

Age and Sex Disparities in Discharge Statin Prescribing in the Stroke Belt: Evidence From the Reasons for Geographic and Racial Differences in Stroke Study

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Background—Stroke is a costly and debilitating disease that disproportionately affects blacks. Despite the efficacy of statins, evidence suggests racial disparities may exist in statin prescribing.

Methods and Results—We analyzed discharge medications for participants hospitalized for an ischemic stroke during follow-up of the REGARDS (Reasons for Geographic and Racial Differences in Stroke) study. Medications on admission and discharge were abstracted from medical records. Among the 666 eligible incident strokes (2003–2013), analyses were restricted to 323 participants who were not statin users at the time of admission and had no history of atrial fibrillation. Overall, 48.7% were prescribed a statin on discharge. In the Stroke Belt, participants aged 65 years and older were 47% less likely to be discharged on a statin compared with those younger than 65 years (relative risk [RR], 0.53; 95% Cl, 0.38–0.74). This association was not observed in non–Stroke Belt residents. Outside the Stroke Belt, blacks were more likely than whites to be discharged on a statin (RR, 1.42; 95% Cl, 1.04–1.94), while no black:white association was present among Stroke Belt residents (RR, 0.93; 95% Cl, 0.69–1.26; *P* for interaction=0.228). Compared with women, men in the Stroke Belt were 31% less likely to be discharged on a statin (RR, 0.69; 95% Cl, 0.50–0.94) while men outside the Stroke Belt were more likely to be discharged on a statin (RR, 0.69; 95% Cl, 0.50–0.94) while men outside the Stroke Belt were more likely to be discharged on a statin (RR, 1.38; 95% Cl, 0.99–1.92; *P* for interaction=0.004).

Conclusions—Statin discharge prescribing may differ among Stroke Belt and non–Stroke Belt residents, particularly in older Americans and men. (J Am Heart Assoc. 2017;6:e005523. DOI: 10.1161/JAHA.117.005523.)

Key Words: disparities • prescribing patterns • secondary prevention • statins • stroke

E ach year, 795 000 people in the United States experience a new or recurrent stroke.¹ Stroke is a leading cause of serious, long-term adult disability, with estimated direct and indirect costs of \$71.6 billion in 2012.¹ The majority of strokes (85%) are ischemic, with an annual recurrence rate of 5% to 15%.¹⁻⁹ The importance of secondary stroke prevention is paramount, since the estimated

Correspondence to: Karen C. Albright, DO, MPH, Geriatric Research, Education and Clinical Center (GRECC), Birmingham VA Medical Center, 700 South 19th Street, Room 8202, Birmingham, AL. E-mail: kalbright@uabmc.edu Received January 7, 2017; accepted June 15, 2017.

© 2017 The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made. 6.6 million adult stroke survivors in the United States are at increased risk for stroke recurrence.¹⁰ Recurrent strokes are often more disabling and costly than incident stroke.¹¹

The SPARCL (Stroke Prevention by Aggressive Reduction in Cholesterol Levels) trial demonstrated the efficacy of HMG-CoA reductase inhibitors (statins) in preventing recurrent stroke in patients without coronary heart disease.^{12,13} A Cochrane review of randomized controlled trials suggests that patients with ischemic stroke or transient ischemic attack, with or without a history of coronary heart disease, should receive statins.¹⁴ Despite the demonstrated efficacy of statins in preventing recurrent stroke, some studies suggest that lipidlowering agents are not being equally prescribed for all patients with stroke at the time of hospital discharge.^{15,16}

Most studies to date have focused only on patients from hospitals participating in quality-improvement programs, thus the overall proportion of the general population of patients with ischemic stroke who receive a statin at discharge, and the association of patient characteristics and discharge statin prescribing remains unknown. The purpose of this analysis is to estimate the proportion of patients with ischemic stroke

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Clinical Perspective

What Is New?

- Among participants hospitalized for ischemic stroke who were not already taking a statin, <49% were prescribed a statin on discharge.
- Older Americans in the Stroke Belt were 47% less likely to be discharged on a statin; this difference was not observed in non–Stroke Belt residents.
- Blacks outside the Stroke Belt were 42% more likely to be prescribed a statin on discharge; no black:white differences were observed among Stroke Belt residents.
- In the Stroke Belt, men were 31% less likely to be discharged on a statin; outside the Stroke Belt, men were 38% more likely to be discharged on a statin.

What Are the Clinical Implications?

- In patients hospitalized for ischemic stroke, opportunities exist to improve statin prescribing on discharge.
- Providers should remain cognizant that a meta-analysis of placebo-controlled and active-comparator trials demonstrated that statins reduce the risk of stroke in patients with coronary heart disease and a randomized controlled trial demonstrated that statin treatment reduces the risk for recurrent stroke in patients with a history of stroke or transient ischemic attack.
- All ischemic stroke survivors should be evaluated to determine whether they could benefit from a statin, regardless of the patient's age, race, sex, or geographic residence.

who receive a statin at discharge and to document differences in discharge statin prescribing by age, race, and sex, in and out of the Stroke Belt¹⁷ using a national cohort of individuals admitted to a variety of US hospitals. Given that patients using a statin on hospital admission for stroke (prevalent users) often differ from patients not actively using a statin by age, risk factors, and comorbidities, this study focuses on patients who were not using a statin at the time of stroke admission.¹⁸

Methods

This report uses data from the REGARDS (Reasons for Geographic and Racial Differences in Stroke) study, a national, prospective cohort trial of 30 239 US adults aged 45 years and older, designed to investigate factors associated with the excess stroke mortality observed among blacks compared with whites and among residents of the Stroke Belt compared with other geographic regions of the United States. The Stroke Belt states include Alabama, Arkansas, Georgia, Indiana, Kentucky, Louisiana, Mississippi, North Carolina,

ogy of the REGARDS study has been previously described.²⁰ Participant recruitment occurred from January 2003 through October 2007. Baseline data were collected using a computer-assisted telephone interview, self-administered questionnaires, and an in-home examination. Demographic information, medical history, and an array of other risk factors were obtained at the baseline telephone interview. Of relevance to the current analysis, the in-home examination was conducted a median of 3 to 4 weeks after the computerassisted telephone interview and included blood pressure measurements, collection of blood and urine samples, anthropometry, and ECG. Participants were contacted every 6 months using the computer-assisted telephone interview and asked whether they have been hospitalized, visited an emergency department, or had a doctor's visit that resulted in an overnight stay in a hospital. If a participant or proxy reported a potential stroke event (hospitalization or an outpatient visit), his/her medical records were requested and the case was adjudicated by an expert panel.²¹ Consent was obtained verbally by phone and later in writing during the in-person evaluation. The institutional review boards of the participating institutions approved the study methods.

South Carolina, Tennessee, and Virginia.^{17,19} The methodol-

From the 1044 adjudicated ischemic strokes occurring among REGARDS participants from January 2003 to October 2012, we excluded participants if they had inadequate medical records available for review (n=32), were discharged from the emergency department (n=37), were seen only in the outpatient setting (n=93), died during stroke hospitalization or were discharged to hospice (n=56), had incomplete medication records (n=2), reported a history of stroke at the time of REGARDS enrollment (n=158), had documented evidence of statin use before admission (n=253), or had evidence of atrial fibrillation (n=90), resulting in 323 adjudicated ischemic strokes in the current analysis (Figure 1). Analyses were restricted to individuals without atrial fibrillation, as individuals with atrial fibrillation were excluded from SPARCL, the trial that set the standard for statin use in secondary stroke prevention.¹³ Because SPARCL was not published until 2006, we also examined the proportion of statin prescribing by year.¹²

Outcomes of Interest

Medications on hospital admission and discharge associated with the physician-adjudicated ischemic stroke events were obtained from medical records by 2 data abstractors. A list of each participant's home medications (medications before hospitalization) was obtained from the admission history and physical examination and the medication reconciliation sheet. Medications prescribed at the time of discharge were obtained from the discharge summary and the inpatient medication reconciliation sheet. Any discrepancy was

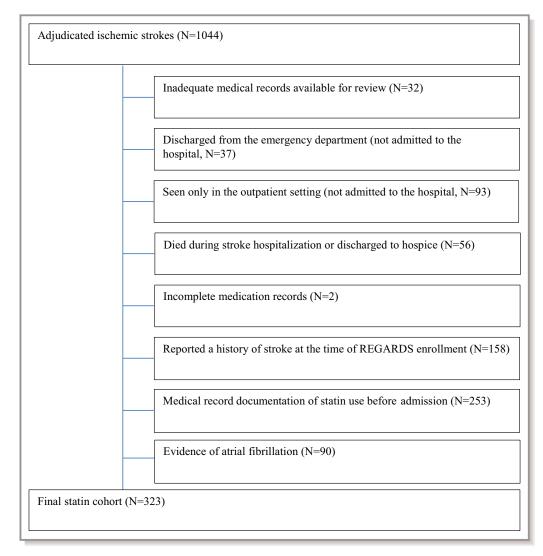


Figure 1. Flow diagram of exclusion criteria applied to achieve the final statin (HMG-CoA reductase inhibitors) cohort. REGARDS indicates Reasons for Geographic and Racial Differences in Stroke study.

adjudicated by 2 or more data abstractors. The primary outcome of interest for this analysis was documented evidence of statin prescribing at the time of discharge ("prescribed").

In an effort to reduce biases, such as confounding, we restricted our analysis to participants who were not prevalent users of statins (n=323) at the time of admission.¹⁸ An individual was categorized as a prevalent user of statins if there was documentation in the medical record of the individual taking a medication from that class before admission. Participants who were not prevalent users of statins before admission and were prescribed a statin at the time of discharge were classified as incident statin users.

Exposures and Covariates

Age at the time of stroke, black race, and male sex were each considered individually as exposures. Stroke Belt residence

was evaluated as an effect modifier by adding a Stroke Beltexposure interaction term to each exposure model. Given that access to medical care has the potential to change with Medicare eligibility, we examined age at the time of stroke as a categorical variable (<65 years versus ≥65 years). All participants self-reported race as either non-Hispanic black or non-Hispanic white at the time of enrollment as described above. Sex was also self-reported. Residence was selfreported at the time of enrollment. Atrial fibrillation was defined by self-report or ECG detection of atrial fibrillation.²² Hypertension was defined by self-report, self-reported use of hypertension medications, or systolic blood pressure \geq 140 mm Hg or diastolic blood pressure \geq 90 mm Hg (average of 2 blood pressure measurements). Dyslipidemia was defined as any of the following: self-reported high cholesterol, total cholesterol >200 mg/dL, high-density lipoprotein <40 mg/dL, or low-density lipoprotein cholesterol >100 mg/dL.²³ Diabetes mellitus was defined by self-report

or a fasting glucose level ≥126 mg/dL or a nonfasting glucose level ≥200 mg/dL.²⁴ Coronary heart disease was defined by self-report of myocardial infarction, percutaneous coronary intervention, or coronary artery bypass graft surgery or ECG evidence of myocardial infarction. Chronic kidney disease was defined as a glomerular filtration rate <60 mL/ min per 1.73 m².²⁵ Impaired cognition was defined as a 6-item screener score of \leq 4 during the baseline computerassisted telephone interview.^{26,27} Variables related to smoking, education, and income were dichotomized as current smoking, obtaining at least a high school education, and having an annual income <\$20 000. US hospital characteristics were obtained from the 2003 through 2013 American Hospital Association Annual Survey of Hospitals.²⁸ The urbanrural status of each hospital was defined according to a modification of the rural-urban continuum classification scheme using county-level data.29

Statistical Analysis

Baseline characteristics were compared between patients prescribed statins and patients not prescribed statins, using ttests for continuous variables and Pearson chi-square or Fisher exact tests, where appropriate, for categorical variables. In an effort to prevent the potential interpretation of the odds ratio as a relative risk, we evaluated the association

100

90

80

70

60

50

40

30

20

10

0

2003

2004

2005

2006

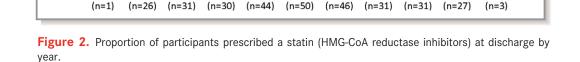
2007

Proportion of Participants Prescribed a Statin at Discharge

between statin prescribing at time of discharge and each exposure of interest with crude and adjusted relative risk (ie, risk ratio [RR]) using the modified Poisson regression method.³⁰ This method applies a robust error variance procedure (ie, sandwich estimation) to account for overestimation in the error term.³⁰ RRs for statin prescribing were calculated for age 65 years and older compared with age younger than 65 years, blacks compared with whites, and men compared with women, after adjustment for hypertension, dyslipidemia, diabetes mellitus, coronary heart disease, chronic kidney disease, impaired cognition, current smoking, high school education, and income. As we observed an increasing trend in statin prescribing over time (Figure 2), we included year of stroke in the multivariable models. Stroke Belt residence was evaluated for effect modification by adding a Stroke Belt-exposure interaction term (eg, male×Stroke Belt residence) to each exposure model. In addition, sensitivity analyses were performed including participants with atrial fibrillation.

Results

Among the 323 participants with an incident stroke, the median age was 74 years (interquartile range, 67–80), 48.9% were black, 45.8% were men, and 55.7% were Stroke Belt



2008

2009

2010

2011

2012

2013

Characteristic	Not Using a Statin before Admission (n=323)	Discharge Statin Not Prescribed (n=158)	Discharge Statin Prescribed (n=165)	P Value
Age, y*	74 (67–80)	75 (68–81)	73 (66–79)	0.113
Age ≥65 y	83.6	86.7	80.6	0.139
Black	48.9	45.6	52.1	0.239
Men	45.8	47.5	44.2	0.561
Hypertension	87.3	85.4	89.1	0.325
Dyslipidemia	87.3	82.3	92.1	0.008
Diabetes mellitus	38.1	38.0	38.2	0.969
Coronary heart disease	28.8	25.9	31.5	0.269
Chronic kidney disease	18.0	17.7	18.2	0.914
Impaired cognition	12.4	12.7	12.1	0.884
Current smoking	19.5	18.4	20.6	0.610
Stroke buckle or belt	55.7	58.2	53.3	0.376
High school education	82.7	81.5	84.2	0.518
Income <\$20 000	20.7	20.9	20.6	0.951

 Table 1. Characteristics of Patients With Ischemic Stroke From the REGARDS Study With No Known History of Atrial Fibrillation

 Who Reported Not Using a Statin Before Admission by Statin Prescribing at Discharge

REGARDS indicates Reasons for Geographic and Racial Differences in Stroke; statin, HMG-CoA reductase inhibitor.

*Values are expressed as percentages except for continuous variables, which are expressed as median (25th percentile–75th percentile).

residents. Table 1 shows the baseline characteristics of eligible participants who were not taking statins (n=323) at the time of admission by those who were and were not discharged on statins. Overall, 48.7% of participants had evidence of a statin prescribed at discharge. Participants who were prescribed a statin at discharge were more likely to have dyslipidemia compared with those who were not prescribed a statin (92.1% versus 82.3%, P=0.008). There were no other statistically significant differences between patients prescribed and not prescribed a statin. Hospitals where participants were prescribed a statin at discharge more frequently reported resident training compared with the hospitals where participants were not prescribed a statin at discharge (53.7% versus 38.5%, P=0.006). There were no other statistically significant differences between hospitals that did and did not prescribe a statin at (Table 2). There was an increasing trend in statin prescribing over time (P for trend <0.001) (Table 3).

After multivariable adjustment, participants aged 65 years and older were less likely to be prescribed a statin at discharge (RR, 0.75; 95% Cl, 0.57–0.99), while those with dyslipidemia were more likely to be prescribed a statin at discharge (RR, 1.67; 95% Cl, 1.10–2.53) (Table 4). Participants were more likely to be prescribed a statin at discharge over time (RR, 1.13; 95% Cl, 1.08–1.18). There were no statistically significant differences in statin prescribing by race (black:white RR, 1.13; 95% Cl, 0.91–1.41) or sex (male: female RR, 0.97; 95% Cl, 0.78–1.21).

Interaction testing by Stroke Belt residence was statistically significant at a 2-sided $\alpha \leq 0.1$ for both age 65 years and older (P=0.086) and male sex in the full models (P=0.004) (Table 5). Within the Stroke Belt, participants aged 65 years and older were 47% less likely to be discharged on a statin compared with patients younger than 65 years (RR, 0.53; 95% Cl, 0.38-0.75). This association was not observed in non-Stroke Belt residents (RR, 1.14; 95% CI, 0.69–1.90; P for interaction=0.086). Among non-Stroke Belt residents, blacks were more likely to be discharged on a statin (RR, 1.42; 95% Cl, 1.04-1.94). This association was not present among black Stroke Belt residents (RR, 0.93; 95% CI, 0.69-1.26; P for interaction=0.228). Male Stroke Belt residents were 31% less likely to be discharged on a statin compared with their female counterparts (RR, 0.69; 95% Cl, 0.50-0.94). In non-Stroke Belt residents, men were more likely to be discharged on a statin (RR, 1.38; 95% Cl, 0.99–1.92; P for interaction=0.004). Results did not change significantly when participants with atrial fibrillation were included in the analyses (data not shown).

Discussion

Although statin prescribing increased over time in the current study, statins were prescribed at discharge to only 49% of patients with ischemic stroke. This represents a treatment gap given current American College of Cardiology/American Heart Association (ACC/AHA) recommendations.¹⁰ Comparing the estimate of statin discharge prescribing in the current study
 Table 2. Characteristics of Hospitals Where Patients With Stroke From the REGARDS Study With No Known History of Atrial

 Fibrillation Who Reported Not Using a Statin Before Admission Were Treated by Statin Prescribing at Discharge

Characteristic	Not Using a Statin Before Admission (n=323)	Discharge Statin Not Prescribed (n=158)	Discharge Statin Prescribed (n=165)	P Value
Hospital in stroke belt state*	57.5	59.6	55.5	0.455
Hospital census region				
Northeast	7.5	7.1	7.9	0.700
Midwest	18.4	16.0	20.7	
South	69.4	71.8	67.1	
West	4.7	5.1	4.3	
Hospital location rural-urban classification			-	
Metro—counties in metro areas of ≥ 1 million population	47.2	43.6	50.6	0.186
Metro-counties in metro areas of 250 000 to 1 million population	29.1	29.5	28.7	
Metro-counties in metro areas of <250 000 population	13.4	12.8	14.0	
Nonmetro—urban population of \geq 20 000, adjacent to a metro area	5.6	6.4	4.9	
Nonmetro-urban population of 2500 to 19 999, adjacent to a metro area	4.1	6.4	1.8	
Nonmetro—urban population of 2500 to 19 999, not adjacent to a metro area	0.6	1.3	0	
Resident training approved by council for GME	46.3	38.5	53.7	0.006

GME indicates graduate medical education; REGARDS, Reasons for Geographic and Racial Differences in Stroke; statin, HMG-CoA reductase inhibitor.

*Values are expressed as percentages except for continuous variables, which are expressed as median (25th percentile–75th percentile). Hospital data were available for 99% (n=320) of events.

with prior reports is difficult because prior studies have used broad definitions that include any lipid-lowering agent.^{10,12} Using these broad definitions, previous studies have reported that 55% to 85% of patients with ischemic stroke receive lipidlowering therapy at discharge.^{15,16,31} Estimates from prior studies were derived from clinical trials and hospitals dedicated to improving the quality of inpatient stroke care. Therefore, it is not surprising that the proportion of patients discharged on a statin is lower in the current study that was derived from a national cohort admitted to a variety of hospitals. While some studies have reported muscle-related side effects in 10% to 25% of patients receiving statin therapy,^{32,33} that proportion is not large enough to account for our observation that only 49% of ischemic stroke survivors were prescribed a statin at discharge.

Further, we did see an increase in statin prescribing over time. The reasons for this are unclear. Since the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) was published in 2001, it is unlikely that these guidelines influenced the prescribing trends. Similarly, since the ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults was not published until 2013, this could not have impacted statin prescribing in our study since the strokes occurred from 2003 to 2013. Instead, the increase may be partially attributed to the SPARCL trial, with results published in 2006. Our data indicate that the first increase in statin prescribing for patients without dyslipidemia began in 2007. Further, results from SPARCL may have focused more attention on statin prescribing for patients with dyslipidemia, as the rates of prescribing for this group also increased after 2006.

Past Get With The Guidelines-Stroke studies have shown that patients admitted to hospitals in the South have lower odds of having a statin prescribed at discharge.³⁴ These lower odds in discharge statin prescribing after stroke have also been described in older individuals,³⁴ women,³⁴ and blacks,¹⁶ but no study has specifically evaluated whether the magnitude of these differences by age, sex, and race is the same inside and outside of the Stroke Belt. By examining Stroke Belt residence as an effect modifier, we were able to examine the direction and magnitude of the age, sex, and race effect inside and outside of the Stroke Belt. In contrast to previous studies that have reported blacks as less likely to be prescribed statins,^{15,16} we found no differences in discharge statin prescribing between blacks and whites. There were, however, statistically significant age and sex differences among Stroke Belt residents.

Reasons for older participants and men being discharged on a statin less frequently among Stroke Belt residents are likely multifactorial. Providers and family members of older individuals and men may have had different goals of care

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	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	P Value For Trend
Participants prescribed a statin at the time of discharge	0 (1)	0 (1) 23.1 (26)	41.9 (31)	50.0 (30)	50.0 (44)	48.0 (50)	50.0 (46)	48.4 (31)	74.2 (31)	77.8 (27)	66.7 (3)	<0.001
Participants with dyslipidemia prescribed a statin at the time of discharge	0 (0)	27.3 (22)	46.4 (28)	57.7 (26)	53.8 (39)	48.9 (45)	53.8 (39)	48.3 (29)	80.0 (25)	73.9 (23)	66.7 (3)	0.001
Participants without dyslipidemia prescribed a statin at the time of discharge	0 (1) 0 (4)	0 (4)	0 (3)	0 (4)	20.0 (5)	40.0 (5)	28.6 (7)	50.0 (2)	50.0 (6)	100 (4)	(0) 0	<0.001

Values are expressed as percentages (counts). REGARDS indicates Reasons for Geographic and Racial Differences in Stroke, statin, HMG-CoA reductase inhibitor.

Table 4. Risk of Statin Prescribing at Discharge for PatientsWith Ischemic Stroke From the REGARDS Study With NoKnown History of Atrial Fibrillation Who Reported Not Using aStatin Before Admission

Characteristics	Crude PR (95% CI)	Adjusted* PR (95% CI)
Age $\geq \!\! 65$ y	0.82 (0.64–1.05)	0.75 (0.57–0.99)
Black	1.14 (0.92–1.41)	1.13 (0.91–1.41)
Men	0.94 (0.76–1.16)	0.97 (0.78–1.21)
Hypertension	1.19 (0.83–1.71)	1.23 (0.84–1.78)
Dyslipidemia	1.70 (1.07–2.70)	1.67 (1.10–2.53)
Diabetes mellitus	1.00 (0.81–1.25)	0.90 (0.73–1.13)
Coronary heart disease	1.14 (0.91–1.42)	1.19 (0.93–1.51)
Chronic kidney disease	1.02 (0.77–1.34)	1.01 (0.77–1.32)
Impaired cognition	0.98 (0.70–1.36)	0.96 (0.69–1.33)
Current smoking	1.07 (0.83–1.39)	1.07 (0.84–1.37)
Stroke buckle or belt	0.91 (0.73–1.12)	0.89 (0.72–1.10)
High school education	1.10 (0.81–1.49)	1.04 (0.77–1.41)
Income <\$20 000	0.99 (0.76–1.29)	1.03 (0.79–1.35)
Admission year	1.11 (1.06–1.16)	1.13 (1.08–1.18)

Values are expressed as risk ratios (RRs) with 95% Cls. REGARDS indicates Reasons for Geographic and Racial Differences in Stroke; statin, HMG-CoA reductase inhibitor. *Full model adjusted for age, race, sex, hypertension, dyslipidemia, diabetes mellitus, coronary heart disease, chronic kidney disease, impaired cognition, current smoking status, stroke buckle or belt residence, education, income, and admission year.

influencing their decisions regarding secondary stroke prevention. They may have had complicated hospital courses resulting from uncontrolled vascular risk factors, inpatient complications, or more severe strokes leading to less aggressive inpatient stroke care.

Study Strengths and Limitations

The current study informs us on discharge statin prescribing over time; the associations between age, race, sex, and discharge statin prescribing; and the impact of Stroke Belt residence on these associations. Unlike the samples used for prior reports, the sampling of the REGARDS study allows for detailed focus on geographic variations in discharge prescribing.²⁰ Particular attention to Stroke Belt residence is essential given that between 2% and 15% of the excess stroke mortality traditionally attributed to race is actually attributable to geography.³⁵

The current study is not without limitations. Defining a participant as a prevalent statin user relied on the available medical documentation. Poor recall on the part of the patient or family could have resulted in prevalent users being misclassified as incident users (not taking a statin at the time of admission). The proportion of participants who were prescribed a statin at discharge could have been

	Crude		Adjusted*			
Characteristic	Non-Stroke Belt (n=143)	Stroke Belt (n=180)	P Value	Non-Stroke Belt (n=143)	Stroke Belt (n=180)	P Value
Age \geq 65 y	1.15 (0.72–1.86)	0.65 (0.48–0.87)	0.044	1.14 (0.69–1.90)	0.53 (0.38–0.75)	0.086
Black	1.31 (0.95–1.80)	0.99 (0.74–1.34)	0.224	1.42 (1.04–1.94)	0.93 (0.69–1.26)	0.228
Men	1.28 (0.94–1.75)	0.69 (0.50–0.96)	0.007	1.38 (0.99–1.92)	0.69 (0.50-0.94)	0.004
Hypertension	1.09 (0.65–1.82)	1.26 (0.76–2.08)	0.664	1.24 (0.72–2.14)	1.07 (0.65–1.76)	0.740
Dyslipidemia	1.49 (0.78–2.86)	1.87 (0.98–3.56)	0.631	1.64 (0.88–3.04)	1.90 (1.05–2.47)	0.576
Diabetes mellitus	0.92 (0.66–1.28)	1.09 (0.81–1.47)	0.465	0.85 (0.61–1.20)	0.94 (0.71–1.25)	0.467
Coronary heart disease	1.26 (0.93–1.70)	1.03 (0.74–1.43)	0.171	1.14 (0.83–1.57)	1.13 (0.80–1.59)	0.554
Chronic kidney disease	0.80 (0.53–1.22)	1.26 (0.88–1.80)	0.109	0.86 (0.57–1.30)	1.42 (1.00–2.03)	0.085
Impaired cognition	0.97 (0.62–1.50)	0.97 (0.59–1.59)	0.993	0.94 (0.62–1.42)	0.91 (0.55–1.49)	0.749
Current smoking	1.22 (0.87–1.71)	0.96 (0.65–1.40)	0.358	1.09 (0.87–1.53)	0.91 (0.65–1.29)	0.190
High school education	1.03 (0.67–1.60)	1.14 (0.76–1.72)	0.745	1.16 (0.71–1.91)	1.06 (0.72–1.57)	0.647
Income <\$20 000	1.09 (0.75–1.58)	0.93 (0.65–1.35)	0.565	1.16 (0.76–1.75)	1.04 (0.72–1.51)	0.737
Admission year	1.08 (1.02–1.15)	1.14 (1.07–1.20)	0.287	1.09 (1.03–1.16)	1.16 (1.09–1.24)	0.259

 Table 5.
 Crude and Fully Adjusted* Risk of Statin Prescribing at Discharge for Patients With Ischemic Stroke From the REGARDS

 Study With No Known History of Atrial Fibrillation Who Reported Not Using a Statin Before Admission by Stroke Belt Residence

Values are expressed as risk ratios (RRs) with 95% CIs. REGARDS indicates the Reasons for Geographic and Racial Differences in Stroke; statin, HMG-CoA reductase inhibitor. *Full model adjusted for age, race, sex, hypertension, dyslipidemia, diabetes mellitus, coronary heart disease, chronic kidney disease, impaired cognition, current smoking status, education, income, and admission year.

underestimated if incident users were not taking statins because of previous statin side effects. Poor documentation in the medical record at the time of discharge would result in participants being misclassified as not prescribed a statin, resulting in overestimates of the proportion not prescribed a statin. We were unable to obtain reliable insurance information, which may have impacted statin prescribing. However, the majority of our sample was 65 years and older, ensuring at least basic insurance coverage through Medicare.

Restricting our analysis to participants who reported not taking a statin at the time of admission reduced our sample size and may have impaired our ability to detect differences in groups,¹⁸ but we employed an incident user design as an attempt to that ensure prescribing patterns are not confounded by prior statin use. Thus, our findings may not be generalizable to all individuals who experience a stroke. most notably past or present statin users.¹⁸ Knowing that individuals taking a statin may differ from those not taking a statin in terms of the duration and severity of existing comorbidities,^{18,36–38} we designed our study to focus on individuals not taking a statin at the time of admission.³⁶ Despite these limitations, this is one of few studies to report on the proportion of patients with ischemic stroke discharged on a statin, a secondary stroke prevention medication class proven effective in reducing recurrent stroke. One strength of this study is its use of the REGARDS cohort data. Using these data permits us to examine Stroke Belt residence, factors related to stroke, and the discharge prescribing of statins at a variety of hospitals nationwide, avoiding the bias introduced by examining only patients treated at hospitals participating in stroke quality-improvement programs.

Conclusions

Although statins have been shown to lower the risk of recurrent stroke, fewer than 50% of participants in a nationwide cohort study were prescribed a statin at the time of stroke hospital discharge. Among Stroke Belt residents, individuals aged 65 years and older and men were less likely to be discharged on a statin—not blacks—leaving the reasons for higher rates of recurrent stroke in blacks unresolved. A next step in our efforts to understand the reasons for the higher rate of recurrent stroke in blacks is to evaluate statin adherence in ischemic stroke survivors.

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References

- Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, Das SR, de Ferranti S, Despres JP, Fullerton HJ, Howard VJ, Huffman MD, Isasi CR, Jimenez MC, Judd SE, Kissela BM, Lichtman JH, Lisabeth LD, Liu S, Mackey RH, Magid DJ, McGuire DK, Mohler ER III, Moy CS, Muntner P, Mussolino ME, Nasir K, Neumar RW, Nichol G, Palaniappan L, Pandey DK, Reeves MJ, Rodriguez CJ, Rosamond W, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Woo D, Yeh RW, Turner MB. Heart disease and stroke statistics–2015 update: a report from the American Heart Association. *Circulation*. 2015;131:e29–e322.
- Matsumoto N, Whisnant JP, Kurland LT, Okazaki H. Natural history of stroke in Rochester, Minnesota, 1955 through 1969: an extension of a previous study, 1945 through 1954. *Stroke*. 1973;4:20–29.
- Sacco RL, Wolf PA, Kannel WB, McNamara PM. Survival and recurrence following stroke. The Framingham study. *Stroke*. 1982;13:290–295.
- Sacco RL, Shi T, Zamanillo MC, Kargman DE. Predictors of mortality and recurrence after hospitalized cerebral infarction in an urban community: the Northern Manhattan Stroke study. *Neurology*. 1994;44:626–634.
- Petty GW, Brown RD Jr, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO. Survival and recurrence after first cerebral infarction: a population-based study in Rochester, Minnesota, 1975 through 1989. *Neurology*. 1998;50:208–216.
- Eriksson SE, Olsson JE. Survival and recurrent strokes in patients with different subtypes of stroke: a fourteen-year follow-up study. *Cerebrovasc Dis.* 2001;12:171–180.
- Lisabeth LD, Smith MA, Brown DL, Moye LA, Risser JM, Morgenstern LB. Ethnic differences in stroke recurrence. *Ann Neurol.* 2006;60:469–475.
- Leoo T, Lindgren A, Petersson J, von Arbin M. Risk factors and treatment at recurrent stroke onset: results from the Recurrent Stroke Quality and Epidemiology (RESQUE) study. *Cerebrovasc Dis.* 2008;25:254–260.
- Allen NB, Holford TR, Bracken MB, Goldstein LB, Howard G, Wang Y, Lichtman JH. Trends in one-year recurrent ischemic stroke among the elderly in the USA: 1994–2002. *Cerebrovasc Dis.* 2010;30:525–532.
- Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, Fang MC, Fisher M, Furie KL, Heck DV, Johnston SC, Kasner SE, Kittner SJ,

Mitchell PH, Rich MW, Richardson D, Schwamm LH, Wilson JA. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/ American Stroke Association. *Stroke*. 2014;45:2160–2236.

- Samsa GP, Bian J, Lipscomb J, Matchar DB. Epidemiology of recurrent cerebral infarction: a medicare claims-based comparison of first and recurrent strokes on 2-year survival and cost. *Stroke*. 1999;30:338–349.
- Amarenco P, Bogousslavsky J, Callahan A III, Goldstein LB, Hennerici M, Rudolph AE, Sillesen H, Simunovic L, Szarek M, Welch KM, Zivin JA. High-dose atorvastatin after stroke or transient ischemic attack. *N Engl J Med.* 2006;355:549–559.
- Amarenco P, Bogousslavsky J, Callahan AS, Goldstein L, Hennerici M, Sillesen H, Welch KM, Zivin JA. Design and baseline characteristics of the stroke prevention by aggressive reduction in cholesterol levels (SPARCL) study. *Cerebrovasc Dis.* 2003;16:389–395.
- Manktelow BN, Potter JF. Interventions in the management of serum lipids for preventing stroke recurrence. *Cochrane Database Syst Rev.* 2009;(3): CD002091.
- Tuhrim S, Cooperman A, Rojas M, Brust JC, Koppel B, Martin K, Chassin M. The association of race and sex with the underuse of stroke prevention measures. *J Stroke Cerebrovasc Dis.* 2008;17:226–234.
- Schwamm LH, Reeves MJ, Pan W, Smith E, Frankel M, Olson D, Zhao X, Peterson E, Fonarow GC. Race/ethnicity, quality of care, and outcomes in ischemic stroke. *Circulation*. 2010;121:1492–1501.
- National Heart Lung and Blood Institute. Stroke Belt Initiative. Project accomplishments and lessons learned. 1996. [online]. Available at: https:// www.nhlbi.nih.gov/files/docs/resources/heart/sb_spec.pdf. Accessed May 12, 2015.
- 18. Johnson E, Bartman B, Briesacher B, Fleming N, Gerhard T, Kornegay C, Nourjah P, Sauer B, Schumock G, Sedrakyan A, Stürmer T, West S, Schneeweiss S. The Incident User Design in Comparative Effectiveness Research [online]. Available at: http://effectivehealthcare.ahrq.gov/index. cfm/search-for-guides-reviews-and-reports/?productid=1086&pageaction=dis playproduct#5641. Accessed May 12, 2015.
- Borhani NO. Changes and geographic distribution of mortality from cerebrovascular disease. Am J Public Health Nations Health. 1965;55:673–681.
- Howard VJ, Cushman M, Pulley L, Gomez CR, Go RC, Prineas RJ, Graham A, Moy CS, Howard G. The reasons for geographic and racial differences in stroke study: objectives and design. *Neuroepidemiology*. 2005;25:135–143.
- Howard VJ, Kleindorfer DO, Judd SE, McClure LA, Safford MM, Rhodes JD, Cushman M, Moy CS, Soliman EZ, Kissela BM, Howard G. Disparities in stroke incidence contributing to disparities in stroke mortality. *Ann Neurol.* 2011;69:619–627.
- 22. Prineas RJ, Soliman EZ, Howard G, Howard VJ, Cushman M, Zhang Z, Moy CS. The sensitivity of the method used to detect atrial fibrillation in population studies affects group-specific prevalence estimates: ethnic and regional distribution of atrial fibrillation in the REGARDS study. *J Epidemiol.* 2009;19:177–181.
- 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.
- 24. American Diabetes Association. Standards of medical care in diabetes–2014. *Diabetes Care*. 2014;37(suppl 1):S14–S80.
- Levey AS, Eckardt KU, Tsukamoto Y, Levin A, Coresh J, Rossert J, De Zeeuw D, Hostetter TH, Lameire N, Eknoyan G. Definition and classification of chronic kidney disease: a position statement from kidney disease: improving global outcomes (KDIGO). *Kidney Int*. 2005;67:2089–2100.
- Callahan CM, Unverzagt FW, Hui SL, Perkins AJ, Hendrie HC. Six-item screener to identify cognitive impairment among potential subjects for clinical research. *Med Care*. 2002;40:771–781.
- Wadley VG, Unverzagt FW, McGuire LC, Moy CS, Go R, Kissela B, McClure LA, Crowe M, Howard VJ, Howard G. Incident cognitive impairment is elevated in the stroke belt: the REGARDS study. *Ann Neurol.* 2011;70:229–236.
- American Hospital Association. The American Hospital Association Annual Survey Database. The American Hospital Association, 2003-2013. [online]. Available at: https://www.ahadataviewer.com/additional-data-products/ AHA-Survey/. Accessed February 25, 2017.
- USDA Economic Research Service. Rural-Urban Continuum Codes. 2013. [online]. Available at: https://www.ers.usda.gov/data-products/rural-urbancontinuum-codes/. Accessed February 25, 2017.
- Zou G. A modified poisson regression approach to prospective studies with binary data. Am J Epidemiol. 2004;159:702–706.
- Park JH, Ovbiagele B. Optimal combination secondary prevention drug treatment and stroke outcomes. *Neurology*. 2015;84:50–56.

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- Bruckert E, Hayem G, Dejager S, Yau C, Begaud B. Mild to moderate muscular symptoms with high-dosage statin therapy in hyperlipidemic patients--the PRIMO study. *Cardiovasc Drugs Ther.* 2005;19:403–414.
- Cohen JD, Brinton EA, Ito MK, Jacobson TA. Understanding statin use in America and gaps in patient education (USAGE): an internet-based survey of 10 138 current and former statin users. *J Clin Lipidol*. 2012;6: 208–215.
- Ovbiagele B, Schwamm LH, Smith EE, Hernandez AF, Olson DM, Pan W, Fonarow GC, Saver JL. Recent nationwide trends in discharge statin treatment of hospitalized patients with stroke. *Stroke*. 2010;41:1508–1513.
- 35. Yang D, Howard G, Coffey CS, Roseman J. The confounding of race and geography: how much of the excess stroke mortality among African Americans is explained by geography? *Neuroepidemiology*. 2004;23:118–122.
- Ray WA. Evaluating medication effects outside of clinical trials: new-user designs. *Am J Epidemiol.* 2003;158:915–920.
- McMahon AD, MacDonald TM. Design issues for drug epidemiology. Br J Clin Pharmacol. 2000;50:419–425.
- Moride Y, Abenhaim L. Evidence of the depletion of susceptibles effect in nonexperimental pharmacoepidemiologic research. J Clin Epidemiol. 1994;47:731–737.





Age and Sex Disparities in Discharge Statin Prescribing in the Stroke Belt: Evidence From the Reasons for Geographic and Racial Differences in Stroke Study

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