ORIGINAL RESEARCH

Statin Use and Adverse Effects Among Adults >75 Years of Age: Insights From the Patient and Provider Assessment of Lipid Management (PALM) Registry

Michael G. Nanna, MD; Ann Marie Navar, MD, PhD; Tracy Y. Wang, MD, MHS, MSc; Xiaojuan Mi, PhD; Salim S. Virani, MD, PhD; Michael J. Louie, MD, MPH, MSc; L. Veronica Lee, MD; Anne C. Goldberg, MD; Veronique L. Roger, MD, MPH; Jennifer Robinson, MD, MPH; Eric D. Peterson, MD, MPH

***Background*—**Current statin use and symptoms among older adults in routine community practice have not been well characterized since the release of the 2013 American College of Cardiology/American Heart Association guideline.

***Methods and Results*—**We compared statin use and dosing between adults >75 and ≤75 years old who were eligible for primary or secondary prevention statin use without considering guideline-recommended age criteria. The patients were treated at 138 US practices in the Patient and Provider Assessment of Lipid Management (PALM) registry in 2015. Patient surveys also evaluated reported symptoms while taking statins. Multivariable logistic regression models examined the association between older age and statin use and dosing. Among 6717 people enrolled, 1704 (25%) were >75 years old. For primary prevention, use of any statin or high-dose statin did not vary by age group: any statin, 62.6% in those >75 years old versus 63.1% in those ≤75 years old (P=0.83); high-dose statin, 10.2% versus 12.3% in the same groups (P=0.14). For secondary prevention, older patients were slightly less likely to receive any statin (80.1% versus 84.2% [P=0.003]; adjusted odds ratio, 0.81; 95% confidence interval, 0.66–1.01 [P=0.06]), but were much less likely to receive a high-intensity statin (23.5% versus 36.2% [P<0.0001]; adjusted odds ratio, 0.54; 95% confidence interval, 0.45–0.65 [P=0.0001]). Among current statin users, older patients were slightly less likely to report any symptoms (41.3% versus 46.6%; P=0.003) or myalgias (27.3% versus 33.3%; P<0.001).

***Conclusions*—**Overall use of statins was similar for primary prevention in those aged >75 years versus younger patients, yet older patients were less likely to receive high-intensity statins for secondary prevention. Statins appear to be similarly tolerated in older and younger adults. **(*J Am Heart Assoc*. 2018;7:e008546. DOI: 10.1161/JAHA.118.008546.)**

Key Words: aging • elderly • primary prevention • secondary prevention • statin • statin therapy

Statins have proved beneficial for the prevention of cardiovascular disease in adults,[1–3] but patients >75 years have been underrepresented in randomized controlled trials.[4,5] In addition, concerns have been raised about the adverse effects of statins and polypharmacy as a reason not to treat older patients as aggressively as younger patients.[1,6] Although data are mixed for primary prevention after the age of 75 years,[7] studies in older patients with atherosclerotic cardiovascular disease (ASCVD) suggest no attenuation of benefit. The 2013 American College of Cardiology (ACC)/American Heart Association (AHA) Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults acknowledges the limitations of existing data on older individuals and recommends individualizing the decision to initiate statins for primary prevention in adults >75 years.[1] For secondary prevention, 3 trials found that high-intensity statin therapy reduced cardiovascular events more than moderate-intensity

From the Duke University Medical Center, Durham, NC (M.G.N.); Duke Clinical Research Institute, Duke University School of Medicine, Durham, NC (A.M.N., T.Y.W., X.M., E.D.P.); Baylor College of Medicine, Houston, TX (S.S.V.); Regeneron Pharmaceuticals, Inc, Tarrytown, NY (M.J.L.); Sanofi, Bridgewater, NJ (L.V.L.); Washington University, St Louis, MO (A.C.G.); Mayo Clinic, Rochester, MN (V.L.R.); and The University of Iowa College of Public Health, Iowa City, IA (J.R.).

An accompanying Table S1 is available at http://jaha.ahajournals.org/content/7/10/e008546/DC1/embed/inline-supplementary-material-1.pdf

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Correspondence to: Michael G. Nanna, MD, Duke University Medical Center, Durham, NC 27710. E-mail: michael.nanna@duke.edu

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Clinical Perspective

What Is New?

- Since the release of the 2013 American College of Cardiology/American Heart Association guideline, older patients (>75 years old) with atherosclerotic cardiovascular disease were less likely than their younger counterparts to receive high-intensity statins.
- Among primary prevention patients, statin use was similar among older and younger patients.
- Statins were similarly tolerated between older and younger patients.

What Are the Clinical Implications?

- Treatment differences between high-risk older and younger patients with atherosclerotic cardiovascular disease may represent a therapeutic opportunity for improvement and highlight the importance of future randomized controlled trials evaluating high-intensity statin use in older adults for secondary prevention.

statin therapy, but these trials enrolled few patients >75 years and none >80 years[8–10]; however, there was sufficient evidence for moderate-intensity statin therapy in secondary prevention patients of any age.[11] The most recent 2016 US Preventive Services Task Force Recommendation Statement on Statin Use for the Primary Prevention of Cardiovascular Disease similarly avoids firm recommendations about statins for older adult patients (>75 years old), as do the European Society of Cardiology/European Atherosclerosis Society guidelines for the management of dyslipidemias in patients >80 years old, with insufficient evidence to make a recommendation in this population.[12,13]

Our study was designed to evaluate patterns of statin use and symptoms in older adults in contemporary community practice. Using the Patient and Provider Assessment of Lipid Management (PALM) registry, we determined whether adults aged >75 were (1) less likely to be treated with a statin, (2) less likely to be treated with a high-intensity statin, or (3) more likely to have patient-reported symptoms than their younger counterparts.

Methods

Data Description and Outcomes of Interest: PALM Registry

The PALM registry is composed of 7736 patients with ASCVD or at high risk for ASCVD from 138 cardiology, primary care, and endocrinology practices nationwide.[14] As described previously,[14] data were collected cross-sectionally at enrollment and included patient demographic and socioeconomic characteristics, comorbidities, medical history, core laboratory lipid panels, patient experiences, and beliefs about lipid-lowering therapy from patient surveys and provider characteristics. 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. All study participants provided informed consent, and all sites obtained institutional review board approval for participation.

For this analysis, patients ≤75 years were included if they would have met a recommendation for high- or moderate-intensity statin therapy under the most recent ACC/AHA cholesterol guideline, and patients >75 years old were included if they would have met an indication for statin therapy independent of their chronologic age.[1] Patients qualified for high-intensity statin therapy for purposes of secondary prevention if they had a history of clinical ASCVD. Patients were classified as having ASCVD if they had prior myocardial infarction, coronary artery disease, coronary artery bypass grafting, percutaneous coronary intervention, stroke/transient ischemic attack, abdominal aortic aneurysm, peripheral arterial disease, carotid artery stenosis, or noncoronary arterial revascularization. Patients qualified for high-intensity statin therapy for primary prevention if they had the following: (1) low-density lipoprotein cholesterol ≥190 mg/dL or (2) diabetes mellitus with a 10-year ASCVD risk ≥7.5%. Patients qualified for at least moderate-intensity statin therapy if they had no indication for high-intensity statin and one of the following: (1) diabetes mellitus with a 10-year ASCVD risk <7.5% or (2) 10-year ASCVD risk ≥7.5% on the basis of the pooled cohort risk equation and no diabetes mellitus. Because the 10-year risk calculator is meant to be used for those 40 to 79 years old, we calculated risk for those ≥80 years as if they were 79 years, which represents the minimum risk for these adults given increased risk with age.

Any statin and high-intensity statin therapy were considered outcomes of interest. Statin intensity was defined on the basis of the daily dose at the time of enrollment using the previously defined 2013 ACC/AHA cholesterol guideline schema.[1] High-intensity statin therapy was defined as atorvastatin ≥40 mg or rosuvastatin ≥20 mg daily. Covariates included patient demographics and socioeconomic characteristics, medical history, laboratory results, patient beliefs about statins, adverse effects, and willingness for change. Patient surveys were administered via an iPad before being seen in the clinic. These surveys included questions on beliefs about statins, adverse effects, and willingness for change. Symptoms were assessed in patients ≤75 and >75 years, within subgroups of patients currently receiving statin therapy or specifically receiving high-intensity statin therapy and those previously receiving statin therapy who had since stopped therapy (Table S1).

Missing data were infrequent, except for the income variable. For multivariable modeling, missing values of

continuous variables were imputed using the median, and missing values of categorical variables were imputed to the most common value. Missing/do not know/prefer not to answer responses for the income variable were imputed to the 2014 median census household income on the basis of the patient residence zip code or the enrolling site zip code if the patient zip code was missing.

Statistical Analysis

Overall and by subgroups, we described patient characteristics of the study population by age group (>75 versus ≤75 years) using frequencies with percentages for categorical variables and medians with interquartile range for continuous variables. For categorical variables, we tested for differences between age groups using χ^2 tests when the cell number was ≥5 and Fisher's exact tests when the cell number was <5. We used Kruskal-Wallis tests for continuous variables.

We then estimated the unadjusted and adjusted association between age and outcomes (statin and high-intensity statin use) using logistic regression models overall and by subgroups of primary and secondary prevention. In the unadjusted model, age was the only independent variable. Prespecified clinically relevant variables possibly associated with statin use were included in the multivariable model to control for potential confounding, and they were retained in the models regardless of statistical significance. In the adjusted (multivariable) model, independent variables included age and covariates (sex, race, ASCVD, including myocardial infarction, coronary artery disease, coronary artery bypass grafting, percutaneous coronary intervention, stroke/transient ischemic attack, abdominal aortic aneurysm, peripheral arterial disease, carotid artery stenosis, noncoronary arterial revascularization, diabetes mellitus, heart failure, chronic kidney disease, smoking, body mass index, insurance status by type, annual income, and whether the patient saw a cardiologist). For primary prevention, the models did not include history of ASCVD. We reported the estimated odds ratios (ORs) and 95% confidence intervals (CIs). We used a 2-tailed α=0.05 to establish statistical significance of all tests. All analyses were performed using SAS, version 9.4 (SAS Institute, Inc, Cary, NC).

Results

A total of 6717 patients (n=3425 with clinical ASCVD) had an indication for statin therapy, including 1704 (25%) >75 years. The baseline characteristics of older adults differed from younger adults in the PALM registry (Table 1). Older patients were more frequently white than younger adults (88.4% versus 79.5% [P<0.001] in primary prevention; 92.9% versus 84.6% [P<0.0001] in secondary prevention). Overall, older patients had higher rates of established ASCVD compared with younger adults (60.9% versus 47.6%; P<0.0001). Among those with a history of ASCVD, older adults more frequently had peripheral artery disease (20.9% versus 17.1%; P=0.008), coronary artery disease (80.0% versus 75.3%; P=0.003), carotid stenosis (20.9% versus 17.1%; P=0.008), prior coronary artery bypass grafting (28.3% versus 21.1%; P<0.0001), and abdominal aortic aneurysm (6.7% versus 3.9%; P<0.001), but less frequently had a history of myocardial infarction (25.9% versus 30.9%; P=0.003) or percutaneous coronary intervention (37.8% versus 42.8%; P=0.006) (Table 1). Compared with younger adults, older patients had a higher prevalence of heart failure and chronic kidney disease, but a lower prevalence of diabetes mellitus and a lower body mass index. Older adults were somewhat more likely to receive moderate-intensity statin therapy for secondary prevention (56.6% versus 47.9%; P<0.0001) (Figure 1). Nevertheless, in secondary prevention settings, older individuals were less likely to be treated with any statin overall (80.1% versus 84.2%; P=0.003) and much less likely to receive high-intensity statins (23.5% versus 36.2%; P<0.0001). In multivariable analyses, there was no difference in statin use or high-intensity statin use between older and younger adults eligible for statins for purposes of primary prevention (statin OR, 1.07 [95% CI, 0.88–1.30]; high-intensity statin OR, 0.92 [95% CI, 0.68–1.24]) (Figure 2). Yet, older adults with prior ASCVD had a trend toward lower ORs of overall statin use (OR, 0.81; 95% CI, 0.66–1.01; P=0.06) and were less likely to be treated with a high-intensity statin (OR, 0.54; 95% CI, 0.45–0.65; P=0.0001).

Patient-reported symptoms while receiving statins, statin discontinuation rates, and reasons for discontinuation were analyzed by age group (Table 2). The prevalence of prior statin discontinuation was similar among older versus younger adults (11.4% for those >75 versus 9.8% for those ≤75 years; P=0.09). Adverse effects were also noted as a reason for stopping at similar rates in older versus younger individuals (58.0% versus 53.4%; P=0.35). Among adults currently receiving a statin, older patients were actually less likely to report experiencing any adverse symptoms (41.3% versus 46.6%; P=0.003) or myalgias specifically (27.3% versus 33.3%; P<0.001). These trends were similar among older versus younger patients who were taking a high-intensity statin.

Discussion

Patients >75 years have been poorly represented in large primary and secondary ASCVD prevention statin trials. Consequently, the ACC/AHA and more recent US Preventive Services Task Force guidelines do not recommend statins for primary prevention in older adults, although the former allows for risk

Table 1. Baseline Characteristics by Age (n=6717)

	Primary Prevention (n=3292)			Secondary Prevention (n=3425)		
Characteristics	Aged ≤75 y (n=2626)	Aged >75 y (n=666)	*P* Value	Aged ≤75 y (n=2387)	Aged >75 y (n=1038)	*P* Value
Male sex	1260 (48.0)	275 (41.3)	0.002	1555 (65.1)	611 (58.9)	<0.001
Age, y	66.0 (58.0–70.0)	80.0 (77.0–83.0)	<0.0001	67.0 (60.0–71.0)	80.5 (78.0–84.0)	<0.0001
Race			<0.001			<0.0001
White	2088 (79.5)	589 (88.4)		2020 (84.6)	964 (92.9)	
Black	476 (18.1)	67 (10.1)		308 (12.9)	57 (5.5)	
Other/unknown	62 (2.4)	10 (1.5)		59 (2.5)	17 (1.6)	
Hispanic	414 (15.8)	74 (11.1)	0.003	172 (7.2)	71 (6.8)	0.70
10-y risk (among those without ASCVD*)	14.4 (9.5–22.0)	32.4 (26.2–43.3)	<0.0001			
Prior MI	. . .	. . .	. . .	738 (30.9)	269 (25.9)	0.003
Prior stroke	. . .	. . .	. . .	232 (9.7)	109 (10.5)	0.48
PAD	. . .	. . .	. . .	408 (17.1)	217 (20.9)	0.008
Coronary artery disease	. . .	. . .	. . .	1798 (75.3)	830 (80.0)	0.003
Prior CABG	. . .	. . .	. . .	504 (21.1)	294 (28.3)	<0.0001
Prior PCI	. . .	. . .	. . .	1021 (42.8)	392 (37.8)	0.006
Abdominal aortic aneurysm	. . .	. . .	. . .	93 (3.9)	70 (6.7)	<0.001
Carotid artery stenosis	. . .	. . .	. . .	408 (17.1)	217 (20.9)	0.008
History of TIA	. . .	. . .	. . .	165 (6.9)	86 (8.3)	0.16
Prior noncoronary arterial revascularization	. . .	. . .	. . .	108 (4.5)	49 (4.7)	0.80
Total cholesterol, mg/dL	181.0 (156.0–212.0)	176.5 (152.0–205.0)	0.002	158.0 (137.0–189.0)	155.0 (134.0–185.0)	0.04
LDL-C, mg/dL	105.0 (83.0–131.0)	99.0 (79.0–123.0)	<0.0001	87.0 (68.0–110.0)	83.0 (66.0–107.0)	0.03
LDL-C on treatment, mg/dL	94.0 (75.0–116.0)	89.0 (72.0–107.0)	0.002	82.0 (66.0–102.0)	79.0 (63.0–97.0)	0.001
LDL-C not on treatment, mg/dL	123.0 (100.0–146.0)	118.0 (95.0–140.0)	0.005	114.0 (84.0–143.0)	110.0 (83.0–132.0)	0.17
HDL-C, mg/dL	52.0 (43.0–64.0)	58.0 (47.0–69.0)	<0.0001	49.0 (40.0–59.0)	52.0 (44.0–62.0)	<0.0001
Diabetes mellitus	1367 (52.1)	185 (27.8)	<0.0001	1022 (42.8)	354 (34.1)	<0.0001
Hypertension	2008 (76.5)	523 (78.5)	0.26	2008 (84.1)	908 (87.5)	0.01
Heart failure	87 (3.3)	54 (8.1)	<0.0001	334 (14.0)	195 (18.8)	<0.0001
Chronic kidney disease	180 (6.9)	88 (13.2)	<0.0001	267 (11.2)	179 (17.2)	<0.0001
BMI, kg/m^2	30.7 (27.3–35.6)	27.1 (24.5–31.4)	<0.0001	30.3 (26.6–34.8)	27.5 (24.8–31.3)	<0.0001
Smoking status			<0.0001			<0.0001
Current smoker	304 (12.4)	24 (3.9)		320 (14.1)	33 (3.4)	
Quit/former smoker	904 (37.0)	266 (43.0)		1080 (47.6)	529 (54.4)	
Never smoked	1236 (50.6)	329 (53.2)		868 (38.3)	411 (42.2)	
College or above	1525 (62.9)	344 (56.4)	0.003	1507 (66.7)	540 (55.7)	<0.0001
Insurance†						
Private	1465 (60.2)	317 (51.5)	<0.0001	1377 (57.7)	514 (49.5)	<0.0001
Medicare	1305 (53.7)	537 (87.0)	<0.0001	1324 (55.5)	854 (82.3)	<0.0001
Medicaid	264 (10.9)	68 (11.0)	0.90	287 (12.0)	77 (7.4)	<0.0001
No insurance	76 (3.1)	7 (1.1)	0.007	39 (1.6)	8 (0.8)	0.05
Other	59 (2.2)	8 (1.2)	0.09	44 (1.8)	19 (1.8)	0.98

Continued

Table 1. Continued

Characteristics	Primary Prevention (n=3292)			Secondary Prevention (n=3425)		
	Aged ≤75 y (n=2626)	Aged >75 y (n=666)	*P* Value	Aged ≤75 y (n=2387)	Aged >75 y (n=1038)	*P* Value
Income‡			<0.0001			<0.0001
<$35 000	598 (34.9)	147 (43.5)		537 (35.2)	242 (44.6)	
$35 000–$75 000	586 (34.1)	115 (34.0)		473 (31.0)	195 (36.0)	
$75 000–$100 000	197 (11.5)	38 (11.2)		182 (11.9)	47 (8.7)	
≥$100 000	334 (19.5)	38 (11.2)		334 (21.9)	58 (10.7)	
Seen by a cardiologist	723 (27.5)	295 (44.3)	<0.0001	1861 (78.0)	815 (78.5)	0.72
Seen by an endocrinologist	506 (19.3)	66 (9.9)	<0.0001	451 (18.9)	119 (11.5)	<0.0001

All values are expressed as median (interquartile range) or number (percentage), where appropriate. ASCVD indicates atherosclerotic cardiovascular disease; BMI, body mass index; CABG, coronary artery bypass grafting; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

*ASCVD includes prior MI, coronary artery disease, CABG, PCI, stroke, abdominal aortic aneurysm, peripheral arterial disease, carotid artery stenosis, noncoronary arterial revascularization, or prior TIA.

†Insurance: "other" includes all answers that are not "no," "private," "Medicare," or "Medicaid."

‡Income: excludes "I do not know" and "prefer not to answer" from denominator. Income is based on self-report; when missing, we used zip code–based median income for modeling.

discussion, while suggesting less intense therapy for secondary prevention.[1,12] Despite a lack of evidence and firm treatment guidelines, clinicians need to make therapeutic decisions about lipid management in older patients. In our large, contemporary, practice-based study, we found that many patients >75 years in primary prevention are receiving a statin. What is unclear is

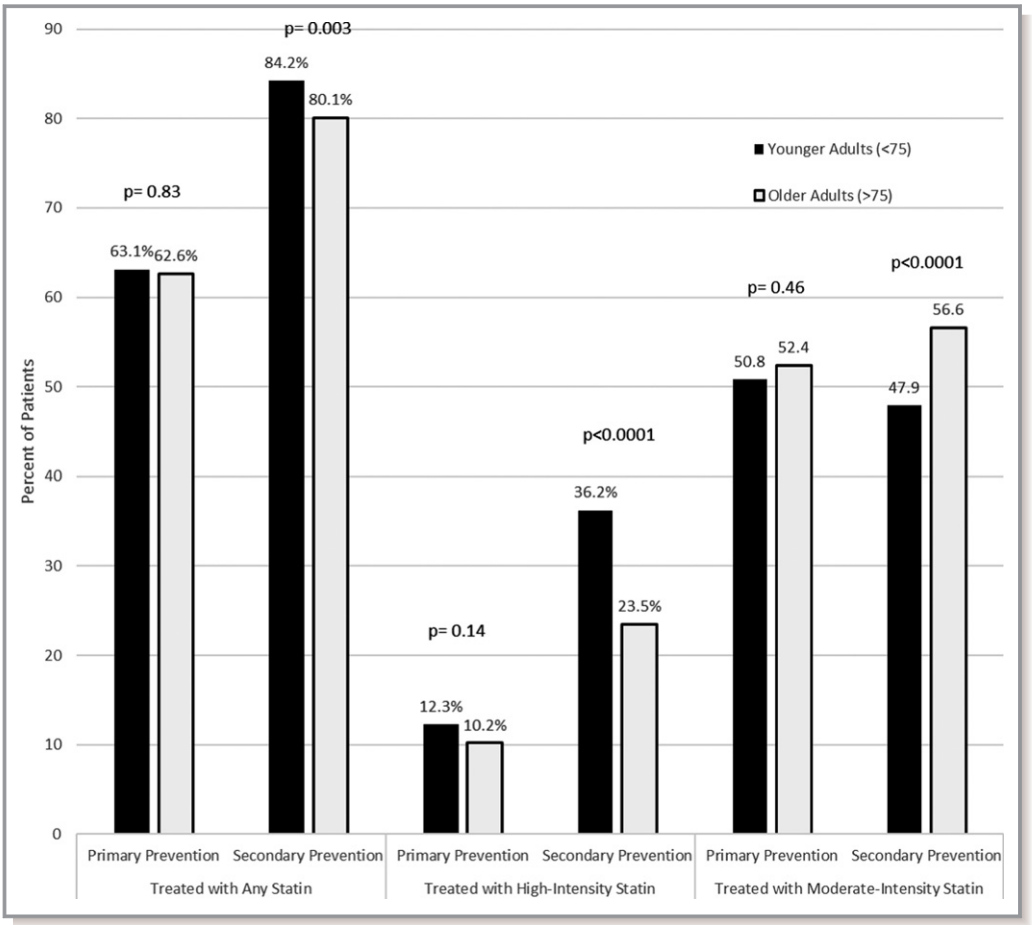

Figure 1. Statin use in older vs younger adults. Primary and secondary prevention statin use in older vs younger adults, according to those treated with any statin, a high-intensity statin, and a moderate-intensity statin.

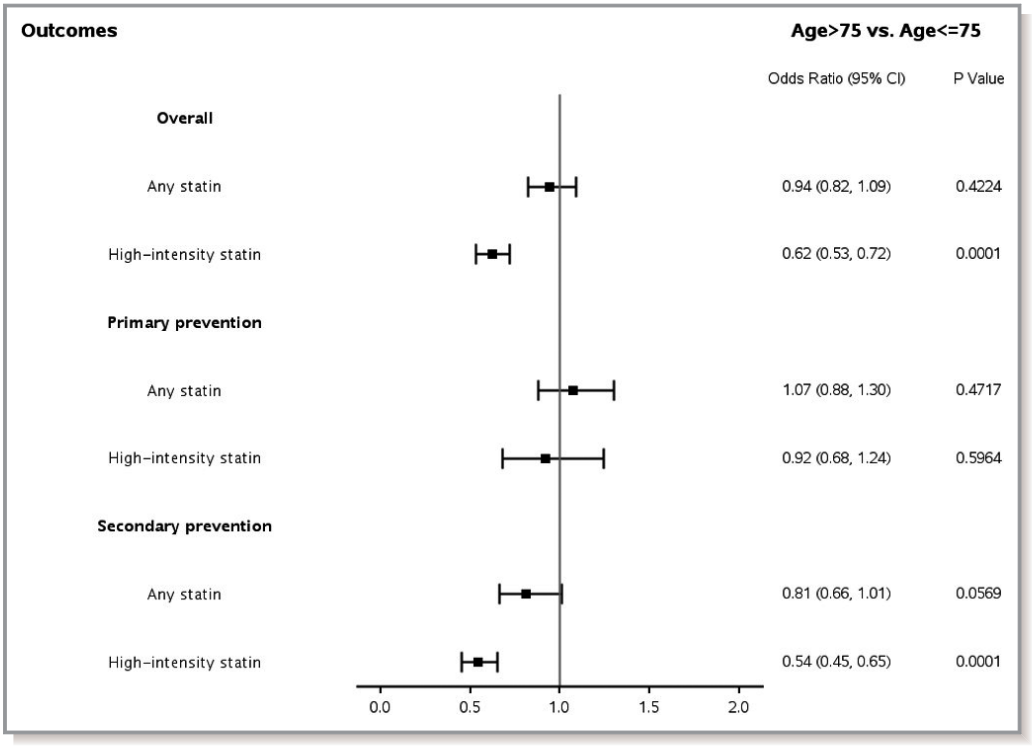

Figure 2. Adjusted association between age (>75 vs ≤75 years) and statin use. For overall and secondary prevention, model adjusted for sex, race, atherosclerotic cardiovascular disease (including myocardial infarction, coronary artery disease, coronary artery bypass grafting, percutaneous coronary intervention, stroke, abdominal aortic aneurysm, peripheral arterial disease, carotid artery stenosis, noncoronary arterial revascularization, and prior transient ischemic attack), diabetes mellitus, heart failure, chronic kidney disease (CKD), smoking, body mass index (BMI), insurance, income, and whether the patient saw a cardiologist. For primary prevention, model adjusted for sex, race, diabetes mellitus, heart failure, CKD, smoking, BMI, insurance, income, and whether the patient saw a cardiologist. CI indicates confidence interval.

whether physicians are extrapolating treatment algorithms used for their younger patients and applying these algorithms to their older patients, particularly for primary prevention. In the setting of primary prevention, older and younger patients had a similar likelihood of receiving statin therapy, including high-intensity statin therapy. Nonetheless, in secondary prevention, physicians appeared to follow the ACC/AHA guidelines and prescribed lower-dose statins in older individuals with ASCVD. Finally, relative to younger patients, we found that older individuals treated with any or high-intensity statins specifically had similar likelihoods of having adverse symptoms as their similarly treated younger peers.

Although the absolute risk of cardiovascular disease increases with advancing age, prior studies have demonstrated that older adults were less likely to be treated with statins than their younger counterparts.[15,16] Older adults in the PALM registry represent a high-risk population, with higher rates of ASCVD than younger patients, and had a higher prevalence of being treated with statins, particularly moderate-intensity statins. Older adults in the lower-risk primary prevention cohort were equally likely to be treated with any statin or a high-intensity statin for primary prevention. Conversely, higher-risk older adults with a history of ASCVD were less likely than their younger counterparts to be treated with statins overall or with high-intensity statin therapy. The treatment difference in high-intensity statin use among patients with known ASCVD was particularly striking, and older patients more frequently received moderate-intensity statin therapy, which suggests that clinicians have been applying the most recent ACC/AHA guideline recommendation for moderate-intensity statins to older patients with an ASCVD history.[1] Other factors affecting access to statins may also affect statin use, such as lower income, varying insurance coverage, competing illnesses and comorbidities, and higher likelihood of being homebound, although differences in high-intensity statin use persisted even after correction for heart failure, income, and insurance status. Differences in type of ASCVD between older and younger populations may also contribute to differences in statin treatment patterns, with younger populations more frequently having a history of myocardial infarction or percutaneous coronary intervention, which may be more likely to prompt

Table 2. Statin Experience and Willingness to Try a Cholesterol-Lowering Medication Among Those Previously Not Receiving a Statin

Variable	Those Aged ≤75 y	Those Aged >75 y	*P* Value*
Among those currently receiving a statin (n=4641)			
Experienced any symptoms	1519 (46.6)	446 (41.3)	0.003
Experienced myalgias	1083 (33.3)	294 (27.3)	<0.001
Among those currently receiving a high-intensity statin (n=1358)			
Experienced any symptoms	493 (48.2)	89 (35.3)	<0.001
Experienced myalgias	352 (34.5)	49 (19.5)	<0.0001
Among those previously receiving a statin (n=525)			
Reason for stopping			
No longer needed	68 (18.6)	27 (18.9)	0.95
Did not like taking daily	23 (6.3)	3 (2.1)	0.07
Cost/expense or lost/changed insurance	30 (8.2)	6 (4.2)	0.11
Did not notice improvement	18 (4.9)	3 (2.1)	0.21
Prefer natural remedies	28 (7.7)	7 (4.9)	0.27
Adverse effects	195 (53.4)	83 (58.0)	0.35
Friend/relative/other information suggested stopping	22 (6.0)	6 (4.2)	0.42
Do not know/cannot remember	38 (10.4)	15 (10.5)	0.98
Among those who were never receiving a statin (n=1551)			
Ever recommended (% yes)	137 (18.8)	45 (18.2)	0.83
Willingness to try a cholesterol-lowering medication			
Not at all or unlikely	89 (16.7)	38 (20.4)	0.02
Possibly	173 (32.5)	46 (24.7)	
Very likely or almost certainly	233 (43.8)	78 (41.9)	
Do not know	37 (7.0)	24 (12.9)	

Data are presented as number (percentage), with the percentage generated as a percentage of the number of patients in that particular age (≤75 vs >75 years old) and statin treatment status subgroup (currently receiving a statin, currently receiving a high-intensity statin, previously receiving a statin, or never receiving a statin). All percentages were calculated as a percentage of nonmissing.

*χ^2 Tests were used when the cell number was ≥5. Fisher's exact tests were used when the cell number was <5.

high-intensity statin use than other forms of ASCVD. Among very old patients, limited life expectancy may lead to joint decisions between the patient and provider to lower statin intensity or discontinue therapy entirely.

Despite their high risk of ASCVD, the evidence for primary prevention statin therapy and high-intensity statin therapy in secondary prevention in older adults is incomplete.[4,5,17,18] Clinical trial data suggest a clinical benefit of moderate-intensity statins in those aged ≥75 years when used for secondary prevention, and prior observational studies have demonstrated a significant risk reduction gleaned from statin therapy in this population.[11,15,16,19] Similarly, a recent observational study suggests a significant survival advantage exists among older adults with ASCVD treated with high- versus moderate-intensity statins, amplified at maximal doses of high-intensity statins.[20] On the other hand, a recent post hoc analysis from the ALLHAT-LLT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial) found a signal (*P*=0.07) for possible increased all-cause mortality among older adults treated with statins.[7] These findings highlight the necessity for clinical trials to evaluate the efficacy and safety of statin therapy, including high-intensity therapy, for both primary and secondary prevention of cardiovascular disease, specifically in older adults. One such example is the ongoing STAREE (Statin Therapy for Reducing Events in the Elderly) trial (NCT02099123). This trial is randomizing older adults (≥70 years) without prior ASCVD to high-intensity statin therapy with atorvastatin 80 mg or placebo, and it features several relevant geriatric end points, including measures of cognitive function, disability, frailty, and quality of life.

Although some cite adverse effect risk as a potential cause for statin underuse in older populations, we observed similar

rates of reported statin symptoms in older versus younger patients. In fact, older adults currently receiving statins were less likely to report symptoms than younger adults. These findings are significant, particularly given the perceived increased risk of statin adverse effects in older adults that is prevalent in the literature, despite prior studies suggesting otherwise[1,6,21–24]; whether providers hold similar beliefs about statins deserves further exploration.

This study captures a large number of outpatient older adults from 138 different sites, representing a highly generalizable cohort that is likely representative of the larger US population. In addition, this is the first study to characterize statin treatment patterns among older adults since the release of the 2013 ACC/AHA guideline, as well as the first study to capture patient-related perceptions and beliefs about statins (both of which are important contributions to cardiology and geriatrics literature). Despite these strengths, our study had some limitations. First, we were unable to capture specific clinician perceptions and beliefs that may have influenced treatment patterns; this information would have provided a more comprehensive understanding of the forces influencing statin use in older adults. Second, recall bias may affect the ability of older individuals to remember an adverse effect, because of age-related cognitive changes. Third, individuals currently receiving a statin are less likely to have had a prior adverse effect, which may lead to selection bias. Fourth, it was impossible to determine whether symptoms described by patients were directly attributable to statin therapy, and it is unlikely that reported symptoms were all directly attributed to statin use. Fifth, for the primary prevention subgroup, we estimated ASCVD risk with the pooled cohort equation, which is meant for use in patients 40 to 79 years old. As a result, this method may not have accurately estimated ASCVD risk in patients ≥80 years old. Sixth, we did not collect information on the timing of initiation or duration of statin therapy. Finally, we did not capture detailed information on geriatric impairments and frailty that may play a role in therapeutic decision making in the older adult population.

In conclusion, older and younger patients in the PALM registry were similarly likely to receive statins for primary prevention; however, older individuals less frequently received statin therapy and, in particular, high-intensity statin therapy for secondary prevention. Statins were similarly tolerated in older and younger adults. Future clinical trials are needed to more definitively identify the proper statin treatment approach in older patients.

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Author Contributions

All authors have been involved in the study design, analysis, and article revision. All authors read and approved the final article. Nanna is the guarantor who accepts full responsibility for the work and the conduct of the study, had access to the data, and controlled the decision to publish. Nanna had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Nanna contributed to the conception and design of the study, the data interpretation, the article drafting, and the critical revision of the article. Navar contributed to the conception and design of the study, the data analysis, the data interpretation, the article drafting, and the critical revision of the article. Wang, Mi, Virani, Louie, Lee, Goldberg, Roger, and Robinson contributed to the conception and design of the study, the data interpretation, and the critical revision of the article. Peterson contributed to the conception and design of the study, the supervision, data acquisition, and interpretation, the article drafting, and the critical revision of the article.

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SUPPLEMENTAL MATERIAL

Table S1. Adverse Symptom Example Survey Questions.

Example side effect and symptom related questions from the PALM patient survey.

Have you experienced any of the following symptoms while taking a statin? Please select all that apply. ***If currently or previously on a statin***
[ ] muscle aches/cramps
[ ] memory loss, forgetfulness, or confusion
[ ] weakness
[ ] nausea/vomiting/stomach upset
[ ] constipation
[ ] fatigue
[ ] hives/itching
[ ] other (free text)
[ ] I have not experienced any symptoms
[ ] I don't know/can't remember
What was the reason for stopping your last statin? Please select all that apply. ***If not on a statin now, but previously on a statin***
[ ] My doctor felt it was no longer needed
[ ] I didn't like taking a medication every day
[ ] Too expensive/cost
[ ] I lost/changed my insurance
[ ] I did not notice any improvement in how I felt while on this medication
[ ] I prefer natural remedies or supplements instead of prescription medicines
[ ] I had side effects
[ ] A friend or relative recommended I stop
[ ] Information I read (online, magazine) or heard suggested that I stop
[ ] Other ____
[ ] I don't know/can't remember