Statin treatment and adherence to national cholesterol guidelines after ischemic stroke

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Abstract—Background: National cholesterol guidelines have defined high vascular risk individuals as those who could potentially benefit most from statin therapy. The authors aimed to determine the rate of statin use, its predictors, and the achievement of national guideline target lipid goals among ischemic stroke survivors. **Methods:** The authors abstracted data from the Vitamin Intervention for Stroke Prevention (VISP) study database from the United States and Canada to incorporate into algorithms for initiating statin therapy according to the National Cholesterol Education Program (NCEP) guidelines for high-risk individuals. The authors applied these algorithms to all study subjects. Univariate as well as multivariate associations for target lipid levels and statin implementation were then evaluated utilizing pertinent demographic, clinical, and laboratory data. **Results:** Of 2,894 subjects in the analysis dataset, 38% were women; 71% were recruited in the United States and 29% in Canada. Of 769 high-risk subjects, 262 (34%) had a low-density lipoprotein (LDL) level ≥ 130 mg/dL and 124 of these (47%) were not on statin. Among those high-risk persons on statin treatment, only 42% had an LDL ≤ 100 mg/dL. Subjects in the overall cohort were more likely to be on a statin if they were treated in the United States or had a history of hypertension or coronary artery disease. **Conclusions:** Approximately one out of three guideline-eligible high vascular risk ischemic stroke patients in this study had low-density lipoprotein cholesterol concentrations above qualifying levels for pharmacologic therapy, but half of these patients were not taking a statin, and of those receiving statin treatment, less than half were within recommended lipid goals.

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National Cholesterol Education Program Adult Treatment Panel (ATP) guidelines provide clinicians with recommendations for the clinical management of abnormal blood cholesterol to reduce the risk of cardiovascular events.^{1,2} However, single center studies of stroke survivors suggest that an unacceptably high proportion of these individuals with dyslipidemia are neither on lipid lowering therapy nor managed aggressively enough to achieve recommended target cholesterol levels.^{3,4} This is an important issue since mounting evidence indicates that aggressive lipid-lowering, particularly with statin therapy, will be of benefit to the majority of patients with ischemic stroke.⁵

Additional material related to this article can be found on the *Neurology* Web site. Go to www.neurology.org and scroll down the Table of Contents for the April 25 issue to find the title link for this article.

The Vitamin Intervention for Stroke Prevention (VISP) trial was a multicenter, double-blind, randomized controlled clinical trial performed at centers across the United States (n = 45) and Canada (n = 10) designed to determine whether best medical therapy and a multivitamin containing high-dose folic acid, pyridoxine, and cobalamin given to lower total homocysteine levels would reduce the incidence of recurrent cerebral infarction in patients with a nondisabling cerebral infarction.⁶

In this study, we aimed to 1) evaluate the percent utilization of statin treatment among the subset of ATP-eligible high vascular risk individuals who had experienced a recent stroke and the change in utilization over the course of the VISP study; 2) determine the proportion of such high-risk individuals with a recent stroke whose lipid levels were within the target range recommended by national guide-

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lines; and 3) describe lipid profiles among all individuals with a recent ischemic stroke and to identify factors associated with statin utilization in them.

Methods. We reviewed data from the VISP trial.⁶ The methods and results of this trial have previously been described.⁶ Pertinent to this report, the VISP population included individuals who neurologists had identified as having experienced an ischemic stroke from September 1996 through May 2003. Demographic, clinical, and laboratory data including fasting lipid panels were collected at baseline, with subsequent clinical and laboratory information, obtained at follow-up visits 6, 12, and 24 months. Lipid panels were measured locally at VISP sites, and baseline values were obtained a minimum of 21 days from the time of the stroke. Participants were asked to fast for 12 hours before enrollment and follow-up visits, but blood was drawn regardless of fasting state.

We evaluated the achievement of target lipid goals and statin utilization in the VISP cohort at baseline enrollment, to define their determinants in patients with ischemic stroke. Algorithms for initiating statin therapy in high-risk individuals were those defined by the ATP II guidelines that were in effect for most of the VISP study enrollment period. For the VISP cohort, the ATP II indicator conditions for high risk were the presence of coronary artery disease or history of carotid endarterectomy or other obstructive vascular disease. To examine hypothetical treatment rates and lipid level targets for the VISP population under the 2001 ATP III guidelines (which were only partly in effect during the study period), criteria for initiating statin therapy in high-risk individuals were those defined by that panel.² ATP III differed from ATP II principally due to expansion of the highest risk group for whom treatment should be initiated at a low-density lipoprotein (LDL) cholesterol above 130 mg/dL with a target of <100 mg/dL. This included the addition of patients with diabetes and those whose 10-year absolute coronary artery disease (CAD) risk exceeded 20% according to the Framingham Coronary Artery Disease Risk Model.⁷⁻⁹

To calculate absolute 10-year CAD risk in the patients free of vascular disease or diabetes in the VISP cohort, we collected the following data corresponding to the CAD risk factors in the Framingham profile: age; sex; systolic blood pressure and blood pressure treatment; total cholesterol; high-density lipoprotein (HDL) cholesterol; use of antihypertensive therapy; and current cigarette smoking. These factors were used to arrive at each individual's absolute CHD risk using the ATP III Coronary Heart Disease Risk Assessment Calculator tool.¹⁰

For each patient meeting a clinical condition indication under ATP II, and ATP III, we assessed LDL cholesterol concentrations at baseline, and applied thresholds for therapy initiation that had been specified in the various panel guidelines. We calculated LDL cholesterol using Friedewald's formula because this method has been used in clinical trials documenting the benefits of cholesterol-lowering therapy and is recommended by the ATP.¹¹

We compared actual treatment rates and target lipid levels achieved in the VISP cohort to those specified under the governing national guidelines of the time (ATP II) and under the ATP III guidelines. Subjects were excluded if they did not have a complete lipid panel ($n = 382$), had missing lipid lowering agent data ($n = 179$), had triglycerides >400 mg/dL, or if the relative difference between the recorded LDL and that estimated for the individual using the Friedewald formula based on the total cholesterol, triglyceride, and HDL cholesterol exceeded 5% ($n = 120$). After these exclusions, the final sample size was $n = 2,894$. We also collected data on statin use at baseline, 6, 12, and 24 months.

Statistical analysis. Various demographic and clinical factors were compared between patients at high risk and those not at high risk according to ATP II. Significance was assessed between these two independent groups using a standard χ^2 test for categorical variables and a t test for continuous variables.

Univariate and multivariate associations were examined to identify significant predictors of lipid levels above target ATP II goals in high-risk subgroup, as well as the frequency of statin use in the overall VISP cohort. For multivariable association, we established the logistic regression models using all the prognostic factors chosen a priori as explanatory variables regardless of their statistical significance and model predictability, and the individual association was summarized in terms of OR with all other risk factors adjusted.

Table 1 Demographic and clinical information* on patients in high-risk and low-risk groups according to Adult Treatment Panel (ATP) II ($n = 2,894$)

Variable	Patients not at high risk, $n = 2,125$	Patients at high risk, $n = 769$	p Value†
Mean age, y	66 (11)	69 (10)	<0.001
Male	1,221 (57)	577 (75)	<0.001
Race			<0.001
White	1,665 (78)	654 (85)	
Black	326 (15)	80 (10)	
Other	134 (6)	35 (5)	
Country			0.003
US	1,469 (69)	575 (75)	
Canada	656 (31)	194 (25)	
Mean BMI	28 (6)	28 (5)	0.079
History			
Ever smoker	1,370 (64)	550 (72)	<0.001
Hypertension	1,552 (73)	583 (76)	0.170
Diabetes	523 (25)	267 (35)	<0.001
Lipid profile‡			
Total cholesterol	203 (43)	190 (42)	<0.001
Triglycerides	159 (74)	161 (76)	0.635
LDL cholesterol	126 (38)	117 (39)	<0.001
HDL cholesterol	47 (16)	43 (15)	<0.001
Statin	797 (38)	453 (59)	<0.001

* Mean (SD) for continuous variables; n (%) for categorical variables.

† p Value is for testing the difference of each characteristic between high- and low-risk groups.

‡ Values are in mg/dL.

BMI = body mass index; LDL = low-density lipoprotein; HDL = high-density lipoprotein.

We also assessed the prevalence of statin use over the entire study period. The trend over time was tested using the Cochran-Armitage statistic.¹²

A determination was then made of the proportion of high vascular risk patients at baseline who were within target LDL-C range, and who were receiving statin treatment according to treatment initiation goals as specified by the various ATP guidelines. For all tests for univariate associations, the standard χ^2 test was used. Two sided hypotheses are assumed for statistical testing and inference.

Results. Clinical profiles. A total of 3,680 patients with ischemic stroke were admitted during the study period. A total of 2,894 individuals had complete, verifiable data, and did not meet any exclusion criteria. Of these, mean and median ages were 66.5 and 68 years; 38% were women. We identified 769 patients (27% of the cohort) deemed to be at high cardiovascular risk, and thereby eligible for the intensive treatment of hyperlipidemia, according to the ATP II Guidelines for Secondary Prevention.¹ Table 1 shows demographic characteristics and the frequency of various clinical variables in high-risk and low-risk groups according to ATP II in the VISP study.

Table 2 Demographic and clinical information on high-risk subjects with baseline LDL-C level ≥ 130 mg/dL (above NCEP II treatment initiation goal) and OR for exceeding the initiation level in univariate and multivariate models (n = 769)

Variable	LDL-C ≥ 130 mg/dL, n = 262, 34%	LDL-C <130 mg/dL, n = 507, 66%	Univariate OR (95% CI)	p Value*	Multivariate OR (95% CI)	p Value*
Age, y	69 (10)	71 (9)	0.7 (0.5,1.0)	0.021	0.6 (0.5,0.9)	0.006
Sex						
Female	73 (38)	119 (62)	1		1	
Male	189 (33)	388 (67)	0.8 (0.6,1.1)	0.182	0.7 (0.5,1.1)	0.093
Race						
White	227 (35)	427 (65)	1		1	
Black	27 (34)	53 (66)	1.0 (0.6,1.6)	0.865	0.9 (0.5,1.5)	0.609
Other	8 (23)	27 (77)	0.6 (0.3,1.3)	0.150	0.6 (0.3,1.4)	0.221
Country						
US	203 (35)	372 (65)	1.3 (0.9,1.8)	0.214	1.3 (0.9,1.9)	0.146
Canada	59 (30)	135 (70)	1		1	
Body mass index	28 (5)	27 (5)	1.2 (0.9,1.6)	0.222	1.2 (0.9,1.6)	0.309
History						
Coronary artery disease						
Yes	205 (32)	440 (68)	0.5 (0.4,0.8)	0.002	0.6 (0.4,0.9)	0.011
No	57 (46)	66 (54)	1		1	
Stroke†						
Yes	71 (34)	135 (66)	1.0 (0.7,1.4)	0.901	1.0 (0.7,1.5)	0.823
No	191 (34)	371 (66)	1		1	
Smoker						
Yes	35 (34)	67 (66)	1.0 (0.7,1.6)	0.956	0.9 (0.6,1.5)	0.699
No	227 (34)	440 (66)	1		1	
Hypertension						
Yes	197 (34)	386 (66)	1.0 (0.7,1.3)	0.772	0.9 (0.6,1.4)	0.709
No	65 (35)	121 (65)	1		1	
Diabetes						
Yes	77 (29)	190 (71)	0.7 (0.5,1.0)	0.024	0.7 (0.5,1.0)	0.035
No	185 (37)	316 (63)	1		1	
Statin						
Yes	138 (30)	315 (70)	0.7 (0.5,0.9)	0.012	0.7 (0.5,0.9)	0.010
No	124 (39)	192 (61)	1		1	

Mean (SD) for continuous variables; n (%) for categorical variables. For OR, continuous variables are dichotomized by median and OR assesses above median condition, OR = 1 denotes reference level.

* p Value is for testing the association of each characteristic and the treatment initiation goal, i.e., for testing if OR is equal to 1.

† Prior to Vitamin Intervention for Stroke Prevention (VISP) trial qualifying stroke.

LDL = low-density lipoprotein.

Patients at high risk were older, more likely to be male, white, be recruited in the United States, have a history of smoking or diabetes, and have lower total and LDL cholesterol as well as lower HDL cholesterol. High-risk subjects were also more likely to be treated with a statin.

Low-density lipoprotein cholesterol concentrations above the ATP II treatment initiation level. The ATP II guidelines specified an LDL cholesterol of 130 mg/dL as a level that should trigger initiation of therapy in high-risk patients. For the VISP cohort 262/769 high-risk patients had LDL cholesterol ≥ 130 . Characteristics of patients that led them to exceed this threshold are outlined in table 2. Multivariate predictors of LDL-C ≥ 130 mg/dL were younger age (for example, those above the median age had 60% of the adjusted odds of exceeding the initiation level as those below the median age), no history of CAD, no history of diabetes, and not being on statin treatment. Of 262 high-risk subjects (United States + Canada) who had an LDL level ≥ 130 mg/dL, 47% were not on statin therapy.

Low-density lipoprotein cholesterol concentrations above the ATP II target goal. The ATP-II guidelines identified an LDL-C ≤ 100 mg/dL as a goal for high-risk patients. A total of 278/769 (36%) high-risk VISP subjects met this goal at the time of baseline enrollment, while 491 patients had LDL cholesterol that exceeded 100 mg/dL. Characteristics of these patients are outlined in table 3. Multivariate predictors of LDL-C >100 mg/dL were no history of CAD, hypertension, and diabetes, as well as not being on statin treatment. A total of 228 subjects with LDL cholesterol over 100 mg/dL were not taking a statin. Of all those patients on statin treatment (n = 453), 42% had LDL <100 mg/dL.

Comparison of the application of various ATP guidelines to VISP high-risk subjects. Table 4 shows the proportion of VISP high-risk subjects in the United States and Canada with baseline LDL-C concentrations above target and treatment initiation goals according to the ATP II and ATP III guidelines (published during the course of the study),

Table 3 Demographic and clinical information on high-risk subjects with baseline LDL-C level >100 mg/dL (above NCEP II target goal) and OR for exceeding the target goal in univariate and multivariate models (n = 769)

Variable	LDL-C >100 mg/dL, n = 278, 36%	LDL-C ≤100 mg/dL, n = 491, 64%	Univariate OR (95% CI)	p Value*	Multivariate OR (95% CI)	p Value*
Age, y	70 (10)	71 (9)	0.9 (0.6,1.2)	0.294	0.8 (0.6,1.1)	0.201
Sex						
Female	122 (64)	70 (36)	1		1	
Male	369 (64)	208 (36)	1.0 (0.7,1.4)	0.918	1.0 (0.7,1.4)	0.762
Race						
White	420 (64)	234 (36)	1		1	
Black	49 (61)	31 (39)	0.9 (0.6,1.4)	0.602	0.9 (0.6,1.6)	0.760
Other	22 (63)	13 (37)	0.9 (0.5,1.9)	0.870	1.1 (0.5,2.3)	0.795
Country						
US	371 (65)	204 (35)	1.1 (0.8,1.6)	0.504	1.2 (0.8,1.7)	0.333
Canada	120 (62)	74 (38)	1		1	
Body mass index	28 (5)	27 (5)	1.2 (0.9,1.6)	0.348	1.3 (0.9,1.7)	0.161
History						
Coronary artery disease						
Yes	400 (62)	245 (38)	0.6 (0.4,0.9)	0.011	0.6 (0.4,1.0)	0.050
No	91 (74)	32 (26)	1		1	
Stroke†						
Yes	134 (65)	72 (35)	1.1 (0.8,1.5)	0.697	1.2 (0.8,1.6)	0.442
No	357 (64)	205 (36)	1		1	
Smoker						
Yes	64 (63)	38 (37)	1.0 (0.6,1.5)	0.803	0.9 (0.6,1.4)	0.612
No	427 (64)	240 (36)	1		1	
Hypertension						
Yes	359 (62)	224 (38)	0.7 (0.5,0.9)	0.020	0.7 (0.4,1.0)	0.026
No	132 (71)	54 (29)	1		1	
Diabetes						
Yes	157 (59)	110 (41)	0.7 (0.5,1.0)	0.031	0.7 (0.5,1.0)	0.035
No	185 (37)	316 (63)	1		1	
Statin						
Yes	263 (58)	190 (42)	0.5(0.4,0.7)	<0.001	0.5 (0.4,0.7)	<0.001
No	228 (72)	88 (28)	1		1	

Mean (SD) for continuous variables; n (%) for categorical variables. For OR, continuous variables are dichotomized by median and OR assesses above median condition, OR = 1 denotes reference level.

* p Value is for testing the association of each characteristic and the treatment initiation goal, i.e., for testing if OR is equal to 1.

† Prior to Vitamin Intervention for Stroke Prevention (VISP) trial qualifying stroke.

LDL = low-density lipoprotein.

and their relationship to statin use. There was a significant difference in statin utilization between both countries among these high-risk persons with LDL-C concentrations above target lipid goals. There also appeared to be a decrease in adherence to the more expansive ATP III target treatment initiation goals and lipid levels compared to ATP II in the United States.

Statin utilization profiles. Table 5 describes the predictors of being on a statin among subjects in the overall VISP cohort in univariate and multivariate regression models. For the multivariate analysis, non-black race, treatment in the United States, history of coronary artery disease, and history of hypertension remained significantly associated with being on a statin prescription.

Table E-1 (on the *Neurology* Web site at www.neurology.org) displays percent statin utilization rates over the period of the VISP study, revealing an increase in statin use from baseline enrollment (46%) to 24-month study completion (58%) in the United States, and 36% to 52% in Canada, demonstrating significant increases with $p < 0.001$.

There was also a significant increase in statin use following the issuance of the 2001 ATP III guidelines as evidenced by a comparison of 12-month and 24-month visits done throughout the study (table E-2).

Discussion. We found in our cross-sectional analysis of baseline lipid levels in individuals who have experienced a recent ischemic stroke that only one out of every three high vascular risk persons were within target of ATP II guideline goal (LDL cholesterol concentration 100 mg/dL or less). Numerous studies of individuals with cardiac disease have implied that appropriate treatment of cholesterol levels has been suboptimal.¹³⁻¹⁷ This study suggests that the same may be true for patients with ischemic stroke at high vascular risk.

Perhaps even more worrisome was that almost half of the high vascular risk subjects were not prescribed a statin even though they had LDL-C concen-

Table 4 Number and percentage of Vitamin Intervention for Stroke Prevention (VISP) trial high vascular risk subjects in the United States and Canada with baseline LDL-C concentrations above target and treatment initiation goals according to Adult Treatment Panel (ATP) II and ATP III guideline criteria, and their relationship to statin utilization

Guideline/above goal cutoff	Country	Total, n	Not on statin, n (%)	<i>p</i> Value*
ATP II				
LDL >100 mg/dL	US	371	159 (43)	0.0052
	Canada	120	69 (58)	
LDL ≥130 mg/dL	US	203	88 (43)	0.0167
ATP III	Canada	59	36 (61)	
LDL ≥100 mg/dL	US	743	362 (49)	<0.001
	Canada	277	177 (64)	
LDL ≥130 mg/dL	US	407	188 (46)	<0.001
	Canada	155	96 (62)	

* For difference in statin use between United States and Canada.

LDL = low-density lipoprotein.

trations above the ATP target for treatment initiation. When we applied the more aggressive LDL-C target goals recommended in the more recent ATP III guidelines, we found an even higher rate of potential undertreatment among high-risk persons, as expected.

With widening indications for statins, as per recent Food and Drug Administration labeling to include individuals with any evidence of cerebrovascular disease, and more recent studies suggesting that pretreatment with statins may result in lesser stroke severity,¹⁸ and better functional outcomes after a stroke,¹⁹ we evaluated the correlates of treatment with statins among ischemic stroke survivors regardless of ATP-defined risk status. As was shown, CAD patients tended to receive statin treatment more often, and statin therapy was more prevalent in the United States than in Canada.

One possible reason for the underutilization of lipid treatment in ischemic stroke survivors may be decades of prior research which have yielded inconsistent results regarding the role of cholesterol in ischemic stroke,²⁰⁻²² and this may have generally fostered a reluctance on the part of clinicians to take the treatment of lipid levels in patients with ischemic stroke very seriously. The more recent ATP III guidelines suggest an expanded role for the use of statins in preventing coronary events among ischemic stroke survivors because in addition to those with known CAD, it recommends aggressive lipid lowering treatment for those with indicator conditions such as diabetes, and other CAD risk equivalents.² Indeed, we noted a significant increase over the course of the VISP study period particularly around the time the ATP III guidelines were issued, suggesting perhaps some penetration of guideline recommendations among caregivers, albeit clearly

insufficient. However, the potential for further expansion may exist, since only patients with cerebral ischemia due to symptomatic carotid artery disease are regarded as harboring a CAD risk equivalent, and not those with atherosclerotic disease in the aortic arch, the vertebral arteries, the basilar artery, the middle cerebral arteries, and intracranial branch atheromatosis.²³ The results of the SPARCL study will shed further light on the role of lipid-lowering and statin therapy in patients with ischemic stroke without known CAD.²⁴

The implementation of vascular protection strategies as a whole among patients with stroke has been variable and suboptimal.²⁵⁻²⁸ It is not uncommon to find that among health care professionals attending to patients with stroke, the focus is primarily on secondary stroke prevention. It is true that shortly after an ischemic stroke the highest vascular risk is for another stroke,²⁹ however, patients with stroke are at a greater long-term risk of death due to recurrent cardiac events (which make up 40% of deaths over 5 years of follow-up) than recurrent stroke.³⁰ Aggressive management of risk factors, like cholesterol, could have a significant and positive impact on the natural history of atherosclerotic cardiovascular disease.

With heightened recognition of vascular risk factors, recent clinical trial evidence, and updated national guidelines, there is likely to be a gradual trend toward an increase in the statin eligible patients with stroke. As such, the issue of underdiagnosis and undertreatment of high vascular risk individuals may be compounded. It would appear that a number of directed quality improvement interventions are needed to improve the quality of cholesterol management in patients with CVD. Alongside the implementation of prompt diet and lifestyle modification, the screening and initiation of treatment with statins before hospital discharge may be a simple and effective intervention with the potential to substantially reduce cardiovascular morbidity and mortality in this vulnerable population. Indeed, the systematic predischARGE treatment initiation strategy has been shown to be feasible,^{31,32} predict longer-term community care,³³ and result in improved vascular outcomes.^{32,34}

In this study we directly compared dyslipidemia management in a high-risk population in the United States and Canada. Although it appeared that statin treatment was more prevalent in the United States than Canada, the percent of high-risk patients above the LDL concentration initiation threshold (130 mg/dL) for statin treatment and below the LDL concentration upper goal (= or <100 mg/dL) appeared to be similar in the United States and Canada.

This study has limitations. We used the ATP II guidelines for the major analyses of the VISP cohort because these were the guidelines in place during its study enrollment, and although we performed an analysis applying the current ATP III guidelines to the VISP subjects, it is difficult to predict how VISP-

Table 5 Demographic and clinical information on subjects on statins in the overall Vitamin Intervention for Stroke Prevention (VISP) cohort (n = 2,894)

Variable	Statin users, n = 1,250, 43%	Non-statin users, n = 1,644, 57%	Univariate OR (95% CI)	p Value*	Multivariate OR (95% CI)	p Value*
Age, y	67 (10)	68 (11)	1.0 (0.8, 1.1)	0.562	0.9 (0.8, 1.0)	0.133
Sex						
Female	472 (43)	624 (57)	1		1	
Male	778 (43)	1,020 (57)	1.0 (0.9, 1.2)	0.914	0.9 (0.8, 1.1)	0.190
Race						
White	1,007 (43)	1,312 (57)	1		1	
Black	165 (41)	241 (59)	0.9 (0.7, 1.1)	0.296	0.8 (0.6, 1.0)	0.027
Other	78 (46)	91 (54)	1.1 (0.8, 1.5)	0.490	1.0 (0.7, 1.4)	0.982
Country						
US	944 (46)	1,100 (54)	1.5 (1.3, 1.8)	<0.001	1.5 (1.3, 1.8)	<0.001
Canada	306 (36)	544 (64)	1		1	
Body mass index	28 (6)	27 (6)	1.2 (1.0, 1.4)	0.017	1.1 (0.9, 1.3)	0.451
History						
Coronary artery disease						
Yes	392 (61)	253 (39)	2.5 (2.1, 3.0)	<0.001	2.5 (2.1, 3.0)	<0.001
No	855 (38)	1,382 (62)	1		1	
Stroke†						
Yes	268 (42)	369 (58)	0.9 (0.8, 1.1)	0.512	0.9 (0.7, 1.0)	0.110
No	982 (44)	1,274 (56)	1		1	
Smoker						
Yes	190 (40)	280 (60)	0.9 (0.7, 1.1)	0.183	0.9 (0.7, 1.1)	0.379
No	1,060 (44)	1,363 (56)	1		1	
Hypertension						
Yes	965 (45)	1,170 (55)	1.4 (1.2, 1.6)	<0.001	1.3 (1.1, 1.6)	0.004
No	282 (38)	470 (62)	1		1	
Diabetes						
Yes	382 (48)	408 (52)	1.3 (1.1, 1.6)	0.001	1.1 (0.9, 1.3)	0.239
No	868 (41)	1,233 (59)	1		1	
Lipid profile						
Total-C	196 (46)	198 (42)	0.9 (0.48, 1.1)	0.284		
TG	148 (74)	139 (74)	1.2 (1.0, 1.4)	0.020	1.1 (0.9, 1.3)	0.295
LDL-C	119 (40)	123 (37)	0.9 (0.8, 1.1)	0.174	1.0 (0.8, 1.1)	0.689
HDL-C	42 (14)	43 (17)	0.9 (0.8, 1.0)	0.054	1.0 (0.8, 1.2)	0.723

Mean (SD) for continuous variables; n (%) for categorical variables. For OR, continuous variables are dichotomized by median and OR assesses above median condition, OR = 1 denotes reference level.

* p Value is for testing the association of each characteristic and the statin utilization if OR is equal to 1.

† Prior to VISP trial qualifying stroke.

TG = triglycerides; Total-C, LDL-C, HDL-C = total, low-density, and high-density lipoprotein cholesterol.

associated physicians or VISP patients would have fared under the newer guidelines. However, if recent stroke studies^{35,36} showing that fewer than 50% of hospitalized patients with stroke receive a lipid panel are relevant, it would appear unlikely that there has been substantial improvement. Another important consideration is that we do not know if and how many patients might have been offered and declined, started and discontinued, or received inadequate doses of statins,³⁷ in the outpatient setting prior to VISP enrollment. Furthermore, we lack information on potential complications of statin therapy, such as myalgias, that may have limited statin use. We excluded investigation of use of lipid lowering agents other than statins from this study, because most of the landmark lipid lowering trials used statins, recent guidelines focus on statins,⁵ and

statins remain the most effective and best-tolerated drugs for lowering LDL-C. It should also be pointed out that since VISP patients were encountered in a research oriented setting, they were probably better and more aggressively treated than stroke survivors seen in routine medical practice. Finally, in our application of ATP III criteria, we may have underestimated the proportion of high-risk individuals because some individuals identified as low risk by Framingham score were on statins, and the effect of statins on total cholesterol concentration may have led to their misclassification.

In order to reduce the burden of vascular disease, particularly CAD, the diagnosis of dyslipidemia and treatment with therapeutic targets must be improved. Our study suggests that despite the availability of ATP guidelines for the identification and

management of high blood cholesterol, appropriate use of ATP therapeutic algorithms remains inadequate. More specifically, statins were underutilized for the secondary prevention of CAD in this at-risk population. This is of concern since patients at high risk for initial or recurrent CHD events constitute the population most likely to benefit from comprehensive risk factor management.

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