Non-ST-Elevation Myocardial Infarction in the United States: Contemporary Trends in Incidence, Utilization of the Early Invasive Strategy, and In-Hospital Outcomes

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Background—There has been a paradigm shift in the definition of timing of early invasive strategy (EIS) for patients admitted with non-ST-elevation myocardial infarction (NSTEMI) in the last decade. Data on trends of EIS for NSTEMI and associated in-hospital outcomes are limited. Our aim is to analyze temporal trends in the incidence, utilization of early invasive strategy, and in-hospital outcomes of NSTEMI in the United States.

Methods and Results—We analyzed the 2002–2011 Nationwide Inpatient Sample databases to identify all patients ≥40 years of age with the principal diagnosis of acute myocardial infarction (AMI) and NSTEMI. Logistic regression was used for overall, age-, sex-, and race/ethnicity-stratified trend analysis. From 2002 to 2011, we identified 6 512 372 patients with AMI. Of these, 3 981 119 (61.1%) had NSTEMI. The proportion of patients with NSTEMI increased from 52.8% in 2002 to 68.6% in 2011 (adjusted odds ratio [OR; per year], 1.055; 95% confidence interval [CI], 1.054 to 1.056) in the overall cohort. Similar trends were observed in age-, sex-, and race/ethnicity-stratified groups. From 2002 to 2011, utilization of EIS at day 0 increased from 14.9% to 21.8% (P_{trend}<0.001) and utilization of EIS at day 0 or 1 increased from 27.8% to 41.4% (P_{trend}<0.001). Risk-adjusted in-hospital mortality in the overall cohort decreased during the study period (adjusted OR [per year], 0.976; 95% CI, 0.974 to 0.978).

Conclusions—There have been temporal increases in the proportion of NSTEMI and, consistent with guidelines, greater utilization of EIS. This has been accompanied by temporal decreases in in-hospital mortality and length of stay. (*J Am Heart Assoc*. 2014;3: e000995 doi: 10.1161/JAHA.114.000995)

Key Words: early invasive strategy • in-hospital mortality • non-ST-elevation myocardial infarction • temporal trends

A cute coronary syndromes (ACS) continue to be a major cause of morbidity and mortality.[1] Data from the United States and Europe have reported a decrease in the incidence of ST-elevation myocardial infarction (STEMI) with an increase

in non-ST-elevation myocardial infarction (NSTEMI) in the past decade.[2-6] Current 2012 American College of Cardiology/ American Heart Association (ACC/AHA) guidelines recommend early invasive strategy (EIS) for management of patients with NSTEMI and refractory angina or electrical or hemodynamic insufficiency (class IB), initially stabilized patients with NSTEMI, and high risk of clinical events (class IA). The early invasive approach (within 12 to 24 hours of presentation) to reduce ischemic complications is also recommended in initially stabilized high-risk patients with NSTEMI (class IIA).[7] The optimal timing of EIS has been debated and undergone a paradigm shift in the last decade. The transition from 48 hours to within 24 hours occurred after the publication of the Timing of Intervention in Acute Coronary Syndromes (TIMACS) trial in 2009.[8,9] However, there is a paucity of information with regard to the secular trends in utilization of EIS in patients with NSTEMI and how this may vary among different NSTEMI patient populations. Using a large nationwide administrative database, the present study aimed to analyze and describe age-, sex-, and race/ethnicity-specific

trends in the incidence, utilization of EIS, and in-hospital outcomes for NSTEMI in the United States from 2002 to 2011.

Methods

Data Source

Data were obtained from the 2002 to 2011 Nationwide Inpatient Sample (NIS) databases. The NIS, sponsored by the Agency for Healthcare Research and Quality as a part of the Healthcare Cost and Utilization Project (HCUP), is the largest publicly available all-payer inpatient care database in the United States. It contains discharge-level data from ≈8 million hospital stays from approximately 1000 hospitals designed to approximate a 20% stratified sample of all community hospitals in the United States. Criteria used for stratified sampling of hospitals include hospital ownership, bed size, teaching status, urban or rural location, and geographic region. Discharge weights are provided for each patient discharge record, which were used to obtain national estimates. Discharge weights are calculated for NIS data by first stratifying the NIS hospitals on the same variables used for creating the sample. A weight is then calculated for each stratum by dividing the number of universe discharges in that stratum (obtained from American Hospital Association data) by the number of NIS discharges in the stratum. Weighted estimates are calculated by uniformly applying stratum weights to the discharges according to the stratum from which the discharge was drawn. Weights are assigned to each discharge and are stored in each record in the data element, DISCWT. When the discharge weights are applied to the unweighted NIS data, the result is an estimate of the number of discharges for all inpatient discharges from community hospitals in the United States. This study was deemed exempt by the New York Medical College Institutional Review Board (Valhalla, NY) because HCUP-NIS is a public database with no personal identifying information.

Study Population

We used the International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM), codes 410.xx to identify all patients ≥40 years of age with the principal diagnosis of acute myocardial infarction (AMI; N=6 512 372). Patients with the principal diagnosis of NSTEMI were then identified using ICD-9-CM codes 410.7x (n=3 981 119). We chose the principal diagnosis because it is considered the primary reason for hospital admission. EIS was defined as coronary angiography (ICD-9-CM procedure codes 88.55, 88.66, 37.22, or 37.23) with or without revascularization (ie, percutaneous coronary intervention (PCI; ICD-9-CM

procedure codes 00.66, 36.01, 36.02, 36.05, 36.06 and 36.07) or coronary artery bypass graft surgery (CABG; ICD-9-CM procedure code 36.1x) on day 0 (considered within 24 hours of admission) or on days 0 or 1 (considered within 48 hours of admission).

Outcomes Measured

We initially studied the overall age-, sex-, and race/ethnicity-specific trends in the incidence of NSTEMI. We then examined the trends in utilization of the EIS in patients with NSTEMI. Our primary outcome of interest was all-cause, in-hospital mortality, defined as death during the hospitalization encounter in the NIS database. We used the average length of stay and total hospital cost as secondary outcomes. We analyzed the overall age-, sex-, and race/ethnicity-specific trends in utilization of the EIS, risk-adjusted in-hospital mortality, average length of stay, and total hospital cost in patients with NSTEMI. The NIS provides total charges, which reflect the amount a hospital billed for services, rather than actual costs or the amount a hospital received in payment. In this study, we used the HCUP Cost-to-Charge Ratio File developed by the Agency for Healthcare Research and Quality (AHRQ) to translate total charges into costs. Each file contains hospital-specific cost-to-charge ratios based on all-payer inpatient cost for nearly every hospital in the NIS databases. Cost information

Table 1. International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) and Clinical Classifications Software (CCS) Codes Used to Identify Comorbidities

Comorbidities	Source	Code(s)
Smoking	ICD-9-CM	V15.82, 305.1
Dyslipidemia	CCS	53
Coronary artery disease	ICD-9-CM	414.00-414.07
Family history of coronary artery disease	ICD-9-CM	V17.3
Previous myocardial infarction	ICD-9-CM	412
Previous transient ischemic attack/stroke	ICD-9-CM	V12.54
Previous percutaneous coronary intervention	ICD-9-CM	V45.82
Previous coronary artery bypass grafting	ICD-9-CM	V45.81
Carotid artery disease	ICD-9-CM	433.10
Atrial fibrillation	ICD-9-CM	427.31
Dementia	ICD-9-CM	290.xx, 294.1x, 294.2x, 294.8, 331.0-331.12, 331.82, 797

is obtained from the hospital accounting reports collected by the Centers for Medicare and Medicaid Services.

Patient and Hospital Characteristics

Baseline patient characteristics used included demographics (age, sex, race/ethnicity, primary expected payer, weekday versus weekend admission), 29 Elixhauser co-morbidities as defined by the AHRQ and other clinically relevant comorbidities (smoking, dyslipidemia, known coronary artery disease [CAD], family history of CAD, previous myocardial infarction [MI], previous transient ischemic attack or stroke, previous PCI, previous CABG, carotid artery disease, dementia, and atrial fibrillation). A list of ICD-9-CM and Clinical Classifications Software codes used to identify comorbidities and in-hospital procedures is provided in Table 1. Hospital characteristics, such as hospital region (Northeast, Midwest, South, and West), bed size (small, medium, and large), location (rural or urban), and teaching status were also included.

Statistical Analysis

Weighted data were used for all statistical analyses. For trend analysis, we used Mantel-Haenszel's chi-square (χ^2) test of linear association for categorical variables and linear regression for continuous variables. To assess whether the incidence of NSTEMI, utilization of EIS, or in-hospital mortality has changed over time, unadjusted and multivariable adjusted logistic regression models were constructed. Our independent variable, calendar year, was initially entered as a continuous variable in the regression models to obtain unadjusted and adjusted odds ratios (ORs; per year) for the temporal trends. To determine whether there was a temporal variability from year to year in the incidence of NSTEMI, utilization of EIS, or in-hospital mortality, we also evaluated calendar year as a categorical variable, with 2002 as the reference year. The regression models adjusted for all demographics (except sex and race/ethnicity for sex and race/ethnicity-specific trends, respectively), hospital characteristics, and all Elixhauser and other clinically relevant comorbidities. The methodology has been utilized in our previous analysis of NIS databases.[10,11] We graphically displayed the unadjusted and adjusted ORs and 95% confidence intervals (CIs) for incidence of NSTEMI, utilization of EIS for NSTEMI, or in-hospital mortality over time.

Statistical analysis was performed using IBM SPSS Statistics 20.0 (IBM Corp., Armonk, NY). All *P* values were 2 sided with a significance threshold of *P*<0.001 (a lower-than-usual *P*-value threshold was selected to correct for the effects of a large sample size as well as inflation of type I error because of repeated testing using a large
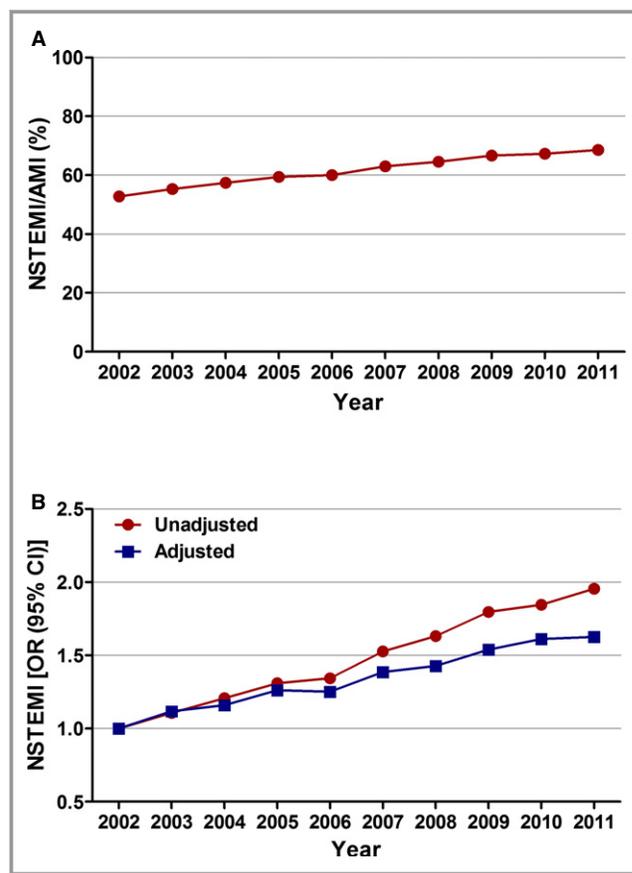
Figure 1. Temporal trends in incidence of non-ST-elevation myocardial infarction (STEMI). A, NSTEMI (%) was calculated as the number of patients with NSTEMI divided by the number of patients with acute myocardial infarction (AMI) per year×100; P_{trend}<0.001. B, Trends in NSTEMI presented as unadjusted and adjusted odds ratio and 95% confidence interval (CI) for each year relative to 2002 (reference year). Regression model adjusted for demographics, hospital characteristics, and 29 Elixhauser and other clinically relevant comorbidities. 95% CIs are depicted, but are too narrow to be visualized outside the marker width.

number of variables). Categorical variables are expressed as percentage and continuous variables as mean± SEM. OR, and 95% CI were used to report the results of logistic regression.

Results

Temporal Trends in NSTEMI

From 2002 to 2011, we identified 6 512 372 patients ≥40 years of age admitted with AMI. Of these, 3 981 119 (61.1%) had NSTEMI. Among patients with AMI, the proportion of those presenting with NSTEMI increased from 52.8% in 2002 to 68.6% in 2011 (P_{trend}<0.001). After adjusting for baseline demographics, hospital characteristics, and

Table 2. Adjusted Temporal Trends of Proportion of Non-ST-Elevation Myocardial Infarction: Overall Cohort, Age, Sex, and Race/Ethnicity Stratified

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Adjusted OR (Per Year)
Overall	1.00	1.12 (1.11 to 1.13)	1.16 (1.15 to 1.17)	1.26 (1.25 to 1.27)	1.25 (1.24 to 1.26)	1.39 (1.37 to 1.40)	1.43 (1.42 to 1.44)	1.54 (1.53 to 1.55)	1.61 (1.60 to 1.63)	1.63 (1.61 to 1.64)	1.055 (1.054 to 1.056)
Age, y											
40 to 64	1.00	1.10 (1.08 to 1.11)	1.17 (1.15 to 1.18)	1.26 (1.25 to 1.28)	1.24 (1.23 to 1.26)	1.35 (1.33 to 1.37)	1.36 (1.34 to 1.38)	1.48 (1.46 to 1.50)	1.50 (1.48 to 1.53)	1.50 (1.48 to 1.52)	1.045 (1.044 to 1.046)
65 to 74	1.00	1.12 (1.10 to 1.14)	1.17 (1.15 to 1.19)	1.26 (1.24 to 1.29)	1.25 (1.23 to 1.27)	1.46 (1.44 to 1.49)	1.41 (1.39 to 1.44)	1.54 (1.51 to 1.57)	1.63 (1.60 to 1.66)	1.65 (1.62 to 1.68)	1.056 (1.055 to 1.058)
≥75	1.00	1.14 (1.12 to 1.16)	1.15 (1.13 to 1.16)	1.26 (1.24 to 1.28)	1.27 (1.25 to 1.29)	1.39 (1.37 to 1.41)	1.52 (1.50 to 1.55)	1.62 (1.60 to 1.64)	1.74 (1.71 to 1.76)	1.80 (1.77 to 1.83)	1.066 (1.065 to 1.068)
Sex											
Men	1.00	1.12 (1.11 to 1.14)	1.16 (1.15 to 1.17)	1.25 (1.24 to 1.27)	1.22 (1.21 to 1.24)	1.33 (1.32 to 1.35)	1.37 (1.35 to 1.38)	1.46 (1.44 to 1.47)	1.52 (1.50 to 1.53)	1.53 (1.51 to 1.54)	1.046 (1.045 to 1.047)
Women	1.00	1.11 (1.09 to 1.12)	1.15 (1.14 to 1.17)	1.27 (1.25 to 1.29)	1.29 (1.27 to 1.31)	1.47 (1.45 to 1.49)	1.52 (1.50 to 1.54)	1.67 (1.65 to 1.70)	1.77 (1.75 to 1.80)	1.80 (1.78 to 1.83)	1.070 (1.069 to 1.071)
Race/ethnicity											
White	1.00	1.12 (1.11 to 1.13)	1.16 (1.15 to 1.17)	1.25 (1.24 to 1.26)	1.23 (1.22 to 1.24)	1.37 (1.36 to 1.38)	1.41 (1.40 to 1.43)	1.53 (1.52 to 1.55)	1.60 (1.58 to 1.62)	1.63 (1.61 to 1.64)	1.055 (1.054 to 1.055)
African American	1.00	1.04 (1.01 to 1.07)	1.11 (1.08 to 1.14)	1.24 (1.20 to 1.28)	1.31 (1.27 to 1.35)	1.45 (1.41 to 1.49)	1.47 (1.43 to 1.52)	1.50 (1.45 to 1.54)	1.83 (1.78 to 1.89)	1.75 (1.70 to 1.80)	1.070 (1.068 to 1.073)
Hispanic	1.00	1.24 (1.20 to 1.28)	1.26 (1.22 to 1.30)	1.38 (1.33 to 1.42)	1.43 (1.39 to 1.48)	1.46 (1.41 to 1.50)	1.60 (1.54 to 1.65)	1.74 (1.69 to 1.80)	1.59 (1.54 to 1.64)	1.78 (1.73 to 1.84)	1.056 (1.053 to 1.059)
Asian/ Pacific Islander	1.00	1.09 (1.03 to 1.16)	1.20 (1.13 to 1.27)	1.32 (1.24 to 1.41)	1.23 (1.16 to 1.31)	1.67 (1.58 to 1.78)	1.56 (1.47 to 1.65)	1.51 (1.42 to 1.60)	1.63 (1.53 to 1.73)	1.48 (1.40 to 1.57)	1.051 (1.046 to 1.056)

Multivariable adjustment for baseline demographics, hospital characteristics, and 29 Elixhauser and other clinically relevant comorbidities as outlined in the methodology. Adjusted odds ratios (OR; per year) for trend were determined using logistic regression models evaluating calendar year as a continuous variable. Numbers in parenthesis represent 95% confidence interval.

comorbidities, we observed an increasing trend in the proportion of patients hospitalized with NSTEMI from 2002 to 2011 (adjusted OR [per year], 1.055; 95% CI, 1.054 to 1.056; $P<0.001$; Figure 1; Table 2).

The increase in proportion of NSTEMI was observed in all age groups. During the study period, it increased from 45.4% to 60.2% in those 40 to 64 years of age (adjusted OR [per year], 1.045; 95% CI, 1.044 to 1.046; $P<0.001$), from 54.5% to 70.7% in those 65 to 74 (adjusted OR [per year], 1.056; 95% CI, 1.055 to 1.058; $P<0.001$), and from 59% to 77.1% in patients ≥75 (adjusted OR [per year], 1.066; 95% CI, 1.065 to 1.068; $P<0.001$). When stratified according to sex, women (56.1% to 73.6%; adjusted OR [per year], 1.070; 95% CI, 1.069 to 1.071; $P<0.001$) had a steeper proportional increase, compared to men (50.4% to 65.3%; adjusted OR [per year], 1.046; 95% CI, 1.045 to 1.047; $P<0.001$). Increase in NSTEMI proportions were also observed across all races. African-American patients showed the greatest proportional increase (Figure 2; Table 2).

Changing Baseline Characteristics of Patients With NSTEMI

Table 3 depicts the baseline demographic, hospital, and clinical characteristics of patients admitted with NSTEMI from 2002 to 2011. There was a slight decrease in mean age at admission during the study period (70.36±13.11 years in 2002 versus 69.87±13.53 in 2011; $P<0.001$). More specifically, there was an increase in the proportion of NSTEMI patients aged 40 to 64 years and decrease in those aged ≥75 years from 2002 to 2011 ($P_{trend}<0.001$). Similarly, there was a small, but statistically significant, increase in the proportion of men (56% in 2002 to 57.5% in 2011; $P_{trend}<0.001$) and a consequent decrease in the proportion of women (44.0% in 2002 to 42.5% in 2011; $P_{trend}<0.001$) with NSTEMI during the study period. The prevalence of smoking, dyslipidemia, CAD, previous MI, carotid artery disease, diabetes mellitus, hypertension, obesity, peripheral vascular disease, chronic renal failure, alcohol abuse, deficiency anemias, coagulopathy, fluid/electrolyte disorders, and previous PCI increased from 2002 to 2011 ($P_{trend}<0.001$ for all). The prevalence of heart failure and chronic pulmonary diseases remained relatively constant throughout the study period.

Trends in EIS

Utilization of EIS on day 0 of presentation increased from 14.9% in 2002 to 21.8% in 2011 (adjusted OR [per year], 1.065; 95% CI, 1.064 to 1.066; $P<0.001$). The adjusted temporal trends for utilization of EIS were similar across all age, sex, and racial/ethnic groups. Patients ≥75 years of age
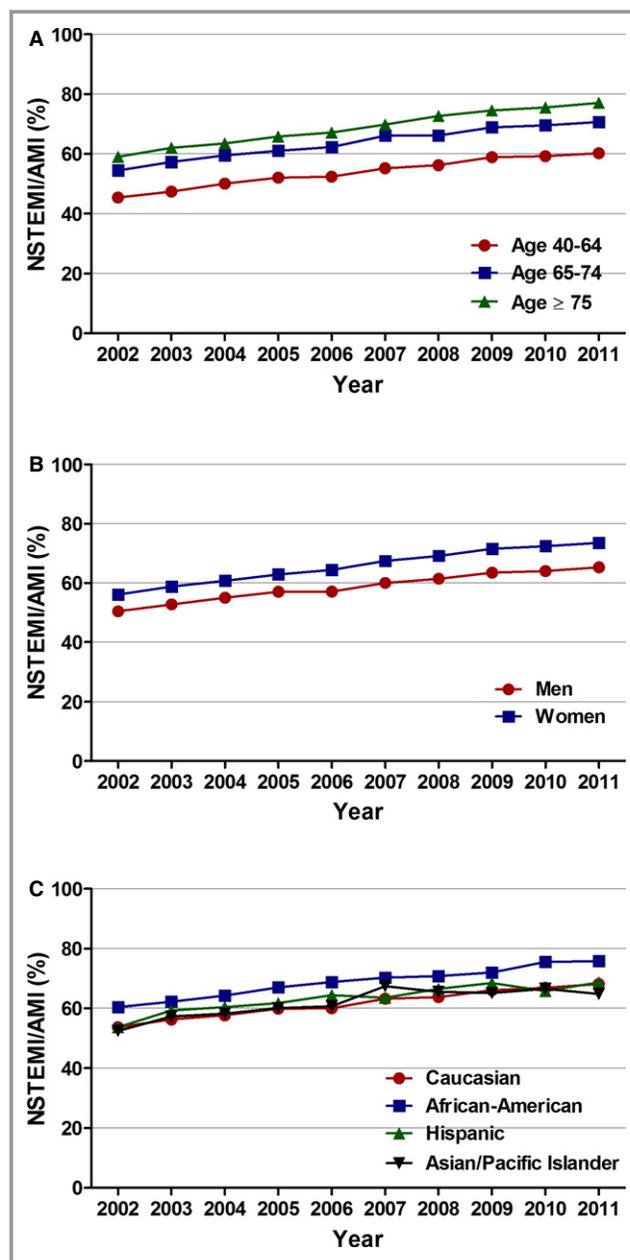
Figure 2. Age, sex, and race/ethnicity specific trends in incidence rates of non-ST-elevation myocardial infarction. A, Age stratified; $P_{trend}<0.001$, (B) sex stratified; $P_{trend}<0.001$, and (C) race/ethnicity stratified; $P_{trend}<0.001$. AMI indicates acute myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction.

had the highest proportional increase in utilization of EIS (adjusted OR [per year], 1.072; 95% CI, 1.069 to 1.074; $P<0.001$; Figures 3 and 4; Table 4).

We also analyzed the utilization of EIS at day 0 or 1. Results showed a temporal increase in the overall as well as the age-, race/ethnicity-, and sex-stratified cohorts (Figures 3 and 4; Table 5).

Table 3. Baseline Demographics, Hospital Characteristics, Comorbidities, Utilization of Early Invasive Strategy, and Overall In-Hospital Mortality in Patients With Non-ST-Elevation Myocardial Infarction

Variable	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	P Value
No. of cases (weighted)	393 937	405 415	390 093	384 392	395 477	384 373	406 566	412 679	397 624	410 563	—
Age (mean, y)	70.36	70.40	70.29	70.32	69.83	69.90	70.19	69.66	69.72	69.87	<0.001
Age-stratified cases, y (% of total)											<0.001
40 to 64	32.8	33.3	33.8	34.4	36.0	36.0	35.4	37.0	37.2	36.7	
65 to 74	24.1	23.3	23.4	22.4	22.4	22.8	22.4	23.0	22.9	23.4	
≥75	43.1	43.4	42.8	43.3	41.6	41.2	42.2	40.0	39.9	39.9	
Gender, %											<0.001
Men	56.0	56.1	56.4	56.5	56.8	56.4	56.4	57.2	57.1	57.5	
Women	44.0	43.9	43.6	43.5	43.2	43.6	43.6	42.8	42.9	42.5	
Race, %											<0.001
White	79.2	77.4	78.3	79.6	77.4	76.2	77.0	76.1	75.4	74.8	
African American	9.2	9.3	9.7	7.8	9.4	10.6	9.6	9.7	12.3	11.7	
Hispanic	6.5	8.5	7.0	7.5	7.9	7.1	6.6	7.3	6.8	7.9	
Asian/Pacific Islander	1.8	2.1	2.1	1.7	1.9	2.4	2.4	2.1	2.3	2.0	
Other	3.2	2.7	2.8	3.5	3.4	3.8	4.8	3.3	3.4	3.5	
Primary expected payer, %											<0.001
Medicare	65.7	66.4	64.8	65.5	63.5	62.8	62.9	62.3	62.3	64.0	
Medicaid	4.0	4.6	4.5	4.9	4.7	4.7	5.1	5.6	6.1	5.7	
Private insurance	25.3	23.8	24.6	23.7	25.0	25.2	24.7	24.1	23.8	22.6	
Uninsured	2.8	3.0	3.7	3.8	4.0	4.3	4.3	5.1	5.0	4.8	
Other	2.2	2.2	2.4	2.2	2.8	3.0	3.0	2.9	2.8	2.9	
Weekend admission, %	24.8	24.3	24.7	24.8	24.3	24.7	25.6	25.3	25.7	25.7	<0.001
Hospital characteristics											
Region, %											<0.001
Northeast	24.1	23.6	23.3	24.1	23.1	21.7	19.0	20.6	20.5	19.6	
Midwest	21.1	23.0	23.3	20.4	21.9	23.0	24.7	22.2	24.8	21.7	
South	39.5	38.8	37.7	39.8	40.5	39.3	40.1	41.3	38.2	40.5	
West	15.4	14.6	15.7	15.7	14.5	16.0	16.2	15.9	16.5	18.2	
Bed size, %											<0.001
Small	9.4	9.7	10.2	7.0	11.1	9.4	10.3	8.9	10.1	9.9	
Medium	24.4	25.0	23.7	24.6	25.1	25.2	23.1	21.9	21.8	24.1	
Large	66.2	65.3	66.1	68.4	63.8	65.4	66.7	69.1	68.1	66.0	
Urban location	86.6	86.8	89.1	89.9	90.7	89.2	88.7	89.6	88.1	89.8	<0.001
Teaching hospital	43.8	44.4	46.8	45.4	51.1	49.3	45.4	47.3	46.5	47.9	<0.001
Comorbidities, %											
Smoking	20.5	20.1	21.6	23.9	25.4	27.0	27.9	31.8	33.0	35.0	<0.001
Dyslipidemia	35.6	36.5	40.3	43.8	47.4	50.6	52.4	56.4	59.2	62.1	<0.001
CAD	68.2	68.8	69.6	70.5	72.0	72.0	72.9	76.2	75.9	77.4	<0.001
Family h/o CAD	3.3	3.2	4.0	4.9	5.0	5.7	6.0	7.3	8.2	8.3	<0.001
Previous myocardial infarction	8.9	8.5	9.1	9.0	9.7	10.2	10.5	11.6	12.3	13.1	<0.001

Continued

Table 3. Continued

Variable	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	*P* Value
Previous TIA/stroke*	—	—	—	—	—	0.8	4.4	5.9	6.7	7.4	<0.001
Previous PCI	7.0	7.0	7.2	7.8	9.1	10.0	10.7	12.4	13.5	15.5	<0.001
Previous CABG	9.2	8.9	8.6	8.3	8.5	8.4	8.8	9.7	9.8	10.9	<0.001
CAD	1.3	1.3	1.3	1.4	1.6	1.8	2.1	2.4	2.4	2.7	<0.001
Atrial fibrillation	18.5	18.5	18.4	18.9	19.0	18.5	17.1	17.8	18.1	19.2	<0.001
Dementia	5.1	5.4	5.5	5.8	6.0	6.2	7.1	7.1	7.3	7.8	<0.001
AIDS	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.1	<0.001
Alcohol abuse	1.8	1.8	2.0	2.1	2.4	2.4	2.5	2.7	2.8	2.8	<0.001
Deficiency anemias	11.9	12.6	12.4	12.7	13.5	15.8	17.7	18.3	18.5	20.3	<0.001
RA/collagen vascular diseases	1.8	1.7	1.8	1.9	2.0	2.1	2.3	2.3	2.4	2.6	<0.001
Chronic blood loss anemia	1.6	1.6	1.6	1.7	1.7	1.7	1.3	1.2	1.0	1.0	<0.001
Congestive heart failure	35.2	36.1	37.0	36.6	34.6	34.6	34.0	34.4	34.9	35.5	<0.001
Chronic pulmonary disease	22.2	22.2	22.2	23.3	23.0	23.5	22.9	22.9	22.5	23.6	<0.001
Coagulopathy	2.8	3.1	3.4	3.4	3.5	3.9	3.8	4.6	4.8	5.5	<0.001
Depression	3.9	4.3	4.4	4.9	5.3	6.0	6.7	7.1	7.5	8.1	<0.001
Diabetes (uncomplicated)	27.0	27.7	27.5	27.3	28.4	29.1	29.6	30.4	30.9	31.8	<0.001
Diabetes (complicated)	6.1	6.1	6.0	6.1	6.0	6.9	7.1	7.0	7.3	8.3	<0.001
Drug abuse	0.7	0.8	1.0	1.2	1.4	1.5	1.4	1.7	1.8	1.9	<0.001
Hypertension	51.0	59.3	61.0	62.4	65.5	66.7	69.3	71.2	72.6	74.3	<0.001
Hypothyroidism	7.8	8.1	8.0	8.5	8.7	9.8	10.9	11.0	11.4	12.4	<0.001
Liver disease	0.7	0.7	0.9	0.9	0.9	1.1	1.1	1.2	1.3	1.4	<0.001
Lymphoma	0.5	0.4	0.5	0.5	0.5	0.5	0.6	0.5	0.5	0.6	<0.001
Fluid and electrolyte disorder	14.5	15.5	16.3	17.5	17.7	18.9	20.4	20.5	20.9	22.6	<0.001
Metastatic cancer	0.8	0.7	0.9	0.9	0.9	1.0	1.0	1.0	0.9	1.0	<0.001
Other neurological disorders	5.6	5.1	5.1	5.3	5.6	6.1	6.7	6.7	6.5	6.9	<0.001
Obesity	6.6	6.7	7.0	7.6	8.1	9.5	11.1	12.4	12.1	14.2	<0.001
Paralysis	1.9	1.8	1.7	1.6	1.7	1.8	2.3	1.9	1.9	2.0	<0.001
Peripheral vascular disease	9.5	9.7	10.2	10.0	10.9	12.2	12.7	13.3	12.7	14.2	<0.001
Psychoses	1.3	1.4	1.4	1.4	1.5	1.7	2.2	2.2	2.4	2.7	<0.001
Pulmonary circulation disorders	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2	<0.001
Renal failure (chronic)	8.5	9.4	9.6	11.9	17.9	20.4	20.1	21.6	22.8	24.8	<0.001
Solid tumor without metastasis	6.7	1.4	1.5	1.5	1.5	1.6	1.6	1.6	1.6	1.6	<0.001
Peptic ulcer (nonbleeding)	1.5	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	<0.001
Valvular disease	0.4	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	<0.001
Weight loss	1.1	1.3	1.4	1.4	1.5	1.8	2.4	2.7	2.6	3.3	<0.001

Table 3. Continued

Variable	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	P Value
Invasive strategy, %											
Day 0	14.9	15.5	17.0	18.2	21.0	20.0	19.8	23.1	21.9	21.8	<0.001
Day 0 or 1	27.8	29.2	31.1	33.3	36.4	35.2	35.3	41.1	40.9	41.4	<0.001
In-hospital mortality, %	5.5	5.5	5.2	4.9	4.6	4.4	4.4	4.1	4.0	3.9	<0.001

AIDS indicates acquired immunodeficiency syndrome; CABG, coronary artery bypass graft surgery; CAD, coronary artery disease; h/o, history of; PCI, percutaneous coronary intervention; RA, rheumatoid arthritis; TIA, transient ischemic attack.

*Data for previous transient ischemic attack/stroke were available from 2007.

Primary Outcome: In-Hospital Mortality

In-hospital mortality decreased from 5.5% in 2002 to 3.9% in 2011 in all patients with NSTEMI (adjusted OR [per year], 0.976; 95% CI, 0.974 to 0.978; $P<0.001$). On age-stratified analysis, those ≥75 years of age had the greatest decrease in in-hospital mortality (adjusted OR [per year], 0.968; 95% CI, 0.966 to 0.971; $P<0.001$). Women had a steeper temporal decline in in-hospital mortality, compared to men, from 2002 to 2011 (adjusted OR [per year], 0.965; 95% CI, 0.962 to 0.968; $P<0.001$ in women and adjusted OR [per year], 0.986; 95% CI, 0.984 to 0.989; $P<0.001$ in men). Statistically significant decline in mortality was also observed in all racial/ethnic groups.

In patients receiving EIS on day 0 of presentation, in-hospital mortality was 2.5% in 2002 and 2.0% in 2011. However, the overall trend in this decrease was not statistically significant (adjusted OR [per year], 0.998; 95% CI,
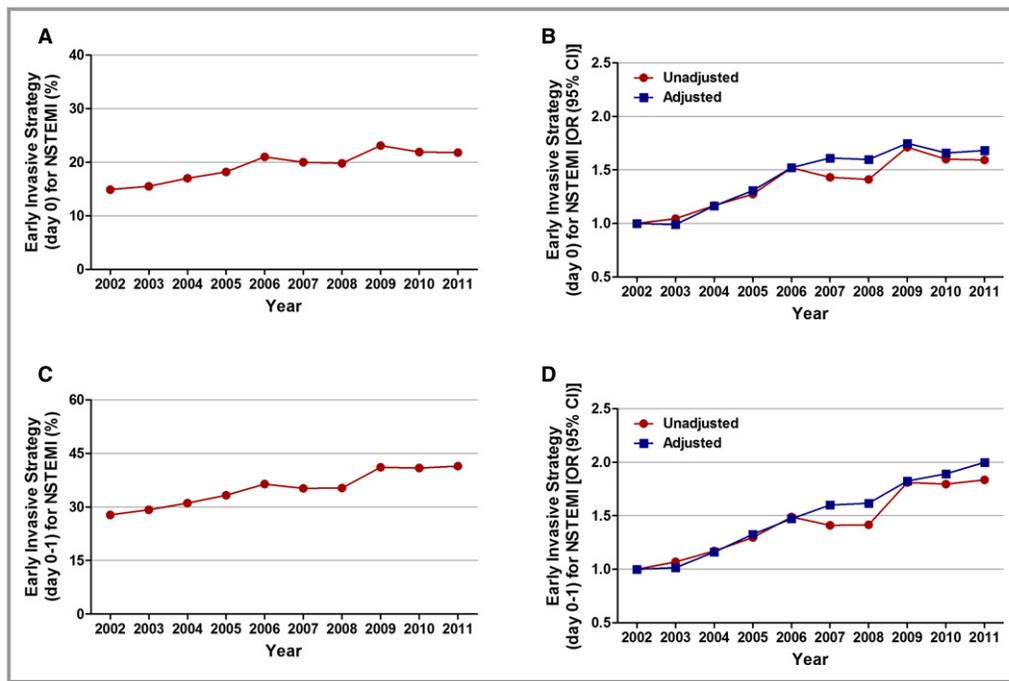

Figure 3. Trends in utilization of early invasive strategy for non-ST-elevation myocardial infarction. A, Early invasive strategy at day 0; $P_{trend}<0.001$. B, Trends in early invasive strategy at day 0 presented as unadjusted and adjusted odds ratio and 95% confidence interval (CI) for each year relative to 2002 (reference year). Regression model adjusted for demographics, hospital characteristics, and 29 Elixhauser and other clinically relevant comorbidities. C, Early invasive strategy at day 0 or 1; $P_{trend}<0.001$. D, Trends in early invasive strategy at day 0 or 1 presented as unadjusted and adjusted odds ratio and 95% confidence interval (CI) for each year relative to 2002 (reference year). Regression model adjusted for demographics, hospital characteristics, and 29 Elixhauser and other clinically relevant comorbidities. 95% CIs are depicted, but are too narrow to be visualized outside the marker width. NSTEMI indicates non-ST-elevation myocardial infarction.
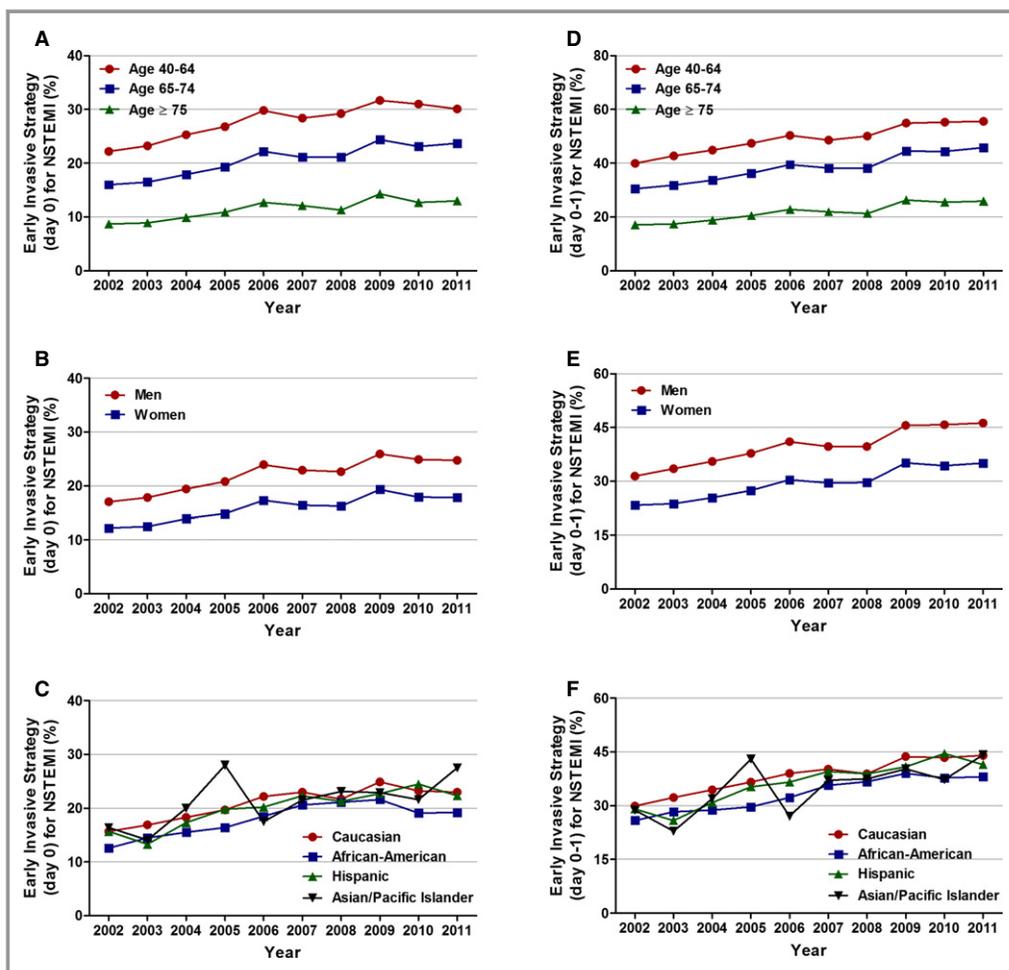
Figure 4. Age, sex, and race/ethnicity specific trends in utilization of early invasive strategy (EIS) for non-ST-elevation myocardial infarction. A, Age stratified, EIS day 0; P_{trend}<0.001, (B) sex stratified, EIS day 0; P_{trend}<0.001, (C) race/ethnicity stratified, EIS day 0; P_{trend}<0.001, (D) age stratified, EIS day 0 or 1; P_{trend}<0.001, (E) sex stratified, EIS day 0 or 1; P_{trend}<0.001, and (F) race/ethnicity stratified, EIS day 0 or 1; P_{trend}<0.001. NSTEMI indicates non-ST-elevation myocardial infarction.

0.991 to 1.004; P=0.471). A temporal decline in in-hospital mortality was observed in patients treated with invasive strategy on day 0 or 1 (2.4% in 2002 to 1.8% in 2011; adjusted OR [per year], 0.988; 95% CI, 0.983 to 0.993; P<0.001; Figures 5 and 6; Table 6). In patients not receiving EIS, in-hospital mortality decreased from 6.7% in 2002 to 5.4% in 2011 (adjusted OR [per year], 0.977; 95% CI, 0.975 to 0.979; P<0.001; Figure 6; Table 6).

Secondary Outcomes: Cost and Length of Stay

For secondary outcome analysis, we studied the temporal trends in cost and length of stay. Detailed results of the length and cost of stay temporal trends stratified by age, sex, and race/ethnicity are shown in Tables 7 and 8, respectively. The mean (±SEM, in days) length of stay decreased in the overall cohort of patients during the study period (5.7±0.01

in 2002 to 4.8±0.01 in 2011; P_{trend}<0.001). Patients with NSTEMI undergoing EIS within day 0 had the shortest length of stay, and the length of stay declined in all patients undergoing EIS, irrespective of timing (from 4.4±0.03 in 2002 to 3.9±0.02 in 2011 for those with EIS at day 0 and from 4.8±0.02 in 2002 to 4.1±0.01 in 2011 for those with EIS within day 0 or 1; P_{trend}<0.001 for all; Figure 7; Table 7).

Mean (±SEM, in dollars) cost of stay in the overall patient population admitted with NSTEMI increased from $14 774±30 from 2002 to $20 269±35 in 2011 ($P_{trend}$<0.001). The mean (±SEM, in dollars) costs accrued by those undergoing EIS were higher and showed a similar increasing trend (from $17 385±80 in 2002 to $24 345±76 in 2011 for those with EIS at day 0 and from $17 534±59 in 2002 to $23 971±55 in 2011 for those with EIS within day 0 or 1; P_{trend}<0.001 for all; Figure 8; Table 8).

Table 4. Adjusted Temporal Trends of Non-ST-Elevation Myocardial Infarction With Utilization of the Early Invasive Strategy at Day 0: Overall Cohort, Age, Sex, and Race/Ethnicity Stratified

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Adjusted OR (Per Year)
Overall	1.00	0.99 (0.97 to 1.01)	1.17 (1.15 to 1.18)	1.31 (1.29 to 1.33)	1.52 (1.50 to 1.54)	1.61 (1.59 to 1.64)	1.60 (1.58 to 1.62)	1.75 (1.72 to 1.77)	1.66 (1.63 to 1.68)	1.68 (1.66 to 1.71)	1.065 (1.064 to 1.066)
Age, y											
40 to 64	1.00	1.00 (0.98 to 1.02)	1.22 (1.19 to 1.24)	1.34 (1.31 to 1.37)	1.52 (1.49 to 1.56)	1.62 (1.59 to 1.66)	1.71 (1.67 to 1.75)	1.77 (1.73 to 1.80)	1.75 (1.71 to 1.79)	1.73 (1.70 to 1.77)	1.068 (1.066 to 1.070)
65 to 74	1.00	1.00 (0.97 to 1.03)	1.12 (1.08 to 1.15)	1.24 (1.21 to 1.28)	1.49 (1.44 to 1.53)	1.57 (1.52 to 1.61)	1.52 (1.48 to 1.57)	1.68 (1.63 to 1.73)	1.58 (1.53 to 1.62)	1.64 (1.59 to 1.69)	1.061 (1.059 to 1.064)
≥75	1.00	0.97 (0.95 to 1.00)	1.16 (1.12 to 1.19)	1.37 (1.33 to 1.40)	1.60 (1.56 to 1.65)	1.73 (1.68 to 1.78)	1.58 (1.53 to 1.62)	1.90 (1.85 to 1.95)	1.70 (1.66 to 1.75)	1.77 (1.72 to 1.82)	1.072 (1.069 to 1.074)
Sex											
Men	1.00	0.99 (0.97 to 1.01)	1.15 (1.13 to 1.17)	1.32 (1.29 to 1.34)	1.52 (1.49 to 1.54)	1.62 (1.59 to 1.65)	1.62 (1.59 to 1.65)	1.75 (1.72 to 1.78)	1.68 (1.65 to 1.71)	1.71 (1.68 to 1.75)	1.067 (1.066 to 1.069)
Women	1.00	0.99 (0.96 to 1.01)	1.19 (1.16 to 1.22)	1.30 (1.26 to 1.33)	1.53 (1.50 to 1.57)	1.60 (1.56 to 1.64)	1.56 (1.53 to 1.60)	1.75 (1.71 to 1.79)	1.63 (1.59 to 1.67)	1.63 (1.60 to 1.67)	1.061 (1.059 to 1.063)
Race/ethnicity											
White	1.00	1.01 (0.99 to 1.03)	1.19 (1.17 to 1.21)	1.31 (1.28 to 1.33)	1.53 (1.51 to 1.56)	1.66 (1.63 to 1.68)	1.59 (1.57 to 1.62)	1.84 (1.81 to 1.87)	1.71 (1.68 to 1.74)	1.72 (1.69 to 1.75)	1.068 (1.067 to 1.070)
African American	1.00	1.15 (1.09 to 1.22)	1.31 (1.24 to 1.38)	1.39 (1.31 to 1.47)	1.63 (1.55 to 1.72)	1.87 (1.78 to 1.97)	1.96 (1.86 to 2.06)	1.90 (1.81 to 2.00)	1.64 (1.57 to 1.73)	1.75 (1.67 to 1.84)	1.057 (1.053 to 1.061)
Hispanic	1.00	0.85 (0.80 to 0.90)	1.09 (1.03 to 1.16)	1.25 (1.18 to 1.32)	1.36 (1.29 to 1.44)	1.51 (1.43 to 1.60)	1.47 (1.39 to 1.56)	1.61 (1.53 to 1.70)	1.81 (1.71 to 1.91)	1.57 (1.49 to 1.66)	1.072 (1.068 to 1.077)
Asian/Pacific Islander	1.00	0.88 (0.79 to 0.99)	1.05 (0.95 to 1.17)	1.63 (1.46 to 1.81)	1.12 (1.00 to 1.26)	1.18 (1.06 to 1.31)	1.40 (1.27 to 1.55)	1.33 (1.20 to 1.47)	1.47 (1.32 to 1.63)	1.66 (1.50 to 1.83)	1.055 (1.047 to 1.064)

Multivariable adjustment for baseline demographics, hospital characteristics, and 29 Elixhauser and other clinically relevant comorbidities as outlined in the methodology. Adjusted odds ratios (OR; per year) for trend were determined using logistic regression models evaluating calendar year as a continuous variable. Numbers in parenthesis represent 95% confidence interval.

Table 5. Adjusted Temporal Trends of Non-ST-Elevation Myocardial Infarction With Utilization of the Early Invasive Strategy at Day 0 to 1: Overall Cohort, Age, Sex, and Race/Ethnicity Stratified

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Adjusted OR (Per Year)
Overall	1.00	1.02 (1.00 to 1.03)	1.16 (1.15 to 1.18)	1.33 (1.31 to 1.35)	1.47 (1.45 to 1.49)	1.60 (1.58 to 1.62)	1.62 (1.60 to 1.64)	1.82 (1.80 to 1.85)	1.89 (1.87 to 1.92)	2.00 (1.97 to 2.03)	1.084 (1.083 to 1.085)
Age, y											
40 to 64	1.00	1.07 (1.05 to 1.09)	1.26 (1.23 to 1.29)	1.44 (1.41 to 1.47)	1.54 (1.51 to 1.57)	1.72 (1.68 to 1.75)	1.86 (1.82 to 1.90)	1.99 (1.95 to 2.03)	2.11 (2.07 to 2.15)	2.26 (2.21 to 2.31)	1.096 (1.094 to 1.097)
65 to 74	1.00	1.00 (0.97 to 1.02)	1.10 (1.07 to 1.13)	1.23 (1.25 to 1.31)	1.43 (1.40 to 1.47)	1.56 (1.51 to 1.60)	1.51 (1.48 to 1.55)	1.74 (1.70 to 1.78)	1.82 (1.78 to 1.87)	1.94 (1.90 to 1.99)	1.082 (1.080 to 1.084)
≥75	1.00	0.97 (0.95 to 1.00)	1.14 (1.11 to 1.16)	1.31 (1.28 to 1.34)	1.51 (1.47 to 1.54)	1.64 (1.60 to 1.67)	1.58 (1.54 to 1.61)	1.89 (1.85 to 1.93)	1.92 (1.88 to 1.96)	2.01 (1.96 to 2.05)	1.089 (1.087 to 1.091)
Sex											
Men	1.00	1.04 (1.02 to 1.06)	1.19 (1.17 to 1.21)	1.37 (1.34 to 1.39)	1.49 (1.46 to 1.52)	1.65 (1.62 to 1.68)	1.68 (1.65 to 1.70)	1.88 (1.85 to 1.91)	1.97 (1.94 to 2.01)	2.10 (2.06 to 2.13)	1.088 (1.087 to 1.090)
Women	1.00	0.98 (0.96 to 1.00)	1.13 (1.10 to 1.15)	1.27 (1.25 to 1.30)	1.45 (1.42 to 1.48)	1.54 (1.51 to 1.57)	1.54 (1.50 to 1.57)	1.75 (1.71 to 1.78)	1.78 (1.74 to 1.82)	1.87 (1.83 to 1.91)	1.078 (1.077 to 1.080)
Race/ethnicity											
White	1.00	1.04 (1.03 to 1.06)	1.19 (1.17 to 1.21)	1.34 (1.32 to 1.36)	1.49 (1.47 to 1.51)	1.64 (1.62 to 1.67)	1.60 (1.58 to 1.62)	1.90 (1.87 to 1.92)	1.94 (1.91 to 1.97)	2.05 (2.02 to 2.09)	1.086 (1.085 to 1.087)
African American	1.00	1.11 (1.06 to 1.16)	1.20 (1.14 to 1.25)	1.23 (1.18 to 1.29)	1.43 (1.37 to 1.50)	1.68 (1.61 to 1.75)	1.79 (1.71 to 1.87)	1.86 (1.78 to 1.94)	1.80 (1.73 to 1.87)	1.99 (1.91 to 2.07)	1.079 (1.076 to 1.082)
Hispanic	1.00	0.89 (0.85 to 0.94)	1.09 (1.03 to 1.14)	1.27 (1.21 to 1.33)	1.46 (1.39 to 1.53)	1.58 (1.51 to 1.66)	1.63 (1.55 to 1.71)	1.78 (1.69 to 1.86)	2.13 (2.03 to 2.23)	1.83 (1.74 to 1.91)	1.092 (1.086 to 1.097)
Asian/Pacific Islander	1.00	0.75 (0.68 to 0.83)	0.92 (0.83 to 1.01)	1.53 (1.39 to 1.70)	0.90 (0.81 to 0.99)	1.22 (1.11 to 1.34)	1.35 (1.23 to 1.48)	1.48 (1.35 to 1.62)	1.62 (1.48 to 1.78)	1.65 (1.50 to 1.81)	1.079 (1.071 to 1.087)

Multivariable adjustment for baseline demographics, hospital characteristics, and 29 Elixhauser and other clinically relevant comorbidities as outlined in the methodology. Adjusted odds ratios (OR; per year) for trend were determined using logistic regression models evaluating calendar year as a continuous variable. Numbers in parenthesis represent 95% confidence interval.
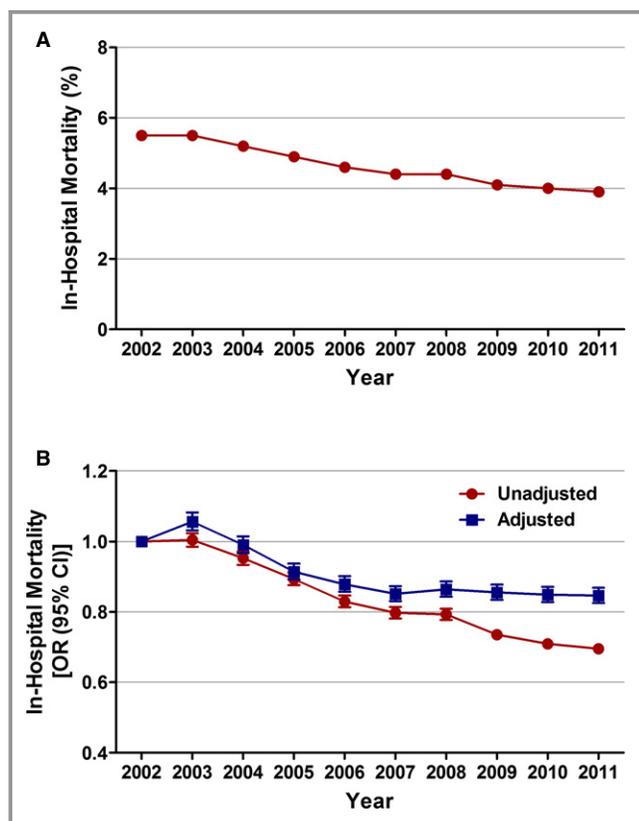
Figure 5. Trends in in-hospital mortality in patients with non-ST-elevation myocardial infarction. A, In-hospital mortality (%) was calculated as the number of patients who died during the hospitalization divided by the number of patients with NSTEMI per year×100; P_{trend}<0.001. B, Trends in in-hospital mortality presented as unadjusted and adjusted odds ratio (OR) and 95% confidence interval (CI) for each year relative to 2002 (reference year). Regression model adjusted for demographics, hospital characteristics, and 29 Elixhauser and other clinically relevant comorbidities. NSTEMI indicates non-ST-elevation myocardial infarction.

Discussion

We report an increasing trend in the proportion of NSTEMI admissions for the overall cohort and in the age-, sex-, and race/ethnicity-stratified subgroups from 2002 to 2011. This is associated with an increase in utilization of EIS, decreased in-hospital mortality, and decreased length of stay during the same period.

Analysis of the National Registry of Myocardial Infarction from 1990 to 2006 reported an increase in the proportion of NSTEMI from 14.2% in 1990 to 59.1% in 2006 (P<0.001).[2] The proportional increase in NSTEMI may be the result of an aging population, increasing chronic comorbidities, and reduction in smoking. Part of the increase in the proportion of NSTEMI in our study may be attributable to increased utilization and higher sensitivity of cardiac biomarkers (troponins). In the

age- and sex-stratified analysis, patients ≥75 years and women had the greatest proportional increase in NSTEMI. Women are also more likely to present with NSTEMI, compared to men.[12] Older patients are more likely to be women and have significant comorbidities that predispose them to NSTEMI.

On trend analysis of baseline characteristics, we report an increase in the proportion of patients in the 40 to 64 years of age group. This is in concordance with the analysis of Get With The Guidelines Coronary Artery Disease Registry from 2003 to 2008,[13] with that age group representing the fastest-growing segment of our population over the years.

Importantly, there was a temporal increase in utilization of the EIS in the NSTEMI patient population. Meta-analysis of randomized, control trials has consistently shown a benefit of EIS in the setting of NSTEMI, especially in the high-risk patient population.[14,15] Definition of optimal timing of invasive management has undergone a paradigm shift in the last decade. The 2002 ACC/AHA guidelines for management of NSTEMI[16] and the 2007 ACC/AHA guidelines[17] for management of NSTEMI in the elderly patient population defined the EIS as routine cardiac catheterization within 48 hours of presentation. The more recent TIMACS trial[8] compared the routine early intervention (≤24 hours of presentation; median time, 14 hours) to delayed intervention (≥36 hours after presentation; median time, 50 hours). There was no significant difference in the primary endpoint, other than in the prespecified subgroup with high Global Registry of Acute Coronary Events scores. After 6 months, they reported a 28% relative reduction in secondary outcome of death, MI, and refractory ischemia in the early intervention group (OR, 0.72; 95% CI, 0.58 to 0.89; P=0.003).

The results of the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the ACC/AHA Guidelines) Quality Improvement Initiative from 2000 to 2002 indicated that the EIS (within 48 hours) was not utilized in a majority of high-risk patients with NSTEMI.[18] They reported male sex, ischemic electrocardiographic changes, younger age, positive biomarkers, lack of congestive heart failure, lack of renal insufficiency, and white race as predictors of early invasive management. We analyzed the trends in both day 0 and day 0 or 1 of presentation. Utilization of EIS at day 0 increased from 14.9% in 2002 to 21.8% in 2011 (P<0.001), and utilization of EIS at day 0 or 1 increased from 27.8% in 2002 to 41.4% in 2011 (P<0.001). The increase in utilization was consistent among all age-, race/ethnicity-, and sex-stratified subgroups after multivariable adjustment. Men had a higher proportional increase in EIS at both day 0 and day 0 or 1 of presentation. Previous studies have discussed the sex differences in the invasive management of ACS, with women being managed less aggressively than men.[19,20]
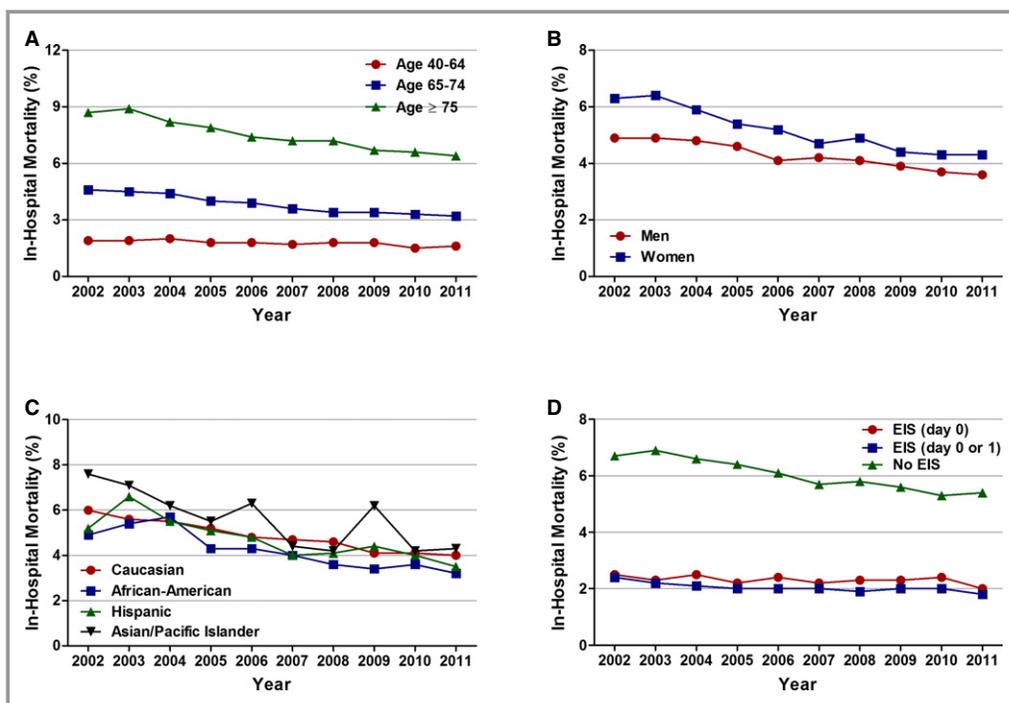
Figure 6. Age, sex, race/ethnicity, and utilization of invasive strategy-specific trends in in-hospital mortality in patients with non-ST-elevation myocardial infarction. A, Age stratified, (B) sex stratified, (C) race/ethnicity stratified, and (D) stratified according to utilization of invasive strategy (P_{trend}<0.001 for all). No EIS was defined as patients who did not receive coronary angiography with intent to revascularize within day 0 or 1. EIS indicates early invasive strategy.

Interestingly, patients ≥75 years of age had a higher proportional increase in EIS at day 0 and patients 40 to 64 years of age had an overall higher proportional increase at day 0 or 1. Chin et al.,[21] using the linked CRUSADE registry and Medicare and Medicaid claims data, reported an increased utilization of evidence based NSTEMI care and decline in in-hospital mortality in 2006, compared with 2003 (OR, 0.82; 95% CI, 0.67 to 1.00; *P*=0.045) in patients ≥65 years of age with NSTEMI. Recent trend analysis from Denmark also reported an increase in initiation of coronary angiography for first-time NSTEMI admissions at 3 days from 18.2% in 2001 to 55.7% to 2009.[22]

We also report a decrease in risk-adjusted in-hospital mortality and length of stay for patients admitted with NSTEMI. The decline in in-hospital mortality was observed in patients receiving EIS as well as those not receiving EIS. This observation is consistent with improvement in, or better adherence to, medical therapy, independent of EIS utilization. The lower in-hospital mortality observed in the EIS-managed patients is likely the result of patient selection bias, as previously demonstrated by analysis of the CRUSADE registry,[18] and no causal association between EIS and in-hospital mortality can be inferred from the results of our study.

The decline in overall in-hospital mortality was most prominent in those ≥75 years of age. We have previously reported a 24% relative reduction of in-hospital mortality in octogenarians treated with the early invasive approach versus the initial conservative strategy (OR, 0.76; 95% CI, 0.74 to 0.78; *P*<0.001).[23] However, it is not possible to conclusively establish a causal relationship between increasing utilization of EIS and decreasing in-hospital mortality from this study.

Limitations

This study has certain limitations. Because this is a retrospective, observational study, the possibility of selection bias and residual measured and unmeasured confounding cannot be completely eliminated. NIS is an administrative database; there is the potential for unrecognized miscoding of diagnostic and procedure codes. There is a possibility that widespread troponin utilization in the last decade may have contributed to the increase in NSTEMI diagnosis and also potentially decreased case severity of those classified as NSTEMI. Also, conditions other than ACS may have led to troponin elevations and hence miscoding of NSTEMI exists. Clinical presentation and medication utilization variables are not available in this administrative database. It is our assumption that day 0 corresponds to ≤24 hours and days 0 or 1 corresponds to ≤48 hours, because the database does not provide the timing of procedure in hours. For trends in

Table 6. Adjusted Temporal Trends of Risk-Adjusted In-Hospital Mortality in Patients With Non-ST-Elevation Myocardial Infarction: Overall Cohort, Age, Sex, Race/Ethnicity, and Early Invasive Strategy Stratified

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Adjusted OR (Per Year)
Overall	1.00	1.06 (1.03 to 1.08)	0.99 (0.97 to 1.01)	0.91 (0.89 to 0.94)	0.88 (0.86 to 0.90)	0.85 (0.83 to 0.87)	0.86 (0.84 to 0.88)	0.86 (0.83 to 0.88)	0.85 (0.83 to 0.87)	0.85 (0.83 to 0.87)	0.976 (0.974 to 0.978)
Age, y											
40 to 64	1.00	0.98 (0.91 to 1.05)	1.07 (0.99 to 1.15)	0.92 (0.86 to 0.99)	0.96 (0.90 to 1.03)	0.84 (0.78 to 0.90)	0.92 (0.86 to 0.98)	0.97 (0.90 to 1.03)	0.85 (0.80 to 0.91)	0.87 (0.82 to 0.94)	0.983 (0.977 to 0.988)
65 to 74	1.00	1.08 (1.02 to 1.14)	1.04 (0.99 to 1.10)	0.91 (0.86 to 0.97)	0.88 (0.83 to 0.93)	0.80 (0.76 to 0.85)	0.83 (0.79 to 0.88)	0.89 (0.84 to 0.94)	0.88 (0.83 to 0.93)	0.88 (0.83 to 0.93)	0.977 (0.972 to 0.982)
≥75	1.00	1.07 (1.04 to 1.10)	0.96 (0.93 to 0.99)	0.90 (0.88 to 0.93)	0.85 (0.83 to 0.88)	0.85 (0.82 to 0.88)	0.83 (0.81 to 0.86)	0.80 (0.77 to 0.82)	0.81 (0.79 to 0.84)	0.79 (0.77 to 0.82)	0.968 (0.966 to 0.971)
Sex											
Men	1.00	1.06 (1.02 to 1.09)	1.03 (0.99 to 1.07)	0.98 (0.95 to 1.02)	0.90 (0.86 to 0.93)	0.93 (0.90 to 0.97)	0.91 (0.88 to 0.94)	0.96 (0.92 to 0.99)	0.93 (0.90 to 0.97)	0.92 (0.88 to 0.95)	0.986 (0.984 to 0.989)
Women	1.00	1.06 (1.02 to 1.09)	0.95 (0.92 to 0.98)	0.85 (0.82 to 0.88)	0.86 (0.83 to 0.90)	0.78 (0.75 to 0.81)	0.82 (0.80 to 0.85)	0.76 (0.73 to 0.79)	0.77 (0.75 to 0.80)	0.78 (0.76 to 0.81)	0.965 (0.962 to 0.968)
Race/ethnicity											
White	1.00	1.02 (0.99 to 1.05)	0.95 (0.92 to 0.97)	0.90 (0.88 to 0.93)	0.87 (0.84 to 0.89)	0.85 (0.83 to 0.88)	0.87 (0.84 to 0.89)	0.84 (0.81 to 0.86)	0.83 (0.81 to 0.86)	0.85 (0.82 to 0.87)	0.978 (0.975 to 0.980)
African American	1.00	1.19 (1.10 to 1.30)	1.21 (1.12 to 1.31)	0.98 (0.90 to 1.07)	0.94 (0.87 to 1.03)	0.92 (0.84 to 0.99)	0.86 (0.79 to 0.94)	0.83 (0.76 to 0.91)	0.93 (0.85 to 1.01)	0.84 (0.76 to 0.92)	0.967 (0.960 to 0.973)
Hispanic	1.00	1.32 (1.21 to 1.44)	1.15 (1.05 to 1.27)	1.02 (0.93 to 1.12)	1.03 (0.93 to 1.13)	0.90 (0.81 to 0.99)	0.93 (0.84 to 1.03)	1.08 (0.98 to 1.19)	1.06 (0.96 to 1.17)	0.92 (0.83 to 1.01)	0.978 (0.971 to 0.986)
Asian/Pacific Islander	1.00	1.04 (0.89 to 1.21)	0.90 (0.77 to 1.05)	0.87 (0.73 to 1.03)	0.76 (0.64 to 0.90)	0.64 (0.54 to 0.76)	0.60 (0.51 to 0.71)	0.91 (0.78 to 1.07)	0.60 (0.51 to 0.72)	0.72 (0.61 to 0.86)	0.952 (0.939 to 0.965)
EIS											
Day 0	1.00	0.92 (0.84 to 1.01)	1.02 (0.94 to 1.11)	0.87 (0.80 to 0.95)	0.96 (0.88 to 1.04)	0.91 (0.84 to 0.99)	0.92 (0.85 to 0.99)	0.96 (0.88 to 1.04)	1.02 (0.94 to 1.11)	0.89 (0.82 to 0.97)	0.998 (0.991 to 1.004)
Day 0 to 1	1.00	0.92 (0.86 to 0.98)	0.93 (0.87 to 0.99)	0.84 (0.78 to 0.89)	0.84 (0.78 to 0.89)	0.88 (0.83 to 0.94)	0.85 (0.80 to 0.91)	0.91 (0.86 to 0.97)	0.90 (0.84 to 0.96)	0.80 (0.75 to 0.85)	0.988 (0.983 to 0.993)
No EIS	1.00	1.08 (1.05 to 1.11)	1.01 (0.99 to 1.04)	0.94 (0.92 to 0.97)	0.91 (0.88 to 0.93)	0.87 (0.84 to 0.89)	0.88 (0.86 to 0.91)	0.86 (0.84 to 0.89)	0.86 (0.84 to 0.88)	0.88 (0.86 to 0.91)	0.977 (0.975 to 0.979)

Multivariable adjustment for baseline demographics, hospital characteristics, and 29 Elixhauser and other clinically relevant comorbidities as outlined in the methodology. Adjusted odds ratios (OR; per year) for trend were determined using logistic regression models evaluating calendar year as a continuous variable. Numbers in parenthesis represent 95% confidence interval. EIS indicates early invasive strategy.

Table 7. Temporal Trends in Length of Stay (Mean±SE) in Days

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Overall	5.72 (±0.01)	5.72 (±0.01)	5.71 (±0.01)	5.53 (±0.01)	5.42 (±0.01)	5.25 (±0.01)	5.18 (±0.01)	5.10 (±0.01)	4.89 (±0.01)	4.78 (±0.01)
Age, y										
40 to 64	4.54 (±0.01)	4.69 (±0.02)	4.61 (±0.02)	4.41 (±0.01)	4.52 (±0.02)	4.37 (±0.02)	4.37 (±0.01)	4.37 (±0.01)	4.24 (±0.01)	4.15 (±0.01)
65 to 74	6.11 (±0.02)	6.02 (±0.02)	6.04 (±0.02)	5.82 (±0.02)	5.64 (±0.02)	5.59 (±0.02)	5.45 (±0.02)	5.45 (±0.02)	5.16 (±0.02)	5.04 (±0.02)
≥75	6.40 (±0.02)	6.35 (±0.01)	6.40 (±0.02)	6.28 (±0.02)	6.09 (±0.02)	5.84 (±0.02)	5.73 (±0.01)	5.57 (±0.01)	5.35 (±0.01)	5.20 (±0.01)
Sex										
Men	5.44 (±0.01)	5.48 (±0.01)	5.50 (±0.01)	5.32 (±0.01)	5.25 (±0.01)	5.07 (±0.01)	5.01 (±0.01)	5.01 (±0.01)	4.77 (±0.01)	4.70 (±0.01)
Women	6.08 (±0.02)	6.03 (±0.01)	5.98 (±0.02)	5.80 (±0.02)	5.65 (±0.02)	5.48 (±0.02)	5.40 (±0.01)	5.22 (±0.01)	5.05 (±0.01)	4.89 (±0.01)
Race/ethnicity										
White	5.77 (±0.01)	5.63 (±0.01)	5.65 (±0.01)	5.51 (±0.01)	5.38 (±0.01)	5.19 (±0.01)	5.11 (±0.01)	4.98 (±0.01)	4.82 (±0.01)	4.66 (±0.01)
African American	6.23 (±0.04)	6.64 (±0.04)	6.64 (±0.05)	8.99 (±0.05)	6.06 (±0.04)	5.67 (±0.04)	5.73 (±0.04)	5.59 (±0.03)	5.29 (±0.03)	5.24 (±0.03)
Hispanic	6.05 (±0.04)	6.59 (±0.04)	6.55 (±0.05)	6.02 (±0.05)	5.92 (±0.05)	5.70 (±0.05)	5.85 (±0.05)	5.72 (±0.04)	5.52 (±0.04)	4.89 (±0.03)
Asian/Pacific Islander	7.49 (±0.17)	7.02 (±0.10)	6.29 (±0.10)	6.60 (±0.11)	6.56 (±0.10)	5.66 (±0.08)	5.30 (±0.06)	5.69 (±0.09)	5.15 (±0.06)	5.10 (±0.07)
Early invasive strategy										
Day 0	4.38 (±0.03)	4.36 (±0.02)	4.43 (±0.02)	3.97 (±0.02)	4.17 (±0.02)	4.04 (±0.02)	4.01 (±0.02)	4.09 (±0.02)	3.98 (±0.02)	3.87 (±0.02)
Day 0 to 1	4.75 (±0.02)	4.61 (±0.02)	4.63 (±0.02)	4.27 (±0.01)	4.40 (±0.01)	4.32 (±0.02)	4.30 (±0.01)	4.33 (±0.01)	4.19 (±0.01)	4.08 (±0.01)

Table 8. Temporal Trends in Total Hospital Cost (Mean±SE) in U.S. Dollars

|	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Overall	$14 774 (±30)	$16 145 (±33)	$17 750 (±34)	$18 142 (±34)	$19 484 (±33)	$18 971 (±35)	$20 004 (±36)	$19 587 (±34)	$19 632 (±35)	$20 269 (±36)
Age, y										
40 to 64	$14 457 (±46)	$16 501 (±54)	$17 914 (±54)	$18 353 (±53)	$19 983 (±53)	$19 495 (±58)	$21 193 (±59)	$20 372 (±54)	$20 597 (±55)	$21 287 (±56)
65 to 74	$16 827 (±73)	$17 800 (±75)	$19 980 (±81)	$20 154 (±80)	$21 517 (±77)	$21 287 (±79)	$22 268 (±84)	$22 110 (±80)	$22 125 (±84)	$22 888 (±83)
≥75	$13 875 (±44)	$14 998 (±48)	$16 429 (±52)	$16 958 (±53)	$17 956 (±51)	$17 239 (±51)	$17 767 (±55)	$17 382 (±52)	$17 265 (±53)	$17 785 (±56)
Sex										
Men	$15 266 (±40)	$16 924 (±45)	$18 571 (±46)	$19 166 (±47)	$20 522 (±45)	$20 003 (±48)	$21 154 (±49)	$20 884 (±48)	$20 712 (±46)	$21 665 (±50)
Women	$14 143 (±44)	$15 153 (±47)	$16 695 (±52)	$16 816 (±50)	$18 123 (±50)	$17 642 (±50)	$18 527 (±55)	$17 850 (±49)	$18 191 (±54)	$18 382 (±51)
Race/ethnicity										
White	$14 727 (±42)	$15 614 (±43)	$17 080 (±43)	$18 054 (±45)	$18 934 (±43)	$19 114 (±47)	$19 349 (±44)	$18 900 (±42)	$18 919 (±40)	$19 649 (±42)
African American	$14 863 (±118)	$17 546 (±139)	$17 702 (±134)	$16 952 (±142)	$19 202 (±132)	$18 322 (±114)	$19 142 (±142)	$18 724 (±112)	$18 050 (±95)	$19 018 (±111)
Hispanic	$19 282 (±189)	$19 695 (±191)	$22 802 (±255)	$22 484 (±203)	$21 509 (±152)	$22 132 (±175)	$23 788 (±199)	$22 989 (±175)	$24 329 (±173)	$28 558 (±168)
Asian/Pacific Islander	$25 936 (±485)	$21 668 (±364)	$24 790 (±422)	$28 487 (±562)	$26 611 (±448)	$23 703 (±358)	$27 373 (±395)	$26 322 (±380)	$24 509 (±340)	$29 743 (±434)
Early invasive strategy										
Day 0	$17 385 (±80)	$19 542 (±94)	$21 783 (±92)	$21 965 (±86)	$23 475 (±80)	$22 912 (±80)	$23 860 (±84)	$22 572 (±68)	$23 673 (±76)	$24 345 (±78)
Day 0 to 1	$17 534 (±59)	$19 097 (±63)	$21 280 (±64)	$21610 (±61)	$23 099 (±57)	$22 594 (±59)	$23 873 (±62)	$22 823 (±53)	$23 489 (±55)	$23 971 (±55)
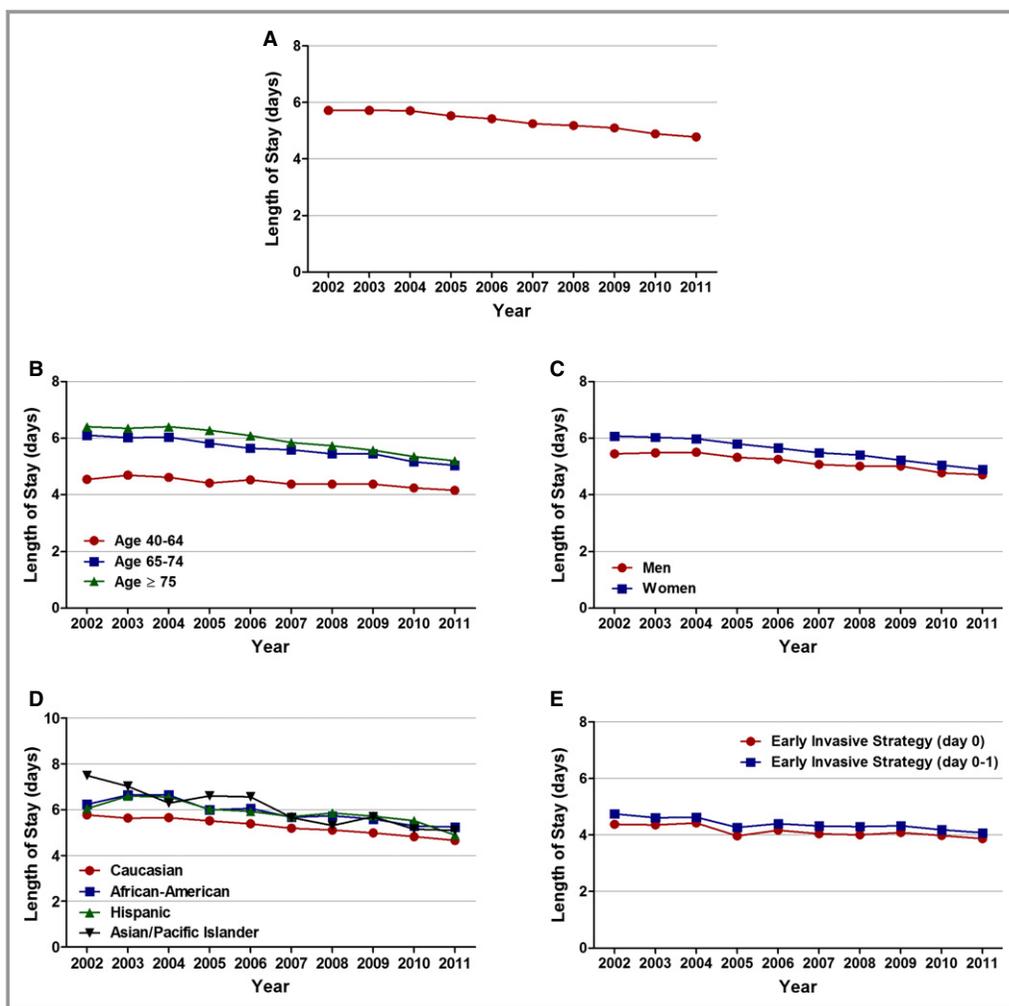
Figure 7. Temporal trends in length of stay, in days. A, Overall, (B) age, (C) sex, (D) race/ethnicity, and (E) timing of invasive strategy (P_{trend}<0.001 for all).

total hospital costs, we did not convert hospital costs into inflation-adjusted constant dollars. The NIS databases do not include NSTEMI hospitalizations for veterans hospitalized in Veterans Affairs hospitals. We could also not account for patients transferred in from other hospitals. Last, outcomes in the NIS database are limited to in-hospital events and causes of death are not differentiated. However, these potential limitations may be partially compensated by the large size of the database and the ability to obtain nationwide estimates using the discharge weights provided.

Conclusions

In this large, nationwide analysis of patients with MI, we report an increase in proportion of NSTEMI with increasing utilization of EIS in the United States. We also report a decrease in in-hospital mortality and decrease in length of stay during the study period. The improved outcomes may reflect greater adherence to the evolving guideline-recommended therapies. Nevertheless, age-, sex-, and race/ethnicity-specific differences in the management and outcomes of NSTEMI were observed, and further studies are needed to develop strategies to ensure more equitable care for NSTEMI.

Disclosures

Dr Bhatt discloses the following relationships: advisory board: Elsevier Practice Update Cardiology, Medscape Cardiology, and Regado Biosciences; board of directors: Boston VA Research Institute and Society of Cardiovascular Patient Care; chair: American Heart Association Get With The Guidelines Steering Committee; data monitoring committees: Duke Clinical Research Institute, Harvard Clinical Research Institute, Mayo Clinic, and Population Health Research Institute; honoraria: American College of Cardiology (editor, Clinical Trials, Cardiosource), Belvoir Publications (editor in chief,
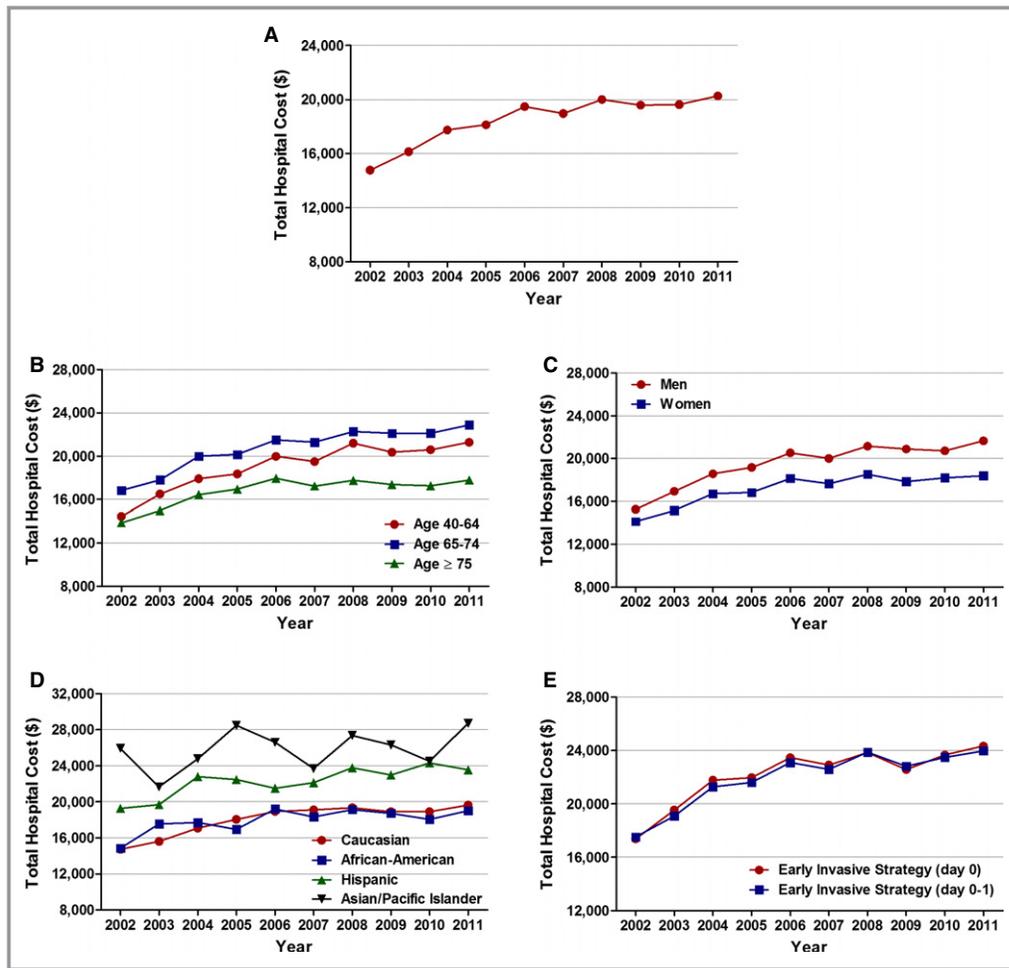
Figure 8. Temporal trends in cost of stay, in U.S. dollars. (A) Overall, (B) age, (C) sex, (D) race/ethnicity, and (E) timing of invasive strategy (P_{trend}<0.001 for all).

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