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Statin Use and Gait-Speed Decline in Community-Dwelling Older Adults

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AUTHOR CONTRIBUTIONS

Drs. Lo-Ciganic and Hanlon had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Lo-Ciganic, Perera, Gray, Boudreau, Zgibor, Strotmeyer, Donohue, Bunker, Hanlon
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Analysis and interpretation of data: Lo-Ciganic, Perera, Gray, Boudreau, Zgibor, Strotmeyer, Donohue, Bunker, Hanlon
Drafting of the manuscript: Lo-Ciganic, Perera, Gray, Boudreau, Zgibor, Strotmeyer, Donohue, Bunker, Hanlon
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Abstract

BACKGROUND/OBJECTIVES—The association between statin use and physical function is uncertain. The objective of this study was to examine the association between statin use and objectively assessed gait-speed decline in community-dwelling older adults.

DESIGN—Longitudinal cohort study.

SETTING—Health, Aging, and Body Composition (Health ABC) study.

PARTICIPANTS—Two thousand five participants aged 70–79 years at baseline, with medication and gait speed data at years 1998–1999, 1999–2000, 2001–2002 and 2002–2003.

MEASUREMENTS—The independent variables were any statin use, their standardized daily doses (low, moderate, high) and lipophilicity. The primary outcome measure was gait speed decline ≥ 0.1 m/s in the following year of statin use. Multivariable generalized estimating equations were used, adjusting for demographic, health-related behaviors, health status and access to health care factors.

RESULTS—Statin use increased from 16.2% in 1998–1999 to 25.6% in 2002–2003. The overall proportions of those with gait speed decline ≥ 0.1 m/s increased from 22.2 to 23.9% between 1998–2003. Compared to non-users, any statin use was not associated with gait speed decline ≥ 0.1 m/s (adjusted odds ratio [AOR] = 0.90, 95% CI [0.77, 1.06]). Similar non-significant trends were also seen with the use of hydrophilic or lipophilic statins. Only low-dose statin users were found to have a 22% lower risk of gait speed decline (AOR = 0.78, 95% CI [0.61, 0.99]), which was mainly driven by the results from 1999–2000 follow-up.

CONCLUSION—These results suggest no detrimental effects of statin use on gait speed decline in community-dwelling older adults.

Keywords

hydroxymethylglutaryl-CoA reductase inhibitors; statins; gait speed; physical function; aged

INTRODUCTION

Gait speed is a simple, but important indicator of functional status in older adults, and a strong predictor for mortality and other health-related outcomes.[1, 2] A growing body of evidence has identified a relationship between chronic inflammation and age-related functional decline, and risk of disability.[3] Several studies indicate that statins have anti-inflammatory effects, beyond their cholesterol-lowering and anti-atherosclerosis properties.[4] For these reasons, statins could potentially have a protective effect on age-related functional decline.

Current evidence on the association between statin use and physical function decline in older adults is mixed.[5–13] Studies whose sample constitute primarily of those with peripheral artery disease (PAD) have reported that statin users had less annual decline in walking speed or distance.[5–8] However, these observed beneficial effects were modest and their clinical relevance is unclear. In addition, among studies that were not restricted to PAD samples, 4 of them did not find associations between statin use and self-reported or other physical function measures,[9–12] whereas one study found that fast walking speed decline was 25% slower in lipid-lowering medication users.[13] Previous studies show that criteria for substantial change in gait speed decline for clinical and research use are approximately 0.10 m/s, which was strongly associated with morbidity and mortality in older adults.[2, 14]

Given these conflicting findings and the importance of maintaining adequate physical function, the objective of study was to examine the association between statin use and risk of gait speed decline ≥ 0.1 m/s in community-dwelling older adults. Our hypothesis was that statin use would be protective for the development of gait speed decline ≥ 0.1 m/s.

METHODS

Study Design, Sample, and Data Source

This longitudinal study used data from the Health, Aging and Body Composition (Health ABC) Study, that enrolled 3,075 white and black adults aged 70–79 years without mobility problems.[15] Participants were recruited in 1997–1998 from a random sample of Medicare beneficiaries residing in Pittsburgh, PA and Memphis, TN. The sample of 2,405 for the current study was based on those included measurement when 20-meter gait speed was measured in 1998–1999 and medication one year prior to the gait speed measure. The study was approved by the Institutional Review Boards of the Universities of Pittsburgh, Tennessee, and California at San Francisco, and written informed consent was obtained from each participant.

Data collection and Management

The data collected during annual in-person visits included from 1998–2003 included blood tests, a battery of physiological measurements using standardized methods and responses to structured questionnaires regarding demographics, multiple aspects of health behavior and status.[15] Several incident comorbidities examined in the current study (i.e., coronary heart disease [CHD), congestive heart failure [CHF], stroke and PAD) were centrally adjudicated by the morbidity and mortality committee based on conclusive evidence from hospitalization or death records.[15] Prevalent disease is based on self-reports and/or medications.

Prescription medication information was collected annually from 1998–2003, except year 2000–2001. Participants were asked to bring all prescription medications taken in the previous month, and trained research assistants transcribed the drug name, strength, and dosage form from the medication bottle and participants reported number of units taken in the previous day/week/month, and whether taken regularly or as needed. This medication information was coded using the Iowa Drug Information Service (IDIS) and entered into a computerized database.[16]

Primary Outcome Measures

Usual gait speed was measured over a 20-m course in an unobstructed corridor annually from 1998 to 2003, and was summarized in meters per second (m/s). Timing started with the first step over the starting line and ended at the first footfall over the finishing line. Our primary outcome variable was gait speed decline ≥ 0.1 m/s in the following year based on previous studies.[2, 14]

Primary and Secondary Independent Variables

Statins were identified via corresponding IDIS codes of 24060202–24060208. The primary independent variable was use versus no use of statins at baseline (1998–1999) and annually (as a time-varying variable). We created several secondary independent variables for lipophilicity, and standardized daily dose (SDD). To create the SDD measure, we first calculated the daily dose by multiplying the number of dosage forms taken the previous day by medication strength. Then we divided the daily dose by the statin's equivalent dose reported to decrease LDL-C by 37%.[17] The following daily doses were considered to equal one unit of equivalent dose (atorvastatin 10 mg, fluvastatin 80 mg, lovastatin 40 mg, pravastatin 40 mg, simvastatin 20 mg, rosuvastatin 5 mg).[17] The SDD were categorized into low-dose (< 1 SDD), moderate-dose (1 SDD), and high-dose (>1 SDD), based on the distribution of the data and clinical relevance. Finally, we created a dichotomous measures in which statins were categorized as being lipophilic (i.e., lovastatin, simvastatin, atorvastatin, fluvastatin) or hydrophilic (i.e., pravastatin and rosuvastatin).[18]

Covariates

Several characteristics that could confound or modify the association between statin use and gait speed were adjusted for in the analyses, and were grouped into four domains: (1) demographics, (2) health-related behaviors, (3) health status, and (4) access to health care factors. Demographic variables included baseline age, sex, race (black or white), study site, education (postsecondary education, high school graduate, or less than high school graduate), and living status (alone or not alone) as a time-varying variable.

Health-related behaviors were characterized from smoking status, alcohol use (current, past, or never), and self-report of doing moderate-to-high intensity exercise in the previous week (yes vs. no) as time-varying variables. Health status factors for which statins may be indicated were characterized as time-varying, dichotomous measures (present vs. absent) for adjudicated comorbidities including CHD, stroke, and PAD.[19] Time-varying, dichotomous measures (present vs. absent) were used for self-reported hypertension, diabetes, CHF, pulmonary disease (baseline), osteoarthritis, and Parkinson's disease (baseline). Chronic kidney disease (CKD) was defined by a time-varying, dichotomous measure when the estimated glomerular filtration rate was less than 60 ml/min.[20] A time-varying dichotomous variable was created for self-rated health (good to excellent vs. fair/poor). A time-varying, categorical variable for body mass index (BMI: underweight or normal [<25.0 kg/m^2], overweight [25.0–29.9 kg/m^2], or obese [≥30.0 kg/m^2]) along with a continuous variable for average total body mass (kg) were created. In addition, voluntary isokinetic knee extensor strength (i.e., average maximum torque [Nm]) was considered as a time-varying continuous variable.[21] Time-varying, dichotomous variables were created for cognitive impairment

(Modified Mini-Mental State < 80),[22] and high depressive symptoms (Center for Epidemiologic Studies Depression Scale score >15).[23] Several time-varying, dichotomous medications use (yes vs. no) related to falls and mobility problems that were controlled for in the analyses included benzodiazepines, angiotensin converting enzyme inhibitors (ACEIs), anticholinergic medications, non-steroidal anti-inflammatory drugs (NSAIDs) and other medications with anti-inflammatory effects (i.e., systematic glucocorticoids, immunosuppressive medications, and some medications for rheumatoid arthritis, asthma, inflammatory bowel diseases, systemic lupus erythematous and other systemic inflammatory diseases).[24] A time-varying, continuous variable of the number of overall prescription medications (excluding statins, benzodiazepine, ACEIs, and other medications with anti-inflammatory effects) was included.[25]

Two time-varying, dichotomous access to health care factors (yes versus no) were created, having a flu shot in the past year (as a proxy related to an individual's care seeking behavior and access to health care to adjust for healthy user effect, as well as a provider's availability),[26] and having prescription drug coverage, accounting for patients who were on and off insurance over time.

Primary and Secondary Statistical Analyses

Appropriate descriptive statistics were used to summarize participant characteristics and main analytic variables. Statin exposure was defined as use in the year preceding ascertainment of gait speed measures. Multivariable generalized estimating equations [GEEs] models were used to examine the association between statin use and gait speed decline ≥ 0.1 m/s.[27] An autoregressive working correlation structure was used to account for potential multiple years of data from the same participants and the resulting stochastic non-independence of observations.[27] In the final multivariable models, adjusted odds ratios (AORs) and 95% confidence intervals (CI) for statin use were computed adjusted for demographics, potential confounders by indication, gait speed measures at previous years, a factor related to access to health care and covariates with a p-value less than 0.15 from a forward selection procedure. Secondary analyses used a similar approach that adjusted for the same covariates but included other operational definitions of statin use as main predictors to test dose-response and lipophilicity relationships. All analyses were performed using SAS® version 9.3 (SAS Institute Inc. Cary, NC).

RESULTS

Of the 2,405 sample participants, the mean age was 74.6 years, 51% were female, 37% were black, 63% had prescription medication coverage, and 390 (16.2%) used statins (Table 1). Statin users were younger on average and more likely to be white and from the Pittsburgh site and, have prescription drug coverage, smoke previously, drink alcohol currently, perform high-or-moderate-intensity exercise, and have more chronic comorbidities (i.e., hypertension, diabetes, CHD, CHF, stroke, PAD, and CKD) than nonusers. Statin users were also more likely to take benzodiazepines, ACEIs and multiple prescription drugs.

At baseline, among statin users, 48% used low doses, and 86% took lipophilic statins (Table 2). Any use of statin increased steadily to 20.1% in 1999–2000 to 25.6% in 2001–2002. The

overall proportions of gait speed decline ≥ 0.1 m/s ranged from 22.2 to 23.9% between 1998–2003. Statin users only experienced less gait speed decline (18.0% vs. 23.3%, p =0.03) than nonusers in 1999–2000. However, this trend was not seen (p>0.05) in 2000–2001 (25.7% vs. 22.0%) or 2002–2003 (23.6% vs. 24.0%).

Any statin use was not associated with gait speed decline ≥ 0.1 m/s (AOR 0.90; 95% CI= 0.77–1.06) compared to nonusers (Table 3). Statistically non-significant findings were also seen in high or moderate-dose, and lipophilic or hydrophilic statin use. However, only a 22% risk reduction in the gait speed decline was found statistically significant among low-dose users compared to statin nonusers (AOR 0.78; 95% CI [0.61, 0.99])., which was mainly driven from the results from 1999–2000 follow-up.

DISCUSSION

The overall results of this study demonstrated no substantial associations between statin use and gait speed decline ≥ 0.1 m/s, which has been related to outcomes of self-reported motility and mortality, in a large elderly community dwelling sample. These overall results are consistent with studies conducted in those without PAD.[9–12] Large cohort studies found that statin use was not associated with self-reported mobility limitations,[9] objective physical performance measures[10] and incidence of frailty in postmenopausal women[11], and muscle strength, balance, mobility and falls.[12] However, two randomized trials[7, 8] and three longitudinal studies [5, 6, 13] in individuals with PAD have reported that statin use was associated with lower risk of gait speed decline. Possible explanations of these differences include use of varied populations (e.g., women only, younger baseline age), less precise self-reported outcomes, modest improvement in using continuous outcomes but might lack of clinical relevance, and lack of attention to dose-response.

What are the clinical implications of these study findings for older adults? Given that statin use may continue to increase due to new 2013 ACC/AHA guideline on the Treatment of Blood Cholesterol,[28] the overall non-significant association of statin use in gait speed decline is reassuring since it was possible that statin-related muscular adverse events in older adults could have resulted in slower gait speed. Generally, the muscle-related adverse events of statin use are associated with higher doses and blood levels.[29] These adverse events may occur in up to 10% of the adults receiving high-dose statins,[30] however, the precise estimate is unknown for older frail adults. Low-dose statin use as shown in our results may minimize muscle-related adverse effects in older adults, and therefore may be less likely to counteract beneficial effects of statins.

Strengths of this study include the prospective design in a large sample of community-dwelling older adult population, medication information collected using a state of the art approach, availability of serially obtained, standardized gait speed measures, and adjustment for numerous potential confounders. However, inherent to longitudinal studies examining older adults, potential survivor bias should be considered. The results from a sensitivity analysis, restricted to participants alive during all study years 1998–2003, yielded similar results (data not shown). Second, medication data were collected at fixed nearly yearly points in time, preventing us from being able to document the exact date on which statins

were initiated, dosage was changed, or discontinued, or adverse events that could affect gait speed occurred. Moreover, unmeasured confounders such as adherence to medications cannot be ruled out. Lastly, this sample was drawn from two US cities and may not be generalizable to other populations.

CONCLUSION

These results suggest no detrimental effects of statin use on gait speed decline in community-dwelling older adults. Future studies are needed to confirm the inconclusive, observed decreased risk of low-dose statin use in varied older adult populations.

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Conflict of Interest Disclosures

None of the authors has relevant financial interests, activities, relationships, or affiliations, or other potential conflicts of interest to report.

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	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Employment or Affiliation		X		X		X		X		X		X		X		
Grants/Funds		X		X		X		X		X		X		X		
Honoraria		X		X		X		X		X		X		X		
Speaker Forum		X		X		X		X		X		X		X		
Consultant		X		X		X		X		X		X		X		
Stocks		X		X		X		X		X		X		X		
Royalties		X		X		X		X		X		X		X		
Expert Testimony		X		X		X		X		X		X		X		
Board Member		X		X		X		X		X		X		X		
Patents		X		X		X		X		X		X		X		
Personal Relationship		X		X		X		X		X		X		X		

Elements of Financial/ Personal Conflicts	Anne Newman		Eleanor Simonsick		Douglas Bauer		Suzanne Satterfield		Paolo Caserotti		Tamara Harris		Ronald Shorr		Joseph Hanlon	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Employment or Affiliation		X		X		X		X		X		X		X		
Grants/Funds		X		X		X		X		X		X		X		
Honoraria		X		X		X		X		X		X		X		

Elements of Financial/ Personal Conflicts	Anne Newman		Eleanor Simonsick		Douglas Bauer		Suzanne Satterfield		Paolo Caserotti		Tamara Harris		Ronald Shorr		Joseph Hanlon	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Speaker Forum		X		X		X		X		X		X		X		
Consultant		X		X		X		X		X		X		X		
Stocks		X		X		X		X		X		X		X		
Royalties		X		X		X		X		X		X		X		
Expert Testimony		X		X		X		X		X		X		X		
Board Member		X		X		X		X		X		X		X		
Patents		X		X		X		X		X		X		X		
Personal Relationship		X		X		X		X		X		X		X		

References

1. Abellan van Kan G, Rolland Y, Andrieu S, et al. Gait speed at usual pace as a predictor of adverse outcomes in community-dwelling older people an International Academy on Nutrition and Aging (IANA) Task Force. J Nutr Health Aging. 2009; 13:881–889. [PubMed: 19924348]
2. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. JAMA. 2011; 305:50–58. [PubMed: 21205966]
3. Corsonello A, Garasto S, Abbatecola AM, et al. Targeting inflammation to slow or delay functional decline: where are we? Biogerontology. 2010; 11:603–614. [PubMed: 20549351]
4. Bu DX, Griffin G, Lichtman AH. Mechanisms for the anti-inflammatory effects of statins. Curr Opin Lipidol. 2011; 22:165–170. [PubMed: 21412153]
5. Giri J, McDermott MM, Greenland P, et al. Statin use and functional decline in patients with and without peripheral arterial disease. J Am Coll Cardiol. 2006; 47:998–1004. [PubMed: 16516084]
6. McDermott MM, Guralnik JM, Greenland P, et al. Statin use and leg functioning in patients with and without lower-extremity peripheral arterial disease. Circulation. 2003; 107:757–761. [PubMed: 12578881]
7. Mondillo S, Ballo P, Barbati R, et al. Effects of simvastatin on walking performance and symptoms of intermittent claudication in hypercholesterolemic patients with peripheral vascular disease. Am J Med. 2003; 114:359–364. [PubMed: 12714124]
8. Mohler ER 3rd, Hiatt WR, Creager MA. Cholesterol reduction with atorvastatin improves walking distance in patients with peripheral arterial disease. Circulation. 2003; 108:1481–1486. [PubMed: 12952839]
9. Gray SL, Boudreau RM, Newman AB, et al. Angiotensin-converting enzyme inhibitor and statin use and incident mobility limitation in community-dwelling older adults: the Health, Aging and Body Composition study. J Am Geriatr Soc. 2011; 59:2226–2232. [PubMed: 22092102]
10. Gray SL, Aragaki AK, LaMonte MJ, et al. Statins, angiotensin-converting enzyme inhibitors, and physical performance in older women. J Am Geriatr Soc. 2012; 60:2206–2214. [PubMed: 23176078]
11. LaCroix AZ, Gray SL, Aragaki A, et al. Statin use and incident frailty in women aged 65 years or older: prospective findings from the Women's Health Initiative Observational Study. J Gerontol A Biol Sci Med Sci. 2008; 63:369–375. [PubMed: 18426960]
12. Haerer W, Delbaere K, Bartlett H, et al. Relationships between HMG-CoA reductase inhibitors (statin) use and strength, balance and falls in older people. Intern Med J. 2012; 42:1329–1334. [PubMed: 22032261]
13. Dumurgier J, Singh-Manoux A, Tavernier B, et al. Lipid-lowering drugs associated with slower motor decline in the elderly adults. J Gerontol A Biol Sci Med Sci. 2014; 69:199–206. [PubMed: 24097424]
14. Perera S, Mody SH, Woodman RC, et al. Meaningful change and responsiveness in common physical performance measures in older adults. J Am Geriatr Soc. 2006; 54:743–749. [PubMed: 16696738]

15. Simonsick EM, Newman AB, Nevitt MC, et al. Measuring higher level physical function in well-functioning older adults: expanding familiar approaches in the Health ABC study. J Gerontol A Biol Sci Med Sci. 2001; 56:M644–649. [PubMed: 11584038]
16. Pahor M, Chrischilles EA, Guralnik JM, et al. Drug data coding and analysis in epidemiologic studies. Eur J Epidemiol. 1994; 10:405–411. [PubMed: 7843344]
17. Jones PH, Davidson MH, Stein EA, et al. Comparison of the efficacy and safety of rosuvastatin versus atorvastatin, simvastatin, and pravastatin across doses (STELLAR* Trial). Am J Cardiol. 2003; 92:152–160. [PubMed: 12860216]
18. Hamelin BA, Turgeon J. Hydrophilicity/lipophilicity: relevance for the pharmacology and clinical effects of HMG-CoA reductase inhibitors. Trends Pharmacol Sci. 1998; 19:26–37. [PubMed: 9509899]
19. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002; 106:3143–3421. [PubMed: 12485966]
20. Fried LF, Boudreau R, Lee JS, et al. Kidney function as a predictor of loss of lean mass in older adults: health, aging and body composition study. J Am Geriatr Soc. 2007; 55:1578–1584. [PubMed: 17908060]
21. Scott D, Blizzard L, Fell J, et al. Statin therapy, muscle function and falls risk in community-dwelling older adults. QJM. 2009; 102:625–633. [PubMed: 19633029]
22. Teng EL, Chui HC. The Modified Mini-Mental State (3MS) examination. J Clin Psychiatry. 1987; 48:314–318. [PubMed: 3611032]
23. Radloff LS. The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. Appl Psych Measur. 1977; 1:385–401.
24. Peron EP, Gray SL, Hanlon JT. Medication use and functional status decline in older adults: a narrative review. The American journal of geriatric pharmacotherapy. 2011; 9:378–391. [PubMed: 22057096]
25. Schneeweiss S, Wang PS, Avorn J, et al. Improved comorbidity adjustment for predicting mortality in Medicare populations. Health Serv Res. 2003; 38:1103–1120. [PubMed: 12968819]
26. Shrank WH, Patrick AR, Brookhart MA. Healthy user and related biases in observational studies of preventive interventions: a primer for physicians. J Gen Intern Med. 2011; 26:546–550. [PubMed: 21203857]
27. Diggle, PJ.; Heagerty, P.; Liang, K-Y., et al. Analysis of Longitudinal Data. 2. New York: Oxford University Press Inc; 2002.
28. Stone NJ, Robinson J, Lichtenstein AH, et al. ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013
29. Thompson PD, Clarkson PM, Rosenson RS. An assessment of statin safety by muscle experts. Am J Cardiol. 2006; 97:69C–76C.
30. Bruckert E, Hayem G, Dejager S, et al. Mild to moderate muscular symptoms with high-dosage statin therapy in hyperlipidemic patients--the PRIMO study. Cardiovasc Drugs Ther. 2005; 19:403–414. [PubMed: 16453090]

Table 1

Baseline Characteristics of the Study Sample Overall and According to Statin Use[a]

	Full Sample (N= 2405)	Statin Users (N= 390)	Statin Nonusers (N= 2015)
Demographics			
Age, mean ± SD	74.6 ± 2.8	74.3 ± 2.7*	74.7 ± 2.9
Female sex	1235 (51.4)	195 (50.0)	1040 (51.6)
Black race	894 (37.2)	114 (29.2)***	780 (38.7)
Pittsburgh site	1257 (52.3)	239 (61.3)****	1018 (50.5)
Education			
Postsecondary	1084 (45.2)	192 (49.4)	892 (44.4)
High school	793 (33.1)	129 (33.1)	664 (33.0)
Less than high school graduate	522 (21.8)	68 (17.5)	454 (22.6)
Living alone	697 (29.0)	105 (26.9)	592 (29.4)
Health-related behaviors			
Smoking status			
Current	206 (8.6)	22 (5.6)***	184 (9.2)
Past	1119 (46.6)	219 (56.2)	900 (44.7)
Never	1077 (44.8)	149 (38.2)	928 (46.1)
Alcohol use			
Current	1226 (51.2)	223 (57.2)*	1003 (50.0)
Past	507 (21.2)	79 (20.3)	428 (21.3)
Never	663 (27.7)	88 (22.5)	575 (28.7)
Doing moderate-to-high intensity exercise in the past week	690 (28.7)	141 (36.2)***	549 (27.3)
Health Status Factors			
Hypertension	1104 (45.9)	220 (56.4)****	884 (43.9)
Diabetes mellitus	363 (15.1)	75 (19.2)*	288 (14.3)
Coronary heart disease	450 (18.7)	165 (42.3)****	285 (14.1)
Stroke	133 (5.5)	33 (8.5)**	100 (5.0)
Peripheral artery disease	151 (6.3)	48 (12.3)****	103 (5.1)
Congestive heart failure	103 (4.3)	28 (7.2)**	75 (3.7)
Chronic kidney disease	484 (20.3)	108 (27.8)****	376 (18.8)
Pulmonary disease	99 (4.1)	10 (2.6)	89 (4.4)
Osteoarthritis	1345 (55.9)	219 (56.2)	1126 (55.9)
Parkinson disease	15 (0.6)	0 (0)	15 (0.7)
Health Status Factors			
Good/Excellent rated health	2057 (85.5)	327 (83.9)	1730 (85.9)
Body mass index			

	Full Sample (N= 2405)	Statin Users (N= 390)	Statin Nonusers (N= 2015)
Under/Normal	798 (33.2)	110 (28.2)*	688 (34.1)
Overweight	1030 (42.8)	187 (48.0)	843 (41.8)
Obese	577 (24.0)	93 (23.8)	484 (24.0)
Body composition: Total body lean mass (Kg), Mean ± SD	48.8 ± 10.3	48.6 ± 9.7	48.8 ± 10.4
Voluntary isokinetic knee extensor strength: Average maximum torque (Nm), Mean ± SD	104.6 ± 37.3	106.1 ± 38.5	104.4 ± 37.1
Cognitive impairment (3MS < 80)	187 (7.8)	22 (5.6)	165 (8.2)
Severe depression (CES-D >15)	102 (4.3)	16 (4.1)	86 (4.3)
Anticholinergic use	345 (14.4)	52 (13.3)	293 (14.5)
Benzodiazepines	146 (6.1)	33 (8.5)*	113 (5.6)
ACEI	402 (16.7)	90 (23.1)***	312 (15.5)
NSAID	513 (21.3)	71 (18.2)	442 (21.9)
Other anti-inflammatory drugs	96 (4.0)	17 (4.4)	79 (3.9)
Number of prescription drugs, mean ± SD	2.7 ± 2.4	3.4 ± 2.5****	2.6 ± 2.3
Health-care Access Factors			
Prescription drug coverage	1521 (63.3)	282 (72.3)***	1239 (61.6)
Having a flu shot in the past year?	1798 (74.8)	317 (81.3)	1481 (73.5)

Abbreviations: ACEI: angiotensin converting enzyme inhibitors; CES-D: Center for Epidemiologic Studies-Depression scale; 3MS: Mini-Mental Status examination; NSAID: non-steroidal anti-inflammatory drugs; SD: standard deviation

[a] Data represented as N (%), unless otherwise stated; Numbers were not summed up to total due to missing information.

* P <0.05,

** P < 0.01,

*** P<0.001,

**** P<0.0001 from chi-square or t-test between statin users and non-users.

Table 2

Prevalence of Statin Use Over Time[a]

Statin Use	1998–1999 (N= 2405)	1999–2000 (N= 2206)	2001–2002 (N= 1968)
Any users	390 (16.2)	444 (20.1)	504 (25.6)
High-dose (>1 SDD)	59 (2.5)	76 (3.5)	137 (7.0)
Moderate-dose (1 SDD)	143 (6.0)	195 (8.8)	235 (11.9)
Low-dose (< 1 SDD)	188 (7.8)	173 (7.8)	132 (7.0)
Lipophilic[b]	334 (13.9)	398 (18.0)	461 (23.4)
Hydrophilic[b]	56 (2.3)	46 (2.1)	43 (2.2)

Abbreviations: ACEI: angiotensin converting enzyme inhibitors; SDD: standardized daily dose;

[a] Data represented as N (%);

[b] Lipophilic: atorvastatin, lovastatin, fluvastatin and simvastatin; hydrophilic: pravastatin and rosuvastatin

Table 3

Multivariable Generalized Estimating Equations Models of Statin Use and Gait Speed Decline

Statin Use	Gait speed decline ≥ 0.1 m/s (yes/no), AOR (95% CI)[b]	P value
Non-users	Reference	--
Any users	0.90 (0.77, 1.06)	0.21
High-dose (>1 SDD)	0.90 (0.67, 1.22)	0.50
Moderate-dose (1 SDD)	1.02 (0.82, 1.27)	0.86
Low-dose (< 1 SDD)	0.78 (0.61, 0.99)	0.04
Lipophilic[a]	0.93 (0.79, 1.09)	0.37
Hydrophilic[a]	0.72 (0.47, 1.12)	0.15

Abbreviations: AOR: adjusted odds ratio; SDD: standardized daily dose;

[a] Lipophilic: atorvastatin, lovastatin, fluvastatin and simvastatin; hydrophilic: pravastatin and rosuvastatin.

[b] Separate multivariable Generalized Estimating Equation analysis were used to adjust for baseline demographics (race, sex, site). Final models also included time-varying statin use, age, coronary heart disease, diabetes, stroke, peripheral artery disease, self-rated health, gait speed at previous year, anticholinergics, benzodiazepines, angiotensin converting enzyme inhibitors, nonsteroidal anti-inflammatory drugs, other anti-inflammatory drugs, number of prescription drugs, and having a flu shot in the past 12 months.