ORIGINAL RESEARCH

Effects of Race on Statin Prescribing for Primary Prevention With High Atherosclerotic Cardiovascular Disease Risk in a Large Healthcare System

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Background—Although guidelines recommend statins with a high level of evidence for 4 primary prevention benefit groups, prescribing disparities still exist. The objective of this study was to evaluate the effects of race on statin prescribing for primary prevention.

Methods and Results—A retrospective cohort analysis of patients within a large academic health system was performed to investigate statin prescribing among primary prevention groups. The statin benefits groups were patients diagnosed with diabetes mellitus, with an low-density lipoprotein ≥190 mg/dL, or with an atherosclerotic cardiovascular disease (ASCVD) 10-year risk ≥7.5%. Statin prescribing was 20% in the ASCVD ≥7.5% group, followed by 37.8% in the low-density lipoprotein ≥190 mg/dL group and 40.5% in the diabetes mellitus group. Blacks were less likely to be prescribed a statin compared with whites in the diabetes mellitus (odds ratio, 0.64; 95% CI, 0.49–0.82; *P*=0.001) and ASCVD ≥7.5% groups (odds ratio, 0.38; 95% CI, 0.26–0.54; *P*<0.0001). Blacks 60 to 69 years of age (odds ratio, 7.97; 95% CI, 3.14–20.2; *P*=0.003) and 70 to 79 years of age (odds ratio, 4.21; 95% CI, 1.81–9.79; *P*=0.008) were more likely to be prescribed a statin compared with blacks <60 years of age in the ASCVD ≥7.5% group.

Conclusions—Blacks are less likely to be prescribed statins in diabetes mellitus and ASCVD ≥7.5% groups compared with whites. Younger blacks with ASCVD risk ≥7.5% are less likely to be prescribed statins compared with older blacks. Future research should focus on tailored interventions to address statin prescribing disparities in blacks. **(*J Am Heart Assoc*. 2019;8:e014709. DOI: 10.1161/JAHA.119.014709.)**

Key Words: disparities • race • statin therapy

Primary prevention of incident atherosclerotic cardiovascular disease (ASCVD) is explained by traditional risk factors, such as age, blood pressure, cholesterol, smoking status, and diabetes mellitus.[1] Statins remain one of the most effective therapies to prevent ASCVD. Since the 2013 update, the American College of Cardiology/American Heart Association guidelines for the management of blood cholesterol have identified 4 statin benefit groups: clinical ASCVD, severe hypercholesterolemia (low-density lipoprotein cholesterol [LDL-C] ≥190 mg/dL), diabetes mellitus in adults, and those with an ASCVD 10-year risk ≥7.5%.[2] Although these guidelines recommend statins with a high level of evidence, prescribing disparities still exist.[3–5]

Improved efforts for primary prevention of ASCVD are even more paramount in blacks. Blacks often have a higher incident rate of stroke and coronary artery disease compared with whites.[6–9] This excess risk is directly related to the elevated risk factors, such as blood pressure, cholesterol, smoking, and diabetes mellitus, in black individuals. In the ARIC (Atherosclerosis Risk in Communities) Study, the proportion of blacks with optimal risk factors was 3.8% compared with 7.5% in white participants.[5] Furthermore, ≈90% of the ASCVD events in blacks compared with ≈70% of the events in white participants were explained by risk factors.

The objective of this study was to evaluate the effects of race on statin prescribing for primary prevention with high ASCVD risk in a large healthcare system. These results could provide valuable insights for future interventions to improve statin prescribing in various primary prevention groups.

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An accompanying Table S1 is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.014709

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Clinical Perspective

What Is New?

- Statin therapy is less likely to be prescribed to blacks compared with whites.
- Patients <60 years of age are less likely to be prescribed statin therapy compared with older patients.
- Younger blacks are particularly vulnerable to these disparities in statin prescribing.

What Are the Clinical Implications?

- Health systems should identify population health strategies to reduce the disparities in statin prescribing among blacks.
- Studies are needed to determine successful interventions to address statin prescribing disparities in blacks.

Methods

Study Design

A retrospective cohort analysis of patients within a large academic health system in the United States was performed to investigate differences in statin prescribing among the primary prevention ASCVD groups following the 2013 American College of Cardiology/American Heart Association Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults. The initial patient cohort was active patients at Michigan Medicine, the University of Michigan Health System, who were at least 18 years old and had at least one cholesterol panel result between June 2017 and June 2018. All data were obtained from the University of Michigan electronic health record (EHR) data warehouse. The University of Michigan Institutional Review Board approved this study with a waiver of informed consent. The authors declare that all supporting data are available within the article and its online supplementary files.

Cohort Identification

Patients were identified for the initial cohort using phase 1 from the Phenotype Knowledgebase algorithm for identifying familial hypercholesterolemia.[10] Phase 1 of the familial hypercholesterolemia Phenotype Knowledgebase algorithm identifies patients with primary hypercholesterolemia and excludes patients with secondary causes of hypercholesterolemia. The patient index date for analysis refers to the date of the patient's highest recorded LDL-C level among all historical laboratory results. Patients were excluded if they had triglyceride levels reach 500 mg/dL on at least 2 occurrences or secondary causes of hypercholesterolemia within 1 year before the index date. The secondary causes of hypercholesterolemia are identified on the basis of abnormal laboratory values defined in the Phenotype Knowledgebase familial hypercholesterolemia algorithm. To account for the November 2013 American College of Cardiology/American Heart Association guidelines, patients with index dates before December 1, 2013 (n=25 797), were excluded. Patients with existing ASCVD before the index date were removed from the analysis (n=6072). These previous diagnoses were identified using *International Classification of Diseases, Ninth Revision* (*ICD-9*), codes from those published with the Phenotype Knowledgebase algorithm and its corresponding *International Classification of Diseases, Tenth Revision* (*ICD-10*), codes. Patients without race information in the EHR were excluded from the cohort (n=542). A full list of patient identification procedures can be found in Figure 1.

Statin Benefit Groups

Of the remaining 33 298 patients, those between 20 and 79 years of age who had an LDL-C level ≥190 mg/dL at the index date were assigned to the LDL-C ≥190 mg/dL group. Patients 40 to 79 years of age at the index date and who were diagnosed with diabetes mellitus using *ICD-9* code 250.xxx and *ICD-10* code E10.xxx, E11.xxx, or E13.xxx (n=3233) were assigned to the diabetes mellitus group.

ASCVD risk was estimated using the pooled cohort equation in the residual patients. Patients who did not have complete information on smoking status (n=201), systolic blood pressure (n=250), high-density lipoprotein cholesterol (HDL-C), and total cholesterol (n=21) were also excluded. Patients' date of birth, race, ethnicity, and sex information were obtained from the EHR. Their ages at index date were calculated on the basis of the date of birth and index date. LDL-C, HDL-C, triglyceride, and systolic blood pressure were measured within 3 months before the index date until 3 months after the index date. If any patient had multiple records within this 6-month period, we used the mean of the measurements in the analysis. Patients' responses to smoking status within 3 months before the index date until 3 months after the index were identified. A list of antihypertensive drugs was used to define if patients were on hypertension treatment around the index date.[11] Using these variables, 10-year ASCVD risk scores were calculated on the basis of the published pooled cohort equation.[12] Patients with an ASCVD 10-year risk ≥7.5% were assigned to the ASCVD ≥7.5% group. The 3 groups, diabetes mellitus, LDL ≥190 mg/dL, and ASCVD ≥7.5%, were also combined into one group called the all benefit group. This group represents all primary prevention statin benefit patients. Because of the definitions, patients can be in both the diabetes mellitus and LDL ≥190 mg/dL groups but are only represented once in the all benefit group.

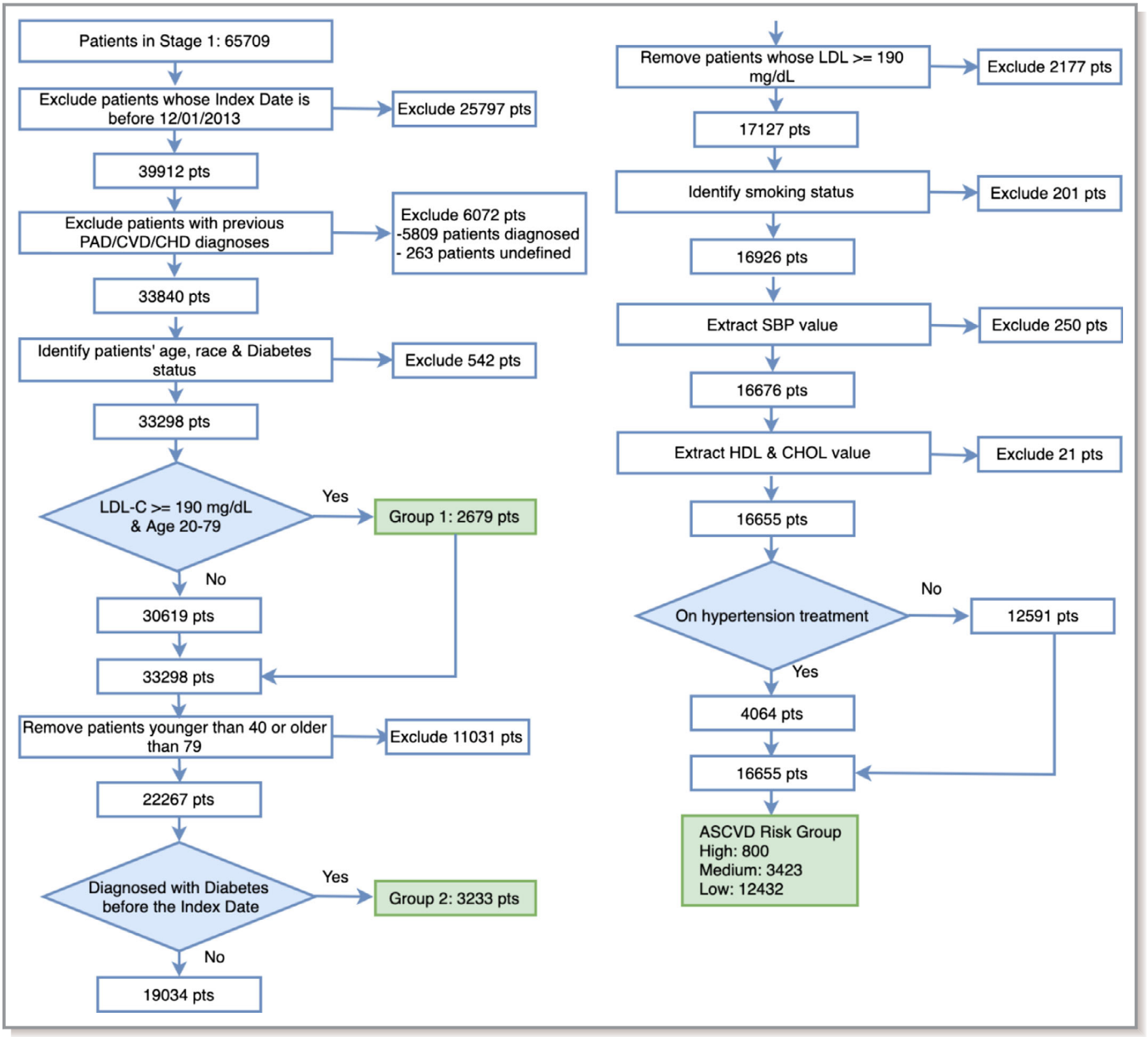

Figure 1. Flow chart for patient identification. ASCVD indicates atherosclerotic CVD; CHD, coronary heart disease; CHOL, total cholesterol; CVD, cardiovascular disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LDL-C, LDL cholesterol; PAD, peripheral arterial disease; SBP, systolic blood pressure.

Statin Treatment at Index Date

Medication histories in the EHR were used to determine if patients were prescribed statin treatment around the index date. A list of statin medications was used, which included combination therapy. The start and stop date of the prescription had to follow one of the following criteria to be considered as on statin treatment during the index date: (1) Index date minus 30 days was less than or equal to start date and less than or equal to the index date. (2) The start date was less than or equal to the index date and the stop date was greater than or equal to the index date. (3) If the stop date is missing in the prescription, the stop date was estimated on the basis of the formula: Stop Date=(Quantity/Frequency)×(Refills+1). The start date had to be less than or equal to the index date, and the estimated stop date was greater than or equal to the index date.

Statistical Analyses

Categorical variables were defined as frequencies and percentages, and differences between the groups were assessed by the χ^2 test or the Fisher exact test, where appropriate. Continuous variables were characterized by the

Table. Demographics by Race

Variables	White (n=7696)	Black (n=1004)	Asian (n=706)	Other (n=247)	Overall (n=9653)
Sex		*P*=0.002			
Women	3518 (45.7)	522 (52.0)	331 (46.9)	119 (48.2)	4490 (46.5)
Age, y		*P*<0.0001			
Mean (SD)	61.0 (10.4)	57.0 (10.3)	58.7 (12.0)	56.8 (12.1)	60.3 (10.7)
Ethnicity		*P*<0.0001			
Non-Hispanic or Latino	7280 (94.6)	962 (95.8)	681 (96.5)	118 (47.8)	9041 (93.7)
Hispanic or Latino	79 (1.0)	10 (1.0)	2 (0.3)	115 (46.6)	206 (2.1)
Missing	337 (4.4)	32 (3.2)	23 (3.3)	14 (5.7)	406 (4.2)
LDL-C level, mg/dL		*P*=0.726			
Mean (SD)	156 (57.4)	154 (62.4)	155 (63.1)	153 (90.6)	156 (59.5)
HDL-C, mg/dL		*P*<0.0001			
Mean (SD)	55.2 (16.9)	55.8 (17.0)	53.3 (14.0)	51.2 (15.1)	55.0 (16.7)
Triglycerides, mg/dL		*P*<0.0001			
Mean (SD)	162 (125)	128 (87.8)	166 (110)	186 (148)	160 (122)
Total cholesterol, mg/dL		*P*<0.0001			
Mean (SD)	220 (52)	212 (52)	220 (53)	217 (87)	219 (53)
Smoking status		*P*<0.0001			
Yes	920 (12.0)	161 (16.0)	56 (7.9)	27 (10.9)	1164 (12.1)
Missing	37 (0.5)	5 (0.5)	3 (0.4)	0 (0)	45 (0.5)
On hypertension treatment		*P*<0.0001			
Yes	3610 (46.9)	660 (65.7)	271 (38.4)	133 (53.8)	4674 (48.4)
History of diabetes mellitus		*P*<0.0001			
Yes	2446 (31.8)	414 (41.2)	295 (41.8)	143 (57.9)	3298 (34.2)
Statin prescribed		*P*=0.052			
Yes	2309 (30)	272 (27.1)	208 (29.5)	88 (35.6)	2877 (29.8)

Data are given as number (percentage), unless otherwise indicated. HDL-C indicates high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

mean and SD or median (quartile 1–quartile3), and a Student *t* test determined differences between the groups. Stepwise logistic regression was performed in each statin benefit group to determine the predictors of statin prescribing in the cohort, with a *P* value cutoff of 0.05 for inclusion in the model. The outcome variable was statin prescribing (yes/no), and the predictors of statin prescription for each model were age (categorized by <60, 60–69, and 70–79 years of age), race, ethnicity, sex, hypertension treatment (yes/no), smoking status, systolic blood pressure, total cholesterol, LDL-C, and HDL-C.

Results

Study Population

A total of 9653 patients were identified for the all benefit group, with 3233 patients in the diabetes mellitus group, 2679 patients in the LDL ≥190 mg/dL group, and 4223 patients in the ASCVD ≥7.5% group. In the all benefit group, the average age was 60±11 years, systolic blood pressure was 131±18 mm Hg, and LDL-C was 156±59 mg/dL. Most patients were nonsmokers (87.5%), white (79.7%), and on hypertension treatment (48.4%). Table shows demographics by race. Table S1 shows demographics by statin benefit group.

Statin Prescribing

Statin prescribing in the all benefit group was 29.8%. The lowest proportion of statin prescribing was in the ASCVD ≥7.5% group (20%), followed by 37.8% in the LDL ≥190 mg/dL group and 40.5% in the diabetes mellitus group. Figure 2 demonstrates the proportion of patients prescribed statins over time by statin benefit group.

In the all benefit group, race was a significant predictor of statin prescribing. Patients identified as black were less likely

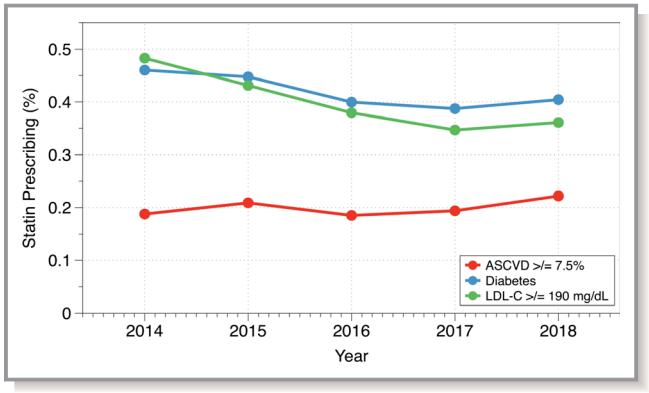

Figure 2. Plot of statin prescribing over time by benefit group. ASCVD indicates atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol.

to receive a statin compared with white patients (odds ratio [OR], 0.58; 95% CI, 0.49–0.69; $P<0.0001$) when adjusting for age, on hypertension treatment, systolic blood pressure, HDL-C, total cholesterol, and LDL-C. This effect was similar in the diabetes mellitus (OR, 0.64; 95% CI, 0.49–0.82; $P=0.001$) and ASCVD ≥7.5% groups (OR, 0.38; 95% CI, 0.26–0.54; $P<0.0001$) when adjusting for age, on hypertension treatment, HDL-C, total cholesterol, and LDL-C. In the LDL ≥190 mg/dL, race was not a significant predictor of statin prescribing. Only LDL-C, total cholesterol, smoking status, and age remained statistically significant in the stepwise logistic regression model. Figure 3 represents a plot of the adjusted ORs.

Age was also a significant predictor of statin prescribing in the all benefit group and each individual group in the same stepwise logistic regression model. In the all benefit group, those 70 to 79 years of age were more likely to be prescribed a statin than those <60 years of age (OR, 1.37; 95% CI, 1.19–1.57; $P<0.0001$) when adjusting for race, on hypertension treatment, systolic blood pressure, HDL-C, total cholesterol, and LDL-C, but there was no difference in those 60 to 69 years of age and those <60 years of age. In the diabetes mellitus, LDL ≥190 mg/dL, and ASCVD ≥7.5% groups, those patients 60 to 69 years of age and 70 to 79 years of age were more likely to be prescribed a statin compared with those <60 years of age. Figure 4 represents a plot of the adjusted ORs for all groups. An age by race statistical interaction existed in the ASCVD ≥7.5% group ($P=0.011$), controlling for all other predictors of statin prescribing. Blacks 60 to 69 years of age (OR, 7.97; 95% CI, 3.14–20.2; $P=0.003$) and 70 to 79 years of age (OR, 4.21; 95% CI, 1.81–9.79; $P=0.008$) were more likely to be prescribed a statin compared with blacks <60 years of age.

Discussion

Since 2013, the guidelines have recommended statin therapy in 4 primary prevention groups: clinical ASCVD, diabetes

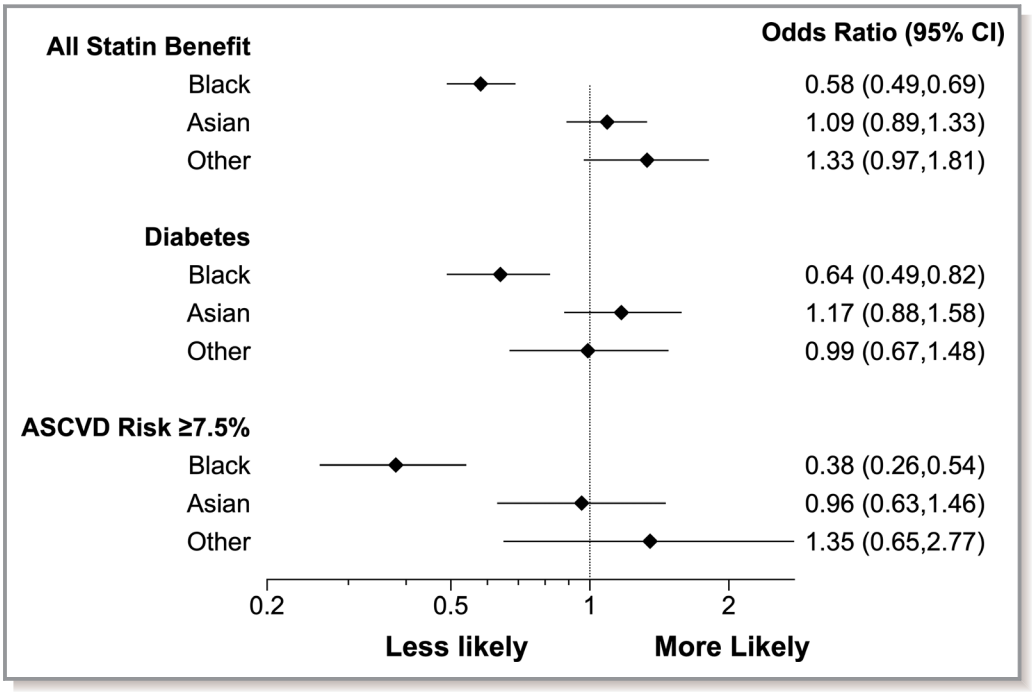

Figure 3. Adjust odds of statin prescribing by race (vs white) for benefit groups. Odds ratios from stepwise logistic regression. All statin benefit adjusted by age, on hypertension treatment, high-density lipoprotein cholesterol (HDL-C), systolic blood pressure, total cholesterol, and low-density lipoprotein cholesterol (LDL-C). Diabetes mellitus and atherosclerotic cardiovascular disease (ASCVD) risk ≥7.5% adjusted by age, on hypertension treatment, HDL-C, total cholesterol, and LDL-C.

mellitus, LDL ≥190 mg/dL, and ASCVD risk ≥7.5%. Our study demonstrates that a significant proportion of patients in 3 of these groups are not prescribed a statin after the release of the 2013 guidelines, with the lowest percentage of patients prescribed statins in the ASCVD ≥7.5% group. Blacks were less likely than whites to be prescribed statins in the diabetes mellitus and ASCVD ≥7.5% groups when controlling for all clinical factors associated with statin prescribing. We did not, however, identify this same association in the LDL ≥190 mg/dL group. Last, we found that younger blacks (<60 years of age) are less likely to be prescribed statins if their ASCVD risk is ≥7.5% after adjusting for other predictors of statin prescribing.

Two prospective cohort studies have demonstrated disparities in the treatment of cardiovascular disease before the release of the 2013 guidelines. The ARIC Study compared disparities in risk in blacks compared with whites in 14 162 adults free from stroke or coronary artery disease.[6] A lower proportion of blacks demonstrated optimal risk levels when compared with whites. Blacks were also more likely to have at least one elevated risk factor compared with whites. After adjustment of these risk factors, event rates in blacks and whites were similar. The REGARDS (Reasons for Geographic and Racial Differences in Stroke) population study investigated disparities in statin use in 18 216 participants enrolled from 2003 to 2007.[13] All race and sex groups were less likely to use statins when compared with white men. In addition, as the number of cumulative vulnerabilities (age, being a woman, being black, living in poverty, and no health insurance) a patient had increased, statin use decreased significantly. These results support our study but also highlight that we are not addressing disparities that have existed for decades.

Explanation of the reasons for the lack of statin prescribing in blacks is complex. The PALM (Patient and Provider Assessment of Lipid Management) registry investigated racial disparities of statin prescribing in 138 primary care, cardiology, and endocrine practices in 2015.[14] Blacks were less likely than whites to receive a statin at guideline-recommended intensity for primary and secondary prevention. Also, blacks were less likely to believe statins were safe and less likely to trust their clinicians. An analysis of Medicare patients showed that blacks are less likely to be adherent to statin therapy compared with whites after an ischemic stroke.[15] A study of >1000 Kaiser Permanente members in Georgia demonstrated women and blacks were less likely to be adherent to statins over time.[16] Furthermore, in the REGARDS cohort study, there was a lower level of agreement between patient self-reported lipid-lowering therapy and Medicare claims in black men compared with black women, white women, and white men.[17] In an intervention study, copayment reduction for statins increased medication adherence in black

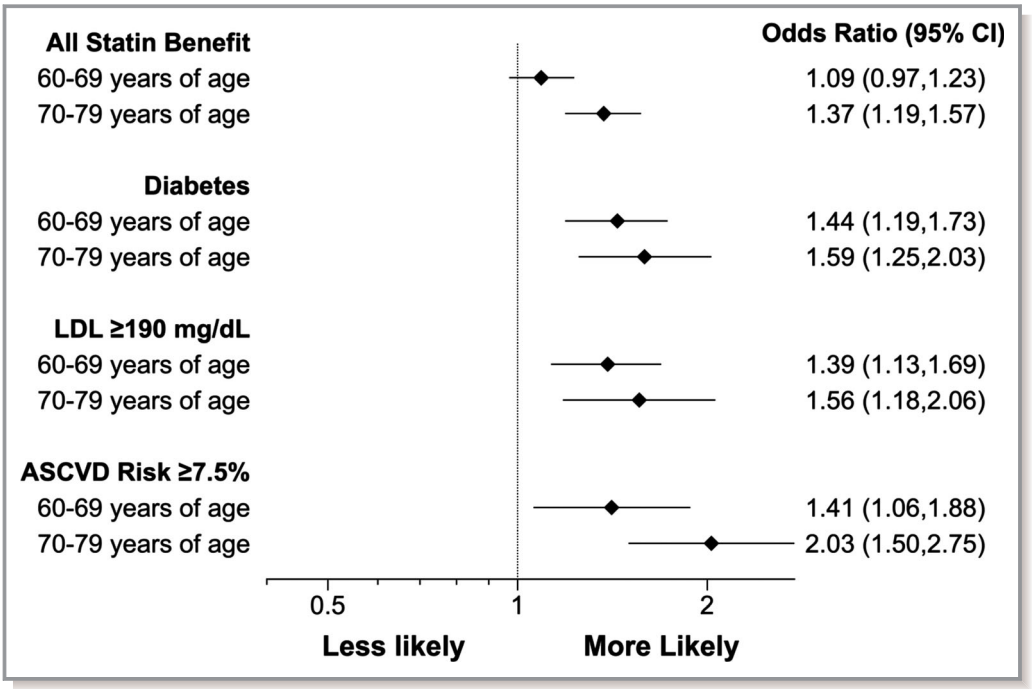

Figure 4. Adjust odds of statin prescribing by age category (vs <60 years of age) for benefit groups. Odds ratios from stepwise logistic regression. All statin benefit adjusted by age, on hypertension treatment, high-density lipoprotein cholesterol (HDL-C), systolic blood pressure, total cholesterol, and low-density lipoprotein cholesterol (LDL-C). Diabetes mellitus and atherosclerotic cardiovascular disease (ASCVD) risk ≥7.5% adjusted by age, on hypertension treatment, HDL-C, total cholesterol, and LDL-C.

patients, even after adjusting for income.[18] More research needs to be done to identify the patient and provider barriers for not prescribing statins and then patient and provider interventions should be created to optimize statin therapy and reduce disparities. Patient interventions may focus on social barriers to treatment and provide culturally appropriate health programs tailored to the individual. Provider interventions could address potential bias, access to care, and quality of care.

Several limitations exist in this study. Our findings are limited to a single health system that primarily serves southeastern Michigan. All data were obtained from the EHR, which limits the research to certain variables and could have missing data, leading to unmeasured residual confounding. The statin prescribing was defined from electronic medical record data. Clinician reasoning could not be obtained to determine the thought process of prescribing a statin. We did not have access to pharmacy prescription fill records, so adherence could not be assessed. Future studies should pool data from EHRs and pharmacy claims data.

Conclusions

In this retrospective cohort of patients from 2013 to 2018 in a large health system, statin prescribing among the 3 primary prevention statin groups remains low. Blacks are less likely to be prescribed a statin in the diabetes mellitus and ASCVD >7.5% groups compared with whites. Blacks <60 years of age are less likely to be prescribed statins compared with those 60 to 69 and 70 to 79 years of age. Future research in this area should focus on tailored interventions to increase statin prescribing to address these disparities.

Disclosures

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