

CLINICAL RESEARCH

Coronary Artery Disease

Cardiac Rehabilitation and Survival in Older Coronary Patients

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- Objectives** This study assessed the effects of cardiac rehabilitation (CR) on survival in a large cohort of older coronary patients.
- Background** Randomized controlled trials and meta-analyses have shown that CR improves survival. However, trial participants have been predominantly middle-aged, low- or moderate-risk, white men.
- Methods** The population consisted of 601,099 U.S. Medicare beneficiaries who were hospitalized for coronary conditions or cardiac revascularization procedures. One- to 5-year mortality rates were examined in CR users and nonusers using Medicare claims and 3 analytic techniques: propensity-based matching, regression modeling, and instrumental variables. The first method used 70,040 matched pairs, and the other 2 techniques used the entire cohort.
- Results** Only 12.2% of the cohort used CR, and those users averaged 24 sessions. Each technique showed significantly lower ($p < 0.001$) 1- to 5-year mortality rates in CR users than nonusers. Five-year mortality relative reductions were 34% in propensity-based matching, 26% from regression modeling, and 21% with instrumental variables. Mortality reductions extended to all demographic and clinical subgroups including patients with acute myocardial infarctions, those receiving revascularization procedures, and those with congestive heart failure. The CR users with 25 or more sessions were 19% relatively less likely to die over 5 years than matched CR users with 24 or fewer sessions ($p < 0.001$).
- Conclusions** Mortality rates were 21% to 34% lower in CR users than nonusers in this socioeconomically and clinically diverse, older population after extensive analyses to control for potential confounding. These results are of similar magnitude to those observed in published randomized controlled trials and meta-analyses in younger, more selected populations. (J Am Coll Cardiol 2009;54:25–33) © 2009 by the American College of Cardiology Foundation

Coronary heart disease (CHD) is the leading cause of death worldwide. It is also a major driver of medical care costs and economic costs of death and disability, especially in older people. Worldwide in 2002, more than 7.2 million deaths were attributed to CHD (1). In the U.S. alone, more than 13 million people had CHD, more than 860,000 people had acute myocardial infarctions (AMIs), and 480,000 people died of CHD in 2003 (2). Older Americans (age 65 years or older) account for more than 55% of AMIs and 86% of CHD deaths (3). Cardiac rehabilitation (CR), which uniformly includes

monitored aerobic exercise and varying protocols for lipid control, weight loss, or stress modification, is recommended for patients after MIs, with stable angina, or after revascularization with coronary artery bypass graft (CABG) surgery or coronary angioplasty (4–9). Meta-analyses of randomized controlled trials of CR have demonstrated 15% to 28% reductions in all-cause mortality (10–14). However, these trials included

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very few older persons, women, members of racial/ethnic minorities, or high-risk patients (e.g., patients with congestive heart failure [CHF]). Hence, their results may not accurately reflect effects in older or more sociodemographically diverse populations.

This study examined 1- to 5-year mortality in 601,099 Medicare beneficiaries who were hospitalized in 1997 for coronary disease or revascularization procedures with follow-up extended through 2002. We compared mortal-

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**Abbreviations
and Acronyms****AMI** = acute myocardial infarction**CABG** = coronary artery bypass graft**CHD** = coronary heart disease**CHF** = congestive heart failure**CR** = cardiac rehabilitation**IV** = instrumental variable**PCI** = percutaneous coronary intervention

ity in CR users and nonusers using 3 statistical techniques: propensity-based matching, regression modeling, and instrumental variables (IVs).

Methods

Study cohort. We included all Medicare beneficiaries age 65 years and older who were hospitalized in 1997 in nonfederal, acute care hospitals in the 50 U.S. states or District of Columbia for coronary diagnoses or procedures paid by Medicare, the

almost-universal health insurance for older and disabled Americans. The principal diagnosis codes used to identify beneficiaries were 410.xx for AMI, 411.xx for other acute coronary syndromes, 413.xx for stable coronary syndrome, and 414.xx for other chronic ischemic heart disease conditions. Procedure codes included 36.1 for CABG surgery and 36.01, 36.02, 36.05, or 36.06 for percutaneous coronary intervention (PCI)—angioplasty or stent. Other inclusion criteria were a hospital stay of 30 days or less (to identify probable candidates for CR), being alive for at least 30 days after hospital discharge, and uninterrupted enrollment in fee-for-service Medicare Part A and Part B during the index hospitalization and for at least 12 months after discharge (to obtain complete billing information). The study cohort consisted of the 601,099 Medicare beneficiaries who met the inclusion criteria.

Data sources and definition of CR use. Medicare's National Claims History File was the primary data source. Medicare's master enrollment database included information on date of birth, sex, race, date of death (when applicable), residence zip code, enrollment status over time, Medicare entitlements (Part A and Part B), and group health plan membership. Census 2000 data were linked to residence zip code statistics as proxies for the patient's socioeconomic, educational, and disability statuses. American Hospital Association and Medicare data were used to determine hospital characteristics for index admissions. Use of CR services was defined by Medicare reimbursement for at least 1 CR session (denoted by Current Procedure Terminology codes 93797 and 93798) within 1 year following discharge.

Primary outcome. The primary outcome was all-cause mortality within 5 years of discharge from the index hospitalization. Because these survival data formed the basis of eligibility for government benefits, there was virtually no loss to follow-up for mortality; therefore, patients were censored only at the end of the follow-up period if they were still alive.

Statistical analysis. The patient was the unit of analysis. Explanatory variables included patient sociodemographic

characteristics (age, sex, race/ethnicity, Medicare/Medicaid dual eligibility), distance from the center of the patient's residence zip code to the nearest available CR facility within the state of residence, health-related characteristics (type of coronary event, type of coronary intervention, duration of the index hospitalization, and comorbid conditions), characteristics of the index hospital (state, size, teaching status, and availability of angiography, angioplasty, and cardiac surgery), and the socioeconomic characteristics of the patient's zip code (median household income, proportion below poverty line, average education, and prevalence of disability) and geography (census division).

Relationship between CR and mortality using propensity-based matching. Propensity-based matching paired CR users with nonusers using all observable risk factors (15–17). Using the entire study cohort, we fit a multiple logistic regression model of CR use as a function of the explanatory variables. We adjusted for clustering within index admission hospitals and used generalized estimating equations via the GENMOD procedure in SAS software (version 9.1, SAS Institute Inc., Cary, North Carolina). This model provided the adjusted predicted probabilities (propensity scores) of CR use from 0 to 1 for each patient. Then we matched each CR user with a nonuser who had the closest propensity score for CR use and matched exactly on sex, race, type of cardiac event (AMI, CABG, or PCI), age category (65 to 74 years, 75 to 84 years, or 85 years and older), presence of a diagnosis of CHF, Medicare/Medicaid dual eligibility, and census division.

Nonusers were accepted as matches only if they were alive for at least as many days after their hospital discharge as the interval between the matched CR user's hospital discharge and the CR user's first CR session. Using the GREEDY algorithm and a macro developed by Kosanke and Bergstralh (18), all possible matches were identified (using a propensity caliper of 60% of the pooled SD of the logit propensity score). These procedures yielded 70,040 matched pairs of CR users and nonusers, the subset of the entire cohort used in our propensity-based matching analyses. The large size of this cohort did not require trying to match more than 1 nonuser to each user. Standardized differences, defined as the difference between means divided by the pooled SD of the 2 groups (19), were used to describe the magnitudes of differences between groups (CR users and nonusers). Standardized differences >10% were considered meaningful (19).

Mortality differences between matched pairs of CR users and nonusers overall and for demographically- and clinically-defined subgroups were estimated using Kaplan-Meier survival curves. They were tested for their homogeneity with the Wilcoxon signed rank test for matched pairs. Differences in mortality rates were assessed for 5 years after discharge from index hospitalizations, and their statistical significances were evaluated using the McNemar test.

To evaluate these differential effects of CR by sex, race, and age groups, we ran a multiple logistic regression model

on the paired matches using 5-year mortality as the dependent variable. The dichotomous predictors were CR use, female, white, age 75 to 84 years, age 85 years and older, AMI, CABG, percutaneous transluminal coronary angioplasty, CHF, and all first-order interaction terms between CR use, sex, race, and age categories. The model also accounted for matched pairs.

Dose-response relationships between CR and mortality using propensity-based matching. The CR users were divided into low- and high-user groups based on the median number of CR sessions received (1 to 24 sessions and 25 or more sessions, respectively). The propensity-based matched pair analysis required that the dose be treated as a dichotomous variable. Each high-CR user was matched with a low-CR user on the closest logit of propensity scores and exact matches for sex, race, type of cardiac event (AMI, CABG, or PCI), age category (65 to 74 years, 75 to 84 years, or 85 years and older), and Medicare/Medicaid dual eligibility. Low-CR users were accepted as matches only if they were alive the same number of days after discharge from their index hospitalizations as their high-user counterparts when they received their 25th CR session.

Relationships between CR use and mortality using regression modeling. Regression modeling fit estimated the impact of CR on mortality with the same risk factors as matching but applied to the entire cohort of 601,099 Medicare beneficiaries. We regressed 1- to 5-year mortality by fitting a single-equation probit model with CR use and all available patient and hospital characteristics as independent variables. After calculating each patient's probability of death with and without CR use at each time point, we then estimated changes in mortality associated with CR as the difference between these 2 mortality rates and averaged over the entire cohort.

Relationships between CR and mortality using IVs. We enhanced regression modeling by using IVs to protect against residual confounding by unobserved variables (15–17). The IV method consists of selecting 1 or more variables (instruments) that are correlated with the use of CR but without any direct effect on survival (except through the use of CR). Using the entire cohort, we examined 2 IVs that would affect CR participation rates but should not otherwise affect mortality outcomes: 1) distance to the CR facility from the center of the patient's residence zip code within his/her state of residence; and 2) density of CR facilities per 10,000 population age 65 years or older by state. To establish the validity of these 2 variables, we stratified the cohort into 2 equal-sized groups: 1) patients living closer versus more distant from the CR facility; and 2) patients living in low-versus high-density CR facility areas. Although the use of CR was higher in patients living closer to CR facilities or in high-density CR areas, there were no significant differences in sociodemographic, number of coronary illness episodes, and comorbidities between these 2 equal-sized groups. These very similar characteristics between these groups, and the steps below, supported our assumption that classifying

patients on the basis of distance to CR or density of CR facilities were not independently associated with mortality. Because further analysis found the effects were not linear, each IV was entered as a set of dummy variables based on quintiles of distributions among CR users. We confirmed that each set of dummy variables was a strong predictor of CR use by fitting a multivariable single-equation probit model of CR use with and without the IVs but with all measured patient and hospital characteristics. Use of CR declined significantly with increasing distance from the closest CR facility and increased significantly with a higher density of CR facilities.

The 2 instruments combined increased the pseudo R^2 of the model from 0.156 to 0.199 ($p < 0.001$). Finally, to determine that the instruments were not directly related to survival, we fit a multivariable single-equation probit model of mortality including the IVs, CR use, and measured patient and hospital characteristics. The results indicated a small, but not clinically meaningful, change in the pseudo R^2 associated with the IVs (for 5-year survival from 0.2188 to 0.2190, representing a relative improvement of only 0.09%). We concluded that the instruments were valid and used them to estimate CR benefits.

The first stage of the IV model determined how much variance in CR use was explained by the IVs after adjusting for measured patient and hospital characteristics (15). The second stage predicted survival based on the predicted probability of CR use from the first-stage model coupled with all the explanatory factors except for IVs in the first-stage model. The resulting coefficient was considered to be the unbiased estimate of CR effect on survival. We used the biprobit procedure in STATA (version 10, StataCorp., College Station, Texas) with adjustment for hospital clustering of patients to obtain efficient standard error estimates. As with regression modeling, we calculated each patient's probability of death with and without CR use at each time point and then estimated mortality reduction as the difference between these 2 rates and averaged for the entire cohort.

Role of residual confounding in the relationships between CR and mortality. To quantify residual confounding from unobserved characteristics, we contrasted estimated CR effects obtained from the IV analysis with those from regression modeling; we then used the result to adjust findings from matching.

Sensitivity analysis. As a sensitivity analysis, we repeated the propensity-based matched analysis including only the pairs with AMI and/or CABG, the most straightforward indications for Medicare reimbursement of CR.

Results

Of the 601,099 Medicare beneficiaries who met the study's eligibility criteria, 12.2% ($n = 73,049$) received 1 or more CR outpatient sessions, and CR users received a mean of 24 (SD 12.4) (Table 1). The CR users were more likely to be

Table 1 Baseline Characteristics of Overall Cohort and Matched Pairs

Characteristic	Entire Cohort			Matched Pairs (CR Use)			Matched Pairs (CR Dose)			
	CR Users	Nonusers	Standardized Difference*	CR Users	Nonusers	Standardized Difference*	Low-CR Users	High-CR Users	Standardized Difference*	
Sample size	73,049	528,050	NA	70,040	70,040	NA	17,298	17,298	NA	
Propensity score (mean)	NA	NA	NA	0.257	0.251	0.0%	0.532	0.532	0.0%	
Standard deviation	NA	NA	NA	(0.170)	(0.162)	NA	(0.115)	(0.115)	NA	
Sociodemographic characteristics of patients										
Male	64.0%	50.0%	28.6%	63.6%	63.6%	0.0%	67.2%	67.2%	0.0%	
White	96.5%	90.0%	26.3%	96.5%	96.5%	0.0%	99.2%	99.2%	0.0%	
Age group (yrs)										
65–74	65.7%	47.3%	37.8%	65.2%	65.2%	0.0%	70.0%	70.0%	0.0%	
75–84	32.3%	40.0%	16.1%	32.7%	32.7%	0.0%	29.5%	29.5%	0.0%	
≥85	2.0%	12.7%	41.9%	2.1%	2.1%	0.0%	0.5%	0.5%	0.0%	
Medicaid at discharge	3.3%	14.1%	38.9%	3.4%	3.4%	0.0%	0.7%	0.7%	0.0%	
Index hospitalization (not exhaustive groups)										
AMI as principal diagnosis at discharge	36.7%	31.5%	11.0%	37.1%	37.1%	0.0%	33.8%	33.8%	0.0%	
CABG as coronary procedure	37.5%	11.6%	63.1%	35.4%	35.4%	0.0%	38.4%	38.4%	0.0%	
PCI as coronary procedure	20.3%	17.9%	6.2%	21.0%	21.0%	0.0%	18.9%	18.9%	0.0%	
Comorbid conditions										
Cardiovascular disease										
Prior acute myocardial infarction	2.7%	3.6%	5.0%	2.7%	2.7%	0.3%	2.7%	2.8%	0.7%	
Prior any other coronary diagnosis	13.9%	24.4%	26.7%	14.1%	14.4%	0.7%	14.0%	14.0%	0.1%	
Hypertensive heart disease	54.0%	54.8%	1.5%	54.1%	53.0%	2.3%	53.3%	53.6%	0.6%	
Cardiac arrest	5.6%	5.5%	0.3%	5.5%	5.6%	0.4%	5.2%	5.3%	0.4%	
CHF	19.4%	31.2%	27%	19.8%	19.8%	0.0%	18.9%	18.8%	0.3%	
Peripheral vascular disease	15.0%	18.5%	9.5%	15.1%	15.4%	0.8%	14.8%	14.7%	0.5%	
Cerebrovascular disease	7.1%	10.2%	11.0%	7.1%	7.4%	0.9%	6.9%	7.1%	0.9%	
Musculoskeletal condition	15.9%	20.7%	12.5%	15.9%	15.4%	1.3%	15.6%	15.3%	0.7%	
Chronic pulmonary disease	15.0%	21.7%	17.4%	15.2%	15.6%	1.1%	15.5%	15.2%	0.6%	
Diabetes without complications	22.8%	26.5%	8.5%	23.0%	23.1%	0.4%	23.0%	23.1%	0.2%	
Diabetes with complications	2.7%	5.1%	12.0%	2.8%	2.8%	0.2%	2.6%	2.7%	0.5%	
Census division of index hospital										
New England	5.7%	5.1%	2.7%	5.9%	5.9%	0.0%	5.7%	5.8%	0.3%	
Mid Atlantic	12.0%	15.9%	11.4%	12.5%	12.5%	0.0%	12.9%	12.9%	0.0%	
South Atlantic	15.4%	21.9%	16.9%	16.0%	16.0%	0.0%	16.6%	17.0%	1.0%	
East North Central	25.2%	18.4%	16.6%	25.6%	25.6%	0.0%	23.8%	23.1%	1.5%	
East South Central	5.2%	8.7%	13.9%	5.4%	5.4%	0.0%	5.5%	5.8%	1.4%	
West North Central	17.2%	6.9%	31.9%	14.5%	14.5%	0.0%	16.5%	16.0%	1.5%	
West South Central	7.8%	11.3%	11.7%	8.1%	8.1%	0.0%	8.0%	8.3%	1.2%	
Mountain	4.2%	3.9%	1.8%	4.2%	4.2%	0.0%	4.4%	4.2%	1.1%	
Pacific	7.4%	8.0%	2.0%	7.7%	7.7%	0.0%	6.6%	6.9%	1.3%	
Index hospitalization										
Length of stay >4 days	54.5%	40.4%	28.6%	53.3%	53.2%	0.2%	53.7%	53.9%	0.5%	
Any-cause hospitalization in prior year	22.8%	36.3%	30.0%	23.1%	23.4%	0.7%	22.7%	22.6%	0.4%	
Facility characteristics of index hospitalization										
Availability of cardiac catheterization										
Yes	69.0%	62.3%	14.1%	68.4%	69.0%	1.2%	83.5%	83.3%	0.6%	
Unknown	16.7%	18.2%	3.9%	17.0%	16.8%	0.3%	16.6%	16.7%	0.5%	
Medical school affiliation										
Yes	46.9%	41.3%	11.3%	46.3%	45.0%	2.7%	49.0%	48.2%	1.5%	
Unknown	3.8%	3.9%	0.5%	3.8%	3.9%	0.4%	3.9%	3.7%	0.7%	

*Standardized difference is the mean difference between groups as a percentage of their pooled SD.

AMI = acute myocardial infarction; CABG = coronary artery bypass graft; CHF = congestive heart failure; CR = cardiac rehabilitation; NA = not applicable; PCI = percutaneous coronary intervention.

male, white, younger, and not on Medicaid (a health program for individuals and families with low incomes and resources), and to have been admitted for an AMI, CABG, or PCI procedure than nonusers. They also had fewer comorbid conditions and were less likely to have had prior admissions for AMI or CHD, coexisting CHF, peripheral vascular or cerebrovascular diseases, musculoskeletal conditions, chronic pulmonary disease, or diabetes.

Although CR users and nonusers differed considerably on clinical and location-of-care measures, matched co-

horts were well balanced on all observable characteristics. Successful matches were obtained for 70,040 CR users with a like number of nonusers and for 17,298 high-dose CR users (25 or more sessions) with an equal number of low-CR users.

In the matched-pair analysis, CR users were less likely to have died at each time point. For example, cumulative mortality rates were 2.2% in CR users versus 5.3% in nonusers at 1 year and 16.3% versus 24.6% at 5 years. These mortality reductions represented relative reduc-

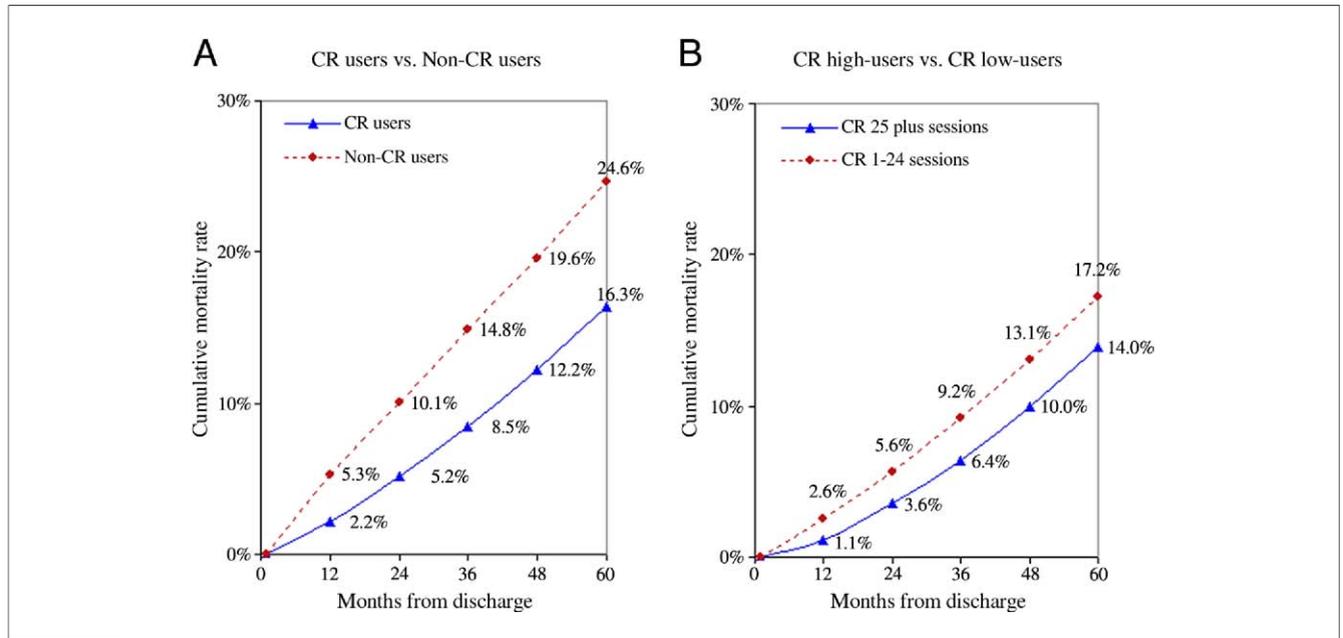


Figure 1. Estimates of Cumulative Mortality Rates for Propensity-Based Matched Groups of CR Use

All curves begin 1 month after discharge. Differences in cumulative mortality rates between cardiac rehabilitation (CR) users and nonusers at each time point shown were significant ($p < 0.0001$). Differences in cumulative mortality rates between low- and high-CR users were all significant ($p < 0.001$). Differences in annual mortality rates between CR users and nonusers were 3.1% in year 1, 2.0% in year 2, 1.8% in year 3, 1.5% in year 4, and 1.6% in year 5 (all at $p < 0.001$). Differences in annual mortality rates between high- and low-CR users were 1.4% in year 1, 0.7% in year 2, 0.8% in year 3, 0.5% in year 4, and 0.3% in year 5 (all significant at $p < 0.011$).

tions of 58% at 1 year and 34% at 5 years and were statistically significant ($p < 0.001$) (Fig. 1A). In addition, high-dose CR users were less likely to die than low-dose CR users (1.1% vs. 2.6% at 1 year and 14.0% vs. 17.2% at 5 years; $p < 0.001$ in each case) (Fig. 1B). These mortality reductions from more sessions represented relative reductions of 58% at 1 year and 19% at 5 years.

All sex, age, and racial groups had lower mortality rates among CR users than among matched nonusers (Table 2). Mortality reductions increased progressively with older age

and were greater in women than men in each age group. Overall, the cumulative 5-year mortality reduction was greater in women than men (10.4% vs. 7.1%). Nonwhites benefited more than whites (9.9% vs. 8.3%, respectively). In addition, multivariate analysis in matched pairs found a greater benefit from CR in older age groups ($p < 0.001$ for 75 to 84 years and $p < 0.013$ for 85 years and older) compared with age 65 to 74 years and in women compared with men ($p < 0.001$), but no statistically significant difference for race ($p = 0.442$).

Table 2. All-Cause 5-Year Cumulative Mortality Rates for Matched Pairs of CR Users and Nonusers by Demographic Characteristics

Participant Groups	Number of Matched Pairs	Cumulative Mortality Rates		
		CR Users	Nonusers	Difference*
All matched pairs	70,040	16.3%	24.6%	8.3%
By sex and age group				
Men	44,550	18.1%	25.2%	7.1%
Age 65–74 yrs	30,003	14.2%	19.9%	5.7%
Age 75–84 yrs	13,790	24.9%	34.7%	9.8%
Age ≥85 yrs	757	47.3%	61.8%	14.5%
Women	25,490	14.2%	24.5%	10.4%
Age 65–74 yrs	15,678	11.5%	19.7%	8.2%
Age 75–84 yrs	9,135	17.2%	30.7%	13.4%
Age ≥85 yrs	677	34.4%	53.9%	19.5%
By race				
Whites	67,569	16.6%	24.9%	8.3%
Nonwhites	2,471	18.1%	28.1%	9.9%

*Estimated mortality rate differences between nonusers and cardiac rehabilitation (CR) users were all significantly different than 0 at $p < 0.001$.

Table 3 All-Cause 5-Year Cumulative Mortality Rates for Matched Pairs of CR Users and Nonusers by Clinical Groups

Participant Groups	Number of Matched Pairs	Cumulative Mortality Rates		
		CR Users	Nonusers	Difference*
All matched pairs	70,040	16.3%	24.6%	8.3%
By presence of AMI diagnosis				
AMI	25,966	18.9%	30.9%	12.0%
Without coexistence of CHF	19,044	13.9%	23.2%	9.3%
With coexistence of CHF	6,922	32.5%	52.0%	19.5%
Non-AMI	44,074	14.9%	21.0%	6.1%
Without coexistence of CHF	37,136	12.1%	17.2%	5.0%
With coexistence of CHF	6,938	29.4%	41.3%	11.9%
By type of treatment				
CABG	24,809	13.7%	19.0%	5.3%
Without coexistence of CHF	20,185	11.1%	15.3%	4.2%
With coexistence of CHF	4,624	25.1%	35.3%	10.2%
PCI	14,679	14.7%	20.8%	6.1%
Without coexistence of CHF	12,459	12.1%	16.9%	4.8%
With coexistence of CHF	2,220	29.4%	43.1%	13.7%
No coronary procedure	30,552	20.0%	31.8%	11.8%
Without coexistence of CHF	23,536	15.2%	24.6%	9.4%
With coexistence of CHF	7,016	36.4%	56.2%	19.8%
By coexistence of CHF				
No	56,180	12.7%	19.2%	6.5%
Yes	13,860	30.9%	46.6%	15.7%

*Estimated mortality rate differences between nonusers and CR users were all significantly different than 0 at $p < 0.001$. Abbreviations as in Table 1.

CR use was associated with lower mortality in all clinical subgroups. Reductions in 5-year cumulative mortality were greater in patients with AMIs than in those without AMIs (12.0% vs. 6.1%, respectively, $p < 0.001$) and in patients with coexisting CHF than in those without CHF (15.7% vs. 6.5%, respectively, $p < 0.001$) (Table 3). When the cohort of matched pairs was stratified by both AMI diagnosis and CHF, the largest difference in 5-year cumulative mortality rates was in patients with AMIs who also had CHF (32.5% in CR users vs. 52.0% in nonusers).

Figure 2 displays the observed and estimated mortality rates for the full cohort of beneficiaries. In CR nonusers, observed mortality rates (Fig. 2A) were slightly higher than rates adjusted by either regression modeling (Fig. 2B) or IVs (Fig. 2C). In CR users, however, estimated mortality rates from regression modeling and IVs were noticeably higher than observed rates. These comparisons indicate some selection effects and confounding with CR users being healthier overall than nonusers on both observed and unobserved characteristics.

Table 4 summarizes the observed and estimated 1- and 5-year mortality rates in CR users and nonusers. Several points deserve emphasis. First, mortality rates for both CR users and nonusers were dramatically lower in the matched-pairs analysis than in analyses that included the entire cohort. This is because matched pairs represent a relatively healthier subgroup of the cohort. Second, mortality reductions associated with CR use were lower from each of the analytic techniques than were observed reductions (e.g.,

range of 21.2% to 33.7% at 5 years compared with 58.9%). Hence, adjustment for observed explanatory factors is important to reduce confounding. Third, the IV model, which adjusts for both observed and unobserved variables, provided the lowest mortality reduction associated with CR. Even then, 1-year mortality was 43.4% and 5-year mortality was 21.2% relatively lower in CR users than nonusers (both $p < 0.001$). In addition, although the relative reduction in mortality decreases between 1 and 5 years of follow-up, the absolute reduction increases over this period. Similarly, the annual mortality reductions are highly significant even in year 5 in both matched pairs and IV analyses (Figs. 1 and 2).

Finally, under the propensity-based matched analysis limited to the 46,889 matched pairs with AMI and/or CABG, CR users were associated with an 8.9-percentage point lower 5-year mortality rate compared with their nonuser counterparts.

Discussion

This study of older Americans with CHD provides strong evidence of a beneficial relationship between the use of CR and improved patient survival. The finding that 5-year mortality in CR users was 21% lower than in comparable beneficiaries who did not use CR is very similar to the 20% and 23% reductions reported in the 2 most recent meta-analyses of randomized trials (14). Moreover, the findings extend to a much broader spectrum of individuals than did the randomized clinical trials: older patients with CHD, individuals with diverse socioeco-

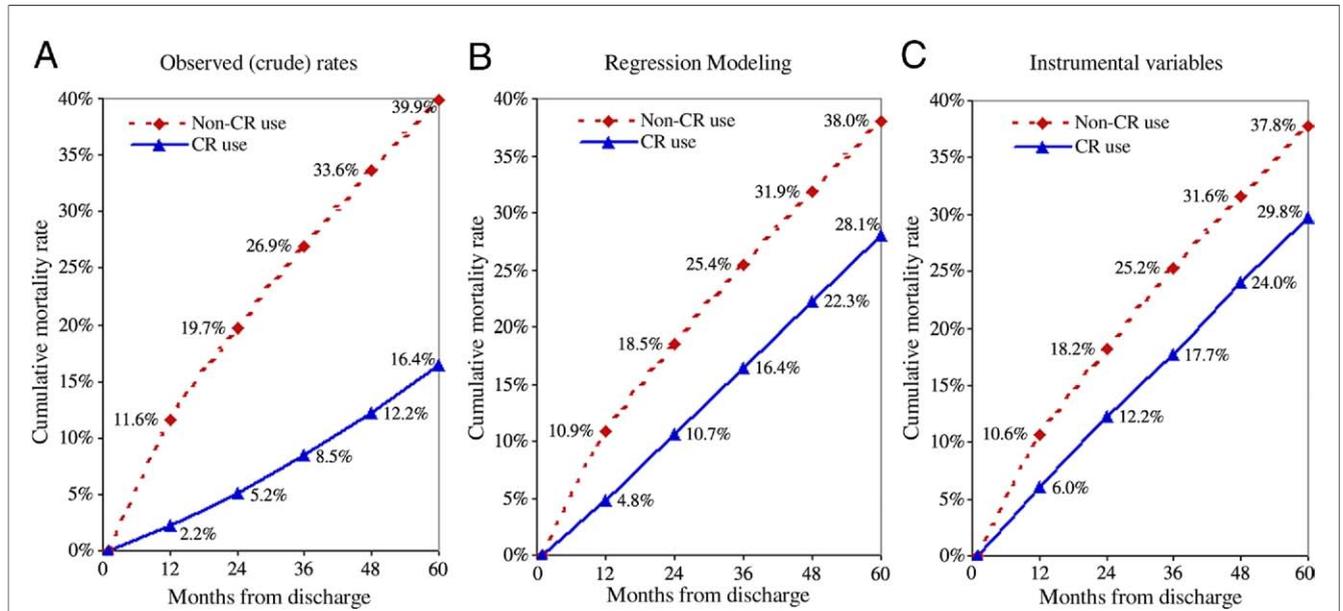


Figure 2 Crude and Adjusted Cumulative Mortality Rates for CR Use and Nonuse in the Entire Study Cohort of Medicare Beneficiaries (N = 601,099)

All curves begin 1 month after discharge. Observed and adjusted differences in cumulative mortality rates between cardiac rehabilitation (CR) users and nonusers at each time point shown were significant ($p < 0.0001$). Adjusted cumulative mortality rates for CR use from instrumental variables were lower at each time point than rates from single probit ($p < 0.001$ for 12 months, $p < 0.01$ for 24 and 48 months, and $p < 0.05$ for 36 and 60 months). Adjusted differences in annual mortality rates between CR use and non-CR use from instrumental variables were 6.0% in year 1, 2.4% in year 2, 2.9% in year 3, 1.5% in year 4, and 1.5% in year 5 (all at $p < 0.001$).

nomics and demographic characteristics, and a broader range of clinical severity of cardiac disease and comorbidities.

The study was based on an analysis of administrative data and used a variety of analytic approaches to control for potential confounding and increase the validity of findings. These techniques include the use of matching, regression modeling, and IVs to control for potential confounding. The validity of findings is further supported by a clear dose-response effect among CR users. Because the 8.9-percentage point improvement among AMI and CABG patients observed in the sensitivity analysis was close to the 8.3-percentage point difference observed in the entire cohort, our results are robust to alternative cohort specifications.

Favorable associations between CR use and survival were found in all race, sex, and age groups and in all clinical subgroups including patients with coexisting CHF. The differences in mortality rates in the matched-pair analysis imply that one 5-year death would be averted for every 12 patients who receive CR (20). Furthermore, the significant reduction in year 5 under both matched-pairs and IV analyses suggest that the benefits associated with CR persist for at least 5 years. The findings strongly suggest the need to increase the use of CR in a broad range of patients who are recovering from AMIs or coronary artery revascularization procedures.

Study strengths and limitations. Important strengths of the study are the large size and diverse sociodemographic and

Table 4 One- and 5-Year Benefit of CR Use by Analytic Technique

Mortality Rates*	Observation (N = 601,099)	Propensity-Based Matching (70,040 Pairs)	Regression Modeling (N = 601,099)	Instrumental Variables (N = 601,099)
1 yr				
CR use	2.2%	2.2%	4.8%	6.0%
Nonuse	11.6%	5.3%	10.9%	10.6%
Absolute difference†	9.4%	3.1%	6.1%	4.6%
Relative reduction‡	81.0%	58.5%	56.0%	43.4%
5 yrs				
CR use	16.4%	16.3%	28.1%	29.8%
Nonuse	39.9%	24.6%	38.0%	37.8%
Absolute difference†	23.5%	8.3%	9.9%	8.0%
Relative reduction‡	58.9%	33.7%	26.1%	21.2%

*Absolute differences between cardiac rehabilitation (CR) users and nonusers were all significantly different than 0 at $p < 0.001$. †Absolute difference is in percentage point difference. ‡Relative reductions in mortality rates are for CR use compared with nonuse.

clinical characteristics of the population examined and the 5-year follow-up period available that provided nearly 3 million person-years of data. The study population included a broad range of older Americans with coronary disease who were receiving “real world” medical treatment. This contrasts with the randomized controlled trials of CR, which generally enrolled selected, less severely ill, and younger individuals. The large size and diverse characteristics of the cohort and breadth of medical and sociodemographic variables permitted close matching of CR users with CR nonusers and increased the validity of our results. Additionally, the inclusion of IVs in the analysis helped to control for potential confounding of results by unobserved differences in disease severity, risk factors, adherence, or lifestyle variables that were not available in the Medicare database. Comparisons among the 3 techniques show the value of multiple analytic approaches. The fact that mortality reductions were one-third lower using IVs than with propensity-based matching suggests that extensive matching on observed variables did not completely eliminate selection effects.

Limitations of the study derive from its reliance on Medicare claims data as the major data source and the fact that the study period was from 1997 through 2002. These data were compiled by Medicare as a special, one-time study. Although the claims data allowed for adjustment for principal diagnoses and the presence of comorbidities, they did not permit explicit adjustment for important measures of heart disease severity such as left ventricular ejection fraction, cardiac risk factors such as smoking or obesity, important laboratory test results, or medication regimens. Moreover, the matched-pair analysis could not control for the level of patient motivation as a potential confounder. The benefits of CR would be overstated if motivation to modify lifestyles and to adhere to medication regimens were stronger in CR users than among nonusers. However, the use of the IV approach should control for such unobserved characteristics.

Finally, changes in treatment protocols for CHD since the 1997 to 2002 period may have influenced the use of CR and patient survival. Eligibility for Medicare reimbursement of CR was expanded in 2006 to include patients who received coronary angioplasty or cardiac transplantation and valve replacement, in addition to the previous indications of stable angina, AMI, and CABG surgery (8). Hence, more patients covered by Medicare may be receiving CR today than in 1997. However, CR use remained low in 2005 (21), and the number of CR facilities changed little between 1997 and 2004 (22). Treatment for CHD, however, has become more intense since 1997 with the increased use of early coronary angioplasty in patients with AMIs, the advent of drug-eluting stents, and more aggressive use of cardiac medications such as statins, antiplatelet agents, beta-blockers, and angiotensin-converting enzyme inhibitors. There is no a priori reason, however, to think that these treatments would differentially benefit CR users more than nonusers. Despite its limitations, this study is the largest analysis to date of CR in the elderly, a growing

population segment in the U.S. and worldwide and a growing share of CR users (23).

Implications of findings. This study verified the low overall use of CR in patients with coronary artery disease (12.2%) shown in prior studies in the U.S. (14% after AMI and 31% after CABG [24] and 35% after AMI in 21 states [21]), 29% in the United Kingdom (25), 23% in France after AMI (26), <8% in Japan after AMI (27), and 41% in Ontario, Canada, after CABG (28). Low use of CR is a global phenomenon. The confluence of low use of CR and higher survival in CR users highlights important clinical, policy, and research challenges. Low CR use occurs despite the endorsement of CR by important professional organizations including the American Heart Association, American College of Cardiology, American Association of Cardiovascular and Pulmonary Rehabilitation (5–7); the Canadian Association of Cardiac Rehabilitation (29); and the European Society of Cardiology (30). Possible reasons for low use of CR include physicians’ skepticism over its benefits, variations in access to CR programs in different parts of the country and in different countries, preference for exercise or rehabilitation at home over in an institution, and physicians’ primary emphasis on cardiac medications and revascularization procedures. Patient-related factors may also be operative, including their reluctance to commit to 8 to 12 weeks of CR sessions and logistic or financial impediments. Finally, compared with other interventions, current reimbursement levels for CR may be too low to cover costs (31,32) or encourage active marketing of programs by hospitals or free-standing facilities.

Conclusions

Our study provides strong support for the concept that CR participation decreases mortality in older cardiac patients as has been demonstrated in younger patients in randomized controlled trials. This evidence suggests the importance of initiatives to further evaluate its clinical benefits and cost effectiveness and to consider options for stimulating expanded use. Options might include: 1) examining the resource costs of providing CR services so that reimbursement rates can be adjusted and appropriate incentives for use created (33,34); 2) implementing quality-of-care performance measures for hospitals and physicians to encourage referrals to and use of CR (35,36); and 3) considering including CR use as a criterion in value-based purchasing initiatives (37).

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