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The impact of paradoxical comorbidities on risk-adjusted mortality of Medicare beneficiaries with cardiovascular disease

Abstract
Background: Persistent uncertainty remains regarding assessments of patient comorbidity based on administrative data for mortality risk adjustment. Some models include comorbid conditions that are associated with improved mortality while other models exclude these so-called paradoxical conditions. The impact of these conditions on patient risk assessments is unknown.
Objective: To examine trends in the prevalence of conditions with a paradoxical (protective) relationship with mortality, and the impact of including these conditions on assessments of risk adjusted mortality.
Methods: Patients age 65 and older admitted for acute myocardial infarction (AMI) or coronary artery bypass graft (CABG) surgery during 1994 through 2005 were identified in Medicare Part A files. Comorbid conditions defined using a common algorithm were categorized as having a paradoxical or non-paradoxical relationship with 30-day mortality, based upon regression coefficients in multivariable logistic regression models.
Results: For AMI, the proportion of patients with one or more paradoxical condition and one or more non-paradoxical condition increased by 24% and 3% respectively between 1994 and 2005. The odds of death for patients with one-or-more paradoxical comorbidities, relative to patients with no paradoxical comorbidity, declined from 0.69 to 0.54 over the study period. In contrast, the risk associated with having one or more non-paradoxical comorbidities increased from 2.66 to 4.62 for AMI. This pattern was even stronger for CABG. Risk adjustment models that included paradoxical comorbidities found larger improvements, in risk-adjusted mortality for AMI and CABG, over time than models that did not include paradoxical comorbidities.
Conclusion: The relationship between individual comorbid conditions and mortality is changing over time, with potential impact on estimates of hospital performance and trends in mortality. Development of a standard approach for handling conditions with a paradoxical relationship to mortality is needed.

Key words: comorbidity, International Classification of Diseases, mortality, quality of health care, risk adjustment, performance measures.

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Background

Administrative health data are large collections of insurance claims generally collected for billing purposes. Centers for Medicare & Medicaid Services (CMS) is the single largest source of administrative data on acute care hospitalizations, compiling data on more than 11 million hospital admissions for more than 38 million people in 2005. Although not originally intended for research, administrative databases contribute enormously to ongoing health services research (Iezzoni, 2002; Riley, 2009; Wunsch, Harrison, & Rowan, 2005), and their use in assessing provider-level outcomes has become standard (Krumholz et al., 2006). More recently, claims based analyses have served as the source of data for estimating hospital quality based on risk-standardized mortality; such measures are widely available to the public (Krumholz & Normand, 2008). However, a limitation of these measures is persistent uncertainty about the adequacy of the methods to adjust for differences in patient complexity (Iezzoni, 1997). Failure to account for patient differences makes it difficult to discern whether differences in outcomes are due to differences in quality of care or to unmeasured patient complexity.

A critical element in risk-adjustment using administrative data is the assessment of comorbidity. Comorbidity is defined as the presence of one or more pre-existing conditions, in addition to the primary reason for admission, that increase the likelihood of an adverse outcome (Elixhauser, Steiner, Harris, & Coffey, 1998). In administrative data, comorbidity is captured using International Classification of Diseases, 9th Clinical Modification (ICD 9-CM) diagnosis codes. While a number of investigators have developed comorbidity indices for use with administrative data (Deyo, Cherkin, & Ciol, 1992; Quan et al., 2005; Romano, Roos, & Jollis, 1993; Elixhauser et al., 1998), assignment of ICD-9-CM codes in administrative data is highly variable, and uncertainty about the precise meaning of specific codes persists. A limited number of prior studies have found that some conditions, such as diabetes and hypertension, were protective of mortality in their analyses despite clinical evidence to the contrary (Jencks, Williams, & Kay, 1988; Iezzoni et al., 1992). Such relationships violate the fundamental definition that comorbidity is a factor that complicates treatment and increases the risk of adverse outcomes. More troubling, there is no standard approach for handling comorbidities with paradoxical effects on mortality, and the impact of these conditions on assessments of patient risk has not been systematically evaluated. In addition, the incentives for coding of secondary diagnoses have changed over time due to payment mechanisms and hospital performance measurement systems that increasingly depend on patient characteristics recorded in claims data, possibly exacerbating variability in coding.

This study examined 12-year trends in the prevalence of specific comorbid conditions and the relationship of comorbidity to 30-day mortality using Medicare administrative data. In particular, we examined trends in the prevalence of conditions with a paradoxical relationship to mortality and the impact of these conditions on assessments of risk adjusted mortality for patients admitted for acute myocardial infarction (AMI) or undergoing coronary artery bypass graft (CABG). Comorbid conditions are defined using a widely available algorithm (Quan et al., 2005).

Methods

Data

We identified all patients age 65 and older admitted with a primary diagnosis of Acute Myocardial Infarction (AMI) or undergoing Coronary Artery Bypass Graft (CABG) during 1994 through 2005 using Medicare Provider and Analysis Review (MedPAR) Part A files. The MedPAR files contain hospital discharge abstract data for 100% of Medicare Part A fee-for-service patients discharged from acute care hospitals. AMI patients were identified on the basis of primary International Classification of Diseases, 9th Clinical Medication (ICD-9-CM) diagnosis code '410.xx,' excluding patients with fifth digit ='2,' as these represent admissions to evaluate or treat an AMI that received initial treatment in a prior admission. Patients admitted for AMI who were transferred from another hospital were excluded (n=322,548), providing 2,653,451 total AMI admissions during 1994–2005. CABG patients were identified using ICD-9-CM procedure codes 36.10–36.19, resulting in 2,007,807 total CABG admissions. Other data elements on the MedPAR files include patient demographics; patients' ZIP Code and state of residence; primary and secondary diagnoses and procedures, as captured by ICD-9-CM codes; the diagnosis related group (DRG); admission source (e.g., transfer from another hospital, emergency room); admission priority (elective, urgent, or emergent); admission and discharge dates; disposition at the time of hospital discharge; dates of death up to two years after discharge; and a six-digit unique hospital identifier.

Mortality was defined as deaths within 30 days of admission (for AMI) or within 30 days of surgery (for CABG). These definitions are consistent with standard methods for evaluating short-term mortality that may reflect quality of care (Krumholz & Normand, 2008).

Comorbid conditions were identified based on secondary ICD-9-CM diagnosis codes on the hospital discharge record and algorithms published by Quan et al. (2005), based on original work of Charlson (Deyo et al., 1992; Romano et al., 1993) and Elixhauser et al., (1998). These algorithms map ICD-9 codes to 47 conditions that are unlikely to represent hospital-acquired complications. After eliminating overlap in conditions defined by Charlson and Elixhauser, we identified 32 unique comorbid conditions (Table 1).

Table 1. Thirty seven comorbid conditions described by Quan et al (2005), based on algorithms developed by Elixhauser et al (1998) and Deyo et al (1992).

Acquired Immune Deficiency	Diabetes	Paralysis
Alcohol Abuse Disorder	Drug Abuse	Peripheral Vascular Disease
Arrhythmia	Fluid/Electrolyte Disorder	Pulmonary/Circulation Disorder
Blood Anemia	Hemi-paraplegia	Psychosis
Cerebrovascular Disorder	Hypertension	Obesity
Chronic Heart Failure (CHF)	Hypothyroid	Renal Failure
Chronic Obstructive Pulmonary Dis. (COPD)	Liver Disease	Rheumatic Disease
Coagulation Disorder	Metastatic Cancer	Ulcer without bleeding
Deficiency Anemia	Myocardial Infarction	Valve Disorder
Dementia	Neurological Disorder	Weight Loss
Depression	Non-Metastatic Cancers	

Source: Authors' calculations using Centers for Medicare and Medicaid Services (CMS) Medicare Provider Analysis and Review (MedPAR) files for years 1994 through 2005.

Statistical analyses

First, trends in age, sex, race, admission source and priority, and prevalence of comorbid characteristics of patients admitted for AMI, or undergoing CABG, were examined after collapsing data into two-year increments (1994/95; 1996/97; 1998/99; 2000/01; 2002/03; 2004/05). Significant trends over the entire study period were detected using the Cochran-Armitage trend test for each patient characteristic. All analyses were conducted separately for the AMI and CABG cohorts.

Second, we developed risk-adjustment models for mortality within 30 days of AMI admission or CABG procedure using patients discharged during 2004/05. First, bivariate relationships between mortality and patient demographics, admission source and priority, and individual comorbid conditions, were determined using the chi-square test for categorical variables and Wilcoxon rank test for ordinal or continuous variables. Variables significantly related to mortality in bivariate analyses ($p<.01$) were considered candidate variables for inclusion in stepwise logistic regression risk adjustment models. Age was included in models as a continuous variable (although the inclusion of age as a categorical variable expressed in 5-year increments produced nearly identical results). Race and ethnicity were expressed using two indicator variables for patients who were classified in the database as either "non-Hispanic black" or "Hispanic and other non-white," with the reference category being non-Hispanic white patients. Admission priority was expressed using two indicator variables for emergent and urgent admissions, relative to elective admissions. Admission source was expressed as indicator variables for patients transferred to the hospital from another acute-care facility and patients admitted through the emergency department, with a referent category that primarily included patients referred by a physician. Finally, all models included indicators for each two-year increment.

Final logistic regression models (shown in Appendix) for AMI and CABG were generated using random intercepts for hospitals to control for the clustering of patients within hospitals (Raudenbush & Bryk, 2002).

Using the final models, comorbid conditions that were significantly related to mortality were categorized as either ‘paradoxical’ comorbidities (i.e., regression coefficients indicated a protective effect) or ‘non-paradoxical’ comorbidities (i.e., coefficients indicated an adverse effect on mortality, as expected). Comorbidities with paradoxical relationship to mortality after AMI included hypertension, diabetes, hypothyroidism, obesity, blood anemias, deficiency anemias, valvular heart disorder, depression, drug abuse, and ulcer with no bleeding. Non-paradoxical comorbidities for AMI mortality included chronic heart failure (CHF), arrhythmias, cerebrovascular disease, paralysis, neurological disorders, renal failure, liver disease, metastatic cancer, non-metastatic cancer, coagulation disorders, weight loss, fluid or electrolyte disorders, dementia, and chronic obstructive pulmonary disease. Paradoxical comorbidities for CABG included all of those with a paradoxical relationship for AMI identified above plus three additional conditions: alcohol abuse, psychosis, and dementia. Additional non-paradoxical comorbidities for CABG included valvular disorder, pulmonary circulation disorder, hemiparaplegia, peripheral vascular disease, and acute myocardial infarction.

Separate multivariable models for each two-year increment further evaluated the consistency of the relationship of paradoxical comorbidities to mortality over time. For AMI, comorbidities with a paradoxical relationship to mortality during 2004/05 were also paradoxical during all other two-year periods, with the exception of diabetes. Diabetes was associated with higher AMI mortality during 1994/95, but the relationship changed over time and was paradoxically related to mortality by 2004/05. For CABG, all conditions that were paradoxical during 2004/05 were paradoxical throughout the observation period in multivariable models.

Next, we examined trends in the likelihood of having one or more paradoxical condition and the overall relationships of paradoxical and non-paradoxical conditions to 30-day mortality during 1994 through 2005. For these analyses, the proportions of AMI and CABG patients with any paradoxical and any non-paradoxical comorbidity during each two-year increment, and the odds of death associated with having one or more paradoxical or one or more non-paradoxical conditions, were compared during successive two-year periods. Finally, the odds of death in each two-year increment, relative to 1994/95, were determined based on multivariable logistic regression models that did and did not include indicators for paradoxical conditions. These models allowed us to examine the impact of including paradoxical conditions on changes in 30-day mortality that were observed between 1994 and 2005.

All p-values are two-tailed, with p-values less than .05 deemed statistically significant. All statistical analyses were performed using SAS 9.0 (SAS Institute Inc., Cary, NC). This project was approved by the University of Iowa Institutional Review Board.

RESULTS

Patient characteristics and prevalence of comorbid conditions that were significantly related to mortality in logistic regression models, are displayed in Tables 2 and 3, respectively. All differences over time are statistically significant, although not necessarily clinically significant. Mean age increased by roughly two years for AMI and CABG. The proportion of patients who were female increased slightly for AMI, but decreased slightly for CABG. For both groups, the proportion of patients who were black or other non-white race increased from 1994 through 2005. There was little change in the proportion of admissions through the ER for either group, but the proportion of CABG admissions with urgent or emergent priority status decreased during the period (Table 2).

Table 2. Patient demographics and race/ethnicity significantly related to mortality for Medicare beneficiaries admitted for AMI or undergoing CABG in 1994/95 and 2004/05

	AMI				CABG			
	1994/95		2004/05		1994/95		2004/05	
Total Patients	506,454		455,859		347,534		267,430	
Demographics								
Age, mean, years (sd)	76.4	(7.5)	78.5	(8.1)	72.5	(5.2)	74.5	(5.8)
Sex, women	245,244	(48.4%)	228,009	(50.0%)	121,869	(35.1%)	90,404	(33.8%)
Race/Ethnicity								
White (Non-Hisp.)	460,204	(90.9%)	402,936	(88.4%)	324,754	(93.4%)	242,943	(90.8%)
Black	30,388	(6.0%)	33,337	(7.3%)	12,038	(3.5%)	12,991	(4.9%)
Other	15,861	(3.1%)	19,586	(4.3%)	10,742	(3.1%)	11,496	(4.3%)
Indicators Of Severity								
Admit through ER	342,772	(67.7)	305,894	(67.1)	65,521	(18.9)	52,137	(19.5)
Priority = Urgent	125,185	(24.8)	113,278	(24.9)	114,267	(33.0)	73,645	(27.6)
Priority = Emergent	350,154	(69.4)	309,605	(68.0)	100,264	(29.0)	64,418	(24.1)

Source: Authors' calculations using CMS MedPAR files for years 1994 through 2005.

The prevalence of several comorbid conditions changed over the study period (Table 3). For AMI, increases greater than 100% were observed for renal failure, liver disease, coagulation disorders, and depression; increases greater than 50% were additionally observed for obesity, weight loss, hypothyroidism, drug abuse, and blood anemia. The largest increase in terms of absolute patient volume occurred with hypertension, which increased by 48%, representing

Table 3. Patient comorbid conditions and indicators of severity significantly related to mortality for Medicare beneficiaries admitted for AMI or undergoing CABG in 1994/95 and 2004/05

	AMI				CABG			
	1994/95		2004/05		1994/95		2004/05	
Total Patients	506,454		455,859		347,534		267,430	
Comorbid Conditions								
Alcohol Abuse		-		-	1,993	(0.6)	2,995	(1.1)
Arrhythmia	203,629	(40.2)	174,847	(38.4)	149,187	(42.9)	127,376	(47.6)
Blood Anemia	6,031	(1.2)	8,839	(1.9)	3,173	(0.9)	3,517	(1.3)
Cerebrovascular Disorder	35,879	(7.1)	30,634	(6.7)	31,586	(9.1)	21,739	(8.1)
CHF	205,846	(40.6)	195,390	(42.9)	80,008	(23.0)	73,688	(27.6)
COPD	90,263	(17.8)	111,282	(24.4)		-		-
Coagulation Disorder	7,126	(1.4)	16,499	(3.6)	11,700	(3.4)	25,744	(9.6)
Deficiency Anemia	6,782	(1.3)	7,285	(1.6)	1,794	(0.5)	1,799	(0.7)
Dementia	14,217	(3.1)	11,737	(2.3)	509	(0.1)	691	(0.3)
Depression	8,323	(1.6)	14,999	(3.3)	3,129	(0.9)	5,192	(1.9)
Diabetes	121,454	(24.0)	118,935	(26.1)	80,158	(23.1)	72,877	(27.3)
Drug Abuse	1,163	(0.2)	1,733	(0.4)	1,085	(0.3)	1,535	(0.6)
Fluid/Electrolyte Disorder	92,271	(18.2)	86,444	(19.0)	55,671	(16.0)	41,981	(15.7)
Hemiparaplegia		-		-	2,834	(0.8)	781	(0.3)
Hypertension	201,367	(39.8)	268,669	(58.9)	155,769	(44.8)	167,648	(62.7)
Hypothyroidism	24,111	(4.8)	38,251	(8.4)	13,385	(3.9)	17,106	(6.4)
Liver disease	2,655	(0.5)	5,349	(1.2)	1,155	(0.3)	2,255	(0.8)
Metastatic Cancer	4,344	(0.9)	5,193	(1.1)		-		-
Myocardial Infarction		-		-	121,508	(35.0)	84,493	(31.6)
Non-Metastatic Cancer	9,982	(2.0)	11,252	(2.5)		-		-
Neurological Disorders	24,445	(4.8)	23,991	(5.3)	7,329	(2.1)	7,028	(2.6)
Obesity,	10,600	(2.1)	14,644	(3.2)	10,510	(3.0)	14,412	(5.4)
Paralysis	7,531	(1.5)	2,285	(0.5)		-		-
Peripheral Vasc. Disease		-		-	28,919	(8.3)	30,730	(11.5)
Psychosis		-		-	1,033	(0.3)	1,134	(0.4)
Pulmonary Circ. Disorder		-		-	6,646	(1.9)	6,419	(2.4)
Renal failure	22,769	(4.5)	47,064	(10.3)	8,807	(2.5)	17,652	(6.6)
Ulcer		-		-	4,469	(1.3)	1,475	(0.5)
Valve disorder	70,056	(13.8)	80,501	(17.7)	60,376	(17.4)	74,851	(28.0)
Weight loss	5,523	(1.1)	9,167	(2.0)	2,622	(0.7)	3,725	(1.4)

Source: Authors' calculations using CMS MedPAR files for years 1994 through 2005.

more than 67,000 additional AMI patients with hypertension during 2004/05 than during 1994/95, despite the fact that total AMI admission volume decreased by roughly 50,000 during that time period. For CABG, patterns over time in the prevalence of individual conditions were generally similar to those seen for AMI.

Risk adjusted mortality

Unadjusted mortality after AMI decreased from 20.9% to 16.5% from 1994/95 to 2004/05 (a relative reduction of 21%). During that same time frame, the proportion of patients with one or more paradoxical comorbid conditions increased from 63% to 78% (a relative increase of 24%), while the proportion of patients with any non-paradoxical condition increased by only 3%. Similarly, unadjusted mortality after CABG decreased from 5.3% to 4.6% (a 13% relative reduction), while the prevalence of paradoxical conditions increased by 23% and the prevalence of non-paradoxical conditions increased by 6% (Table 4).

Table 4. Unadjusted time trends for AMI and CABG patients

	Acute Myocardial Infarction Patients			CABG Patients		
Year	Unadjusted 30-Day Mortality	Any Paradoxical Comorbidity	Any Non-Paradoxical Comorbidity	Unadjusted 30-Day Mortality	Any Paradoxical Comorbidity	Any Non-Paradoxical Comorbidity
1994/95	20.9%	63%	77%	5.3%	60%	81%
1996/97	19.8	68	77	5.2	64	82
1998/99	19.5	70	77	5.1	68	82
2000/01	19.0	73	77	4.8	71	83
2002/03	17.8	76	78	4.7	73	84
2004/05	16.5	78	79	4.6	74	86
Percent Change	-21.0%	+24%	+3%	-13%	+23%	+6%

Source: Authors' calculations using CMS MedPAR files for years 1994 through 2005.

The relative odds of death associated with paradoxical and non-paradoxical comorbidities also changed considerably during the time period (Table 5). For AMI, the odds of death for patients with one or more paradoxical comorbidities compared to patients with no paradoxical comorbidity were 0.69 during 1994/95 (Odds Ratio [OR]=0.69), and decreased to 0.54 during 2004/05; a 22% decrease in the relative odds. The change for CABG was even greater, with relative odds of death associated with paradoxical comorbidities decreasing from OR=0.57 in 1994/95 to OR=0.31 in 2004/05—a 46% decrease. In contrast, the relative odds of death associated with non-paradoxical comorbidities increased. During 1994/95, AMI patients with one or more non-paradoxical comorbidities were 2.66 times more likely to die compared to persons without any non-paradoxical comorbidity, while by 2004/05 AMI patients with non-paradoxical comorbidities were 4.6 times more likely to die. Similarly, the relative odds of death associated with non-paradoxical comorbidities for CABG increased from 3.67 to 6.13.

Table 5. Relative odds of death (and 95% confidence interval) associated with Paradoxical and Non-Paradoxical comorbidities for AMI and CABG patients

	AMI		CABG	
Assessment Period	Odds of death for person with ANY paradoxical comorbidity relative to person with NO paradoxical comorbidity	Odds of death for person with ANY non-paradoxical comorbidity relative to person with NO non-paradoxical comorbidity	Odds of death for person with ANY paradoxical comorbidity relative to person with NO paradoxical comorbidity	Odds of death for person with ANY non-paradoxical comorbidity relative to person with NO non-paradoxical comorbidity
1994-95	0.69 (0.68-0.70)	2.66 (2.61-2.72)	0.57 (0.55-0.59)	3.67 (3.45-3.90)
1996-97	0.69 (0.68-0.70)	3.10 (3.03-3.16)	0.51 (0.49-0.52)	4.16 (3.90-4.43)
1998-99	0.67 (0.66-0.68)	3.53 (3.45-3.61)	0.46 (0.45-0.48)	4.57 (4.26-4.89)
2000-01	0.63 (0.62-0.64)	3.90 (3.81-4.00)	0.39 (0.38-0.41)	5.05 (4.67-5.45)
2002-03	0.59 (0.58-0.60)	4.37 (4.26-4.49)	0.35 (0.34-0.36)	5.39 (4.94-5.89)
2004-05	0.54 (0.53-0.55)	4.62 (4.48-4.76)	0.31 (0.30-0.32)	6.13 (5.49-6.83)
1994 to 2005 Percent Change	-22%	+74%	-46%	+67%

Source: Authors' calculations using CMS MedPAR files for years 1994 through 2005.

Finally, we assessed the change in risk adjusted mortality over time in models that did and did not include paradoxical conditions (Table 6). First, we examined risk-adjusted mortality using multivariable models that controlled for patient demographics (e.g., age, sex), hospital characteristics, and non-paradoxical comorbidities only. Second, we ran models that included all of these factors plus paradoxical comorbidities; comparing estimates from the two models allowed us to examine how estimates of AMI and

Table 6. Odds of death (and 95% confidence interval) by year, relative to 1994/95, based on risk adjustment models that do and do not control for paradoxical comorbidities

	AMI		CABG	
Odds of death (and confidence interval) relative to 1994/95 for given period	Model controls for paradoxical comorbidity	No control for paradoxical comorbidity	Model controls for paradoxical comorbidity	No control for paradoxical comorbidity
1994/95	1.00	1.00	1.00	1.00
1996/97	0.94 (0.93-0.95)	0.90 (0.89-0.91)	0.96 (0.94-0.98)	0.92 (0.90-0.94)
1998/99	0.95 (0.94-0.96)	0.89 (0.88-0.91)	0.95 (0.93-0.97)	0.88 (0.86-0.90)
2000/01	0.94 (0.93-0.96)	0.87 (0.86-0.88)	0.88 (0.86-0.90)	0.80 (0.78-0.81)
2002/03	0.89 (0.88-0.90)	0.80 (0.79-0.81)	0.82 (0.80-0.84)	0.72 (0.71-0.74)
2004/05	0.79 (0.78-0.81)	0.71 (0.70-0.72)	0.73 (0.71-0.75)	0.64 (0.63-0.66)
1994 to 2005 % Change	-21%	-29%	-27%	-36%

Source: Authors' calculations using CMS MedPAR files for years 1994 through 2005.

CABG mortality differ depending upon inclusion or exclusion of paradoxical comorbidities. For AMI, there was a 21% decrease in the relative odds of death from 1994-1995 through 2004-05, when the risk adjustment model controlled for both paradoxical and non-paradoxical comorbidities (OR=0.79; p<.001). With only non-paradoxical comorbidities, the *decrease* in the relative odds of death was larger at 29% (i.e., OR = 0.71; p<.001). Similarly, we found a larger decrease in risk adjusted mortality for CABG using risk-adjustment models that only control for non-paradoxical comorbidities. The odds of death during 2004-05, relative to 1994-95, is 0.73 when controlling for all comorbidities, and 0.64 when only controlling for non-paradoxical comorbidities.

Discussion

A critical element in risk-adjustment using administrative data is the assessment of comorbidity. This study demonstrates significant changes in the coding of comorbid conditions in administrative data over time. These findings have important implications for policy makers and researchers attempting to measure hospital quality and evaluate changes in patient outcomes over time.

We found that the increase in the proportion of patients with a paradoxical comorbid condition was at least four times greater than the increase for non-paradoxical conditions. Moreover, while the risk of death associated with non-paradoxical conditions increased during the study period, the risk of death associated with paradoxical conditions moved in the opposite direction. This suggests a greater likelihood of survival for patients with paradoxical conditions in later years compared to earlier years. Most importantly, estimates of improvement in AMI and CABG mortality differed markedly depending upon whether our models included or excluded paradoxical comorbidities. This is far from a trivial issue.

Conditions with a paradoxical relationship to mortality have been noted previously. Jencks, Williams, and Kay (Jencks et al., 1988) found that patients with secondary diagnosis of diabetes mellitus, unspecified anemia, hypertension, angina, ischemic heart disease, mitral valvular disease, ventricular premature beats, and unclassified arrhythmias were significantly less likely to die within 30 days than patients without these recorded diagnoses. Similarly, Iezzoni et al. (1992) demonstrated protective relationships to mortality for many comorbid conditions (e.g., type II diabetes, essential hypertension, angina), with odds ratios ranging from 0.37 to 0.70 in separate analyses of mortality after admission for stroke, pneumonia, AMI, or CHF. To our knowledge, this is the first study to investigate paradoxical comorbidities using administrative data in nearly 20 years.

The reason for the paradoxical relationship between specific conditions and mortality is unclear, although three possible explanations are offered. First, although few studies have investigated paradoxical comorbidities using administrative data, multiple clinical studies have noted paradoxical relationships between specific comorbid conditions and outcomes for specific diseases. In particular, conventional markers of cardiovascular risk such as obesity, hypertension, and hyperlipidemia have been linked to better survival among patients with coronary artery disease and heart failure (Oreopoulos et al., 2009; Uretsky et al., 2007; Habbu, Lakkis, & Dokainish, 2006; Romero-Corral et al., 2006.). One explanation is that selection bias in the admitting and referral process may, at least in part, account for the apparent paradoxical relationships. Notably, Oreopoulos et al. (2009) found that patients with coronary artery disease who were overweight or had mild or moderate obesity were also more likely to undergo revascularization procedures compared to patients with normal body mass, despite having lower risk coronary anatomy. They also found better survival among overweight and obese patients. The authors concluded that patients with obesity may present and receive treatment earlier compared to patients with normal body mass. These results suggest that selection bias may cause the paradox if individuals with certain comorbid conditions receive treatment at an earlier stage of disease. Indeed, the fact that, in our study, the paradoxical comorbidities appear to reduce mortality more for CABG than for AMI supports this notion—CABG is an elective procedure with greater clinical discretion for admission compared to AMI, and thus may be more subject to selection bias. Moreover, the larger change over time in the impact of paradoxical comorbidites on CABG mortality may also reflect changes in the willingness of surgeons to operate on some patients over time. If selection bias drives the paradoxical relationships, statistical processes to control for selection should be explored.

Second, some clinical studies suggest that the perceived paradoxical relationships may, in fact, represent real clinical phenomena that are not yet understood (Kalantar-Zadeh, Block, Horwich, & Fonarow, 2004). For example, malnutrition has been linked to several poor outcomes, and nutrition-related comorbid conditions may reflect the absence of malnutrition for a given patient (e.g., obesity, hyperlipidemia). Alternatively, the comorbid conditions themselves may be a marker for a poor outcome. For example, hypertension may be a marker for the absence of low blood pressure, which may be caused by cardiac pump failure and therefore indicate greater cardiac disease severity. These clinical explanations suggest that additional research is warranted to investigate whether conventional risk factors for cardiovascular disease in the general population apply to hospitalized patients.

Finally, paradoxical relationships may reflect coding bias in administrative data, in that patients with serious disease or complications are less likely to have certain common conditions coded, even when present. Comorbid illness may also be under-reported for patients with acute conditions due to bias that favors recording secondary diagnoses associated with the cause of the acute condition, rather than diagnoses associated with unrelated chronic illnesses (Iezzoni et al., 1992; Jencks et al., 1988). Despite the fact that several studies have documented deficiencies in the coding of comorbidity in administrative data (Benchimol et al., 2011), few studies have attempted to investigate how these deficiencies impact the assessment of patient risk. It is noteworthy that some comorbidities were paradoxical for AMI and not CABG, and vice versa, which suggests that the mechanism underlying the paradox differs across comorbidities and diseases. For example, valvular heart disease was protective of death for AMI, and associated with increased risk of death for CABG. It is possible that the AMI's are detected earlier for patients with valvular heart disease, compared to patients without valvular heart disease, which improves survival after AMI. In contrast, valvular heart disease may increase risks associated with CABG surgery. We also believe that part of the differential effects of individual comorbidities represents selection bias. An example of this is dementia, which is associated with increased risk of death for AMI, but decreased risk of death for CABG. AMI patients with dementia are likely older and less healthy compared to AMI patients without dementia, leading to higher risk of death. Patients with very severe dementia may also be less likely to be referred for CABG, so that only relatively healthy persons with dementia undergo CABG.

The apparent *increase* we found in the presence of specific conditions on the hospital discharge record over time may be due to multiple reasons. First, the actual prevalence of some conditions, such as obesity and diabetes, is known to be increasing in the general population and thus an increase in these conditions on patient medical records is logical. For some conditions, however, the increase we found is substantially greater than documented in the general population. For example, the prevalence of hypertension in the general population age 60 and older increased by 10% from 1988 through 2004 (Ostchega, Dillon, Hughes, Carroll, & Yoon, 2007). In contrast, the proportion of AMI and CABG patients with hypertension increased in our data by nearly 50% and 40%, respectively. The increase may be due to greater attention to coding of secondary conditions on medical records, or a change in the actual characteristics of patients admitted for AMI or undergoing CABG. For some conditions, the increase may be attributed to better diagnostic procedures in more recent years, allowing better identification of conditions that were previously not recognized. Some have even argued that current medical practices 'overdiagnose,' so that current diagnostic methods are able to identify conditions well before they pose any risk, leading to additional interventions without any benefit to survival (Welch, Schwartz, & Woloshin, 2011). Finally, thresholds for defining some conditions have changed over time. For example, guidelines for defining hypertension changed during our observation period, so that the diagnosis now applies to persons who were previously not considered hypertensive. One approach for addressing such conditions in risk assessment is to use and/or refine administrative diagnosis codes to better delineate severity (e.g., uncontrollable hypertension versus controlled hypertension). Toward that end, the proposed adoption of ICD-10-CM diagnosis codes in CMS administrative data, which is scheduled for 2013, is intended to provide greater sensitivity and specificity for risk assessment (Health and Human Services, 2008). Studies to investigate appropriate risk assessment under the new coding system are warranted.

The findings of the study hold significant implications for refining the measurement of comorbidity and underscore the complexity of comorbidity assessment in administrative data, which is often taken for granted. Presently, there is no standard approach for dealing with paradoxical conditions, although it is generally believed that risk-adjustment models should have clinical validity (Krumholz et al, 2006a). In their assessment of the CMS Hierarchical Conditions Classification (HCC) model, Pope et al. (2004) recommend that providers should never be penalized for recording additional diagnoses. Nevertheless, paradoxical conditions are frequently included in risk adjustment models to assess hospital performance (Krumholz & Normand, 2008; Render et al., 2008; Johnston et al., 2002; Krumholz et al., 2006), including the models currently used to assess hospital performance for AMI and CHF for CMS (Krumholz et al, 2010). Such relationships violate the underlying concept of comorbidity as a factor that complicates treatment and increases the risk of adverse outcomes. Some investigators have supplemented diagnoses on the inpatient record with diagnoses from prior health care encounters (Krumholz & Normand, 2008), which may minimize the impact of coding bias that exists on admission records. Nevertheless, this approach is often difficult to operationalize and may yield widely different estimates of the impact of the comorbid condition on outcomes (Abrams, Vaughan Sarrazin, Rosenthal, et al., 2008). In addition, the use of risk-adjustment for performance measurement usually creates incentives for hospitals to record all indicators of comorbidity in order to make patients appear 'sicker'. However, the use of paradoxical comorbid conditions for risk-adjustment actually creates disincentives to record those conditions. Ultimately, skepticism among clinicians, regarding the validity of the risk-adjustment process, may threaten the acceptance of performance measures derived from multivariable risk-adjustment.

Some limitations to the study should be noted. First, we are unable to accurately state the reason for the increase in prevalence of some conditions. We believe that the change may be attributed to a combination of factors including changes in hospital coding practices, changes in actual patient characteristics, and changes in the use of specific tests to screen for conditions. Nevertheless, this study highlights the possibility that the changing prevalence of specific conditions on hospital discharge records over time may not necessarily reflect true changes in underlying patient severity. Second, it is important to note that this study does not attempt to provide a comprehensive assessment of factors reflecting patient risk; this study examines comorbidity estimates only.

The increasing availability of administrative data, combined with public-use algorithms to identify comorbid conditions and user-friendly statistical software, has made it easier to examine hospital quality using multivariable risk-adjustment methods. Such analyses are commonly conducted by researchers, policy makers, and for-profit businesses with results being published, sold, and disseminated to news media and on the Internet. At the same time, the ease with which analyses can be conducted means that individuals performing the analyses may be unfamiliar with the limitations of administrative data and the potential for bias in the coding of specific conditions. Unrecognized systematic differences in coding practices, across facilities or over time, makes it difficult to discern differences in true patient mix from differences in coding bias. Unfortunately, naïve application of common risk adjustment tools can produce misleading results, potentially impacting conclusions regarding hospital performance and general trends in risk-adjusted mortality. Nevertheless, the impact of paradoxical comorbidities on conclusions of analyses based on administrative data is rarely acknowledged in published research. We recommend that journal reviewers and other stakeholders be mindful when reviewing methods used to handle paradoxical comorbidities in multivariable analyses, and that the potential impact of paradoxical comorbidities on results be acknowledged. Moreover, refinement of methods for measuring comorbidity is paramount given the resources invested in these efforts, the potential consequences to individuals and organizations of incorrectly identifying both high and low performing sites, and the resources that might be wasted investigating hospitals that are unfairly targeted. In light of findings presented here, development of a standard approach to model conditions with paradoxical relationships is warranted.

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