Does Physician Specialty Affect the Survival of Elderly Patients with Myocardial Infarction?

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Objective. To determine the effect of treatment by a cardiologist on mortality of elderly patients with acute myocardial infarction (AMI, heart attack), accounting for both measured confounding using risk-adjustment techniques and residual unmeasured confounding with instrumental variables (IV) methods.

Data Sources/Study Setting. Medical chart data and longitudinal administrative hospital records and death records were obtained for 161,558 patients aged ≥ 65 admitted to a nonfederal acute care hospital with AMI from April 1994 to July 1995. Our principal measure of significant cardiologist treatment was whether a patient was admitted by a cardiologist. We use supplemental data to explore whether our analysis would differ substantially using alternative definitions of significant cardiologist treatment.

Study Design. This retrospective cohort study compared results using least squares (LS) multivariate regression with results from IV methods that accounted for additional unmeasured patient characteristics. Primary outcomes were 30-day and one-year mortality, and secondary outcomes included treatment with medications and revascularization procedures.

Data Collection/Extraction Methods. Medical charts for the initial hospital stay of each AMI patient underwent a comprehensive abstraction, including dates of hospitalization, admitting physician, demographic characteristics, comorbid conditions, severity of clinical presentation, electrocardiographic and other diagnostic test results, contraindications to therapy, and treatments before and after AMI.

Principal Findings. Patients admitted by cardiologists had fewer comorbid conditions and less severe AMIs. These patients had a 10 percent (95 percent CI: 9.5–10.8 percent) lower absolute mortality rate at one year. After multivariate adjustment with LS regression, the adjusted mortality difference was 2 percent (95 percent CI: 1.4– 2.6 percent). Using IV methods to provide additional adjustment for unmeasured differences in risk, we found an even smaller, statistically insignificant association between physician specialty and one-year mortality, relative risk (RR) 0.96 (0.88– 1.04). Patients admitted by a cardiologist were also significantly more likely to have a cardiologist consultation within the first day of admission and during the initial hospital stay, and also had a significantly larger share of their physician bills for inpatient treatment from cardiologists. IV analysis of treatments showed that patients treated by cardiologists were more likely to undergo revascularization procedures and to receive thrombolytic therapy, aspirin, and calcium channel-blockers, but less likely to receive beta-blockers.

Conclusions. In a large population of elderly patients with AMI, we found significant treatment differences but no significant incremental mortality benefit associated with treatment by cardiologists.

Key Words. Acute myocardial infarction, mortality, cardiovascular treatment effects, instrumental variables methods

Although clinical trials have shown that the mortality from acute myocardial infarction (AMI) can be significantly reduced through the use of primary angioplasty (Gibbons, Holmes, Reeder, et al. 1993; Grines, Browne, Marco, et al. 1993; Michels and Yusuf 1995), thrombolytic therapy (Fibrinolytic Therapy Trialists' Collaborative Group 1994), aspirin (Krumholz, Radford, Ellerbeck, et al. 1995), beta-blockers (MIAMI Trial Research Group 1985; Infarct Survival Collaborative Group 1986), and angiotensin-converting enzyme inhibitors (ACE-inhibitors) (Latini, Maggioni, Flather, et al. 1995; Pfeffer, Braunwald, Moye, et al. 1992), physicians frequently fail to prescribe these therapies (Ryan, Anderson, Antman, et al. 1996; Brand et al. 1995). Since cardiologists have been shown to be more knowledgeable about the appropriate utilization of therapies to treat AMI (Ayanian, Hauptman, Guadagnoli, et al. 1994), a recommendation that cardiologists have primary treatment responsibility for all patients with AMI might improve the quality of care and outcomes of these patients.

In fact, one study showed that patients admitted by cardiologists were 12 percent less likely to die in the first year compared to patients admitted by internists (Jollis, DeLong, Peterson, et al. 1996). A subsequent study with limited statistical power did not confirm this association (Ayanian et al. 1997). Recently, a study of California Medicare beneficiaries with AMI confirmed

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that patients admitted by cardiologists had a lower mortality rate than patients admitted by internists, family practitioners, or medical subspecialists (Frances, Go, Dauterman, et al. 1999). However, adjustment for patient and hospital characteristics markedly reduced the association between physician specialty and patient mortality, whereas additional adjustment for measured treatments had little effect. Frances and colleagues (1999) postulated that the remaining benefit of cardiologist care might be due to residual confounding, but they could not distinguish the possibility that cardiologists perform better at unmeasured processes of care from their presumption that cardiologists care for healthier patients. In these studies, adjusting for other treatments received can be problematic, because the use of specific treatments may be correlated with unmeasured patient variables, just as treatment by a cardiologist may be. In the absence of a randomized controlled trial, which will likely never be performed, experts have suggested that resolving the debate over the benefits of care by a cardiologist may require better means of risk adjustment and of accounting for other beneficial treatments that are not causally related to cardiologist care (Ayanian et al. 1997).

One potential approach to removing residual selection bias is instrumental variables (IV) (Newhouse and McClellan 1998). IV methods have been used extensively in economics and have recently been used to account for unmeasured patient differences in observational medical studies (Mc-Clellan, McNeil, and Newhouse 1994). To use these methods, researchers must first identify observable variables for use as IVs that can effectively "randomize" patients into groups with different likelihoods of receiving the treatment of interest, while maintaining balance across the groups with respect to potential confounding health characteristics. For example, a prior study used the differential distance, defined as the distance from a patient's home to the nearest hospital offering angiography minus the distance from a patient's home to the nearest hospital that did not offer angiography, as an instrumental variable to separate patients into those more or less likely to receive invasive therapy for AMI. Patients with small differential distances, those who lived near a hospital with angiography, had similar health characteristics to patients who lived farther away, but they had a significantly higher likelihood of receiving coronary angiography and cardiac revascularization procedures (angioplasty and bypass surgery). By using IV, the researchers were able to adjust for potential unmeasured risk factors that could not be accounted for by standard risk-adjustment methods, and thereby obtained an estimate of the health benefits of the additional or incremental use of intensive procedures that was not confounded by selection bias (McClellan, McNeil, and Newhouse 1994).

Given the inability of prior studies to determine whether cardiologists' patients with AMI actually have a lower mortality rate than patients treated by other physicians, we used both traditional risk adjustment and IV methods to evaluate the association of physician specialty and one-year mortality among 161,558 Medicare beneficiaries with AMI. Our analysis used a large national sample of elderly patients with a very extensive set of risk adjusters, and also assessed whether IV methods indicated substantial residual confounding. In addition, our analysis also explored the relationship between being admitted by a cardiologist and the intensity of treatment by cardiologists throughout the initial hospital stay. Virtually all previous studies have simply evaluated admission by a cardiologist. Thus, our study provides a significantly better opportunity to isolate the effect of cardiologist care from that of measured and unmeasured confounding variables for a nationally representative population.

METHODS

Data Sources

Our principal data were collected by the Cooperative Cardiovascular Project (CCP), a major policy initiative undertaken by the Health Care Financing Administration (HCFA) to improve health care quality for Medicare beneficiaries with AMI. CCP medical record abstracts for each patient include dates of hospitalization, demographic characteristics, comorbid conditions, severity of clinical presentation, electrocardiographic and other diagnostic test results, contraindications to therapy, and treatments before and after AMI (Normand et al. 1996). The reliability of the data abstraction process, which included more than 150 variables, has been demonstrated previously (Marciniak, Ellerbeck, Radford, et al. 1998). The clinical data from the CCP file were linked to longitudinal Medicare hospital discharge records, also maintained by HCFA, which identify the attending physician of each patient based on a Unique Physician Identification Number (UPIN). The UPIN file for 1995 identifies the practice setting and self-reported specialty for all physicians treating Medicare patients. The discharge records also provide detailed information on intensive procedures performed, including cardiac catheterization and revascularization (angioplasty and bypass surgery). The clinical data were linked to death records from the HCFA Denominator file,

which includes complete date of death information for Medicare beneficiaries. Each patient's residence was characterized as urban or rural based on its location within one of 320 metropolitan statistical areas.

Study Subjects

We identified 210,996 Medicare beneficiaries across the United States who were hospitalized with AMI between April 1994 and July 1995. The diagnosis of AMI was confirmed by chart review for each patient. The definition of AMI required either a creatine kinase–MB index ≥ 5 percent or an elevated lactate dehydrogenase level (LDH) with LDH-1 \geq LDH-2; or two of the following three criteria: chest pain, creatine kinase greater than or equal to twice the normal value, and electrocardiogram (ECG) evidence of AMI (Ellerbeck, Jencks, Radford, et al. 1995). We excluded patients who did not have a confirmed AMI (n = 23,480); and patients who had been transferred from another acute care hospital (14,137), since we lacked information regarding their presenting clinical characteristics. Patients whose records lacked information regarding their treating physician (63) or the geographical location of their home (15,803) were also excluded because our analyses depended on these variables. Only the first admission of a patient was included in the analysis. A total of 161,558 patients were evaluated.

To evaluate the possibility that patients treated by noncardiologists might have achieved a differential benefit from transfer to a second acute care hospital, we repeated all analyses excluding patients who were transferred out of the hospital within three days of admission. When we evaluated the remaining 148,325 patients, the results were virtually unchanged.

Treatment Variables

Admitting physicians were categorized based on their self-reported specialty in the UPIN file, which has been shown to have a high correlation with board certification status (Jollis, DeLong, Peterson, et al. 1996; Ayanian et al. 1997). Physicians who reported their primary or secondary specialty to be cardiology were defined as "cardiologists." All other physicians were classified as "noncardiologists."

To determine whether admitting physician specialty was correlated with intensity of treatment by cardiologists throughout a patient's initial hospital stay, we conducted a supplemental analysis of all physician billing records during the hospital stay from the Medicare Physician/Supplier (Part B) File for an approximately 5 percent random sample of Medicare beneficiaries admitted to the hospital with a primary diagnosis of new AMI during the time period of our analysis and for whom complete billing data could be obtained. We used these data to construct other patient variables, in addition to admission by a cardiologist, to describe the intensity of cardiologist treatment more completely. The additional cardiologist treatment variables were: whether or not the patient had at least one cardiology consultation during the first 24 hours of admission; whether the patient had at least one cardiology consultation at some time during the initial admission; the share of total Medicare physician payments during the initial hospital stay made to cardiologists; and the percent of all physician expenditures allocated to cardiologists. We defined patients as being in the "large cardiology share" (30 percent of all patients) if the proportion of all physician payments made to cardiologists exceeded 39 percent. We used this 5 percent sample to explore the relationship between being admitted by a cardiologist and these other aspects of cardiology care.

Hospitals were categorized along two dimensions to allow us to assess the impact of more intensive cardiologist care as well as whether other treatment and outcome effects are correlated with but not causally related to treatment by a cardiologist. First, we defined a hospital as a "cardiologist hospital" if cardiologists treated >50 percent of CCP patients admitted with AMI to that hospital. Second, we defined hospitals as "high volume" if they treated more than 50 Medicare patients with AMI in the CCP (Newhouse and McClellan 1998). Hospitals were also described based on their capacity to provide coronary angiography and revascularization.

Outcome Variables

Our primary outcomes were 30-day and one-year patient mortality rates by physician specialty. Secondary outcomes included treatment decisions that we hypothesized may be causally related to treatment by a cardiologist: the use of medical treatments and cardiac procedures. Medical treatments included in-hospital treatment with thrombolytic therapy, aspirin, beta-blockers, ACEinhibitors, and intravenous nitroglycerin; and discharge treatment with aspirin, beta-blockers, ACE-inhibitors, and calcium channel-blockers. Procedure outcomes included the use of coronary angiography, percutaneous transluminal coronary angioplasty (PTCA), and coronary artery bypass graft surgery (CABG) during hospitalization.

Missing Data

Missing data were handled with an imputation process. Missing data for an individual patient nearly always occurred in clusters. For example, ECG lead

results or chemistry values were nearly always absent collectively rather than individually. Because the values of these variables do not vary independently, we imputed values by cluster using a hotdeck procedure based on approximately 50 demographic and clinical variables that were almost always present (Meng 1997; Fitzmaurice and Laird 1997; McClellan and Noguchi 1998). To evaluate the effect of imputed data, we repeated all analyses without the imputed variables and verified that the results did not change significantly.

Analytic Approach

To evaluate the effect of treatment by a cardiologist, we initially compared the populations of patients treated by cardiologists and noncardiologists. Pairwise comparisons between groups were made using chi-square tests for dichotomous data and the student's *t*-test for continuous data. Because of our very large sample size, quantitatively small differences in characteristics that had no substantial effect on patient outcomes were often statistically significant.

We then employed robust (heteroscedasticity-consistent) least-squares (LS) multivariate linear regression to risk adjust for measured differences between the two populations. We first adjusted for demographic and geographic variables only (see Appendix for list of covariate categories). We then adjusted for comorbid illnesses and measures of disease severity. Our final models also included the effect of admission to a hospital that treated a high volume of AMI patients. We did not include patient receipt of medications or procedures, as these may be causally related to treatment by a cardiologist and may also be subject to confounding. The absolute 30-day and one-year mortality rates associated with treatment by cardiologists versus treatment by noncardiologists were calculated in each analysis.

Because LS risk-adjustment methods can only adjust for measured patient characteristics, we used IV methods to adjust for potential unmeasured confounding in the patients treated by cardiologists and by high-volume hospitals. IV analysis requires a variable that is not correlated with patient characteristics (e.g., comorbidity or severity of illness) that directly affect outcomes (e.g., mortality), but that is associated with the probability of the patient receiving the treatment of interest. We hypothesized that the location of a patient's residence would independently predict the likelihood of being treated by a cardiologist. We grouped patients geographically based on their differential distance to a cardiologist hospital, a hospital where over half of CCP patients were treated by a cardiologist. Our differential distance was defined as the distance from a patient's home to the nearest cardiologist hospital minus the distance from a patient's home to a noncardiologist hospital. Patients with smaller differential distances are thus closer to hospitals where cardiologists treat a majority of AMI patients. Approximate geographic locations of patient homes and hospitals were estimated using the geographic centroid of their respective ZIP codes. We then used an algorithm to estimate the distance between patient and hospital ZIP codes and to identify the minimum distance to each type of hospital for each patient.

To evaluate the validity of our instrumental variable, we stratified the entire cohort into two groups based on their differential distance to a cardiologist hospital. We used the median differential distance (6.6 miles) to separate the population approximately in half. This initial comparison validated our primary assumption that differential distance to a cardiologist hospital was not associated with the health status of the patients but was a strong predictor of treatment by a cardiologist.

To utilize the full range of the differential difference variation, we applied more general IV estimation techniques by stratifying the population into a larger number of groups. Urban residents were categorized into groups based on differential distances of less than -2.8 miles, -2.8 to 0.00, 0.01 to 2.20, 2.21 to 4.70, 4.71 to 9.80, 9.81 to 20.8, and greater than 20.8 miles; rural residents were categorized by differential distances of less than 9.7 miles, 9.8 to 22.6, 22.7 to 33.4, 33.5 to 48.0, and greater than 48 miles. Urban and rural residents were categorized differently since larger differential distances were needed to establish equal groups of rural residents. Separating the population into these cells extended the two-group IV comparison across a larger number of differential distance groups that did not differ substantially in their measured characteristics. We included variables for patient demographic, comorbidity, and severity of illness information in our multivariate IV models (Rubin 1997).

Because we found that cardiologists and cardiology hospitals tended to be associated with larger, more experienced, and more intensive facilities, we also repeated our IV models including the effect of treatment by a highvolume hospital (independent of treatment by a cardiologist). Our goal was to remove at least some of the confounding caused by potentially beneficial treatments that were associated with but not causally related to greater likelihood of treatment by a cardiologist, in order to obtain the least confounded estimate possible of the mortality rate difference by physician specialty. Comparisons between cardiologists and noncardiologists are primarily expressed as adjusted percentage-point differences in outcomes; for certain examples, these are converted to relative risks (SAS Institute 1996).

Utilization of Treatments and Procedures

To determine whether there are differences in practice patterns between cardiologists and noncardiologists, we compared their respective utilization of medications and therapies. We used IV models that adjusted for both hospital volume and detailed patient characteristics to remove potential biases in our estimates of the effect of more intensive cardiologist care on use of medications and cardiac procedures.

RESULTS

Characteristics of Patients Treated by Cardiologists and Noncardiologists

Medicare patients admitted by cardiologists (38 percent) were younger and more likely to be white and male than patients treated by other physicians (Table 1). These patients were less likely to have chronic illnesses, such as diabetes mellitus, congestive heart failure, cerebrovascular disease, chronic obstructive pulmonary disease, and dementia but were more likely to have had prior angina, PTCA, and CABG surgery. Patients with a prior MI were slightly less likely to be treated by cardiologists. Severity of illness measures generally indicated that patients treated by cardiologists were less critically ill than those treated by other physicians. Cardiologists' patients were more likely to receive early medical attention after developing symptoms, have normal vital signs and a low Killip class, and be verbally oriented compared with noncardiologists' patients.

We also found differences in hospital characteristics between patients treated by cardiologists and those treated by other physicians. Patients treated by cardiologists were more likely to be admitted to hospitals that cared for a higher volume of elderly AMI patients and that provided coronary angiography and revascularization.

Mortality Rates Using LS Method

Patients treated by cardiologists had lower unadjusted 30-day mortality (RR = 0.77; 95 percent CI: 0.75–0.79) and one-year mortality (RR = 0.73; 95 percent CI: 0.72–0.75) compared with patients treated by other physicians (Table 2). Adjusting for demographic and geographic characteristics reduced the one-year mortality difference attributable to cardiologists by over 30 percent (RR = 0.81; 95 percent CI: 0.80–0.83). Further adjustment for patient

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	Cardiologist- Treated (%) (N = 62,114)	Noncardiologist- Treated (%) (N = 99,444)	P-value
Demographic characteristics			
Age	73.7	76.6	< 0.001
Female	43.0	51.9	< 0.001
Black	6.2	8.3	< 0.001
Rural	28.3	28.2	0.65
Comorbidity variables			
Diabetes	28.9	33.1	<0.001
Hypertension	60.1	62.9	< 0.001
Congestive heart failure	18.0	26.0	<0.001
Prior stroke	12.3	16.4	< 0.001
Current smoker	18.6	15.3	< 0.001
Prior angina	51.3	44.7	< 0.001
Prior myocardial infarction	5.8	6.7	< 0.001
Prior PTCA	10.3	4.9	< 0.001
Prior CABG surgery	17.3	10.3	< 0.001
Chronic obstructive pulmonary disease	18.6	23.4	< 0.001
Peripheral vascular disease	11.0	12.0	< 0.001
Dementia	3.4	8.8	< 0.001
Walks independently	82.6	72.0	< 0.001
Depression	7.5	10.4	< 0.001
Continent	92.2	86.4	< 0.001
Measures of severity			
Verbally oriented	93.1	88.2	< 0.001
Heart rate > 100 beats/min.	20.5	29.2	< 0.001
Mean arterial pressure: ≥ 40mm Hg and < 80 mm Hg	16.0	14.9	<0.001
Time since chest pain started: < 6 hours	22.6	20.8	< 0.001
Time since chest pain started: 6–12 hours	29.2	26.6	< 0.001
Anterior myocardial infarction	45.6	44.9	0.006
Myocardial infarction on electrocardiogram	79.4	76.3	< 0.001
Blood urea nitrogen $> 40 \text{ mg/dl}$	6.4	10.2	< 0.001
Killip class			
Killip class 1	54.5	46.1	
Killip class 2	12.2	12.2	
Killip class 3	30.0	39.1	
Killip class 4	3.3	2.6	
Admitting hospital			
Admission to high-volume hospital	86.3	68.2	< 0.001
Admission to cardiac catheterization hospital	93.0	74.6	< 0.001
Admission to revascularization hospital	80.1	55.3	< 0.001
Admission to cardiologist hospital	62.1	22.8	<0.001
Outcomes			
30-day absolute mortality rate	17.2	22.3	<0.001
1-year absolute mortality rate	28.2	38.4	<0.001

Table 1: Baseline Characteristics Among AMI Patients Treated byCardiologists and Noncardiologists

Table 2:Absolute Differences in Mortality Among AMI PatientsTreated by Cardiologists Compared to Patients Treated byNoncardiologists, Using Lease-Squares Method of MultivariateRisk Adjustment

	30-Da	y Mortality	1-Year Mortality		
	Treatment Effect (P-Value)	95% Confidence Interval	Treatment Effect (P-Value)	95% Confidence Interval	
Unadjusted	-5.1	(-5.5~-4.7)	-10.2	(-10.6~-9.7)	
	(<0.001)		(<0.001)		
Adjusted for demographic and geographic variables	-2.9	(-3.3~-2.5)	-6.4	(-6.9~-6.0)	
00r	(<0.001)		(<0.001)		
Adjusted for demographic, geographic, comorbidity.	-1.1	(-1.5~-0.7)	-2.6	(-3.0~-2.1)	
and severity variables	(<0.001)		(<0.001)		
Adjusted for demographic,	-0.6	(-1.0~-0.2	-2.0	(-2.4~-1.5)	
and hospital volume variables	(0.004)		(<0.001)		

comorbidity and severity of illness markedly reduced, but did not eliminate, the attributable difference in one-year mortality associated with treatment by a cardiologist (RR = 0.94; 95 percent CI: 0.93–0.96). Thus, adjusting for measured selection bias decreased the mortality benefit associated with cardiologist treatment by over 75 percent.

Preliminary IV Comparisons Using Stratification by Differential Distances

To test the hypothesis that the differential distance to a cardiologist hospital is not associated with patient comorbidity or severity of illness characteristics, we stratified our population into two groups based on differential distance less than or greater than -6.6 miles (Table 3). In contrast to Table 1, the two groups were nearly identical with respect to most of the measured characteristics that predict mortality. Although rural location and race are not equally distributed in the two groups, we adjusted for these variables in our multivariate models. The effective randomization in terms of similarity of measured characteristics

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	$\frac{Differential}{Distance} \\ \leq 6.6 \text{ miles (%)} \\ (N = 84.090)$	$\begin{array}{l} Differential \\ Distance \\ \geq 6.6 \text{ miles (\%)} \\ (N = 77.468) \end{array}$	P-value
Demographic Characteristics			
Are	75.6	754	<0.001
Female	18.8	18 2	0.001
Black	40.0	56	<0.01
Bural	03	48 7	<0.001
Comorbidity Variables	5.0	40.7	NO.001
Diabetes	313	31.8	0.05
Hypertension	62.8	60.7	<0.001
Congestive Heart Failure	22.0	23.0	0.001
Prior Stroke	14.7	14.0	0.00
Current Smoker	16.4	14.5	0.17
Prior Angina	10.4	471	0.01
Prior Myocardial Infarction	69	47.1 66	0.001
Prior PTCA	73	6.6	<0.001
Prior CABG Surgery	13.9	12.8	0.001
Chronic Obstructive Pulmonary Disease	20.8	12.0 22.4	<0.01
Perinheral Vascular Disease	11.8	113	0.001
Dementia	60	6.5	0.001
Walks Independently	76.7	75.4	<0.004
Depression	8.8	00	<0.001
Continent	89.0	88 3	<0.001
Measures of Severity	00.0	00.0	NO.001
Verbally Oriented	00.3	80.0	0.02
Heart Rate > 100 heats/min	26.5	25.1	<0.02
Mean Arterial Pressure: > 40 mm Hg and < 80	14.9	15.7	<0.001
mm Ha	14.5	10.7	NO.001
Time since chest pain started: < 6 hours	91.1	<u> 22 0</u>	<0.001
Time since chest pain started: 6-19 hours	26.9	22.0	<0.001
Anterior Myocardial Infarction	44.9	45.4	014
Myocardial Infarction on Electrocardiogram	77.6	77 4	<0.001
Blood urea nitrogen $> 40 \text{ mg/dl}$	9.0	85	<0.001
Killin Class	0.0	0.0	<0.001
Killin Class 1	48 9	49 7	-0.001
Killin Class 2	11.9	12.5	
Killin Class 3	36.2	34.9	
Killin Class 4	30	2.8	
Admitting Hospital	0.0	2.0	
Admission to high-volume hospital	84.2	70.5	<0.001
Admission to cardiac catheterization hospital	84.9	67.3	<0.001
Admission to revascularization hospital	62.7	46.8	<0.001
Admission to cardiologist hospital	51.1	23.5	< 0.001
Admitting Physician	• • • •	2010	101001
Cardiologist	43.8	32.7	<0.001
Outcomes			
30-day absolute mortality rate	19.7	21.0	<0.001
1-year absolute mortality rate	34.1	34.9	< 0.001
			-

Table 3:Comparison of Elderly AMI Patients Stratified byDifferential Distance to a Cardiologist Hospital

remained when the cohort was divided into 12 groups of equal size based on differential distances.

Despite their similar characteristics, the two groups showed important differences with respect to their treatment (Table 3). Patients with differential distance less than 6.6 miles were more likely to be treated in a high-volume hospital, a catheterization hospital, or a revascularization hospital, and they were 40 percent more likely to be treated by a cardiologist.

Table 4 presents evidence on the relationship between the widely applied definition of significant treatment by a cardiologist, based on whether the patient was admitted by a cardiologist, and several reasonable alternative definitions. Because these alternative definitions required complete physician billing data that we were only able to obtain for approximately 5 percent of new AMI patients admitted to the hospitals during the time period of our analysis, the sample sizes for this table are much smaller. Table 4 shows that, regardless of the definition of cardiologist treatment used, our IV approach distinguishes patient groups treated more and less intensively by cardiologists.

Mortality Rates Using IV Methods

In our most complete adjustment for observed and unobserved differences in patient characteristics using detailed risk adjustment plus the multivariate IV method, treatment by a cardiologist was no longer associated with significantly lower mortality rates at 30 days or one year (Table 5). Compared to the LS results in Table 2, the IV estimates of the cardiologist effect on 30-day

Variable (%)	Differential Distance ≤ 6.6 miles	Differential Distance > 6.6 miles
Measure available from full chart review sample	(N = 84,090)	(N = 77,468)
Admitted by cardiologist (full sample)	43.8	32.7
Measures available from 5% complete billing record sample	(N = 3,728)	(N = 3,823)
Treated by cardiologist withing 24 hrs of admission	51.8	37.1
Treated by cardiologist during initial hospitalization	76.4	64.7
Share of physican expenditures from cardiologists	28.4	23.4
High share of physican expenditures from cardiologists*	33.0	27.3

Table 4:Comparison of Alternative Definitions of Intensity ofCardiologist Treatment

*High share defined as more than 39 percent of expenditures from cardiologists as a share of total physician expenditures during initial hosiptal stay.

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Table 5: Effect of Admission to a High-Volume Hospital andTreatment by a Cardiologist for Patients with AMI, Adjusted forDemographic, Geographic, Comorbidity, and Severity Variables usingInstrumental Variable Methods

	30-Day Mortality		1-Year Mortality		
	F-Test for IVs	Treatment Effect (P-Value)	95% Confidence Interval	Treatment Effect (P-Value)	95% Confidence Level
Admission to high-volume hospital	278.7	-2.9	(-4.1~-1.8)	-2.1	(-3.5~-0.8)
		(<0.001)		(0.002)	
Treatment by cardiologist	104.9	-1.6	(-3.9~0.6)	-1.3	(-4.0~1.3)
		(0.16)		(0.31)	

Note: The results are adjusted for demographic, comorbidity, severity, and hospital volume variables (see Appendix for details).

and one-year mortality remain small, and the one-year effect is even closer to 0. The confidence intervals for this estimate are considerably wider; we discuss the causes and implications of the wider confidence interval in the next section. In contrast to the insignificant effect for treatment by a cardiologist, admission to a hospital treating a high volume of AMI patients remained associated with a statistically significant 2 percent mortality benefit. As in our LS models (Table 2), accounting for the fact that intensive treatment by cardiologists is correlated with treatment by a high-volume hospital significantly reduces the apparent effect of cardiologist treatment.

Mortality Rates Using Fewer Predictor Variables

To test the impact of the instrumental variable on risk adjustment with a more limited number of predictor variables, we repeated our analyses using only the predictors that Jollis, DeLong, Peterson, et al. (1996) used in their study (see Appendix). Using LS analysis, we found a point estimate for the relative risk associated with treatment by a cardiologist, 0.86 (95 percent CI: 0.85–0.88), that was similar to that reported by Jollis, DeLong, Peterson, et al. (1996). However, when we utilized the IV analysis to adjust for unmeasured confounding, the estimate for the relative risk was 0.96 (95 percent CI: 0.88–1.04). Thus, detailed covariate adjustment had a substantial effect on our LS estimates but essentially no effect on our IV estimates.

Utilization of Medications and Procedures

Although we observed no significant benefit in mortality associated with treatment by cardiologists, cardiologists were more likely to utilize the most proven medications. After complete adjustment for measured and unmeasured confounding variables, cardiologists were more likely to utilize thrombolytic therapy, aspirin, intravenous nitroglycerin, and smoking cessation counseling (Table 6). However, they were also more likely to prescribe calcium channelblockers at discharge and less likely to prescribe beta-blockers. We found no significant differences in the use of ACE-inhibitors by physician specialty. Patients treated by cardiologists had utilization rates for coronary angiography and revascularization (PTCA or CABG) 28 percent and 19 percent higher than patients of noncardiologists. These differences increased to 33 percent and 29 percent after IV adjustment.

DISCUSSION

As previously demonstrated by other studies, we found that cardiologists treat AMI patients who generally have better survival prospects than patients treated by other physicians (Jollis, DeLong, Peterson, et al. 1996; Ayanian et al. 1997; Frances, Go, Dauterman, et al, 1999). Compared with noncardiologist patients, patients admitted by cardiologists were more likely to have demographic characteristics associated with lower mortality from AMI, including younger age, male sex, and white race (Normand et al. 1996; Vaccarino et al. 1995). In addition, patients treated by cardiologists were more likely to be able to walk independently and were less likely to have a comorbid illness associated with worse outcomes after AMI, including diabetes (Miettinen, Lehto, Salomaa, et al. 1998), hypertension (Gustafsson, Køber, Torp-Pedersen, et al. 1998), congestive heart failure (Normand et al. 1996), and depression (Barefoot, Helms, Mark, et al. 1996). Finally, consistent with prior studies, patients admitted by cardiologists appeared to have less severe AMIs, as assessed by Killip class and hemodynamic status (Donohoe 1998).

Although the outcomes of patients treated by cardiologists clearly differ from those of patients treated by other physicians, the two large prior studies that evaluated the association of physician specialty and patient mortality from AMI found that measurable selection bias explained only part of the observed benefit from cardiologist care (Jollis, DeLong, Peterson, et al. 1996; Frances, Go, Dauterman, et al. 1999). Although treatment differences between cardiologists and other physicians could account for the residual differences

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	Proportion of Patients Treated	Unadjusted Differences in Utilization	Instrumental Variable Adjusted Differences in Utilization	
		Treatment Effect (P-Value)	Treatment Effect (P-Value)	95% Confidence Interval
Thrombolytics during hospitalization	12.3	5.5	5.2	(3.2~7.1)
		(<0.001)	(<0.001)	
Aspirin during hospitalization	76.7	8.2	9.0	(6.6~11.5)
		(<0.001)	(<0.001)	
Aspirin at discharge	69.1	9.8	15.9	(12.6~19.1)
		(<0.001)	(<0.001)	
Beta-blocker during hospitalization	43.8	8.8	-9.5	(-12.4~-6.6)
		(<0.001)	(<0.001)	
Beta-blocker at discharge	37.8	7.6	-8.4	(-11.7~-5.0)
		(<0.001)	(<0.001)	
Nitroglycerin (IV) during hospitalization	47.6	13.2	9.5	(6.4~12.5)
		(<0.001)	(<0.001)	
ACE-inhibitor during hospitalization	39.2	-2.1	-2.7	(-5.6~0.3)
		(<0.001)	(0.07)	
ACE-inhibitor at discharge	35.4	-2.3	-3.0	(-6.3~0.3)
-		(<0.001)	(0.07)	
Calcium channel-blocker at discharge	38.0	3.1	5.2	(1.8~8.6)
		(<0.001)	(0.003)	
Coronary angiography during hospitalization	38.2	28.1	33.3	(30.7~35.9)
		(<0.001)	(<0.001)	
PTCA during hospitalization	15.5	19.4	24.7	(22.5~26.8)
		(<0.001)	(<0.001)	
CABG during hospitalization	8.8	-0.3	4.1	(2.4~5.8)
		(<0.001)	(<0.001)	
Smoking Cessation	7.1	2.4	1.5	(0.2~2.9)
Counseling during hospitalization		(<0.001)	(0.03)	

Table 6:Comparison of Treatments Used by Cardiologists Relativeto Noncardiologists

in patient mortality by physician specialty, one study found that differences in measured processes of care could account for only a small portion of the lower mortality rate associated with treatment by cardiologists (Frances, Go, Dauterman, et al. 1999). Traditional methods of risk adjustment cannot determine whether the mortality reduction associated with cardiologist care results from residual unmeasured differences in patient characteristics or in physician treatment decisions.

Our analysis used both extensive risk-adjustment methods and IV methods to assess selection bias. Our risk-adjustment methods differed from previous studies in our use of a much larger sample size and a much more extensive set of risk adjusters, as well as controls for hospital volume, which we hypothesized would diminish the amount of unmeasured confounding. By estimating our risk-adjustment models, including only predictors that Jollis, DeLong, Peterson, et al. (1996) used in their study (see Appendix), we were able to demonstrate more fully the significance of unmeasured confounding. We found a point estimate for the relative risk of one-year mortality associated with treatment by a cardiologist, 0.86 (95 percent CI: 0.85–0.88), that was similar to that reported by Jollis, DeLong, Peterson, et al. (1996). Our more detailed LS model significantly reduced the apparent association between cardiologist treatment and mortality to a relative risk of 0.94 (CI: 0.93–0.96).

To determine whether our risk adjustment results still suffered from significant residual confounding despite our very detailed multivariate model, we used IV methods as well. We postulated that patients who live relatively close to a hospital where most patients are treated by cardiologists would be similar to patients who live farther from such a hospital. This assumption is intuitive since people are unlikely to choose their residence based on whether AMI patients are primarily treated by cardiologists at hospitals that are relatively close by. We demonstrated that the differential distance to a hospital where most patients are treated by cardiologists, our instrumental variable, allowed us to construct groups that did not differ meaningfully in measured patient characteristics that predict mortality. We also found that patients who live relatively near a hospital where cardiologists care for most MI patients were 40 percent more likely to be treated by a cardiologist. Since the differential distance to a cardiologist hospital effectively randomized patients by creating groups with very similar health characteristics that differed in their likelihood of being treated by a cardiologist, it satisfied the required prerequisites of an instrumental variable.

Our IV analysis showed that the slightly lower one-year mortality rate apparent in the LS models after accounting fully for observable patient differences and for treatment at high-volume centers may still overstate the effect of cardiologist care. Because the fully risk-adjusted estimate of the cardiologist effect was small in absolute magnitude, the IV methods had only a quantitatively modest further effect, even though the point estimate was 35 percent smaller (relative risk of 0.96 compared to 0.94). The IV-estimated effect was virtually identical (relative risk of 0.96) in models that included only a more limited set of risk adjusters, as in the Jollis, DeLong, Peterson, et al. (1996) study, confirming the finding in Table 3 that the IV analysis does not appear to be confounded by differences in case mix. However, the confidence intervals of our IV estimates were considerably wider than the confidence intervals of the LS estimates. This is a general feature of IV analyses: because the estimates are based on a much more limited (albeit "cleaner") source of variation in treatment compared to actual (but potentially biased) treatment choice, the residual variance tends to be considerably wider than in LS models. While the wider intervals imply that our fully adjusted LS estimate and all of our IV estimates are not significantly different, the IV analyses consistently suggest that a favorable residual bias exists in the very precise LS estimate of the cardiologist effect. Since our sample essentially was the entire population of elderly AMI patients admitted to the participating hospitals during the study period, we conclude that, at least for elderly AMI patients in the time period we studied, the long-term mortality benefit of more intensive treatment by a cardiologist was extremely close to 0. Our results suggest that an incremental reduction in the use of cardiologists, as in our "low-cardiologist" hospitals, would have no substantial adverse mortality consequences.

Although greater treatment by a cardiologist was not associated with substantially lower one-year mortality, important differences were observed in the utilization of medications and procedures. As prior studies have also shown, patients treated by cardiologists were more likely to receive thrombolytic therapy, primary angioplasty, aspirin within a day of admission, and revascularization with angioplasty or bypass surgery during hospitalization (Jollis, DeLong, Peterson, et al. 1996; Ayanian et al. 1997; Frances, Go, Dauterman, et al. 1999; Borowsky, Kravitz, Laouri, et al. 1995). In contrast to a prior study (Jollis, DeLong, Peterson, et al. 1996), however, we found that noncardiologists were more likely to use beta-blockers both in the hospital and at discharge than cardiologists after adjustment for selection bias. A recent study that evaluated CCP patients who were "ideal" candidates for beta-blockers found, after adjusting for measured variables, that cardiologists were more likely to prescribe beta-blockers (Krumholz, Radford, Wang, et al.

1998). Using analyses that adjust for both measured and unmeasured forms of patient and hospital selection bias and that accounted for other hospital factors such as volume that were also associated with cardiologist treatment, we found that patients treated by noncardiologists were actually more likely to receive beta-blockers. While this particular finding regarding beta-blocker use might be anomalous, we note that it appears only in our fully adjusted IV model that includes both very detailed covariate adjustment and careful controls for treatment by high-volume hospitals. Thus, it is possible that the difference between our study and other recent studies can be explained by the following. (1) We included more extensive comorbidity controls. Because less severely ill patients are more likely to be treated with beta-blockers, this difference in methods will reduce any apparent cardiologist benefit. (2) We accounted for the correlation between treatment by a cardiologist and treatment by a high-volume hospital in a way that did not introduce new selection bias. In our study, higher-volume hospitals treated somewhat more severely ill patients and were more likely to adopt current standards of best practice, so that this difference in methods will also reduce any apparent cardiologist benefit. This finding highlights the need for use of adjustment methods in observational studies that go beyond accounting for measured differences in patient severity and use care to account for other, correlated treatments that might also be subject to selection bias. However, efforts to improve quality of care might be more profitably directed to areas other than cardiologist-noncardiologist comparisons. Not only do the incremental health benefits of greater cardiologist treatment appear quite modest, more importantly, regardless of physician specialty, fewer than half of patients received beta-blocker therapy in the hospital or at discharge regardless of physician specialty.

The primary strength of our study is the utilization of a comprehensive risk-adjustment model and IV techniques to control for measured and unmeasured selection bias. Prior studies have been unable to distinguish treatment effect attributable to specialty care from residual selection bias. Our analysis was able to determine the relative impact of patient and hospital characteristics on the mortality difference observed between patients treated by cardiologists and noncardiologists. In addition, in contrast to prior studies that focused on specific geographic regions (Ayanian et al. 1997), we analyzed the entire population of Medicare patients with MI covered by fee-for-service health insurance during a 16-month period, making this a true national study.

Our study has several limitations. First, much as we tried to overcome all of the inherent limitations of the data, our analysis was observational and relied on the accuracy of the data abstraction process of the CCP. Only a well-executed clinical trial randomizing patients to receive treatment with either cardiologists or noncardiologists can definitively determine whether and how physician specialty affects patient outcomes. Such a study will likely never be performed for a representative national sample of Medicare AMI patients, so evidence on this question using the best possible techniques to account for residual biases is important on a practical level. Moreover, even an "ideal" trial would not directly answer policy questions about the health consequences of incremental increases or reductions in the use of cardiologists in providing acute MI care. Our incremental IV analysis that compares similar populations with more or less access to cardiologists seems best-suited to such questions.

Second, we used self-reported data reporting physician specialty, so we may have misclassified physicians and obscured a possible benefit associated with cardiologist care; however, self-reported and actual physician specialty are highly correlated (Ayanian et al. 1997; Jollis, DeLong, Peterson, et al. 1996). Third, our analysis focused on comparing patients admitted by a cardiologist to those admitted by other physicians as our principal measure of the intensity of cardiologist care. Although our analysis of billing data for a subset of our patient population indicated that this measure of cardiologist use is highly correlated with a broad range of other measures of cardiologist use, further studies should address in more detail whether cardiology consultation and other particular aspects of cardiologist care have differential effects on mortality for patients with AMI. In particular, our results suggest that more limited cardiology consultations are likely to have virtually no long-term mortality consequences. Fourth, we lack information on the physicians treating patients who were transferred out to a second acute care facility; nonetheless, when these patients were excluded, the results remained unchanged. Finally, a one-year follow-up time may have been too short for all the benefits of cardiologists' increased utilization of revascularization procedures to emerge. However, after one year, over one-third of our elderly cohort had expired, and we found no trend over time toward increasing benefit associated with cardiologist treatment.

In conclusion, we found that patients with AMI who were treated primarily by cardiologists did not have substantially lower mortality than patients who relied more extensively on other types of physicians for treatment. This is true even though greater reliance on cardiologists led to better adherence to best practices in many dimensions, and especially to more use of intensive and costly cardiac procedures. The larger mortality differences previously reported between patients treated by cardiologists and noncardiologists were attributable in large part to patient and hospital characteristics. For outcome studies with extensive selection problems, such as the differences in the characteristics of patients treated by physicians of different specialties, IV methods combined with risk-adjustment methods can be a powerful tool for eliminating confounding.

	Current Study	Jollis, DeLong, Peterson, et al. (1996)
Demographic and geographic	Age, sex, race, rural/urban	Age, sex, race, rural/urban
Comorbidity	History of: incontinence, peptic ulcer disease, internal bleeding, bleeding disorder, recent trauma, dementia/Alzheimer disease, diabetes, recent surgical procedure, terminal illness, allergic reaction, stroke, angina, congestive heart failure or pulmonary edema, peripheral vascular disease/claudication, hypertension, chronic obstructive pulmonary disease, coronary artery bypass surgery, percutaneous transluminal coronary angioplasty, prior myocardial infarction, other cardiac surgery, current ambulatory status, and tobacco use.	History of diabetes, stroke, hypertension, coronary artery bypass surgery, prior myocardial infarction, prior use of thrombolytic therapy.
Measures of severity	Ability to respond to verbal commands, motor status, heart rate, temperature, mean arterial blood pressure, respiratory rate, height, body mass index, S3 gallop, conduction disorder, findings of congestive heart failure on exam.	Heart rate, height, weight, systolic blood pressure.
Diagnostic test results	Sodium, glucose, albumin, hematocrit, leukocyte count, platelet count, blood urea nitrogen, cardiomegaly on chest radiography, and electrocardiogram findings.	Electrocardiographic findings, Killip class

APPENDIX

REFERENCES

Ayanian, J. Z., P. J. Hauptman, E. Guadagnoli, E. M. Antman, C. L. Pashos, and B. J. McNeil. 1994. "Knowledge and Practices of Generalist and Specialist Physicians Regarding Drug Therapy for Acute Myocardial Infarction." New England Journal of Medicine 331 (17): 1136-42.

- Ayanian J. Z., E. Guadagnoli, B. J. McNeil, and P. D. Cleary. 1997. "Treatment and Outcomes of Acute Myocardial Infarction Among Patients of Cardiologists and Generalist Physicians." Archives of Internal Medicine 157 (22): 2570-76.
- Barefoot, J. C., M. J. Helms, D. B. Mark, J. A. Blumenthal, R. M. Califf, T. L. Haney, C. M. O'Connor, I. C. Siegler, and R. B. Williams. 1996. "Depression and Long-Term Mortality Risk in Patients with Coronary Artery Disease." *American Journal* of Cardiology 78 (6): 613-17.
- Borowsky, S. J., R. L. Kravitz, M. Laouri, B. Leake, J. Partridge, V. Kaushik, L. J. Haywood, and R. H. Brook. 1995. "Effect of Physician Specialty on Use of Necessary Coronary Angiography." *Journal of the American College of Cardiology* 26 (6): 1484-91.
- Brand, D.A., L. N. Newcomer, A. Freiburger, and H. Tian. 1995. "Cardiologists' Practices Compared with Practice Guidelines: Use of Beta-Blockade After Acute Myocardial Infarction." *Journal of the American College of Cardiology* 26 (6): 1432– 36.
- Donohoe, M. T. 1998. "Comparing Generalist and Specialty Care: Discrepancies, Deficiencies, and Excesses." Archives of Internal Medicine 158 (15): 1596-1608.
- Ellerbeck, E. F., S. F. Jencks, M. J. Radford, T. F. Kresowik, A. S. Craig, J. A. Gold, H. M. Krumholz, and R. A. Vogel. 1995. "Quality of Care for Medicare Patients with Acute Myocardial Infarction. A Four-State Pilot Study from the Cooperative Cardiovascular Project." *Journal of the American Medical Association* 273 (19): 1509-14.
- Fibrinolytic Therapy Trialists' Collaborative Group. 1994. "Indications for Fibrinolytic Therapy in Suspected Acute Myocardial Infarction: Collaborative Overview of Early Mortality and Major Morbidity Results from All Randomized Trials of More Than 1000 Patients." *Lancet* 343 (8893): 311–22.
- Fitzmaurice, G. M., and N. M. Laird. 1997. "Regression Models for Mixed Discrete and Continuous Responses with Potentially Missing Values." *Biometrics* 53 (1): 110-22.
- Frances, C. D., A. S. Go, K. W. Dauterman, K. Deasaransingh, D. L. Jung, S. Gettner, I. M. Newman, B. M. Massie, and W. S. Browner. 1999. "Outcome Following Acute Myocardial Infarction: Are Differences among Physician Specialties the Result of Quality of Care or Case Mix?" Archives of Internal Medicine 159 (13): 1429-36.
- Gibbons, R. J., D. R. Holmes, G. S. Reeder, K. R. Bailey, M. R. Hopfenspirger, and B. J. Gersh. 1993. "Immediate Angioplasty Compared with the Administration of a Thrombolytic Agent Followed by Conservative Treatment for Myocardial Infarction." New England Journal of Medicine 328 (10): 685-91.
- Grines, C.L., K. F. Browne, J. Marco, D. Rothbaum, G. W. Stone, J. O'Keefe, P. Overlie, B. Donohue, N. Chelliah, G. C. Timmis, R. E. Vlietstra, N. Strzelecki, S. Puchrocicz-Ochocki, and W. W. O'Neill. 1993. "A Comparison of Immediate Angioplasty with Thrombolytic Therapy for Acute Myocardial Infarction." New England Journal of Medicine 328 (10): 673–79.

- Gustafsson, F., L. Køber, C. Torp-Pedersen, P. Hildebrandt, M. H. Ottesen, B. Sonne, and J. Carlsen. 1998. "Long-Term Prognosis after Acute Myocardial Infarction in Patients with a History of Arterial Hypertension." *European Heart Journal* 19 (4): 588-94.
- Infarct Survival Collaborative Group. 1986. "Randomized Trial of Intravenous Atenolol among 16 027 Cases of Suspected Acute Myocardial Infarction." *Lancet* 2 (8498): 57–66.
- Jollis, J. G., E. R. DeLong, E. D. Peterson, L. H. Muhlbauer, D. E. Fortin, R. M. Califf, and D. B. Mark. 1996. "Outcome of Acute Myocardial Infarction According to the Specialty of the Admitting Physician." New England Journal of Medicine 335 (25): 1880-87.
- Krumholz, H. M., M. J. Radford, E. F. Ellerbeck, J. Hennen, T. P. Meehan, M. Perillo, Y. Wang, T. F. Kresowik, and S. F. Jencks 1995. "Aspirin in the Treatment of Acute Myocardial Infarction in Elderly Medicare Beneficiaries. Patterns of Use and Outcomes." *Circulation* 92 (10): 2841-47.
- Krumholz, H. M., M. J. Radford, Y. Wang, J. Chen, A. Heiat, and T. A. Marciniak. 1998. "National Use and Effectiveness of Beta-Blockers for the Treatment of Elderly Patients after Acute Myocardial Infarction: National Cooperative Cardiovascular Project." Journal of the American Medical Association 280 (7): 623-29.
- Latini, R., A. P. Maggioni, M. Flather, P. Sleight, and G. Tognoni. 1995. "ACE Inhibitor Use in Patients with Myocardial Infarction. Summary of Evidence from Clinical Trials." *Circulation* 92 (10): 3132–37.
- Marciniak, T. A., E. F. Ellerbeck, M. J. Radford, T. F. Kresowick, J. A. Gold, H. M. Krumholz, C. I. Kiefe, R. M. Allman, R. A. Vogel, and S. F. Jencks. 1998.
 "Improving the Quality of Care for Medicare Patients with Acute Myocardial Infarction: Results from the Cooperative Cardiovascular Project." *Journal of the American Medical Association* 279 (17): 1351-57.
- McClellan, M., B. J. McNeil, and J. P. Newhouse. 1994. "Does More Intensive Treatment of Acute Myocardial Infarction in the Elderly Reduce Mortality? Analysis Using Instrumental Variables." Journal of the American Medical Association 272 (11): 859-66.
- McClellan, M., and H. Noguchi. 1998. "Validity and Interpretation of Treatment Effect Estimates Using Observational Data: Treatment of Heart Attacks in the Elderly." Stanford University mimeograph.
- Meng, X. L. 1997. "The EM Algorithm and Medical Studies: A Historical Link." Statistical Methods in Medical Research 6 (1): 3-23.
- MIAMI Trial Research Group. 1985. "Metoprolol in Acute Myocardial Infarction Mortality." American Journal of Cardiology 56 (14): 15G-22G.
- Michels, K. B., and S. Yusuf. 1995. "Does PTCA in Acute Myocardial Infarction Affect Mortality and Reinfarction Rates? A Quantitative Overview (Meta-Analysis) of the Randomized Clinical Trials." *Circulation* 91 (2): 476–85.
- Miettinen, H., S. Lehto, V. Salomaa, M. Mähönen, M. Niemelä, S. M. Haffner, K. Pyörälä, and J. Tuomilehto. 1998. "Impact of Diabetes on Mortality after the First Myocardial Infarction." *Diabetes Care* 21 (1): 69-75.

- Newhouse, J. P., and M. McClellan. 1998. "Econometrics in Outcomes Research: The Use of Instrumental Variables." Annual Review of Public Health 19: 17-34.
- Normand, S. T., M. E. Glickman, R. G. Sharma, and B. J. McNeil. 1996. "Using Admission Characteristics to Predict Short-Term Mortality from Myocardial Infarction in Elderly Patients. Results from the Cooperative Cardiovascular Project." Journal of the American Medical Association 275 (17): 1322-28.
- Pfeffer, M. A., E. Braunwald, L. A. Moye, L. Basta, E. J. Brown, Jr., T. E. Cuckly, B. R. Davis, E. M. Geltman, S. Goldman, G. C. Flaker, M. Klein, G. A. Lamas, M. Packer, J. Rouleau, J. L. Rouleau, J. Rutherford, J. H. Wertheimer, and C. M. Hawkins. 1992. "Effect of Captopril on Mortality and Morbidity in Patients with Left Ventricular Dysfunction after Myocardial Infarction. Results of the Survival and Ventricular Enlargement Trial." New England Journal of Medicine 327 (10): 669-77.
- Rubin, D. B. 1997. "Estimating Causal Effects from Large Data Sets using Propensity Scores." Annals of Internal Medicine 127 (8, Part 2): 757-63.
- Ryan, T. J., J. L. Anderson, E. M. Antman, B. A. Braniff, N. H. Brooks, R. M. Califf, L. D. Hillis, L. F. Hratzka, E. Rapaport, B. T. Riegel, R. O. Russell, E. E. Smith III, and W. D. Weaver. 1996. "ACC/AHA Guidelines for the Management of Patients with Acute Myocardial Infarction: Executive Summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines." Circulation 94 (9): 2341-50.
- Statistical Analysis System (SAS) Institute. 1996. SAS Release 6.11. Cary, NC: SAS Institute.
- Vaccarino, V., H. M. Krumholz, L. F. Berkman, and R. I. Horwitz. 1995. "Sex Differences in Mortality after Myocardial Infarction. Is there Evidence for an Increased Risk for Women?" *Circulation* 91 (6): 1861-71.