

Recent Nationwide Trends in Discharge Statin Treatment of Hospitalized Patients With Stroke

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Background and Purpose—The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial showed statins reduce vascular risk among patients with atherosclerotic stroke or transient ischemic attack. In this study, we assessed recent nationwide trends in discharge statin treatment after acute stroke and the influence of SPARCL on clinical practice.

Methods—Using data from eligible patients with stroke and transient ischemic attack admitted to Get With The Guidelines–Stroke (GWTG–Stroke) -participating hospitals between January 1, 2005, and December 31, 2007, we assessed discharge statin use over time and in relation to dissemination of the SPARCL results.

Results—Among 173 284 patients with ischemic stroke and transient ischemic attack, overall discharge statin treatment was 83.5%. Discharge statin prescription climbed steadily but modestly over the 2-year study period from 75.7% to 84.8% ($P < 0.001$) with a nonsignificant increase during SPARCL reporting but a return to prior levels thereafter. Factors associated with lower discharge statin use in patients without contraindications included female sex and South region.

Conclusions—Discharge statin prescription among hospitalized patients with stroke increased over time, but 1 in 5 patients still leaves the hospital without treatment. Primary drivers of increased use were secular trends and individual/hospital site characteristics. (*Stroke*. 2010;41:00-00.)

Key Words: clinical trials ■ GWTG ■ health services ■ practice patterns ■ prevention ■ statins
■ stroke ■ transient ischemic attack ■ utilization

Randomized clinical trials have established that β -hydroxy- β -methylglutaryl-coenzyme A reductase inhibitors (statins) prevent ischemic stroke in patients with dyslipidemia, coronary artery disease (CAD), or stroke.^{1–3} The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial showed that among individuals with recent symptomatic cerebrovascular disease and no known CAD, the incidence of vascular events, including stroke, was significantly lower in those treated with a high dose of a statin compared with placebo.⁴ This study and other evidence led the American Heart Association/American Stroke Association (AHA/ASA) to recommend in-hospital initiation of statin therapy for patients with stroke or transient ischemic attack (TIA) of atherosclerotic origin.³

Before SPARCL, serum cholesterol management was underused in eligible patients with ischemic stroke and TIA,^{5,6} and prior studies of lipid modifier treatment during the hospital encounter were based on regional, not nationwide data. Stroke hospitalization provides a window of opportunity to assure

initiation of management⁷ ([http://stroke.ahajournals.org/cgi/content/full/35/12-R17-417899](http://stroke.ahajournals.org/cgi/content/full/35/12/R17-417899)) and starting treatment during the acute stroke hospital encounter promotes drug adherence⁸ and enhances clinical outcomes in the postdischarge setting.^{9,10}

The objective of this study was 1-fold; first, to assess recent nationwide trends in discharge statin treatment among patients with ischemic stroke and to see if such treatment changed in response to the dissemination of SPARCL trial results, and second, to identify correlates of statin treatment among individuals hospitalized with a cerebrovascular event.

Methods

Database and Procedures

We used data from the Get With The Guidelines–Stroke (GWTG–Stroke) program database. GWTG–Stroke is a nationwide quality improvement initiative geared at fostering improved adherence to guideline-based care in patients hospitalized with stroke and TIA.^{11,12} Briefly, participating hospitals use an Internet-based Patient Management Tool (Outcome Sciences Inc, Cambridge Mass) to enter data, receive decision support, and obtain feedback through

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on-demand reports of performance on quality measures. GWTG-Stroke participating hospitals record data from consecutive stroke and TIA hospital admissions. Case ascertainment is done through clinical identification during the hospital encounter, retrospective surveillance of International Classification of Diseases, 9th Revision codes, or both. Trained hospital personnel abstract data on demographics, medical history, neuroimaging, in-hospital treatment, and discharge characteristics. A performance measure of the GWTG-Stroke program is that each patient with stroke or TIA is discharged on lipid-lowering therapy in accordance with prevailing expert consensus national guidelines. Each participating hospital received either human research approval to enroll cases without individual patient consent under the common rule or a waiver of authorization and exemption from subsequent review by their Institutional Review Board.

Main Predictors and Covariates

Main predictors of interest were time periods related to dissemination of the SPARCL trial results. Covariates included age, sex, race (analyzed for this article as white, black, Hispanic, or other), type of index event (ischemic stroke versus TIA), comorbid medical conditions (atrial fibrillation, prosthetic heart valve, previous stroke/TIA, coronary artery disease or prior myocardial infarction, carotid stenosis, diabetes, peripheral vascular disease, hypertension, dyslipidemia, and smoking), use of lipid-lowering treatment before admission, and hospital characteristics (bed size, annual number of stroke discharges, academic teaching status, and geographical region). Hospital bed size was used as a continuous variable, whereas annual number of stroke discharges were categorized as 0 to 100, 101 to 300, or >300. Hospital teaching status and hospital region (defined as Northeast, Midwest, South, or West) were determined using statistics published by the AHA.

Outcomes

Primary outcome of interest was percent discharged on statin treatment. Secondary outcome of interest, analyzed only in an unadjusted manner, was percent discharged on lipid-modifying treatment, which included use of statins, fibrates, or unspecified lipid modifier therapy.

Study Periods

We analyzed the GWTG-Stroke data set for patients hospitalized with stroke or TIA from January 2005 to December 2007. Time periods were categorized in relation to dissemination of the SPARCL results through conference and print publication: (1) pre-SPARCL reporting, January 2005 to April 2006; (2) during SPARCL reporting, May 2006 to August 2006 (SPARCL trial results were first presented at an international conference in May 2006 and then published in print form as an article in August 2006); and (3) post-SPARCL reporting, September 2006 to December 2007.

Overall Cohort

Between January 1, 2005, and December 31, 2007, 1056 hospitals contributed data on 529 287 stroke and TIA discharges. Only patients with ischemic stroke or TIA were included in this analysis. Patients who died before discharge ($n=15\,374$), were discharged to hospice care ($n=9204$), were transferred to another acute care hospital ($n=8632$), left against medical advice ($n=2453$), or in whom discharge status was missing ($n=6361$) were excluded because these patients would not be eligible for lipid-lowering treatment at discharge. We also excluded patients with known contraindications to lipid-lowering treatment ($n=34\,528$) and those with discharge lipid therapy status missing ($n=3523$). For analyses aimed at assessing how SPARCL influenced clinical practice, we also excluded those with measured low-density lipoprotein cholesterol level <100 mg/dL (unless on cholesterol reducer at admission, $n=89\,717$), those with a history of atrial fibrillation or newly diagnosed atrial fibrillation during the index hospitalization ($n=34\,213$), and patients with prosthetic heart valves ($n=3173$). These additional exclusionary criteria were made to accommodate

the SPARCL trial subject population, which did not include those with low-density lipoprotein cholesterol levels <100 mg/dL or presumed cardioembolic stroke mechanisms.⁴ However, for analyses aimed at assessing what factors were associated with statin prescription at discharge, these 3 latter groups of subjects were included. Therefore, for analyses pertaining to SPARCL, there were 173 284 patients (32.7% of overall cohort) eligible patients from 981 sites, whereas for the discharge statin prescription analysis, there were 299 079 patients (56.5% of overall cohort) eligible patients from 997 sites. Covariate missing rate was low (approximately 2%). Missing data were imputed to the most prevalent category for use in regression modeling.

Statistical Analyses

Univariate changes in discharge treatment use of statins and lipid-modifying treatment over time were tested using the Cochran-Mantel-Haenszel row-mean score test. Patient-level characteristics and hospital-level variables were then compared across the pre-SPARCL, during SPARCL, and post-SPARCL periods. Piecewise logistic multivariable regression models were then fit to track statin use at discharge (reported as estimated ORs of a given month compared with the previous month) in the 3 SPARCL time periods. Individual and hospital-level confounders were also controlled for in the regression models. The generalized estimating equation method with exchangeable working correlation matrix was used to provide valid inference after accounting for within hospital correlation. Models that contain only time effects are referred to as "unadjusted," whereas models with complete adjustment for patient and hospital characteristics, in addition to the time effects, are referred to as "adjusted." All probability values are 2-sided. Analyses were performed using SAS Version 9.1.3 (SAS Institute, Cary, NC).

Results

The study population for the SPARCL analysis consisted of 119 746 patients with ischemic stroke and 53 538 patients with TIA. Overall, the mean age was 68.3 years and a slight majority were women (Table 1). Other sociodemographic and clinical characteristics in the overall cohort, as well as in the pre-, during-, and post- SPARCL periods among patients admitted with ischemic stroke or TIA, are shown in Table 1. Discharge use of lipid-lowering medication was 83.5% with statin prescription occurring in 79.2% (Table 1). The statin treatment rate was 96 373 of 119 746 (80.5%) in patients with ischemic stroke and 40 889 of 53 538 (76.4%) in patients with TIA. Admission use of lipid-lowering therapy was 56.7%. Patients who were receiving lipid-lowering therapy before hospitalization were more likely to be discharged on a statin (89.2%) compared with those not previously receiving lipid-lowering medication (66.3%; $P<0.0001$). The rates of discharge statin use by hospital varied substantially (10th to 90th percentile: 59.5% to 91%).

The frequency of statin prescription at discharge climbed steadily and linearly throughout the almost 3-year observation period, from 75.7% in January 2005 to 84.8% in December 2007 ($P<0.0001$), without any acceleration or deceleration during or after the period of SPARCL reporting (Figure). Discharge lipid modifier prescription also climbed steadily and linearly over the study period (Figure). Although not statistically significant, over the period when the SPARCL trial result was disseminated (during SPARCL versus pre-SPARCL), discharge statin use increased more than expected based on the prior pattern but returned to the pre-SPARCL pattern of acceleration afterward (Table 2). This pattern was also reflected in the adjusted estimated odds

Table 1. Sociodemographic and Clinical Characteristics in the Overall Cohort as Well as in Pre-, During, and Post-SPARCL Periods Among Patients Admitted With Ischemic Stroke or TIA

Variable	Description	Overall Cohort (n=173 284)	Pre-SPARCL (n=53 606)	During SPARCL (n=22 125)	Post-SPARCL (n=97 553)	
Age, years	Mean (SD)	68.30 (13.54)	68.25 (13.46)	68.09 (13.50)	68.37 (13.60)	
Sex	Female, %	51.64	51.16	51.42	51.96	
Race	White, %	73.14	73.65	73.23	72.83	
Ethnicity	Hispanic, %	4.75	4.16	4.87	5.04	
Stroke type	Ischemic stroke, %	69.10	71.49	69.28	67.75	
Medical history	Stroke or TIA	30.99	30.93	30.51	31.14	
	CAD/myocardial infarction	27.78	28.39	28.21	27.35	
	Carotid stenosis	5.16	5.36	5.29	5.03	
	Diabetes	32.35	32.44	32.34	32.31	
	Peripheral artery disease	4.93	5.04	5.00	4.86	
	Hypertension	75.94	75.75	75.63	76.11	
	Dyslipidemia	50.58	50.05	50.42	50.90	
	Recent smoker	19.55	18.97	19.97	19.77	
	Lipid modifier use	Before admission	56.74	56.37	56.91	56.90
	National Institutes of Health Stroke Scale score	Mean (SD)	4.55 (5.65)	4.71 (5.65)	4.54 (5.61)	4.48 (5.65)
Median (25th, 75th)		3 (1, 6)	3 (1, 7)	3 (1, 6)	2 (1, 6)	
Missing values, %		57.31	61.68	58.60	54.61	
Serum total cholesterol	Mean (SD)	188.16 (48.11)	191.21 (47.87)	188.45 (48.10)	186.50 (48.15)	
Serum LDL-C	Mean (SD)	118.17 (41.48)	120.43 (41.08)	118.66 (41.50)	116.90 (41.63)	
	Median (25th, 75th)	116 (91, 141)	118 (95, 143)	117 (92, 142)	115 (88, 141)	
	Missing values, %	16.18	19.26	16.82	14.35	
Hospital no. of beds	Median (25th, 75th)	378 (263, 564)	394 (270, 574)	382 (264, 572)	369 (260, 557)	
Hospital type	Academic, %	62.13	64.85	63.36	60.35	
No. of stroke discharges	0–100	8.61	7.46	8.12	9.35	
	101–300	50.82	48.37	49.84	52.39	
	>300	40.57	44.17	42.04	38.26	
Region	Northeast, %	25.95	25.91	27.33	25.65	
	Midwest, %	19.31	20.41	19.21	18.72	
	South, %	39.16	36.63	38.36	40.73	
	West, %	15.58	17.05	15.09	14.89	
Lipid modifier treatment	At discharge	83.48	80.41	83.03	85.27	
Statin treatment	At discharge	79.21	76.31	79.15	80.82	

Excludes patients with LDL-C <100 mg/dL, history or presence of atrial fibrillation, and prosthetic heart valves.
LDL-C indicates low-density lipoprotein cholesterol.

of change in statin use per month during periods related to conference/print dissemination of the SPARCL trial results (Table 2). Calendar time over the entire study period was associated with greater odds of discharge statin use (unadjusted monthly OR 1.019, 95% CI=1.017 to 1.022, quarterly OR 1.058, 95% CI=1.050 to 1.067; yearly OR 1.255, 95% CI=1.218 to 1.294; all $P<0.0001$).

Characteristics independently associated with discharge statin prescription are displayed in Table 3. Notably, patients who had lower adjusted odds of receiving a discharge statin prescription were more likely to be female, present with TIA rather than ischemic stroke, have known CAD or peripheral vascular disease, to be admitted to academic hospitals, and hospitals in the South or Midwest (versus West) of the

country. Patients with known dyslipidemia or taking a cholesterol reducer at the time of admission were more likely to receive discharge statin therapy.

Discussion

In this nationwide study, we found that the use of statin medications at discharge in hospitalized patients with ischemic stroke and TIA increased from 2005 to 2007. However, SPARCL trial reporting did not contribute significantly to this modest boost in discharge treatment and 18 months after SPARCL was first reported, almost 1 in 5 statin-eligible patients with ischemic stroke or TIA was being discharged from the hospital without a statin.

The lack of a significant effect of SPARCL reporting on discharge statin treatment prescription in hospitalized patients

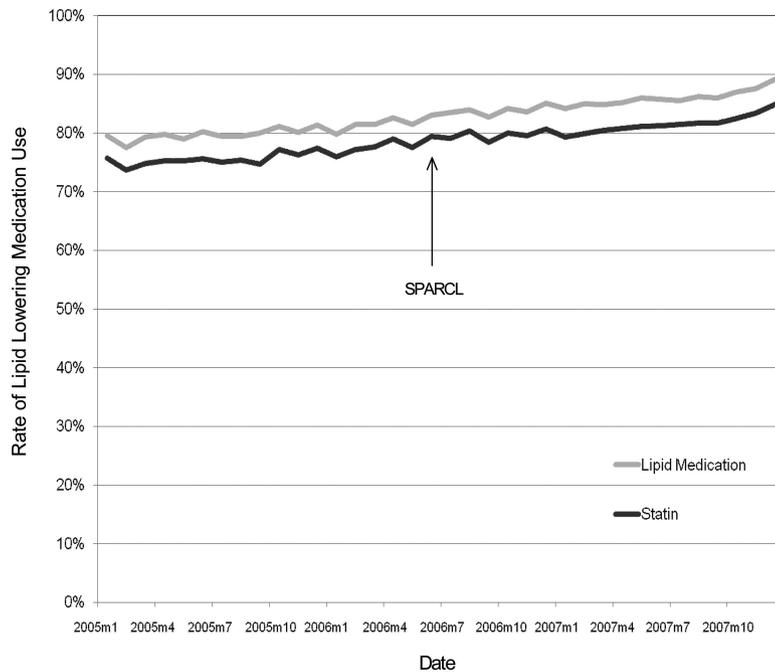


Figure. Frequency of hospital discharge use of lipid-lowering medications, including statins, among GTWG-Stroke patients hospitalized with ischemic stroke (IS) or TIA between January (Month 1) 2005 to December (Month 12) 2007. Arrow indicates period during which SPARCL results were reported.

with ischemic stroke and TIA may have been because clinicians had already made up their minds regarding the effectiveness of statin use before publication of SPARCL based on indirect evidence supporting benefit for statins in reducing vascular events after stroke.¹³ Treatment rates in prior studies have ranged from 36% to 50%, but these were either not nationwide in scope or were limited to tertiary institutions.^{5,14–16} Higher treatment rates observed in the GWTG-Stroke database were associated with calendar time underscoring the influence of secular trends on the results.

Our multivariable analyses showed that many avenues on the patient- and hospital-level could be explored to enhance discharge statin treatment rates further. Some of these avenues have previously been identified.^{5,14–16} For instance, patients with TIA or those with relatively fewer comorbidities tend to be less likely to receive discharge statin therapy even when they are at eligible. On the other hand, certain patients seem to be more likely to leave the hospital on a statin, and

these individuals are those with known dyslipidemia or who were on a cholesterol reducer at the time of hospital admission.^{5,16} Mounting data indicate that women who survive a stroke have less optimal in-hospital management and less favorable outcomes than men^{17–19} with recent trends showing a widening of these disparities.²⁰ Indeed, women hospitalized with stroke receive lipid modifier treatment less frequently at the time of discharge than their male counterparts.^{21,22} Even patients with prior CAD/myocardial infarction or peripheral vascular disease were less likely to receive lipid-lowering therapy despite long-established benefits in these patients. This finding is consistent with a recent observation from the AHA's GWTG that patients with polyvascular disease paradoxically receive less intense secondary prevention therapy.²³

Another constituency with established poorer stroke outcomes are individuals living in the South region of the United States, and they had the lowest discharge statin use rates in this study. Stroke incidence and stroke-related deaths are

Table 2. Estimated ORs of Change in Statin Use Per Month Among Hospitalized Patients With Ischemic Stroke and TIA During Periods Related to Conference/Print Dissemination of the SPARCL Trial Results

Effect of Interest	Adjusted*				Unadjusted			
	OR	Lower 95% CI	Upper 95% CI	P	OR	Lower 95% CI	Upper 95% CI	P
Pre-SPARCL (per month)	1.024	1.017	1.032	<0.0001	1.019	1.013	1.025	<0.0001
During SPARCL (per month)	1.030	1.010	1.050	0.0034	1.025	1.009	1.040	0.0016
Post-SPARCL (per month)	1.022	1.016	1.029	<0.0001	1.017	1.012	1.022	<0.0001
Post- versus pre- SPARCL	0.998	0.988	1.008	0.7114	0.998	0.990	1.005	0.5465
During SPARCL versus pre-SPARCL	1.005	0.982	1.029	0.6608	1.005	0.987	1.024	0.5592

Excludes patients with LDL-C <100 mg/dL, history or presence of atrial fibrillation, and prosthetic heart valves.

*Adjusted for age, sex, race, index cerebrovascular event (stroke versus TIA), medical histories (previous stroke/TIA, CAD/prior myocardial infarction, carotid stenosis, diabetes, peripheral vascular disease, hypertension, dyslipidemia, smoking), taking cholesterol reducer at admission, and hospital characteristics (no. of beds, hospital type, no. of stroke discharge, region).

LDL-C indicates low-density lipoprotein cholesterol.

Table 3. Estimated ORs for Discharge Statin Use by Covariates Among Hospitalized Patients With Ischemic Stroke and TIA

Covariates	Description	OR	Lower 95% CI	Upper 95% CI	P
Age	Per 10 years	0.929	0.919	0.940	<0.0001
Sex	Female versus male	0.869	0.852	0.886	<0.0001
Race	White versus other	0.870	0.822	0.921	<0.0001
Index hospitalization	TIA versus ischemic stroke	0.640	0.620	0.660	<0.0001
History of stroke or TIA	Yes versus no	0.857	0.837	0.877	<0.0001
History of CAD/prior myocardial infarction	Yes versus no	0.953	0.929	0.978	0.0003
History of carotid stenosis	Yes versus no	1.100	1.040	1.163	0.0009
History of diabetes	Yes versus no	0.992	0.968	1.016	0.5122
History of hypertension	Yes versus no	1.048	1.023	1.073	0.0001
History of peripheral vascular disease	Yes versus no	0.903	0.860	0.947	<0.0001
History of smoker	Yes versus no	1.234	1.195	1.274	<0.0001
History of dyslipidemia	Yes versus no	1.988	1.914	2.064	<0.0001
Taking cholesterol reducer at Admission	Yes versus no	8.467	7.862	9.117	<0.0001
History of or current atrial fibrillation	Yes versus no	0.704	0.682	0.726	<0.0001
Prosthetic heart valve	Yes versus no	0.787	0.726	0.853	<0.0001
No. of hospital beds	Per 100-unit change	1.033	1.004	1.063	0.0275
Hospital type	Academic versus nonacademic	0.746	0.669	0.832	<0.0001
Region	Midwest versus West	0.717	0.597	0.862	0.0004
	Northeast versus West	0.907	0.760	1.082	0.2767
	South versus West	0.656	0.555	0.775	<0.0001
No. of stroke discharges	0–100 versus 301+	0.669	0.572	0.782	<0.0001
	101–300 versus 301+	0.882	0.772	1.007	0.0643

much higher in the South than the rest of the country.²⁴ Our results emphasize the need to find better ways of bridging these sex and geographic disparities in stroke care.

Even at academic institutions, which harbor the experts who often write the consensus guidelines many practitioners rely on, there remains substantial room for improvement in discharge treatment use after stroke.¹⁴ Our finding that academic hospitals participating in GWTG-Stroke were less likely to implement discharge statin treatment when compared with nonacademic hospitals was not consistent with prior data,¹⁶ and this may be due to differences in the size and composition between that single-state registry,¹⁶ and ours but will require further study. Finally, 2 lifestyle-related vascular risk factors, smoking and overall adiposity (higher body mass index), were linked to higher odds of being discharged on a statin. We are unaware that such links have been reported before. It could be that the presence of these deleterious behavioral characteristics, not easily amenable to ready modification, keyed the clinicians to optimizing pharmacotherapy.

This study has limitations. Study data were collected based on the medical record and depend on the accuracy and completeness of clinical documentation. We were unable to explore the relationship between stroke severity and odds of statin treatment because the National Institutes of Health Stroke Scale is not routinely collected in clinical practice and therefore incompletely available in the registry. Another important consideration is that use of a statin medication at hospital discharge does not necessarily indicate the patient

was treated with the most appropriate agent, dose, or achieved goal. Lastly, although we controlled for known confounders, unmeasured confounding could have affected our results.

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Disclosures

L.H.S. serves as chair of the AHA GWTG Steering Committee; serves as a consultant to the Research Triangle Institute, CryoCath, and to the Massachusetts Department of Public Health; and has provided expert medical opinions in malpractice lawsuits regarding stroke treatment and prevention. E.E.S. serves as a member of the GWTG Science Subcommittee and receives research support from the National Institutes of Health (National Institute of Neurological Disorders and Stroke R01 NS062028) and the Canadian Stroke Network and salary support from the Heart and Stroke Foundation of Canada and the Canadian Institute for Health Research. A.F.H. is a member of the AHA GWTG analytical center at the Duke Clinical Research Institute and reports receiving research support from Johnson & Johnson, Medtronic, and Merck; honoraria from Astra-Zeneca; and is serving on the speakers' bureau for Novartis. A.F.H. has made available online a detailed listing of financial disclosures (www.dcri.duke.edu/research/coi.jsp). W.P. and D.M.O. are members of the Duke Clinical Research Institute that serves as the AHA

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