Changes in Geographic Variation in the Use of Percutaneous Coronary Intervention for Stable Ischemic Heart Disease After Publication of the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) Trial

Arun V. Mohan, MD, MBA; Reza Fazel, MD, MSc; Pei-Hsiu Huang, MD; Yu-Chu Shen, PhD; David Howard, PhD

Background—Clinical uncertainty is cited as a cause of geographic variation. However, little is known about the effect of comparative effectiveness research on variation. We examined whether geographic variation in the use of percutaneous coronary intervention (PCI) for stable ischemic heart disease (SIHD) declined after publication of the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial.

Methods and Results—We examined changes in utilization and geographic variation in 67 hospital referral regions using the State Inpatient Databases. We compared age- and sex-adjusted rates of PCI for SIHD before (2006) and after (2008) publication of the COURAGE trial and compared those with contemporaneous changes in PCI volume for acute coronary syndrome. A total of 272,659 PCIs for SIHD from 526 hospitals were included in the analysis. After the publication of the COURAGE trial, PCI volume for SIHD declined by 25% (P<0.001) and decreased by 12% for acute coronary syndrome (P<0.001). This was predominantly attributable to changes in hospital referral regions with the highest levels of utilization pre-COURAGE trial (35% decline in the highest tertile versus 18% in the lowest). As measured by the systematic component of variation, there was substantial geographic variation in the use of PCI for SIHD preceding the publication of the COURAGE trial. Variation declined by 28% (0.53 versus 0.40) after publication, but geographic variation remained higher for SIHD than acute coronary syndrome (0.40 versus 0.17).

Conclusions—There was a substantial decline in the use of and geographic variation in PCI for SIHD after the publication of the COURAGE trial. However, geographic variation in the use of PCI for SIHD remained high. (Circ Cardiovasc Qual Outcomes. 2014;7:125-130.)

Key Words: coronary artery disease ■ health policy ■ outcome assessment (health care) ■ percutaneous coronary intervention

A large body of research demonstrates substantial geographic variation in healthcare utilization that is not explained by differences in patient characteristics, is inconsistent with evidence-based practice, and does not deliver superior clinical outcomes.1–4 As such, reducing geographic variation has been a major focus of healthcare planners and policymakers.5 Geographic variation in the use of healthcare resources is often attributed to variation in physicians’ opinions about the best course of treatment.6–9 That is, the best approach to diagnosing and treating many clinical conditions remains unknown, leading clinicians to disagree about optimal management. It follows that evidence from comparative effectiveness studies should reduce variation.

Until 2007, the role of percutaneous coronary intervention (PCI) in the management of stable ischemic heart disease (SIHD) without high-risk clinical or anatomic features was a matter of debate.8,10,11 The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial, published in 2007, was a multicenter, randomized, controlled trial comparing medical therapy with medical therapy plus PCI for patients with SIHD.12 The trial showed that PCI did not improve survival or prevent myocardial infarction compared with medical...
WHAT IS KNOWN

• Clinical uncertainty is thought to be an important cause of geographic variation in medical practice.
• Comparative effectiveness research is thought to reduce geographic variation, but this has not been well tested.

WHAT THE STUDY ADDS

• This article measures geographic variation in the use of percutaneous coronary intervention for stable ischemic heart disease using hospital discharge data.
• There were substantial changes in utilization and geographic variation in the use of percutaneous coronary intervention for stable ischemic heart disease after the publication of the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial.

therapy alone. The COURAGE trial was highly regarded, was well publicized, and ultimately led to changes in the clinical guidelines for the management of SIHD. Previous research has demonstrated a decline in PCI volume for SIHD and a small increase in the proportion of patients who received optimal medical therapy post-COURAGE trial. However, changes in geographic variation in the use of PCI after COURAGE use have not been previously examined.

In this study, we compare utilization and geographic variation in the use of PCI for SIHD before and after publication of the COURAGE trial. We also evaluate trends in the use of PCI for acute coronary syndrome (ACS) to account for secular trends in PCI use. Research has consistently demonstrated that revascularization reduces the incidence of major adverse events in patients with ACS.

Methods

Data Sources

We combined data from the State Inpatient Databases (SIDs) and Dartmouth Atlas for Healthcare for 3 years (2006–2008). The SIDs are a component of the Healthcare Cost and Utilization Project produced by the Agency for Healthcare Research and Quality. The SIDs contain all-payer, inpatient discharge data from nearly 100% sample of hospitals in participating states. The SIDs include both visits requiring inpatient services as well as observation visits or so-called 23-hour admissions, although previous work suggests inconsistency in the coding of observation services that may limit the utility of these data. The SIDs include data elements routinely captured in discharge abstracts from inpatient stays such as diagnoses, procedures, and demographics. We examined SIDs data for 7 states—Arizona, California, Florida, Massachusetts, Maryland, New Jersey, and New York. These databases captured discharge data from 95% (range, 80%–100%) of hospitals in these states for the study period. Smaller hospitals are over-represented among nonresponders, leading the share of admissions captured to exceed 95%.

The Dartmouth Atlas for Healthcare provides several measures of regional healthcare supply and demand at the hospital referral region (HRR) level. Each HRR represents a regional healthcare market for tertiary medical care that requires the services of a major referral center. HRRs were defined by the Dartmouth Atlas through an analysis of referral patterns for Medicare patients for major cardiovascular surgical procedures and neurosurgery. The Atlas also contains demographic data for all residents in each HRR drawn from the US census.

Study Sample

The study sample includes patients aged ≥40 years who underwent PCI (International Classification of Diseases, Ninth Revision codes 36.01, 36.02, 36.05, 36.06, 36.07, and 36.09) during a hospitalization. These patients were grouped into 2 mutually exclusive categories based on the International Classification of Diseases, Ninth Revision codes in the first through tenth positions: (1) ACS, and (2) SIHD. The first group (ACS) includes patients with the codes for acute myocardial infarction or unstable angina (410.x, 411.1). The second group includes all other patients. SIHD is rarely recorded as a diagnosis in claims and thus it is not possible to specifically identify these patients. Although patients in the SIHD group also include those who are asymptomatic, recent analyses of data from the CathPCI Registry demonstrate that the majority (>68%) of patients undergoing PCI for nonacute indications would meet COURAGE trial entry criteria.

Statistical Analysis

The unit of analysis was the HRR. There are 306 HRRs in the United States, 73 of which we initially included in the analysis. We excluded 5 because they overlapped other states (Burlington, VT; Philadelphia, PA; Morristown, NJ; Las Vegas, NV; Washington, DC). We also excluded Santa Cruz, CA, because no hospitals performed PCI in 2006 and 2007.

We calculated annual age- and sex-adjusted rates of PCI for SIHD and ACS per 1000 residents for each HRR (weighted to HRR population) for each of the 3 years examined as well as on a quarterly basis. We calculated changes in mean PCI rates pre- (2006) and post-COURAGE (2008) trial in aggregate and by tertile of pre-COURAGE PCI utilization rates. Changes in mean PCI rates pre-COURAGE trial were compared with changes post-COURAGE trial using the Student t test.

We assessed changes in geographic variation across HRRs over time using 2 measures commonly used for this purpose: the interquartile range and the systematic component of variation (SCV). The interquartile ratio is the ratio between the rate in the region ranked at the 75th percentile and the region ranked at the 25th percentile. The SCV measures the relative SCV in rates between regions by subtracting the random component of variance from the total variance. The SCV is calculated as follows:

\[
SCV = 1 \frac{1}{I} \sum_{i=1}^{I} \left( \frac{y_i - \bar{y}}{e_i} - \frac{\sum_{i=1}^{I} y_i}{I \bar{e}} \right)
\]

where \(y_i\) is the observed cases in region \(i\), \(e_i\) is the expected number of cases in region \(i\), and \(I\) is the number of regions.

We used least squares regression to estimate the number of PCI cases by diagnosis (SIHD versus ACS) at the HRR-year level as a function of the number of men aged 40 to 64 years, the number of men aged 65 years, the number of women aged 50 to 64 years, and the number of women aged 65 years. The regressions included random effects for HRR. The \(R^2\) values exceeded 75%. We used predicted values from the regression as a proxy for the number of expected cases in each region. When calculating predictions, we set the random effects to zero.

The interquartile range describes the distribution of rates, whereas the SCV uses differences between expected and observed cases. SCV is a more robust measure of geographic variation and is less sensitive to procedural volume and the underlying distribution of procedures per patient. Stata 11.0 (College Station, TX) was used for all analyses. The study was reviewed by the Institutional Review Board of Emory University and considered exempt.

Results

A total of 272,659 PCIs for SIHD and 333,196 PCIs for ACS were performed between 2006 and 2008 in the 67 HRRs at 526 hospitals. Changes in utilization of PCI are shown in
After the publication of the COURAGE trial, age- and sex-adjusted PCI volume for SIHD declined by 25% (mean=1.18 per 1000 residents aged >40 years; P≤0.001) in contrast to a 9% decline for ACS (mean=1.35–1.23; P≤0.001). There is a considerable persistence in region-level PCI rates over time. PCI rates in the HRRs in the highest tertile, 1.96 per 100,000 residents, were well above rates among HRRs in the lowest tertile, 0.55 per 100,000 residents, in 2006 and remained so in 2008 (1.27 versus 0.46). Between 2006 and 2008, PCI rates declined in all tertiles. PCI rates decreased by 18% in HRRs in the lowest tertile, 1.96 per 100,000 residents, were well above rates among HRRs in the lowest tertile, 0.55 per 100,000 residents, in 2006 and remained so in 2008 (1.27 versus 0.46). Between 2006 and 2008, PCI rates declined in all tertiles. PCI rates decreased by 18% in HRRs in the lowest tertile of utilization and 35% in the highest. Changes in PCI for ACS were more balanced, falling 10% in the lowest tertile and 16% in the highest. Tertile-specific declines in PCI rates for SIHD were largest in percentage terms compared with declines in PCI rates for ACS.

As shown in Table 2, the interquartile range for SIHD fell by 30% during the study period (1.00–0.70), whereas it increased by 8% for ACS (0.89–0.96). The SCV for SIHD fell by 25% (0.53–0.40) but was unchanged for ACS (0.17–0.17). This is shown graphically in the Figure.

### Discussion

Our study of hospital discharge data from 7 states demonstrated a substantial decline in use and geographic variation in the use of PCI after publication of the COURAGE trial. For a control condition not studied in the COURAGE trial, namely, ACS, we found a modest decline in PCI use consistent with the reported decline of myocardial infarction in the United States and little change in geographic variation. Geographic variation in the use of PCI for SIHD remains considerably higher than for ACS.

Our finding that the use of PCI for SIHD declined by 25% after publication of the COURAGE trial is consistent with previous research demonstrating a 16% to 20% decline. Other authors have pointed out that the COURAGE trial was only one of many factors that may have conspired to affect utilization of PCI. During this same period, there were concerns raised that drug-eluting stents, as well as declines in incidence of coronary artery disease, may have led to an overall decrease in PCI. However, recent work demonstrates that changes in utilization occurred well before concerns about drug-eluting stents were first raised. Although there was a 13% decline in the prevalence of coronary artery disease during this period, this would not explain the magnitude of the decrease in PCI for SIHD that we observed nor would it explain the differential decrease relative to ACS. The fact that this decrease in utilization was proportional to baseline utilization and associated with a decrease

### Table 1. Changes in Age and Sex Standardized Rate of PCI per 1000 Residents >40 Years of Age by Tertile of Utilization

<table>
<thead>
<tr>
<th>Tertile</th>
<th>n</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>Change 2006 to 2008 (SE)</th>
<th>P Value</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIHD</td>
<td>67</td>
<td>1.18</td>
<td>0.96</td>
<td>0.89</td>
<td>0.25 (0.05)</td>
<td>&lt;0.001</td>
<td>−25</td>
</tr>
<tr>
<td>Lowest</td>
<td>22</td>
<td>0.55</td>
<td>0.46</td>
<td>0.46</td>
<td>0.18 (0.03)</td>
<td>0.003</td>
<td>−18</td>
</tr>
<tr>
<td>Middle</td>
<td>22</td>
<td>1.09</td>
<td>0.99</td>
<td>0.97</td>
<td>0.11 (0.06)</td>
<td>0.041</td>
<td>−11</td>
</tr>
<tr>
<td>Highest</td>
<td>23</td>
<td>1.96</td>
<td>1.49</td>
<td>1.27</td>
<td>0.35 (0.08)</td>
<td>&lt;0.001</td>
<td>−35</td>
</tr>
<tr>
<td>ACS</td>
<td>67</td>
<td>1.35</td>
<td>1.25</td>
<td>1.23</td>
<td>0.09 (0.03)</td>
<td>&lt;0.001</td>
<td>−9</td>
</tr>
<tr>
<td>Lowest</td>
<td>22</td>
<td>0.91</td>
<td>0.85</td>
<td>0.82</td>
<td>0.10 (0.02)</td>
<td>0.001</td>
<td>−10</td>
</tr>
<tr>
<td>Middle</td>
<td>22</td>
<td>1.38</td>
<td>1.33</td>
<td>1.37</td>
<td>0.01 (0.05)</td>
<td>0.859</td>
<td>−1</td>
</tr>
<tr>
<td>Highest</td>
<td>23</td>
<td>1.80</td>
<td>1.60</td>
<td>1.52</td>
<td>0.16 (0.05)</td>
<td>&lt;0.001</td>
<td>−16</td>
</tr>
</tbody>
</table>

Lowest, middle, and highest refer to hospital referral region tertiles of baseline (2006) utilization of PCI. ACS indicates acute coronary syndrome; PCI, percutaneous coronary intervention; and SIHD, stable ischemic heart disease.

### Table 2. Changes in Geographic Variation of PCI Use

<table>
<thead>
<tr>
<th>Year</th>
<th>% Change (2006–2008)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIHD (n=67)</td>
<td></td>
</tr>
<tr>
<td>IQR</td>
<td>0.70</td>
</tr>
<tr>
<td>SCV</td>
<td>0.40</td>
</tr>
<tr>
<td>ACS (n=67)</td>
<td></td>
</tr>
<tr>
<td>IQR</td>
<td>0.96</td>
</tr>
<tr>
<td>SCV</td>
<td>0.17</td>
</tr>
</tbody>
</table>

ACS indicates acute coronary syndrome; IQR, interquartile range; PCI, percutaneous coronary intervention; SCV, systematic component of variation; and SIHD, stable ischemic heart disease.

### Figure

Distribution of age and sex standardized rate of percutaneous coronary intervention (PCI) per 1000 residents >40 years of age by hospital referral region. The boxplots are of the 25th and 75th percentiles, with whiskers at 5% and 95%. ACS indicates acute coronary syndrome; and SIHD, stable ischemic heart disease.
in geographic variation further supports its validity. Thus, although other factors may have affected PCI volumes during the study period, our study reinforces other data that suggest a role for the COURAGE trial.

In addition to a reduction in the utilization of PCI for SIHD, we found an ≈25% decline in geographic variation in its use—a question that has not previously been studied. Yet, geographic variation in the use of PCI for SIHD remains more than twice as high as ACS. Again, the extent to which these changes are attributable to the COURAGE trial is unclear. However, to the extent that concerns about the safety of drug-eluting stents13 increased clinical uncertainty, we would have expected to see an increase in regional variation.

Our findings highlight the challenges and opportunities for comparative effectiveness research. It has long been known that some research findings are easily adopted by physicians, whereas others are not. For example, the use of taxane-based chemotherapy among women with early stage breast tumors increased rapidly after the presentation of favorable trial results at an oncology conference, even before the results were vetted by the U.S. Food and Drug Administration and published.35 Likewise, prepublication release of favorable results from carotid endarterectomy trials were associated with steep increases in use, including use in older patients who were excluded from the trials. Negative results from trials of high-dose chemotherapy for women with breast cancer and arthroscopic surgery for patients with osteoarthritis of the knee were followed by immediate reductions in use.36,37 There are also many instances where results have failed to have a substantial and timely impact. Examples include trials of percutaneous coronary angioplasty (PCI) in patients with occluded infarct-related arteries identified >24 hours post-myocardial infarction38 and radiotherapy in older women with smaller, early stage breast tumors.39

This variable adoption of evidence-based practice is thought to be the result of a complex interplay of numerous factors including financial, organizational, social, cultural, and cognitive.40 In the case of medical technologies that are proven to be ineffective (eg, COURAGE), the same factors that may have led to their rapid adoption—fee for service reimbursement, marketing, etc—may have retarded their abandonment.41 Although this may be true, several recent studies demonstrate a significant impact of negative comparative effectiveness studies on clinical practice.36,37,42-45 These findings, in conjunction with ours, lend credence to the theory that new evidence that resolves ambiguity about the benefits of a treatment will reduce variation in its use.45 In the case of the COURAGE trial, the study may have further benefited from widespread media attention both preceding and following announcement of the results,46 reflecting the business risk faced by stent manufacturers, significant publicity by the American College of Cardiology before the meeting, as well as a significant gap between the volume of PCI for SIHD and evidence of its benefit. These factors may have increased uptake of findings from the COURAGE trial.

Despite the impact on clinical practice, the fact that we find persistent geographic variation in the use of PCI for SIHD even after a large, well-conducted, and highly regarded clinical trial demonstrates the challenges facing comparative effectiveness research. These variations likely reflect continued uncertainty about the degree to which the findings of the COURAGE trial are generalizable,49,7,48 and the utility of immediate versus delayed relief from angina symptoms.48 In addition, the findings may be driven by factors other than clinical uncertainty (eg, variation in competition, reimbursement levels, or medical training) related to the effective translation of comparative effectiveness research.

Our study has several important limitations. First, we are unable to assess the underlying distribution of procedures per patient, thus impacting our estimation of geographic variation. However, the SCV is less sensitive to this than other measures of geographic variation.27 Second, we do not know the extent to which the patients in our study would have met eligibility criteria for the COURAGE trial and thus whether it may have affected physician decision making. Our approach is justified, however, by the high positive predictive value of coding for ACS9,50 and data from the CathPCI Registry, which demonstrate that a majority of patients undergoing PCI for nonacute indications meet COURAGE trial entry criteria.17,26 Third, our study uses data from only 7 states. However, these states include 35% of the US population. Most previous studies of geographic variation use national Medicare data. The advantage of our approach is that it includes procedures performed in patients with private insurance, Medicaid, and other sources of coverage. Prior work indicates that geographic variations in spending by private insurers are uncorrelated with variations in Medicare spending.51 Fourth, the SIDs do not consistently capture PCIs performed on an outpatient basis. Although the shift from inpatient to outpatient PCI may explain some of the decline in utilization, we observed it is unlikely to fully explain our findings. In 2008, the vast majority of PCIs were performed on an inpatient basis with relatively little change between 2001 and 2008.52 Furthermore, the proportion of PCI for ACS and SIHD in our study is consistent with that from registry data.53 Exclusion of observation PCI should increase the proportion of PCI for ACS, which is done on a nonelective basis. And, to the extent that the rate of change in the use of outpatient PCI varied across regions during the study period or was coded inconsistently, we would have expected variation in PCI rates to increase. Fifth, we do not know whether the changes observed in 2008 has been maintained to the present or whether the 25% decline in PCI volumes was more short lived. As such, our findings may simply represent a regression to the mean phenomenon.

Despite its limitations, our study is the first to examine patterns of geographic variation in PCI usage for SIHD. Our study suggests that there were substantial changes in utilization and geographic variation in the use of PCI for SIHD after the publication of the COURAGE trial that were proportionate to baseline PCI utilization. However, geographic variation in the use of PCI for SIHD remains considerably higher than for ACS. Understanding the underlying causes of this variation and reducing it through more effective translation of the findings of comparative effectiveness studies into clinical practice ought to be a focus of professional societies and regulatory agencies.

Acknowledgments

We acknowledge Danny McCormick, MD, and Leslee Shaw, PhD, for their review of our manuscript.


Changes in Geographic Variation in the Use of Percutaneous Coronary Intervention for Stable Ischemic Heart Disease After Publication of the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) Trial
Arun V. Mohan, Reza Fazel, Pei-Hsiu Huang, Yu-Chu Shen and David Howard

Circ Cardiovasc Qual Outcomes. 2014;7:125-130; originally published online December 17, 2013;
doi: 10.1161/CIRCOUTCOMES.113.000282
Circulation: Cardiovascular Quality and Outcomes is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2013 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-7705. Online ISSN: 1941-7713

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circoutcomes.ahajournals.org/content/7/1/125

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Quality and Outcomes can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Quality and Outcomes is online at:
http://circoutcomes.ahajournals.org//subscriptions/