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MORTALITY AFTER ACUTE MYOCARDIAL INFARCTION IN HOSPITALS THAT DISPROPORTIONATELY TREAT AFRICAN-AMERICANS

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Abstract

Background—African-Americans are more likely be seen by physicians with less clinical training or treated at hospitals with deficient times to acute reperfusion therapies. Less is known about differences in health outcomes. This paper compares risk-adjusted mortality following Acute Myocardial Infarction (AMI) between U.S. hospitals with high and low fractions of elderly black AMI patients.

Methods and Results—A prospective cohort study was performed for fee-for-service Medicare patients hospitalized for AMI during 1997–2001 (N = 1,136,736). Hospitals (N = 4289) were classified into approximate deciles depending on the extent to which the hospital served the African-American population. The lowest category (12.5 percent of AMI patients) included hospitals without any African-American AMI admissions during 1997–2001. Decile 10 (10 percent of AMI patients) included hospitals with the highest fraction of black AMI patients (33.6 percent). The main outcome measures were 90-day and 30-day mortality following AMI.

Patients admitted to hospitals disproportionately serving African-Americans experienced no greater level of morbidities or severity of the infarction. Yet hospitals in Decile 10 experienced risk-adjusted 90-day mortality rate of 23.7 percent (95% CI: 23.2–24.2) compared to 20.1 percent (95% CI: 19.7–20.4) in Decile 1 hospitals. Differences in outcomes between hospitals were not explained by income, hospital ownership status, hospital volume, Census region, urban status, or hospital surgical treatment intensity.

Conclusions—Risk-adjusted mortality following AMI is significantly higher in U.S. hospitals that disproportionately serve African-Americans. A reduction in overall mortality at these hospitals could reduce dramatically black-white disparities in health care outcomes.

The Institute of Medicine study on racial disparities in health and health care has documented the sharp differences in the treatment of diseases for African-Americans,

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None.

particularly for cardiovascular diseases.^{1–24} Less well understood is the mechanism generating disparities in health outcome. Do physicians or hospitals provide poorer quality care to their black patients compared to their white patients? Or are African-American patients more likely to be treated by a physician or hospital where all patients receive lower quality care, regardless of race?^{25–27} The importance of the latter hypothesis has been demonstrated recently in studies showing African-Americans are more likely to be seen by physicians with less clinical training than those treating whites,²⁸ and treated at hospitals with higher risk-adjusted surgical mortality and lower rates of evidence-based treatments and protocols.^{29–33} However, the association between the racial composition of hospitals and health outcomes such as mortality is not known.

This study compares outcomes, measured by 90-day and 30-day adjusted mortality rates after Acute Myocardial Infarction (AMI), for hospitals that disproportionately treat African-American patients relative to those that do not. To address this question, we draw on a nearly 100 percent sample of fee-for-service Medicare patients with an index AMI between January 1997 and September 2001, comprising 1.14 million individuals. We measure the percentage of all AMI patients in a hospital who were African-American and categorize hospitals into 10 approximate deciles ranked by the extent to which a hospital serves the African-American community. Risk-adjusted mortality is examined across these deciles, under the hypothesis that hospitals with a large share of African-American patients are different from hospitals with a smaller (or zero) share. The importance of factors such as income, hospital ownership, surgical treatment intensity, racial composition, region, and unmeasured health status are considered separately as potential confounders.

Methods

Data

The primary data set is a longitudinal sample from the 100 percent Medicare fee-for-service population hospitalized for AMI between January 1997 and September 2001. The criterion for determining the presence of AMI from the claims is a primary diagnosis code of AMI (41000–41091) without evidence of an old MI. Federal hospitals are excluded. The initial sample with valid provider and location identification was 1,254,786 individuals. Patients were assigned to their hospital of initial admission for heart disease treatment, even if the patient was later treated at another hospital. Using information from the Medicare Denominator File, the race of each patient was determined as black, other, which includes Hispanic enrollees, and the residual group. Because of concerns about the statistical power required for discerning outcome differences, and the low sensitivity of Hispanic responses³⁴ we exclude respondents in the “other” category (N = 42,200), leaving two groups, African-American, and the residual group which we denote as “white.” There is a very strong correlation between African-American racial measures in the Medicare claims data and self-reported racial identity.³⁴

Observations were excluded if there was evidence from claims data of a previous MI (N = 54,357), or if patients enrolled in an HMO during the calendar year following the AMI index event (N = 17,160). (Patients enrolled in a risk-bearing HMO at the time of the AMI were not in this sample, because there is no record of the AMI on the claims data.) Additional criterion for exclusion was inability to match the patient’s zip code to region of residence (N = 114), lack of valid income data for that zip code (N = 2,819), and hospitals with fewer than 10 AMIs over the entire period of analysis (N = 1,400) leaving a sample of 1,136,736.

This sample was used to calculate the percent of all AMI patients in a hospital who were African-American. We then created approximate deciles of this measure to provide a summary measure of the extent to which a hospital serves the African-American

community. The lowest “decile” comprised the 12.5 percent of patients admitted to hospitals without any black AMI patient during the period 1997–2001. Using this slightly larger grouping avoided splitting the sample in an arbitrary way. Decile 2 is attenuated as a result, so that the bottom two groups comprise one-fifth of the sample. The remaining deciles are defined conventionally. Patient counts in each of these higher deciles were not exactly 10 percent since patients in a given hospital were retained in the same decile category.

Measuring Health Care Outcomes

The primary measure of outcomes is risk adjusted 90-day mortality rates. While risk adjusted 30-day mortality rates are also presented, we favor 90-day rates because they are less likely to penalize hospitals with high rates of revascularization and subsequent operative mortality. Previous uses of these outcome data have been described elsewhere.^{35–38} As noted by previous studies, measures of hospital performance using patient outcome data can be biased by differences across hospitals in the average severity of disease.³⁹ However, measures of risk-adjusted AMI mortality have been shown to be valid indicators of hospital quality, and have been incorporated into hospital profiling efforts, for example those developed by the Agency for Healthcare Research and Quality.⁴⁰

Flexible quadratic age and gender interaction terms (age, age², sex, age × sex, and age² × sex) were included in all analyses. As well, the following disease categories were entered separately as categorical variables: vascular disease, dementia, renal, pulmonary, diabetes (with and without complications), liver (with and without complications), and cancer (non-metastatic and metastatic). Also included were year categorical variables (with the year 2001 the reference year) and categorical variables indicating the severity of the AMI: whether anterior, inferior, sub-endocardial, or a reference “other” category.

Analysis

Multivariable logistic regression models were estimated for risk-adjusted 90-day (and 30-day) mortality across the deciles of percent African-American in each hospital. In each model reported in the paper, standard-errors are clustered at the hospital level and all statistical analysis was performed in STATA v8.0.41 We wish to facilitate exposition and to avoid misinterpreting odds-ratios as relative-risks when the underlying event is not rare,⁴² and so report expected probabilities rather than odds-ratios. We use the ADJUST command in STATA which sets all covariates to their mean values, and then “turns on” each of the decile categorical variables in turn. For each decile, an estimate and confidence interval is calculated in log-odds ratios; these are then converted into probability units. This is the expected mortality rate (and confidence interval) for a representative patient, one with average risk characteristics.

Potential Explanations for Differences in Risk-Adjusted Mortality Outcome Measures

We examine the role of six observable factors that might explain differences in hospital-level mortality outcomes. The first is that the different racial composition of the deciles could lead to unmeasured confounding if African-American patients exhibited higher rates of mortality even after adjusting for risk factors. We address this hypothesis in two ways. The first is to estimate the logistic model with race-decile interaction terms, which allows for two separate mortality gradients, one for black and the other for white AMI patients. The disadvantage of this approach is that there are very few African-American AMI patients in the lower deciles, with a corresponding deficiency in statistical power. We therefore combined deciles 2–6 into one group comprising 11.4 percent of black patients and 39.8 percent of white patients. The second approach is to estimate a logistic model separately for black and white patients, but with a single variable, the percentage of black AMI patients in

the hospital (a hospital-level variable), to test for a linear race-specific gradient in the logistic regression.

Second, hospitals admitting African-American AMI patients have been shown to be less likely to perform surgical interventions.^{3–19,43} To capture these effects, hospital-specific rates of coronary artery bypass grafts (CABG) and percutaneous coronary interventions (PCI) in the sample are included in one specification of the regression. Third, hospitals may differ with respect to average volume of treatment.^{30,44–46} The hospital-specific AMI volume is therefore included as an additional explanatory variable. Fourth, the ownership status of hospitals could confound racial effects if African-American patients are more likely to be admitted to government hospitals. We therefore use indicator variables to adjust for the teaching and ownership status of the hospital (government (non-federal), not-for-profit, for-profit). As noted by others, these variables are markers for multiple competing factors,⁴⁷ and should not be interpreted as measuring the effect of ownership, volume, or treatment intensity *per se*.

Fifth, there may be systematic differences in income levels across regions, and so we adjust by median household income by zip code from the 2000 Census. Finally, we adjust for location of residence using the four U.S. Census regions and whether the individual lives in an urban area. We note that adjusting for geography can lead to underestimates (or overestimates) of true racial disparities.²⁷ If a large fraction of African-Americans live in the South, then adjusting for Southern residence automatically removes one factor – average mortality differences between Southern and Non-Southern hospitals – that can explain overall racial disparities in outcomes.

Unmeasured confounding factors could bias estimates. Specifically, if patients seen in hospitals that disproportionately treated African-Americans experienced a higher prevalence of comorbidities not observed in the data, we would spuriously attribute elevated mortality rates to such hospitals. To examine this hypothesis we constructed an index of disease severity, as proxied by *observed* comorbidities and the location of the infarct. This index is estimated using a logistic regression that predicts 90-day mortality, and includes race, age, sex, all measured comorbidities, and the severity of the AMI. Differences in the severity of the comorbidities and location of the AMI generate variation in the index of predicted mortality, and are presented by hospital racial decile in terms of predicted 90-day mortality. When there are no differences across hospital deciles in the comorbidity index, the role for unmeasured confounding variables to bias estimates is circumscribed. The reason is that confounding variables tend to be correlated with one another; smokers for example (an unmeasured variable) tend to have lower incomes and are more likely to present with COPD or cancer (measured variables). Finding that the measured variables are unassociated with hospital deciles therefore reduces the likelihood that the unmeasured (correlated) covariates are positively associated with hospital deciles.⁴⁸

Results

Table 1 presents summary statistics for fee-for-service Medicare beneficiaries who were treated for AMI between January 1st 1997 and September 30th 2001. The table illustrates the construction of the deciles used in the analysis. The average Medicare AMI patient was treated in a hospital where 6.9 percent of the patients were African-American. The bottom “decile” accounted for 12.5 percent of the population who were admitted to 1369 hospitals (comprising 32 percent of all hospitals) that saw no African-American AMI patients over the duration of the study period. These hospitals constitute Decile 1 (the lowest decile) of percent African-American patients in the hospital. On the other end of the spectrum, 33.6 percent of patients in Decile 10 hospitals were African-American. Patients admitted to

hospitals with the highest fraction of African-American patients were more likely to live in the South, and less likely to live in an urban setting. Differences across the deciles are significant statistically ($p < .001$).

There was large variation in ownership status and treatment intensity between hospitals based on the extent to which they treat the African-American population (Table 2). Relative to the hospital that the average AMI patient was treated at, hospitals that disproportionately treat African-Americans are more likely to be teaching hospitals, more likely to be government (non-federal), and less likely to be not for profit. These hospitals are similar in terms of CABG and PTCA intensity, but have lower AMI volume. All differences across the deciles are highly significant statistically ($p < .001$).

With the exception of hospitals that treat no African-Americans, the distribution of comorbidities and severity of the AMI across hospitals (adjusted for age, race and sex) is similar (Figure 1). In decile 2 hospitals (where only 0.3 percent of patients were African-American), the index of predicted 90-day mortality based solely on comorbidities and severity of the AMI was 22.2 percent (95% CI: 22.1–22.3%). It was 22.1 percent (95% CI: 22.0–22.2%) and 22.0 (95% CI: 21.9–22.1%) for hospitals in deciles 9 and 10 respectively. The noticeable exception to the similarity in comorbidities across deciles of percent African-American is seen for patients in Decile 1 hospitals. These patients, all of whom are white, have predicted 90-day mortality of 23.7% (95% CI: 23.6–23.8%), 7 percent higher than the expected mortality in the other deciles. While not reported in the table, the elevated mortality in decile 1 is attributable largely to the elevated prevalence of renal failure (2.9 percent in this decile compared to 2.2 percent for other deciles; $p < 0.001$), and a lower likelihood of being diagnosed with a subendocardial infarction (39.0 versus 49.0 percent for other deciles; $p < 0.001$).

Figure 2 illustrates risk-adjusted 90-day mortality across hospital deciles. Hospitals that have a greater share of African-American AMI patients have substantially higher risk-adjusted mortality. Even though patients in decile 1 hospitals are the sickest (as measured by the index of comorbidities) they experience the lowest risk-adjusted mortality following AMI. Figure 2 presents results from two models. In the first, outcomes are adjusted for age, race, sex and comorbidities. In the second, we further adjusted for income, hospital ownership, region, and treatment characteristics. The two models yield similar results suggesting that the hospital characteristics and income are not significant explanatory variables once comorbidities have been adjusted for. The area under the Receiver Operator Curve (ROC) is 0.679 for the first model, and 0.681 for the second.

Figure 3 presents estimated adjusted mortality separately by race. Because of the small number of African-American AMI patients in deciles 2–6, these deciles were combined to improve statistical power in estimating race-specific adjusted mortality. Estimated mortality for African-Americans in decile 10 hospitals are significantly higher than for decile 2–6 hospitals ($p = .04$). The difference between black and white adjusted mortality rates is not significant within each hospital decile, but a joint test of significance rejects the null hypothesis of equality ($p < 0.001$). For the logistic regressions estimated separately for white and black AMI patients, the mortality gradient (by fraction of African-American admissions to the hospital) was significant for both white ($p < .001$) and black ($p = .007$) patients.

We obtained similar results regarding the association between hospital deciles and mortality using 30-day mortality. In these models, which also adjusted age, race, gender, comorbidities, hospital teaching status, region, ownership and treatment intensity, 30-day mortality in Decile 1 hospitals is 14.9% (95% CI: 14.6–15.2%), in Decile 2 15.6% (95% CI: 15.2–16.1%), and in Decile 10 17.6% (95% CI: 17.2–18.0%). Using these estimates,

hospitals in decile 10 experienced 18 percent higher mortality relative to decile 1 hospitals. However, 30-day mortality within hospitals was not significantly higher among African-American patients.

Any potential burdens of higher mortality risk in hospitals that serve African-Americans is borne disproportionately by African-American patients, since a large fraction of this population is seen in the hospitals that comprise decile 9 and decile 10 hospitals. As Figure 4 shows, nearly half of African-Americans are seen in decile 10 hospitals, those with among the highest risk-adjusted mortality. Sixty-nine percent of African-American patients are seen in the 21 percent of hospitals that constitute decile 9 and 10 hospitals.

Discussion

Risk-adjusted mortality following AMI is significantly higher in hospitals that disproportionately serve African-Americans, and this result holds even after adjusting for a variety of potential confounding factors. Our results may appear inconsistent with those in Kahn et al., who found African-Americans with a variety of clinical conditions were more likely to be admitted to higher-quality urban teaching hospitals.⁴⁹ However, their study used a different time period (1981–86), and their sample was limited to 5 states. More recently, several studies have noted that African-American patients are treated by physicians with less clinical training,²⁸ referred to lower quality cardiac surgeons,⁵⁰ and treated at hospitals with higher risk-adjusted surgical mortality.³⁰ Other studies have also found a negative association between the fraction African-American admitted to the hospital and the use of emerging medical technologies³³ and favorable birth outcomes.^{51,52}

Within hospitals, 90-day mortality rates for African-Americans were somewhat higher than for whites. These results contrast with most studies using data from earlier periods that have not generally found elevated mortality risks among African-American AMI patients.^{6,12,13,20,49,53,54} More recent studies, however, have found higher rates of mortality and functional disability among African-American AMI patients.^{18,19}

The most important limitation of this paper is the possibility that unobservable health status of AMI patients in neighborhoods served by hospitals with a disproportionate number of African-American AMI admissions is systematically different from the average. If so, the higher mortality rates observed in these hospitals could be the result of unmeasured confounding factors, rather than hospital performance *per se*. One obvious difference across hospital deciles is simply that there are more African-American patients in the higher deciles, and if they are systematically sicker—conditional on covariates—then the estimates could be biased. However, even if outcomes are measured using white mortality rates or African-American mortality rates separately a significant mortality gradient is obtained.

Another limitation arises if risk adjustment does not adjust adequately for underlying illness. If the categorical comorbidity variables do not measure the severity of the disease, for example if diabetes is more severe among African-American AMI patients in decile 2 hospitals than among African-American AMI patients in decile 10 hospitals, then the results could be biased. It could also be the case that *unmeasured* confounding factors play a role in the elevated rates of mortality in the high-decile hospitals, for example smoking or exercise behavior. But the role for unmeasured confounding factors is constrained. For unmeasured confounding to bias the results, they would need to be unassociated with the measured confounders, which, as shown in Figure 1, explain none of the observed mortality gradient.

As well, hospitals serving a disproportionate number of African-American AMI patients tend to be located in low income neighborhoods, so the race variable could reflect socioeconomic status. A parallel analysis (not reported) assigning hospitals to deciles of zip

code income (rather than deciles of the proportion of African-American AMI patients) failed to show any consistent patterns: risk-adjusted mortality in decile 10 (high income) hospitals was not significantly different from risk-adjusted mortality in decile 1 (low income) hospitals. Similarly, accounting for the broad region of residence or urban status did not alter our results.

Why is risk-adjusted mortality – for both African-Americans and whites -- associated with a higher fraction of African-American hospital admissions? One hypothesis is that African-American AMI patients are more likely to be admitted to hospitals with lower volume, and lower volume has predicted worse outcomes in other studies.^{44–46} Similarly, it could be the case that overall revascularization rates in hospitals with a large fraction of African-American patients could be lower, as suggested by previous research documenting racial gaps in surgical treatment of cardiovascular disease.^{3–19,43} These explanations alone cannot explain the gradient, since the regression analysis adjusts for such factors. A plausible explanation is differences in hospital-level quality not adequately adjusted for in our analysis but highlighted in recent studies, such as time to reperfusion, the prescription of beta-blockers, post-surgical mortality, or the quality of physicians, could explain observed differences in outcomes.^{28,30–32,55,56}

Another limitation of the study is that it does not address racial disparities that take place within the hospital because of differences in the use of effective treatments or lack of communication between African-American patients and a largely white clinical staff. For example, Barnato et. al. documented substantially lower rates of PTCA and CABG for African-American AMI patients even after adjusting for the hospital to which they were admitted.³² Statistical analysis that distinguishes between these two explanations – disparities within hospitals, and disparities occurring because blacks go to different hospitals than whites – are therefore critical for future research on disparities.⁵⁷

The potential benefits that come from increasing quality of care are well understood.^{58–61} One implication of this study is that reducing mortality rates in high-mortality hospitals can have implications for reducing racial disparities in health outcomes. Because 21 percent of hospitals treat 69 percent of elderly African-American AMI patients, targeting quality improvements at hospitals that disproportionately serve African-Americans could dramatically reduce black-white disparities in care. As well, since many African-American Medicare beneficiaries live in urban areas with more than one hospital, efforts to better direct patients towards high quality hospitals may also be an effective means of reducing disparities.

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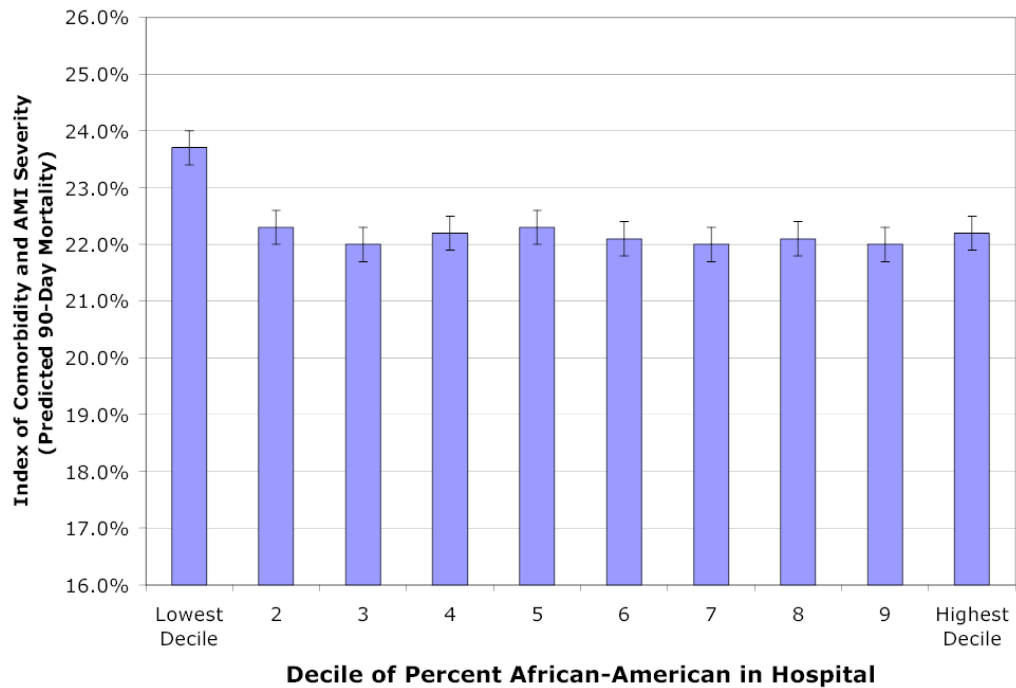


Figure 1. Index of Comorbidity and AMI Severity by the Average Percentage of African-American AMI Patients Admitted to the Hospital

Legend: The graph reports the average index of Comorbidity and AMI Severity by hospital decile according to the average percentage of African-American AMI patients admitted to that hospital. Multiple indicators for severity are used: the presence of vascular disease, pulmonary disease, dementia, diabetes, renal failure, cancer, and the location of the infarct, anterior, inferior, sub-endocardial, or other. These indicators are combined into one index using as weights the coefficients from a prediction model for 90-day mortality. Thus the index predicts 90-day mortality based on comorbidities and severity of the AMI, after adjusting for age, gender, and race. This index is intended to test the hypothesis that AMI patients are sicker in hospitals that disproportionately admit African-Americans. The graph indicates that this hypothesis is rejected; indeed those patients admitted to the lowest decile (no African-American admissions) experience elevated risk factors.

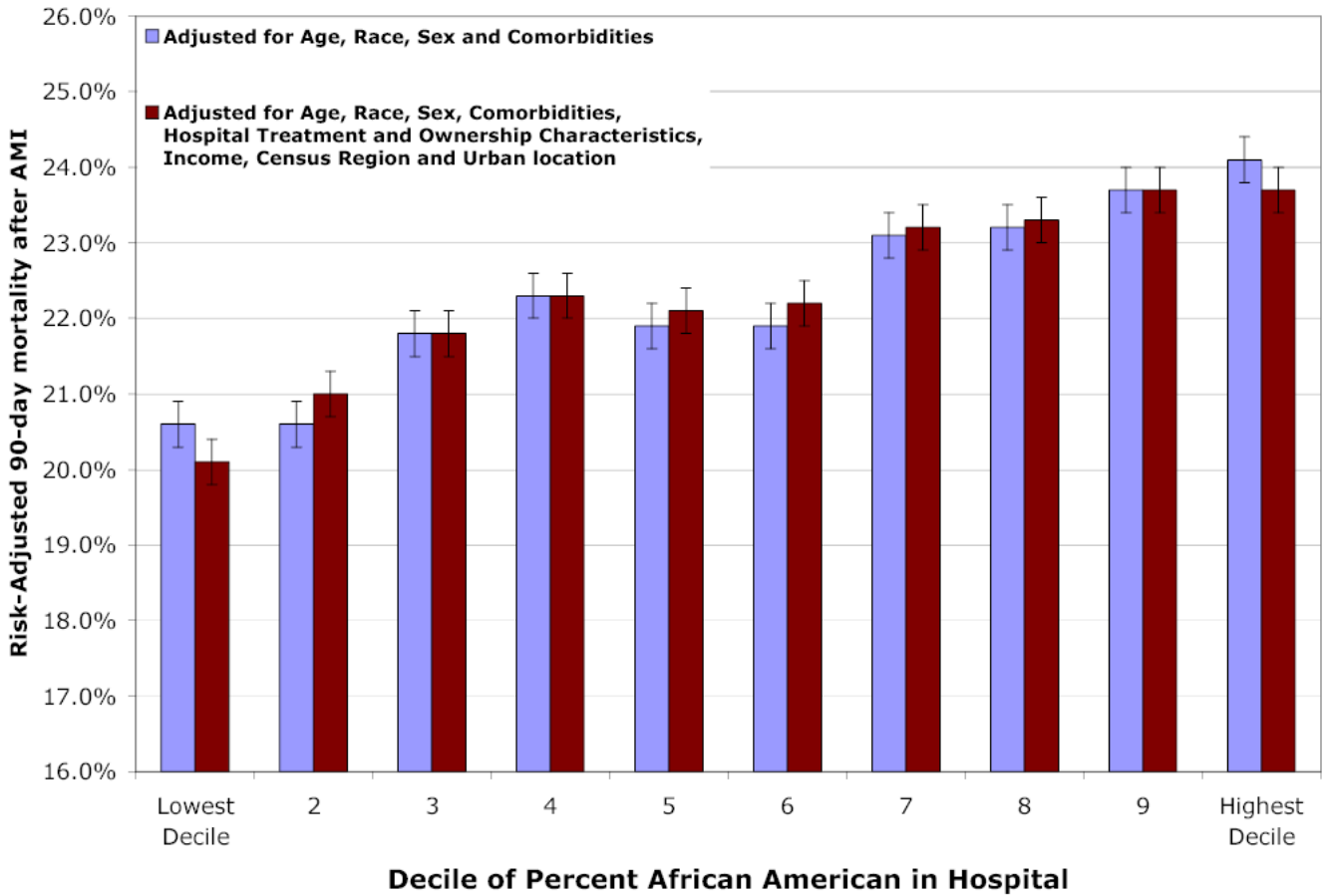


Figure 2. Risk-Adjusted 90-Day Mortality after AMI, by the Average Percentage of African-American AMI Patients Admitted to the Hospital

Legend: The graph reports 90 day mortality after adjusting for age, gender, race, comorbidities, and location of the infarct (anterior, inferior, sub-endocardial, other). Comorbidities include presence of vascular disease, pulmonary disease, dementia, diabetes, renal failure, and cancer. Hospital ownership and treatment characteristics are listed in Table 2, and include teaching hospital, government non-federal ownership, non-government not for profit, investor owned (for profit), hospital PTCA and CABG rates and annual AMI volume. Income refers to beneficiary’s zip-code income. Region refers to the 4 Census regions. A joint test of the importance of hospitals deciles is significant at the $p < .001$ level.

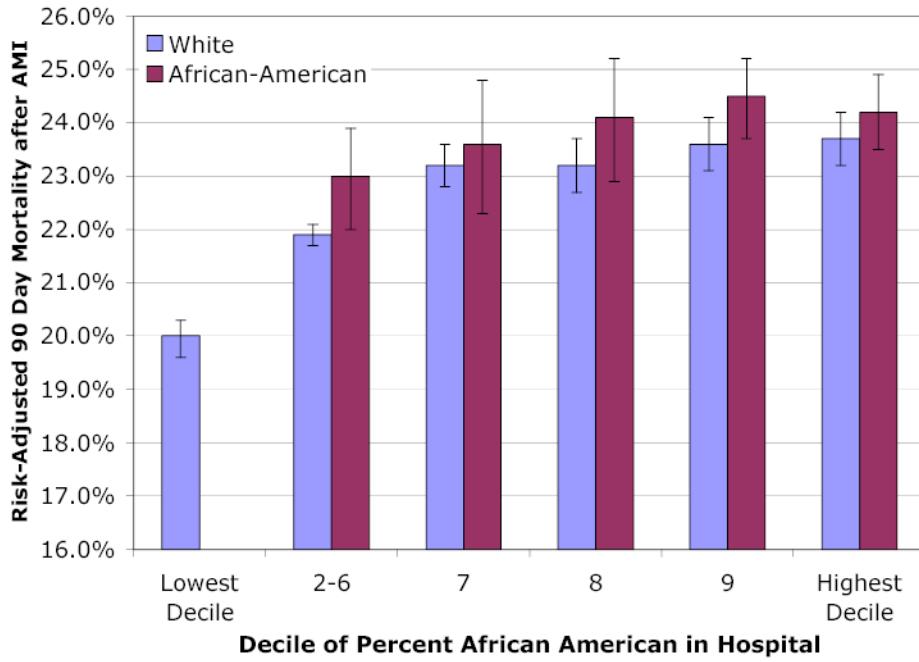


Figure 3. Risk-Adjusted 90-Day Mortality after AMI, by Race and Average Percentage of African-American AMI Patients Admitted to the Hospital

Legend: This regression includes all covariates described in the Legend for Figure 2, but with black and white hospital decile effects allowed to differ. To improve statistical power, Deciles 2–6, which together comprise 11 percent of the black AMI sample, are combined.

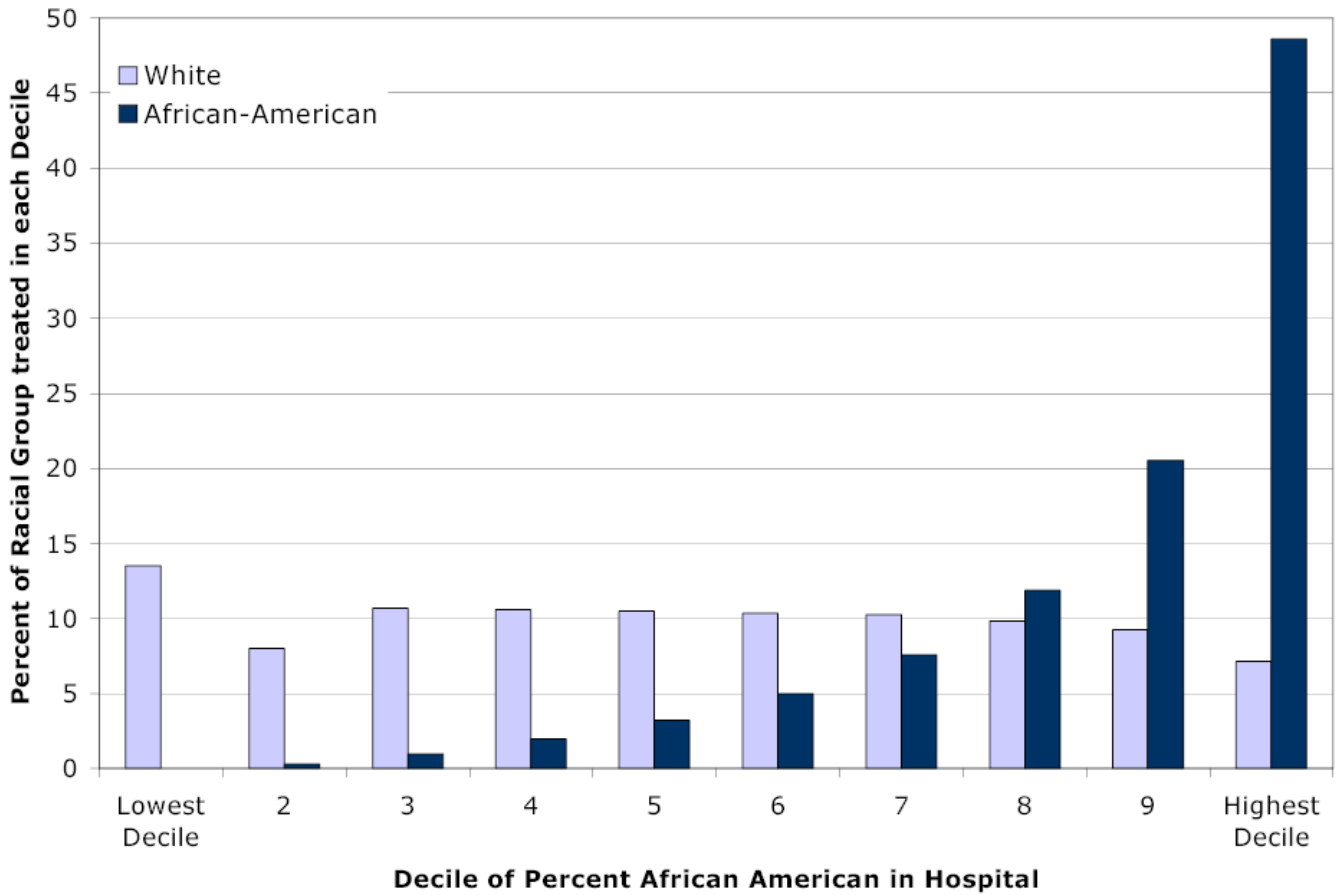


Figure 4. Distribution of African-American and White Patients, by the Average Percentage of African-American AMI Patients Admitted to the Hospital

Legend: The graph reports the share of each racial group (relative to all African-American or white AMI patients in the Medicare fee-for-service population) treated in hospitals within each decile category. A joint test of the importance of hospitals deciles is significant at the $p < .001$ level.

Table 1

Characteristics of AMI Patients and Hospitals, by the Average Percentage of African-American AMI Patients in the Admitting Hospital

Deciles of Percent African American in Hospital	Average Percentage of patients who are African American	Range (Min-Max)	Number of Hospitals	Percent of Patients in an Urban Area	Percent of Patients in the South	Number of Patients
Lowest Decile	0.0%	0-0%	1,369	24.0%	12.5%	142,666
2	0.3%	0.0-0.4%	162	40.1%	9.7%	84,971
3	0.7%	0.4-0.9%	276	47.8%	21.3%	113,853
4	1.4%	0.9-1.8%	342	43.9%	29.8%	113,526
5	2.2%	1.8-2.8%	287	48.4%	36.9%	113,769
6	3.4%	2.8-4.2%	291	43.9%	38.3%	112,265
7	5.2%	4.2-6.4%	326	41.2%	39.9%	114,056
8	8.2%	6.4-10.4%	337	43.6%	51.2%	114,348
9	14.2%	10.4-19.4%	358	43.8%	71.6%	114,686
Highest Decile	33.6%	19.5-98.6%	541	35.2%	68.9%	115,596
Total	6.9 %	0.0-98.6%	4,289	40.8%	38.0%	1,136,736

Notes: AMI index events from January 1, 1997 to September 30, 2001 for beneficiaries enrolled in fee-for-service Medicare. In calculating averages, each hospital is weighted by the number of patients treated over the study period. Urban areas are defined as counties which are classified being part of a Metropolitan Statistical Area (MSA). States are classified as being in the South or West using United States Census Bureau definitions for these regions. All differences across deciles are jointly significant at the $p < .001$ level.

Table 2

Hospital Ownership Characteristics and Hospital Treatment Characteristics, by the Average Percentage of African-American AMI Patients in the Admitting Hospital

Percent African American in Hospital (Deciles)	Hospital Teaching and Ownership Status			Hospital Treatment Characteristics			
	Teaching	Govt. Non-Federal	Not for Profit	For Profit	Average CABG Rate after AMI	Average PTCA Rate after AMI	Annual AMI Volume
Lowest	3%	18%	76%	7%	9%	16%	48
2	7%	6%	91%	3%	12%	25%	143
3	8%	7%	77%	15%	12%	22%	139
4	8%	9%	82%	9%	11%	21%	117
5	16%	8%	81%	11%	13%	23%	154
6	15%	7%	83%	11%	13%	24%	154
7	23%	8%	80%	13%	12%	23%	152
8	28%	14%	74%	12%	12%	23%	143
9	20%	17%	70%	13%	12%	23%	129
Highest	30%	17%	70%	13%	11%	20%	107
Average	16%	11%	78%	11%	12%	22%	126

Source: AMI index events from January 1, 1997 to September 30, 2001 for beneficiaries enrolled in fee-for-service Medicare. Each hospital is weighted by the number of patients treated over the study period. Annual AMI Volume is the average number of patients aged 65 and over in the Medicare program admitted to the hospital for AMI. All differences across deciles are jointly significant at the p < .001 level