Title
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Journal
Journal of the American Heart Association, 4(3)

ISSN
2047-9980

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Publication Date
2015-03-10

DOI
10.1161/jaha.114.001445

Peer reviewed

Differential Time Trends of Outcomes and Costs of Care for Acute Myocardial Infarction Hospitalizations by ST Elevation and Type of Intervention in the United States, 2001–2011

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***Background*—**Little is known whether time trends of in-hospital mortality and costs of care for acute myocardial infarction (AMI) differ by type of AMI (ST-elevation myocardial infarction [STEMI] vs. non-ST-elevation [NSTEMI]) and by the intervention received (percutaneous coronary intervention [PCI], coronary artery bypass grafting [CABG], or no intervention) in the United States.

***Methods and Results*—**We conducted a serial cross-sectional study of all hospitalizations for AMI aged 30 years or older using the Nationwide Inpatient Sample, 2001–2011 (1 456 154 discharges; a weighted estimate of 7 135 592 discharges). Hospitalizations were stratified by type of AMI and intervention, and the time trends of in-hospital mortality and hospital costs were examined for each combination of the AMI type and intervention, after adjusting for both patient- and hospital-level characteristics. Compared with 2001, adjusted in-hospital mortality improved significantly for NSTEMI patients in 2011, regardless of the intervention received (PCI odds ratio [OR] 0.68, 95% CI 0.56 to 0.83; CABG OR 0.57, 0.45 to 0.72; without intervention OR 0.61, 0.57 to 0.65). As for STEMI, a decline in adjusted in-hospital mortality was significant for those who underwent PCI (OR 0.83; 0.73 to 0.94); however, no significant improvement was observed for those who received CABG or without intervention. Hospital costs per hospitalization increased significantly for patients who underwent intervention, but not for those without intervention.

***Conclusions*—**In the United States, the decrease in in-hospital mortality and the increase in costs differed by the AMI type and the intervention received. These non-uniform trends may be informative for designing effective health policies to reduce the health and economic burdens of AMI. **(*J Am Heart Assoc*. 2015;4:e001445 doi: 10.1161/JAHA.114.001445)**

Key Words: acute myocardial infarction • hospital costs • in-hospital mortality • time trend

Both the incidence[1–11] of and in-hospital mortality[1–7,12–15] from acute myocardial infarctions (AMI), particularly ST-elevation AMI (STEMI), has declined in the United States during the last decade. Regardless of such improvements in disease management, AMI remains the leading cause of death in the United States.[12] Several studies have examined the time trend in the clinical outcome (eg, in-hospital mortality rate, 30-day mortality rate) and costs of care for AMI both at regional and national levels.[1–9,13–18] But to the best of our knowledge, no study has evaluated whether time trend differs by the type of AMI and the intervention the patients received.

In this context, we examined whether the time trends for in-hospital mortality and hospital costs for AMI hospitalizations differ by the type of AMI and the intervention performed during hospitalization from 2001 to 2011 using nationally representative data of AMI hospitalizations in the United States.

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Received September 16, 2014; accepted February 19, 2015.

Methods

Design and Settings

We conducted a serial cross-sectional analysis of hospitalizations from 2001 through 2011, using the Healthcare Cost and Utilization Project (HCUP) Nationwide Impatient Sample (NIS).[19] The NIS is a stratified, single-stage cluster sample, which represents one of the largest all-payer inpatient care data in the United States. NIS samples approximately 8 million hospital discharges per year from hospitals in those states participating in HCUP (eg, NIS 2011—1045 hospitals from 46 states). NIS offers a weight variable and study design variables that enable production of national estimates and their variances of all hospitalizations in the United States during the year. The institutional review boards of Massachusetts General Hospital (Boston, MA) and the University of Tokyo (Tokyo, Japan) approved this study.

Study Participants

All hospitalizations between 2001 and 2011 for patients aged 30 years or older with principal diagnosis of AMI were included in this study. We excluded patients with the hospital length of stay of zero (LOS) because they may have resulted from coding errors, our interest was in ordinary AMI patients who stayed longer than 1 day and the characteristics of the AMI patients with zero LOS (eg, those who were transferred to other institutions or who died within 24 hours of admission) are likely to be different from them, and technically we could not calculate the geometric mean of LOS when the data include zeros. We identified an AMI hospitalization using the *International Classification of Diseases—Ninth Revision, Clinical Modification* (*ICD-9-CM*) primary discharge diagnosis code for AMI (*ICD-9-CM* codes 410.x0 and 410.x1). We excluded *ICD-9-CM* codes 410.x2 which represents an AMI episode of care following the initial episode (eg, hospital transfers). The primary unit of analysis was a patient hospitalization, counted at discharge. We further classified the hospitalizations into 2 groups by the type of AMI: STEMI and NSTEMI. STEMI was identified by using codes for AMIs of the anterolateral wall (*ICD-9-CM* codes of 410.00 and 410.01), other anterior wall (410.10 and 410.11), inferolateral wall (410.20 and 410.21), inferoposterior wall (410.30 and 410.31), other inferior wall (410.40 and 410.41), other lateral wall (410.50 and 410.51), true posterior wall (410.60 and 410.61), or other specified sites (410.80 and 410.81). NSTEMI was identified using codes for subendocardial infarction (410.70 and 410.71) or AMI of unspecified site (410.90 and 410.91). Because each discharge has a unique primary discharge diagnosis code, all included in our sample were classified as either STEMI or NSTEMI. We also collected information about the intervention received (percutaneous coronary intervention [PCI] and coronary artery bypass grafting [CABG]) using the ICD-9-CM procedure code. We considered discharges as having undergone PCI during hospitalization when they had procedure codes of percutaneous transluminal coronary angioplasty or coronary atherectomy (00.66, 36.01, 36.02, 36.05), insertion of non-drug-eluting coronary artery stent(s) (36.06), or insertion of drug-eluting coronary artery stent(s) (36.07). We considered discharges as having undergone CABG during hospitalization when they had procedure codes of bypass anastomosis for heart revascularization (36.1x). Patients "without intervention" were defined as those having neither of PCI nor CABG during hospitalizations.

Outcome Measures

Primary outcomes of this study were the all-cause in-hospital mortality and costs per hospitalization for AMI. Secondary outcome measures included total costs per hospitalization and hospital length of stay (LOS). Although hospital charges per discharge (physician fees not included) were available in NIS, actual cost data were not available in NIS. Therefore, we used hospital-specific cost-to-charge ratios (CCRs) provided by HCUP and converted charges into costs.[20] When hospital-specific CCRs were not available, we used group average CCRs instead. The hospital accounting reports collected by the Centers for Medicare and Medicaid Services were used to obtain CCR information. The cases without any CCR information were excluded from the analyses (missing data in <10% of eligible cases), and the data were appropriately reweighted to calculate the national estimates of the costs, as suggested by the HCUP.[20] To facilitate direct comparisons between years for hospital costs, we converted all hospital costs to 2011 US dollars using the Consumer Price Index (CPI).[21]

Other Variables

We collected information about both patient- and hospital-level characteristics that are associated with the mortality and costs of care, and used them as adjustment variables in our regression models. The collected patient characteristics include age at admission, gender, primary health insurance type, hospitalization source, and comorbidities. We did not include race/ethnicity in our analyses because the data were missing for quite a large portion of units (26% missing in 2001), and the race/ethnicity information in the HCUP data was considered to be missing not at random. Age at admission was categorized by 10 years. Health insurance type was categorized as Medicaid, Medicare, private, or others including the uninsured. Hospitalization source was dichotomized into elective hospitalization or not. Comorbidities were assessed using *Clinical Classifications Software* (CCS) developed by AHRQ based on the methods by Elixhauser et al,[22] and all comorbidities included in the Elixhauser Comorbidity Index were adjusted except congestive heart failure. The hospital factors include bed size, hospital ownership, hospital region, and a category made of urban/rural distinction and teaching status. With regard to hospital characteristics, bed size was categorized as small, medium, or large based on the number of hospital beds using cut-off points specific to the hospital's region, location, and teaching status. Ownership of the hospital was grouped as government nonfederal, private non-profit, and private investor-own. Hospital regions consist of Northeast, Midwest, South, and West. Hospital location (urban or rural) and teaching status were jointly categorized as rural, urban non-teaching, and urban teaching.

Statistical Analyses

All analyses used SAS-callable SUDAAN, version 11.0 (Research Triangle Institute, Research Triangle Park, NC) to obtain appropriate variance estimations that accounted for the complex survey sampling design. We calculated AMI hospitalization incidence rates (the number of estimated hospitalizations per 1000 populations) using the population estimates.[23] Poisson regression was used to calculate *P* values for the trend (P_{trend}) for the incidence rates. The proportion of STEMI among all AMI hospitalizations was calculated, and the time trend was assessed using the logistic regression models using the year indicator as continuous variable. Weighted estimates of patient and hospital characteristics for each year were described for all AMI discharges, and also separately for STEMI and NSTEMI cases. We also calculated the proportion of cases with PCI and CABG for STEMI and NSTEMI hospitalizations. Logistic regression analyses with year variable used as continuous were used to assess the time trends of the proportions of PCI and CABG use.

Next, we examined the trends of in-hospital mortality stratified by the type of AMI and the intervention received. We classified AMI hospitalizations into 6 groups: (1) STEMI with PCI, (2) STEMI with CABG, (3) STEMI without intervention, (4) NSTEMI with PCI, (5) NSTEMI with CABG, and (6) NSTEMI without intervention. We evaluated both unadjusted and adjusted time trend by fitting logistic regression models with the year indicator used as a continuous variable. The patient- and hospital-level characteristics adjusted in the evaluation of the adjusted association are listed in Other Variables. In order to account for the clustering of the hospitalizations at hospital-level, we used generalized estimating equations (GEE) with logistic link function. An exchangeable working correlation structure was selected, as this correlation matrix is most widely used for health data and any permutation is valid.[24]

We also examined the temporal trends of hospital costs per hospitalization. Because hospital costs per hospitalization were not normally distributed, we log-transformed the costs per hospitalization, took the average of the logarithmic values, and then back-transformed the average, calculating a geometric mean. We then constructed linear regression models with log-transformed costs as the outcome variable to estimate the percent changes of hospital costs per hospitalization from 2001. We used similar methods for the analysis of the temporal trends of LOS.

We also estimated aggregate national hospital costs on AMI hospitalizations in the United States adjusted for CPI by means of aggregating all the CPI-adjusted costs of all AMI hospitalizations for each year.

Results

From 2001 through 2011, we identified a total of 1 456 154 patient discharges of AMI in the United States, corresponding to a weighted estimate of 7 135 592 discharges. Characteristics of the hospitalized patients with AMI over the 11-year period are presented in Table 1. There was missing information for each demographic variable as follows: 158 (0.01%) missing gender, 2608 (0.2%) missing payer, 139 082 (9.6%) missing type of admission, 5969 (0.4%) missing bed size and location/teaching status, and 17 799 (1.2%) missing ownership of hospital. There was no missing value with regard to age and hospital region.

Incidence

The overall rate of AMI hospitalizations declined significantly during the study period (4.5 per 1000 populations in 2001 to 3.2 per 1000 populations in 2011; 29% decrease; P_{trend}<0.001, Table 1). The proportion of STEMI among AMI hospitalizations also decreased (40.2% in 2001 to 26.9% in 2011; 33% decrease; P_{trend}<0.001). In more recent years, patients hospitalized for AMI were more likely to be male, less likely to be admitted as elective hospitalization, more likely to be admitted to private investor-owned hospitals, and less likely to be admitted to rural hospitals.

Use of PCI and CABG for AMI

The weighted proportion of PCI and CABG use was calculated and shown in Table 2. During the study period, the use of PCI increased significantly for both the STEMI (75% increase; P_{trend}<0.001) and NSTEMI patients (54% increase; P_{trend}< 0.001). By contrast, the CABG use decreased for both STEMI (39% decrease; P_{trend}<0.001) and NSTEMI (14% decrease; P_{trend}=0.005). Both the proportion of PCI use and the rate of increase in PCI use among STEMI hospitalizations were greater compared with those among NSTEMI hospitalizations.

In-Hospital Mortality

We observed differential time trends of unadjusted in-hospital mortality by the type of AMI and the type of intervention (Table 3). For STEMI, in-hospital mortality increased among those who did not receive intervention (20% increase, P_{trend}<0.001). On the other hand, the mortality did not change significantly among those who received PCI (3.5% increase, P_{trend}=0.12) or CABG (1.6% decrease, P_{trend}=0.14). Among

Table 1. Patient and Hospital Characteristics of US Adults 30 Years or Older Hospitalized for Acute Myocardial Infarction, 2000–2011

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	P_{trend}*
Unweighted sample, n	147 587	151 171	150 131	136 881	129 655	132 811	121 067	126 316	121 060	116 631	122 844	
Weighted sample, n	738 365	730 786	718 838	664 507	635 145	647 880	599 749	619 657	609 417	582 861	588 387	
Incidence rates of AMI hospitalizations per 1000 population	4.5	4.4	4.2	3.9	3.7	3.7	3.4	3.5	3.4	3.2	3.2	<0.001
STEMI among AMI hospitalization, unweighted %	59 363 (40.2%)	59 251 (39.1%)	56 116 (37.3%)	47 232 (34.6%)	43 056 (33.1%)	44 546 (33.4%)	37 631 (31.0%)	37 670 (29.8%)	34 186 (28.2%)	32 626 (28.0%)	33 114 (26.9%)	<0.001
Patient variables												
Age, mean, year (SD)	68.4 (14.0)	68.2 (14.2)	68.1 (14.3)	68.2 (14.3)	68.2 (14.5)	67.6 (14.4)	67.7 (14.5)	67.9 (14.5)	67.5 (14.4)	67.5 (14.4)	67.7 (14.3)	0.64
Female gender, unweighted n (weighted %)	60 665 (41.1%)	61 980 (41.1%)	61 425 (41.0%)	55 922 (40.8%)	52 840 (40.8%)	52 810 (39.9%)	48 852 (40.4%)	50 977 (40.4%)	47 758 (39.5%)	46 154 (39.6%)	48 373 (39.4%)	<0.001
Health insurance, unweighted n (weighted %)												
Medicare	87 078 (59.1%)	89 234 (59.3%)	89 242 (59.7%)	80 398 (58.8%)	76 738 (59.3%)	75 492 (57.1%)	68 328 (56.6%)	71 087 (56.4%)	67 502 (56.1%)	65 162 (55.9%)	70 433 (57.6%)	<0.001
Medicaid	6630 (4.5%)	6707 (4.5%)	7492 (5.0%)	6601 (4.8%)	6664 (5.1%)	6515 (4.9%)	5980 (5.0%)	6861 (5.4%)	7101 (5.9%)	7681 (6.6%)	7651 (6.3%)	<0.001
Private	44 675 (30.4%)	45 138 (29.8%)	42 879 (28.5%)	39 067 (28.6%)	36 229 (28.0%)	39 038 (29.4%)	35 598 (29.5%)	36 515 (29.0%)	34 258 (28.2%)	32 317 (27.8%)	32 493 (26.5%)	<0.001
Others	8809 (5.9%)	9848 (6.5%)	10 267 (6.8%)	10 707 (7.7%)	9885 (7.6%)	11 586 (8.6%)	10 927 (8.9%)	11 642 (9.2%)	11 936 (9.8%)	11 255 (9.7%)	11 900 (9.7%)	<0.001
Admission Type—Elective, unweighted n (weighted %)	12 790 (9.5%)	11 613 (8.4%)	13 201 (9.7%)	11 244 (8.9%)	8875 (7.8%)	10 707 (8.7%)	9023 (8.2%)	8053 (7.0%)	6219 (5.6%)	7686 (7.3%)	6960 (6.3%)	<0.001
Hospital variables												
Bed size, unweighted n (weighted %)												
Small	13 769 (9.2%)	15 543 (9.6%)	15 198 (9.6%)	14 830 (9.9%)	9474 (7.2%)	15 606 (11.4%)	12 631 (9.1%)	12 870 (10.0%)	10 273 (8.5%)	12 293 (9.7%)	11 638 (9.4%)	0.97
Medium	35 165 (23.4%)	35 957 (24.0%)	37 116 (24.2%)	33 046 (23.1%)	31 180 (24.0%)	32 499 (24.5%)	29 494 (24.5%)	28 989 (22.5%)	25 205 (21.4%)	24 237 (20.9%)	27 535 (23.6%)	0.42
Large	98 653 (67.5%)	99 671 (66.3%)	97 746 (66.2%)	89 005 (67.0%)	89 001 (68.9%)	84 339 (64.1%)	78 795 (66.3%)	84 337 (67.4%)	83 368 (70.1%)	78 554 (69.4%)	82 168 (67.0%)	0.49
Ownership of hospital, unweighted n (weighted %)												
Government, nonfederal	14 983 (10.0%)	13 994 (9.1%)	17 016 (11.1%)	15 187 (10.7%)	16 145 (11.5%)	13 103 (9.7%)	14 671 (11.7%)	15 328 (11.0%)	11 729 (9.7%)	12 602 (11.1%)	10 200 (8.1%)	0.86
Private, non-profit	112 612 (79.2%)	120 350 (80.6%)	111 414 (76.6%)	103 560 (77.6%)	94 693 (75.1%)	97 854 (76.1%)	88 826 (75.3%)	92 556 (74.2%)	91 908 (77.1%)	86 443 (74.8%)	93 852 (77.5%)	0.11

Continued

Table 1. Continued

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	P_{trend}*
Private, investor-own	17 177 (10.8%)	16 168 (10.3%)	19 310 (12.2%)	16 285 (11.7%)	18 027 (13.4%)	19 988 (14.2%)	15 525 (13.0%)	18 312 (14.8%)	15 209 (13.2%)	16 039 (14.1%)	17 289 (14.4%)	0.03
Region, unweighted n (weighted %)												
Northeast	31 587 (21.7%)	31 498 (22.6%)	31 393 (21.3%)	28 796 (20.8%)	27 396 (21.6%)	24 985 (20.3%)	22 081 (20.3%)	22 434 (18.0%)	22 761 (19.7%)	22 785 (19.7%)	22 394 (18.7%)	0.18
Midwest	30 285 (22.2%)	32 016 (21.5%)	33 790 (23.3%)	29 893 (23.4%)	28 130 (22.0%)	29 225 (23.0%)	27 991 (24.0%)	30 148 (24.6%)	27 346 (22.5%)	29 014 (25.1%)	27 789 (22.2%)	0.54
South	62 269 (40.8%)	61 255 (39.2%)	61 507 (39.2%)	54 938 (38.6%)	52 253 (39.9%)	56 728 (40.8%)	48 466 (38.8%)	52 418 (40.5%)	50 079 (41.3%)	43 147 (37.5%)	49 851 (40.2%)	0.99
West	23 446 (15.3%)	26 402 (16.6%)	23 441 (16.1%)	23 254 (17.3%)	21 876 (16.5%)	21 873 (15.9%)	22 529 (16.9%)	21 316 (16.8%)	20 874 (16.5%)	21 685 (17.7%)	22 810 (18.9%)	0.28
Location/teaching status, unweighted n (weighted %)												
Rural	20 775 (14.4%)	20 160 (13.7%)	18 472 (13.6%)	14 512 (11.2%)	13 399 (10.7%)	11 983 (9.5%)	13 517 (10.8%)	14 062 (11.0%)	12 063 (9.8%)	14 249 (11.3%)	10 518 (9.2%)	0.003
Urban nonteaching	64 892 (41.9%)	65 739 (42.5%)	66 250 (42.7%)	60 638 (43.9%)	61 874 (46.8%)	57 116 (41.5%)	51 857 (42.3%)	55 873 (44.8%)	50 533 (43.6%)	50 072 (43.5%)	53 060 (42.8%)	0.76
Urban teaching	61 920 (43.7%)	65 272 (43.8%)	65 338 (43.7%)	61 731 (44.8%)	54 382 (42.5%)	63 345 (49.0%)	55 546 (46.9%)	56 261 (44.2%)	56 250 (46.6%)	50 763 (45.3%)	57 763 (47.9%)	0.26

AMI indicates acute myocardial infarction; SD, standard deviation; STEMI, ST-elevation acute myocardial infarction; US, United States.
*P_{trend} was calculated by Poisson regression for incident rate of hospitalization, and logistic regression for categorical outcomes.

Table 2. Weighted Proportion of STEMI/NSTEMI Hospitalizations by Type of Intervention (Only PCI, CABG, and Without Intervention), 2001–2011

		2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	
	Unweighted n	Weighted % Among STEMI or NSTEMI											P_{trend}*
STEMI													
Only PCI	285 799	43.7%	46.7%	50.3%	53.7%	57.9%	62.3%	65.4%	69.7%	73.0%	75.3%	76.6%	<0.001
CABG	46 303	10.9%	11.1%	10.6%	10.3%	9.7%	9.9%	9.2%	8.2%	8.2%	6.7%	6.7%	<0.001
Without intervention	152 689	45.4%	42.2%	39.2%	36.0%	32.4%	27.8%	25.4%	22.1%	18.8%	18.0%	16.8%	<0.001
NSTEMI													
Only PCI	278 784	22.0%	22.6%	24.6%	27.2%	28.9%	31.3%	29.8%	30.8%	33.0%	32.6%	33.9%	<0.001
CABG	95 007	10.5%	10.7%	10.2%	9.8%	9.3%	10.1%	9.4%	9.3%	9.9%	9.3%	9.0%	0.005
Without intervention	597 572	67.6%	66.7%	65.2%	63.0%	61.9%	58.6%	60.9%	59.9%	57.2%	58.1%	57.1%	<0.001

CABG indicates coronary artery bypass grafting; CI, confidence interval; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.
*P_{trend} was calculated using logistic regression models with a continuous year variable as the independent variable.

NSTEMI cases, in-hospital mortality decreased significantly, especially among those who did not receive intervention (29% decrease; P_{trend}<0.001) and those who underwent CABG (41% decrease; P_{trend}<0.001). We did not find a systematic pattern as to the in-hospital mortality among NSTEMI patients who received PCI (16% decrease, P_{trend}=0.29).

Table 3. Unadjusted Trend of in-Hospital Mortality and Geometric Means of Hospital Costs, and Hospital Length of Stay, by STEMI/NSTEMI and PCI/CABG Use

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	P_{trend}*
In-hospital mortality, %												
STEMI with only PCI	3.40	3.33	3.12	3.05	3.21	3.14	3.32	3.48	3.41	3.35	3.52	0.12
STEMI with CABG	5.79	5.23	5.41	5.43	6.23	5.13	4.92	5.04	5.15	4.53	5.70	0.14
STEMI without intervention	12.43	12.96	13.01	12.92	13.18	12.94	14.52	14.57	15.21	14.51	14.91	<0.001
NSTEMI with only PCI	1.73	1.69	1.47	1.59	1.48	1.52	1.58	1.64	1.71	1.52	1.45	0.29
NSTEMI with CABG	4.97	4.77	4.66	4.31	4.30	3.72	3.96	3.59	3.60	2.97	2.91	<0.001
NSTEMI without intervention	8.87	8.79	8.64	8.49	8.05	7.57	6.88	6.96	6.47	6.33	6.26	<0.001
Hospital costs, dollars in 2011												
STEMI with only PCI	17 182	18 230	18 820	20 605	20 661	20 266	19 729	19 917	19 661	19 782	19 614	<0.001
STEMI with CABG	36 923	38 635	40 097	41 992	43 968	42 777	44 962	44 919	45 282	45 647	45 935	<0.001
STEMI without intervention	8746	9207	9196	9368	9077	9242	9660	9917	9969	10,183	10,246	<0.001
NSTEMI with only PCI	15 636	16 519	17 776	19 983	19 874	19 342	18 532	18 954	18 607	18 766	18 733	<0.001
NSTEMI with CABG	35 700	36 456	39 278	41 338	42 319	40 959	42 746	41 885	42 428	42 652	43 182	<0.001
NSTEMI without intervention	7837	8220	8553	8859	8701	8866	8698	8771	8627	8617	8474	<0.001
Hospital length of stay, days												
STEMI with only PCI	3.57	3.56	3.50	3.46	3.37	3.29	3.27	3.22	3.19	3.14	3.07	<0.001
STEMI with CABG	9.42	9.38	9.39	9.33	9.52	9.34	9.57	9.62	9.55	9.31	9.31	0.69
STEMI without intervention	3.47	3.51	3.44	3.43	3.39	3.37	3.43	3.48	3.48	3.40	3.32	0.09
NSTEMI with only PCI	3.14	3.12	3.21	3.17	3.04	2.94	2.85	2.88	2.91	2.90	2.86	<0.001
NSTEMI with CABG	10.03	9.86	10.09	10.44	10.45	10.15	10.46	10.31	10.25	9.95	10.31	0.22
NSTEMI without intervention	3.84	3.81	3.85	3.78	3.75	3.68	3.55	3.60	3.48	3.39	3.27	<0.001

CABG indicates coronary artery bypass grafting; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.
*P_{trend} was calculated using logistic regression models for mortality and linear regression models for continuous outcome variables.

Table 4. Adjusted* Trend of in-Hospital Mortality by STEMI/NSTEMI and PCI/CABG Use

		2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
	Unweighted n (%)†	Odds Ratio (95% CI) Compared to 2001										
STEMI with only PCI	253,624 (88.7%)	Ref.	0.95 (0.84 to 1.06)	0.95 (0.84 to 1.07)	0.93 (0.82 to 1.06)	0.93 (0.83 to 1.06)	0.90 (0.80 to 1.01)	0.92 (0.82 to 1.04)	0.91 (0.81 to 1.02)	0.88 (0.77 to 0.99)	0.86 (0.76 to 0.98)	0.83 (0.73 to 0.94)
STEMI with CABG	40,322 (87.1%)	Ref.	0.98 (0.80 to 1.20)	1.06 (0.88 to 1.29)	0.99 (0.81 to 1.20)	1.11 (0.89 to 1.39)	0.87 (0.70 to 1.09)	0.85 (0.68 to 1.06)	0.82 (0.65 to 1.04)	0.92 (0.73 to 1.16)	0.80 (0.62 to 1.04)	0.92 (0.72 to 1.19)
STEMI without intervention	128,741 (84.3%)	Ref.	0.94 (0.88 to 1.01)	1.00 (0.93 to 1.07)	0.96 (0.89 to 1.03)	0.91 (0.84 to 0.98)	0.86 (0.80 to 0.94)	0.94 (0.86 to 1.03)	0.99 (0.90 to 1.08)	0.99 (0.89 to 1.09)	0.93 (0.84 to 1.03)	0.98 (0.88 to 1.09)
NSTEMI with only PCI	248,827 (89.3%)	Ref.	1.10 (0.92 to 1.30)	0.94 (0.79 to 1.13)	0.96 (0.80 to 1.15)	0.85 (0.71 to 1.02)	0.89 (0.76 to 1.06)	0.91 (0.76 to 1.09)	0.90 (0.75 to 1.08)	0.89 (0.74 to 1.08)	0.76 (0.63 to 0.91)	0.68 (0.56 to 0.83)
NSTEMI with CABG	83,905 (88.3%)	Ref.	1.08 (0.89 to 1.31)	1.09 (0.90 to 1.32)	0.96 (0.79 to 1.16)	0.95 (0.78 to 1.16)	0.76 (0.62 to 0.94)	0.82 (0.67 to 0.99)	0.76 (0.62 to 0.94)	0.79 (0.66 to 0.95)	0.66 (0.53 to 0.82)	0.57 (0.45 to 0.72)
NSTEMI without intervention	522,220 (87.4%)	Ref.	0.91 (0.86 to 0.96)	0.93 (0.88 to 0.98)	0.88 (0.83 to 0.93)	0.82 (0.77 to 0.87)	0.74 (0.70 to 0.79)	0.67 (0.63 to 0.71)	0.67 (0.63 to 0.71)	0.63 (0.59 to 0.68)	0.63 (0.59 to 0.67)	0.61 (0.57 to 0.65)

CABG, coronary artery bypass grafting; CI, confidential interval; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; Ref, reference; STEMI, ST-elevation myocardial infarction.
*Adjusted for patient-level characteristics (ie, age category, gender, primary payer, admission source, and all comorbidity variables from Elixhauser Comorbidity Index but the variable for congestive heart failure) and hospital-level characteristics (hospital bed size, ownership of the hospital, hospital regions, and the variable for hospital location and teaching-status) in multiple regressions stratified by STEMI/NSTEMI and PCI/CABG use.
†Number of observations in each regression and the proportion in the subgroup was presented.

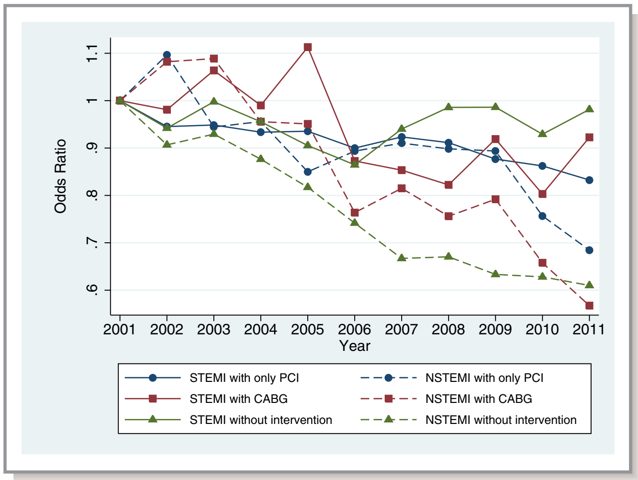

Figure 1. Temporal trends of in-hospital mortality for acute myocardial infarction hospitalizations in the United States by ST-elevation/non-ST-elevation and percutaneous coronary intervention/cardiac bypass graft stenting use. Year 2001 was used as the reference. CABG indicates coronary artery bypass grafting; PCI, percutaneous coronary intervention; STEMI, non-ST-elevation myocardial infarction.

After controlling for both patient- and hospital-level characteristics, we found that in-hospital mortality improved dramatically among NSTEMI patients regardless of the type of treatments they received. The patient outcomes improved for those patients who received PCI (OR 0.68, 95% CI 0.56 to 0.83), CABG (OR 0.57, 95% CI 0.45 to 0.72), or without intervention (OR 0.61, 95% CI 0.57 to 0.65) (Table 4 and Figure 1). As for STEMI patients, adjusted in-hospital mortality improved for those who received PCI (OR 0.83, 95% CI 0.73 to 0.94), but no significant improvement was seen for those who underwent CABG (OR 0.92, 95% CI 0.72 to 1.19) or those without intervention (OR 0.98, 95% CI 0.88 to 1.09).

Hospital Costs per Hospitalization

The trends in hospital costs were assessed using unadjusted (Table 3) and adjusted analyses (Table 5 and Figure 2). From 2001 to 2011, the hospital costs increased significantly across the subgroups. In the adjusted analyses, the increases in geometric means in 2011 compared with those in 2001 were larger among those with PCI or CABG than among those without intervention. The largest increase was found among STEMI hospitalizations that underwent CABG (20.7% increase; 95% CI, 14.6% to 27.1%).

Length of Stay

The LOS of AMI hospitalizations decreased, especially among those with PCI or those without intervention (eg, STEMI with PCI: 18.3% decrease, 95% CI, −20.5% to −16.1%). The decrease of LOS among those with CABG appeared smaller, and the trend was not statistically significant among NSTEMI hospitalization that underwent CABG (1.2% decrease, 95% CI, −4.5% to 2.3%) (Table 6).

Aggregate National Hospital Costs

The aggregated national hospital costs in the United States are illustrated in Table 7. After adjusting for the inflation, hospital costs for AMI hospitalizations decreased nationally from $12.4 billion in 2001 to $11.3 billion in 2011 (9% decrease).

Discussion

By using a large, nationally representative database of US hospitalizations from 2001 to 2011, we found that differential time trends of in-hospital mortality and hospital costs by the type of AMI and the type of intervention received. Most notably, adjusted in-hospital mortality declined significantly for NSTEMI regardless of the type of intervention received. In contrast, among STEMI patients, the improvement in in-hospital mortality was statistically significant only for those who underwent PCI, and no improvement was observed for those who received CABG or those without any intervention. Hospital costs increased significantly for those who received intervention; the rate of increase in hospital costs was most prominent among those patients who received CABG.

Previous studies have investigated the temporal trends of mortality and hospital costs for AMI patients. An analysis using the Kaiser Permanente Northern California dataset reported that 30-day mortality of NSTEMI patients decreased, whereas the mortality of STEMI patients did not improve.[4] Their sample was not a nationally representative sample of the US population, and the patients who underwent PCI and those who received CABG were not assessed separately. They also did not evaluate the cost data. Movahed et al examined the in-hospital mortality for STEMI and NSTEMI patients using the HCUP NIS datasets,[10,11,15,16] but they did not stratify their analysis by the intervention received. Zhao and colleagues compared hospital costs by the intervention performed using a dataset of commercially insured individuals in the United States.[25] Their data were again not a nationally representative sample, and they did not look into the time trends of hospital costs. To the best of our knowledge, this is the first study showing that the trends of in-hospital mortality and hospital costs differ by type of AMI and intervention received during hospitalization.

There are multiple possible reasons for the observed decrease in mortality for NSTEMI without intervention and NSTEMI who underwent CABG. Consistent improvement in primary and secondary prevention of AMI—eg, appropriate prescription of aspirin, β-blockers, and statins[26]—may affect

Table 5. Adjusted* Trend of Geometric Means of Hospital Costs by STEMI/NSTEMI and PCI/CABG Use

		2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
	n (%)[†]	Odds Ratio (95% CI) Compared to 2001										
STEMI with only PCI	234,627 (82.1%)	Ref.	+7.0% (2.6 to 11.6%)	+10.9% (5.2 to 17.0%)	+18.6% (12.4 to 25.2%)	+19.8% (14.2 to 25.6%)	+17.5% (12.3 to 23.0%)	+12.3% (7.1 to 17.7%)	+14.4% (9.2 to 19.9%)	+11.2% (6.4 to 16.3%)	+7.3% (1.5 to 13.5%)	+10.0% (4.9 to 15.3%)
STEMI with CABG	36,682 (79.2%)	Ref.	+7.6% (3.4 to 12.0%)	+14.4% (8.6 to 20.5%)	+16.7% (11.0 to 22.6%)	+21.4% (15.7 to 27.5%)	+20.4% (14.5 to 26.6%)	+23.7% (18.0 to 29.8%)	+25.3% (19.2 to 31.7%)	+22.1% (16.1 to 28.3%)	+20.0% (12.4 to 28.2%)	+20.7% (14.6 to 27.1%)
STEMI without intervention	117,756 (77.1%)	Ref.	+4.8% (1.9 to 7.8%)	+4.1% (0.9 to 7.3%)	+3.7% (0.1 to 7.5%)	+1.9% (−1.4 to 5.2%)	+1.7% (−1.7 to 5.3%)	+2.3% (−1.6 to 6.4%)	+5.0% (1.1 to 9.0%)	+0.9% (−3.5 to 5.6%)	−1.8% (−6.4 to 3.0%)	+1.9% (−2.7 to 6.7%)
NSTEMI with only PCI	231,900 (83.2%)	Ref.	+7.3% (2.2 to 12.6%)	+16.2% (9.2 to 23.6%)	+25.0% (17.0 to 33.7%)	+24.2% (17.7 to 31.2%)	+23.6% (17.4 to 30.0%)	+15.7% (10.0 to 21.7%)	+18.3% (12.8 to 24.1%)	+15.0% (9.3 to 20.9%)	+9.3% (2.1 to 17.0%)	+10.5% (5.0 to 16.3%)
NSTEMI with CABG	77,578 (81.7%)	Ref.	+7.4% (3.6 to 11.4%)	+14.6% (9.1 to 20.3%)	+16.3% (11.3 to 21.6%)	+19.3% (14.5 to 24.2%)	+18.7% (13.1 to 24.6%)	+20.6% (15.5 to 25.8%)	+23.0% (18.1 to 28.1%)	+20.1% (15.3 to 25.1%)	+15.4% (9.1 to 22.0%)	+18.4% (13.3 to 23.7%)
NSTEMI without intervention	484,894 (81.1%)	Ref.	+5.4% (2.7 to 8.1%)	+9.8% (6.7 to 13.0%)	+9.6% (6.5 to 12.8%)	+9.3% (6.3 to 12.3%)	+7.6% (4.6 to 10.8%)	+4.5% (0.9 to 8.3%)	+6.4% (3.4 to 9.4%)	+1.8% (−1.4 to 5.1%)	−1.7% (−5.7 to 2.4%)	+0.5% (−2.6 to 3.7%)

CABG indicates coronary artery bypass grafting; CI, confidential interval; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; Ref, reference; STEMI, ST-elevation myocardial infarction.

*Adjusted for patient-level characteristics (ie, age category, gender, primary payer, admission source, and all comorbidity variables from Elixhauser Comorbidity Index but the variable for congestive heart failure) and hospital-level characteristics (hospital bed size, ownership of the hospital, hospital regions, and the variable for hospital location and teaching-status) in multiple regressions stratified by STEMI/NSTEMI and PCI/CABG use.

†Number of observations in each regression and the proportion in the subgroup was presented. The numbers in cost analyses were fewer than others due to the missingness with regard to cost-charge ratio; modified weight was used for cost analyses considering the missingness.

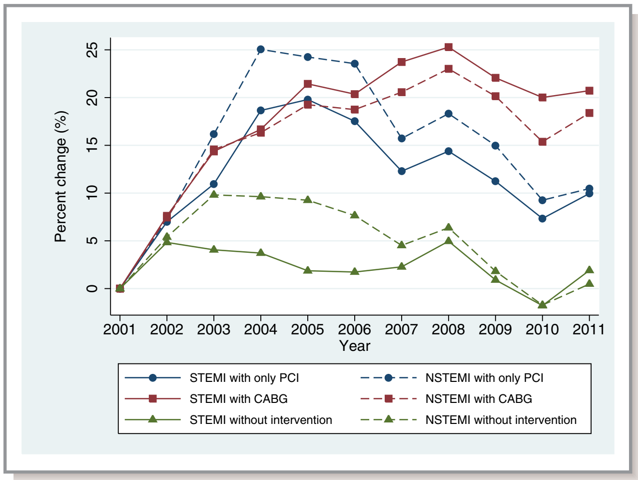

Figure 2. Temporal trends of percent change of hospital costs for acute myocardial infarction hospitalizations in the United States by ST-elevation/non-ST-elevation and percutaneous coronary intervention/cardiac bypass graft stenting use. Year 2001 was used as the reference. CABG indicates coronary artery bypass grafting; PCI, percutaneous coronary intervention; STEMI, non-ST-elevation myocardial infarction.

mortality especially among these populations. Alternatively, patients with NSTEMI in more recent study periods may include patients diagnosed only by highly sensitive troponin but with less severe myocardial damage.[4,14] This could have led to the observed lower mortality in NSTEMI in recent years. Additionally, the indication of CABG for NSTEMI may have changed over time and become highly selective, thereby leading to lower mortality.

The increased hospital costs among AMI patients may come from the increasing trend in general medical spending.[27] But the costs of devices and procedures supposedly increased faster than general medical spending considering the prominent increase of costs among those who received intervention. We observed that LOS was shortened for patients with PCI and for patients with CABG (albeit slowly) during the study period; however, the increased costs per unit of intervention might have outweighed the effect of shortened LOS on total costs per hospitalization.

At the national level, aggregate national hospital costs for AMI hospitalizations decreased by 9% during the study period (these figures did not include physician fees). The drastically decreased incidence of AMI hospitalizations was mostly offset by the increased hospital costs per hospitalization, especially for AMI with intervention. Curbing the increasing hospital costs per hospitalization may be critical to reduce total health expenditure spent on the treatment of AMI in the United States.

Our study has several limitations. First, as with any studies using administrative data, errors in recording diagnoses are possible. However, HCUP data are shown to be relatively accurate, and widely used to estimate diagnoses, procedures, and healthcare expenditures.[28,29] Second, due to advances in technology related to PCI, severe AMI cases who would have been treated with CABG a decade ago, are more likely to be treated by PCI in recent years. This does not affect a consistent improvement across the treatment type among NSTEMI patients, but it may explain non-significant improvement in mortality among the STEMI patients who underwent CABG. Third, the HCUP NIS contains discharge-level records, not patient-level records, and thus we were unable to identify multiple hospitalizations for each patient. Fourth, the lack of patient identifiers in the NIS precluded us from using other mortality measures such as 30-day mortality. Previous studies using data from MIDAS in New Jersey found that in-hospital declines in mortality were observed but the post-discharge AMI mortality in fact increased.[30] Our findings cannot be extrapolated to the other outcome measures of the AMI patients, but we believe that the national estimates of the in-hospital mortality over time are valuable information for clinicians and policy makers. Fifth, although we adjusted for both patient- and hospital-level characteristics in evaluating the change in in-hospital mortality and hospital costs, there may be unmeasured time-varying confounders. Sixth, the HCUP charges do not include physician fees, thereby leading to underestimation of total costs per AMI hospitalization. However, it is unlikely the proportion of physician fees out of total costs has increased over time differently across the type of AMI and the intervention received; therefore, this may not confound our findings. Lastly, due to the nature of HCUP NIS dataset, costs of care after discharges were unknown. Likosky and colleagues showed more rapid increase in expenditures occurring after discharge using data of fee-for-service Medicare beneficiaries.[31] Additional data and analyses are needed to obtain broader understanding about financial burden of AMI incidence.

This study has several important implications. Because AMI continues to be one of the major public health burdens in our healthcare system, the rising spending for AMI hospitalizations should encourage policy makers and health services researchers to develop more cost-effective approaches for the management of AMI. Identification and development of strategies for reducing the costs of AMI hospitalizations accompanied by interventions (ie, PCI and/or CABG) may be an effective approach to reducing the net financial burden of AMI on healthcare systems. For clinicians, the observed decline in the mortality in patients with NSTEMI is encouraging and supports the prior optimism that AMI morbidity and mortality can be prevented.

Conclusions

In summary, using a large nationally representative database of US hospitalizations in 2001–2011, we found that in-hospital

Table 6. Adjusted* Trend of Geometric Means of Length of Stay by STEMI/NSTEMI and PCI/CABG Use

	n (%)†	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
STEMI with only PCI	253,760 (88.8%)	Ref.	−0.5% (−2.7 to 1.7%)	−1.4% (−3.8 to 1.0%)	−3.0% (−5.2 to −0.8%)	−6.3% (−8.9 to −3.7%)	−7.7% (−10.2 to −5.2%)	−8.7% (−11.1 to −6.3%)	−10.9% (−13.3 to −8.5%)	−12.7% (−14.9 to −10.5%)	−15.5% (−17.6 to −13.3%)	−18.3% (−20.5 to −16.1%)
STEMI with CABG	40,410 (87.3%)	Ref.	+2.4% (−0.5 to 5.5%)	+5.5% (2.3 to 8.8%)	+2.7% (−0.4 to 5.8%)	+2.3% (−1.3 to 6.0%)	+1.3% (−2.3 to 4.7%)	+3.7% (−0.1 to 7.7%)	+2.6% (−1.3 to 6.7%)	+1.3% (−2.7 to 5.5%)	−0.7% (−4.5 to 3.3%)	−4.1% (−8.2 to 0.2%)
STEMI without intervention	128,937 (84.4%)	Ref.	+0.5% (−1.6 to 2.7%)	−2.9% (−5.0 to −0.8%)	−4.4% (−6.6 to −2.2%)	−6.2% (−8.4 to −3.9%)	−9.9% (−12.2 to −7.4%)	−10.9% (−13.2 to −8.5%)	−10.7% (−13.2 to −8.1%)	−13.8% (−16.4 to −11.1%)	−16.7% (−19.2 to −14.0%)	−18.1% (−20.9 to −15.1%)
NSTEMI with only PCI	248,942 (89.3%)	Ref.	−0.7% (−3.7 to 2.5%)	0.7% (−2.3 to 3.8%)	−2.4% (−5.7 to 0.9%)	−6.0% (−9.2 to −2.7%)	−8.6% (−11.6 to −5.4%)	−11.0% (−14.0 to −7.9%)	−12.2% (−15.5 to −8.9%)	−14.5% (−17.2 to −11.6%)	−17.4% (−20.3 to −14.4%)	−20.6% (−23.3 to −17.8%)
NSTEMI with CABG	84,087 (88.5%)	Ref.	+2.6% (−0.5 to 5.7%)	+6.5% (3.3 to 9.7%)	6.6% (3.5 to 9.9%)	5.0% (1.8 to 8.4%)	+2.8% (−0.9 to 6.6%)	+5.6% (2.4 to 8.9%)	+4.8% (1.5 to 8.2%)	+3.7% (0.8 to 6.8%)	−0.1% (−3.5 to 3.4%)	−1.2% (−4.5 to 2.3%)
NSTEMI without intervention	522,812 (87.5%)	Ref.	−0.0% (−1.6 to 1.5%)	+0.0% (−1.6 to 1.5%)	−2.7% (−4.3 to −1.1%)	−5.5% (−7.2 to −3.8%)	−10.0% (−11.6 to −8.4%)	−12.9% (−14.4 to −11.4%)	−12.9% (−14.5 to −11.2%)	−16.7% (−18.2 to −15.1%)	−20.2% (−21.7 to −18.7%)	−22.1% (−23.5 to −20.6%)

CABG indicates coronary artery bypass grafting; CI, confidential interval; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; Ref, reference; STEMI, ST-elevation myocardial infarction.
*Adjusted for patient-level characteristics (ie, age category, gender, primary payer, admission source, and all comorbidity variables from Elixhauser Comorbidity Index but the variable for congestive heart failure) and hospital-level characteristics (hospital bed size, ownership of the hospital, hospital regions, and the variable for hospital location and teaching-status) in multiple regressions stratified by STEMI/NSTEMI and PCI/CABG use.
†Number of observations in each regression and the proportion in the subgroup was presented.

Table 7. Aggregate National Hospital Costs on AMI Hospitalization, Adjusted for CPI, 2001–2011

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Aggregate national hospital costs, billion dollars (SE)	12.4 (0.9)	13.1 (1.0)	13.2 (0.9)	13.1 (1.0)	12.7 (0.9)	13.1 (0.9)	11.6 (0.8)	12.1 (0.8)	11.9 (0.8)	11.3 (0.7)	11.3 (0.7)

AMI indicates acute myocardial infarction; CPI, consumer price index; SE, standard error.

mortality decreased significantly for NSTEMI regardless of the type of treatment they received. By contrast, we found significant improvement only for STEMI with PCI; no significant improvement was observed for STEMI patients who received CABG and those without intervention. Hospital costs increased significantly for those who received intervention, and the rate of increase in hospital costs was most prominent among those patients who underwent CABG. These non-uniform temporal trends may be informative for designing effective health policies that reduce the health and economic burdens of AMI in the United States.

Acknowledgments

We would like to acknowledge Neil S. Wenger, MD, MPH (Division of General Internal Medicine & Health Services Research, David Geffen School of Medicine at University of California, Los Angeles, Los Angeles, California) for his comments. We thank Satoshi Toyokawa, PhD and Fumiaki Nakamura, MD, PhD (Department of Public Health/ Health Policy, Graduate School of Medicine, the University of Tokyo, Tokyo, Japan) for their technical support.

Sources of Funding

This study was supported by St. Luke's Life Science Institute, Tokyo, Japan. Dr Tsugawa is funded by Harvard University and Honjo International Scholarship Foundation.

Disclosures

None.

References

1. Khera S, Kolte D, Palaniswamy C, Mujib M, Aronow WS, Singh T, Gotsis W, Silverman G, Frishman WH. ST-elevation myocardial infarction in the elderly—temporal trends in incidence, utilization of percutaneous coronary intervention and outcomes in the United States. *Int J Cardiol*. 2013;168:3683–3690.
2. Kolte D, Khera S, Aronow WS, Mujib M, Palaniswamy C, Sule S, Jain D, Gotsis W, Ahmed A, Frishman WH, Fonarow GC. Trends in incidence, management, and outcomes of cardiogenic shock complicating ST-elevation myocardial infarction in the United States. *J Am Heart Assoc*. 2014;3:e000590 doi:10.1161/JAHA.113.000590.
3. Parikh NI, Gona P, Larson MG, Fox CS, Benjamin EJ, Murabito JM, O'Donnell CJ, Vasan RS, Levy D. Long-term trends in myocardial infarction incidence and case fatality in the National Heart, Lung, and Blood Institute's Framingham Heart study. *Circulation*. 2009;119:1203–1210.
4. Yeh RW, Sidney S, Chandra M, Sorel M, Selby JV, Go AS. Population trends in the incidence and outcomes of acute myocardial infarction. *N Engl J Med*. 2010;362:2155–2165.
5. Rosamond WD, Chambless LE, Heiss G, Mosley TH, Coresh J, Whitsel E, Wagenknecht L, Ni H, Folsom AR. Twenty-two-year trends in incidence of myocardial infarction, coronary heart disease mortality, and case fatality in 4 US communities, 1987-2008. *Circulation*. 2012;125:1848–1857.
6. 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.
7. Fang J, Alderman MH, Keenan NL, Ayala C. Acute myocardial infarction hospitalization in the United States, 1979 to 2005. *Am J Med*. 2010;123:259–266.
8. Towfighi A, Markovic D, Ovbiagele B. National gender-specific trends in myocardial infarction hospitalization rates among patients aged 35 to 64 years. *Am J Cardiol*. 2011;108:1102–1107.
9. Chen J, Normand SL, Wang Y, Drye EE, Schreiner GC, Krumholz HM. Recent declines in hospitalizations for acute myocardial infarction for Medicare fee-for-service beneficiaries: progress and continuing challenges. *Circulation*. 2010;121:1322–1328.
10. Movahed MR, Ramaraj R, Hashemzadeh M, Hashemzadeh M. Nationwide trends in the age adjusted prevalence of non-ST elevation myocardial infarction (NSTEMI) across various races and gender in the USA. *Acute Card Care*. 2010;12:58–62.
11. Movahed MR, Ramaraj R, Hashemzadeh M, Jamal MM, Hashemzadeh M. Rate of acute ST-elevation myocardial infarction in the United States from 1988 to 2004 (from the Nationwide Inpatient Sample). *Am J Cardiol*. 2009;104:5–8.
12. Miniño AM. Death in the United States, 2011. US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, 2013. http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.309.2559&rep=rep1&type=pdf. Accessed March 19, 2015.
13. Hines A, Stranges E, Andrews RM. Trends in hospital risk-adjusted mortality for select diagnoses by patient subgroups, 2000-2007. HCUP Statistical Brief #98, 2010.
14. 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.
15. Movahed MR, John J, Hashemzadeh M, Hashemzadeh M. Mortality trends for non-ST-segment elevation myocardial infarction (NSTEMI) in the United States from 1988 to 2004. *Clin Cardiol*. 2011;34:689–692.
16. Movahed MR, John J, Hashemzadeh M, Jamal MM, Hashemzadeh M. Trends in the age adjusted mortality from acute ST segment elevation myocardial infarction in the United States (1988–2004) based on race, gender, infarct location and comorbidities. *Am J Cardiol*. 2009;104:1030–1034.
17. Gibson CM, Pride YB, Frederick PD, Pollack CV Jr, Canto JG, Tiefenbrunn AJ, Weaver WD, Lambrew CT, French WJ, Peterson ED, Rogers WJ. Trends in reperfusion strategies, door-to-needle and door-to-balloon times, and in-hospital mortality among patients with ST-segment elevation myocardial infarction enrolled in the National Registry of Myocardial Infarction from 1990 to 2006. *Am Heart J*. 2008;156:1035–1044.
18. Nagamine M, Jiang HJ, Merrill CT. Trends in elderly hospitalizations, 1997–2004. HCUP Statistical Brief #14, 2006.
19. Agency for Healthcare Research and Quality. HCUP Databases. Healthcare Cost and Utilization Project (HCUP). Available at: www.hcup-us.ahrq.gov/nisoverview.jsp. Accessed August 30, 2014.

20. Agency for Healthcare Research and Quality. Cost-to-Charge Ratio Files. Healthcare Cost and Utilization Project (HCUP). Available at: http://www.hcup-us.ahrq.gov/db/state/costtocharge.jsp. Accessed August 30 2014.

21. Bureau of Labor Statistics. Consumer Price Index. Available at: http://www.bls.gov/cpi/. Accessed August 30 2014.

22. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care*. 1998;36:8–27.

23. US Census Bureau. Population Estimates. Available at: https://www.census.gov/popest/. Accessed August 30 2014.

24. Hanley JA, Negassa A, Edwardes MD, Forrester JE. Statistical analysis of correlated data using generalized estimating equations: an orientation. *Am J Epidemiol*. 2003;157:364–375.

25. Zhao ZX, Winget M. Economic burden of illness of acute coronary syndromes: medical and productivity costs. *BMC Health Serv Res*. 2011;11:35.

26. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, Dai S, Ford ES, Fox CS, Franco S, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Huffman MD, Judd SE, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Mackey RH, Magid DJ, Marcus GM, Marelli A, Matchar DB, McGuire DK, Mohler ER, Moy CS, Mussolino ME, Neumar RW, Nichol G, Pandey DK, Paynter NP, Reeves MJ, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Wong ND, Woo D, Turner MB. Heart disease and stroke statistics—2014 update: a report from the American Heart Association. *Circulation*. 2014;129:e28–e292.

27. Roehrig C, Turner A, Hughes-Cromwick P, Miller G. When the cost curve bent—pre-recession moderation in health care spending. *N Engl J Med*. 2012;367:590–593.

28. Sun BC, Emond JA, Camargo CA Jr. Direct medical costs of syncope-related hospitalizations in the United States. *Am J Cardiol*. 2005;95:668–671.

29. Hasegawa K, Tsugawa Y, Brown DFM, Mansbach JM, Camargo CA. Trends in bronchiolitis hospitalizations in the United States, 2000–2009. *Pediatrics*. 2013;132:28–36.

30. Kostis WJ, Deng Y, Pantazopoulos JS, Moreyra AE, Kostis JB. Trends in mortality of acute myocardial infarction after discharge from the hospital. *Circ Cardiovasc Qual Outcomes*. 2010;3:581–589.

31. Likosky DS, Zhou W, Malenka DJ, Borden WB, Nallamothu BK, Skinner JS. Growth in medicare expenditures for patients with acute myocardial infarction: a comparison of 1998 through 1999 and 2008. *JAMA Intern Med*. 2013;173:2055–2061.