Title

Impact of ST-Segment—Elevation Myocardial Infarction Regionalization Programs on the Treatment and Outcomes of Patients Diagnosed With Non—ST-Segment—Elevation Myocardial Infarction

Authors

Montoy, Juan Carlos C
Shen, Yu-Chu
Brindis, Ralph G
et al.

Journal of the American Heart Association

ORIGINAL RESEARCH

Impact of ST-Segment–Elevation Myocardial Infarction Regionalization Programs on the Treatment and Outcomes of Patients Diagnosed With Non–ST-Segment–Elevation Myocardial Infarction

Juan Carlos C. Montoy [iD], MD, PhD; Yu-Chu Shen [iD], PhD; Ralph G. Brindis [iD], MD, MPH; Harlan M. Krumholz [iD], MD, SM; Renee Y. Hsia [iD], MD, MSc

BACKGROUND: Many communities have implemented systems of regionalized care to improve access to timely care for patients with ST-segment–elevation myocardial infarction. However, patients who are ultimately diagnosed with non–ST-segment–elevation myocardial infarctions (NSTEMIs) may also be affected, and the impact of regionalization programs on NSTEMI treatment and outcomes is unknown. We set out to determine the effects of ST-segment–elevation myocardial infarction regionalization schemes on treatment and outcomes of patients diagnosed with NSTEMIs.

METHODS AND RESULTS: The cohort included all patients receiving care in emergency departments diagnosed with an NSTEMI at all nonfederal hospitals in California from January 1, 2005 to September 30, 2015. Data were analyzed using a difference-in-differences approach. The main outcomes were 1-year mortality and angiography within 3 days of the index admission. A total of 293 589 patients with NSTEMIs received care in regionalized and nonregionalized communities. Over the study period, rates of early angiography increased by 0.5 and mortality decreased by 0.9 percentage points per year among the overall population (95% CI, 0.4–0.6 and –1.0 to –0.8, respectively). Regionalization was not associated with early angiography (–0.5%; 95% CI, –1.1 to 0.1) or death (0.2%; 95% CI, –0.3 to 0.8).

CONCLUSIONS: ST-segment–elevation myocardial infarction regionalization programs were not statistically associated with changes in guideline-recommended early angiography or changes in risk of death for patients with NSTEMI. Increases in the proportion of patients with NSTEMI who underwent guideline-directed angiography and decreases in risk of mortality were accounted for by secular trends unrelated to regionalization policies.

Key Words: angiography ■ mortality ■ non–ST-segment–elevation myocardial infarction ■ ST-segment–elevation myocardial infarction

See Editorial by Ward and Nallamothu

Many communities have established regionalized systems of care for ST-segment–elevation myocardial infarction (STEMI) over the past decade.[1–3] Although this focus on the organization and delivery of care may improve treatment and outcomes for patients with STEMI, regionalization could have unintended effects on patients with non–ST-segment–elevation myocardial infarction (NSTEMI), a condition with high prevalence and significant mortality, and for which angiography and

<div style="border: 2px solid red;">

CLINICAL PERSPECTIVE

What Is New?

- In this study of almost 300 000 patients with non–ST-segment–elevation myocardial infarction, likelihood of early angiography increased by 0.5 and mortality decreased by 0.9 percentage points per year over the course of >10 years.
- Regionalization of care for ST-segment–elevation myocardial infarction was not associated with changes in angiography, percutaneous coronary intervention, or 1-year mortality of patients presenting with non–ST-segment–elevation myocardial infarction.

What Are the Clinical Implications?

- Treatment and outcomes for non–ST-segment–elevation myocardial infarction have improved recently, but ST-segment–elevation myocardial infarction regionalization programs were not responsible for these changes and policy makers should not expect ST-segment–elevation myocardial infarction regionalization programs to have large unintended consequences for patients presenting with non–ST-segment–elevation myocardial infarction.

</div>

percutaneous coronary intervention (PCI) are associated with better outcomes.[4–13]

Specifically, STEMI regionalization could affect volume and staffing in both PCI and non-PCI centers, potentially influencing the type of care given to patients with NSTEMI.[14,15] It also could improve outcomes through several mechanisms, including through increased adherence to guidelines recommending angiography, via a volume-outcomes relationship, or through external factors, such as better follow-up care.[16] However, whether regionalization of STEMI care impacts treatments and outcomes for patients experiencing NSTEMIs, whether beneficial, neutral, or harmful, remains unexplored.

In this study, we set out to determine whether and to what extent STEMI regionalization might impact treatment and outcomes for patients with NSTEMIs. We hypothesized that risk-adjusted outcomes for patients with NSTEMIs improved more in regionalized compared with nonregionalized communities. We also hypothesized that the probability of receiving invasive therapy (ie, guideline-directed angiography and possible PCI within 72 hours) increased for patients with NSTEMI in regionalized communities compared with nonregionalized communities.

METHODS

Because of the sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to the California Office of Statewide Health Planning and Development at oshpd.ca.gov.

Conceptual Model

STEMI regionalization could change the type of care given to patients with NSTEMI in several ways. First, after regionalization, a greater proportion of patients with NSTEMIs could receive care at PCI-capable hospitals if emergency medical services providers transport them to PCI centers because of immediate concern for a possible STEMI or if they self-present to PCI-capable centers. Second, patients with NSTEMI may be more likely to undergo timely invasive therapy (ie, a PCI within 72 hours during index hospitalization).[17] This is particularly important given mounting evidence and an American College of Cardiology/ American Heart Association guideline recommending that most patients with NSTEMI should receive timely invasive therapy (ie, PCI within 72 hours) as a first-line treatment.[5,11–13] Third, PCI centers may provide better NSTEMI care because of experience derived from a higher volume of treated patients.[15] Finally, regionalized centers may provide better follow-up care, including medical optimization for secondary prevention.[16]

However, there is a possibility that treatment and outcomes could worsen under certain conditions: first, if the focus on STEMIs leads physicians at either PCI or non-PCI centers to focus less on caring for patients with NSTEMIs; second, if non-PCI centers fall out of practice because they admit and treat fewer NSTEMIs; and, finally, if regionalization results in fragmentation of local care and thus poorer follow-up and secondary prevention.

A difference-in-differences approach compares the changes in treatment and outcomes for counties that regionalized (difference between preregionalization and postregionalization) compared with the difference over the same time period for counties that were not regionalized. This approach helps identify the association between the change in policy and changes in treatment and outcomes separate from the trends in treatment and outcomes occurring for reasons other than the change in policy, such as changes in the epidemiological features of NSTEMI.

Study Sample and Data Sources

We linked nonpublic discharge data and nonpublic emergency department data from the California Office of Statewide Health Planning and Development for the study period from January 1, 2005 to September 30, 2015. As Office of Statewide Health Planning and Development records data from all emergency department and inpatient encounters

at all nonfederal, general acute-care hospitals, and patients are identified by record linkage number, we comprehensively observed procedures and diagnoses for all patients with NSTEMI during the study period. All patient encounters in the data, identified as having an *International Classification of Diseases, Ninth Revision* (*ICD-9*), code for NSTEMI (410.70 and 410.71) or STEMI (410.xx, except 410.7x and 410.x2) during the study period, were included in our analysis. We linked each patient observation to California Vital Statistics data through 2013 (the most recent data available) using a unique patient identifier.

Hospitals and counties were linked to the STEMI Network Database and Hospital STEMI Designation data set, 2 data sets we previously collected for related research.[18,19] These data sets contain the degree of regionalization and dates of implementation of California's 33 local emergency medical services agencies, which provide emergency medical services for California's 58 counties. Although the term regionalization is used broadly in the literature as "matching of medical resources to patient needs to maximize health benefits and outcomes while minimizing cost and use of resources over a specified geographic area,"[20] this leaves some degree of subjectivity in defining regionalization. Following previous work conducted by the research team,[18,19] we denoted a county as achieving complete regionalization on and after the year that 95% of its local emergency medical services system has: (1) emergency medical systems that direct prehospital transport to bypass the nearest hospitals that do not offer emergent PCI to facilities that offer emergent PCI for patients with STEMI; and (2) interhospital transfer protocols specifically for patients with STEMI.[20]

Outcomes

The primary outcomes were angiography within 3 days and death at 1 year. We chose angiography instead of PCI because this represents an *attempt* at an invasive strategy regardless of whether a culprit lesion was identified or subject to intervention. We identified angiography using *ICD-9* procedure codes 3721-3 and 8850-7. Secondary outcomes included death at 7, 30, and 90 days, as identified through the linked vital statistics files. As a sensitivity analysis, we also used receipt of PCI as another outcome (Table S1).

Statistical Analysis

We used a multivariable linear regression model to measure the association between regionalization status of each patient's county of residence and risk of death within 1 year of NSTEMI diagnosis. The model included regionalization status, year, patient

characteristics, hospital characteristics, and treatments. An indicator for regionalization was specified as one on and after the year in which a community achieved STEMI regionalization, and zero otherwise. Our model included year of encounter to account for secular trends common across all counties, regardless of regionalization status. Patient characteristics included sex, age group, race/ethnicity, comorbidities (categorized according to Elixhauser comorbidity index), and expected insurance. Race/ethnicity categories included Asian, Black, Hispanic, and Native American. Age groups were defined as <40, 40 to 64, 65 to 69, 70 to 74, 75 to 79, 80 to 84, and ≥85 years. Hospital characteristics included annual emergency department volume, critical access designation, teaching hospital designation, government hospital, not-for-profit status, and whether the hospital was PCI capable (defined as capable for a given year if that year's PCI procedures were ≥5) or non-PCI capable. We included an interaction term between PCI capability and regionalization status to measure differences between non-PCI centers and PCI centers separately within nonregionalized and regionalized communities. Angiography (without PCI) within 3 days and PCI within 3 days were both included as indicators. We analyzed secondary outcomes for death (7, 30, and 90 days) using the same model specification. We used a multivariable linear regression model to measure the association between regionalization status of each patient's county of residence and the likelihood of undergoing angiography within 3 days of diagnosis. This model used angiography as the outcome of interest and excluded PCI; it was otherwise identical to the mortality model. The PCI model used as a sensitivity analysis used the same specification as the angiography model, with PCI as the outcome of interest. All models used county fixed effects to account for unobserved differences across counties that did not vary over the study period. Given our sample size of ≈290 000, we had 80% power at an α of 0.05 to detect a 1 percentage point difference in likelihood of angiography or death. SEs were clustered at the county level for all models. All analyses were conducted using STATA 15 (StataCorp, College Station, TX). Permission to conduct this study was granted by the University of California, San Francisco, Institutional Review Board with a waiver of informed consent.

RESULTS

During our 10-year study period, we evaluated 293 589 patients with NSTEMI; of these patients, 78 923 (26.8%) received care in communities that were not regionalized the year of their admission

and 214 666 (73.2%) received care in hospitals in STEMI-regionalized communities (Table 1). Patients in regionalized communities were more likely to be minorities and had more comorbidities than patients in nonregionalized communities; they did not differ by age or sex.

Over the study period, the incidence of NSTEMI increased. As more counties became regionalized, an increasing proportion of patients received care in regionalized communities and a decreasing proportion received care at nonregionalized communities (Figure 1). By 2014, all communities had regionalized. Over the study period, most patients with NSTEMI received care in PCI-capable hospitals; they had a higher likelihood of doing so in regionalized than in nonregionalized communities (69.9% regionalized and 63.3% nonregionalized; χ^2 $P<0.0005$).

When controlling for patient and hospital characteristics, the multivariable regression examining regionalization and probability of undergoing angiography (Table 2) did not show any impact from regionalization (–0.3 percentage points; 95% CI, –1.2 to 0.5 percentage points). The probability of undergoing angiography increased by 0.5 percentage points each year (95% CI, 0.4–0.6 percentage points) across all counties, regardless of regionalization status. The strongest predictor of whether a patient underwent angiography was whether the hospital was PCI capable (49.4 percentage points; 95% CI, 48.8–50.2 percentage points). There was no difference in this association between regionalized and nonregionalized communities (interaction, –0.2 percentage points; 95% CI, –1 to 0.6 percentage points). Patients were less likely to undergo angiography at critical access hospitals (–10.0 percentage points; 95% CI, –15.7 to –4.3 percentage points) or teaching hospitals (–3.5 percentage points; 95% CI, –4.1 to –2.8 percentage points). In terms of patient demographics, increasing age (>70 years) and most (23 of 29) comorbidities were associated with a lower likelihood of angiography (coefficients for comorbidities not presented). Patients with Medicare and Medicaid insurance were less likely to undergo angiography than those with private insurance (–2.8 percentage points [95% CI, –3.3 to –2.2 percentage points] and –3.5 percentage points [95% CI, –4.2 to –2.8 percentage points], respectively). Black patients had a 5.6 percentage point lower probability of receiving angiography (95% CI, –6.3 to –4.9 percentage points) compared with non-Hispanic White patients.

Figure 2 shows trends for the proportion of patients with NSTEMI undergoing angiography within 30 days of diagnosis. There was a steady increase in the proportion of patients who received angiography over the study period; most of this was attributable to the increased proportion of patients undergoing angiography within 2 days of diagnosis.

The probability of death within 1 year of NSTEMI diagnosis decreased over time across all counties in the multivariable model (–0.9 percentage points per year; 95% CI, –1.0 to –0.8 percentage points per year; Table 3). No significant association between regionalization and death was found (0.0 percentage points; 95% CI, –0.8 to 0.7 percentage points). Receiving care in a PCI center was associated with a 3.7 percentage point increased risk of death (95% CI, 3.0–4.3 percentage points). This relationship did not differ between regionalized and nonregionalized communities: interaction between PCI capability and regionalization was 0.4 percentage points (95% CI, –0.3 to 1.2 percentage points). The probability of death increased with increasing age and with most (21 of 29) comorbidities. Undergoing angiography within 3 days of NSTEMI diagnosis was associated with a 10.1 percentage point decrease in risk of death (95% CI, –10.5 to 9.7 percentage points), and PCI within 3 days was associated with a 10.5 percentage point decrease in mortality (95% CI, –11.0 to –10.1 percentage points). Regionalization was not associated with risk of death across different time horizons: 7 days, 30 days, 90 days, and 1 year (Figure S1).

DISCUSSION

In this retrospective cohort study from 2005 through 2015 of nearly 294 000 patients with NSTEMIs, we found that regionalization was not associated with significant changes in the likelihood of patients who received timely angiography or decreased mortality. Over the 10-year study period, the proportion of patients with NSTEMI undergoing angiography increased and their risk of death decreased, but these changes were not attributable to regionalization.

Our study is, to our knowledge, the first analysis of the relationship between regionalization of STEMI care and the treatment and outcomes for patients with NSTEMI. Previous work on STEMI regionalization has focused on the process of establishing such programs and intermediate outcomes, such as door-to-balloon times.[19,21,22] These studies address primary questions about STEMI regionalization programs, but do not consider possible impacts on the management of patients with NSTEMI. The recent literature on NSTEMIs does include evaluations of incidence (eg, the impact of newer troponin assays and changes in patient demographics),[23] treatment (timing of and selection of patients for PCI),[11,24,25] and outcomes (mortality).[26] However, such analyses have not considered these trends and outcomes vis-à-vis STEMI regionalization programs.

Table 1. Patient and Hospital Characteristics

Characteristics	Not Regionalized (n=78 923)	Regionalized (n=214 666)	P Value
Patient characteristics			
Women	33 126 (42)	89 864 (41.9)	0.545
Age, median (IQR), y	70.0 (58–80)	69.0 (58–80)	0.7942
Race/ethnicity			
White	53 194 (67)	122 510 (57)	<0.0005
Black	5205 (7)	18 143 (8)	
Hispanic	10 712 (14)	43 799 (20)	
Asian	6589 (8)	20 883 (10)	
Insurance			
Private	19 257 (24)	46 797 (22)	<0.0005
Medicare	49 875 (63)	134 368 (63)	
Medicaid	5176 (7)	20 901 (10)	
Indigent	1225 (2)	3617 (2)	
Self-pay	2194 (3)	5726 (3)	
Other	1184 (2)	3253 (2)	
Comorbidities			
Anemia	17 311 (22)	52 943 (25)	<0.0005
Arrhythmia	129 (0)	416 (0)	0.094
Arthritis	1804 (2)	5480 (3)	<0.0005
Cancer	741 (1)	2313 (1)	0.001
Congestive heart failure	27 663 (35)	77 918 (36)	<0.0005
Coagulopathy	3088 (4)	11 495 (5)	<0.0005
COPD	17 913 (23)	46 073 (21)	<0.0005
Depression	5403 (7)	13 732 (6)	<0.0005
Dementia	2420 (3)	6076 (3)	<0.0005
Diabetes mellitus, uncomplicated	22 036 (28)	60 246 (28)	0.408
Diabetes mellitus with chronic complications	8883 (11)	31 158 (15)	<0.0005
Fluid and electrolyte disorders	15 492 (20)	48 712 (23)	<0.0005
HIV	159 (0)	420 (0)	0.796
Hypertension	59 367 (75)	170 802 (80)	<0.0005
Hypothyroid	9226 (12)	26 955 (13)	<0.0005
Liver disease	1374 (2)	4782 (2)	<0.0005
Lymphoma	423 (1)	1377 (1)	0.001
Metastatic cancer	1945 (12)	5459 (3)	0.249
Neurological disorder	4998 (6)	14 915 (7)	<0.0005
Obesity	10 211 (13)	33 701 (16)	<0.0005
Paralysis	2221 (3)	6016 (3)	0.805
Psychoses	1925 (2)	8287 (4)	<0.0005
Pulmonary circulation disorder	3445 (4)	11 428 (5)	<0.0005
Renal failure	16 995 (22)	62 573 (29)	<0.0005
Substance abuse	3853 (5)	12 352 (6)	<0.0005
Ulcer, peptic	71 (0)	91 (0)	<0.0005
Vascular disease	10 456 (13)	34 381 (16)	0.153
Valvular disease	11 201 (14)	30 097 (14)	<0.0005
Weight loss	1534 (2)	8702 (4)	<0.0005
Hospital characteristics			
ED annual volume, median (IQR)	40 210 (27 035–53 291)	45 995 (29 908–66 346)	<0.0005

(*Continued*)

Table 1. Continued

Characteristics	Not Regionalized (n=78 923)	Regionalized (n=214 666)	P Value
Critical access hospital	135 (0.2)	185 (0.1)	<0.0005
Teaching hospital	7034 (9)	20 829 (10)	<0.0005
Government hospital	10 511 (13)	29 243 (14)	0.028
Not for profit	57 746 (73)	147 468 (69)	<0.0005
Catheterization laboratory in hospital	49 945 (63)	150 034 (70)	<0.0005

Values are number (percentage) unless otherwise stated. Race/ethnicity: Native American, other, and invalid combine to <5% of the sample. P values for age and ED volume calculated using t test; all other P values from the Pearson χ^2 test for independence between samples. COPD indicates chronic obstructive pulmonary disease; ED, emergency department; and IQR, interquartile range.

The absence of a positive finding contributes to an increased understanding of the implications of STEMI regionalization programs. In previous work, we found that regionalization was not associated with a significant impact on whether patients with NSTEMI received care in PCI-capable hospitals: likelihood of patients with NSTEMI receiving care in PCI-capable hospitals increased by only 2.2 percentage points. We thus did not expect to find a difference in treatment or outcomes caused by increased likelihood of care in PCI-capable hospitals and herein focused on whether the care patients received (ie, angiography and possible PCI) changed over the regionalization process.

Our analysis tested for differences in treatment and outcomes between regionalized and nonregionalized communities, and tested for differences between PCI and non-PCI centers within regionalized communities. This approach is important because there could be changes at the population level, and changes within the population that are obscured by a population-level analysis. For example, regionalization could lead to improvements in treatment and outcomes at PCI centers and worsening at non-PCI centers, but if these
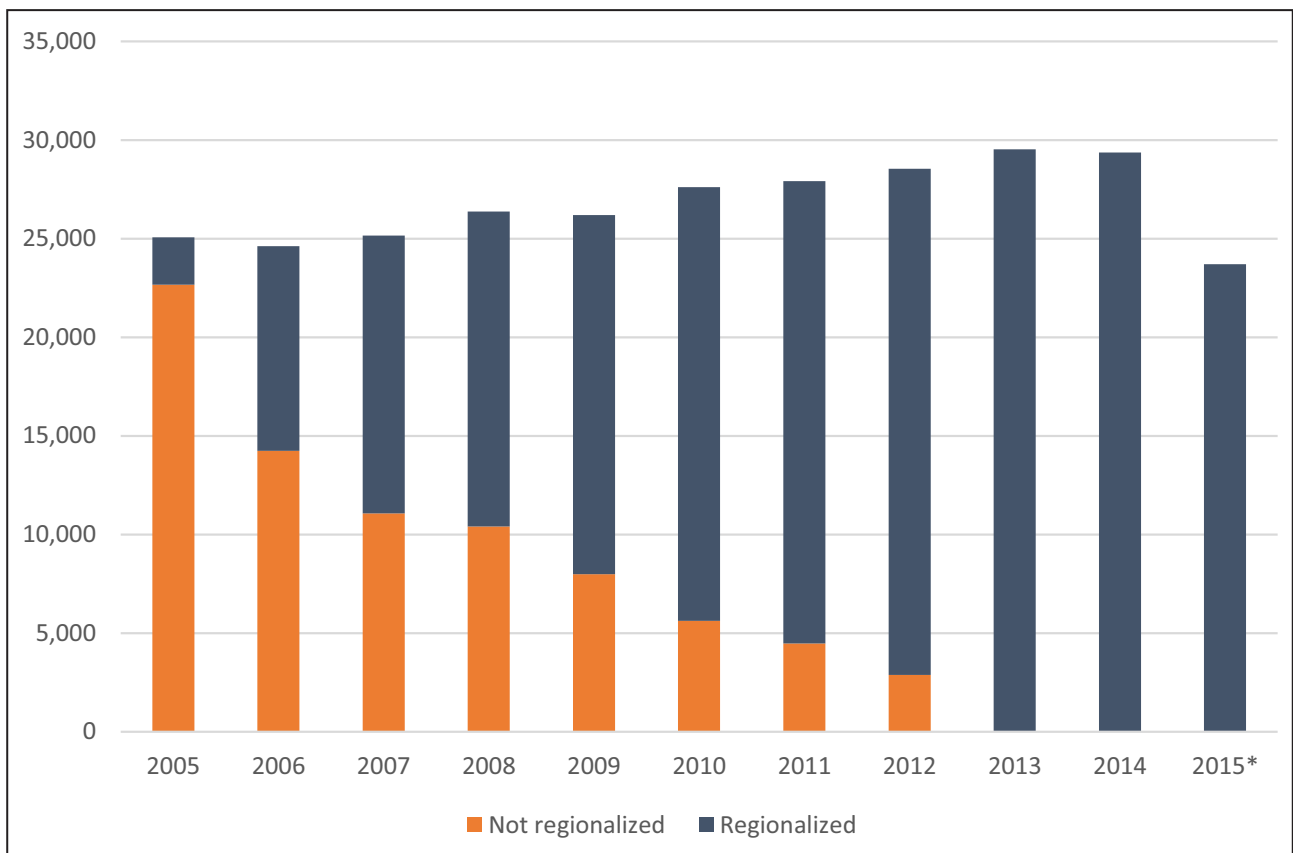

Figure 1. Non–ST-segment–elevation myocardial infarction (NSTEMI) incidence, according to regionalization status.
Cases of NSTEMI per year for both regionalized and not regionalized communities. *Data end on September 30, 2015.

Table 2. Probability of Undergoing Catheterization Within 3 Days of Admission

Variable	Coefficient	95% CI	P>t
Regionalized	−0.003	−0.012 to 0.005	0.415
Year	0.005	0.004 to 0.006	<0.0005
Patient characteristics			
Women	−0.031	−0.034 to −0.027	<0.0005
Age group, y			
40–64	0.014	0.000 to 0.027	0.048
65–69	−0.003	−0.018 to 0.012	0.689
70–74	−0.024	−0.039 to −0.009	0.001
75–79	−0.060	−0.075 to −0.046	<0.0005
80–84	−0.128	−0.142 to −0.113	<0.0005
85–99	−0.289	−0.303 to −0.274	<0.0005
Race/ethnicity			
Black	−0.056	−0.063 to −0.049	<0.0005
Hispanic	0.001	−0.003 to 0.006	0.56
Asian	0.002	−0.004 to 0.008	0.594
Insurance			
Medicare	−0.028	−0.033 to −0.022	<0.0005
Medicaid	−0.035	−0.042 to −0.028	<0.0005
Indigent	0.039	0.026 to 0.052	<0.0005
Self-pay	−0.009	−0.019 to 0.002	0.102
Other	−0.007	−0.021 to 0.007	0.316
Hospital characteristics			
Catheterization laboratory within hospital	0.495	0.488 to 0.502	<0.0005
Catheterization laboratory×regionalized	−0.002	−0.010 to 0.006	0.58
ED volume (log)	0.006	0.003 to 0.009	<0.0005
Critical access hospital	−0.100	−0.157 to −0.043	0.001
Teaching hospital	−0.035	−0.041 to −0.028	<0.0005
Government hospital	0.009	0.002 to 0.016	0.008
Not for profit	0.002	−0.003 to 0.007	0.376
County population (log)	0.439	0.340 to 0.538	<0.0005

Multivariable regression also includes other race/ethnicity categories (Native American, other, and invalid) and comorbidities (indicator variable for each Elixhauser category). Comorbidities are not presented. Catheterization laboratory×regionalized is an interaction term equal to 1 if catheterization laboratory is present and community is regionalized. Reference categories include the following: not regionalized, year 2005, men, aged <40 years, White race, no comorbidities, privately insured, and no catheterization laboratory in hospital. ED indicates emergency department.

are similar in magnitude, a population-level analysis will find no net effect. We did not find this was the case; there was no evidence that regionalization led to changes compared with nonregionalized communities, nor was there evidence that treatment and outcomes changed within regionalized communities. The most likely interpretation of our finding is that STEMI regionalization may not have impacted the management strategy of NSTEMIs, with no discernable effect on 1-year mortality.

Because of the mounting evidence of the use of early PCI for patients with NSTEMI that became apparent around the same time that STEMI regionalization programs took shape, it is possible that hospitals adopted timely PCI for NSTEMI before regionalization and thus there was no apparent effect of regionalization. Alternatively, hospitals could have increased their angiography capability in preparation for regionalization and thus had no apparent change in treatment because of regionalization. However, the lack of association between regionalization and treatment and outcomes suggests that neither of these changes took place, with instead slow adoption of a timely invasive strategy in the management of NSTEMI over the study period separate from regionalization. The proportion of patients we observed undergoing timely angiography was similar to the proportion found in other observational studies over similar time periods,[17,27,28] although lower than that reported by the NCDR (National Cardiovascular Data Registry) ACTION (Acute Coronary Treatment
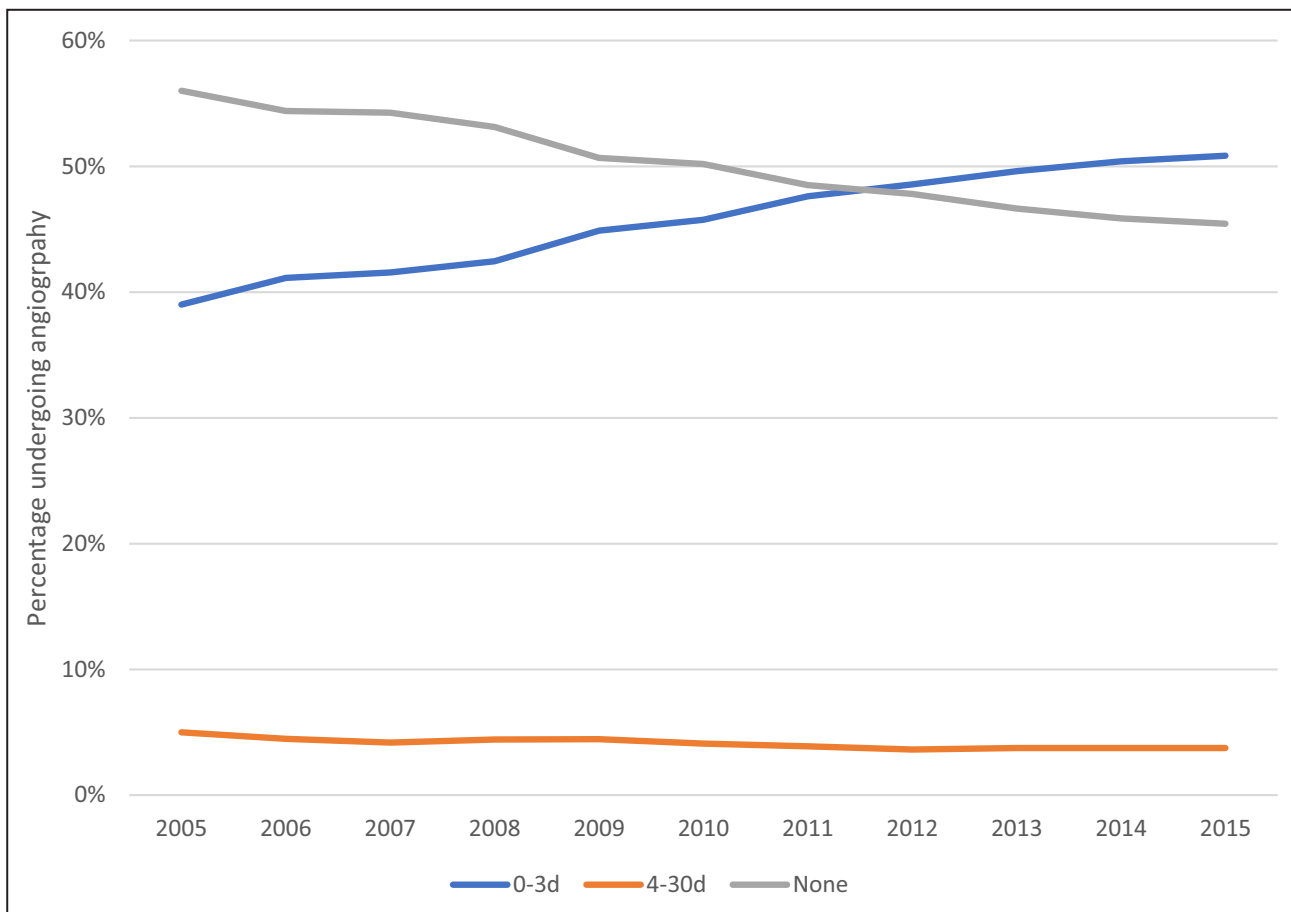
Figure 2. Percentage of patients with non–ST-segment–elevation myocardial infarction (NSTEMI) undergoing angiography.
Percentage of patients in each year with NSTEMI who underwent angiography within 3 days of diagnosis (0–3d), who underwent angiography between 4 and 30 days of diagnosis (4–30d), or who did not undergo angiography (None).

and Intervention Outcomes Network) Registry–Get With The Guidelines.[29] This likely suggests that the patients, severity of illness, and hospitals we observed are similar to those seen in other population-based studies, whereas the ACTION Registry–Get With The Guidelines has a larger share of larger, tertiary care centers with greater resources.

Regionalization of STEMI care has been established in much of the United States and in other countries, but many areas still do not have such a system in place and, in those that do, its execution has been heterogeneous.[30,31] Beyond the initial calls for regionalization by the American Heart Association and American College of Cardiologists, the Mission: Lifeline initiative has identified these systems as an important intervention to improve the outcomes of STEMI care; implementation and evaluation are ongoing.[23,32,33] Understanding the collateral effects on a related condition, NSTEMI, is relevant to communities considering regionalization, particularly in communities with fewer resources.[34,35] Our results may improve policy makers' expectations about the unintended consequences of establishing

a regionalized system of STEMI care on patients with NSTEMI.

Our results also suggest that further research is needed to determine how patients are being selected for angiography and possible PCI. Our finding that angiography (without PCI) and PCI were both associated with a 10 percentage point decrease in 1-year mortality suggests that undergoing angiography selects for healthier patients; our analysis of the predictors of angiography and PCI corroborates this, showing that younger patients with fewer comorbidities were more likely to undergo angiography. However, the administrative nature of our data set does not allow us to observe patient stability or other clinical factors informing the decision of whether to undergo angiography; patients may have been appropriately deemed too sick to undergo an invasive strategy. Alternatively, an invasive strategy may not have been within the goals of care of some older patients with more comorbidities. Although our retrospective design precludes causal inferences between early invasive therapy and mortality, it does

Table 3. Probability of Death Within 1 Year of NSTEMI

Variable	Coefficient	95% CI	*P>t*
Regionalized	0.000	−0.008 to 0.007	0.99
Year	−0.009	−0.010 to −0.008	<0.0005
Patient characteristics			
Women	−0.019	−0.022 to −0.015	<0.0005
Age group, y			
40–64	0.015	0.003 to 0.028	0.018
65–69	0.028	0.015 to 0.042	<0.0005
70–74	0.048	0.035 to 0.062	<0.0005
75–79	0.074	0.061 to 0.088	<0.0005
80–84	0.122	0.108 to 0.136	<0.0005
85–99	0.220	0.206 to 0.233	<0.0005
Race/ethnicity			
Black	−0.008	−0.015 to −0.002	0.008
Hispanic	−0.015	−0.020 to −0.011	<0.0005
Asian	−0.017	−0.022 to −0.011	<0.0005
Insurance			
Medicare	0.014	0.009 to 0.019	<0.0005
Medicaid	0.007	0.001 to 0.014	0.03
Indigent	−0.015	−0.026 to −0.003	0.011
Self-pay	−0.005	−0.014 to 0.005	0.332
Other	0.000	−0.013 to 0.012	0.947
Hospital characteristics			
ED volume (log)	−0.001	−0.003 to 0.002	0.553
Critical access hospital	0.015	−0.036 to 0.066	0.564
Teaching hospital	−0.010	−0.016 to −0.004	0.001
Government hospital	0.014	0.007 to 0.020	<0.0005
Not for profit	−0.011	−0.015 to −0.006	<0.0005
County population (log)	0.150	0.055 to 0.245	0.002
Catheterization laboratory within hospital	0.037	0.030 to 0.043	<0.0005
Catheterization laboratory×regionalized	0.004	−0.003 to 0.012	0.246
Patient care			
Angiography without intervention within 3 d	−0.101	−0.105 to −0.097	<0.0005
PCI within 3 d	−0.105	−0.110 to −0.101	<0.0005

Multivariable regression also includes other race/ethnicity categories (Native American, other, and invalid) and comorbidities (indicator variable for each Elixhauser category). Comorbidities are not presented. Catheterization laboratory×regionalized is an interaction term equal to 1 if catheterization laboratory is present and community is regionalized. Reference categories include the following: not regionalized, year 2005, men, aged <40 years, White race, no comorbidities, privately insured, and no catheterization laboratory in hospital. ED indicates emergency department; NSTEMI, non–ST-segment–elevation myocardial infarction; and PCI, percutaneous coronary intervention.

inform how angiography and PCI are used in practice and raises questions such as whether guidelines are being applied appropriately and whether and why subpopulations receive this intervention at different rates.

Limitations

Our study was limited to nonfederal hospitals in California, which is not necessarily representative of hospitals in other states or regions. It is, however, a large state with a diverse population and a wide range of urban and rural regions and could reflect trends seen in other regions and states within the United States. The increasing NSTEMI incidence and the increased likelihood of undergoing angiography reported in this study are consistent with trends reported for other populations, as is the finding that the proportion of patients undergoing angiography is still suboptimal.[27,36–38] Second, as with many administrative data sets, the data sets we used did not provide detailed information about nonprocedural patient care (such as adherence to medical management guidelines), nor did it offer the opportunity to examine

social determinants of health, what treatments were offered but not rendered, or access to and quality of outpatient care. This also limited our ability to investigate whether other care recommendations were followed, such as immediate angiography and revascularization for hemodynamically unstable patients or angiography within 24 hours for patients with high risk scores. Furthermore, coding could affect apparent incidence if hospitals updated what they define as an NSTEMI during the regionalization process.[39] Also, our inclusion criteria relied on a primary diagnosis of NSTEMI acute myocardial infarction and could have mistakenly included patients with type 2 myocardial infarction who were misclassified as having NSTEMI or excluded patients with NSTEMI who had this listed as a secondary diagnosis. However, unless there was a systematic difference in the way these were coded across regionalization areas, it is unlikely to pose significant problems in interpreting our final model.

Third, there are known changes in the epidemiological features of acute myocardial infarction, in particular NSTEMIs, caused in part by increased sensitivity of troponin assays and changes in patient demographics and health-related risk factors, but it was beyond the scope of this study to investigate which assays were used or investigate state-wide changes in case mix.[24,40] Last, the decision by any given community to undergo regionalization of STEMI care may have been because of unobserved factors that also influenced care. For example, a community may have regionalized because it already functioned as if it were regionalized and thus the cost of regionalization was low, or because care was so poor or disorganized that the potential benefits of regionalization were large. Similarly, we used a dichotomous variable for regionalization, although in practice regionalization exists on a spectrum, so the change from nonregionalized to regionalized may be large for one agency and small for another. Thus, we could not make any causal inferences between regionalization and changes in treatment and outcomes for NSTEMI, but rather report the association between these 2 variables. Because there is considerable heterogeneity in how regionalization has been implemented in other communities, our findings may not generalize to other regions.[32]

CONCLUSIONS

We found that STEMI regionalization policies were not associated with changes in angiography, PCI, or 1-year mortality of patients presenting with NSTEMI. Mortality from NSTEMI is decreasing, and early invasive therapy is becoming increasingly common, but these trends are not attributable to STEMI

regionalization policies and nearly half of patients with NSTEMIs still do not receive guideline-directed timely angiography. Policy makers should not expect STEMI regionalization programs to have either positive or negative unintended consequences for patients presenting with NSTEMIs.

REFERENCES

1. Nissen SE, Brush JE, Krumholz HM. President's page: GAP-D2B: an alliance for quality. *J Am Coll Cardiol*. 2006;48:1911–1912.
2. Menees DS, Peterson ED, Wang Y, Curtis JP, Messenger JC, Rumsfeld JS, Gurm HS. Door-to-balloon time and mortality among patients undergoing primary PCI. *N Engl J Med*. 2013;369:901–909.
3. O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;127:529–555.
4. Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR Jr, Jaffe AS, Jneid H, Kelly RF, Kontos MC, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:e344–e426.

5. King SB, Smith SC, Hirshfeld JW, Jacobs AK, Morrison DA, Williams DO. 2007 Focused update of the ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (2007 Writing Group to Review New Evidence and Update the 2005 ACC/AHA/SCAI Guideline Update for Percutaneous Coronary Intervention). *Circulation*. 2008;117:261–295.

6. Plakht Y, Gilutz H, Shiyovich A. Temporal trends in acute myocardial infarction: what about survival of hospital survivors? Disparities between STEMI & NSTEMI remain: Soroka acute myocardial infarction II (SAMI-II) project. *Int J Cardiol*. 2016;203:1073–1081.

7. El-Menyar A, Ahmed E, Albinali H, Al-Thani H, Gehani A, Singh R, Al SJ. Mortality trends in women and men presenting with acute coronary syndrome: insights from a 20-year registry. *PLoS One*. 2013;8:e70066.

8. Montalescot G, Dallongeville J, Van Belle E, Montalescot G, Dallongeville J, Van Belle E, Rouanet S, Baulac C, Degrandsart A, Vicaut E. STEMI and NSTEMI: are they so different? 1 Year outcomes in acute myocardial infarction as defined by the ESC/ACC definition (the OPERA registry). *Eur Heart J*. 2007;28:1409–1417.

9. Polonski L, Gasior M, Gierlotka M, Polonski L, Gasior M, Gierlotka M, Osadnik T, Kalarus Z, Trusz-Gluza M, Zembala M, et al. A comparison of ST elevation versus non-ST elevation myocardial infarction outcomes in a large registry database: are non-ST myocardial infarctions associated with worse long-term prognoses? *Int J Cardiol*. 2011;152:70–77.

10. García-García C, Subirana I, Sala J, Bruguera J, Sanz G, Valle V, Arós F, Fiol M, Molina L, Serra J, et al. Long-term prognosis of first myocardial infarction according to the electrocardiographic pattern (ST elevation myocardial infarction, non-ST elevation myocardial infarction and non-classified myocardial infarction) and revascularization procedures. *Am J Cardiol*. 2011;108:1061–1067.

11. Bavry AA, Kumbhani DJ, Rassi AN, Bhatt DL, Askari AT. Benefit of early invasive therapy in acute coronary syndromes: a meta-analysis of contemporary randomized clinical trials. *J Am Coll Cardiol*. 2006;48:1319–1325. DOI: 10.1016/j.jacc.2006.06.050.

12. Wallentin L, Lagerqvist B, Husted S, Kontny F, Ståhle E, Swahn E; FRISC II Investigators. Fast Revascularisation during Instability in Coronary artery disease. Outcome at 1 year after an invasive compared with a non-invasive strategy in unstable coronary-artery disease: the FRISC II invasive randomised trial. *Lancet*. 2000;356:9–16. DOI: 10.1016/S0140-6736(00)02427-2.

13. Fox KAA, Poole-Wilson PA, Henderson RA, Clayton TC, Chamberlain DA, Shaw TR, Wheatley DJ, Pocock SJ; Randomized Intervention Trial of Unstable Angina Investigators. Interventional versus conservative treatment for patients with unstable angina or non-ST-elevation myocardial infarction: the British Heart Foundation RITA 3 randomised trial: Randomized Intervention Trial of Unstable Angina. *Lancet*. 2002;360:743–751.

14. Ruff CT, Braunwald E. The evolving epidemiology of acute coronary syndromes. *Nat Rev Cardiol*. 2011;8:140–147. DOI: 10.1038/nrcardio.2010.199.

15. Harrison RW, Simon D, Miller AL, de Lemos JA, Peterson ED, Wang TY. Association of hospital myocardial infarction volume with adherence to American College of Cardiology/American Heart Association performance measures: insights from the National Cardiovascular Data Registry. *Am Heart J*. 2016;178:95–101. DOI: 10.1016/j.ahj.2016.04.002.

16. Cohen D, Manuel DG, Tugwell P, Ramsay T, Sanmartin C. Inequity in primary and secondary preventive care for acute myocardial infarction? Use by socioeconomic status across middle-aged and older patients. *Can J Cardiol*. 2013;29:1579–1585. DOI: 10.1016/j.cjca.2013.06.004.

17. Khera S, Kolte D, Aronow WS, Palaniswamy C, Subramanian KS, Hashim T, Mujib M, Jain D, Paudel R, Ahmed A, et al. Non-ST-elevation myocardial infarction in the United States: contemporary trends in incidence, utilization of the early invasive strategy, and in-hospital outcomes. *J Am Heart Assoc*. 2014;3:e000995. DOI: 10.1161/JAHA.114.000995.

18. Rokos IC, Sporer K, Savino PB, Mercer MP, Shontz SS, Sabbagh S, Hsia RY. A novel survey tool to quantify the degree and duration of STEMI regionalization across California. *Crit Pathw Cardiol*. 2016;15:103–105. DOI: 10.1097/HPC.0000000000000085.

19. Hsia R, Sabbagh S, Sarkar N, Sporer K, Rokos I, Brown J, Brindis R, Guo J, Shen Y-C. Trends in regionalization of care for ST-segment elevation myocardial infarction. *West J Emerg Med*. 2017;18:1010–1017. DOI: 10.5811/westjem.2017.8.34592.

20. Kocher KE, Sklar DP, Mehrotra A, Tayal VS, Gausche-Hill M, Myles RR. Categorization, designation, and regionalization of emergency care: definitions, a conceptual framework, and future challenges. *Acad Emerg Med*. 2010;17:1306–1311. DOI: 10.1111/j.1553-2712.2010.00932.x.

21. Henry TD, Sharkey SW, Burke MN, Chavez IJ, Graham KJ, Henry CR, Lips DL, Madison JD, Menssen KE, Mooney MR, et al. A regional system to provide timely access to percutaneous coronary intervention for ST-elevation myocardial infarction. *Circulation*. 2007;116:721–728.

22. Jollis JG, Al-Khalidi HR, Roettig ML, Berger PB, Corbett CC, Doerfler SM, Fordyce CB, Henry TD, Hollowell L, Magdon-Ismail Z, et al. Impact of regionalization of ST-segment-elevation myocardial infarction care on treatment times and outcomes for emergency medical services-transported patients presenting to hospitals with percutaneous coronary intervention: mission: lifeline accelerator-2. *Circulation*. 2018;137:376–387.

23. Roger VL, Weston SA, Gerber Y, Killian JM, Dunlay SM, Jaffe AS, Bell MR, Kors J, Yawn BP, Jacobsen SJ. Trends in incidence, severity, and outcome of hospitalized myocardial infarction. *Circulation*. 2010;121:863–869.

24. Elgendy IY, Kumbhani DJ, Mahmoud AN, Wen X, Bhatt DL, Bavry AA. Routine invasive versus selective invasive strategies for non-ST-elevation acute coronary syndromes: an updated meta-analysis of randomized trials. *Catheter Cardiovasc Interv*. 2016;88:765–774.

25. Milasinovic D, Milosevic A, Marinkovic J, Milasinovic D, Milosevic A, Marinkovic J, Vukcevic V, Ristic A, Asanin M, Stankovic G. Timing of invasive strategy in NSTE-ACS patients and effect on clinical outcomes: a systematic review and meta-analysis of randomized controlled trials. *Atherosclerosis*. 2015;241:48–54.

26. Kolte D, Khera S, Dabhadkar KC, Agarwal S, Aronow WS, Timmermans R, Jain D, Cooper HA, Frishman WH, Menon V, et al. Trends in coronary angiography, revascularization, and outcomes of cardiogenic shock complicating non-ST-elevation myocardial infarction. *Am J Cardiol*. 2016;117:1–9.

27. Rashid M, Fischman DL, Martinez SC, Capers Q, Savage M, Zaman A, Curzen N, Ensor J, Potts J, Mohamed MO, et al. Temporal trends and predictors of time to coronary angiography following non-ST-elevation acute coronary syndrome in the USA. *Coron Artery Dis*. 2019;30:159–170.

28. Birkhead JS, Weston CFM, Chen R. Determinants and outcomes of coronary angiography after non-ST-segment elevation myocardial infarction: a cohort study of the Myocardial Ischaemia National Audit Project (MINAP). *Heart*. 2009;95:1593–1599.

29. Masoudi FA, Ponirakis A, de Lemos JA, Jollis JG, Kremers M, Messenger JC, Moore JW, Moussa I, Oetgen WJ, Varosy PD, et al. Trends in U.S. cardiovascular care: 2016 report from 4 ACC National Cardiovascular Data Registries. *J Am Coll Cardiol*. 2017;69:1427–1450.

30. Bagai A, Al-Khalidi HR, Sherwood MW, Muñoz D, Roettig ML, Jollis JG, Granger CB. Regional systems of care demonstration project: Mission: Lifeline STEMI Systems Accelerator: design and methodology. *Am Heart J*. 2014;167:15–21.e3.

31. Rhudy JP, Bakitas MA, Hyrkäs K, Jablonski-Jaudon RA, Pryor ER, Wang HE, Alexandrov AW. Effectiveness of regionalized systems for stroke and myocardial infarction. *Brain Behav*. 2015;5:e00398.

32. Green JL, Jacobs AK, Holmes D, Chiswell K, Blanco R, Bates ER, French W, Kupas DF, Mears G, Roe M, et al. Taking the reins on systems of care for ST-segment–elevation myocardial infarction patients. *Circ Cardiovasc Interv*. 2018;11:e005706. DOI: 10.1161/CIRCINTERVENTIONS.117.005706.

33. Kontos MC, Gunderson MR, Zegre-Hemsey JK, Lange DC, French WJ, Henry TD, McCarthy JJ, Corbett C, Jacobs AK, Jollis JG. Prehospital activation of hospital resources (PreAct) ST-segment–elevation myocardial infarction (STEMI): a standardized approach to prehospital activation and direct to the catheterization laboratory for STEMI recommendations from the American Heart Association's Mission: Lifeline Program. *J Am Heart Assoc*. 2020;9:e011963. DOI: 10.1161/JAHA.119.011963.

34. Glickman SW, Delgado MK, Hirshon JM, Hollander JE, Iwashyna TJ, Jacobs AK, Kilaru AS, Lorch SA, Mutter RL, Myers SR, et al. Defining and measuring successful emergency care networks: a research agenda. *Acad Emerg Med*. 2010;17:1297–1305.

35. Nallamothu BK. A race for the base. *Circ Cardiovasc Qual Outcomes*. 2013;6:5–6.

36. Lloyd-Jones D, Adams RJ, Brown TM; Writing Group Members, Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G, Ferguson TB, et al. Executive summary: heart disease and stroke statistics—2010 update: a report from the American Heart Association. *Circulation*. 2010;121:948–954.

37. McManus DD, Gore J, Yarzebski J, Spencer F, Lessard D, Goldberg RJ. Recent trends in the incidence, treatment, and outcomes of patients with STEMI and NSTEMI. *Am J Med*. 2011;124:40–47.

38. Hall M, Dondo TB, Yan AT, Goodman SG, Bueno H, Chew DP, Brieger D, Timmis A, Batin PD, Deanfield JE, et al. Association of clinical factors and therapeutic strategies with improvements in survival following non-ST-elevation myocardial infarction, 2003–2013. *JAMA*. 2016;316:1073–1082.

39. Steinberg BA, French WJ, Peterson E, Frederick PD, Cannon CP; National Registry of Myocardial Infarction Investigators. Is coding for myocardial infarction more accurate now that coding descriptions have been clarified to distinguish ST-elevation myocardial infarction from non-ST elevation myocardial infarction? *Am J Cardiol*. 2008;102:513–517.

40. Veerasamy M, Edwards R, Ford G, Kirkwood T, Newton J, Jones D, Kunadian V. Acute coronary syndrome among older patients: a review. *Cardiol Rev*. 2015;23:26–32.

SUPPLEMENTAL MATERIAL

Table S1. Probability of percutaneous coronary intervention (PCI) within 3 days of admission.

	Coefficient	[95% Conf. Interval]	P>t
Regionalized	-0.002	-0.008,0.004	0.508
Year	0.005	0.004,0.006	<0.0005
Patient characteristics			
Female	-0.044	-0.047,-0.040	<0.0005
Age group			
40-64	0.071	0.058, 0.084	<0.0005
65-69	0.048	0.034, 0.062	<0.0005
70-74	0.035	0.021, 0.049	<0.0005
75-79	0.013	-0.002, 0.027	0.08
80-84	-0.017	-0.031, -0.002	0.022
85-99	-0.082	-0.096, -0.068	<0.0005
Race / ethnicity			
Black	-0.053	-0.060, -0.047	<0.0005
Hispanic	-0.025	-0.029, -0.020	<0.0005
Asian	-0.022	-0.028, -0.016	<0.0005
Comorbidities no presented			
Insurance			
Medicare	-0.026	-0.031, -0.021	<0.0005
Medicaid	-0.045	-0.051, -0.038	<0.0005
Indigent	0.018	0.006, 0.031	0.003
Self-pay	-0.018	-0.028, -0.009	<0.0005
Other	-0.014	-0.027, -0.001	0.041
Hospital characteristics			
ED volume (log)	-0.007	-0.009, -0.004	<0.0005
Critical access hospital	-0.014	-0.069, 0.041	0.617
Teaching hospital	-0.002	-0.008, 0.004	0.506
Government hospital	-0.004	-0.011, 0.003	0.227
Not for profit hospital	0.002	-0.003, 0.007	0.438
County population (log)	0.371	0.276, 0.466	<0.0005
Cath lab within hospital	0.311	0.307, 0.315	<0.0005

ED – emergency department
Multivariable regression also includes other race categories (Native American, other, invalid) and comorbidities (indicator variable for each Elixhauser category).

Figure S1. Probability of death for NSTEMI patients associated with regionalization.
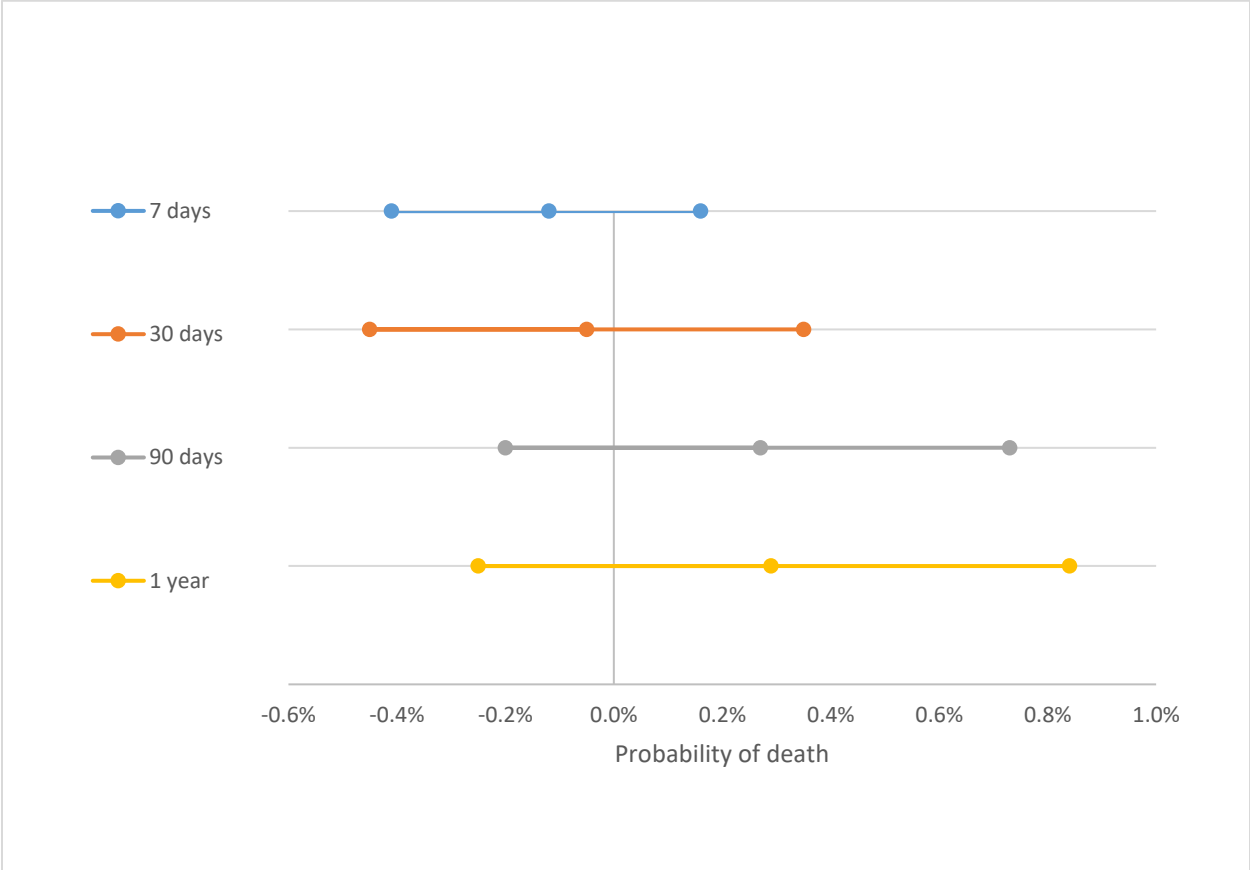
Point estimate and 95% confidence intervals for the association between regionalization status and risk of death at various time points. Values were calculated from a series of multivariable regressions with death as the dependent variable, as presented in Table 3.