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Sex and Racial Disparities in Cardiac Rehabilitation Referral at Hospital Discharge and Gaps in Long-Term Mortality

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Background—Cardiac rehabilitation (CR) referral is recommended for eligible patients, regardless of sex or race. It is unclear whether inequality in CR referral practices was associated with patients' long-term survival.

Methods and Results—We linked the American Heart Association Get With The Guidelines Coronary Artery Disease registry with Medicare claims data for 48 993 coronary artery disease patients from 365 hospitals across the United States between 2003 and 2009. We used generalized estimation equations to estimate the association between CR referral and mortality accounting for clustering within hospitals. Between 2003 and 2009, only 40% of eligible patients received CR referrals. Females were 12% less likely to receive CR referral compared with males. Black, Hispanic, and Asian patients were 20%, 36%, and 50% less likely, respectively, to receive CR referral than white patients. CR referral was associated with 40% lower 3-year all-cause mortality. Women and minorities who received CR referral at hospital discharge had significantly lower mortality compared with those who did not (odds ratios=0.61 [95% confidence interval, 0.56–0.66] for women, 0.75 [95% confidence interval, 0.63–0.88] for black, 0.62 [95% confidence interval, 0.50–0.79] for Hispanic, and 0.63 [95% confidence interval, 0.46–0.85] for Asian patients). Seven percent of the black versus white mortality gap could potentially be reduced by equitable CR referral.

Conclusions—CR referral rates at hospital discharge remained low. Gaps in receiving CR referral at hospital discharge were large for women and minorities, and the mortality gap could potentially be reduced through elimination of inequality in CR referral. (*J Am Heart Assoc.* 2018;7:e008088. DOI: 10.1161/JAHA.117.008088.)

Key Words: cardiac rehabilitation • cardiovascular disease • epidemiology • mortality

Cardiovascular disease accounts for one third of all deaths in the United States,¹ and 31% of all deaths globally.^{2,3} Cardiac rehabilitation (CR), which emphasizes smoking cessation, physical activity, and weight management, can improve physical function, psychosocial well-being, and quality of life for myocardial infarction (MI) survivors.^{4–6} Despite the many benefits of CR, referral and participation

rates are surprisingly low.^{7–9} The Million Hearts Initiatives from the Centers for Disease Control and Prevention set a goal to achieve >70% participation in CR/secondary prevention programs by the year 2022.¹⁰ The American Heart Association and the American College of Cardiology recommend CR referral before hospital discharge as a Class I recommendation and listed assessing the impact of better CR referral, initiation, and participation on population outcomes as priority areas.¹¹ In order to participate in a CR program, patients must first receive a referral from their physician. CR referral is recommended for eligible patients regardless of their sex, race, or geographic location. Prior studies suggest that the most easily overcome barrier to CR participation is the lack of CR referral at hospital discharge.^{9,12–16} It is unclear whether inequality in CR referral practices by physicians was associated with patients' long-term survival.

Prior research on CR mainly focused on 2 areas: (1) identifying predictors for CR referral and initiation^{8,9,17–21} and (2) estimating the effects of CR participation with subsequent outcomes, such as mortality.^{22–24} For (1), the majority of evidence was collected from white males.²⁵ Evidence from females and minorities was limited. For (2),

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Accompanying Tables S1 through S3 are available at <http://jaha.ahajournals.org/content/7/8/e008088/DC1/embed/inline-supplementary-material-1.pdf>

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Clinical Perspective

What Is New?

- Disparities in receiving cardiac rehabilitation referral at hospital discharge were associated with lower long-term survival.

What Are the Clinical Implications?

- Sex and race disparities in cardiovascular health could potentially be reduced through higher rates of cardiac rehabilitation referral.

studies were focused on actual CR participation and mainly based on trials²⁶ or administrative databases.²⁷ However, the administrative databases did not include information regarding CR referral. Furthermore, CR referral and participation could be influenced by patients' underlying health status. Information on detailed clinical conditions as well as quality of care received is limited in claims databases. Can inequality in CR referral at hospital discharge lead to subsequent differences in long-term mortality? The answer to this question is currently unknown and could provide insights into reducing cardiovascular health disparities. The magnitude of potential improvement in mortality that may be achieved by reducing the sex and racial gaps in referral rates remains to be determined.

The Get With The Guidelines–Coronary Artery Disease (GWTG-CAD) program is a national program organized by the American Heart Association.^{28,29} It is a large, multicenter, observational registry started in 2000 to support and facilitate improvement of the quality of care for patients with cardiovascular disease. CR referral, physical activity, weight management, and smoking cessation counseling recommendations were part of the quality of care performance measures. By linking this large registry in the United States with Medicare claims data containing diverse patient and hospital characteristics, we have a unique opportunity to address the abovementioned knowledge gaps. We hypothesized that (1) receipt of CR referral at hospital discharge would be associated with lower 1- and 3-year mortality; (2) there should be no differences in CR referral rates by sex, race, and regional differences; and (3) elimination of gaps in CR referral could potentially be associated with reduced sex and racial disparities in cardiovascular health.

Methods

In accordance with existing policies regarding data availability in the GWTG database, the data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

Study Population

We linked 125 135 patients in the GWTG-CAD registry with Medicare inpatient data from 551 hospitals across the United States. The GWTG Program uses a web-based Patient Management Tool (Outcome Sciences Inc, Cambridge, MA) to collect clinical data and provide decision support with real-time online reporting features. The GWTG-CAD program enrolls patients hospitalized with a confirmed diagnosis of CAD (*International Classification of Diseases Ninth Revision [ICD-9]* codes 410–414 included). Trained data abstractors at participating hospitals in GWTG-CAD collected detailed information on baseline demographic and clinical characteristics, in-hospital care processes and outcomes, and discharge treatment using a standardized set of data elements and definitions. Using an internet-based system, data quality was monitored to assure the completeness and accuracy of the submitted data. Outcome Sciences, Inc. serves as the data collection and coordination center for GWTG. Hospital participation in the GWTG-CAD registry was voluntary and nationwide, and information included met *ICD-9*, Diagnosis code 410 to 414 (diagnosis of acute MI, unstable angina, chronic stable angina, and ischemic heart disease) inclusion criteria or criteria for symptomatic peripheral vascular disease. Case findings were based on clinical identification of patients with qualifying clinical diagnoses or *ICD-9*, identification with clinical verification from data abstraction. Participating hospitals submit clinical data regarding patients' in-hospital care and outcomes.

The Medicare linkage includes Part A (inpatient) claims and the associated denominator file from 2003 to 2009, which linked with data from the GWTG-CAD registry.^{30,31} The study population for this analysis was from hospitals in the GWTG-CAD registry consisting of 125 134 patients in the database linked to Centers for Medicare and Medicaid Services from 551 hospitals in the United States from January 2003 to December 2009 (Figure 1). We included those that had at least 75% complete data on medical history, had a principal cardiac or principal CAD diagnosis (as recorded in the GWTG-CAD registry), were 65 years older with a GWTG-CAD registry hospitalization linked to Medicare, were discharged between January 1, 2003 and December 31, 2009, were discharged alive, but did not leave against medical advice and were not discharged or transferred to either another short-term hospital or hospice or discharge destination missing (as recorded in the GWTG-CAD registry), were enrolled in fee-for-service Medicare at discharge, and had available information on sex, race, and region. If multiple hospitalizations existed for a patient, the first hospitalization was selected as the index hospitalization for this analysis (Figure 1). Our final analytic sample consisted of 48 993 patients, aged 65 years or older, from 365 hospitals.

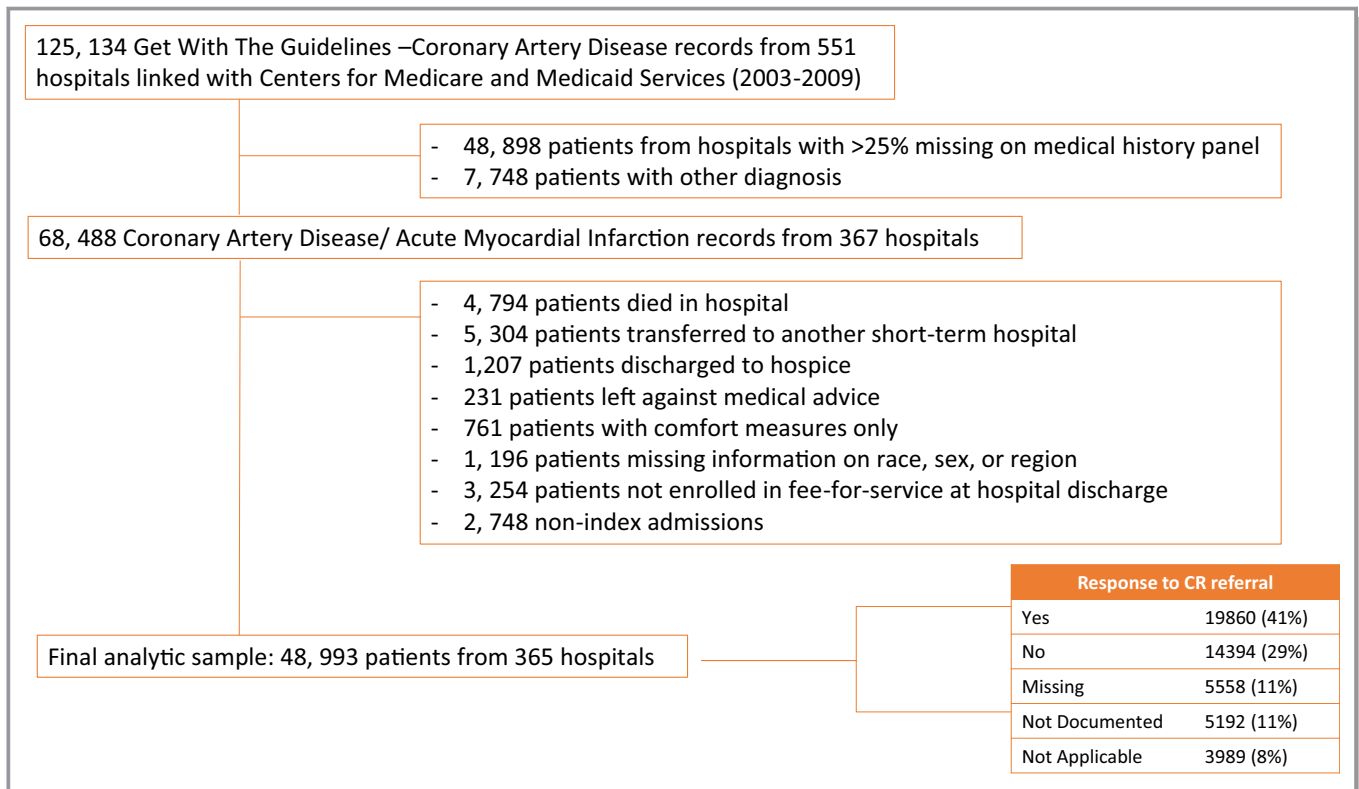


Figure 1. Inclusion and exclusion criteria. CR indicates cardiac rehabilitation.

Measures and Methods of Ascertainment

CR referral and other risk interventions

Outpatient CR program information was collected through the standard performance management form, and extracted from medical records by professionally trained personnel. It is part of the information captured by the GWTG registry data collection form. It was coded as “yes, no, not documented, or not applicable.” For all of our analyses, we included eligible patients as our denominator. There were 3989 (8%) patients with not applicable recorded for the outpatient CR program variable. For each eligible patient ($n=48\,993$), information was extracted regarding whether the patients received outpatient CR referral, and whether patients received physical activity recommendation. For patients who were overweight or obese ($n=28\,063$, body mass index ≥ 25 kg/m²), receipt of weight management was recorded as part of the CAD quality of care measure. For patients who were current smokers ($n=7007$), information on whether smoking cessation counseling was given was also recorded as part of the GWTG performance measure.

Sex, race/ethnicity, and geographic region

Our primary exposures of interest include sex (male or female), race/ethnicity (white, black, Asian, Hispanic, other), and geographic region (Northeast, Midwest, South, West).

Information was extracted from medical records that were collected during patient hospitalization through patient self-reporting and recorded separately by trained hospital personnel.

Mortality

Our outcomes were 1- and 3-year all-cause mortality. Death events were ascertained on the basis of the death date recorded in the denominator/vital status file.

Covariates

In our multivariable analysis, we considered the following variables to be potential confounders for our main analysis and mediation analysis, including patients’ sociodemographic and lifestyle information, insurance status, medical history, cardiac diagnosis, hospital characteristics, medications before hospital admission, medications prescribed at hospital discharge, as well as quality of care received during hospitalization. Quality of care was measured using the GWTG-CAD quality of care composite performance score, which is a composite performance measure documenting 100% compliance (ie, defect-free care). It includes adherence to 6 measures, including angiotensin-converting enzyme inhibitor or angiotensin receptor blocker treatment for patients with left ventricular systolic dysfunction, β -blockers at discharge, lipid-lowering medications, aspirin within 24 hours of

admission and at discharge, and smoking cessation. All covariate information was extracted from medical records as well the GWTG-CAD performance measures form.

Statistical Analyses

We first examined outpatient CR referral rates for the overall sample, and by sex, race, geographic region, and calendar year. For outpatient CR referral and physical activity recommendations, we performed analyses among all CAD patients. For weight management and smoking cessation recommendations, we restricted our analyses to eligible patients only (patients with body mass index ≥ 25 kg/m² for weight management, and smokers for smoking cessation). We also calculated the proportion of CR-referred patients who were white men for each follow-up year.

To examine the generalizability of our findings, we compared patient and hospital characteristics among those included and excluded from our analytic sample. The Pearson χ^2 test was used to compare binary or nominal categorical variables, and the Kruskal–Wallis test was used to compare continuous variables or ordinal categorical variables. Percent standardized differences between groups are also provided (standardized difference $\times 100$).³²

We first estimated the associations between CR referral with 1- and 3-year mortality using a generalized estimation

equation model accounting for clustering within hospital. We tested interaction by sex, race, and region using likelihood ratio tests. To estimate the effect of CR on mortality independent of insurance status and quality of care received, we further adjusted for patients' insurance status, medication use before and after hospital discharge, as well as quality of care received during hospitalization. We examined whether there were sex, racial, and regional differences in CR and other risk intervention recommendation rates using a generalized estimation equation model accounting for clustering within hospitals.

To examine the proportion of sex, racial, and regional gap in mortality that could potentially be reduced through optimal CR referral, we performed a causal mediation analysis.^{33,34} We estimated the association between sex, race, and region with 1- and 3-year mortality using the generalized estimation equation model. The proportion of the disparity in sex/race-mortality relation that could potentially be reduced through CR referral was computed, on the risk difference scale, as $[\text{odds ratio (OR)}_{\text{NDE}} \times (\text{OR}_{\text{NIE}} - 1)] / [\text{OR}_{\text{NDE}} \times \text{OR}_{\text{NIE}} - 1] \times 100$ (NDE, Natural Direct Effect; NIE, Natural Indirect Effect).³³

As a sensitivity analysis, we modified logistic regressions in the original MEDIATION SAS macro to include the generalized estimation equation statement accounting for within-hospital correlations. We also performed sensitivity analysis to estimate the influence of unmeasured confounding factors on our effect estimates.³⁵

Table 1. CR Referral and Other Risk Intervention Rates in Patients With CAD at Hospital Discharge

	N Total (%)	Outpatient CR Referral	Physical Activity Recommendations	Weight Management*	Smoking Cessation [†]
		N (%)	N (%)	N (%)	N (%)
N eligible/overall	48 993 (100.00)	48 993 (100.00)	48 993 (100.00)	28 063 (57.28)	7007 (14.30)
N yes/N eligible	48 993 (100.00)	19 860 (40.54)	37 764 (77.08)	23 199 (82.67)	6140 (87.63)
Sex					
Male	25 830 (52.72)	11 267 (43.62)	20 360 (78.82)	13 232 (83.63)	3508 (87.31)
Female	23 163 (47.28)	8593 (37.10)	17 404 (75.14)	9967 (81.42)	2632 (88.06)
Race					
White	40 573 (82.81)	17 169 (42.32)	31 319 (77.19)	19 364 (82.68)	5052 (87.94)
Black	2775 (5.66)	1012 (36.47)	2042 (73.59)	1296 (79.95)	437 (91.81)
Hispanic	2476 (5.05)	752 (30.37)	2023 (81.70)	1291 (86.59)	314 (85.56)
Asian	1191 (2.43)	265 (22.25)	861 (72.29)	335 (78.64)	90 (73.17)
Other	1978 (4.04)	662 (33.47)	1519 (76.79)	913 (82.55)	247 (83.45)
Region					
Northeast	9232 (18.84)	2739 (29.67)	6794 (73.59)	4316 (83.66)	1156 (88.72)
Midwest	13 781 (28.13)	7370 (53.48)	10 905 (79.13)	7053 (82.95)	1628 (87.15)
South	17 433 (35.58)	6505 (37.31)	13 556 (77.76)	8254 (81.93)	2450 (89.06)
West	8547 (17.45)	3246 (37.98)	6509 (76.16)	3576 (82.66)	906 (83.50)

BMI indicates body mass index; CAD, coronary artery disease; CR, cardiac rehabilitation.

*Among patients with BMI >25 kg/m² only.

[†]Among smokers only.

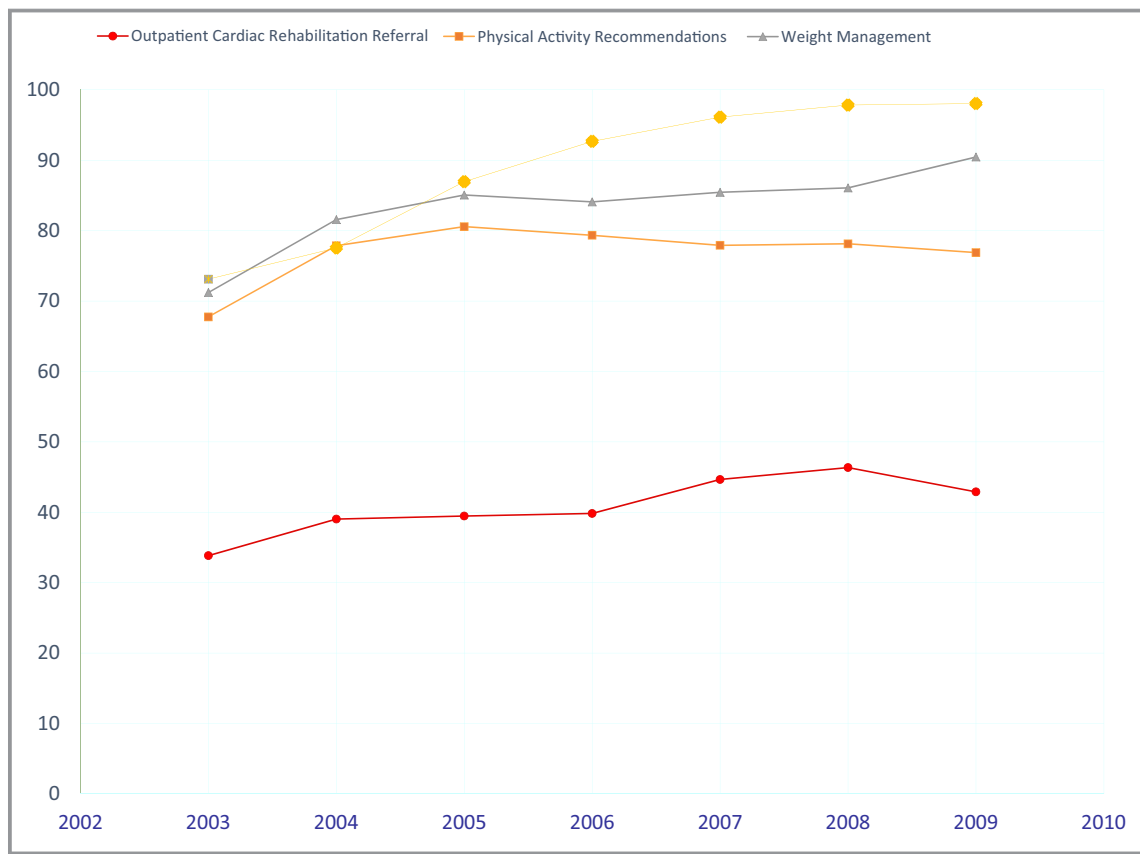


Figure 2. Time trends of cardiac rehabilitation referral rate and other risk intervention rates at hospital discharge from 2003 to 2009.

This study was approved by an institutional review board at the American Heart Association–GWTG committee. All participating institutions were required to comply with local regulatory and privacy guidelines and, if required, to secure institutional review board approval. Because data were used primarily at the local site for quality improvement, sites were granted a waiver of informed consent under the common rule. Quintiles (Cambridge, MA) served as the registry coordinating center. The Duke Clinical Research Institute (Durham, NC) served as the data analysis center, and institutional review board approval was granted to analyze aggregate de-identified data for research purposes.

Results

Among 48 993 patients from 365 fully participating GWTG-CAD sites, 40.5% patients were referred by their physician to an outpatient rehabilitation program at discharge, and 77.1% received a physical activity recommendation (Table 1). Among 28 063 patients who were overweight, 82.7% received weight management recommendation. Among 7007 smokers, 87.6% received smoking cessation recommendations. As part of the quality of care performance measures of the AHA-GWTG program, the CR referral rate remained low from 2003 to

2009. We observed little improvement in CR referral from 34% in 2003 to 43% in 2009 (Figure 2). Greater improvements were observed for smoking cessation, from 70% in 2003 to 98% in 2009. Similarly, improvements were seen for physical activity and weight management recommendations. Among 19 860 CR referred patients, 50% were white males, with level referral rates of 48% in 2003 to 52% in 2009.

Patient and hospital characteristics were overall similar comparing those included with those excluded from our analytic sample (Table S1). Patients who received CR referral tended to be younger, had higher body mass index, and were more likely to receive coronary angiography or percutaneous coronary intervention during hospitalization, less likely to have in-hospital procedures panel missing, and were more likely to be located in the Midwest region (Table 2).

CR referral and other risk interventions were all significantly inversely associated with 1- and 3-year all-cause mortality (Table 3). The significant inverse associations remained after we further adjusted for patients' insurance status, medications, as well as quality of care received. We found significant effect modification by sex for physical activity recommendation (P for interaction=0.0009, Table 4), and for smoking cessation counseling (P for interaction=0.04, Table 4) for 1-year mortality, but no significant interactions for 3-year mortality. Overall,

Table 2. Patients' Characteristics by CR Referral Status at Hospital Discharge

Variable	Overall	Referred	Not Referred	P Value	Standardized Difference, %
	N=48 993	N=19 860	N=29 133		
Demographics					
Age, y*	77 (71–83)	75 (70–80)	78 (71–84)	<0.0001	35.3
Sex				<0.0001	13.5
Female	23 163 (47.3)	8593 (43.3)	14 570 (50.0)		
Male	25 830 (52.7)	11 267 (56.7)	14 563 (50.0)		
Race				<0.0001	
White	40 573 (82.8)	17 169 (86.5)	23 404 (80.3)		16.5
Black	2775 (5.7)	1012 (5.1)	1763 (6.1)		4.2
Hispanic	2476 (5.1)	752 (3.8)	1724 (5.9)		9.9
Asian	1191 (2.4)	265 (1.3)	926 (3.2)		12.4
Other	1978 (4.0)	662 (3.3)	1316 (4.5)		6.1
Insurance				<0.0001	
No insurance/ND/UTD	914 (2.0)	341 (1.8)	573 (2.2)		2.6
Medicare	27 996 (62.0)	11 250 (59.8)	16 746 (63.6)		7.9
Medicaid	2662 (5.9)	816 (4.3)	1846 (7.0)		11.6
Other	13 572 (30.1)	6409 (34.1)	7163 (27.2)		14.9
Cardiac diagnosis				<0.0001	
Heart failure with CAD	13 919 (28.4)	5454 (27.5)	8465 (29.1)		3.5
Confirmed AMI—non-STEMI	4590 (9.4)	2492 (12.5)	2098 (7.2)		18.0
Confirmed AMI—STEMI	22 524 (46.0)	8141 (41.0)	14 383 (49.4)		16.9
Unstable angina	2756 (5.6)	1245 (6.3)	1511 (5.2)		4.7
Coronary artery disease	5204 (10.6)	2528 (12.7)	2676 (9.2)		11.4
Year				<0.0001	14.5
2009	3084 (6.3)	1323 (6.7)	1761 (6.0)		
2008	6680 (13.6)	3096 (15.6)	3584 (12.3)		
2007	7270 (14.8)	3247 (16.3)	4023 (13.8)		
2006	7105 (14.5)	2830 (14.2)	4275 (14.7)		
2005	9500 (19.4)	3749 (18.9)	5751 (19.7)		
2004	8076 (16.5)	3152 (15.9)	4924 (16.9)		
2003	7278 (14.9)	2463 (12.4)	4815 (16.5)		
Medical history					
Atrial fib/atrial flutter	5482 (11.7)	1810 (9.4)	3672 (13.3)	<0.0001	12.3
COPD or asthma	7967 (17.0)	3025 (15.7)	4942 (17.9)	<0.0001	5.9
Diabetes mellitus	15 743 (33.6)	6181 (32.1)	9562 (34.6)	<0.0001	5.4
Hyperlipidemia	23 065 (49.2)	10 747 (55.8)	12 318 (44.6)	<0.0001	22.5
Hypertension	34 850 (74.4)	14 404 (74.8)	20 446 (74.1)	0.08	1.6
Peripheral vascular disease (PVD)	5460 (11.6)	2116 (11.0)	3344 (12.1)	0.0002	3.5
CAD	8459 (18.0)	3592 (18.6)	4867 (17.6)	0.004	2.6
Prior MI	9891 (21.1)	3940 (20.5)	5951 (21.6)	0.003	2.7
Cerebrovascular accident/transient ischemic attack	5255 (11.2)	1738 (9.0)	3517 (12.7)	<0.0001	12.0

Continued

Table 2. Continued

Variable	Overall	Referred	Not Referred	P Value	Standardized Difference, %
	N=48 993	N=19 860	N=29 133		
Implantable cardioverter defibrillator	261 (0.6)	105 (0.5)	156 (0.6)	0.77	0.3
Heart failure	8443 (18.0)	2633 (13.7)	5810 (21.0)	<0.0001	19.6
Anemia	1394 (3.0)	405 (2.1)	989 (3.6)	<0.0001	8.9
Pacemaker—biventricular/resync/ cardiac resynchronization	739 (1.6)	260 (1.3)	479 (1.7)	0.001	3.1
Dialysis (chronic)	911 (1.9)	251 (1.3)	660 (2.4)	<0.0001	8.1
Renal insufficiency	5411 (11.5)	1811 (9.4)	3600 (13.0)	<0.0001	11.6
Depression	1241 (2.6)	464 (2.4)	777 (2.8)	0.007	2.5
Prior PCI or CABG	2186 (4.7)	947 (4.9)	1239 (4.5)	0.03	2.0
Valvular heart disease	277 (0.6)	118 (0.6)	159 (0.6)	0.61	0.5
Medical history panel missing	2121 (4.3)	595 (3.0)	1526 (5.2)	<0.0001	11.3
Smoking	7007 (14.6)	3193 (16.4)	3814 (13.4)	<0.0001	8.6
Measures					
Systolic blood pressure, mm Hg*	123 (110–138)	122 (110–136)	124 (110–140)	<0.0001	9.5
BMI*	26.63 (23.49–30.41)	27.2 (24.2–30.86)	26.3 (23.03–30.07)	<0.0001	15.2
Ejection fraction*	50 (38–60)	50 (40–60)	50 (35–60)	<0.0001	6.5
Ejection fraction <40% or moderate or severe dysfunction	10 973 (25.9)	4132 (23.0)	6841 (28.1)	<0.0001	11.5
Medications before admission					
ACE-inhibitors	4936 (32.0)	2180 (31.7)	2756 (32.2)	0.56	0.9
Aspirin	7706 (49.9)	3592 (52.3)	4114 (48.0)	<0.0001	8.5
β-Blocker	3202 (20.7)	1397 (20.3)	1805 (21.1)	0.26	1.8
Lipid-lowering agents	7663 (49.6)	3547 (51.6)	4116 (48.1)	<0.0001	7.2
Prior medication missing	33 558 (68.5)	12 991 (65.4)	20 567 (70.6)	<0.0001	11.1
In-hospital procedures					
No procedure	6402 (15.1)	1036 (5.5)	5366 (22.7)	<0.0001	51.1
Cardiac cath/coronary angiography	28 025 (66.0)	13 917 (73.8)	14 108 (59.8)	<0.0001	30.1
Cardioversion	156 (0.4)	89 (0.5)	67 (0.3)	0.0015	3.1
CABG or cardiac valve surgery	5467 (12.9)	3550 (18.8)	1917 (8.1)	<0.0001	31.7
PCI or PCI with stent	22 056 (52.0)	11 602 (61.5)	10 454 (44.3)	<0.0001	35.0
CRT-P or CRT-D	88 (0.2)	36 (0.2)	52 (0.2)	0.50	0.7
Implantable cardioverter defibrillator only	162 (0.4)	70 (0.4)	92 (0.4)	0.75	0.3
Dialysis or ultrafiltration, or unspecified	135 (0.3)	40 (0.2)	95 (0.4)	0.0005	3.4
Mechanical ventilation	1093 (2.6)	673 (3.6)	420 (1.8)	<0.0001	11.1
Right cardiac catheterization	671 (1.6)	441 (2.3)	230 (1.0)	<0.0001	10.7
In-hospital procedures panel missing	6545 (13.4)	1006 (5.1)	5539 (19.0)	<0.0001	43.9
Medications at discharge					
ACE inhibitors	27 505 (56.9)	11 949 (60.7)	15 556 (54.3)	<0.0001	13.0
Aspirin	43 971 (90.0)	18 743 (94.6)	25 228 (86.8)	<0.0001	26.9
β-Blockers	41 997 (86.4)	17 564 (88.9)	24 433 (84.7)	<0.0001	12.6
Lipid-lowering agents	38 484 (80.6)	17 303 (88.3)	21 181 (75.2)	<0.0001	34.2

Continued

Table 2. Continued

Variable	Overall	Referred	Not Referred	P Value	Standardized Difference, %
	N=48 993	N=19 860	N=29 133		
Hospital characteristics					
Number of beds*	342 (226–527)	373 (265–536)	323 (208–507)	<0.0001	7.6
Region				<0.0001	
West	8547 (17.4)	3246 (16.3)	5301 (18.2)		4.9
South	17 433 (35.6)	6505 (32.8)	10 928 (37.5)		10.0
Midwest	13 781 (28.1)	7370 (37.1)	6411 (22.0)		33.6
Northeast	9232 (18.8)	2739 (13.8)	6493 (22.3)		22.2
Academic hospital	28 873 (59.0)	12 567 (63.4)	16 306 (56.0)	<0.0001	15.2
Rural location	6020 (12.5)	1704 (8.6)	4316 (15.2)	<0.0001	20.4
Primary PTCA performed for AMI	44 180 (91.3)	18 737 (95.3)	25 443 (88.6)	<0.0001	24.8
Cardiac surgery performed on-site	39 751 (82.7)	17 240 (88.1)	22 511 (79.0)	<0.0001	24.6
Heart transplants performed at site	5541 (11.6)	1739 (8.9)	3802 (13.4)	<0.0001	14.5

ACE indicates angiotensin-converting enzyme; AMI, acute myocardial infarction; BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CR, cardiac rehabilitation; CRT, cardiac resynchronization therapy; IQR, interquartile range; MI, myocardial infarction; ND, not documented; non-STEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty; PVD, peripheral vascular disease; STEMI, ST-elevation myocardial infarction; UD, undetermined.

*Continuous variables presented as median (IQR).

the significant inverse association with mortality by CR referral was consistently seen for both male and female patients, and for all racial groups (Table 4).

We observed significant sex, racial, and regional differences in CR referral at hospital discharge (Table 5). Females were 12% less likely to receive CR referral compared with males (OR=0.88, 95% confidence interval [CI], 0.85–0.92, Table 5). Compared with white patients, black, Hispanic, and Asian patients were 20%, 36%, and 50% less likely to receive CR referral (P for interaction=0.008). Patients in the Midwest region were 2.5 times more likely to receive CR referral compared with those in the Northeast region. Compared with males, females were less likely to receive physical activity recommendations (OR=0.91, 95% CI, 0.86–0.96). No difference was observed for weight management and smoking cessation.

To examine the proportion of sex, racial, and regional gap in mortality that could be reduced through equitable CR referral, we first examined the association between sex, race, and region with 1- and 3-year mortality (Table S2). We found a racial difference in mortality (P for interaction=0.004 for 1-year mortality and 0.001 for 3-year mortality). Compared with white patients, black patients were 1.3 times more likely to die at year 1 and year 3 post hospital discharge (OR=1.31, 95% CI, 1.16–1.47 for 1-year mortality, OR=1.36, 95% CI: 1.23–1.50 for 3-year mortality). This elevated mortality risk among black patients persisted regardless of referral to outpatient CR, having received activity recommendations, or weight management at discharge. Mediation analysis results indicated that CR referral was a significant mediator for the association between

sex and race with mortality (P for natural indirect effect <0.0001 for women, 0.003 for black, 0.0002 for Hispanic, and 0.002 for Asians patients, Table S3). Results were similar after we accounted for within-hospital correlations. Seven percent (95% CI, 6–12%) of the black–white mortality gap could potentially be reduced through equitable CR referral.

For the observed inverse associations of CR referral with 3-year mortality (OR=0.60) to be completely because of unmeasured confounders, the unmeasured confounders would need to be associated with both the CR referral and the mortality by a risk ratio of 3.0-fold each, above and beyond the measured confounders. The unmeasured confounders needed to be associated with both the risk interventions and the mortality by a risk ratio of 2.3-fold each for physical activity and weight management and 1.8-fold each for smoking cessation, to completely explain away the observed lower mortality.

Discussion

In this large cardiovascular disease registry of patients in the United States linked with a database that included long-term mortality, receipt of CR referral at hospital discharge was significantly inversely associated with all-cause mortality. Despite improvements in other risk interventions, CR referral rates remained low, particularly for females, black, Hispanics, and Asian patients, who were 12%, 20%, 36%, and 50% less likely to receive CR referral, respectively. Eliminating inequality in CR referral at hospital discharge could potentially reduce long-term mortality in these patient populations. Specifically,

Table 3. Associations Between CR Referral and Other Risk Interventions at Hospital Discharge With 1- and 3-Y All-Cause Mortality

	Deaths	Unadjusted		Adjusted*		Adjusted†	
	N (%)	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
At 1 y							
Cardiac rehabilitation referral							
Yes	1958 (9.86)	0.38 (0.34, 0.42)	<0.0001	0.52 (0.48, 0.56)	<0.0001	0.56 (0.52, 0.60)	<0.0001
No	6474 (22.22)	Reference		Reference		Reference	
Activity recommendations							
Yes	5682 (15.05)	0.60 (0.55, 0.64)	<0.0001	0.67 (0.62, 0.72)	<0.0001	0.71 (0.66, 0.77)	<0.0001
No	2750 (24.49)	Reference		Reference		Reference	
Weight management‡							
Yes	2627 (11.32)	0.55 (0.50, 0.61)	<0.0001	0.65 (0.58, 0.73)	<0.0001	0.69 (0.62, 0.78)	<0.0001
No	945 (19.43)	Reference		Reference		Reference	
Smoking cessation§							
Yes	859 (13.99)	0.58 (0.49, 0.70)	<0.0001	0.65 (0.53, 0.81)	<0.0001	0.66 (0.50, 0.88)	0.004
No	192 (22.15)	Reference		Reference		Reference	
At 3 y							
CR referral							
Yes	4330 (21.80)	0.42 (0.39, 0.46)	<0.0001	0.56 (0.53, 0.60)	<0.0001	0.60 (0.57, 0.64)	<0.0001
No	11 527 (39.57)	Reference		Reference		Reference	
Activity recommendations							
Yes	11 095 (29.38)	0.62 (0.57, 0.67)	<0.0001	0.68 (0.63, 0.73)	<0.0001	0.72 (0.67, 0.77)	<0.0001
No	4762 (42.41)	Reference		Reference		Reference	
Weight management‡							
Yes	5524 (23.81)	0.60 (0.54, 0.65)	<0.0001	0.69 (0.63, 0.76)	<0.0001	0.73 (0.67, 0.80)	<0.0001
No	1709 (35.14)	Reference		Reference		Reference	
Smoking cessation§							
Yes	1787 (29.10)	0.68 (0.58, 0.79)	<0.0001	0.79 (0.66, 0.95)	0.01	0.69 (0.54, 0.88)	0.003
No	327 (37.72)	Reference		Reference		Reference	

ACE indicates angiotensin-converting enzyme; AMI, acute myocardial infarction; BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CR, cardiac rehabilitation; GWTC-CAD, Get With The Guidelines—Coronary Artery Disease; MI, myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; OR, odds ratio; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty; PVD, peripheral vascular disease; STEMI, ST-elevation myocardial infarction.

*Adjusted for patients sociodemographic and lifestyles information (age, calendar year, BMI, smoking status), patients' medical history (atrial fibrillation/atrial flutter, COPD or asthma, diabetes mellitus, hyperlipidemia, hypertension, PVD, CAD, prior MI, cerebrovascular accident/transient ischemic attack, implantable cardioverter defibrillator, heart failure, anemia, pacemaker—biventricular/resync/cardiac resynchronization therapy, dialysis [chronic], renal insufficiency, depression, prior PCI or CABG, valvular heart disease, systolic blood pressure at discharge, ejection fraction <40% or moderate or severe dysfunction), cardiac diagnosis (STEMI, NSTEMI, AMI unspecified, unstable angina, CAD), and hospital characteristics (geographic region, rural location, teaching status, number of beds, primary PTCA, cardiac surgery, heart transplants site).

†Further adjusted for patients' insurance status (Medicaid, Medicare, other, No insurance/Undetermined/Missing), medication use before hospital admission (ACE inhibitors, β -blocker, aspirin, lipid-lowering agents), medication use at hospital discharge (ACE inhibitors, β -blocker, aspirin, lipid-lowering agents), and the GWTC-CAD quality of care composite performance score.

‡Among patients with BMI >25 kg/m² only.

§Among smokers only.

the odds of mortality could be reduced by 40% for women, 25% for black, 38% for Hispanic, and 37% for Asian patients. Seven percent of the black versus white mortality gap could potentially be reduced by equitable CR referral.

The largest randomized trial of CR among patients with MI demonstrated significant benefits in the subsequent risk of nonfatal MI and other cardiovascular outcomes.^{4,36} Meta-

analyses suggested that CR participation can reduce all-cause mortality by 15% to 28% for patients with MI^{4,37–39} and 45% to 47% for patients with percutaneous coronary intervention.⁴⁰ The effect was estimated to be comparable to improvements associated with aspirin, β -blocker, angiotensin-converting enzyme inhibitor, statin, and anticoagulant therapy.^{5,41–43} However, the generalizability of these results was limited

Table 4. Associations of 1- or 3-Y Mortality and Risk Interventions by Sex and Race

	Adjusted OR (95% CI)	P Value	P for Interaction
1-y mortality			
CR referral			
Sex			
Female	0.58 (0.53, 0.63)	<0.0001	0.17
Male	0.54 (0.49, 0.59)	<0.0001	
Race			
White	0.55 (0.51, 0.59)	<0.0001	0.06
Black	0.73 (0.60, 0.89)	0.001	
Hispanic	0.49 (0.38, 0.63)	<0.0001	
Asian	0.47 (0.27, 0.80)	0.005	
Other	0.66 (0.46, 0.95)	0.02	
Activity recommendations			
Sex			
Female	0.78 (0.72, 0.86)	<0.0001	0.0009
Male	0.65 (0.59, 0.71)	<0.0001	
Race			
White	0.70 (0.65, 0.76)	<0.0001	0.52
Black	0.78 (0.60, 1.00)	0.05	
Hispanic	0.80 (0.62, 1.03)	0.08	
Asian	0.67 (0.43, 1.04)	0.07	
Other	0.85 (0.64, 1.12)	0.24	
Weight management*			
Sex			
Female	0.74 (0.65, 0.85)	<0.0001	0.10
Male	0.65 (0.57, 0.75)	<0.0001	
Race			
White	0.68 (0.61, 0.77)	<0.0001	0.78
Black	0.65 (0.46, 0.91)	0.01	
Hispanic	0.73 (0.49, 1.09)	0.11	
Asian	0.84 (0.39, 1.83)	0.66	
Other	0.93 (0.58, 1.48)	0.74	
Smoking cessation†			
Sex			
Female	0.87 (0.60, 1.26)	0.46	0.04
Male	0.57 (0.42, 0.78)	0.0004	
Race			
White	0.67 (0.50, 0.89)	0.006	0.77
Black	0.54 (0.24, 1.22)	0.13	
Hispanic	0.88 (0.38, 2.04)	0.76	
Asian	1.27 (0.46, 3.55)	0.64	
Other	0.62 (0.25, 1.51)	0.29	
3-y mortality			
CR referral			
Sex			
Female	0.61 (0.56, 0.66)	<0.0001	0.67
Male	0.60 (0.55, 0.64)	<0.0001	

Continued

Table 4. Continued

	Adjusted OR (95% CI)	P Value	P for Interaction
Race			
White	0.60 (0.56, 0.64)	<0.0001	0.06
Black	0.75 (0.63, 0.88)	0.0005	
Hispanic	0.62 (0.50, 0.79)	<0.0001	
Asian	0.63 (0.46, 0.85)	0.002	
Other	0.53 (0.42, 0.67)	<0.0001	
Activity recommendations			
Sex			
Female	0.74 (0.68, 0.81)	<0.0001	0.29
Male	0.70 (0.65, 0.77)	<0.0001	
Race			
White	0.71 (0.66, 0.77)	<0.0001	0.47
Black	0.80 (0.66, 0.98)	0.03	
Hispanic	0.69 (0.54, 0.88)	0.002	
Asian	0.73 (0.53, 1.00)	0.05	
Other	0.87 (0.67, 1.13)	0.29	
Weight management*			
Sex			
Female	0.73 (0.65, 0.82)	<0.0001	0.95
Male	0.74 (0.66, 0.82)	<0.0001	
Race			
White	0.72 (0.65, 0.79)	<0.0001	0.61
Black	0.73 (0.56, 0.95)	0.02	
Hispanic	0.86 (0.59, 1.24)	0.41	
Asian	0.73 (0.39, 1.37)	0.32	
Other	1.01 (0.62, 1.63)	0.98	
Smoking cessation[†]			
Sex			
Female	0.72 (0.52, 0.99)	0.04	0.87
Male	0.70 (0.52, 0.93)	0.01	
Race			
White	0.70 (0.54, 0.90)	0.005	0.88
Black	0.81 (0.39, 1.70)	0.58	
Hispanic	0.80 (0.36, 1.78)	0.58	
Asian	0.90 (0.53, 1.54)	0.71	
Other	0.55 (0.22, 1.33)	0.18	

Adjusted for patients' sociodemographic and lifestyles information (age, calendar year, BMI, smoking status), patients' medical history (atrial fibrillation/atrial flutter, COPD or asthma, diabetes mellitus, hyperlipidemia, hypertension, peripheral vascular disease [PVD], CAD, prior MI, cerebrovascular accident/transient ischemic attack, implantable cardioverter defibrillator, heart failure, anemia, pacemaker—biventricular/resync/cardiac resynchronization therapy, dialysis [chronic], renal insufficiency, depression, prior PCI or CABG, valvular heart disease, systolic blood pressure at discharge, ejection fraction <40% or moderate or severe dysfunction), cardiac diagnosis (STEMI, NSTEMI, AMI unspecified, unstable angina, CAD), hospital characteristics (geographic region, rural location, teaching status, number of beds, primary PTCA, cardiac surgery, heart transplants site), patients' insurance status (Medicaid, Medicare, other, No insurance/Undetermined/Missing), medication use before hospital admission (ACE inhibitors, β -blocker, aspirin, lipid-lowering agents), medication use at hospital discharge (ACE inhibitors, β -blocker, aspirin, lipid-lowering agents), and the GWTG-CAD quality of care composite performance score. ACE indicates angiotensin-converting enzyme; AMI, acute myocardial infarction; BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CR, cardiac rehabilitation; MI, myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; OR, odds ratio; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty; PVD, peripheral vascular disease; STEMI, ST-elevation myocardial infarction.

*Among patients with BMI >25 kg/m² only.

[†]Among smokers only.

because the majority of trial participants were highly selected low-risk white males, with few females, minorities, or elderly patients, and with short duration of follow-up.⁴ Observational

studies with long-term mortality were sparse and mainly focused on CR participation. Prior studies lack detailed clinical and treatment information, data on severity of medical conditions,

Table 5. Sex, Racial, and Regional Differences in CR Referral and Other Risk Interventions

	N Events (%)	Unadjusted OR (95% CI)	P Value	Adjusted OR (95% CI)*	P Value
CR referral					
Sex					
Female	8593 (37.10)	0.79 (0.76, 0.83)	<0.0001	0.88 (0.85, 0.92)	<0.0001
Male	11 267 (43.62)	Reference		Reference	
Race					
			0.04		0.008
Black	1012 (36.47)	0.87 (0.78, 0.97)	0.01	0.80 (0.66, 0.98)	0.02
Hispanic	752 (30.37)	1.00 (0.90, 1.10)	0.94	0.64 (0.47, 0.88)	0.005
Asian	265 (22.25)	1.06 (0.90, 1.24)	0.49	0.50 (0.28, 0.90)	0.02
Other	662 (33.47)	1.06 (0.87, 1.28)	0.56	0.88 (0.67, 1.14)	0.32
White	17 169 (42.32)	Reference		Reference	
Region					
			0.002		0.01
Midwest	7370 (53.48)	2.34 (1.45, 3.78)	0.0005	2.51 (1.38, 4.58)	0.002
South	6505 (37.31)	1.26 (0.79, 1.99)	0.33	1.29 (0.73, 2.30)	0.38
West	3246 (37.98)	1.29 (0.77, 2.14)	0.33	1.58 (0.80, 3.14)	0.19
Northeast	2739 (29.67)	Reference		Reference	
Activity recommendations					
Sex					
Female	17 404 (75.14)	0.91 (0.88, 0.95)	<0.0001	0.91 (0.86, 0.96)	0.001
Male	20 360 (78.82)	Reference		Reference	
Race					
			0.17		0.25
Black	2042 (73.59)	0.95 (0.88, 1.02)	0.17	0.77 (0.59, 1.02)	0.06
Hispanic	2023 (81.70)	1.04 (0.97, 1.12)	0.30	1.28 (0.92, 1.77)	0.14
Asian	861 (72.29)	1.13 (1.00, 1.27)	0.05	1.16 (0.61, 2.19)	0.64
Other	1519 (76.79)	1.07 (0.84, 1.37)	0.56	1.21 (0.87, 1.67)	0.25
White	31 319 (77.19)	Reference		Reference	
Region					
			0.12		0.96
Midwest	10 905 (79.13)	1.27 (0.82, 1.97)	0.28	1.02 (0.60, 1.73)	0.95
South	13 556 (77.76)	1.55 (1.04, 2.31)	0.03	0.97 (0.53, 1.78)	0.92
West	6509 (76.16)	1.10 (0.71, 1.70)	0.67	1.11 (0.62, 1.99)	0.72
Northeast	6794 (73.59)	Reference		Reference	
Weight management**					
Sex					
Female	9967 (81.42)	0.93 (0.89, 0.97)	0.0008	0.96 (0.91, 1.01)	0.11
Male	13 232 (83.63)	Reference		Reference	
Race					
			0.23		0.15
Black	1296 (79.95)	1.00 (0.93, 1.08)	0.97	1.03 (0.93, 1.14)	0.61
Hispanic	1291 (86.59)	1.11 (1.01, 1.21)	0.02	1.16 (1.02, 1.31)	0.02
Asian	335 (78.64)	1.08 (0.92, 1.26)	0.35	1.14 (0.94, 1.39)	0.17
Other	913 (82.55)	0.95 (0.85, 1.07)	0.42	0.99 (0.87, 1.13)	0.92
White	19 364 (82.68)	Reference		Reference	

Continued

Table 5. Continued

	N Events (%)	Unadjusted OR (95% CI)	P Value	Adjusted OR (95% CI)*	P Value
Region			0.24		0.30
Midwest	7053 (82.95)	1.10 (0.68, 1.79)	0.68	1.50 (0.74, 3.04)	0.25
South	8254 (81.93)	1.52 (0.98, 2.37)	0.06	1.70 (0.86, 3.39)	0.12
West	3576 (82.66)	1.28 (0.78, 2.09)	0.32	2.11 (0.99, 4.49)	0.05
Northeast	4316 (83.66)	Reference		Reference	
Smoking cessation [†]					
Sex					
Female	2632 (88.06)	1.03 (0.94, 1.14)	0.51	1.07 (0.93, 1.24)	0.33
Male	3508 (87.31)	Reference		Reference	
Race					
Black	437 (91.81)	1.12 (0.89, 1.41)	0.34	1.09 (0.74, 1.61)	0.67
Hispanic	314 (85.56)	0.96 (0.71, 1.29)	0.76	0.96 (0.61, 1.49)	0.84
Asian	90 (73.17)	0.66 (0.45, 0.99)	0.04	0.73 (0.47, 1.12)	0.15
Other	247 (83.45)	0.81 (0.62, 1.05)	0.10	0.89 (0.62, 1.27)	0.51
White	5052 (87.94)	Reference		Reference	
Region					
Midwest	1628 (87.15)	0.73 (0.44, 1.21)	0.21	0.56 (0.29, 1.08)	0.08
South	2450 (89.06)	1.08 (0.69, 1.70)	0.73	1.04 (0.55, 1.95)	0.90
West	906 (83.50)	0.68 (0.41, 1.11)	0.11	0.72 (0.38, 1.37)	0.32
Northeast	1156 (88.72)	Reference		Reference	

ACE indicates angiotensin-converting enzyme; AMI, acute myocardial infarction; BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CR, cardiac rehabilitation; GWTG-CAD, Get With The Guidelines—Coronary Artery Disease; MI, myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; OR, odds ratio; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty; PVD, peripheral vascular disease; STEMI, ST-elevation myocardial infarction.

*Among smokers only.

**Among patients with BMI >25 kg/m² only.

[†]Adjusted for patients sociodemographic and lifestyles information (age, calendar year, BMI, smoking status), patients' medical history (atrial fibrillation/atrial flutter, COPD or asthma, diabetes mellitus, hyperlipidemia, hypertension, peripheral vascular disease [PVD], CAD, prior MI, cerebrovascular accident/transient ischemic attack, implantable cardioverter defibrillator, heart failure, anemia, pacemaker—biventricular/resync/cardiac resynchronization therapy, dialysis [chronic], renal insufficiency, depression, prior PCI or CABG, valvular heart disease, systolic blood pressure at discharge, ejection fraction <40% or moderate or severe dysfunction), cardiac diagnosis (STEMI, NSTEMI, AMI unspecified, unstable angina, CAD), hospital characteristics (geographic region, rural location, teaching status, number of beds, primary PTCA, cardiac surgery, heart transplants site), patients' insurance status (Medicaid, Medicare, other, No insurance/Undetermined/Missing), medication use before hospital admission (ACE inhibitors, β -blocker, aspirin, lipid-lowering agents), medication use at hospital discharge (ACE inhibitors, β -blocker, aspirin, lipid-lowering agents), and the GWTG-CAD quality of care composite performance score.

and information about other quality of care/risk interventions that patients received, which serve as important factors for CR referral and participation.^{4,22,41,44} Most prior studies were based on claims databases that do not contain information on CR referral. It is unknown whether patients who did not participate in CR therapy did not receive a physician referral, or chose not to participate after referral receipt. Suaya et al used a landmark propensity score analysis as well as 2 instrumental variables derived from the Medicare beneficiary database to estimate the association between CR attendance and mortality. They provided key evidence for a strong inverse association between CR attendance and mortality.²² However, it was unclear how many non-CR attendance patients did not actually receive CR referral. Hammill et al restricted their analyses in

Medicare beneficiaries by examining among patients with at least 1 claim for early outpatient CR services. They reported a significant dose–response relationship between numbers of CR sessions attended and long-term mortality at 4 years.²⁷

Our study builds upon previous studies by looking at an upstream factor for CR participation: receipt of CR referral at hospital discharge. We assessed the association between inequality in CR referral on patients' long-term mortality, a question that has not been previously addressed and could potentially provide beneficial information to policy makers, health professionals, researchers, and patients. The GWTG-CAD database has detailed and rich information on CR referral, as well as other lifestyle intervention recommendations. By linking the GWTG-CAD with an outpatient database,

we were afforded a unique opportunity to examine the association between CR referral with long-term cardiovascular mortality above and beyond quality of care received.^{41,45} The American College of Cardiology and the American Heart Association have issued a Class I recommendation that certain cardiovascular patients (acute MI, percutaneous coronary intervention, coronary artery bypass grafting, heart valve repair/replacement, heart transplant, coronary artery disease, and angina) should be referred to a CR program before hospital discharge. CR participation rates are alarmingly low, particularly with respect to women and minorities.²⁰ Aragam et al reported a minimal influence of patient demographic factors on rates of CR referral among patients with percutaneous coronary intervention.⁸ In our study, among eligible cardiovascular patients, we found that females were 15% less likely to receive CR referral than males. Compared with white patients, minorities, particularly Asian patients, were 54% less likely to receive CR referral. Despite great improvements in the institution of other risk interventions as part of quality measures, CR referral remained alarmingly low from 2003 to 2009. In our study, we showed that CR referral at hospital discharge was significantly associated with reduced mortality for women and minorities, a group of patients that have traditionally been understudied in the literature. Prior studies suggested that the most significant predictor and easily overcome barrier is the lack of CR referral at hospital discharge.⁸ We expanded upon prior study by assessing the degree to which the mortality disparity could be reduced by reducing inequality in CR referral at hospital discharge, using a causal mediation analysis approach. In our study, we found that reducing inequality in CR referral between black and white patients could narrow the mortality gap by 7% in the long term. To the best of our knowledge, no prior study has examined whether and to what extent CR could help reduce cardiovascular health disparities. We also provided evidence that CR referral benefits were independent of other guideline-based therapies, treatments, and quality of care measures.

The major limitation of our study is that we did not have linkage with Medicare Part B files and do not have information about actual CR enrollment and adherence. Future studies with both CR referral and participation data are needed. Our results were limited because the data were available only up to the year 2009. Beatty et al reported an \approx 7% improvement in CR referral from 2007 to 2012 based on the ACTION registry-GWTG data.⁴⁶ Future studies using more recent data on CR referral and any association with mortality are needed. Although our sample consisted of a large number of medical centers located all over the United States, participation in GWTG was purely voluntary, and thus these findings may not be reflective of centers that are not included in this quality initiative. Data were collected by medical chart review and

depend upon the accuracy and completeness of documentation. Counseling regarding lifestyle interventions might have been provided but not recorded in the medical record. The improvements in performance and quality measures over time might have been influenced by factors other than GWTG-CAD participation such as secular trends. Because CR rehabilitation referral, physical activity recommendation, weight management, and smoking cessation counseling are part of the GWTG-quality performance and quality of care measures, CR referral and physical activity recommendations may have some overlap. In practice, physical therapy is also used for CR-eligible patients who have difficulty accessing CR programs, are disabled, with multiple comorbidities, frail, or have limited cognitive function. Since we do not have data on actual levels of activity, this is not possible to explore further. However, our study indicated that despite the improvements in physical activity recommendations at GWTG database, the CR referral rate remained low from 2003 to 2009. Lastly, there are many reasons a clinician takes into consideration when giving a CR referral. A patient could be too old/sick to benefit from CR (eg, frailty, multiple comorbidities, impaired cognition), or too healthy and may not need CR, or may receive CR referral from an outpatient setting, or may have no access to CR programs.^{21,47,48} Our findings may be impacted by residual measured and unmeasured confounding, particularly by these important patient-centered factors related to CR referral. Future research incorporating these patient factors in the GWTG and other related registry databases is needed. From our sensitivity analyses, we believe any residual confounding from these factors was unlikely to be strong. Information on race was collected through patients' self-report and thus subject to misclassification. However, the misclassification was highly likely to be nondifferential and attenuate the effect estimates toward the null. We believe our study represents a best scenario because participating hospitals are part of the GWTG quality of care improvement program, which aims to improve quality of care.

Our study has several strengths. To the best of our knowledge, there are no other data sources at the national level that follow the continuum of CR from referral at hospital discharge to long-term outcomes, so linking GWTG data to Medicare data provides a unique opportunity. Second, the analysis of other lifestyle interventions such as physical activity, weight, and smoking cessation within the same study provides an important context for understanding the magnitude of effect of CR referral. Third, the quantification of the inequality in CR referral on subsequent disparities in mortality reveals an important opportunity to save lives by providing equitable care. As far as we are aware, our study provided the first evidence that inequality in receiving CR referral at hospital discharge was associated with patients' long-term survival. This information could provide insights on

ways to reduce sex and race disparities in cardiovascular health. Our study included patients who were underrepresented in previous studies, including females, black, Hispanic, and Asian patients, and those with more comorbidities. We provided novel insights into the proportion of health disparity that could potentially be reduced through equitable CR referral. Our mediation analysis approach enabled us to address these critical knowledge gaps. Detailed clinical information on ejection fraction, body mass index, smoking, medical treatment, insurance status, and quality of care measures in this unique database also enabled us to control potential confounding more adequately. Additional strengths of our study are the availability of detailed demographic and clinical information before CR referral, and complete ascertainment of long-term mortality. We used rigorous statistical analytical methods to account for clustering within hospitals and also examined the robustness of our results to unmeasured and residual confounding. With additional adjustment for quality of care received during hospitalization, our results remained the same and showed that the association between CR referral and lower mortality was independent of quality of care received. Our sensitivity analysis showed that this observed association is highly unlikely to be completely caused by other unmeasured factors. Other strengths of our study include long-term follow-up and a large sample size with diverse patients and hospital characteristics.

In conclusion, receipt of CR referral at hospital discharge was associated with lower 1- and 3-year mortality. Substantial sex and racial gaps existed for CR referral, especially for females, black, Hispanic, and Asian patients. Eliminating the disparity in CR referral by adopting a policy of providing referrals to all cardiovascular patients at hospital discharge could potentially reduce the racial disparity in long-term mortality by 7%. CR referral rates urgently need improvement, and national targeted CR quality improvement interventions should be supported.

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SUPPLEMENTAL MATERIAL

Table S1. Baseline characteristics of patients and hospitals included and excluded from the analytic sample.

Variable	Overall N=125,134	Included N=48,993	Excluded N=76,141	P-value	Standardized Difference, %
Demographics					
Age, years*	77 (71 - 83)	77 (71 - 83)	78 (71 - 84)	<.0001	10.9
Sex				0.04	1.2
Female	59,606 (47.6)	23,163 (47.3)	36,443 (47.9)		
Male	65,528 (52.4)	25,830 (52.7)	39,698 (52.1)		
Race				<.0001	
White	95,846 (81.9)	40,573 (82.8)	55,273 (81.2)		4.1
Black	6,699 (5.7)	2,775 (5.7)	3,924 (5.8)		0.4
Hispanic	5,658 (4.8)	2,476 (5.1)	3,182 (4.7)		1.8
Asian	3,806 (3.3)	1,191 (2.4)	2,615 (3.8)		8.1
Other	5,019 (4.3)	1,978 (4.0)	3,041 (4.5)		2.1
Missing, %	8,106 (6.5)	0 (0.0)	8,106 (10.6)		
Cardiac Diagnosis					
Heart failure with CAD	3,909 (3.1)	0 (0.0)	3,909 (5.1)	<.0001	-
Confirmed AMI - non-STEMI	39,010 (31.2)	13,919 (28.4)	25,091 (33.0)		9.9
Confirmed AMI - STEMI	11,584 (9.3)	4,590 (9.4)	6,994 (9.2)		0.6
Confirmed AMI - unspecified	50,251 (40.2)	22,524 (46.0)	27,727 (36.4)		19.5
Other	7,240 (5.8)	0 (0.0)	7,240 (9.5)		-
Peripheral vascular disease	47 (0.0)	0 (0.0)	47 (0.1)		-
Cerebral vascular disease	41 (0.0)	0 (0.0)	41 (0.1)		-
Unstable angina	4,498 (3.6)	2,756 (5.6)	1,742 (2.3)		17.2
Coronary artery disease	8,554 (6.8)	5,204 (10.6)	3,350 (4.4)		23.8
Year					
2009	9,798 (7.8)	3,084 (6.3)	6,714 (8.8)	<.0001	18.5
2008	20,031 (16.0)	6,680 (13.6)	13,351 (17.5)		
2007	19,512 (15.6)	7,270 (14.8)	12,242 (16.1)		
2006	19,131 (15.3)	7,105 (14.5)	12,026 (15.8)		
2005	21,566 (17.2)	9,500 (19.4)	12,066 (15.8)		
2004	18,855 (15.1)	8,076 (16.5)	10,779 (14.2)		
2003	16,241 (13.0)	7,278 (14.9)	8,963 (11.8)		
Medical History					
Atrial fib/atrial flutter	12,096 (13.0)	5,482 (11.7)	6,614 (14.3)	<.0001	7.8

Variable	Overall	Included	Excluded	P-value	Standardized Difference, %
	N=125,134	N=48,993	N=76,141		
COPD or asthma	16,576 (17.8)	7,967 (17.0)	8,609 (18.6)	<.0001	4.3
Diabetes	32,261 (34.7)	15,743 (33.6)	16,518 (35.8)	<.0001	4.6
Hyperlipidemia	44,080 (47.4)	23,065 (49.2)	21,015 (45.5)	<.0001	7.4
Hypertension	68,507 (73.6)	34,850 (74.4)	33,657 (72.9)	<.0001	3.4
Peripheral vascular disease (PVD)	11,297 (12.1)	5,460 (11.6)	5,837 (12.6)	<.0001	3.0
CAD	16,453 (17.7)	8,459 (18.0)	7,994 (17.3)	0.003	1.9
Prior MI	21,517 (23.1)	9,891 (21.1)	11,626 (25.2)	<.0001	9.7
Cerebrovascular accident/transient ischemic attack	11,005 (11.8)	5,255 (11.2)	5,750 (12.4)	<.0001	3.8
Implantable cardioverter defibrillator	538 (0.6)	261 (0.6)	277 (0.6)	0.38	0.6
Heart failure	20,071 (21.6)	8,443 (18.0)	11,628 (25.2)	<.0001	17.5
Anemia	2,875 (3.1)	1,394 (3.0)	1,481 (3.2)	0.04	1.3
Pacemaker - Biventricular/Resync/ cardiac resynchronization therapy	1,476 (1.6)	739 (1.6)	737 (1.6)	0.81	0.2
Dialysis (Chronic)	2,178 (2.3)	911 (1.9)	1,267 (2.7)	<.0001	5.3
Renal insufficiency	12,234 (13.1)	5,411 (11.5)	6,823 (14.8)	<.0001	9.6
Depression	2,258 (2.4)	1,241 (2.6)	1,017 (2.2)	<.0001	2.9
Prior PCI or CABG	3,805 (4.1)	2,186 (4.7)	1,619 (3.5)	<.0001	5.9
Valvular heart disease	518 (0.6)	277 (0.6)	241 (0.5)	0.15	0.9
Med history panel missing, %	32,077 (25.6)	2,121 (4.3)	29,956 (39.3)	<.0001	93.6
Smoking	17,037 (14.0)	7,007 (14.6)	10,030 (13.6)	<.0001	2.7
Missing, %	3,592 (2.9)	957 (2.0)	2,635 (3.5)		
Measures					
Systolic blood pressure, mmHg*	124 (110 - 139)	123 (110 - 138)	124 (110 - 140)	0.0005	3.5
Missing, %	45,025 (36.0)	4,959 (10.1)	40,066 (52.6)		
BMI*	26.6 (23.4 - 30.3)	26.6 (23.5 - 30.4)	26.5 (23.2 - 30.2)	<.0001	3.5
Missing, %	38,423 (30.7)	4,898 (10.0)	33,525 (44.0)		
Ejection fraction*	50 (35 - 59)	50 (38 - 60)	47 (35 - 58)	<.0001	11.2
Missing, %	36,108 (28.9)	12,250 (25.0)	23,858 (31.3)		
Ejection fraction <40% or moderate or severe dysfunction	29,585 (29.2)	10,973 (25.9)	18,612 (31.5)	<.0001	12.2
Missing, %	23,683 (18.9)	6,689 (13.7)	16,994 (22.3)		
In-Hospital Procedures					
No procedure	18,190 (21.9)	6,402 (15.1)	11,788 (29.0)	<.0001	34.2
Cardiac cath/coronary angiography	49,363 (59.4)	28,025 (66.0)	21,338 (52.6)	<.0001	27.6
Cardioversion	317 (0.4)	156 (0.4)	161 (0.4)	0.49	0.5
CABG or cardiac valve surgery	9,291 (11.9)	5,467 (12.9)	3,824 (10.7)	<.0001	9.3
PCI or PCI with stent	37,589 (45.3)	22,056 (52.0)	15,533 (38.3)	<.0001	27.8
Cardiac resynchronization therapy -P	160 (0.2)	88 (0.2)	72 (0.2)	0.84	0.5

Variable	Overall N=125,134	Included N=48,993	Excluded N=76,141	P-value	Standardized Difference, %
or CRT-D					
Implantable cardioverter defibrillator only	275 (0.3)	162 (0.4)	113 (0.3)	0.009	1.8
Dialysis or ultrafiltration, or unspecified	326 (0.4)	135 (0.3)	191 (0.5)	<.0001	3.1
Mechanical ventilation	2,388 (2.9)	1,093 (2.6)	1,295 (3.2)	<.0001	3.7
Right cardiac catheterization	1,022 (1.2)	671 (1.6)	351 (0.9)	<.0001	6.5
Procedure panel missing, %	42,098 (33.6)	6,545 (13.4)	35,553 (46.7)	<.0001	78.1
Hospital Characteristics					
Number of beds*	331 (209 - 504)	342 (226 - 527)	327 (202 - 472)	<.0001	19.2
Missing, %	95 (0.1)	0 (0.0)	95 (0.1)		
Region				<.0001	
West	29,090 (23.2)	8,547 (17.4)	20,543 (27.0)		23.1
South	40,506 (32.4)	17,433 (35.6)	23,073 (30.3)		11.3
Midwest	30,813 (24.6)	13,781 (28.1)	17,032 (22.4)		13.3
Northeast	24,725 (19.8)	9,232 (18.8)	15,493 (20.3)		3.8
Academic hospital	67,783 (54.2)	28,873 (59.0)	38,910 (51.2)	<.0001	15.8
Missing, %	160 (0.1)	47 (0.1)	113 (0.1)		
Rural location	15,259 (12.4)	6,020 (12.5)	9,239 (12.3)	0.35	0.5
Missing, %	1,780 (1.4)	753 (1.5)	1,027 (1.3)		
Primary PTCA performed for AMI	107,293 (87.4)	44,180 (91.3)	63,113 (84.9)	<.0001	20.1
Missing, %	2,412 (1.9)	629 (1.3)	1,783 (2.3)		
Cardiac surgery performed on-site	94,128 (76.9)	39,751 (82.7)	54,377 (73.2)	<.0001	23.1
Missing, %	2,724 (2.2)	914 (1.9)	1,810 (2.4)		
Heart transplants performed at site	13,906 (11.5)	5,541 (11.6)	8,365 (11.4)	0.31	0.6
Missing, %	3,715 (3.0)	1,084 (2.2)	2,631 (3.5)		

*Continuous variables presented as median (IQR).

BMI- body mass index; COPD- chronic obstructive pulmonary disease; PVD- peripheral vascular disease; CAD- coronary artery disease; MI- myocardial infarction; PCI- percutaneous coronary intervention; CABG- coronary artery bypass grafting; STEMI- ST-elevation myocardial infarction; NSTEMI- Non-ST-elevation myocardial infarction; AMI- acute myocardial infarction; PTCA- percutaneous transluminal coronary angioplasty

Table S2. The associations between sex, race, and geographic region with 1-year and 3-year all-cause mortality.

		Deaths	Unadjusted Analysis		Adjusted Analysis	
		N (%)	OR (95% CI)	P value	OR (95% CI)	P value
At 1 Year	Overall	8,432 (17.21)				
Sex						
	Female	4,344 (18.75)	1.14 (1.09, 1.20)	<.0001	0.97 (0.92, 1.03)	0.33
	Male	4,088 (15.83)	Reference		Reference	
Race				0.001		0.004
	Black	558 (20.11)	1.24 (1.12, 1.37)	<.0001	1.31 (1.16, 1.47)	<.0001
	Hispanic	378 (15.27)	0.85 (0.75, 0.96)	0.008	0.92 (0.81, 1.05)	0.21
	Asian	248 (20.82)	0.97 (0.80, 1.16)	0.72	0.91 (0.76, 1.09)	0.29
	Other	359 (18.15)	0.98 (0.83, 1.16)	0.80	0.99 (0.86, 1.14)	0.90
	White	6,889 (16.98)	Reference		Reference	
Region				0.004		0.46
	Midwest	2,246 (16.30)	0.65 (0.52, 0.82)	0.0003	0.93 (0.81, 1.06)	0.25
	South	2,917 (16.73)	0.69 (0.56, 0.84)	0.0002	0.91 (0.80, 1.03)	0.13
	West	1,422 (16.64)	0.67 (0.53, 0.86)	0.001	0.91 (0.79, 1.05)	0.17
	Northeast	1,847 (20.01)	Reference		Reference	
At 3 Years	Overall	15,857 (32.37)				
Sex						
	Female	8,150 (35.19)	1.19 (1.14, 1.23)	<.0001	0.98 (0.94, 1.03)	0.41
	Male	7,707 (29.84)	Reference		Reference	
Race				0.0001		0.0001
	Black	1,056 (38.05)	1.31 (1.19, 1.44)	<.0001	1.36 (1.23, 1.50)	<.0001
	Hispanic	730 (29.48)	0.91 (0.85, 0.99)	0.02	0.96 (0.89, 1.04)	0.30
	Asian	456 (38.29)	0.95 (0.84, 1.08)	0.45	0.91 (0.79, 1.06)	0.21
	Other	656 (33.16)	0.95 (0.80, 1.13)	0.55	0.97 (0.84, 1.13)	0.73
	White	12,959 (31.94)	Reference		Reference	
Region				0.008		0.20
	Midwest	4,333 (31.44)	0.70 (0.55, 0.88)	0.002	0.99 (0.87, 1.13)	0.88
	South	5,535 (31.75)	0.72 (0.58, 0.89)	0.002	0.94 (0.84, 1.06)	0.32

West	2,646 (30.96)	0.65 (0.51, 0.84)	0.0007	0.87 (0.75, 1.00)	0.05
Northeast	3,343 (36.21)	Reference		Reference	

Adjusted for patients sociodemographic and lifestyles information (age, calendar year, BMI, smoking status), patients' medical history (atrial fibrillation/atrial flutter, COPD or asthma, diabetes, hyperlipidemia, hypertension, peripheral vascular disease (PVD), CAD, prior MI, cerebrovascular accident/transient ischemic attack, implantable cardioverter defibrillator, heart failure, anemia, pacemaker - biventricular/resync/ cardiac resynchronization therapy, dialysis (chronic), renal insufficiency, depression, prior PCI or CABG, valvular heart disease, systolic blood pressure at discharge, ejection fraction <40% or moderate or severe dysfunction), cardiac diagnosis (STEMI, NSTEMI, AMI unspecified, unstable angina, CAD), and hospital characteristics (geographic region, rural location, teaching status, number of beds, Primary PTCA, cardiac surgery, heart transplants site), patients' insurance status (Medicaid, Medicare, other, No insurance/Undetermined/Missing), medication use prior to hospital admission (ACE inhibitors, beta-blocker, aspirin, lipid-lowering agents), medication use at hospital discharge (ACE inhibitors, beta-blocker, aspirin, lipid-lowering agents), and the GWTG-CAD quality of care composite performance score.

BMI- body mass index; COPD- chronic obstructive pulmonary disease; PVD- peripheral vascular disease; CAD- coronary artery disease; MI- myocardial infarction; PCI- percutaneous coronary intervention; CABG- coronary artery bypass grafting; STEMI- ST-elevation myocardial infarction; NSTEMI- Non-ST-elevation myocardial infarction; AMI- acute myocardial infarction; PTCA- percutaneous transluminal coronary angioplasty

Table S3. Mediation analysis by cardiac rehabilitation referral.

Exposures	Cardiac Rehabilitation Referral	Natural Direct Effect		Natural Indirect Effect		Total Effect	
		OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
1 Year Mortality							
Sex							
Female vs Male	Yes	0.93 (0.87, 0.99)	0.01	1.01 (1.01, 1.02)	<.0001	0.94 (0.89, 1.00)	0.05
	No	Reference		Reference		Reference	
Race							
Black vs White	Yes	1.20 (1.07, 1.34)	0.001	1.01 (1.00, 1.03)	0.0096	1.22 (1.09, 1.37)	0.0006
	No	Reference		Reference		Reference	
Hispanic vs White	Yes	0.81 (0.71, 0.93)	0.002	1.06 (1.04, 1.09)	<.0001	0.86 (0.75, 0.99)	0.03
	No	Reference		Reference		Reference	
Asian vs White	Yes	0.76 (0.62, 0.95)	0.01	1.10 (1.04, 1.17)	0.0019	0.84 (0.69, 1.02)	0.08
	No	Reference		Reference		Reference	
Other vs White	Yes	0.97 (0.83, 1.12)	0.63	1.01 (1.00, 1.03)	0.0749	0.98 (0.85, 1.13)	0.76
	No	Reference		Reference		Reference	
3 Year Mortality							
Sex							
Women vs Men	Yes	0.94 (0.89, 0.98)	0.003	1.01 (1.01, 1.02)	<.0001	0.95 (0.91, 0.99)	0.02
	No	Reference		Reference		Reference	
Race							
Black vs White	Yes	1.25 (1.13, 1.37)	<.0001	1.01 (1.00, 1.02)	0.0037	1.26 (1.14, 1.40)	<.0001
	No	Reference		Reference		Reference	
Hispanic vs White	Yes	0.84 (0.76, 0.93)	0.0006	1.04 (1.02, 1.07)	0.0002	0.88 (0.79, 0.98)	0.01
	No	Reference		Reference		Reference	
Asian vs White	Yes	0.83 (0.69, 1.00)	0.05	1.06 (1.02, 1.11)	0.0024	0.89 (0.75, 1.06)	0.18
	No	Reference		Reference		Reference	
Other vs White	Yes	0.94 (0.82, 1.09)	0.41	1.02 (1.00, 1.04)	0.0093	0.96 (0.83, 1.11)	0.58
	No	Reference		Reference		Reference	

Adjusted for patients sociodemographic and lifestyles information (age, calendar year, BMI, smoking status), patients' medical history (atrial fibrillation/atrial flutter, COPD or asthma, diabetes, hyperlipidemia, hypertension, peripheral vascular disease (PVD), CAD, prior MI, cerebrovascular accident/transient ischemic attack, implantable cardioverter defibrillator, heart failure, anemia, pacemaker - biventricular/resync/ cardiac resynchronization therapy, dialysis (chronic), renal insufficiency, depression, prior PCI or CABG, valvular heart disease, systolic blood pressure at discharge, ejection fraction <40% or moderate or severe dysfunction), cardiac diagnosis (STEMI, NSTEMI, AMI unspecified, unstable angina, CAD), and hospital characteristics (geographic region, rural location, teaching status, number of beds, Primary PTCA, cardiac surgery, heart transplants site), patients' insurance status (Medicaid, Medicare, other, No insurance/Undetermined/Missing), medication use prior to hospital admission (ACE inhibitors, beta-blocker, aspirin, lipid-lowering agents), medication use at hospital discharge (ACE inhibitors, beta-blocker, aspirin, lipid-lowering agents), and the GWTG-CAD quality of care composite performance score.