Editor's Note
The Role of Post–Acute Care in Variation in the Medicare Program

Variation is frequently cited as evidence of unnecessary or wasteful health care, because we would expect a patient's medical condition, not geography or health care professional, to dictate who receives a particular procedure or service. Understanding how much variation is owing to regions vs providers within regions can help in devising strategies to reduce variation.

A 2013 Institute of Medicine report found that differences in individual provider and hospital practices explained variation more than did regional patterns. Hussey, a member of that Institute of Medicine committee, and colleagues analyze in depth some of the Medicare data on variation in their article. They find that conditions that more frequently involved post–acute care explained much of the variation by region. Post–acute care refers to a wide range of services, which include skilled nursing facilities, inpatient rehabilitation facilities, home health aides, outpatient physical and occupational therapy, and long-term care facilities. For example, joint replacement of a lower extremity had more than 4 times as much regional variation as conditions that do not generally involve post–acute care, such as gastrointestinal bleeding. The association of post–acute care with the variation seen by Hussey et al is consistent with a 2011 report from the Medicare Payment Advisory Commission that found that use of post–acute care services explained the largest portion of Medicare variation at the metropolitan statistical-area level.

Medicare spends more than $59 billion on post–acute care, which has more than doubled since 2001. Discharges to post–acute care facilities have increased nearly 50% during the past 15 years. Post–acute care is a major contributor to the costs of a hospitalization episode, because 42% of Medicare beneficiaries are discharged from hospitals to post–acute care. The Medicare Payment Advisory Commission's recommendations to Congress, which promote site-neutral payments for Medicare Payment Advisory Commission's recommenda
tions to Congress, may help reduce variation and increase high-value care for Medicare beneficiaries.

Rita F. Redberg, MD, MSc

Conflict of Interest Disclosures: Dr Redberg reports being a Medicare Payment Advisory Commissioner.


Association Between Opioid Use and Atrial Fibrillation: The Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study

It has been estimated that more than 4.3 million adults in the United States are taking opioids regularly in any given week. Opioid receptors are downregulated in animal models of atrial fibrillation (AF). However, to our knowledge, the association between opioid use and AF has not been examined in population-based studies. We examined the cross-sectional association between prescription opioid use and AF using data from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study.

Methods | Details of the REGARDS study and its design have been published. Briefly, between January 25, 2003, and October 30, 2007, a total of 30,239 participants were recruited using postal mailings and telephone calls from across the United States. Demographic information, medical histories, blood tests, and electrocardiograms were obtained using a computer-assisted telephone interview system and in-home study visits by trained staff. The study was approved by the institutional review boards at all participating centers. Oral informed consent was obtained; the participants received financial compensation. Atrial fibrillation was identified by electrocardiogram and self-reported history of a previous physician-determined diagnosis. Opioid use was ascertained by pill-bottle review during the in-home visit. The association between opioid use and AF was examined in multivariable adjusted logistic regression models using SAS, version 9.3 (SAS Institute Inc). Subgroup analyses were performed.

Results | A total of 24,632 participants (mean [SD] age, 65 [9.4] years; 54.0% women; 40.2% black) were included in the analysis. A total of 1887 participants (7.7%) reported opioid use, and 2086 individuals (8.5%) had AF. The most commonly used opioid was hydrocodone (779 [41.3%] of opioid users), followed by oxycodone (470 [24.9%] of opioid users) and tramadol (378 [20.0%] of opioid users). Several differences were observed between opioid users and nonusers. Opioid users were slightly younger and more likely to be female, black, and have cardiovascular comorbidities (Table 1). The prevalence of AF was higher in opioid users than nonusers (12.5% vs 7.6%; P < .001). As reported in Table 2, opioid use was associated with increased odds of AF (odds ratio [OR], 1.35 [95% CI, 1.16-1.57]) after adjustment for potential confounders, and the results were consistent in several subgroups of the REGARDS study participants. Since it is possible that this association could be confounded by substance abuse, we further adjusted for benzodiazepine and alcohol use. The association remained statistically significant (OR, 1.29 [95% CI, 1.11-1.51]). In addition, given the known cardiotoxic effects of oxycodone, we excluded 434 participants receiving this drug in a sensitivity analysis, and the association remained statistically significant (OR, 1.33 [95% CI, 1.11-1.58]).

Discussion | In this analysis of data from the REGARDS study, opioid use was independently associated with increased...
prevalence of AF. Propoxyphene has been linked with fatal cardiac arrhythmias that led to cessation of its sales in the United States. However, chronic arrhythmias (eg, AF) have not been linked with opioid use. Endogenous opioid peptides open mitochondrial potassium adenosine triphosphate channels, making mitochondria resistant to oxidative stress during episodes of ischemia. Loss of this protective mechanism against oxidative stress may render atrial myocytes amenable to damage, leading to AF.

Our study has limitations, including the cross-sectional design, possibility of residual confounding by unmeasured factors, and lack of data on opioid dosage and length of therapy. In addition, the use of self-reported history of a previous physician diagnosis as one of the methods to ascertain AF is subject to recall bias.

Using data from the REGARDS study, we have shown that opioid use is associated with an increased prevalence of AF. During the past 2 decades, there have been significant increases in both opioid use and AF in the United States. These increases represent a parallel temporal trend that needs further investigation.

Waqas T. Qureshi, MD
Wesley T. O’Neal, MD, MPH
Yulia Khodneva, MD, PhD
Suzanne Judd, PhD
Monika M. Safford, MD
Paul Muntner, PhD
Elsayed Z. Soliman, MD, MSc, MS

Table 1. Characteristics of REGARDS Study Participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Opioid Use (n = 1887)</th>
<th>No Opioid Use (n = 22,745)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic Variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>64 (9.4)</td>
<td>65 (9.4)</td>
<td>.048</td>
</tr>
<tr>
<td>Male sex</td>
<td>656 (34.8)</td>
<td>10,063 (46.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Black race</td>
<td>830 (44.0)</td>
<td>9,069 (39.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Regionb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke buckle</td>
<td>463 (24.5)</td>
<td>4,724 (20.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Stroke belt</td>
<td>706 (37.4)</td>
<td>7,799 (34.2)</td>
<td></td>
</tr>
<tr>
<td>Non-stroke belt</td>
<td>718 (38.0)</td>
<td>10,231 (45.0)</td>
<td></td>
</tr>
<tr>
<td>&lt;High school education</td>
<td>927 (49.1)</td>
<td>8,374 (36.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Annual income, &lt;$20,000</td>
<td>540 (28.6)</td>
<td>3,696 (16.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Clinical Variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current or former smoker</td>
<td>1,171 (62.0)</td>
<td>12,233 (53.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Alcohol usec</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heavy</td>
<td>53 (2.8)</td>
<td>914 (4.0)</td>
<td>.28</td>
</tr>
<tr>
<td>Moderate</td>
<td>457 (24.2)</td>
<td>7,742 (34.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>None</td>
<td>1,377 (73.0)</td>
<td>14,089 (61.9)</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>543 (28.8)</td>
<td>4,551 (20.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Left-ventricular hypertrophy</td>
<td>210 (11.1)</td>
<td>2,196 (9.7)</td>
<td>.04</td>
</tr>
<tr>
<td>History</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHD</td>
<td>428 (22.7)</td>
<td>3,861 (17.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Stroke</td>
<td>170 (9.0)</td>
<td>1,274 (5.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Medication use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>802 (42.5)</td>
<td>9,960 (43.8)</td>
<td>.28</td>
</tr>
<tr>
<td>Antihypertensive</td>
<td>1,237 (65.6)</td>
<td>11,808 (51.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Lipid-lowering agent</td>
<td>728 (38.6)</td>
<td>7,555 (33.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>31 (7.1)</td>
<td>29 (6.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Systolic blood pressure, mean (SD), mm Hg</td>
<td>129 (18)</td>
<td>127 (16)</td>
<td>.002</td>
</tr>
<tr>
<td>Laboratory Variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholesterol, mean (SD), mg/dL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>190 (42)</td>
<td>192 (40)</td>
<td>.10</td>
</tr>
<tr>
<td>HDL-C</td>
<td>51 (16)</td>
<td>52 (16)</td>
<td>.10</td>
</tr>
<tr>
<td>Prior PAD</td>
<td>62 (3.3)</td>
<td>455 (2.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Log(hs-CRP), mean (SD), mg/L</td>
<td>1.2 (1.2)</td>
<td>0.76 (1.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Serum creatinine, mean (SD), mg/dL</td>
<td>0.92 (0.52)</td>
<td>0.91 (0.40)</td>
<td>.14</td>
</tr>
<tr>
<td>Log(ACR), mean (SD), mg/g</td>
<td>2.4 (1.3)</td>
<td>2.3 (1.2)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: ACR, urine albumin-creatinine ratio; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CHD, coronary heart disease; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; PAD, peripheral arterial disease; REGARDS, Reasons for Geographic and Racial Differences in Stroke.

SI conversion factors: To convert total cholesterol and HDL cholesterol to millimoles per liter, multiply by 0.0259; serum creatinine to micromoles per liter, multiply by 88.4.

* Statistical significance was tested using χ² analysis for categorical variables and the Wilcoxon rank sum test for continuous variables.

* Stroke buckle (area of highest incidence of stroke) includes North Carolina, South Carolina, and Georgia. Stroke belt (area of second highest incidence of stroke) includes Alabama, Arkansas, Indiana, Kentucky, Louisiana, Mississippi, Tennessee, and Virginia.

* Alcohol use was classified by the number of drinks per week reported by study participants using the following criteria: none, moderate (1–2 drinks per day for men and 1 drink per day for women), and heavy (>2 drinks per day for men and >1 drink per day for women).
Outcomes in Adults With Acute Pulmonary Embolism Who Are Discharged From Emergency Departments: The Cardiovascular Research Network Venous Thromboembolism Study

Patients with acute pulmonary embolism (PE) have conventionally been hospitalized for their initial management and initiation of anticoagulant treatment. A clinical trial found that patients with PE who were considered at low risk by the PE Severity Index could be safely treated as outpatients. However, it is unclear how often outpatient PE treatment occurs in real-world settings or whether outcomes are as favorable as in the clinical trial. Our study describes the short-term rates of death and hospital admission for patients with acute PE who were discharged from emergency department (ED) settings.

Table 2. Association of Opioid Use With Atrial Fibrillation in REGARDS Participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OR (95% CI)*</th>
<th>P Value</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total population</td>
<td>1.35 (1.16-1.57)</td>
<td>&lt;.001</td>
<td>NA</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65</td>
<td>1.27 (1.01-1.59)</td>
<td>.04</td>
<td>.95</td>
</tr>
<tr>
<td>≥65</td>
<td>1.41 (1.15-1.71)</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1.35 (1.12-1.63)</td>
<td>.002</td>
<td>.70</td>
</tr>
<tr>
<td>Male</td>
<td>1.36 (1.05-1.76)</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>1.51 (1.20-1.91)</td>
<td>&lt;.001</td>
<td>.13</td>
</tr>
<tr>
<td>White</td>
<td>1.27 (1.04-1.55)</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.28 (1.06-1.56)</td>
<td>.01</td>
<td>.54</td>
</tr>
<tr>
<td>Yes</td>
<td>1.44 (1.13-1.83)</td>
<td>.004</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.41 (1.03-1.94)</td>
<td>.03</td>
<td>.86</td>
</tr>
<tr>
<td>Yes</td>
<td>1.33 (1.12-1.58)</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.35 (1.13-1.62)</td>
<td>.001</td>
<td>.94</td>
</tr>
<tr>
<td>Yes</td>
<td>1.32 (1.00-1.73)</td>
<td>.047</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: NA, not applicable; OR, odds ratio; REGARDS, Reasons for Geographic and Racial Differences in Stroke.

* Adjusted for age, sex, race/ethnicity, region of residence, income, educational level, systolic blood pressure, high-density lipoprotein cholesterol level, total cholesterol level, body mass index, smoking, diabetes mellitus, antihypertensive and lipid-lowering medications, aspirin, alcohol use, coronary heart disease, stroke, log(high-sensitivity C-reactive protein), serum creatinine, log(albumin-creatinine ratio), peripheral arterial disease, and left-ventricular hypertrophy.