Temporal Trends of High-Intensity Statin Therapy Among Veterans Treated With Percutaneous Coronary Intervention

Aref A. Bin Abdulhak, MD, MSc; Mary Vaughan-Sarrzin, PhD; Peter Kaboli, MD, MS; Phillip A. Horwitz, MD; Hilary Mosher, MD; Gardar Sigurdsson, MD; Nicholas E. Walker, MD; Robert Wallace, MD, MSc; Jennifer G. Robinson, MD, MPH

Background—The 2013 American College of Cardiology/American Heart Association blood cholesterol guideline recommends high-intensity statin therapy among certain groups of patients, but full implementation of the guideline has not yet been satisfactory. We aimed to investigate the temporal trends and predictors of high-intensity statin therapy among veterans who had been treated with percutaneous coronary intervention (PCI) and followed up by cardiologists within the Veterans Health Administrative system.

Methods and Results—A retrospective cohort study was conducted at the Veterans Health Administrative system including all patients >18 years old who had their PCI procedure between October 2010 and September 2016. National Veterans Health Administrative databases were used to retrieve study participant's demographics, comorbid conditions, statin type and dose within 90 days before and after the PCI procedure. There were 48 862 patients who underwent a PCI procedure during the study period. High-intensity statin use at 90 days post-PCI rose from 23% in 2010 to 37% before release of the 2013 American College of Cardiology/American Heart Association cholesterol guideline, then rose sharply to 80% by 2016. The projected 10-year risk of arteriosclerotic cardiovascular disease events among our study population was projected to be ≈1841 fewer if the cohort had received high-intensity statin therapy versus moderate-intensity statin.

Conclusions—By 2016, the 2013 American College of Cardiology/American Heart Association blood cholesterol guideline was well implemented among veterans who had a PCI procedure in the Veterans Health Administrative system, suggesting systems of care can be improved to increase rates of high-intensity statin initiation. (*J Am Heart Assoc*. 2018;7:e007370. DOI: 10.1161/JAHA.117.007370.)

Key Words: high-intensity statin • quality and outcomes • secondary prevention

Cardiovascular diseases remain the leading causes of mortality and morbidity in the United States, and are associated with significant burden and large healthcare expenditures.[1] The 2013 American College of Cardiology/American Heart Association (ACC/AHA) cholesterol guideline recommended hydroxymethyl glutaryl coenzyme A reductase inhibitors (statins) for cardiovascular risk reduction for secondary and primary prevention patients most likely to benefit.[2] Because cholesterol-lowering efficacy and the cardiovascular risk reduction benefits of statins are largely dependent on the intensity of therapy, high-intensity statins received strong Class I recommendations for patients with clinical cardiovascular disease or primary prevention patients with low-density lipoprotein ≥190 mg/dL.[2]

A meta-analysis of statin trials found that compared with moderate-intensity statin therapy, high-intensity statin

Clinical Perspective

What Is New?

- High-intensity statin therapy utilization dramatically improved among veterans who received their percutaneous coronary intervention within the Veterans Health Administrative System between 2010 and 2016, with the largest increase, from 37% to 80%, following the 2013 American College of Cardiology/American Heart Association cholesterol guideline.
- High-intensity statin therapy as recommended in the 2013 American College of Cardiology/American Heart Association blood cholesterol guideline is well implemented among veterans who had a percutaneous coronary intervention procedure in the Veterans Health Administrative system.

What Are the Clinical Implications?

- Systems of care can be improved to increase rates of high-intensity statin initiation.
- The projected 10-year risk of arteriosclerotic cardiovascular disease events among our study population was projected to be ≈1841 fewer if the cohort had received high-intensity statin therapy versus moderate-intensity statin.

therapy further reduces subsequent major vascular events by 15%, coronary death or nonfatal myocardial infarction by 13%, coronary revascularization by 19%, and ischemic stroke by 16%.[3] Moreover, a recent report has shown a survival benefit from high-intensity statin therapy[4] over moderate-intensity therapy in patients with arteriosclerotic cardiovascular disease (ASCVD). Nonetheless, several reports have shown that statins are underutilized.[5–7] Numerous studies have shown a slow and variable uptake of the guideline within several healthcare systems and specialty practices, and cast doubt upon applicability and implementation of the guideline.[8–10] In addition, the 2014 US Department of Veterans Affairs (VA) and Department of Defense clinical practice guideline for management of dyslipidemia for cardiovascular disease risk reduction advised use of moderate-intensity statin therapy in patients with clinical cardiovascular disease including patients who underwent a percutaneous coronary intervention (PCI).[11] The VA/Department of Defense guideline contradicts the 2013 ACC/AHA guideline and could have further influenced the prescription pattern of statin intensity within the Veterans Health Administrative (VHA) System.

High-intensity statin use among coronary artery disease patients who had a PCI procedure is largely unknown. Given slow and variable adherence to the 2013 ACA/AHA recommendations and release of the contradicting VA/Department of Defense guideline, we hypothesized that high-intensity statin therapy among veterans who had a PCI procedure would be underutilized, which could result in an excess of avoidable atherosclerotic cardiovascular events. Therefore, we sought to study the status and predictors of high-intensity statin therapy among veterans treated with PCI 3 years before and after the publication of the 2013 ACC/AHA cholesterol guideline in the US Veterans Administrative Health Care System.

Methods

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

Study Population

This retrospective cohort study included all veterans age ≥18 years who underwent their PCI in a VHA facility between October 2010 and September 2016. For patients who underwent multiple PCIs during the study period, only the first PCI was retained as the time point from which other variables were derived.

VHA databases were used to retrieve study participants' demographics, comorbid conditions, statin type and dose within 90 days before and after the PCI procedure, and date of PCI.

Receipt of PCI was defined using the Agency for Healthcare Research and Quality clinical classification category for Percutaneous Transluminal Coronary Angioplasty with or without stent placement. For years before Fiscal Year 2016, PCI was defined using *International Classification of Diseases Ninth Revision, Clinical Modification (ICD-9-CM)* and Current Procedural Terminology procedure codes; for Fiscal Year 2016, PCI was defined by *ICD-10-CM* and Current Procedural Terminology procedure codes. The Fiscal Year includes October 1 until September 30.

Statin was defined as prescription that was filled within the 90-day period before and after PCI. Statin intensities were categorized into high intensity (atorvastatin dose of 40–80 mg, and rosuvastatin dose of 20–40 mg), moderate intensity (atorvastatin 10–20 mg, rosuvastatin 5–10 mg, simvastatin 20–40 mg, pravastatin 40–80 mg, lovastatin 40 mg, fluvastatin 80 mg, fluvastatin 40 mg bid, pivastatin 2–4 mg), and low intensity (simvastatin 10 mg, pravastatin 10–20 mg, lovastatin 20 mg, fluvastatin 20–40 mg, pivastatin 1 mg) as defined in the 2013 AHA/ACC blood cholesterol guideline.

Patient characteristics were identified in the VA Corporate Data Warehouse. Specific characteristics included demographics (sex, age, race, ethnicity, and income), comorbid conditions, and history of prior revascularization procedures. Comorbid conditions were identified using *ICD-9-CM* and *ICD-10-CM* diagnosis codes from inpatient and outpatient

encounters during the 12 months before PCI and defined using algorithms originally developed by Elixhauser et al[12] and updated by the Agency for Healthcare Research and Quality.

Statistical Analysis

Associations between statin dose intensity and patient baseline characteristics were evaluated using the χ^2 statistic for proportions and Wilcoxon rank-sum or ANOVA for continuous variables. Trends in statin intensities post-PCI over each year were presented as number and percentage and tested using a χ^2 trend statistic. Subsequently, we used generalized linear mixed models to determine the odds of receiving a high-intensity statin after PCI over time, while controlling for patient demographics, comorbidities, prior revascularization, and prior statin use. For these models, the dependent variable was coded as "1" if a patient received high-intensity statin therapy, and "0" if a patient received statin therapy that was not high intensity or received no statin at all. Time was represented in categories defined by fiscal year of the procedure. Patient characteristics included in multivariable models were determined using stepwise selection after assessing candidate variables for multicollinearity. Model discrimination was assessed using the area under the curve. Given the observed common outcome of receiving high-intensity statin therapy among our cohort, relative risk (RR) ratios were calculated from adjusted odds ratios and reported instead of odds ratios.[13]

Data from the TNT (Treating to New Targets) study[14] were used to calculate the number of ASCVD events that could be avoided by implementing guideline-directed therapy. Specifically, the projected 10-year ASCVD events from the TNT study[15] were used to estimate a 10-year risk of ASCVD events, assuming high-intensity statin use, and assuming moderate-intensity statin use. The risk of ASCVD events was estimated separately for patients with coronary artery disease (CAD) and diabetes mellitus and CAD without diabetes mellitus. The projected 10-year ASCVD risks[15] extrapolated from the TNT trial[14] in patients with CAD without diabetes mellitus on moderate- and high-intensity statin therapies were 20% and 16%, respectively; the 10-year ASCVD risks among patients with CAD and diabetes mellitus on moderate- and high-intensity statin therapy were 37% and 28%, respectively. All statistical analyses were conducted using SAS Version 9.4 (SAS Institute, Cary, NC), and R Version 2.11.1 (Free Software Foundation, Boston, MA). Two-tailed tests were used for statistical significance at a level of 0.05.

The study was approved by a shared institutional review board at Iowa City VA medical center, and University of Iowa Hospital and Clinics, and subjects' informed consent requirement was waived.

Results

Between October 2010 and September 2016, 48 862 patients underwent a PCI procedure. Table 1 lists the baseline characteristics of the study cohort. Mean age was 69 years, 98% were male, 81% were white, 13% were black, and 33% had diabetes mellitus.

In the 90 days before PCI, moderate-intensity statin therapy was the most common regimen (24%) and high-intensity statin therapy was prescribed in 14% in 2010 (Figure 1). Each subsequent year, the rate of high-intensity statin prescriptions filled increased and the rate of moderate-intensity statins fell. By 2016, 38% were taking a high-intensity statin and 8% were taking a moderate-intensity statin in the 90 days before PCI. The rates of low-intensity statin prescriptions remained stable (1.7%–1.3%). The rate of no statin prescription before PCI increased slightly between 2010 and 2016 (38%–43%).

In the 90 days following PCI, the rate of high-intensity statin therapy increased between 2010 and 2016, from 23% to 80% (Figure 2). The largest increase followed the release of the 2013 ACC/AHA guideline, when the rate of high-intensity

**Table 1.** Baseline Characteristics of Study Participants

	Total (n=48 643)	%
Age (y), mean±SD	68.9±9.3	
Male	47 966	98.17
Race		
White	37 835	80.64
Black	6198	13.21
American Indian	349	0.74
Native Hawaiian or other Pacific Islander	331	0.71
Asian	185	0.39
Others	3964	8.1
Diabetes mellitus	16 193	33.29
Stroke	1159	2.38
Peripheral vascular disease	4744	9.75
Myocardial infarction	16 798	34.53
Hypertension	14 693	30.21
Renal failure	6522	13.4
Congestive heart failure	7759	15.95
Intracardiac device	1615	3.32
Valve disease	2328	4.79
Liver disease	1093	2.25
Hypothyroidism	2699	5.55
Atrial fibrillation	4723	9.71
Obstructive sleep apnea	4706	9.67
Depression	3262	6.71

Percentage of Statin Intensities Pre-PCI Procedure
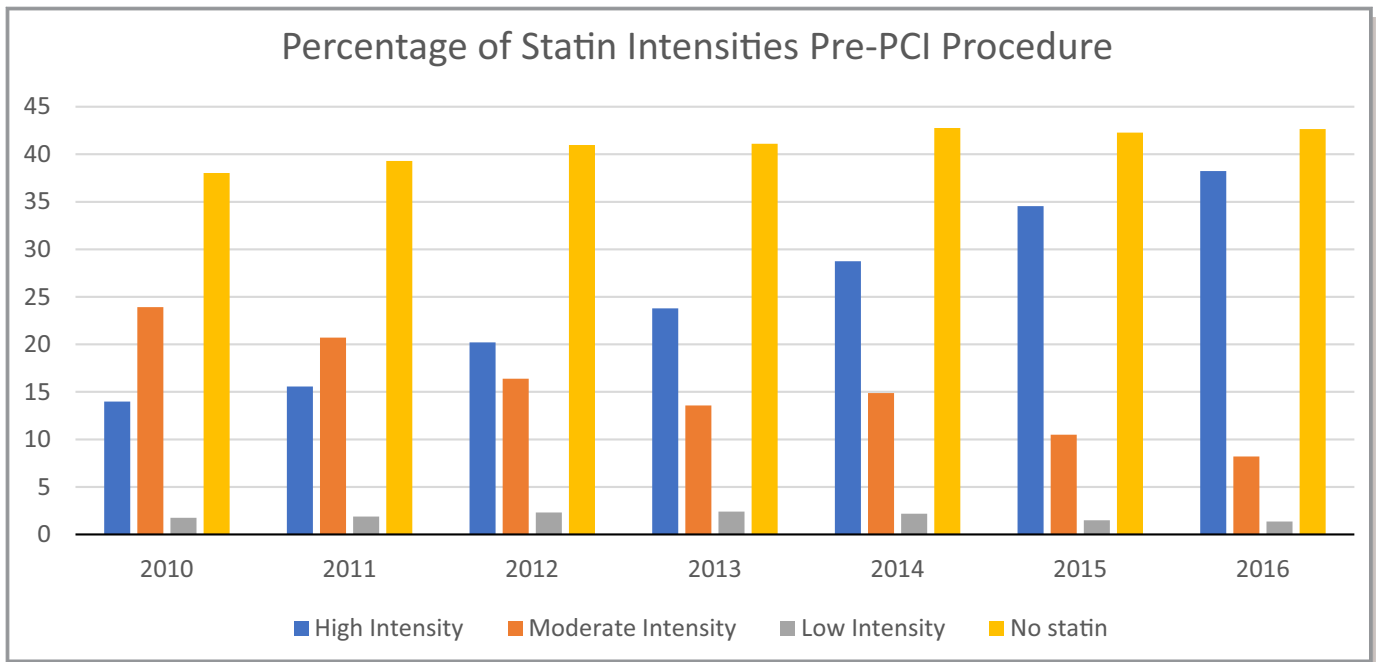
Figure 1. Distribution of statin intensities pre-percutaneous coronary intervention (PCI).

statin increased from 37% in 2012 to 80% by 2015. Moderate-intensity statin therapy steadily declined from being the most commonly prescribed statin therapy in 2012 (41%) to 7% in 2016. Low-intensity statin use in the 90 days post-PCI was uncommon throughout the study period, and no statin use remained relatively stable at 1.4% to 0.5%.

Percentage of Statin Intensity Post-PCI procedure
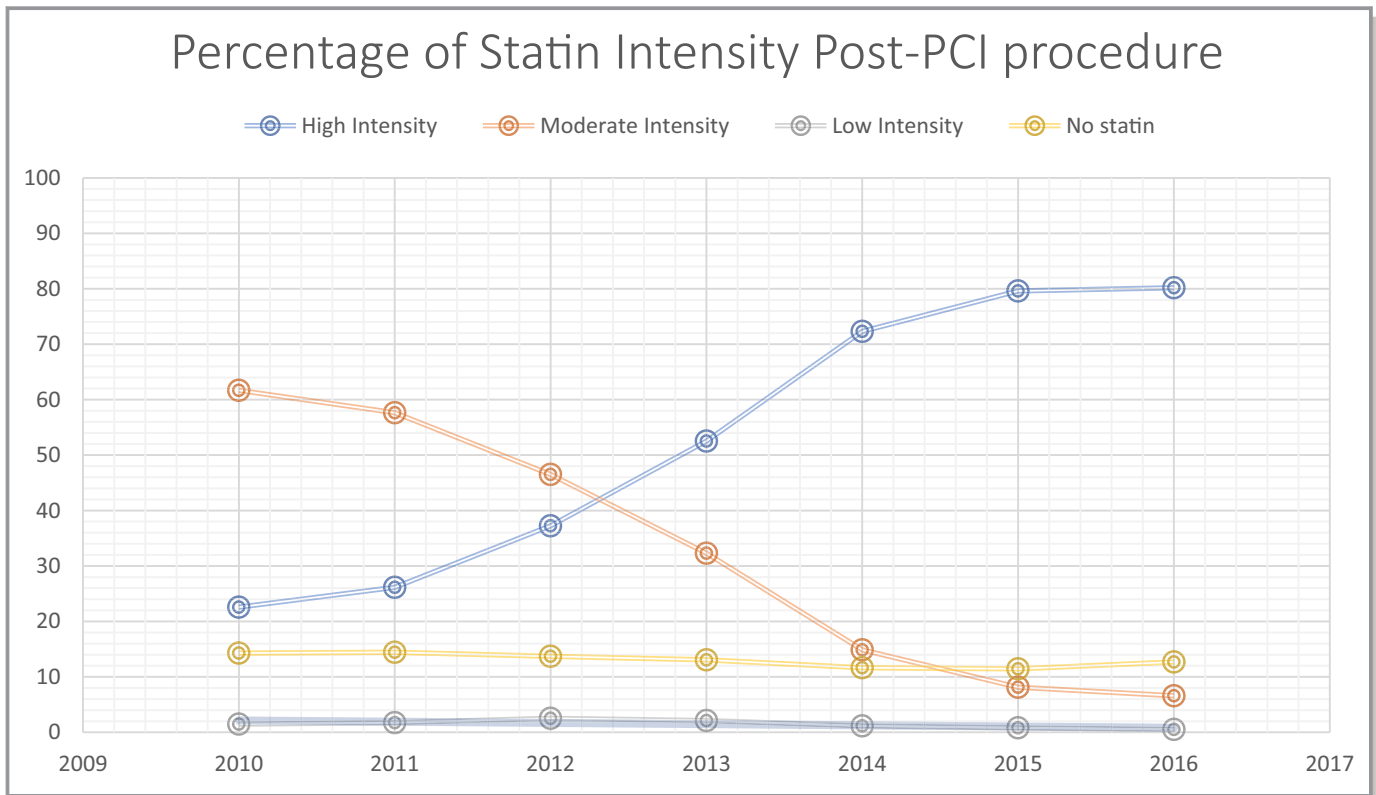
Figure 2. Trend of statin intensity postpercutaneous coronary intervention (PCI).

In the generalized linear mixed logistic regression model, PCI taken place in the fiscal years 2016, 2015, and 2014 was the strongest predictor of receiving high-intensity statin therapy (RR=3.54, 95% confidence interval [CI]=3.46, 3.62; RR=3.43, 95% CI=3.36, 3.51; and RR=3.15, 95% CI=3.07, 3.23, respectively), followed by prior treatment with high-intensity statin therapy before PCI (RR=2.67, 95% CI=2.58, 2.75), PCI taken place in the fiscal year 2013 (RR=2.26, 95% CI=2.16, 2.35), PCI taken place in the fiscal year 2012 (RR=1.56, 95% CI=1.48, 1.65), receiving no statin therapy before PCI (RR=1.29, 95% CI=1.25, 1.34), history of myocardial infarction (RR=1.18, 95% CI=1.16, 1.21), PCI taken place in the fiscal year 2011 (RR=1.12, 95% CI=1.05, 1.19), history of renal failure (RR=1.10, 95% CI=1.06, 1.13), and history of hypertension (RR=1.06, 95% CI=1.04, 1.09).

Increasing age, residence in Midwest or Southern states, and history of AIDS, atrial fibrillation, and liver disease were associated with reduced likelihood of receiving high-intensity statin therapy 90 days post-PCI. Table 2 lists the result of the linear mixed logistic regression model.

Surprisingly, diabetes mellitus, ischemic stroke, and peripheral vascular disease were found not to be statistically significant predictors of receiving high-intensity statin therapy post-PCI in the multivariable model, even though 35% of patients with history of stroke, and 34% of patients with peripheral vascular disease were not on any statin therapy before the PCI. The area under the curve for the final model was 0.84.

The 32 738 PCI patients with CAD without diabetes mellitus could have been expected to experience 6547 ASCVD events over 10 years if they were treated with moderate-intensity statin therapy; 1309 fewer ASCVD events could have been expected to occur if they had been treated with high-intensity statin therapy. Out of 16 124 PCI patients with CAD and diabetes mellitus, there would be 5966 expected ASCVD events if the group was treated with moderate-intensity statin versus 4514 expected events in case of high-intensity statin therapy. Increased use of high-intensity statin therapy could prevent an additional 1841 (based on 80% of study cohort on high-intensity statin therapy) ASCVD events over 10 years.

Discussion

High-intensity statin therapy utilization dramatically improved among veterans who received their PCI within the VHA System between 2010 and 2016, with the largest increase, from 37% to 80%, following the 2013 ACC/AHA cholesterol guideline. This change represents a marked and unprecedented implementation of the 2013 ACC/AHA blood cholesterol guideline, despite the VA Department of Defense guideline not recommending high-intensity statin therapy.

Table 2. RR and 95% CI From Multivariable Logistic Regression Model Predicting High-Intensity Statin Therapy

Variable	RR	95% CI	C Statistic =0.84
Age	0.94	0.93, 0.94	
Myocardial infarction	1.18	1.16, 1.21	
Fiscal year; reference=2010	00	00	
2011	1.12	1.05, 1.19	
2012	1.56	1.48, 1.65	
2013	2.26	2.16, 2.35	
2014	3.15	3.07, 3.23	
2015	3.43	3.36, 3.51	
2016	3.54	3.46, 3.62	
Prior statin use; reference=moderate intensity	00	00	
High-intensity statin	2.67	2.58, 2.75	
Low-intensity statin	0.79	0.79, 0.82	
No statin	1.29	1.25 1.34	
Hypertension	1.06	1.04, 1.09	
Obstructive sleep apnea	1.04	1.00, 1.08	
Renal failure	1.10	1.06, 1.13	
Liver disease	0.81	0.60, 0.83	
Atrial fibrillation	0.86	0.82, 0.90	
Acquired immunodeficiency syndrome	0.68	0.51, 0.86	
Race; reference=White	00	00	
Black	1.06	1.02, 1.09	
Region; reference=West	00	00	
Midwest	0.79	0.76, 0.83	
North	0.96	0.91, 1.00	
South	0.81	0.78, 0.84	

CI indicates confidence interval; RR, relative risk.

Such change is probably driven by a synergism between cardiologists' knowledge of the randomized trial data demonstrating further cardiovascular risk reduction with high- compared with moderate-intensity statin therapy, and adherence to the evidence-based 2013 ACC/AHA guideline. Moreover, availability of generic atorvastatin around the year 2013 within the VHA system could have further facilitated adherence to the 2013 ACC/AHA guideline.

Contemporary reports from the VHA system, Medicare beneficiaries, and US cardiology practices have shown that implementation of the 2013 AHA/ACC blood cholesterol guideline has been low to modest to date.[9,10,16] Rodriguez et al have reported on the uptake of the 2013 AHA/ACC guideline within the VHA system 12 months before and after the release of the guideline among veterans with ASCVD.

Although high-intensity statin therapy has increased from 25% to 35%, it remained disappointingly low relative to the scope of the guideline. Nonetheless, the study has only covered 1 year immediately post release of the guideline and included a heterogeneous group of patients with ASCVD that are followed by different specialty practices. Similarly, Pokharel et al have studied 161 cardiology practices, and found that moderate-high-intensity statin prescriptions improved from 63% (preguideline) to 67% (postguideline) among patients with ASCVD.

Though the increase in high-intensity statin utilization among veterans who underwent a PCI procedure within the VHA system was modest within 1 year from release of the guidelines, rates accelerated over the subsequent 2 to 3 years. Interestingly, the proportion of high-intensity statin started to rise even before the publication of the 2013 ACC/AHA guideline, a trend that was most likely driven by a cardiologist's response to clinical trials findings.[17–19]

High-intensity statin therapy has been shown in several randomized trials[20–23] to be superior to moderate-intensity statin in further reducing major cardiovascular events, and a recent report from observational data has shown a survival benefit of high-intensity statin over submaximal statin therapy. Adherence to guideline recommendation to use high-intensity statins rather than moderate-intensity statin among our cohort could potentially prevent >1800 cardiovascular events over a 10-year period. Nonetheless, a high degree of statin implementation may raise concern about potential statin-related adverse events, most commonly muscle aches or weakness. However, clinical trials have shown similar rates of muscle and other adverse events in the moderate versus high intensity as well as statin versus placebo groups.[24,25]

Several factors could explain our findings. Our cohort is predominantly composed of males, and almost all PCI patients are discharged by and have a follow-up with a cardiologist. Both factors—males sex and care delivered by cardiology specialists—have been shown to be associated with high-intensity statin prescriptions.[8,10] The perceived nature of the PCI intervention might have also influenced more aggressive approach toward cholesterol lowering.

Blacks were more likely to receive high-intensity statin therapy compared with whites, a finding that confirmed a prior report indicating few disparities in medication utilization in the VHA system.[26,27] VA quality improvement initiatives, absence of disparities, and better prescription coverage within the VHA system may have provided a more optimal setting for fully implementing the guideline.[27] However, time since the release date of the guideline appears to be an important predictor of receiving high-intensity statin as shown in Figure 2, suggesting greater improvements may be occurring in other settings.

The rate of no statin use in the 90 days post-PCI remained stable at about 13% between 2010 and 2016. This number is well within the range of the reported prevalence of statin intolerance in the general population, 11% to 15%.[28,29] About 25% of our cohort were older than 75 years, an age group not included in the Class I recommendation for high-intensity statin therapy. Thus, the implementation of the guideline might even have been underestimated.

Conclusion

High-intensity statin therapy as recommended in the 2013 ACC/AHA blood cholesterol guideline is well implemented among veterans who had a PCI procedure in the VHA system. Time since the guideline's release and cardiologist follow-up after an invasive procedure such as PCI are perhaps the driving forces of such an unprecedented degree of implementation of the guideline.

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Disclosures

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