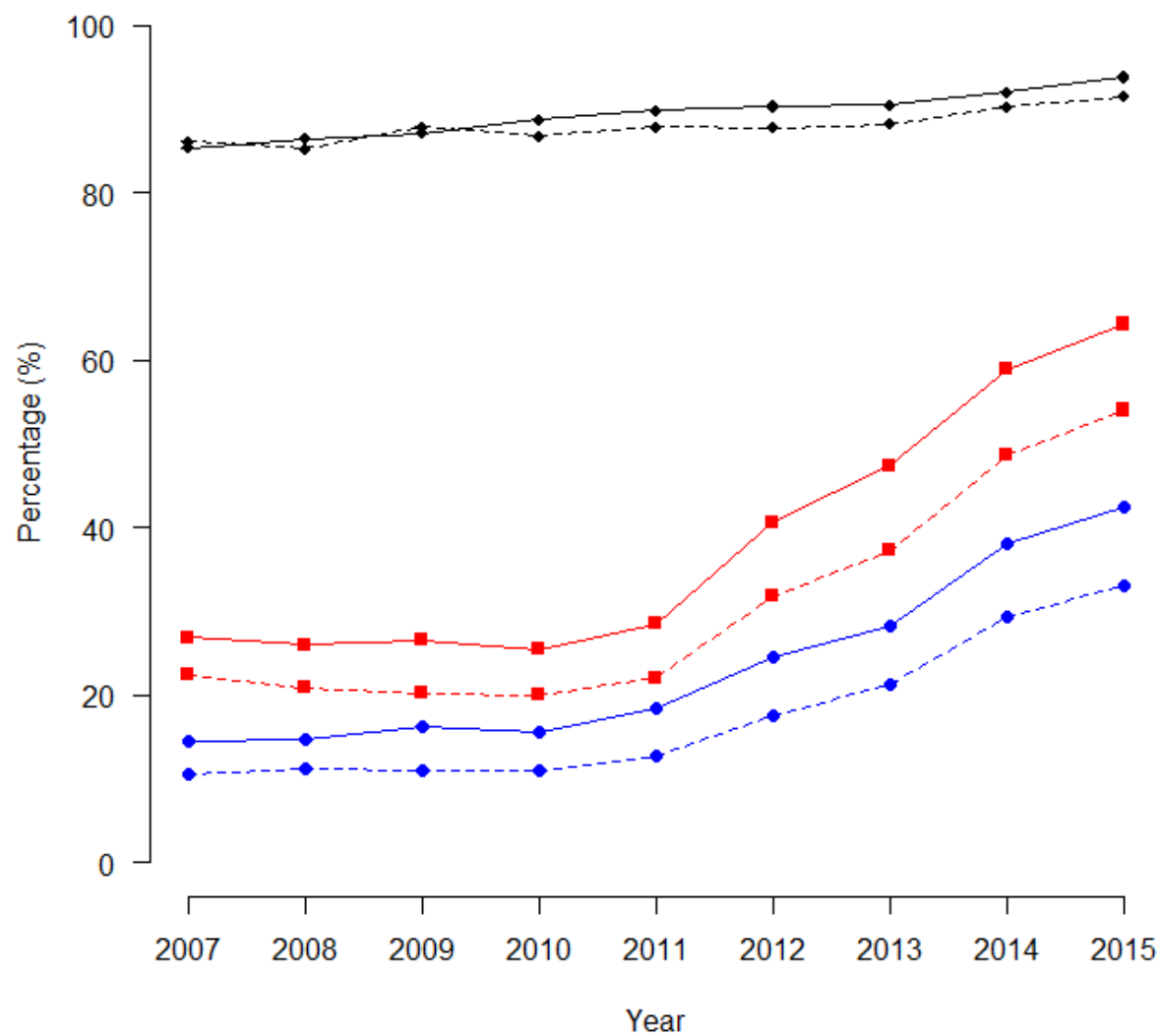


Figure 1

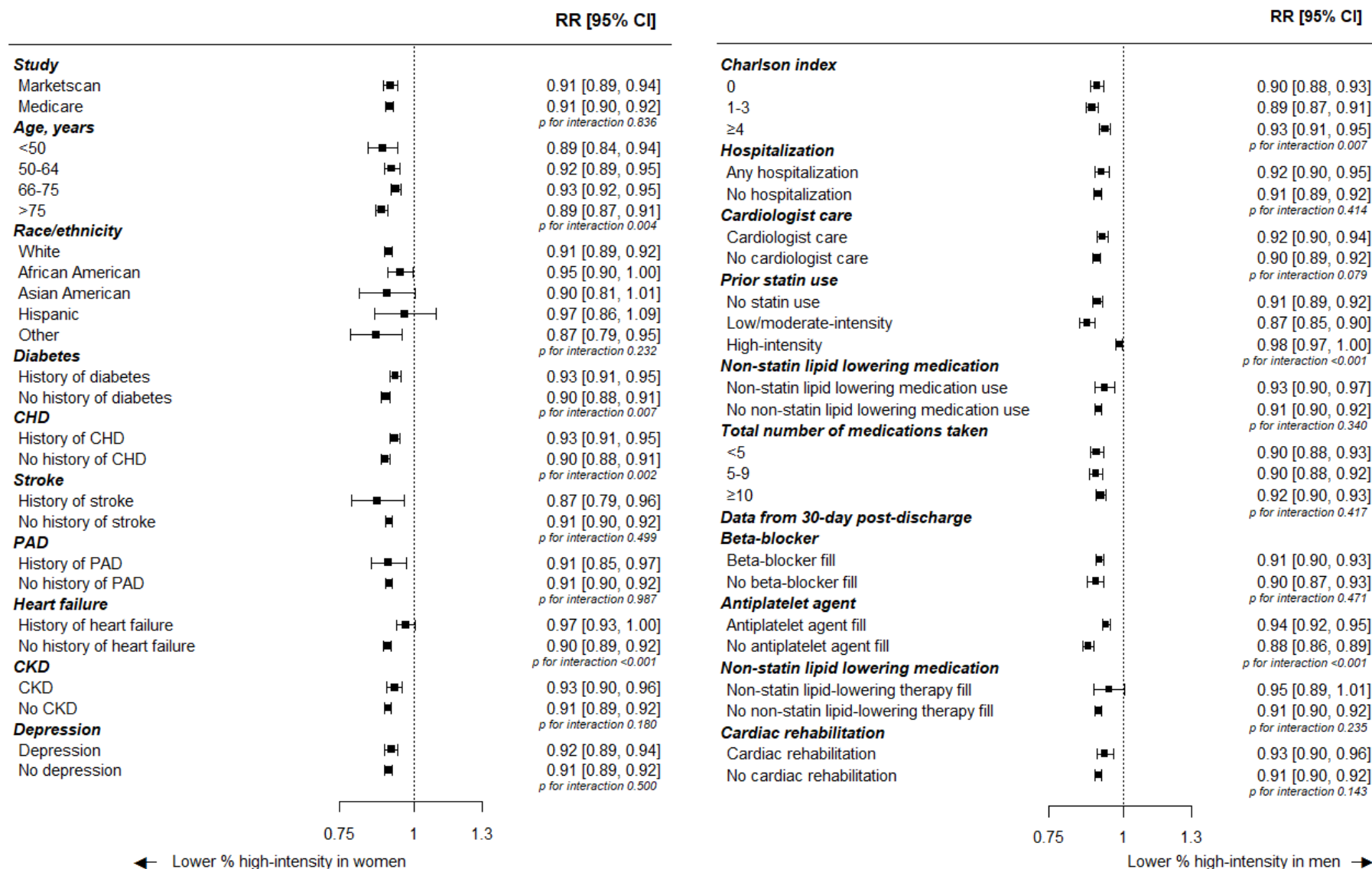


Figure 2

