




ORIGINAL RESEARCH

Contemporary Reevaluation of Race and Ethnicity With Outcomes in Heart Failure

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BACKGROUND: Variation in outcomes by race/ethnicity in adults with heart failure (HF) has been previously observed. Identifying factors contributing to these variations could help target interventions. We evaluated the association of race/ethnicity with HF outcomes and potentially contributing factors within a contemporary HF cohort.

METHODS AND RESULTS: We identified members of Kaiser Permanente Northern California, a large integrated healthcare delivery system, who were diagnosed with HF between 2012 and 2016 and had at least 1 year of prior continuous membership and left ventricular ejection fraction data. We used Cox regression with time-dependent covariates to evaluate the association of self-identified race/ethnicity with HF or all-cause hospitalization and all-cause death, with backward selection for potential explanatory variables. Among 34 621 patients with HF, compared with White patients, Black patients had a higher rate of HF hospitalization (adjusted hazard ratio [HR], 1.28; 95% CI, 1.18–1.38) but a lower rate of death (adjusted HR, 0.78; 95% CI, 0.72–0.85). In contrast, Asian/Pacific Islander patients had similar rates of HF hospitalization, but lower rates of all-cause hospitalization (adjusted HR, 0.89; 95% CI, 0.85–0.93) and death (adjusted HR, 0.75; 95% CI, 0.69–0.80). Hispanic patients also had a lower rate of death (adjusted HR, 0.85; 95% CI, 0.80–0.91). Sensitivity analyses showed that effect sizes for Black patients were larger among patients with reduced ejection fraction.

CONCLUSIONS: In a contemporary and diverse population with HF, Black patients experienced a higher rate of HF hospitalization and a lower rate of death compared with White patients. In contrast, selected outcomes for Asian/Pacific Islander and Hispanic patients were more favorable compared with White patients. The observed differences were not explained by measured potentially modifiable factors, including pharmacological treatment. Future research is needed to identify explanatory mechanisms underlying ongoing racial/ethnic variation to target potential interventions.

Key Words: health disparities ■ hospitalization ■ mortality ■ race and ethnicity

The public health burden of chronic heart failure (HF) is large and growing because of the aging of the population and improvements in prevention and treatment of atherosclerotic cardiovascular disease and its risk factors.^{1,2} Between 2011 and 2017, HF as the listed cause of death has increased 38% and age-adjusted mortality attributed to HF has increased by 21%.² Given the large and increasing burden of HF, additional interventions are needed to improve outcomes among patients with HF, especially in those with HF with preserved ejection fraction (HFpEF). A

better understanding of modifiable factors that may influence HF outcomes among at-risk patient subgroups could help inform such interventions.

Parallel significant demographic changes nationally further highlight the importance of evaluating whether racial/ethnic variation persists in HF outcomes.^{3–10} Earlier studies reported that compared with White patients, Asian, and Pacific Islander (PI) patients had a lower rate of HF hospitalization,⁵ whereas Black and Hispanic patients had higher rates.^{3,5,7–10} Other studies have reported similar rates of hospitalizations

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CLINICAL PERSPECTIVE

What Is New?

- In a large, diverse, and contemporary cohort of adult patients with heart failure, Black patients had a higher rate of heart failure hospitalization and a lower rate of all-cause death compared with White patients.
- In contrast, Asian/Pacific Islander and Hispanic patients had similar rates of heart failure hospitalization but lower rates of death.
- The variation in outcomes was not explained by potentially modifiable factors, including medication use, cardiovascular procedures, and area-based socioeconomic status.

What Are the Clinical Implications?

- Efforts are needed to delineate mechanisms that drive the observed racial/ethnic variation in different types of clinical outcomes.
- Interventions should address racial/ethnic variation while focusing on improving outcomes for all patients with heart failure.

Nonstandard Abbreviations and Acronyms

HFpEF	heart failure with preserved ejection fraction
HFrfEF	heart failure with reduced ejection fraction
KPNC	Kaiser Permanente Northern California
PI	Pacific Islander

between racial/ethnic groups.^{3,7,8,10} With regard to all-cause mortality, compared with White patients, Asian/PI, Black, and Hispanic patients had a lower rate in selected studies.^{3,7-10} In contrast, some studies have found no difference in all-cause mortality for White patients compared with Asian/PI or Hispanic patients.^{7,10} However, variation in populations, time period studied, and ability to control for confounders may have contributed to these conflicting findings, and it is unclear to what extent observed variation in outcomes is attributable to potentially modifiable factors. Furthermore, given HF hospitalization has often been used as a proxy for quality of care,¹¹⁻¹³ it is important to examine concordance between hospitalization rates and death by race/ethnicity.

To address these knowledge gaps, we evaluated outcomes in major racial/ethnic groups within a more contemporary, diverse community-based cohort of adults with HF who had equal access to care in a

large, integrated delivery system. We further examined potentially contributing factors, including cardiovascular and noncardiovascular health status, treatments received, area-based access to care measures, and area-based socioeconomic status (SES) measures.

METHODS

The data, analytic methods, and study materials will not be made available to other researchers for the purposes of reproducing the results or replicating the procedure because of human subject restrictions.

Source Population

The source population was from Kaiser Permanente Northern California (KPNC), an integrated healthcare delivery system currently caring for >4.5 million sociodemographically diverse members across 21 hospitals and >250 offices in northern California. KPNC includes members with coverage through employers, the individual market, Medicaid (Medi-Cal—California's Medicaid program), and Medicare Advantage. More than 35% to 65% of individuals in northern California counties receive care through KPNC, and its membership is highly representative of the local surrounding and statewide population.¹⁴ The primary data source was the KPNC electronic health record system, which contains comprehensive data on demographic characteristics, diagnoses, procedures, echocardiogram results, laboratory results, and medication dispensing and use. The KPNC institutional review board approved this study. Waiver of informed consent was granted because of the nature of the study.

We also used access to care measures from an area deprivation index,¹⁵ a rural-urban county classification scheme,¹⁶ and the Area Health Resource File.¹⁷ The Area Health Resource File is a resource with county-level data on access to care and healthcare utilization that is administered by the Health Resources and Service Administration.¹⁷

Study Sample

We first identified all adult members with diagnosed HF between 2012 and 2016 with follow-up data through 2017. HF was defined as having ≥ 1 hospitalization with a primary discharge code for HF and/or ≥ 3 outpatient visits with a diagnosis code for HF during the study period (2012–2016) (see Table S1 for *International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]*, and *International Classification of Diseases, Tenth Revision, Clinical Modification [ICD-10-CM]*, codes). We defined the index date as the date of the first qualifying diagnosis. This approach has been

previously shown to have a high positive predictive value compared against chart review^{18,19} using Framingham criteria.²⁰ We further categorized HF on the basis of left ventricular ejection fraction (EF) status from echocardiogram reports: preserved (HFpEF: $\geq 50\%$), midrange (HF with midrange EF: 41%–49%), and reduced (HF with reduced EF [HFrEF]: $<40\%$). If a patient had multiple echocardiogram reports, we used the one closest to the date of the index diagnosis. We excluded patients aged <21 years, who had <12 months of prior continuous health plan membership or drug benefit coverage before entry, who had no valid echocardiography data, and who had an organ transplant or who died on the index date (see Figure 1 for sample flow diagram).

Race/Ethnicity Measure

We categorized patients into the following racial/ethnic groups: non-Hispanic White, non-Hispanic Black, Asian/PI, and Hispanic patients. These designations were based on self-identified race and ethnicity. We conceptualized race/ethnicity as a social construct rather than a biological one because race/ethnicity are not meaningful biological categories.²¹

Outcomes

Outcomes included hospitalization for HF, which we defined as hospitalizations with a primary discharge diagnosis code for HF (Table S1), hospitalization for any cause, and all-cause death. Hospitalizations were

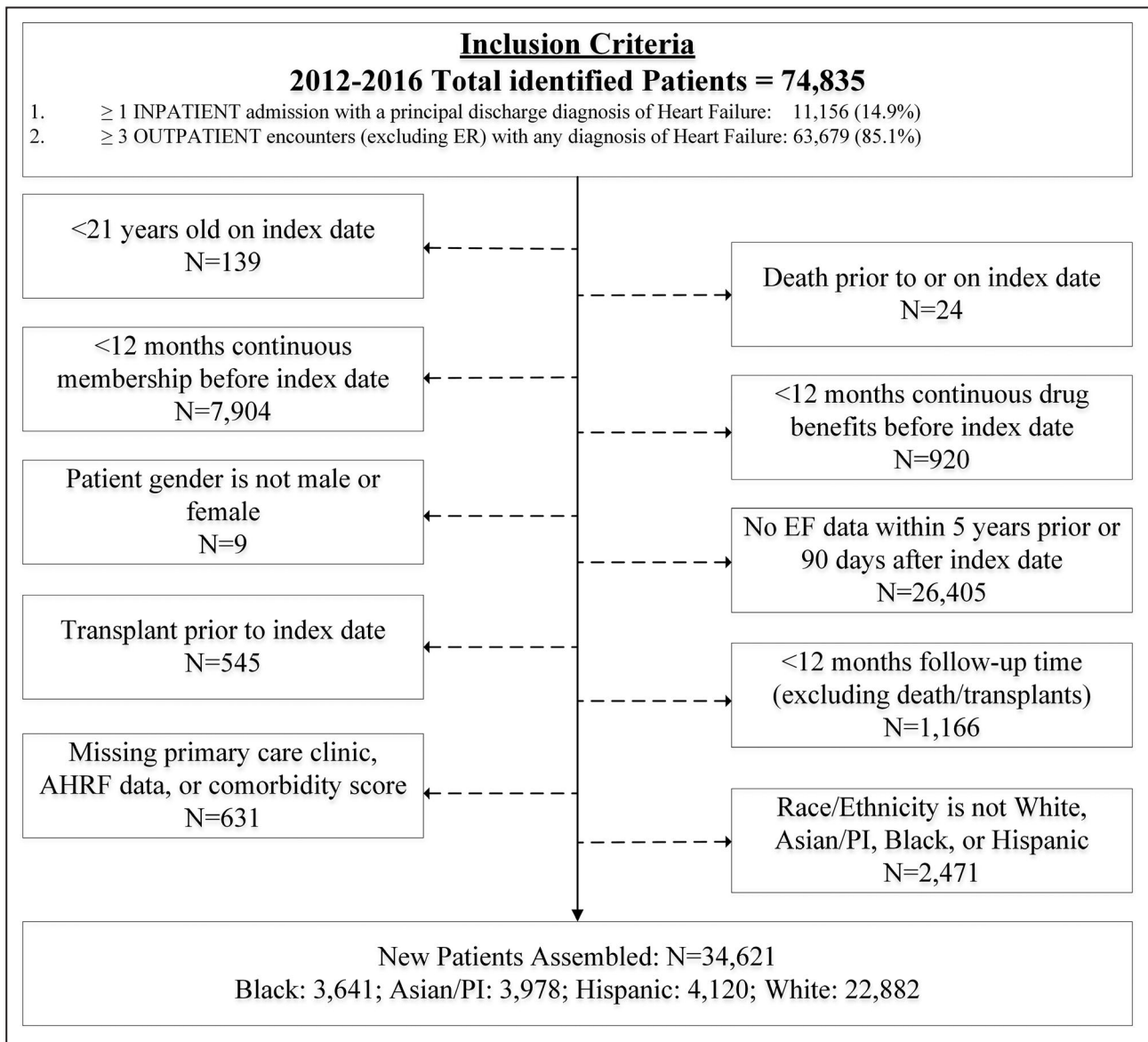


Figure 1. Heart failure cohort assembly.

AHRF indicates Area Health Resource File; EF, ejection fraction; ER, emergency room; and PI, Pacific Islander.

captured through the KPNC comprehensive electronic health record (which includes out-of-network admissions), and deaths were identified from the electronic health record (including proxy reporting), regional cancer registry, and California state death certificate information. We did not attempt to classify potential cause of death because of known substantial misclassification in listed cause(s) of death on death certificates.²²

Explanatory Factors

We categorized potential explanatory factors into 7 distinct domains (Table 1). The first domain was HF characteristics, including EF category (HFpEF, HF with midrange EF, or HFrEF) and presumed incident or prevalent HF. Patients were categorized as having presumed incident HF if they did not have a prior HF diagnosis in the 5 years before the index date; and as having prevalent HF if they did have a prior HF diagnosis in the 5 years before the index date. The second domain included other demographic characteristics, including sex and age (continuous and a quadratic term). The third domain was area-based access-to-care measures (ie, rural status and area health resource file regional medical supply measures). The fourth domain included time-dependent cardiovascular and noncardiovascular comorbidities that may be associated with the outcomes of death and/or hospitalization. The fifth domain was time-dependent cardiovascular procedures (ie, coronary revascularization, pacemaker, implantable cardioverter-defibrillator,

and cardiac resynchronization therapy). The sixth domain included area-based SES measures at the census block-group level (ie, area deprivation index, low area education, and low area income). The seventh and final domain included time-dependent receipt of relevant medications and a proxy for high medication adherence (ie, proportion of days covered >80%). We included time-dependent covariates because it is possible that differences in treatment (cardiovascular procedures and relevant medications) or the management of comorbidities over time could vary across racial/ethnic groups and explain differences in outcomes.

Statistical Analysis

Analyses were performed using SAS 9.4 (SAS Institute Inc, Cary, NC). Baseline characteristics were compared between racial/ethnic groups using standard descriptive statistics. For variables with missing data (ie, selected laboratory results, vital signs, and medication adherence), a “missing” category was included. Cox regression with time-dependent covariates was performed to evaluate the association between race/ethnicity and each outcome of interest, with backward selection of potential explanatory factors. We retained the race/ethnicity variable in all models despite statistical significance because it is the primary predictor variable. Standard errors (SEs) were estimated using a robust sandwich estimator, with the clusters defined as the primary treating facility for each patient. We analyzed 2 models: the

Table 1. Models and Domains of Potential Explanatory Factors

Model	Domain	Covariates
Model 1	Race/ethnicity	Race/ethnicity
	HF characteristics	Presumed incident vs prevalent HF, HF setting, index year
	Other demographic characteristics	Age, sex
	Access to care	PCP shortage area, county bed supply, county cardiologist supply, county PCP supply
	Time-dependent comorbidities	Comorbidity point score, acute myocardial infarction, unstable angina, stroke/transient ischemic attack, atrial fibrillation or flutter, ventricular tachycardia or fibrillation, mitral and/or aortic valvular disease, peripheral artery disease, smoking status, dyslipidemia, hypertension, diabetes mellitus and insulin use, hospitalized bleeding, hyperthyroidism, hypothyroidism, diagnosed dementia, diagnosed depression, chronic lung disease, chronic liver disease, systemic cancer, body mass index (kg/m ²), estimated glomerular filtration rate (mL/min per 1.73 m ²), urine dipstick protein excretion, anemia (hemoglobin <13 g/dL in men, <12 g/dL in women), systolic blood pressure (mm Hg), diastolic blood pressure (mm Hg), high-density lipoprotein (mg/dL), low-density lipoprotein (mg/dL), B-type natriuretic peptide (pg/mL)
	Time-dependent cardiovascular procedures	Coronary artery bypass surgery, percutaneous coronary intervention, pacemaker, ICD, CRT
	Area-based SES	ADI quintiles, low education, low income
Model 2: model 1+time updated measures of medication use and adherence	Time-dependent medication and adherence	ACE inhibitor/angiotensin II receptor blocker, aldosterone, β blocker, calcium channel blocker, diuretic, statins, other lipid-lowering drugs, anticoagulant, medication adherence (time independent)

ACE indicates angiotensin-converting enzyme; ADI, area deprivation index; CRT, cardiac resynchronization therapy; HF, heart failure; ICD, implantable cardioverter-defibrillator; PCP, primary care physician; and SES, socioeconomic status.

first model included all explanatory factors except medication and adherence, and the second model included all explanatory factors as well as medications and adherence. We separately evaluated the impact of adjusting for medications and adherence to evaluate an a priori hypothesis that medication use and adherence are modifiable factors that may explain differences between the racial/ethnic groups. The modeling approach is described below:

1. Model 1: racial/ethnic group+HF characteristics+other demographic characteristics+access-to-care measures+comorbidities+cardiovascular procedures+area-based SES measures.
2. Model 2: model 1+medication use and adherence.

Finally, we performed 5 sensitivity analyses. First, we conducted analyses stratified by presumed incident versus prevalent HF status. Second, we examined associations stratified by HF type (HFpEF, HF with midrange EF, or HFrEF). Third, we examined associations stratified by age at index date (<70, 70–80, and >80 years). Fourth, we examined associations stratified by sex (women and men). Fifth, we reevaluated the models using recurrent events using the Andersen-Gill model²³ instead of time-to-first event for HF and all-cause hospitalization.

RESULTS

Sample Characteristics

We identified 34 621 eligible adults with HF (59.3% HFpEF), of whom 3978 (11.5%) were Asian/PI individuals, 3641 (10.5%) were Black individuals, 4120 (11.9%) were Hispanic individuals, and 22 882 (66.1%) were White individuals (Table 2). White patients were older than Asian/PI, Black, and Hispanic patients, but there were no material differences across racial/ethnic groups in baseline comorbidities, pharmacological treatment, and receipt of cardiovascular procedures. However, White patients were less likely to live in the highest deprivation quintile (12.5%) compared with Black (22.8%) and Hispanic (19.5%) patients, but not Asian/PI patients (9.0%). Follow-up occurred until censoring or end of study follow-up on December 31, 2017, with mean (SD) follow-up of 1080 (638) days.

Rates of Hospitalization and Death by Race/Ethnicity

For the outcome of HF hospitalization, the crude annual incidence was significantly higher for Black patients (17.8 per 100 person-years; 95% CI, 17.0–18.6 per 100 person-years) compared with other racial/ethnic groups (Figure 2A and Table 3). In contrast, for the outcome of hospitalization for any cause, Asian/PI

patients experienced a lower crude annual incidence (53.0 per 100 person-years; 95% CI, 51.7–54.3 per 100 person-years) than the other racial/ethnic groups (Figure 2B and Table 3). Finally, a higher crude annual incidence of all-cause death was observed for White patients (12.4 per 100 person-years; 95% CI, 12.1–12.7 per 100 person-years) compared with Asian/PI, Black, and Hispanic patients (Figure 2C and Table 3).

Multivariable Association of Race/Ethnicity and Outcomes

In a fully adjusted model for HF hospitalization that accounted for any differences in patient characteristics, HF characteristics, access-to-care measures, therapies received, and area-based SES measures, Black patients had a higher adjusted rate than White patients (adjusted hazard ratio [HR], 1.28; 95% CI, 1.18–1.38) (Table 4, model 2; and Figure 3). Compared with White race, Hispanic ethnicity and Asian/PI race were not independently associated with HF hospitalization.

In the fully adjusted model for the outcome of hospitalization for any cause, compared with White patients, Asian/PI patients had a lower adjusted rate (HR, 0.89; 95% CI, 0.85–0.93) (Table 4, model 2; and Figure 3). However, Black and Hispanic patients did not have significantly different adjusted rates of hospitalization for any cause compared with White patients.

For all-cause death, compared with White patients, Asian/PI (HR, 0.75; 95% CI, 0.69–0.80), Black (HR, 0.78; 95% CI, 0.72–0.85), and Hispanic (HR, 0.85; 95% CI, 0.80–0.91) patients had lower adjusted rates of death in fully adjusted models (Table 4, model 2; and Figure 3).

For all 3 outcomes, results from models that did not include time-dependent medication and adherence (Table 4, model 1) were similar in magnitude and the same in terms of statistical significance compared with results of models that included these covariates (Table 4, model 2).

Sensitivity Analyses

Findings were generally similar across the sensitivity analyses examining patients with presumed incident HF; patients with HFpEF only; patients with HFrEF only; age-stratified models (<70, 70–80, and >80 years); and sex-stratified models (Table 5). For HF hospitalization, Black patients had a higher rate compared with White patients, although the differences were not statistically significant for all models, with no significant differences for Asian/PI and Hispanic patients in nearly all models. For all-cause hospitalization, Asian/PI patients had a significantly lower rate than White patients in 6 of the 9 models;

Table 2. Baseline Characteristics of Adults With HF by Race and Ethnicity

Characteristics	Overall (N=34 621)	Asian/Pacific Islander Patients (N=3978)	Black Patients (N=3641)	Hispanic Patients (N=4120)	White Patients (N=22 882)	P Value	Time Dependent
HF characteristics							
EF by categories						<0.001	No
Preserved EF (HFpEF)	20 527 (59.3)	2375 (59.7)	1988 (54.6)	2451 (59.5)	13 713 (59.9)		
Midrange EF (HFmrEF)	6069 (17.5)	653 (16.4)	635 (17.4)	722 (17.5)	4059 (17.7)		
Reduced EF (HFrEF)	8025 (23.2)	950 (23.9)	1018 (28.0)	947 (23.0)	5110 (22.3)		
Prevalent HF	12 285 (35.5)	1324 (33.3)	1534 (42.1)	1502 (36.5)	7925 (34.6)	<0.001	No
HF setting						<0.01	No
Outpatient	28 654 (82.8)	3254 (81.8)	2954 (81.1)	3397 (82.5)	19 049 (83.2)		
Inpatient	5967 (17.2)	724 (18.2)	687 (18.9)	723 (17.5)	3833 (16.8)		
Index year						<0.001	No
2012	13 206 (38.1)	1410 (35.4)	1546 (42.5)	1558 (37.8)	8692 (38.0)		
2013	5351 (15.5)	626 (15.7)	571 (15.7)	621 (15.1)	3533 (15.4)		
2014	4990 (14.4)	602 (15.1)	497 (13.7)	573 (13.9)	3318 (14.5)		
2015	5366 (15.5)	660 (16.6)	519 (14.3)	662 (16.1)	3525 (15.4)		
2016	5708 (16.5)	680 (17.1)	508 (14.0)	706 (17.1)	3814 (16.7)		
Other demographic characteristics							
Age, mean (SD), y	74.3 (12.3)	71.2 (13.7)	69.1 (13.3)	72.3 (12.9)	76.1 (11.3)	<0.001	Yes
Sex						<0.001	No
Women	15 906 (45.9)	1653 (41.6)	1913 (52.5)	1880 (45.6)	10 460 (45.7)		
Men	18 715 (54.1)	2325 (58.4)	1728 (47.5)	2240 (54.4)	12 422 (54.3)		
Access-to-care measure							
PCP shortage area	20 526 (59.3)	2109 (53.0)	1461 (40.1)	2596 (63.0)	14 360 (62.8)	<0.001	No
County bed supply, mean (SD)	24.0 (15.3)	26.4 (13.3)	23.0 (10.4)	23.8 (13.3)	23.8 (16.5)	<0.001	No
County cardiologist supply, mean (SD)	0.7 (0.3)	0.8 (0.4)	0.6 (0.3)	0.7 (0.3)	0.7 (0.3)	<0.001	No
County PCP supply, mean (SD)	9.1 (2.2)	9.8 (2.4)	9.1 (2.1)	8.9 (2.1)	9.0 (2.1)	<0.001	No
Comorbidities							
Comorbidity point score, mean (SD)	74.6 (39.0)	70.4 (38.2)	72.0 (40.1)	76.5 (40.2)	75.4 (38.7)	<0.001	Yes
Acute myocardial infarction	4211 (12.2)	591 (14.9)	406 (11.2)	537 (13.0)	2677 (11.7)	<0.001	Yes
Unstable angina	1296 (3.7)	151 (3.8)	124 (3.4)	179 (4.3)	842 (3.7)	0.13	Yes
Stroke/transient ischemic attack	2460 (7.1)	235 (5.9)	299 (8.2)	305 (7.4)	1621 (7.1)	<0.01	Yes
Atrial fibrillation or flutter	14 379 (41.5)	1430 (35.9)	877 (24.1)	1319 (32.0)	10 753 (47.0)	<0.001	Yes
Ventricular tachycardia or fibrillation	876 (2.5)	78 (2.0)	114 (3.1)	84 (2.0)	600 (2.6)	<0.01	Yes
Mitral and/or aortic valvular disease	7081 (20.5)	777 (19.5)	511 (14.0)	769 (18.7)	5024 (22.0)	<0.001	Yes
Peripheral artery disease	2851 (8.2)	316 (7.9)	310 (8.5)	365 (8.9)	1860 (8.1)	0.35	Yes
Smoking status						<0.001	Yes
Smoker	2027 (5.9)	191 (4.8)	349 (9.6)	176 (4.3)	1311 (5.7)		
Passive smoker	133 (0.4)	9 (0.2)	23 (0.6)	13 (0.3)	88 (0.4)		
Former smoker	16 987 (49.1)	1404 (35.3)	1658 (45.5)	1847 (44.8)	12 078 (52.8)		
Never smoker	15 474 (44.7)	2374 (59.7)	1611 (44.2)	2084 (50.6)	9405 (41.1)		
Dyslipidemia	29 569 (85.4)	3423 (86.0)	3062 (84.1)	3611 (87.6)	19 473 (85.1)	<0.001	Yes
Hypertension	29 821 (86.1)	3391 (85.2)	3349 (92.0)	3655 (88.7)	19 426 (84.9)	<0.001	Yes
Diabetes mellitus and insulin use						<0.001	Yes
No diabetes mellitus	18 974 (54.8)	1807 (45.4)	1716 (47.1)	1642 (39.9)	13 809 (60.3)		

(Continued)

Table 2. Continued

Characteristics	Overall (N=34 621)	Asian/Pacific Islander Patients (N=3978)	Black Patients (N=3641)	Hispanic Patients (N=4120)	White Patients (N=22 882)	P Value	Time Dependent
Diabetes mellitus without insulin use	10 040 (29.0)	1443 (36.3)	1210 (33.2)	1445 (35.1)	5942 (26.0)		
Diabetes mellitus with insulin use	5607 (16.2)	728 (18.3)	715 (19.6)	1033 (25.1)	3131 (13.7)		
Hospitalized bleeding	2127 (6.1)	267 (6.7)	206 (5.7)	280 (6.8)	1374 (6.0)	0.06	Yes
Hyperthyroidism	1680 (4.9)	171 (4.3)	165 (4.5)	219 (5.3)	1125 (4.9)	0.13	Yes
Hypothyroidism	7001 (20.2)	592 (14.9)	377 (10.4)	813 (19.7)	5219 (22.8)	<0.001	Yes
Diagnosed dementia	2481 (7.2)	235 (5.9)	241 (6.6)	310 (7.5)	1695 (7.4)	<0.01	Yes
Diagnosed depression	7251 (20.9)	432 (10.9)	649 (17.8)	918 (22.3)	5252 (23.0)	<0.001	Yes
Chronic lung disease	14 342 (41.4)	1381 (34.7)	1544 (42.4)	1634 (39.7)	9783 (42.8)	<0.001	Yes
Chronic liver disease	1549 (4.5)	199 (5.0)	185 (5.1)	256 (6.2)	909 (4.0)	<0.001	Yes
Systemic cancer	6824 (19.7)	587 (14.8)	729 (20.0)	613 (14.9)	4895 (21.4)	<0.001	Yes
Body mass index, kg/m ²						<0.001	Yes
>40.0	3107 (9.0)	147 (3.7)	601 (16.5)	429 (10.4)	1930 (8.4)		
30.0–39.9	11 346 (32.8)	849 (21.3)	1412 (38.8)	1526 (37.0)	7559 (33.0)		
25.0–29.9	10 771 (31.1)	1337 (33.6)	881 (24.2)	1304 (31.7)	7249 (31.7)		
18.5–24.9	8556 (24.7)	1488 (37.4)	657 (18.0)	790 (19.2)	5621 (24.6)		
<18.5	657 (1.9)	120 (3.0)	65 (1.8)	48 (1.2)	424 (1.9)		
Missing	184 (0.5)	37 (0.9)	25 (0.7)	23 (0.6)	99 (0.4)		
Estimated glomerular filtration rate, mL/min per 1.73 m ²						<0.001	Yes
90–150	5065 (14.6)	655 (16.5)	556 (15.3)	759 (18.4)	3095 (13.5)		
60–89	15 193 (43.9)	1458 (36.7)	1331 (36.6)	1567 (38.0)	10 837 (47.4)		
45–59	6417 (18.5)	655 (16.5)	699 (19.2)	655 (15.9)	4408 (19.3)		
30–44	4152 (12.0)	471 (11.8)	449 (12.3)	498 (12.1)	2734 (11.9)		
15–29	1710 (4.9)	271 (6.8)	230 (6.3)	245 (5.9)	964 (4.2)		
<15	371 (1.1)	94 (2.4)	79 (2.2)	63 (1.5)	135 (0.6)		
Dialysis	1122 (3.2)	256 (6.4)	226 (6.2)	269 (6.5)	371 (1.6)		
Missing	591 (1.7)	118 (3.0)	71 (2.0)	64 (1.6)	338 (1.5)		
Urine dipstick protein excretion						<0.001	Yes
None or trace	15 938 (46.0)	1408 (35.4)	1448 (39.8)	1779 (43.2)	11 303 (49.4)		
≥1	3764 (10.9)	414 (10.4)	478 (13.1)	471 (11.4)	2401 (10.5)		
≥2	2108 (6.1)	306 (7.7)	325 (8.9)	319 (7.7)	1158 (5.1)		
≥3	1328 (3.8)	316 (7.9)	215 (5.9)	283 (6.9)	514 (2.2)		
Missing	11 483 (33.2)	1534 (38.6)	1175 (32.3)	1268 (30.8)	7506 (32.8)		
Anemia (last hemoglobin <13 g/dL in men, <12 g/dL in women)	15 249 (44.0)	1872 (47.1)	1939 (53.3)	2064 (50.1)	9374 (41.0)	<0.001	Yes
Systolic blood pressure, mm Hg						<0.001	Yes
≥180	937 (2.7)	131 (3.3)	198 (5.4)	128 (3.1)	480 (2.1)		
160–179	2311 (6.7)	283 (7.1)	380 (10.4)	315 (7.6)	1333 (5.8)		
140–159	6348 (18.3)	741 (18.6)	816 (22.4)	784 (19.0)	4007 (17.5)		
130–139	7312 (21.1)	820 (20.6)	764 (21.0)	858 (20.8)	4870 (21.3)		
121–129	5712 (16.5)	630 (15.8)	581 (16.0)	722 (17.5)	3779 (16.5)		
<120	11 873 (34.3)	1345 (33.8)	881 (24.2)	1299 (31.5)	8348 (36.5)		
Missing	128 (0.4)	28 (0.7)	21 (0.6)	14 (0.3)	65 (0.3)		
Diastolic blood pressure, mm Hg						<0.001	Yes
≥110	387 (1.1)	54 (1.4)	104 (2.9)	34 (0.8)	195 (0.9)		

(Continued)

Table 2. Continued

Characteristics	Overall (N=34 621)	Asian/Pacific Islander Patients (N=3978)	Black Patients (N=3641)	Hispanic Patients (N=4120)	White Patients (N=22 882)	P Value	Time Dependent
100–109	672 (1.9)	71 (1.8)	150 (4.1)	59 (1.4)	392 (1.7)		
90–99	1920 (5.5)	228 (5.7)	345 (9.5)	197 (4.8)	1150 (5.0)		
85–89	2008 (5.8)	242 (6.1)	290 (8.0)	243 (5.9)	1233 (5.4)		
81–84	2424 (7.0)	266 (6.7)	302 (8.3)	253 (6.1)	1603 (7.0)		
≤80	27 082 (78.2)	3089 (77.7)	2429 (66.7)	3320 (80.6)	18 244 (79.7)		
Missing	128 (0.4)	28 (0.7)	21 (0.6)	14 (0.3)	65 (0.3)		
High-density lipoprotein, mg/dL						<0.001	Yes
≥60	6828 (19.7)	777 (19.5)	853 (23.4)	586 (14.2)	4612 (20.2)		
50–59	6823 (19.7)	814 (20.5)	731 (20.1)	765 (18.6)	4513 (19.7)		
40–49	9786 (28.3)	1179 (29.6)	1020 (28.0)	1240 (30.1)	6347 (27.7)		
35–39	4598 (13.3)	482 (12.1)	409 (11.2)	628 (15.2)	3079 (13.5)		
<35	4621 (13.3)	475 (11.9)	396 (10.9)	674 (16.4)	3076 (13.4)		
Missing	1965 (5.7)	251 (6.3)	232 (6.4)	227 (5.5)	1255 (5.5)		
Low-density lipoprotein, mg/dL						<0.001	Yes
≥200	251 (0.7)	37 (0.9)	34 (0.9)	37 (0.9)	143 (0.6)		
160–199	903 (2.6)	116 (2.9)	132 (3.6)	99 (2.4)	556 (2.4)		
130–159	2577 (7.4)	287 (7.2)	307 (8.4)	297 (7.2)	1686 (7.4)		
100–129	6277 (18.1)	651 (16.4)	702 (19.3)	679 (16.5)	4245 (18.6)		
70–99	12 797 (37.0)	1377 (34.6)	1415 (38.9)	1432 (34.8)	8573 (37.5)		
<70	10 383 (30.0)	1316 (33.1)	898 (24.7)	1414 (34.3)	6755 (29.5)		
Missing	1433 (4.1)	194 (4.9)	153 (4.2)	162 (3.9)	924 (4.0)		
B-type natriuretic peptide, pg/mL						<0.001	Yes
>500	4559 (13.2)	547 (13.8)	498 (13.7)	528 (12.8)	2986 (13.1)		
100–500	9121 (26.3)	909 (22.9)	812 (22.3)	1006 (24.4)	6394 (27.9)		
<100	3304 (9.5)	355 (8.9)	442 (12.1)	392 (9.5)	2115 (9.2)		
Missing	17 636 (50.9)	2167 (54.5)	1889 (51.9)	2194 (53.3)	11 386 (49.8)		
Cardiovascular procedures							
Coronary artery bypass surgery	1542 (4.5)	224 (5.6)	100 (2.7)	198 (4.8)	1020 (4.5)	<0.001	Yes
Percutaneous coronary intervention	4911 (14.2)	673 (16.9)	443 (12.2)	658 (16.0)	3137 (13.7)	<0.001	Yes
ICD	1126 (3.3)	96 (2.4)	115 (3.2)	132 (3.2)	783 (3.4)	<0.05	Yes
Pacemaker or CRT	2854 (8.2)	283 (7.1)	193 (5.3)	338 (8.2)	2040 (8.9)	<0.001	Yes
Area-based SES measures							
ADI quintiles						<0.001	No
Quintile 1	8787 (25.4)	1258 (31.6)	332 (9.1)	688 (16.7)	6509 (28.4)		
Quintile 2	8366 (24.2)	1270 (31.9)	773 (21.2)	994 (24.1)	5329 (23.3)		
Quintile 3	6279 (18.1)	584 (14.7)	734 (20.2)	794 (19.3)	4167 (18.2)		
Quintile 4	6008 (17.4)	498 (12.5)	947 (26.0)	818 (19.9)	3745 (16.4)		
Quintile 5	4845 (14.0)	357 (9.0)	829 (22.8)	802 (19.5)	2857 (12.5)		
Missing	336 (1.0)	11 (0.3)	26 (0.7)	24 (0.6)	275 (1.2)		
Low education	4493 (13.0)	467 (11.7)	983 (27.0)	1077 (26.1)	1966 (8.6)	<0.001	No
Low income	1695 (5.0)	136 (3.5)	384 (10.7)	276 (6.8)	899 (4.0)	<0.001	No
Medication and adherence							
ACE inhibitor/angiotensin II receptor blocker	22 320 (64.5)	2566 (64.5)	2359 (64.8)	2723 (66.1)	14 672 (64.1)	0.11	Yes
Aldosterone	2133 (6.2)	190 (4.8)	301 (8.3)	237 (5.8)	1405 (6.1)	<0.001	Yes

(Continued)

Table 2. Continued

Characteristics	Overall (N=34 621)	Asian/Pacific Islander Patients (N=3978)	Black Patients (N=3641)	Hispanic Patients (N=4120)	White Patients (N=22 882)	P Value	Time Dependent
β Blocker	25 208 (72.8)	2894 (72.8)	2566 (70.5)	2960 (71.8)	16 788 (73.4)	<0.01	Yes
Calcium channel blocker	11 436 (33.0)	1438 (36.1)	1495 (41.1)	1461 (35.5)	7042 (30.8)	<0.001	Yes
Diuretic	23 041 (66.6)	2379 (59.8)	2508 (68.9)	2700 (65.5)	15 454 (67.5)	<0.001	Yes
Statins	23 823 (68.8)	2811 (70.7)	2355 (64.7)	2911 (70.7)	15 746 (68.8)	<0.001	Yes
Other lipid-lowering drugs	1636 (4.7)	186 (4.7)	82 (2.3)	205 (5.0)	1163 (5.1)	<0.001	Yes
Anticoagulant	10 108 (29.2)	969 (24.4)	708 (19.4)	918 (22.3)	7513 (32.8)	<0.001	Yes
Medication adherence						<0.001	No
Adherent	22 596 (65.3)	2453 (61.7)	2003 (55.0)	2515 (61.0)	15 625 (68.3)		
Nonadherent	10 674 (30.8)	1314 (33.0)	1482 (40.7)	1447 (35.1)	6431 (28.1)		
Missing	1351 (3.9)	211 (5.3)	156 (4.3)	158 (3.8)	826 (3.6)		

All results present frequency and overall percentage in parentheses unless otherwise specified. ACE indicates angiotensin-converting enzyme; ADI, area deprivation index; CRT, cardiac resynchronization therapy; EF, ejection fraction; HF, heart failure; HFpEF, HF with preserved EF; HFmrEF, HF with midrange EF; HFrEF, HF with reduced EF; ICD, implantable cardioverter-defibrillator; PCP, primary care physician; and SES, socioeconomic status.

and there were no significant differences for Black or Hispanic patients. For all-cause death, Asian/PI, Black, and Hispanic patients had significantly lower rates compared with White patients in nearly all models. In addition, the magnitude of the difference for Black patients compared with White patients who had HFrEF was greater for rate of HF hospitalization (HR, 1.35; 95% CI, 1.18–1.55) and for death (HR, 0.70; 95% CI, 0.60–0.80) (Table 5, sensitivity analysis 3). In contrast, the respective differences were attenuated for Black patients compared with White patients who had HFpEF for HF hospitalization (HR, 1.19; 95% CI, 1.07–1.33) and for death (HR, 0.82; 95% CI, 0.74–0.91).

DISCUSSION

Within a large, ethnically diverse, contemporary HF cohort with equal access to care within an integrated healthcare delivery system, we observed variation in selected outcomes by race/ethnicity even after accounting for differences in a wide range of individual- and area-based potential confounders, including any differential receipt of pharmacological interventions. Compared with White patients, we found that Black patients experienced a higher adjusted rate of HF hospitalization but lower all-cause mortality and no significant difference in overall hospitalization. In contrast, compared with White patients, Asian/PI patients had lower adjusted rates of hospitalization for any cause and death but no significant difference in HF hospitalization. Hispanic patients had lower adjusted rates of all-cause hospitalization and death but no significant difference in the adjusted rate of HF hospitalization. Sensitivity analyses were largely consistent with the

primary results, with similar or stronger associations when analyzing presumed incident HF cases only and modest variation in the strength of associations by HF characteristics and by age groups.

Our findings support and clarify prior studies suggesting that in the setting of HF, Black patients experience higher rates of hospitalization^{3,7–10} but lower rates of death^{3,7–10} than White patients. Furthermore, our finding that Asian/PI patients had a lower rate of death compared with White patients is consistent with certain previous studies.^{3,7,8} In contrast, we observed that Asian/PI patients had lower rates of all-cause hospitalization compared with White patients, which is consistent with one prior study,⁵ whereas others did not report significant differences.^{3,7,8,10} We found that there was no significant difference between Hispanic ethnicity and the adjusted rate of HF hospitalization and a lower rate of all-cause death compared with White patients, which is in contrast to 2 studies that observed higher rates of HF hospitalization and similar rates of death.^{7,10} Of note, both studies^{7,10} used a hospital-based cohort rather than the more representative cohort we used in our study, which comprehensively included patients with HF identified from both ambulatory and inpatient settings.

Of note, California state-level data in patients with HF from 2014 to 2016 noted that Black patients had a higher, whereas Hispanic and Asian/PI patients had a lower, age-adjusted HF-related death rate compared with White patients (HF-related death defined as having HF being listed on the death certificate).²⁴ With regard to HF hospitalization, Black patients had a higher and Hispanic patients had a similar age-adjusted rate compared with White patients, whereas data were unavailable for Asian/PI patients.²⁴ Several important differences exist between our study and reported

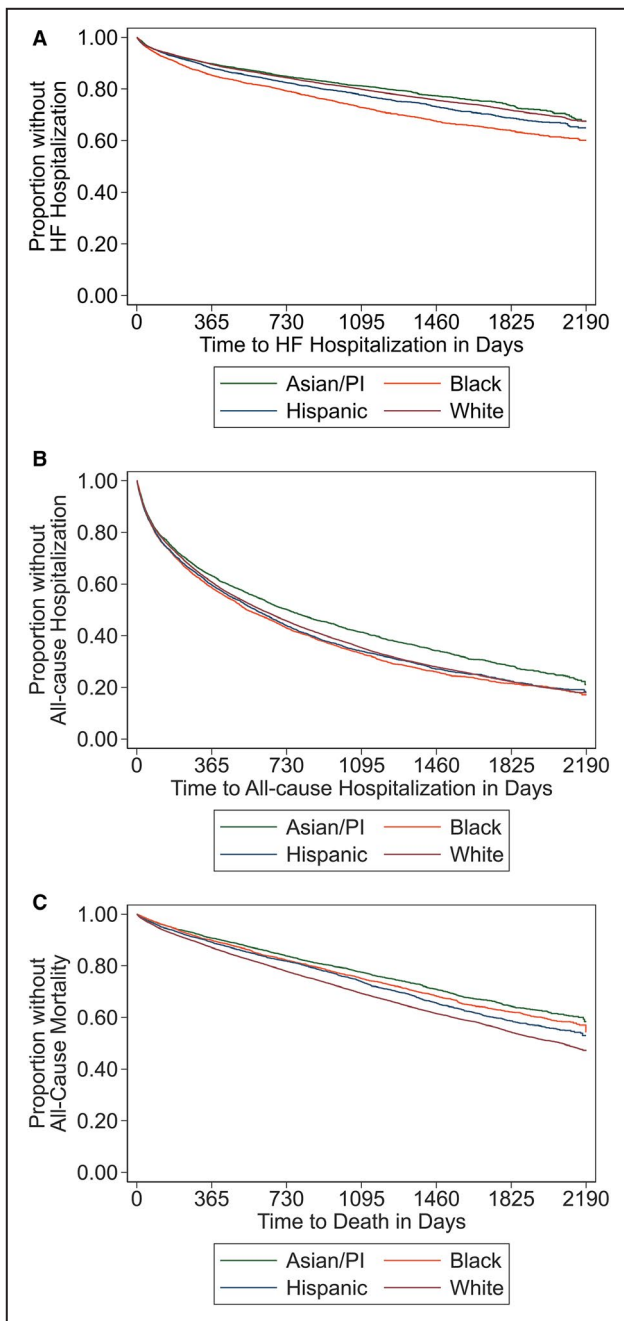


Figure 2. Clinical outcomes by racial/ethnic group among adults with heart failure (HF).

A, Hospitalization for HF. **B**, Hospitalization for any cause. **C**, All-cause death. The *P* value for the log-rank statistic is <0.01 for all 3 outcomes. PI indicates Pacific Islander.

statewide data. First, the statewide data do not adjust for known confounders across racial/ethnic groups other than age or address potentially modifiable factors. Second, our study focused on patients with HF receiving comprehensive care in an integrated delivery system with equal access to care, whereas significant variation in access to care and quality of care exists by race/ethnicity statewide.²⁵ Third, we focused on

Table 3. Crude Rates for Outcomes of Death, Hospitalization for HF, and Hospitalization for Any Cause by Race/Ethnicity

Race/Ethnicity	Rate Per 100 PY (95% CI)
Hospitalization for HF	
Asians/PIs	10.4 (9.8–11.0)
Black patients	17.8 (17.0–18.6)
Hispanic patients	13.0 (12.4–13.6)
White patients	10.9 (10.6–11.1)
Overall	11.8 (11.6–12.0)
Hospitalization for any cause	
Asians/PIs	53.0 (51.7–54.3)
Black patients	71.4 (69.9–73.0)
Hispanic patients	64.8 (63.4–66.3)
White patients	58.2 (57.6–58.8)
Overall	59.8 (59.4–60.3)
All-cause death	
Asians/PIs	8.7 (8.2–9.3)
Black patients	9.6 (9.1–10.2)
Hispanic patients	10.5 (9.9–11.1)
White patients	12.4 (12.1–12.7)
Overall	11.4 (11.2–11.6)

HF indicates heart failure; PI, Pacific Islander; and PY, person-years.

all-cause mortality compared with deaths attributed to HF based on death certificate data, which have known misclassification.²⁶ Fourth, the statewide findings may be driven by a higher prevalence of HF in Black patients than White patients²⁷ and do not directly compare to a cohort of patients with diagnosed HF, such as in our study.

Limited data exist about whether the association between race/ethnicity and clinical outcomes varies by HF characteristics. One study found that the difference in hospitalization for Black patients compared with White patients was greater in patients with HF who had EF $>40\%$ compared with EF $<40\%$,⁹ whereas HF hospitalization and death rates were higher for Black patients in another HFpEF population.⁸ In contrast, we found that the associations between Black race and outcomes were stronger in patients with HFpEF and attenuated in patients with HFrEF.

Our discordant finding that Black patients had higher rates of HF hospitalizations and lower rates of death than White patients, despite extensive adjustment for differences in patient characteristics, treatments received, and area-based measures of access to care and SES, is intriguing. The generally consistent and favorable or neutral findings among Asian/PI patients and Hispanic patients are also of interest. More important, we were unable to identify a clearly modifiable factor (eg, pharmacological treatment) or non-modifiable factor to fully explain our observed racial/

Table 4. Multivariable Association of Race/Ethnicity and Outcomes in Adults With HF

Model	Asian/Pacific Islander vs White Patients			Black vs White Patients			Hispanic vs White Patients		
	Hospitalization for HF	Hospitalization for Any Cause	Death	Hospitalization for HF	Hospitalization for Any Cause	Death	Hospitalization for HF	Hospitalization for Any Cause	Death
Model 1: race/ethnicity, HF characteristics, demographics, access to care, time-dependent comorbidities and cardiovascular procedures, and area-based SES	0.99 (0.91–1.08)	0.88 (0.84–0.93) [†]	0.74 (0.69–0.80) [†]	1.30 (1.20–1.41) [†]	1.00 (0.95–1.05)	0.82 (0.76–0.89) [†]	1.06 (0.98–1.15)	0.97 (0.93–1.02)	0.86 (0.80–0.91) [†]
Model 2: model 1+time-dependent medication use and adherence	1.00 (0.92–1.08)	0.89 (0.85–0.93) [†]	0.75 (0.69–0.80) [†]	1.28 (1.18–1.38) [†]	0.99 (0.94–1.03)	0.78 (0.72–0.85) [†]	1.06 (0.99–1.15)	0.97 (0.93–1.02)	0.85 (0.80–0.91) [†]

Data are given as hazard ratio (95% CI). HF indicates heart failure; and SES, socioeconomic status. [†]*P*<0.001.

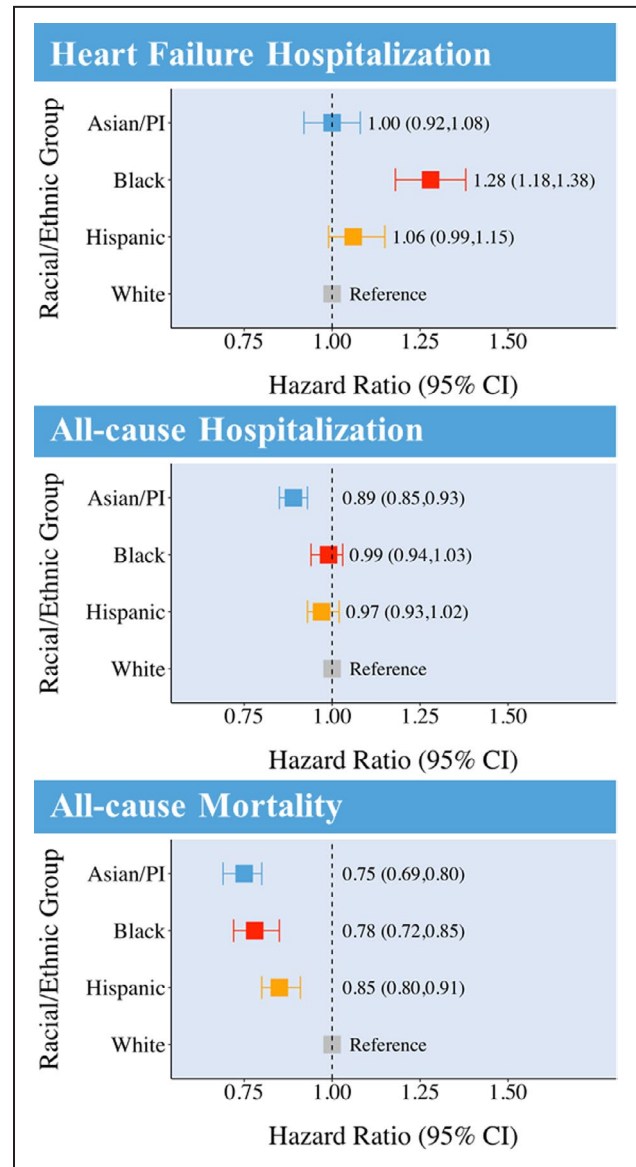


Figure 3. Multivariable association of race and ethnicity with hospitalization for heart failure, hospitalization for any cause, and all-cause mortality in adults with heart failure. The hazard ratios come from model 2 in Table 3. PI indicates Pacific Islander.

ethnic variation in outcomes. A prior analysis of racial/ethnic variation in coronary disease outcomes among KPNC patients found similar results, in which Black, Asian, and Hispanic patients had lower or similar risk of coronary events compared with White patients, and the variation was not explained by modifiable or non-modifiable factors.²⁸ Although we were able to control for many potentially modifiable factors, we were unable to account for certain self-management practices, such as dietary patterns,²⁹ exercise,³⁰ actual medication adherence,³¹ or individual-level SES.³² In addition, hospitalizing a patient for HF exacerbation may also play a different management role in various

Table 5. Sensitivity Analyses of Race/Ethnicity and Outcomes in Adults With HF

Sensitivity Analysis	Asian/Pacific Islander vs White Patients			Black vs White Patients			Hispanic vs White Patients		
	Hospitalization for HF	Hospitalization for Any Cause	Death	Hospitalization for HF	Hospitalization for Any Cause	Death	Hospitalization for HF	Hospitalization for Any Cause	Death
Sensitivity analysis 1: presumed incident HF only	0.99 (0.88–1.10)	0.88 (0.83–0.94)*	0.76 (0.69–0.84)*	1.30 (1.18–1.45)*	0.99 (0.93–1.05)	0.80 (0.71–0.89)*	1.05 (0.95–1.16)	0.96 (0.90–1.02)	0.86 (0.78–0.94)†
Sensitivity analysis 2: preserved EF only	0.95 (0.85–1.06)	0.86 (0.81–0.92)*	0.71 (0.64–0.78)*	1.19 (1.07–1.33)†	0.96 (0.90–1.02)	0.82 (0.74–0.91)*	1.10 (0.99–1.21)	0.98 (0.92–1.03)	0.86 (0.79–0.94)*
Sensitivity analysis 3: reduced EF only	0.93 (0.79–1.10)	0.94 (0.84–1.04)	0.77 (0.66–0.90)*	1.35 (1.18–1.55)*	1.03 (0.94–1.13)	0.70 (0.60–0.80)*	1.02 (0.87–1.19)	1.03 (0.93–1.14)	0.87 (0.76–1.00)
Sensitivity analysis 4: aged <70 y	0.97 (0.84–1.13)	0.86 (0.79–0.94)*	0.73 (0.63–0.85)*	1.39 (1.23–1.57)*	0.97 (0.90–1.05)	0.84 (0.73–0.96)†	1.09 (0.96–1.06)	0.94 (0.87–1.02)	0.77 (0.66–0.89)*
Sensitivity analysis 5: aged 70–80 y	1.02 (0.88–1.17)	0.94 (0.87–1.02)	0.76 (0.67–0.87)*	1.08 (0.94–1.23)	0.96 (0.88–1.04)	0.68 (0.59–0.78)*	0.99 (0.87–1.13)	1.04 (0.97–1.12)	0.84 (0.75–0.94)†
Sensitivity analysis 6: aged >80 y	0.98 (0.85–1.13)	0.89 (0.82–0.97)†	0.76 (0.68–0.85)*	1.32 (1.15–1.54)*	1.09 (0.99–1.19)	0.88 (0.78–1.01)	1.12 (0.99–1.27)	0.94 (0.86–1.02)	0.91 (0.83–1.00)
Sensitivity analysis 7: women	1.10 (0.98–1.25)	0.94 (0.88–1.02)	0.76 (0.67–0.85)*	1.31 (1.18–1.46)*	1.00 (0.93–1.06)	0.82 (0.74–0.92)*	1.08 (0.97–1.21)	1.01 (0.95–1.08)	0.89 (0.81–0.98)†
Sensitivity analysis 8: men	0.93 (0.83–1.04)	0.86 (0.80–0.91)*	0.73 (0.66–0.80)*	1.24 (1.12–1.39)*	0.98 (0.92–1.05)	0.76 (0.68–0.85)*	1.07 (0.96–1.18)	0.95 (0.89–1.01)	0.82 (0.75–0.90)*
Sensitivity analysis 9: recurrent events	0.97 (0.89–1.06)	0.87 (0.83–0.91)*		1.41 (1.29–1.55)*	1.03 (0.98–1.08)		1.09 (1.00–1.18)†	0.96 (0.93–1.00)	

Data are given as hazard ratio (95% CI). All models use backward selection and include all explanatory covariates, including medication and adherence. EF indicates ejection fraction; and HF, heart failure.

*P<0.001.

†P<0.01.

‡P<0.05.

racial/ethnic groups, and may not reflect variable quality of care. We did not find material differences across race/ethnicity in the use of proven HF therapies in our population, and differential patterns of inpatient versus outpatient health care^{33,34} utilization were not associated with survival. It is also possible that there are causative differences across race/ethnicity that impact the development and complications associated with HF. Black patients have a higher incidence of HF than White patients,²⁷ which occurs at an earlier age and is more likely to be attributed to hypertension rather than ischemic heart disease.^{35–37} Prior studies have also found structural, functional, and vascular differences between Black and White patients that may contribute to a higher incidence of HF and worse outcomes for patients who have HF for Black patients compared with White patients. These differences include worse arterial stiffness and microcirculatory function,³⁸ lower levels of natriuretic peptides,^{39,40} differences in the left ventricular structural and functional changes in response to arterial afterload,⁴¹ and a higher prevalence of malignant left ventricular hypertrophy.⁴² Structural or functional cardiac or vascular differences, or responses to therapies, may also potentially explain the differences we found in HF-related outcomes across racial/ethnic groups. It is possible that the clinical factors associated with acute HF symptoms that lead to HF hospitalization may differ from the clinical factors associated with death among patients with HF. If so, then these differences between Black and White patients may contribute to higher HF hospitalization rates in Black patients while not negatively impacting survival. Further studies are needed to determine if specific mechanisms can be identified for the purpose of developing future interventions.

Our study was strengthened by its large sample size, more contemporary study period, inclusion of all major racial/ethnic groups, use of EF data to categorize HF type, comprehensive longitudinal follow-up on key explanatory variables (modifiable and nonmodifiable) and clinical outcomes, and targeted measures at the individual and area level. Our study also had several limitations. For example, despite the broad spectrum of available covariates, we were unable to completely rule out unmeasured confounders, including potential genetic and biologic differences across racial/ethnic groups as well as selected lifestyle factors, such as diet and exercise patterns, alcohol and illicit drug use, and detailed medication adherence, that may influence outcomes. We were also unable to measure potential differences in the clinical severity of HF beyond EF and receipt of different HF-related therapies across racial/ethnic groups. However, we found similar results in the sensitivity analysis that was restricted to patients with presumed incident HF who are likely more comparable in terms

of HF severity than patients with prevalent HF. We used all-cause mortality as an outcome rather than death with HF as a contributing cause because there is substantial misclassification in listed cause(s) of death on death certificates.²² Although it is possible that our findings of lower rates of death among the racial/ethnic minority groups compared with White patients were attributable to using all-cause mortality rather than cause-specific mortality, we were able to adjust for important noncardiovascular comorbidities that are associated with death. Although the findings were of interest, the sensitivity analyses should be considered exploratory given the reduced sample sizes in certain racial/ethnic subgroups and associated limited precision. All studied patients were receiving care within a large integrated healthcare delivery system in northern California, which has an emphasis on cardiovascular prevention and treatment, so the results may not be fully generalizable to all geographic areas and practice settings.

CONCLUSIONS

In summary, within a large, ethnically diverse population with HF, we observed that compared with White patients, Black patients experienced a higher rate of HF hospitalization but a lower rate of death; Asian/PI patients had lower rates of all-cause hospitalization and death; and Hispanic patients had a lower rate of death. Future efforts are needed to better understand explanatory mechanisms for these observations and effective interventions to reduced adverse HF-related outcomes across all racial/ethnic groups.

ARTICLE INFORMATION

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Supplementary Material

Table S1

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SUPPLEMENTAL MATERIAL

Table S1. International Classification of Diseases Ninth Revision (ICD-9) and Tenth (ICD-10) Revision codes for identification of clinical heart failure.

Type	Codes
ICD-9	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 428.0, 428.1, 428.20, 428.21, 428.22, 428.23, 428.30, 428.31, 428.32, 428.33, 428.40, 428.41, 428.42, 428.43, 428.9
ICD-10	I09.81, I11.0, I11.9, I13.0, I13.1, I13.10, I13.11, I13.2, I50, I50.1, I50.2, I50.20, I50.21, I50.22, I50.23, I50.3, I50.30, I50.31, I50.32, I50.33, I50.4, I50.40, I50.41, I50.42, I50.43, I50.9, I97.13