Title

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Abstract

Importance—Muscle pain, fatigue, and weakness are common adverse effects of statin medications and may decrease physical activity in older men.

Objective—Determine whether statin use is associated with physical activity, longitudinally and cross-sectionally.

Design, Setting, and Participants—Men participating in the Osteoporotic Fractures in Men Study, a multicenter prospective cohort study of community-living men age 65+, enrolled between March 2000-April 2002.

Exposure—Statin use as determined by an inventory of medications (taken within last 30 days). In cross-sectional analyses, statin use categories were: users and nonusers. In longitudinal analyses, categories were: prevalent users (baseline use and throughout study), new users (initiated use during the study) and nonusers (never used).

Main Outcomes and Measure—Self-reported physical activity at baseline and 2 follow-up visits using the Physical Activity Scale for the Elderly (PASE). At the third visit, an accelerometer measured metabolic equivalents (METs; kcal/kg/hr) and minutes of moderate activity (METs 3.0), vigorous activity (METs 6.0), and sedentary behavior (METs 1.5).

Results—At baseline, 989 men (24%) were users and 3,148 (76%) were nonusers. The adjusted difference in baseline PASE between users and nonusers was −5.8 points (95% CI, −10.9 to −0.7). A total of 3,039 men met the inclusion criteria for longitudinal analysis: 727 (24%) prevalent users, 845 (28%) new users, 1,467 (48%) nonusers. PASE declined by an average of 2.5 points/ year (2.0–3.0) for nonusers and 2.8 points/year (2.1, 3.5) for prevalent users, a nonstatistical difference (0.3 point, −0.5–1). For new users, annual PASE score declined at a faster rate than nonusers (0.9 point difference; 0.1–1.7). 3,071 men had adequate accelerometry data, 1,542 (50%) were statin users. Statin users expended less METS (0.03 kcal/kg/hr less; 0.02–0.04); engaged in less moderate physical activity (5.4 fewer minutes/day; 1.9–8.8), less vigorous activity (0.6 fewer minutes/day; 0.1–1.1), and more sedentary behavior (7.6 greater minutes/day; 2.6–12.4).

Conclusion and Relevance—Statin use was associated with modestly lower physical activity among community-living men, even after accounting for medical history and other potentially confounding factors. The clinical significance of these findings deserves further investigation.

Introduction

Physical activity is vital for older adults to maintain health, physical function, and independence.[1–3] One objective of Healthy People 2020 is to increase the amount of leisure-time physical activities among older adults.[4] Understanding factors that influence physical activity in older men is both clinically important and of major public health interest.

Muscle symptoms are the most common adverse effects experienced by patients taking statins. Symptoms include diffuse muscle pain, muscle fatigue, and weakness.[5–7] If present, these symptoms are most often observed after initiation of statin therapy, and may cause a decline in physical activity.[8] Several short-term studies have suggested that prevalent use or initiation of a statin use is linked to less physical activity in older adults followed for up to a

year.[8,9] Other studies have demonstrated that initiation of moderate physical activity increased muscle pain and symptoms in statin users.[9–11] Finally, a recent 12-week aerobic exercise study showed that cardiorespiratory fitness and respiratory markers in the muscles were improved for statin nonusers, but did not improve in patients randomized to 40 mg of simvastatin.[12] These studies underscore the possibility that statins may decrease physical activity in older adults, but long-term studies are needed to evaluate if these effects are sustained.

Using a large observational study in older men, the Osteoporotic Fractures in Men Study (MrOS), we evaluated the cross-sectional and longitudinal relationship between self-reported physical activity and statin use up to 6.9 years after baseline. This longer follow-up period allowed us to estimate changes in physical activity in prevalent statin users and initiators of statin medications compared to nonusers. We also evaluated the cross-sectional association between use of statin medication and physical activity measured objectively by an accelerometer.

Methods

Participants

The MrOS study recruited 5,994 community-living men aged 65 years and older from six geographical areas around the United States (Birmingham, AL, Minneapolis, MN, Palo Alto, CA, Pittsburgh, PA, Portland, OR, and San Diego, CA). A baseline examination was completed from March 2000 to April 2002.[13] The MrOS is a study of healthy aging with a focus on osteoporosis and fractures. Men were eligible if they were able to walk without assistance of another person, did not have bilateral hip replacements, had no medical condition expected to cause imminent death, and were able to provide consent. Follow-up clinic visits occurred an average of 4.6 (±0.4) and 6.9 (±0.4) years after baseline, visits 2 and 3 respectively. The MrOS design, rationale, and recruitment have been published elsewhere.[13] The institutional review board at each center approved the study protocol, and written informed consent was obtained from all men.

Medications

At each clinic visit, men were asked to bring all the medications they had taken in the past 30 days. Only prescription medications were included at baseline. Follow-up visits additionally included over-the-counter medications. All medications recorded by study staff were stored in an electronic medications inventory database (San Francisco Coordinating Center, San Francisco, CA). Each medication was matched to its ingredient(s) based on the Iowa Drug Information Service (IDIS) Drug Vocabulary (College of Pharmacy, University of Iowa, Iowa City, IA).[13]

Demographic and health measurements

At all visits, men completed a self-administered questionnaire to ascertain their age, self-identified race, education, marital status, smoking status, self-perceived health, dizziness, and selected self-reported physician-diagnosed conditions, including previous myocardial infarction (MI), stroke, angina, heart failure, hypertension, diabetes, lung disease,

rheumatoid arthritis, and Parkinson's disease. Variables were categorized for this study based on clinically important cut-points as follows: self-identified race as non-white and white; education as some high school or less and high school or more; marital status as married and not married; smoking status as never smoker, past smoker, and current smoker; self-perceived health as very poor, poor, fair, good, and excellent. All self-reported physician-diagnosed conditions were categorized as present and absent. Measured height and weight were used to calculate body mass index. Serum samples were collected at the baseline visit after an overnight fast and total cholesterol was calculated from chemistry assays performed using a standard clinical automated analyzer.

PASE Analyses

At each visit men were asked to complete the Physical Activity Scale for the Elderly (PASE) questionnaire. PASE is a validated, self-administered questionnaire that inquires about the performance of occupational, household, and leisure items over a one-week period.[14] Total PASE score is the weighted sum of participant responses regarding 12 various activities. For this analysis, PASE was adjusted by clinical site and season to reduce their possible effects on physical activity. An average seasonal PASE was calculated according to site. The difference between these mean values and the overall mean PASE at each visit was added to participants' PASE score.

Analytic sample—The primary analytic method was a complete case analysis and the sample consisted of those men with no missing exposure, outcome, or covariates data. Men were excluded for lacking statin use or PASE at baseline (n=239 and n=3, respectively), lacking follow-up statin or PASE information (n=966), or discontinuing statin use during follow-up (n=319 total; 11% of baseline statin users stopped before visit 2 and 9% of visit 2 users stopped before visit 3). An additional 330 men were excluded from the cross-sectional and 1,428 from the longitudinal analysis because of missing covariates.

Statin use—Men were classified as either statin users or nonusers according to their use at baseline for our cross-sectional analysis. For the longitudinal analysis, men were categorized as follows: *Prevalent users* used a statin at all visits; *Nonusers* never reported using a statin; *New users* first reported using a statin either at visit 2 or at visit 3.

Statistical analysis—In order to characterize our baseline analytic sample, t-tests and chi-square tests were used to compare characteristics between baseline statin users and nonusers.

Multivariable linear regression modeling was used to assess the baseline cross-sectional association between statin use and PASE. First, we created a model controlling for age and site only. To account for potential confounding effects, we then constructed a fully adjusted model in which known or suspected risk factors for reduced physical activity were added: fixed-in-time: age, site, and baseline total cholesterol; time-varying: MI, stroke, hypertension, diabetes, perceived health, and body mass index.

Mixed effects linear regression modeling was used to determine the association between statin use and longitudinal changes in PASE. Of interest in our longitudinal models was a

significant statin × time interaction, which estimated the difference in changing PASE scores between the two statin user groups and nonusers. Time was defined as calendar years since baseline, and was used as a continuous variable. As described above, we created an age and site- and a fully adjusted model. Using mixed effects regression allowed us to use both fixed-in-time and time-varying variables in the fully adjusted model. Time-varying variables were considered to account for changes in health status during the follow-up period.

Secondary analysis—To address potential bias in this analysis as a result of missing values, we used data imputation on statin use, PASE, and covariates in fully adjusted models. Data was imputed using the multiple imputation by chained equation (MICE) approach and 20 imputation cycles were performed to generate the data set. Imputation increased the sample size of men to 4,467.

Statistical tests were conducted at the 0.05, two-tailed level of significance. Analyses were performed using STATA version 13.0 (StataCorp, College Station, Texas).

Accelerometer Analyses

As part of visit 3, men were asked to wear an accelerometer, which collected physiological data every minute over a seven-day period (SenseWear® Pro3 Armband, by Body Media, Inc., Pittsburgh, PA). From these data, as well as height, weight, age, handedness, and smoking status, activity level (sedentary, moderate, and vigorous) and time spent at each level were estimated.[15] Outcome variables used in this analysis were daily: 1) Metabolic equivalents (METs; kcal/kg/hr); 2) minutes of moderate physical activity (METs 3.0); 3) minutes of vigorous physical activity (METs 6.0); and, 4) minutes of sedentary behavior (METs 1.5).

Analytic sample—Only men with accelerometer data for at least 90% of the time for at least one 24-hour period were included.

Statin use—Men were classified as statin users or nonusers based on their medication use information collected at visit 3.

Statistical analysis—Multivariable linear regression was used to determine the cross-sectional association between accelerometer outcome measures and statin use. Minutes of moderate physical activity, minutes of vigorous physical activity, and minutes of sedentary behavior were log-transformed to normalize their distributions. For each outcome, a minimally-adjusted model using season, age, and site was created. Fully adjusted models were then created to account for confounding as described above. In models using log-transformed minutes, we reported the ratio of the medians for users versus nonusers and this ratio was interpreted in the text as a percent difference and absolute difference based on the median value.

Results

Statin use and PASE score

At baseline 4,137 men met the criteria of our cross-sectional analytic sample. Nearly a quarter of these men were statin users (N=989) and 76% were nonusers (n=3,148). The average age of users (±SD) was 72.9 (±5.3) and was 72.9 (±5.5) for nonusers. Of these men, statin users were more likely to report a previous MI, a previous stroke, hypertension, diabetes, lower total cholesterol and a lower self-perceived health (Table 1). The fully adjusted estimated difference in baseline PASE between users and nonusers was −5.8 points (95% CI, −10.9 to −0.7) (Table 2).

In our longitudinal analysis of statin use and PASE, 3,039 men were included in the analytic sample. Twenty-four percent (n=727) were prevalent statin users and 48% (n=1467) never used a statin over the approximate 7 years of follow-up. Slightly more than a quarter of men (n=845) first reported statin use during follow-up. On average, a decrease in physical activity was observed in all groups during follow-up (Table 3; Figure 1). According to the fully adjusted model, PASE score for prevalent users declined by roughly the same number of points annually as nonusers. The difference in the annual decline in the two groups (estimated by an interaction term in our fully adjusted model) was 0.3 points (95% CI, −0.5 to 1.1). In new users PASE score declined at a faster rate than nonusers; the difference between groups was 0.9 points/year (95% CI, 0.1 to 1.7). While PASE declined at a statistically significant greater rate than nonusers, the overall difference in PASE decline among the three statin use groups was not significant.

Of the men who used a statin at baseline, 11% discontinued use prior to visit 2 and, of the men who used at visit 2, 9% discontinued use before visit 3. These men had fewer self-reported MIs than men who, during the same timeframe, did not stop. These men also had a nominally greater decline in PASE when compared to their proper counterparts, although no formal statistical tests were performed. All other characteristics were similar.

Our primary analytic approach used complete case analysis for both the cross-sectional and longitudinal analyses of statin use and PASE. To assess the impact of using complete cases, we performed multiple imputation of missing data and reran our models. Multiple imputation of missing data leads to similar estimates of association and did not change our conclusions. In particular, based on the fully adjusted models, cross-sectional difference in baseline PASE was −6.3 points (95% CI, −11.2 to −1.4); and the fully adjusted longitudinal difference in annual decline between persistent and nonusers was 0.2 points (95% CI, to −0.6 to 0.9) and between new and nonusers was 0.8 points (95% CI, 0.1 to 1.5).

Statin use and accelerometer measures

While 4,682 men returned for visit 3, only 3,071 men wore the accelerometer for at least 90% of the time, of which 1,542 (50%) were statin users. As estimated by the fully adjusted models, daily METS was lower in statin users by 0.03 kcal/kg/hr (95% CI, 0.02 to 0.04) (Table 4). Statin users engaged in 9.6% fewer minutes/day of moderate physical activity (95% CI, 3.1% to 16.4%) compared to nonusers; this translates into a difference of 5.4 fewer minutes/day (95% CI, 1.9 to 8.8), given the median minutes/day of moderate physical

activity was 62.0 in nonusers. Similarly, statin users engaged in 9.0% fewer minutes of vigorous activity (95% CI, 1.7% to 16.8%) than nonusers or 0.6 minutes/day less (95% CI, 0.1 to 1.1), given the median minutes/day of vigorous activity was 7.4 minutes/day in nonuser. Statin users were involved in 0.6% more minutes/day of sedentary behavior (95% CI, 0.2% to 1.0%) than nonusers. This was 7.6 more minutes/day of sedentary behavior (95% CI, 2.6 to 12.4), since the median sedentary behavior was 1299.4 minutes/day (21.7 hours/day) in nonusers.

Discussion

In this large observational study in older men, we examined the cross-sectional differences and longitudinal changes in physical activity by statin use. Overall, physical activity declined at similar rates to those observed in a prior study.[16] While short-term studies suggest that statins decrease physical activity in older adults for up to one year, it was unclear if this effect was sustained.[8,9] Our long-term study, that followed men up to an average of 6.9 years, suggests that statins are associated with less physical activity for as long as statins are used. In cross sectional analyses, statin users started with lower physical activity levels compared to nonusers. Longitudinally, prevalent statin users declined at similar rates as nonusers while new statin users declined more rapidly. This association was observed even after adjusting for time-varying health factors, such as MI or stroke.

The exact mechanism by which statins affect muscles is not known. There are a number of possible causes. For example, statins may disrupt mitochondrial function and interfere with ATP production, contributing to fatigue and muscle weakness.[8,18–20] Disruption of mitochondria may also cause myopathy by increasing the production of reactive oxygen species, inducing DNA damage, and initiating apoptosis. Recent studies have also indicated these same mechanisms are precipitated or exacerbated during exercise in statin users.[9–11] If exercise-induced myopathy occurs in older adults taking statin medications, this may explain why we observed prevalent statin users engaged in less physical activity in this study. In addition, new statin users had the largest drop in physical activity; starting off with physical activity similar to nonusers, but ending up with physical activity similar to prevalent statin users.

Prevalent statin use was associated with less physical activity, but perhaps reassuringly, was not associated with a more rapid decline compared to nonusers. While we hypothesized that prevalent statin use would result in a more rapid decline in physical activity, there are two possible reasons we did not observe this. First, those most susceptible to muscle symptoms may have stopped using a statin during this study. Secondly, a decline in one's health may precipitate stopping a statin. Of baseline statin users, 9% stopped before visit 2, and of statin users at visit 2, 11% stopped before visit 3. Of those that stopped, we observed a nominal decrease in physical activity.

We also examined physical activity measured objectively by accelerometry. One measure from the accelerometer included METS, which is a global measure of physical activity. Statin users expended 0.03 fewer METS per day. In clinical terms, and using average body weight of the men in this study (78 kg), the average decrease in energy expenditure was

approximately 56.2 kcal/day, or approximately 151 minutes/week of walking at a typical pace for older adults (2 miles/hour).[21]

The other objective measures included minutes of physical activity during moderate or vigorous activity and minutes of sedentary behavior. While the daily amount of moderate or vigorous activity was modestly less in statin users, it equates to approximately 37.8 minutes/week of less exercise. For comparison, the 2013 American Heart Association and the American College Cardiology (AHA/ACC) Guideline Lifestyle Managements recommends an average of 40 minutes of moderate to vigorous activity for 3–4 sessions per week.[22,23] Finally, more sedentary behavior was observed in statin users, on average about 53 minutes/week, an increase to 21.8 hours/week. Sedentary time is associated with all-cause and CVD mortality.[1,2,24] For example, in one study, >23 hours/week of sedentary behavior was associated with an adjusted hazard ratio of 1.37 (1.01–1.87) compared to <11 hours/week.[24] While it should be noted that 53 more minutes of sedentary behavior per week may not be substantial in terms of CVD risk, clinicians and patients should be aware that more sedentary behavior and less physical activity may be observed with statin use. While accelerometer measurements were only performed once, these are an objective assessment of activity and support the differences observed with self-reported physical activity measured by PASE.

The recent 2013 AHA/ACC Guideline on the Treatment of Blood Cholesterol acknowledges that there are few data available in adults >75 years old and did not clearly support using high-intensity statin therapy in secondary prevention.[17] For the same reason, they also recommend the initiation of statins for primary prevention in this population requires considering comorbidities, safety, and priorities of care. Thus, possible adverse effects on physical activity should be considered.

Limitations

This study was a study of older men, and generalization to older women may not be appropriate. PASE is a self-administered questionnaire and could be subject to measurement error or recall bias. The accelerometer data was only collected at visit 3, thus longitudinal changes could not be assessed for this measure.

As in any observational study of the effect of an intervention, control for confounding by indication was important. It can be difficult to predict whether factors associated with physical activity and statin use might bias the findings toward or away from the null. For example, health issues related to lower physical activity could also relate to statin intolerance or noncompliance, resulting in a weaker apparent effect of statin use on physical activity (bias toward the null). Similarly, low cholesterol in older adults is also associated with worse health and would coincide with lower physical activity and a lack of statin use.[25–27] If residual confounding by health status remains, our results are likely to underestimate the true strength of association between statin use and physical activity. In contrast, the potential that our results overestimate the strength of association also exists. For example, if our adjustments for cardiovascular risk factors are incomplete, there is the possibility that it is these risk factors, and not statin use, that is responsible for the associations we observe with physical activity. Because of these potential biases, we took

care to examine self-reported cardiovascular events that could reasonably be associated both with the use of a statin and physical activity. The collection of these variables over the course of follow-up allowed for adjustment of time-varying confounders, such as MI and stroke, which would be expected to both reduce physical activity and increase the probability of new statin use. Adjustment for cardiovascular events and medications, diabetes, and BMI, which were identified as confounders, minimizes the possibility that the results reported here were due to confounding by indication. However, as in all observational studies, the risk of residual confounding remains. For example, imperfect reporting of cardiovascular events and measurement of cardiovascular risk factors that could affect physical activity leaves room for the possibility of additional, uncontrolled confounding in these analyses.

Information about the duration of statin use was not known prior to the initiation of this study. Consequently, information about prior statin use was not known and participants classified as nonusers may have been former statin users. Classifying participants as new statin users allowed us to explore the association between statin initiation and physical activity. Unfortunately, this does not preclude the possibility that some men were new statin users, then experienced muscular adverse effects, and stopped using a statin prior to the initiation of this study or between visits. Thus, those recorded as being a prevalent or new statin user may have been users that didn't experience muscular symptoms, and perhaps less susceptible to declines in physical activity.

Conclusion

In this prospective observational study in community-living older men, statin use was associated with modestly lower physical activity even after accounting for medical history and other potentially confounding factors. In addition, new statin use was associated with a more rapid decline in physical activity than nonuse. While similar effects have been reported in older adults in short-term studies, this study shows that although physical activity levels remain lower in prevalent statin users than nonusers, they do not continue to decline more rapidly than nonusers over time. The possible reasons for lower physical activity levels in statin users may be general muscle pain caused by statins, a well-known adverse effect; exercise-endured myopathy; or muscular fatigue. The clinical significance of these findings deserves further investigation.

Acknowledgments

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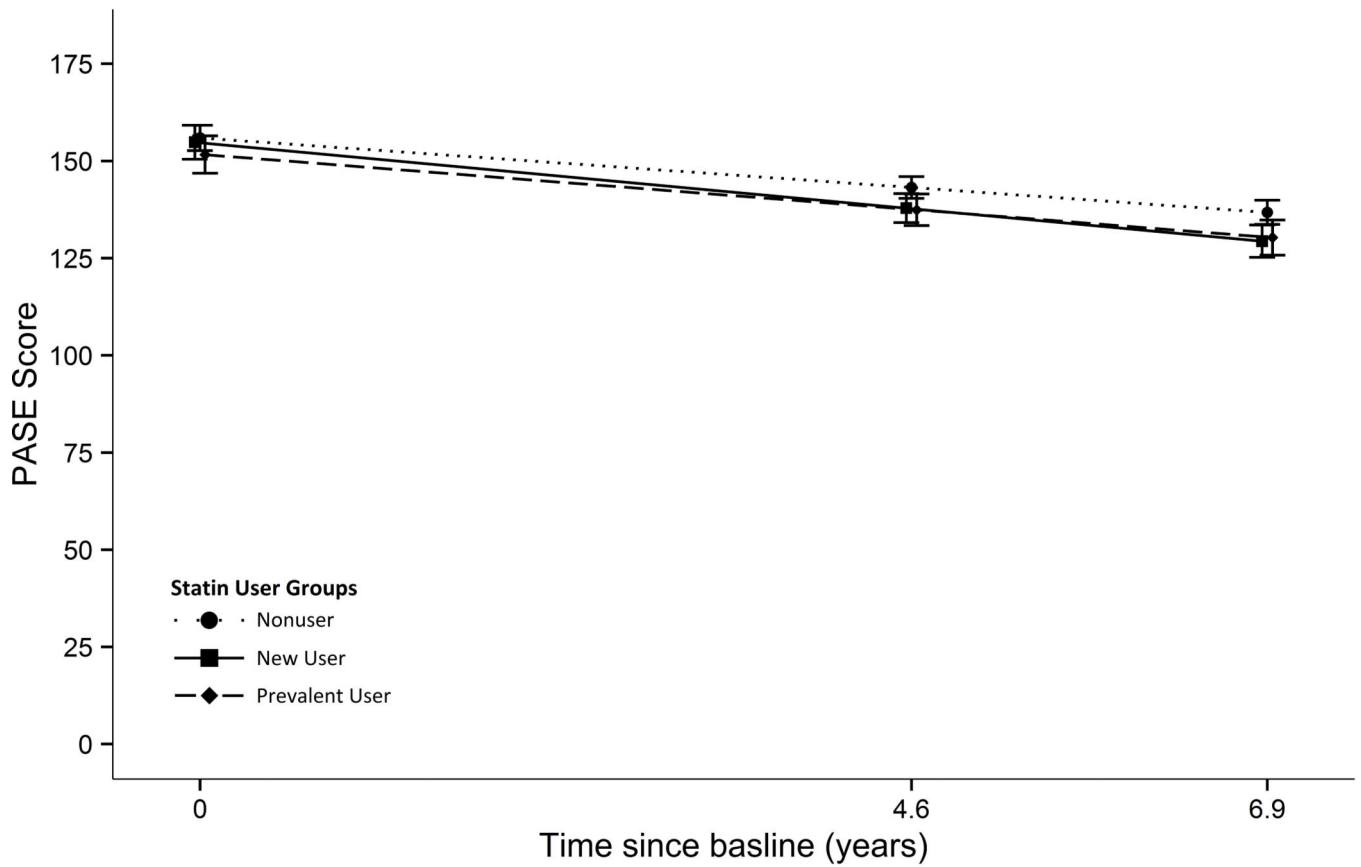
Figure 1.
Mean Physical Activity Scale in the Elderly (PASE) scores according to stain user groups as estimated by mixed effects linear regression adjusted for age, site, and baseline total cholesterol (fixed-in-time), myocardial infarction, stroke, hypertension, diabetes, perceived health and body mass index (time-varying). The error bars represent 95% confidence intervals for the estimated mean PASE at each visit (n=3,039).

Table 1

Baseline characteristics of statin users and nonusers in the cross-sectional PASE analytic sample (N=4,137)[a]

	Statin Users (N=989)	Statin Nonusers (N=3,148)	p-value [b]
Age, mean (SD), years [d]	72.9 (5.3)	72.9 (5.5)	.98
Non-white race/ethnicity	70 (7.1)	257 (8.2)	.27
Education			
Some High School or less	53 (5.4)	188 (6.0)	.47
Married	854 (86.4)	2623 (83.3)	.02
Clinical site [d]			
Birmingham, AL	171 (17.3)	546 (17.3)	
Minneapolis, MN	160 (16.2)	525 (16.7)	
Pittsburg, PA	173 (17.5)	443 (14.1)	.007
Palo Alto, CA	175 (17.7)	574 (18.2)	
Portland, OR	121 (12.2)	516 (16.4)	
San Diego, CA	189 (19.1)	544 (17.3)	
Smoking Status [c]			
Never smoker	363 (36.7)	1249 (39.7)	
Past smoker	608 (61.5)	1791 (56.9)	.003
Current smoker	17 (1.7)	108 (3.4)	
Body Mass Index, mean(SD), kg/m^2 [d]	27.8 (3.8)	27.4 (3.9)	.003
Total cholesterol, mean (SD), mg/dL [d]	177.8 (29.1)	199.7 (33.9)	<.001
Self-reported medical history			
Myocardial Infarction [d]	294 (29.7)	195 (6.2)	<.001
Stroke [d]	76 (7.7)	110 (3.5)	<.001
Angina	297 (30.0)	236 (7.5)	<.001
Heart Failure	65 (6.6)	98 (3.1)	<.001
Hypertension [d]	526 (53.2)	1,172 (37.2)	<.001
Diabetes [d]	136 (13.8)	254 (8.1)	<.001
Lung Disease	100 (10.1)	297 (9.4)	.53
Rheumatoid Arthritis	42 (4.3)	159 (5.1)	.30
Parkinson's Disease	5 (0.5)	19 (0.6)	.72
Dizziness	269 (27.2)	728 (23.1)	.009
ACE Inhibitors & ARB	335 (33.9)	591 (18.8)	<.001
Beta-blockers	333 (33.7)	380 (12.1)	<.001
Calcium channel blockers			
Dihydropyridine	110 (11.1)	192 (6.1)	<.001
Non-dihydropyridine	84 (8.5)	141 (4.5)	

	Statin Users (N=989)	**Statin Nonusers (N=3,148)**	**p-value** [b]
Fibrates [c]	18 (1.8)	48 (1.6)	.59
Niacin [c]	18 (1.8)	51 (1.7)	.75
Total number medications [c]			
0–3	300 (30.3)	1,863 (60.9)	
4–7	453 (45.8)	860 (28.1)	<.001
8–11	182 (18.4)	248 (8.1)	
12+	54 (5.5)	86 (2.8)	
Self-rated health [d]			
Very Poor	3 (0.3)	3 (0.1)	
Poor	18 (1.8)	27 (0.9)	
Fair	143 (14.5)	282 (9.0)	<.001
Good	568 (57.4)	1609 (51.1)	
Excellent	257 (26.0)	1227 (39.0)	

Abbreviations: ACE, angiotensin-converting-enzyme; ARB, angiotensin II receptor blockers; PASE, Physical Activity Scale for the Elderly; SD, standard deviation

[a]Data are presented as number (%) unless otherwise indicated

[b]p-values are from chi-square tests comparing statin user and nonusers for categorical variables and from t-tests for continuous variables

[c]Denominator less than 4137 for these measures due to missing values: smoking status, n=4136; fibrates, n=4046; niacin, n=4046; total number of medications, n=4046

[d]Variables in the fully adjusted PASE models

Table 2

Cross-sectional associations between statins and PASE at baseline (n= 4,137).

	Age & Site Adjusted			Fully Adjusted[1]		
	Mean PASE (95% CI)	Estimated diff. (95% CI)	p-value[2]	Mean PASE (95% CI)	Estimated diff. (95% CI)	p-value[2]
Nonuser	153.3 (151.0, 155.7)	ref		152.0 (149.7, 154.4)	ref	
User	142.1 (138.0, 146.3)	−11.2 (−15.9, −6.4)	<.001	146.3 (141.9, 150.6)	−5.8 (−10.9, −0.6)	.03

Abbreviations: CI, confidence intervals; Diff, difference; PASE, Physical Activity Scale for the Elderly; ref, reference group

[1] Model controlled for the following variables: age, site, myocardial infarction, stroke, hypertension, diabetes, perceived health, body mass index, and total cholesterol

[2] p-value for the estimate difference in PASE at baseline

Table 3

Longitudinal associations between statins and decline in PASE (n= 3,039).

	Age & Site Adjusted			Fully Adjusted[1]		
	Annual decline in PASE (95% CI)	Estimated diff. in decline (95% CI)[2]	p-value[3]	Annual decline in PASE (95% CI)	Estimated diff. in decline (95% CI)[2]	p-value[3]
Nonuser	2.8 (2.3, 3.2)	ref		2.5 (2.0, 3.0)	ref	
Prevalent User	2.9 (2.2, 3.6)	0.1 (−0.7, 0.9)	0.02	2.8 (2.1, 3.5)	0.3 (−0.5, 1.1)	0.07
New User	3.9 (3.3, 4.5)	1.1 (0.3, 1.9)		3.4 (2.8, 4.0)	0.9 (0.1, 1.7)	

Abbreviations: CI, confidence intervals; Diff, difference; PASE, Physical Activity Scale for the Elderly; ref, reference group

[1] Model controlled for the following variables: age, site, and baseline total cholesterol (fixed-in-time); myocardial infarction, stroke, hypertension, diabetes, perceived health, and body mass index (time-varying)

[2] Estimate of the statin use × time interaction with nonusers as a reference group

[3] Type III p-value for the statin use × time interaction

Table 4

Cross-sectional association between statin use and accelerometer outcomes (n=3,071).

	Age & Site Adjusted		Fully Adjusted [1]	
	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value
Mean METS, kcal/kg/hr				
Nonuser	1.25 (1.24–1.26)		1.23 (1.22–1.24)	
User	1.19 (1.18–1.20)		1.20 (1.19–1.21)	
Difference (User-Nonuser)	−0.06 (−0.07- −0.04)	<.001	−0.03 (−0.04- −0.02)	<.001
Median Moderate physical activity, minutes/day [2]				
Nonuser	64.9 (62.1–67.7)		62.0 (59.5–64.7)	
User	53.9 (51.7, 56.3)		56.6 (54.3–59.1)	
User/Nonuser [3]	0.83 (0.78–0.88)	<.001	0.91 (0.86–0.97)	.003
Median Vigorous physical activity, minutes/day				
Nonuser	7.7 (7.3–8.1)		7.4 (7.0–7.8)	
User	6.5 (6.2–6.8)		6.8 (6.5–7.1)	
User/Nonuser	0.84 (0.79–0.90)	<.001	0.92 (0.86–0.98)	.01
Median Sedentary behavior, minutes/day				
Nonuser	1297.0 (1293.6–1300.5)		1299.4 (1296.0–1302.8)	
User	1309.5 (1306.1–1312.9)		1306.9 (1303.5–1310.3)	
User/Nonuser	1.010 (1.006–1.013)	<.001	1.006 (1.002–1.010)	0.003

Abbreviations: CI, confidence intervals, METS, metabolic equivalents,

[1] Covariates include: season, age, site, body mass index, beta-blocker use, ACE inhibitor/ARB use

[2] Estimated medians are reported for outcomes measured in minutes/day since these outcomes were log-transformed for modeling purposes and interpretation of the model coefficients are relative median values

[3] The ratio of user/nonuser was calculated from multivariable linear regression model coefficients estimating the association between statin use and each outcome; since the outcomes were log-transformed, the exponent of model coefficients are a ratio of the median value for users versus nonusers and are interpreted in the text as a percent difference in the outcome