Geographic Variation in Statin Use for Complex Acute Myocardial Infarction Patients

Evidence of Effective Care?

John M. Brooks, PhD,† Elizabeth A. Cook, MS,* Cole G. Chapman, BS,* Puttarin Kulchaitanaroaj, MS,* Elizabeth A. Chrischilles, MS, PhD,† Stephen Welch, PhD,* and Jennifer Robinson, MD, MPH†*

Background: Despite strong evidence to designate statin use for secondary prevention of cardiovascular disease (CVD) as "effective care," observational studies show that many patients with CVD do not receive statins. This suggests that statin prescribing decisions for complex CVD patients are preference sensitive.

Objectives: The aim of this study was to evaluate local area variation in statin prescribing for subsets of complex patients after acute myocardial infarction (AMI) to assess whether current statin prescribing patterns fit profiles of either "effective care" or "preference-sensitive care."

Research Design and Subjects: This was a retrospective cohort study of 124,618 Medicare patients with fee-for-service parts A, B, and D benefits who were hospitalized with AMI in 2008 or 2009 with no evidence of AMI in the past 12 months.

Measures: Patient complexity was defined by the presence of diabetes, heart failure, and chronic kidney disease in the year before AMI admission. Local area practice styles for "no statin," "lower-intensity statins," and "high-intensity statins" were measured using the driving area for clinical care method. Statin prescribing rates for complex patient subsets were contrasted across patients grouped by local areas practice styles.

Results: Lower statin treatment rates were observed for patients with complex conditions, especially among those with heart failure. However, substantial local area variation in statin prescribing is observed across all complex patient groups.

Conclusions: Despite guidelines promoting the use of statins for secondary prevention for CVD patients, substantial local area variation suggests that patient and provider beliefs and preferences weigh heavily in statin prescribing decisions.

Key Words: statins, geographic variation, AMI, effective care, preference-sensitive care

(*Med Care* 2014;52: S37–S44)

Given the strength of evidence from numerous randomized controlled trials (RCTs), statin use for the secondary prevention of future cardiovascular events for patients with cardiovascular disease (CVD) has been designated as "effective care."[1,2] Effective care is defined by the *Dartmouth Atlas* as "services of proven effectiveness that involve no significant tradeoffs—all patients with specific medical needs should receive them."[3,4] Effective care is characterized by strong evidence that provides little clinical discretion so that nonmedical factors should have little influence on treatment choice.[4,5] Clinical guidelines also appear to support the effective care categorization of statin use for patients with CVD.[6,7] In fact, it is thought that most patients will need a high-intensity statin to achieve their cholesterol goals.[8–15]

However, it is not clear whether the designation of statins as effective care for all CVD patients reflects the practice beliefs of providers. CVD patients discharged from hospitals that promoted guideline care had statin discharge prescribing rates ranging from 77% to 90%.[16–18] Only 54% of a sample of Medicare beneficiaries filled a statin prescription within 30 days after an acute myocardial infarction (AMI) discharge,[19] and only 52% of patients, 65 and older, in a managed care plan filled a statin prescription within 90 days after an AMI discharge.[20] In addition, substantial geographic variation in statin spending per Medicare beneficiary was found.[21] Lack of awareness of the clinical evidence does not appear to be a source of this apparent statin underuse as 96% of physicians identify a low-density lipoprotein cholesterol (LDL-C) of <100 mg/dL as the treatment goal for high-risk patients.[22]

Dartmouth provides a contrasting "preference-sensitive" category of medical care in which treatment decisions involve tradeoffs across outcomes.[4,5] It may be that the benefits and adverse-effect risks of statins are heterogenous across patients and that providers believe that the

From the *College of Pharmacy; and †College of Public Health, University of Iowa, Iowa City, IA.

Supported by an Agency for Healthcare Research and Quality grant (1R21HS019574-01) under the American Recovery and Reinvestment Act of 2009.

The authors declare no conflict of interest.

Reprints: John M. Brooks, PhD, College of Pharmacy, University of Iowa, 115S. Grand, S515 PHAR, Iowa City, IA 52242. E-mail: john-brooks@uiowa.edu.

Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Website, www.lww-medicalcare.com.

ISSN: 0025-7079/14/5203-0S37

risks of adverse effects from statins may outweigh statin benefits for many CVD patients. RCTs provide some evidence of heterogenous statin effects across patients. Absolute CVD benefits from statin therapy vary with patient age and are thought to vary with the presence of diabetes (more benefit), heart failure (little or no benefit), and chronic kidney disease (variable benefit).[23–28] Although the statin adverse-effect risks found in RCTs are considered small relative to statin benefits,[29,30] it has been suggested that favorable patient selection in RCTs resulted in adverse-effect risk estimates that are lower than what occurs in practice.[31–34] Statin adverse effects have been shown to vary with statin intensity, patient age, sex, weight, health behaviors, comorbidities, and concomitant drug use.[32,35–41] Given these potential tradeoffs, in its recommended approach for patient-centered care, the American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity used statins as an example of a "preference-sensitive decision" that may "confer long-term benefits but cause short-term harm."[42]

Given that complex CVD patients are often underrepresented in RCTs,[43,44] we theorized that greater CVD patient complexity implies greater evidence uncertainty and the more that statin use would be considered preference-sensitive care by providers. Our objective was to assess whether local area statin prescribing patterns for complex patients discharged with AMI fit the profiles of either "effective care" or "preference-sensitive care." Complex AMI patients were defined here using combinations of conditions suggested to affect statin effectiveness: diabetes, heart failure (HF), and chronic kidney disease (CKD).[23–28] We hypothesized that with evidence less certain for complex AMI patients, statin prescribing rates after AMI will be lower for complex patient and that geographic variation in statin use will increase with patient complexity. We also theorized that with higher adverse-effect risks, prescribing rates for high-intensity statins will fall with patient complexity. This study was approved by the University of Iowa Institutional Review Board.

METHODS

Data and Sample

All Medicare claims files, enrollment information, and part D prescription drug events were obtained from the Chronic Condition Data Warehouse (CCW, www.ccwdata.org) for patients hospitalized with an AMI in 2008 and 2009 using the CCW definition of AMI (an inpatient stay with the primary diagnosis code 410.x1 at any time during the year). The acute hospital admission date for each AMI served as the index date for AMI. The length of stay for each patient with AMI was based on all Medicare institutional claims (acute, long-term care hospital, inpatient rehabilitation facility, critical-access hospital, and short-term nursing facility) with overlapping admission and discharge dates following the initial acute hospital AMI admission. The institutional stay discharge date was the day the patient was discharged home. We excluded AMIs if the patient (1) did not survive the AMI institutional stay; (2) had an AMI within 12 months before the index date; (3) was younger than 66 years at the index date to ensure at least 1 year of Medicare eligibility before the index date; (4) did not have continuous Medicare parts A and B enrollment during the 12 months before the index date; (5) was not continuously enrolled in Medicare part D during the 6 months to the index date; and (6) did not have continuous Medicare Parts A, B, and D enrollment during the period from the discharge date to the minimum of the patient's death month or 12 months after discharge. To ensure a consistent statin measurement period after discharge, we further excluded patients who used hospice or skilled nursing care, were readmitted to inpatient care, or died during the 30 days after the institutional stay discharge date.[45] Finally, we used driving times between ZIP codes to derive local areas. Because driving times have inconsistent meaning for geographically noncontiguous areas (eg, islands not connected by bridges), we restricted our sample to patients living in the continental United States at AMI admission. The final cohort comprised 124,813 patients.

Patient Complexity

We define AMI patient complexity using combinations of diabetes, CKD, and heart failure (HF) diagnosed before the index AMI. Earlier studies suggested that these conditions are associated with statin effectiveness.[23–28] We modified the validated CCW definitions of these conditions to accommodate our 1-year look-back period rather than the 2-year period specified by CCW. The diagnosis codes used to identify each condition can be found in the online Appendix, Supplemental Digital Content 1 (http://links.lww.com/MLR/A565). To identify CKD, we searched for at least 1 Medicare inpatient, skilled nursing facility or home health claim or 2 hospital outpatient or physician claims with the relevant diagnosis codes in any position on the claims. To identify HF and diabetes, we searched for at least 1 inpatient, hospital outpatient, or physician claim with relevant diagnosis codes in any position on the claim. Patients were then stratified into 8 complex combinations, given the following diagnoses before AMI index—(1) no prior HF, CKD, or diabetes; (2) HF only; (3) CKD only; (4) diabetes only; (5) HF and CKD only; (6) HF and diabetes only; (7) CKD and diabetes only; (8) all 3 prior conditions.

Measures of Statin Intensity Prescribing Intent

Our measurement goal was to assess the prescribing intent by statin intensity for each patient at AMI discharge. High-intensity statins were defined as those that can lower LDL-C by 50% or more: atorvastatin 40, 80 mg; and rosuvastatin 20, 40 mg. Lower-intensity statins were defined as those that lower LDL-C <50%: atorvastatin 10, 20 mg; fluvastatin 20, 40, 80 mg; lovastatin 10, 20, 40, 80 mg; rosuvastatin 10 mg; pravastatin 10, 20, 40, 80 mg; rosuvastatin 5 mg; and simvastatin 5, 10, 20, 40, 80 mg.[10] To measure the prescribing intent, we used (1) part D claims during 30 days after the AMI discharge date; and (2) estimates of statins available to the patient at home at AMI discharge based on previous prescription dates and days supplied on part D claims. Two binary treatment variables (lower and high) were specified for each patient. If a patient's first statin

prescription after discharge was a high-intensity statin or if a patient filled ≥2 lower-intensity statin prescriptions of the same drug within 2 days of the first statin prescription with doses summing to high (eg, two atorvastatin 20 mg prescriptions), the patient was assigned lower = 0 and high = 1. All other statin prescription combinations during the 30 days after AMI discharge resulted in lower = 1 and high = 0. It was also possible that a patient was prescribed a statin on AMI discharge but had sufficient statins at home to cover the first 30 days after AMI discharge. To account for this, if a patient had no statin prescriptions in the 30 days after discharge and had at least 30 days of a high-intensity statin at home, the patient was assigned lower = 0 and high = 1. Likewise, if a patient had no statin prescriptions in the 30 days after discharge and had at least 30 days of a lower-intensity statin at home at the patient was assigned lower = 1 and high = 0. All other patients were assigned as "no statin" or lower = 0 and high = 0.

Local Area Practice Style Measures of Statin Intensity

We measured local area statin practice style as the average intent of physicians in the local area around each patient resident ZIP code to prescribe statins by intensity at AMI discharge. Because discharge prescribing intent is less clear for patients with statins available at home on discharge, we used only the patients with no statins at home on their AMI discharge date (N = 79,285) in our measures. Practice styles were measured at the patient ZIP code level using the driving area for clinical care (DACC) method.[46] The DACC method creates "local areas" around each patient residence ZIP code by consecutively adding patients from the next closest ZIP codes based on driving times between zip codes until a threshold number of patients have been reached.[46] Local area practice style measures based on the DACC method have explained a larger portion of treatment variation than other local area definitions and have effectively balanced measured covariates.[46–48] We used a local area size threshold of 100 patients. For the patients in the local areas around each ZIP code using the DACC method, area treatment ratios (ATR) for "no statin," "lower-intensity statins," and "high-intensity statins," were estimated. Each ATR was calculated as the ratio of the number of patients in the local area around a ZIP code who received the respective statin intensity after AMI over the sum across these patients of their predicted probabilities of receiving that statin intensity after AMI. Probabilities were assigned to each patient of receiving no statins, a lower-intensity statin, and a high-intensity statin based on their baseline covariates using a multinomial model of statin intensity choice. The multinomial model specified measures for patient demographics; baseline comorbidities for both the year before the AMI admission and during the index AMI stay including conditions described as statin side effects (myopathy, rhabdomyolysis, renal events, and hepatic events); medications used during the 180 days before the AMI admission; AMI diagnosis type on admission; procedures during the AMI stay; complications during the AMI stay; the number of days of the AMI institutional length of stay spent in intensive care and critical care; other medications filled immediately post-discharge (β-blockers, renin-angiotensin system antagonists); part D variables including premium levels, benefit phase at AMI index date, and beneficiary accumulated total and out-of-pocket drug costs before AMI index; whether patients were Medicaid dual-eligible in their AMI index month; patient low-income status, and socioeconomic characteristics for each patient residence zip code (per capita income, poverty rate, education level, English speaking percentage, rural/urban residence, life expectancy). Full definitions of these variables are included in the online Appendix Supplemental Digital Content 1 http://links.lww.com/MLR/A565. A ZIP code with an ATR >1 for a specific statin intensity had a local area practice style in which that statin intensity was used at a rate higher than average, given the baseline characteristics of the patients in the local area. A ZIP code with an ATR <1 had a local area practice style in which the respective statin intensity was used less than average.

Analysis

Patients in our full sample (N = 124,813) were assigned the ATR values for no-statin, lower-intensity statins, and high-intensity statins based on their residence ZIP code. We then stratified our sample by patient complexity based on combinations of prior CKD, HF, and diabetes. For each complex patient combination, we estimated treatment rates by statin intensity. Patients were grouped based on the quintiles across the full sample of each statin intensity–specific ATR. We then estimated treatment rates by statin intensity for each complex patient combination across ATR quintiles and reported the range in variation in statin treatment rates across quintiles by statin intensity.

RESULTS

Table 1 contains the characteristics of our sample by available statin intensity after AMI discharge. Statins were not available to 38% of patients in our sample, a lower-intensity statin was available to 50%, and a high-intensity statin was available to 12%. Patients with a statin available after discharge tended to be younger; had fewer comorbidities (lower Charlson score); were more likely free of the 3 complex conditions (heart failure, CKD, diabetes); had fewer conditions before AMI or during their AMI stay that are considered to be statin adverse effects; appeared to have more severe AMIs as indicated by a higher percentage of patients having an anterior wall AMI, a lower percentage having a non-ST elevation AMI, and higher percentage having cardiac catheterization during their AMI stay; and were less likely to live in a low-income ZIP code. In addition, patients with a history of statin use were more likely to have statins available after discharge.

Table 2 shows the distribution of patient characteristics after grouping patients by the high-intensity statin ATR associated with their residence ZIP code. The percentage of patients who had a high-intensity statin available after AMI discharge varied from 6% to 20% across the quintiles. The ZIP code with the highest high-intensity ATR had a high-intensity statin treatment rate of 33%, whereas the local areas around 73 ZIP codes had high-intensity statin treatment rates

TABLE 1. Characteristics of Medicare AMI Patients From 2008 to 2009 by Intensity of Initially Prescribed Statin[†]

		Intensity of Initially Prescribed Statin Availability After AMI Discharge			
	Total Population	**None**	**Lower**	**High**	***P*[††]**
N	124,813	47,566	62,316	14,931	
Treatment (%)					<0.0001*
No statin	38	100	0	0	
Lower-intensity statin[†]	50	0	100	0	
High-intensity statin[†]	12	0	0	100	
Age (%) (y)					<0.0001*
66–75	41	33	44	52	
76–85	39	39	39	37	
86+	21	28	17	12	
Sex (%)					<0.0001*
Male	43	40	45	49	
Female	57	60	55	51	
Charlson score[‡] (%)					<0.0001*
0	33	28	36	38	
1+	67	72	64	62	
Complex patient combinations[§] (%)					<0.0001*
No prior heart failure, CKD, or diabetes	25	20	28	30	
Heart failure only	16	19	15	14	
CKD only	5	5	5	5	
Diabetes only	12	10	13	14	
Heart failure and CKD only	10	12	9	8	
Heart failure and diabetes only	12	13	12	11	
CKD and diabetes only	5	5	5	5	
Heart failure, CKD and diabetes	15	17	14	13	
Arterial wall AMI[‖] (%)	6	4	7	9	<0.0001*
NSTEMI AMI[¶] (%)	76	80	74	70	<0.0001*
Catheterization during index stay (%)	59	44	67	75	<0.0001*
Statin Rx in 180 D before index AMI (%)	47	26	60	59	<0.0001*
Conditions related to statin side effects (%)					
Preindex AMI[#]	23	26	21	19	<0.0001*
During index AMI[#]	20	23	18	17	<0.0001*
Low-income ZIP code**	50	51	49	46	<0.0001*

*$P < 0.05$.

[†]On the basis of highest statin intensity in 30 days postindex stay discharge or intensity of 30-day supply available before discharge.

[‡]Klabunde et al.[49]

[§]See Appendix for CKD, HF, and diabetes ICD-9 codes.

[‖]ICD-9 codes 410.0 410.1.

[¶]ICD-9 410.7x.

[#]Acute renal failure/acute tubular necrosis ICD-9 584.xx; acute glomerulonephritis ICD-9 580.xx. myopathy: ICD-9-CM 728.89, 729.1, 359.4,359.8, 359.9, 710.4, 728.9, 729.8X, E942.2; CPT codes 82550, 82552, 82554, 80012, 80016, 80018, or 80019. Acute/sub-acute necrosis of liver ICD-9 570.xx; hepatitis ICD-9 573.3x; other disorders of liver ICD-9 573.8x, 573.9x.

**Percentage of low-income residents was above median in 2000 for beneficiary ZIP code.

[††]Pearson χ^2 statistic calculated by estimating the expected number of observations in each cell of an R-by-C table, and comparing these values with the observed number of observations in each cell of the table. The *P* value is estimated using the χ^2 distribution with $(R-1)\times(C-1)$ degrees of freedom.

AMI indicates acute myocardial infarction; CKD, chronic kidney disease; HF, heart failure; NSTEMI, non-ST elevation AMI, ICD-9 codes 410.7X.

of zero. Trends in the measured covariates remained across the patients grouped by quintiles of the high-intensity statin ATR, but these differences were small relative to the covariate differences when patients were grouped by available statin intensity in Table 1.[50] Similar findings of smaller covariate variation were observed when patients were grouped by the "no statin" and low-intensity statin ATRs (not shown). "No statin" treatment rates ranged from 21% to 69% across the ZIP codes with the minimum and maximum "no statin" ATRs, respectively, and low-intensity statin treatment rates ranged from 15% to 61% across ZIP codes with the minimum and maximum low-intensity statin ATRs, respectively. Figures 1 and 2 contain maps of the northeastern portion of the United States showing the quintile groups of the high-intensity ATR and no-statin ATRs, respectively. These maps illustrate substantial with-region variation in local area statin practice styles. Average "no statin" treatment rates in Figure 2 were 32% in the white areas (first quintile) and 44% in the dark green areas (fifth quintile).

Table 3 shows the percentages of patients with statins available after AMI discharge for the full sample; the sample stratified by whether each patient had prior complex condition (CKD, heart failure, and diabetes); and the sample stratified into complex combinations. Table 3 also shows the range in treatment rates between the first and fifth quintiles by statin intensity for each respective ATR-based local area practice measure. Although 61.9% of our sample had a statin available after AMI discharge, rates were lower for patients with prior complex conditions. Nearly 70% of patients without heart failure, diabetes, or CKD before AMI had a statin available after discharge, whereas only 56.6% of patients with heart failure, 57.2% of patients with CKD,

TABLE 2. Characteristics of Medicare AMI Patients From 2008 to 2009 by Local Area High-intensity Prescribing Style

		Quintile of High-intensity Statin Area Treatment Ratio [Higher Area Treatment Ratio (ATR)→]					
	Total Population	**First**	**Second**	**Third**	**Fourth**	**Fifth**	***P*†††**
N	124,813	24,693	24,691	24,693	24,692	24,694	
High-intensity statin average area treatment ratio	1	0.36	0.67	0.93	1.24	1.84	<0.0001*
Treatment (%)							
No statin	38	40	39	39	38	36	<0.0001*
Lower-intensity statin†	50	54	52	50	48	45	<0.0001*
High-intensity statin†	12	6	9	11	14	20	<0.0001*
Age (%) (y)							
66–75	41	41	42	41	41	39	<0.0001*
76–85	39	39	38	39	38	40	0.0609
86+	21	20	20	20	21	22	<0.0001*
Sex (%)							
Male	43	44	44	43	43	42	<0.0001*
Female	57	56	56	57	57	58	<0.0001*
Charlson score‡ (%)							
0	33	36	34	33	33	31	<0.0001*
1+	67	64	66	67	67	69	
Complex patient combinations§ (%)							<0.0001*
No prior heart failure, CKD, or diabetes	25	27	25	25	24	23	
Heart failure only	16	17	16	16	16	16	0.0775
CKD only	5	5	5	5	5	5	0.3946
Diabetes only	12	12	12	11	12	11	0.5881
Heart failure and CKD only	10	9	10	10	10	11	0.0015*
Heart failure and diabetes only	12	11	12	12	12	13	<0.0001*
CKD and diabetes only	5	5	5	5	5	5	0.3813
Heart failure, CKD and diabetes	15	14	15	15	16	16	<0.0001*
Arterial wall AMI‖	6	6	6	6	6	6	<0.0269*
NSTEMI AMI¶	76	74	75	76	76	78	<0.0001*
Catheterization during index stay	59	62	60	60	58	56	<0.0001*
Statin Rx in 180 days before index AMI	47	45	47	47	47	50	<0.0001*
Conditions related to statin side effects (%)							
Preindex AMI#	23	22	23	23	23	24	<0.0001*
During index AMI#	20	18	20	20	20	21	<0.0001*
Low-income ZIP code** (%)	50	52	50	51	50	46	<0.0001*

*$P<0.05$.

†On the basis of highest statin intensity in 30 days postindex stay discharge or intensity of 30-day supply available before discharge.

‡Klabunde et al.[49]

§See Appendix for CKD, HF, and diabetes ICD-9 codes.

‖ICD-9 codes 410.0 410.1.

¶ICD-9 410.7x.

#Acute renal failure/acute tubular necrosis ICD-9 584.xx; acute glomerulonephritis ICD-9 580.xx. myopathy: ICD-9-CM 728.89, 729.1, 359.4,359.8, 359.9, 710.4, 728.9, 729.8X, E942.2; CPT codes 82550, 82552, 82554, 80012, 80016, 80018, or 80019. Acute/sub-acute necrosis of liver ICD-9 570.xx; hepatitis ICD-9 573.3x; other disorders of liver ICD-9 573.8x, 573.9x.

**Percentage of low-income residents was above median in 2000 for beneficiary ZIP code.

†††The Cochran-Armitage test of trend in characteristic value across patients grouped into quintiles based on local area high-intensity practice style measure. For example, the *P* value for age 76–85 years tests whether a linear trend in the percentage of patients in this age group exists across quintiles of the high-intensity area treatment ratio (ATR)-based patient groups.

AMI indicates acute myocardial infarction; CKD, chronic kidney disease; HF, heart failure; NSTEMI, non-ST elevation AMI, ICD-9 codes 410.7X.

61.5% of patients with diabetes had a statin available after discharge. Comparing rates across complex combinations showed that lower statin rates occur mainly for patients with prior heart failure or CKD. Specifically, patients with both prior heart failure and CKD had the lowest percentage of statin availability after AMI discharge (52.6%), followed by patients with HF only (56.5%) and patients with all 3 prior conditions (56.5%). Patients with only diabetes before AMI had statin availability rates similar to patients with no prior conditions (68.5%). Patients with heart failure and CKD also had the lowest high-intensity statin treatment rate (9.3%), and patients with no prior conditions and patients with only prior diabetes had the highest high-intensity statin treatment rates (14.1% and 14.0%, respectively).

Substantial geographic variation in statin availability existed across all complex combinations after AMI discharge, but the extent of geographic variation was not consistent across the complex combinations. For both the low-intensity statin and high-intensity statin ATRs, the largest rate difference across quintiles was for patients with no prior heart failure, CKD, or diabetes (18 percentage points). Geographic variation in statin use was lowest in more complex patient groups. For example, patients with all 3 prior complex conditions had the lowest rate difference in lower-intensity statins across local area quintiles (11 percentage points) and the second lowest rate difference in high-intensity statins across quintiles (11 percentage points). Patients with prior HF and CKD only had the lowest rate

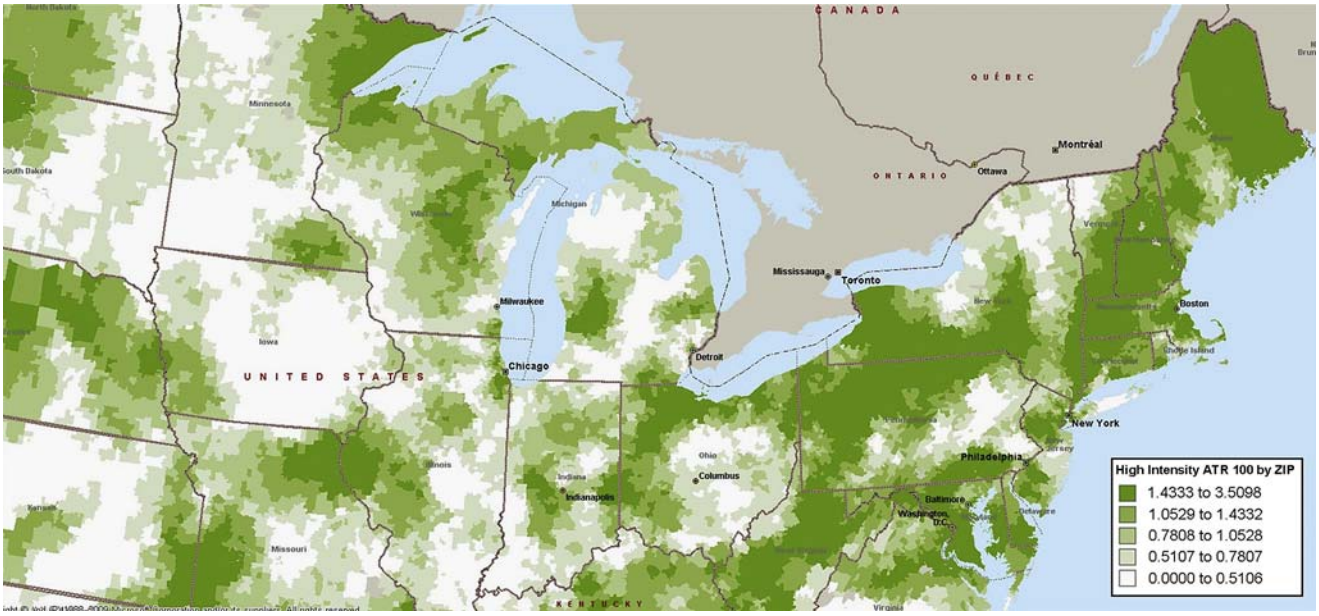

FIGURE 1. Northeastern United States high-intensity statin area treatment ratios by ZIP code. Darker green represents local areas with greater covariate-adjusted use of high-intensity statins after acute myocardial infarction.

difference in high-intensity statins across quintiles (10 percentage points).

DISCUSSION

Our objective was to assess whether local area statin prescribing patterns for complex patients discharged with AMI fit the profiles of either "effective care" or "preference-sensitive care."[4,5] Close to 62% of the Medicare patients in our sample had a statin available during the 30 days after discharge for AMI. This percentage ranged from 69.8% for patients without heart failure, diabetes, and CKD, to little more than half (52.6%) for patients with previous heart failure and CKD. Given that most providers are aware of the cholesterol reduction goals for high-risk CVD patients,[22] these rates suggest that both perceived benefits and risks associated with statins are being incorporated into prescrib-

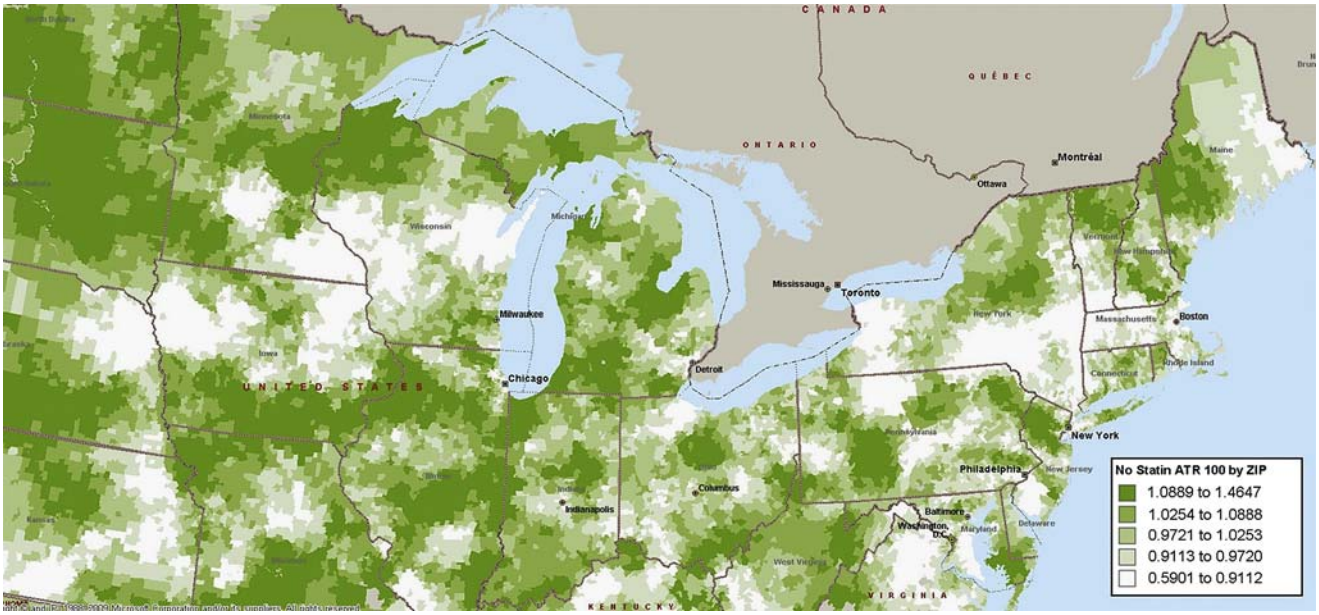

FIGURE 2. Northeastern United States "No Statin" area treatment ratios by ZIP code. Darker green represents local areas with less covariate-adjusted use of any statins after acute myocardial infarction.

TABLE 3. Geographic Variation in Statin Intensity Treatment Rates for Medicare AMI Patients Postdischarge by Patient Complexity

	N	% No Statin (First to Fifth Quintile Range)*	% Lower-intensity Statin (First to Fifth Quintile Range)†	% High-intensity Statin (First to Fifth Quintile Range)‡
Full sample	124,813	38.1 (32–44)	49.9 (43–57)	12.0 (6–20)
Patients with prior condition				
Prior HF	66,644	43.4 (36–49)	46.1 (40–53)	10.5 (6–17)
Prior diabetes	54,125	38.6 (33–44)	49.5 (43–55)	12.0 (7–19)
Prior CKD	43,690	42.8 (36–49)	46.5 (41–53)	10.7 (6–17)
Complex combinations				
No HF, CKD, or D	31,170	30.2 (24–37)	55.7 (47–65)	14.1 (6–24)
HF only	20,451	43.4 (35–51)	46.2 (39–55)	10.3 (5–18)
CKD only	6597	37.8 (33–44)	50.4 (43–57)	11.9 (6–21)
D only	14,364	31.4 (26–38)	54.5 (46–62)	14.0 (8–23)
HF and CKD only	12,470	47.4 (39–54)	43.3 (38–51)	9.3 (5–15)
HF and D only	15,138	40.1 (34–45)	48.7 (43–55)	11.3 (7–18)
CKD and D only	6038	36.4 (32–43)	51.2 (45–58)	12.4 (8–20)
HF, CKD, and D	18,585	43.5 (38–49)	45.7 (40–51)	10.8 (6–17)

*No statin ATR quintiles.
†Low-intensity statin ATR quintiles.
‡High-intensity statin ATR quintiles.
ATR indicates area treatment rate; CKD indicates chronic kidney disease; D, diabetes; HF, heart failure.

ing decisions. Our finding of lower statin rates for more complex patients supports this idea as statin adverse-effect risks have been shown to increase with patient complexity.[32,35–41] It is noted that prior diabetes had little effect on statin rates and that it is consistent with studies suggesting that statin benefits are enhanced for diabetic patients.[23–25] In addition, substantial geographic variation in statin availability after AMI was found across the entire sample and within each complex combination. These results suggest that differences exist across local areas in either the beliefs on relationships between statins and outcomes or in the preferences that providers and patients have over the outcomes associated with statin use. Interestingly, the extent of geographic variation in statin use was lower for more complex patients. There appears to be more agreement across local areas in the lower statin treatment rates for more complex patients than the higher statin treatment rates for the less complex patients.

The ability to make inferences on variation in provider beliefs in this study is limited by the inability of our measures to differentiate between physician and patient choices. The measures used here reflect both physician prescribing behavior and the willingness of patients to fill the statin prescriptions they received. As such, these measures understate the statin prescribing intent of physicians to the extent that prescriptions are unfilled by patients. In addition, it is also possible that the geographic variation in statin use we found could be partially attributable to geographic variation in unmeasured conditions like patient frailty.

Statin rates that diminish with patient complexity and the substantial local area variation in statin rates suggest that providers consider statins to be more "preference-sensitive care" than "effective care" for secondary prevention of CVD. Local area variation in statin use exists across all groups of complex AMI patients. However, our results do not say whether current statin utilization rates represent a correct balancing of statin benefits and risks across complex AMI patients. Further research is needed to assess whether many complex AMI patients in areas with low statin utilization rates are missing benefit opportunities or, in contrast, whether many complex AMI patients in areas with high statin utilization rates are suffering adverse side effects with little benefit gain. In context of statin use for secondary prevention of cardiovascular disease for complex patients, this question is analogous to the question stated many years ago by John Wennberg, "Which rate is right?"[51]

REFERENCES

1. Wallace E, Smith SM, Fahey T. Variation in medical practice: getting the balance right. *Fam Pract*. 2012;29:501–502.
2. National Institute for Health and Clinical Excellence (NICE). Statins for the Prevention of Cardiovascular Events. 2006 [updated 2008]. Available at: http://www.nice.org.uk/nicemedia/pdf/TA094guidance.pdf. Accessed March 1, 2013.
3. Dartmouth Atlas of Health Care. Effective Care. 2013. Available at: http://www.dartmouthatlas.org/keyissues/issue.aspx?con=2939. Accessed March 1, 2013.
4. Fisher ES, Wennberg JE. Health care quality, geographic variations, and the challenge of supply-sensitive care. *Perspect Biol Med*. 2003;46:69–79. Winter 2003.
5. Wennberg JE, Fisher ES, Skinner JGeography and the debate over Medicare reform. *Health Aff*. 2002. Available at: http://www.healthaffairs.org/WebExclusives/Wennberg_Web_Excl_021302.htm. doi: 10.1377/hltaff.w2.115.
6. Grundy SM, Cleeman JI, Merz CNB, et al. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation*. 2004;110:227–239.
7. Smith SC Jr, Allen J, Blair SN, et al. AHA/ACC guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update: endorsed by the National Heart, Lung, and Blood Institute. *Circulation*. 2006;113:2363–2372.
8. Armitage J, Bowman L, Wallendszus K, et al. Intensive lowering of LDL cholesterol with 80 mg versus 20 mg simvastatin daily in 12,064 survivors of myocardial infarction: a double-blind randomised trial. *Lancet*. 2010;376:1658–1669.
9. Baigent C, Blackwell L, Emberson J, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet*. 2010;376:1670–1681.
10. Law MR, Wald NJ, Rudnicka AR. Quantifying effect of statins on low density lipoprotein cholesterol, ischaemic heart disease, and stroke: systematic review and meta-analysis. *Br Med J*. 2003;326:1423–1427.

11. Robinson J, Davidson M. Combination therapy with ezetimibe and simvastatin to acheive aggressive LDL reduction. *Expert Rev Cardiovasc Ther*. 2006;4:461–476.
12. Cannon CP, Steinberg BA, Murphy SA, et al. Meta-analysis of cardiovascular outcomes trials comparing intensive versus moderate statin therapy. *J Am Coll Cardiol*. 2006;48:438–445.
13. Mills EJ, O'Regan C, Eyawo O, et al. Intensive statin therapy compared with moderate dosing for prevention of cardiovascular events: a meta-analysis of >40 000 patients. *Eur Heart J*. 2011;32:1409–U1138.
14. Meek CL, Reston JD, Ramsbottom T, et al. Use of high-intensity statin therapy with simvastatin 80 mg and atorvastatin 80 mg in primary care. *Int J Clin Pract*. 2011;65:120–126.
15. Crouse JR III, Elam MB, Robinson JG, et al. Cholesterol management: Targeting a lower low-density lipoprotein cholesterol concentration increases Adult Treatment Panel-III goal attainment. *Am J Cardiol*. 2006;97:1667–1669.
16. Javed U, Deedwania PC, Bhatt DL, et al. Use of intensive lipid-lowering therapy in patients hospitalized with acute coronary syndrome: an analysis of 65,396 hospitalizations from 344 hospitals participating in Get With The Guidelines (GWTG). *Am Heart J*. 2010;160:1130–1136, 1136 e1131-1133.
17. Lewis WR, Ellrodt G, Peterson E, et al. Trends in the use of evidence-based treatments for coronary artery disease among women and the elderly: findings from the Get With the Guidelines Quality-Improvement Program. *Circulation*. 2009;2:633–641.
18. McGinnis BD, Olson KL, Delate TM, et al. Statin adherence and mortality in patients enrolled in a secondary prevention program. *Am J Manag Care*. 2009;15:689–695.
19. Zuckerman IH, Yin X, Rattinger GB, et al. Effect of exposure to evidence-based pharmacotherapy on outcomes after acute myocardial infarction in older adults. *J Am Geriatr Soc*. 2012;60:1854–1861.
20. Lee HY, Cooke CE, Robertson TA. Use of secondary prevention drug therapy in patients with acute coronary syndrome after hospital discharge. *J Manag Care Pharm*. 2008;14:271–280.
21. Donohue JM, Morden NE, Gellad WF, et al. Sources of regional variation in Medicare Part D drug spending. *N Engl J Med*. 2012;366:530–538.
22. Yan AT, Yan RT, Tan M, et al. Contemporary management of dyslipidemia in high-risk patients: targets still not met. *Am J Med*. 2006;119:676–683.
23. Robinson JG, Stone NJ. Identifying patients for aggressive cholesterol lowering: the risk curve concept. *Am J Cardiol*. 2006;98:1405–1408.
24. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. *Lancet*. 2003;361:2005–2016.
25. Shepherd J, Kastelein JJP, Bittner V, et al. Intensive lipid lowering with atorvastatin in patients with coronary heart disease and chronic kidney disease: the TNT (Treating to New Targets) study. *J Am Coll Cardiol*. 2008;51:1448–1454.
26. Kjekshus J, Apetrei E, Barrios V, et al. Rosuvastatin in older patients with systolic heart failure. *N Engl J Med*. 2007;357:2248–2261.
27. Gissi-HF Investigators. Effect of rosuvastatin in patients with chronic heart failure (the GISSI-HF trial): a randomised, double-blind, placebo-controlled trial. *Lancet*. 2008;372:1231–1239.
28. Desai DA, Zakaria S, Ouyang P. Initiation of statin therapy: are there age limits? *Curr Atheroscler Rep*. 2012;14:17–25.
29. Thompson PD, Clarkson P, Karas RH. Statin-associated myopathy. *JAMA*. 2003;289:1681–1690.
30. Waters DD. Safety of high-dose atorvastatin therapy. *Am J Cardiol*. 2005;96(5A):69F–75F.
31. Bruckert E, Hayem G, Dejager S, et al. Mild to moderate muscular symptoms with high-dosage statin therapy in hyperlipidemic patients—the PRIMO study. *Cardiovasc Drugs Ther*. 2005;19:403–414.
32. Abd TT, Jacobson TA. Statin-induced myopathy: a review and update. *Expert Opin Drug Saf*. 2011;10:373–387.
33. Nichols GA, Koro CE. Does statin therapy initiation increase the risk for myopathy? An observational study of 32,225 diabetic and nondiabetic patients. *Clin Ther*. 2007;29:1761–1770.
34. Golomb BA, McGraw JJ, Evans MA, et al. Physician response to patient reports of adverse drug effects: implications for patient-targeted adverse effect surveillance. *Drug Saf*. 2007;30:669–675.
35. Golomb BA, Evans MA. Statin adverse effects: a review of the literature and evidence for a mitochondrial mechanism. *Am J Cardiovasc Drugs*. 2008;8:373–418.
36. Florentin M, Elisaf MS. Simvastatin interactions with other drugs. *Expert Opin Drug Saf*. 2012;11:439–444.
37. Sathasivam S. Statin induced myotoxicity. *Eur J Intern Med*. 2012;23:317–324.
38. Hedenmalm K, Alvan G, Ohagen P, et al. Muscle toxicity with statins. *Pharmacoepidemiol Drug Saf*. 2010;19:223–231.
39. Holbrook A, Wright M, Sung M, et al. Statin-associated rhabdomyolysis: is there a dose-response relationship? *Can J Cardiol*. 2011;27:146–151.
40. Armitage J. The safety of statins in clinical practice. *Lancet*. 2007;370:1781–1790.
41. Cziraky MJ, Willey VJ, McKenney JM, et al. Statin safety: an assessment using an administrative claims database. *Am J Cardiol*. 2006;97(8A):61C–68C.
42. Ickowicz E, Panel AGSE. Patient-centered care for older adults with multiple chronic conditions: a stepwise approach from the American Geriatrics Society. *J Am Geriatr Soc*. 2012;60:1957–1968.
43. Nallamothu BK, Hayward RA, Bates ER. Beyond the randomized controlled trial: the role of effectiveness studies in evaluating cardiovascular therapies. *Circulation*. 2008;118:1294–1303.
44. Zulman DM, Sussman JB, Chen X, et al. Examining the evidence: a systematic review of the inclusion and analysis of older adults in randomized controlled trials. *J Gen Intern Med*. 2011;26:783–790.
45. Cook EA, Schneider KM, Chrischilles EA, et al. Accounting for immeasurable time bias when using Medicare prescription drug data. *Medicare and Medicaid Research Review*. 2013. (In press).
46. Fang G, Brooks JM, Chrischilles EA. A new method to measure geographic variation in prescription use and its implications for comparative effectiveness research. *Med Care*. 2010;40:710–717.
47. Fang G, Brooks JM, Chrischilles EA. Comparison of instrumental variable analysis using a new instrument with risk adjustment methods to reduce confounding by indication. *Am J Epidemiol*. 2012;175:1142–1151.
48. Brooks JM, Chrischilles EA, Landrum MB, et al. Survival implications associated with variation in mastectomy rates for early-staged breast cancer. *Int J Surg Oncol*. 2012;2012:127854.
49. Klabunde CN, Potosky AL, Legler JM, et al. Development of a comorbidity index using physician claims data. *J Clin Epidemiol*. 2000;53:1258–1267.
50. Armitage P. Tests for linear trends in proportions and frequencies. *Biometrics*. 1955;11:375–386.
51. Wennberg JE. Which rate is right? *N Engl J Med*. 1986;315:810–815.