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Health Status Disparities by Sex, Race/Ethnicity, and Socioeconomic Status in Outpatients With Heart Failure

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Abstract

OBJECTIVES—This study sought to describe the health status of outpatients with heart failure and reduced ejection fraction (HFrEF) by sex, race/ethnicity, and socioeconomic status (SES).

BACKGROUND—Although a primary goal in treating patients with HFrEF is to optimize health status, whether disparities by sex, race/ethnicity, and SES exist is unknown.

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APPENDIX For supplemental tables, please see the online version of this paper.

METHODS—In the CHAMP-HF (Change the Management of Patients with Heart Failure) registry, the associations among sex, race, and SES and health status, as measured by the Kansas City Cardiomyopathy Questionnaire-overall summary (KCCQ-os) score (range 0 to 100; higher scores indicate better health status) was compared among 3,494 patients from 140 U.S. clinics. SES was categorized by total household income. Hierarchical multivariate linear regression estimated differences in KCCQ-os score after adjusting for 31 patient characteristics and 10 medications.

RESULTS—Overall mean KCCQ-os scores were 64.2 ± 24.0 but lower for women (29% of sample; 60.3 ± 24.0 vs. 65.9 ± 24.0 , respectively; p < 0.001), for blacks (60.5 ± 25.0 vs. 64.9 ± 23.0 , respectively; p < 0.001), for Hispanics (59.1 ± 21.0 vs. 64.9 ± 23.0 , respectively; p < 0.001), and for those with the lowest income (<\$25,000; mean: 57.1 vs. 63.1 to 74.7 for other income categories; p < 0.001). Fully adjusted KCCQ-os scores were 2.2 points lower for women (95% confidence interval [CI]: -3.8 to -0.6; p = 0.007), no different for blacks (p = 0.74), 4.0 points lower for Hispanics (95% CI: -6.6 to -1.3; p = 0.003), and lowest in the poorest patients (4.7 points lower than those with the highest income (95% CI: 0.1 to 9.2; p = 0.045; p for trend = 0.003).

CONCLUSIONS—Among outpatients with HFrEF, women, blacks, Hispanics, and poorer patients had worse health status, which remained significant for women, Hispanics, and poorer patients in fully adjusted analyses. This suggests an opportunity to further optimize treatment to reduce these observed disparities.

Keywords

health disparities; heart failure; quality of life

Aprimary goal of U.S. health care, as articulated by the Department of Health and Human Services' *Healthy People 2020* initiative, is to eradicate disparities in health status by sex, race/ethnicity, and socioeconomic status (SES) (1). Prior studies have demonstrated worse outcomes, principally mortality and hospitalization rates, in women, blacks, Hispanics, and patients with lower SES in the setting of heart failure (2,3). However, a primary treatment goal in heart failure is to optimize patients' health status, including their symptoms, function, and quality of life. To date, no studies have described the health status of patients with heart failure and reduced ejection fraction (HFrEF) in routine clinical care. Given the many potential interventions available to improve the health status of patients with HFrEF, identifying differences by sex, race/ethnicity, or SES can highlight new opportunities to further reduce these disparities in care.

To address this gap in knowledge, we compared the health status of patients with HFrEF by sex, race/ethnicity, and SES in the CHAMP-HF (Change the Management of Patients with Heart Failure) registry. CHAMP-HF is a large, prospective, multicenter, observational study of outpatients with HFrEF that captured patients' health status by using the short form of the Kansas City Cardiomyopathy Questionnaire-12 (KCCQ-12), a well-validated measurement of patients' symptoms, function, and quality of life (4). Moreover, as payers increasingly turn to patient-reported outcome measures, such as the KCCQ-12 instrument, to quantify health care quality, identifying populations of patients with worse health status can form the

foundation with which to evaluate whether the use of such performance measures can successfully reduce health status disparities.

METHODS

STUDY DESIGN

CHAMP-HF, as previously described, is a multicenter, observational registry developed with the primary objective of capturing the outcomes and real-world treatment patterns of patients with HFrEF in the United States (5). Briefly, patients with chronic HFrEF (left ventricular ejection fraction [LVEF] 40%) being treated with at least 1 guideline-recommended pharmacotherapy were consecutively recruited from outpatient heart failure clinics. Subjects were excluded if they were enrolled in a hospice program or estimated to have a life expectancy of <1 year or had a history of heart transplantation, left ventricular assist device implantation, or end-stage kidney disease requiring hemodialysis. Eligible sites were identified based upon the completion of a feasibility survey, which provided investigators with the opportunity to ensure broad geographic and provider specialty representation. Study coordinators at each site were responsible for identification and enrollment of subjects during the course of a scheduled outpatient visit. CHAMP-HF was sponsored by Novartis Pharmaceuticals Corp., and all participating sites obtained local or central institutional review board approval before subject enrollment as well as informed consent from each participant. This study leveraged baseline data from all patients enrolled before March 6, 2017.

DATA COLLECTION

At the time of study subject enrollment, site coordinators interviewed patients to collect their self-identified race/ethnicity as well as household income and health status and abstracted their clinical history and medications. The primary outcome for this analysis was disease-specific health status, as assessed by the 12-item KCCQ-12. The KCCQ-12 is a valid, reliable, and sensitive 12-item HF-specific patient-reported outcome form that quantifies patients' HF symptoms, physical and social limitations, and quality of life (4,6). KCCQ-12 domains can be summarized as an overall summary score that ranges from 0 to 100, where higher scores reflect better health status (fewer symptoms, less social or physical limitations, and better quality of life). A 5-point change in KCCQ-os is considered a clinically meaningful difference in scores from both patients' and providers' perspectives (7,8). For descriptive purposes, the KCCQ-os was divided (9) into poor health status (score: <25), fair health status (score: 25 to 49), good health status (score: 50 to 74), and excellent health status (score: 75 to 100). SES was characterized as total annual household income and assessed by asking patients to use ordinal categories of annual household income ranging from <\$25,000 to >\$150,000 per year.

STATISTICAL ANALYSIS

Distribution of continuous KCCQ-os scores was described by mean \pm SD, median, and 25th and 75th percentiles according to patient characteristics that included sex, race/ethnicity, and SES. We then used hierarchical linear regression models, with site as a random effect to account for clustering within sites, to identify patient characteristics associated with

patients' health status. Our first model incorporated patient sociodemographic and clinical characteristics (model 1) with subsequent adjustment for medical therapies (model 2) present on enrollment. Backward selection was performed to obtain the final models. Full models included all variables shown in Table 1, except for laboratory results. Age, sex, and race/ethnicity were permanently retained in the model. The maximum p value for covariates to be retained in the model was set at 0.05. The relationship between mean KCCQ-os score and continuous variables are reported in units of 1 SD, except for age, which was reported per 10 year intervals. We tested the nonlinearity by using restricted cubic splines. There was no evidence of nonlinearity except for age, and therefore we used a linear spline with a knot of 70 for age.

Rates of missing data for patient-level variables, overall, were small (<8%), except for household income, which was not reported by ~24% of patients. Missing values for continuous variables were imputed using the sex/age/KCCQ group-specific median for patient-level covariates. For categorical variables, missing medical history variables were imputed to the most common value. Missing procedures were imputed as "no." All estimates were reported using 95% confidence intervals (CIs) and an $\alpha = 0.05$ was used to determine statistical significance. All analyses were performed using SAS software version 9.4 (SAS Institute, Cary, North Carolina). Analyses were performed independently by Duke Clinical Research Institute, and the lead author takes responsibility for guiding data analysis and interpretation of the results.

RESULTS

A total of 3,552 patients were enrolled in the CHAMPHF registry before March 6, 2017. Of that sample, our final analytic cohort consisted of 3,494 patients across 140 sites after excluding patients with missing KCCQ-os data (n=14), demographic data (n=10), and those ineligible according to the study protocol (n=34) (Figure 1). There was a broad range of patient-reported KCCQ-os scores, encompassing poor (n=228), fair (n=785), good (n=1,101), and excellent (n=1,380) health status.

PATIENT CHARACTERISTICS AND HEALTH STATUS ACROSS SUBGROUPS

Characteristics of the analytic cohort are described in Tables 1 and 2, with information on medication prescription by sex, race/ethnicity, and SES provided in Online Tables 3a to 3d and New York Heart Association (NYHA) functional classification by sex, in Online Table 3e. Of the total sample, the median age was 68.0 (interquartile range [IQR]: 59.0 to 75.0) years, with more men than women (70.8% vs. 29.2%) and white (74.9%) than black (16.4%) or Hispanic (16.9%) patients. The total annual household income was <\$25,000 in 30.8% of participants, whereas 2.7% reported incomes >\$150,000. A significant proportion had concomitant diagnoses of atrial fibrillation, coronary artery disease, chronic obstructive lung disease, diabetes mellitus, and hypertension. Finally, median documented LVEF was 30% (IQR: 23%, 35%). Supporting the stability of this outpatient population, 87.6% of the cohort had no or only one hospitalization within 12 months of enrollment in the registry.

In regard to HF-related quality of life, the mean KCCQ-os score was 64.2 ± 23.9 in the overall sample. Participants with good to excellent health status were more often older

(65), male, and white. Online Table S1 provides a detailed overview of patient subgroup characteristics by ranges of KCCQ-os scores.

DIFFERENCES IN HEALTH STATUS BY SEX, RACE/ETHNICITY, AND SES STATUS

Significant differences in KCCQ-os scores by sex were observed in both unadjusted and adjusted analyses. In the unadjusted model, women had worse KCCQ-os scores than men (-4.8 points; 95% CI: -6.5 to -3.1; p < 0.001). This variability was modestly attenuated after adjusting for other patient-level characteristics in model 1 (-2.2 points; 95% CI: -3.7 to -0.6; p = 0.007) (Online Table S2), and remained statistically significant even after adjusting for HF medications (-2.2 points; 95% CI: -3.8 to -0.6; p = 0.007) (Table 3). Differences by race/ethnicity were observed in unadjusted analyses, with blacks (-4.5 points; 95% CI: -6.7 to -2.2; p < 0.001) and Hispanics (-3.4 points; 95% CI: -6.1 to -0.6; p = 0.016) having worse health status scores than those of whites. For blacks, this difference was fully explained after the addition of other patient characteristics to model 1 (-0.7 points; 95% CI: -2.9 to 1.4; p = 0.52) (Online Table 2) and remained insignificant after adjusting for medical therapies (-0.4 points; 95% CI: -2.5 to 1.8; p = 0.736) (Table 3). For Hispanics, clinically significant differences remained after adjusting only for patient characteristics in model 1 (-3.4 points; 95% CI: -6.0 to -0.8; p = 0.011) (Online Table S2) and then medications (-4.0 points; 95% CI: -6.6 to -1.3; p = 0.003) (Table 3) in model 2.

Finally, large differences by household income were observed between the highest- and lowest-paid groups across unadjusted and adjusted analyses. In the unadjusted model, patients with the highest level had a mean KCCQ-os score that was 15.3 points higher than those with the lowest income (95% CI: 10.4 to 20.1; p < 0.001). This variability was attenuated but still significantly different after adjustment for other patient characteristics in model 1 (5.6 points; 95% CI: 1.0 to 10.2; p = 0.02) (Online Table 2) and persisted after adjusting for medical therapies in model 2 (4.7 points; 95% CI: 0.1 to 9.2; p = 0.045) (Table 3). A test for trend across all income levels was significant for both unadjusted (p < 0.0001) and adjusted (p = 0.003) models. Both unadjusted and fully adjusted models for sex, race/ethnicity, and SES are shown in Figure 2.

DISCUSSION

A primary goal for treating patients with HFrEF is to minimize their symptoms and optimize their function and quality of life (10). To accomplish this goal, clinicians have a range of established and emerging medical and device therapies (11–13), but whether these are applied with similar success to optimize the health status of patients with different sex, race/ethnicity, and SES is unknown. In the present study, we used data from CHAMP-HF to explore disparities in health status by sex, race/ethnicity, and SES. We found that, among a large population of patients with HFrEF in outpatient clinical practice, women, blacks and Hispanics, and lower-income patients had statistically significantly worse HF-specific health status in unadjusted analyses. Moreover, even after adjustment for numerous patient and treatment factors, a small but statistically significant worse KCCQ-os score remained in women, Hispanics, and poorer patients. CHAMP-HF is a contemporary registry that, for the first time, captures the care and outcomes of patients with HFrEF. Our findings describe

significant disparities in the control of HF symptoms and optimization of function and quality of life between women and men, whites and Hispanics, and those with lower and higher SES that warrant further efforts to achieve the goals of equity in health care.

Our findings extend previous efforts to describe disparities in the care of patients with HF by documenting differences in patients' health status across different sociodemographic groups. Thus, although prior efforts have described sociodemographic disparities in relation to cardiovascular mortality and routine implementation of guideline-directed HFrEF therapies, insights into health status disparities are limited (14-16). For example, in regard to sex, our results substantially extend several prior, smaller studies suggesting better (17,18), worse (19–26), or comparable (27) quality of life in women. Our analysis describes health status in a larger, more contemporary stable HFrEF population. When interpreting our findings, we believe it is important to focus upon the unadjusted, as opposed to only adjusted, effect sizes. Although adjusting for confounders is very important in observational research seeking to associate patient characteristics with outcomes, in this case, we do not believe that there is a biologically plausible reason why clinicians should be less capable of controlling the symptoms and optimizing the quality of life of women than that of men. Finding a clinically important difference in KCCQ-os scores in women from this large multicenter registry suggests that we are not being as effective in optimizing the health status of women with HFrEF and that more research is needed to better understand how to overcome these apparent sex-level disparities. For example, prior studies associating female sex with lower adherence to guideline-directed HFrEF therapies may be one possible mechanism of health status inequality, although we did account for differences in treatment in our analyses (17). Whether, as others have suggested, these differences are due to HF management knowledge, perceived control, self-care confidence (28), or competing demands between family responsibilities, sex roles, and self-care (29-31) is unknown and further studies are needed to identify how to deliver care that is more equitable between men and women with HFrEF (32).

Health disparities between whites and nonwhites are well known, but racial variability in HF-specific health status remains understudied (20,33,34). Our findings parallel prior research that has shown poorer perceived HF-related health (18) and steeper functional decline (34) in blacks, although other studies have failed to observe any racially driven associations with health status during outpatient follow-up (35). Although results of our fully adjusted model showed no significant differences in health status between whites and blacks, it remains noteworthy that unadjusted health status differences between those groups were statistically and clinically significant (~5 points lower in blacks). This highlights an important reality in the management of the HFrEF population, in that African Americans have worse health status, whether mediated by an underlying biological mechanism or other sociodemographic patient characteristics, and this should not be overlooked as part of routine outpatient care. Multiple reasons for this variability in health status have been postulated, including cultural differences in what constitutes health and factors considered during self-evaluation of health status (18), although there have been no reports suggesting that these observed differences might not be overcome with more aggressive therapy, an important future research priority.

Our results concerning Hispanics are novel in that they contradict earlier reports that Latin Americans experienced comparable health status, on initial evaluation, compared to other ethnic and racial groups (33,36). As our study is descriptive (and the first to report differences in the health status of Hispanics), we cannot provide causal insights into these observations.

Finally, our findings are most indicative of sizeable variability in HF-specific health status based on financial income, with similar patterns having been previously described (19,37–39). In our study, we leveraged annual household income as a proxy for SES, which coincides with definitions used previously in published reports (18). Overall, our results can be understood in the context of routine HF management, where chronic illness is predictably disabling and thereby forces patients to make significant lifestyle changes that have an impact on overall quality of life. By extension, an adequate financial income provides an uninterrupted layer of insulation against barriers to self-care created by inadequate resources (37).

One strategy that may help address these observed disparities would be to routinely capture and report patient-reported health status in clinical care, a means of transparently and reproducibly documenting the symptoms, function, and quality of life of patients with HF at each and every clinic visit. By consistently capturing and reporting patients' health status, clinicians could readily identify those for whom additional therapeutic strategies may be needed to improve their management. Toward that end, a new Medicare framework (40,41) has been designed to reward providers for collecting patient-reported outcomes measurements through the Centers for Medicare and Medicaid Services Merit-Based Payment System. However, although the Centers for Medicare and Medicaid Services has created a mechanism to encourage the collection of patient-reported outcomes measurements, the means of feasibly collecting, scoring, and reporting these data at the time of a clinical visit will require further work. Although it is possible that the routine collection of patients' health status can reduce these health status disparities, this will require further investigation after the implementation of patient-reported outcome-based performance measures.

STUDY LIMITATIONS

Our findings must be interpreted in context of the following limitations. First, although the CHAMP-HF registry is among the largest cross-sectional assessments of the health status of patients in routine clinical care, it was conducted in voluntary participating sites committed to clinical research. Whether these findings are generalizable throughout the United States is unknown, and our estimates of health status disparities may not accurately reflect the entire country. Second, our analysis assessed health status at a single point in time (enrollment), and further work will be needed to describe the trajectories of patients' health status over time. Third, one-fourth of patients did not report annual household income, and this was treated as a separate category. Fourth, residual measured or unmeasured confounding might have influenced the associations observed. Fifth, the use of multiple comparisons might have influenced the statistical significance and interpretation of final p values. Sixth and finally, this initial, descriptive report was not able to formally test mediators of observed difference

in health status across vulnerable groups nor define practice patterns that might support intervention to reduce these disparities.

CONCLUSIONS

In analyzing a unique, prospective observational registry of patients with chronic HFrEF, we found that women, blacks, and Hispanics and patients with lower socioeconomic status had worse symptoms, function, and health-related quality of life. After multivariate adjustment, clinically significant disparities remained across sex, race/ethnicity, and socioeconomic groups. Our findings indicate that previously reported disparities in survival and hospitalization rates extend to patients' health status and underscore the need for novel strategies to reduce health status disparities as well as future work to better understand their complexity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS AND ACRONYMS

CI confidence interval

HFrEF heart failure and reduced ejection fraction

KCCQ-os Kansas City Cardiomyopathy Questionnaire-overall summary score

LVEF left ventricular ejection fraction

SES socioeconomic status

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE

In the first large assessment of health status in patients with HFrEF, we found that women, blacks, and Hispanics and patients with lower income signify unique populations that may benefit from more aggressive HF follow-up and treatment in the outpatient setting.

TRANSLATIONAL OUTLOOK

This analysis describes the association between HFrEF patients' health status and medical and sociodemographic characteristics at enrollment in an observational registry in a contemporary clinical setting. Future studies will be needed to identify health status trajectories over time as well as detect practice patterns that might reduce health status disparities by sex, race/ethnicity, and socioeconomic status in this high-risk population.

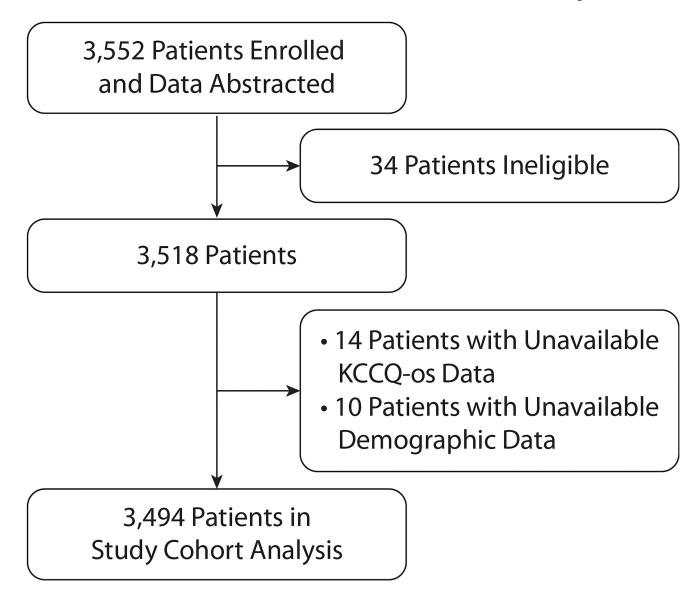


FIGURE 1. Patient Exclusion Flowsheet

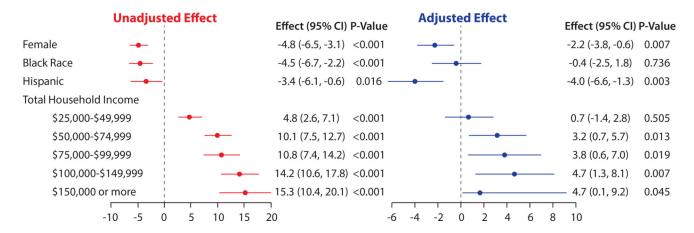


FIGURE 2.Unadjusted and Adjusted Mean KCCQ-os Score Disparities by Sex, Race/Ethnicity, and Socioeconomic Status

Candidate variables considered for multivariate analyses were age, sex, race, BMI, insurance status, highest level of education, house income, employment status, diabetes mellitus, CKD, COPD, depression, tobacco use/smoking, atrial fibrillation, CAD, hypertension, hyperlipidemia, ventricular tachycardia/fibrillation, CRT, number of prior HF hospitalizations, systolic blood pressure, heart rate, LVEF, ACEi/ARB, beta-blocker, MRA, ARNI, loop diuretic agent, hydralazine, digoxin, ivabradine, inotrope, and number of HF medications. Variables included in multivariate analysis after backward selection were age, sex, race, BMI, house income, employment status, CKD, COPD, depression, atrial fibrillation, number of prior HF hospitalizations, systolic blood pressure, heart rate, LVEF, ARNI, loop diuretic therapy, ivabradine, and inotrope. Reference category for sex was male. Reference category for race/ethnicity was white. Reference category for total household income was <\$25,000 (annually). ACEi/ARB = angiotensin-converting enzyme inhibitor/ angiotensin receptor blocker; ARNI = angiotensin-receptor neprilysin inhibitor; BMI = body mass index; CAD = coronary artery disease; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; CRT = cardiac resynchronization therapy; HF = heart failure; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid antagonist; other abbreviations as in Tables 1 and 2.

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TABLE 1

Distribution of Patient Characteristics (N = 3,494)

Age, yrs	68.0 (59.0, 75.0)
<40	111 (3.2)
40–64	1,307 (37.4)
65–80	1,638 (46.9)
>80	438 (12.5)
Male	2,473 (70.8)
White	2,616 (74.9)
Black	572 (16.4)
Hispanic	589 (16.9)
BMI, kg/m ²	29.2 (25.5, 33
Insurance status	
Managed care	574 (16.4)
Private insurance	330 (9.4)
Medicare	2,038 (58.3)
Medicaid	317 (9.1)
Highest level of education	
Less than high school	425 (12.2)
High school	1,187 (34.0)
Some college	1,094 (31.3)
4–yr college	440 (12.6)
Graduate or other professional degree	348 (10.0)
Total household income	
<\$25,000	1,076 (30.8)
\$25,000–\$49,999	685 (19.6)
\$50,000-\$74,999	417 (11.9)
\$75,000–\$99,999	212 (6.1)
\$100,000-\$149,999	184 (5.3)
\$150,000 or more	95 (2.7)
Employee status	
Full-time	496 (14.2)
Part-time	252 (7.2)
Disability for medical reasons	877 (25.1)
Not employed for other reasons	1,869 (53.5)
Medical history	
COPD	1,054 (30.2)

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HbA1c, % 6.4 (5.8, 7.6) Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4)		
Diabetes mellitus	CKD	693 (19.8)
Tobacco use/smoking 689 (19.7) Atrial fibrillation 1,258 (36.0) Coronary artery disease 2,177 (62.3) Hyperlipidemia 2,643 (75.6) Hypertension 2,872 (82.2) VT/VF 661 (18.9) CRT therapy 234 (6.7) NYHA functional classification I I 344 (9.8) II 1,914 (54.8) III 1,004 (28.7) IV 87 (2.5) Unknown 145 (4.1) Number of prior hospitalizations within 12 months of screening 0 2,173 (62.2) 1 886 (25.4) 2 2 435 (12.4) Vital signs on enrollment Systolic pressure, mm Hg 120 (110, 131) Diastolic pressure, mm Hg 72 (64, 80) Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % NT-proBNP, pg/ml 2,013 (794, 5,490) HbA1c, % 6.4 (5.8, 7.6) Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl <td< td=""><td>Depression</td><td>874 (25.0)</td></td<>	Depression	874 (25.0)
Atrial fibrillation 1,258 (36.0) Coronary artery disease 2,177 (62.3) Hyperlipidemia 2,643 (75.6) Hypertension 2,872 (82.2) VT/VF 661 (18.9) CRT therapy 234 (6.7) NYHA functional classification I 344 (9.8) II 1,914 (54.8) III 1,004 (28.7) IV 87 (2.5) Unknown 145 (4.1) Number of prior hospitalizations within 12 months of screening 0 2,173 (62.2) 1 886 (25.4) 2 435 (12.4) Vital signs on enrollment Systolic pressure, mm Hg 120 (110, 131) Diastolic pressure, mm Hg 72 (64, 80) Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % 30 (23, 35) NT-proBNP, pg/ml 2,013 (794, 5,490) HbA1c, % 6.4 (5.8, 7.6) Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² <30 122 (3.5) 30-45 304 (8.7) 45-60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	Diabetes mellitus	1,426 (40.8)
Coronary artery disease 2,177 (62.3) Hyperlipidemia 2,643 (75.6) Hypertension 2,872 (82.2) VT/VF 661 (18.9) CRT therapy 234 (6.7) NYHA functional classification I 344 (9.8) II 1,914 (54.8) III 1,004 (28.7) IV 87 (2.5) Unknown 145 (4.1) Number of prior hospitalizations within 12 months of screening 0 2,173 (62.2) 1 886 (25.4) 2 435 (12.4) Vital signs on enrollment Systolic pressure, mm Hg 120 (110, 131) Diastolic pressure, mm Hg 72 (64, 80) Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % 30 (23, 35) NT-proBNP, pg/ml 2,013 (794, 5,490) HbA1c, % 6.4 (5.8, 7.6) Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² <30 122 (3.5) 30-45 304 (8.7) 45-60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	Tobacco use/smoking	689 (19.7)
Hyperlipidemia 2,643 (75.6) Hypertension 2,872 (82.2) VT/VF 661 (18.9) CRT therapy 234 (6.7) NYHA functional classification I 344 (9.8) II 1,914 (54.8) III 1,004 (28.7) IV 87 (2.5) Unknown 145 (4.1) Number of prior hospitalizations within 12 months of screening 0 2,173 (62.2) 1 886 (25.4) 2 435 (12.4) Vital signs on enrollment Systolic pressure, mm Hg 120 (110, 131) Diastolic pressure, mm Hg 72 (64, 80) Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % 30 (23, 35) NT-proBNP, pg/ml 2,013 (794, 5,490) HbA1c, % 6.4 (5.8, 7.6) Hemoglobin, g/dl 3.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² <30 122 (3.5) 30-45 304 (8.7) 45-60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	Atrial fibrillation	1,258 (36.0)
Hypertension 2,872 (82.2) VT/VF 661 (18.9) CRT therapy 234 (6.7) NYHA functional classification	Coronary artery disease	2,177 (62.3)
VT/VF 661 (18.9) CRT therapy 234 (6.7) NYHA functional classification I II 1,914 (54.8) III 1,004 (28.7) IV 87 (2.5) Unknown 145 (4.1) Number of prior hospitalizations within 12 months of screening 0 0 2,173 (62.2) 1 886 (25.4) 2 435 (12.4) Vital signs on enrollment Systolic pressure, mm Hg Systolic pressure, mm Hg 72 (64, 80) Heart rate, beats/min 72 (64, 80) Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % NT-proBNP, pg/ml 2,013 (794, 5,490 HbA1c, % 6.4 (5.8, 7.6) Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² 30 45-60 491 (14.1) >60 1,200 (34.3) Missi	Hyperlipidemia	2,643 (75.6)
CRT therapy 234 (6.7) NYHA functional classification I 344 (9.8) II 1,914 (54.8) III 1,004 (28.7) IV 87 (2.5) Unknown 145 (4.1) Number of prior hospitalizations within 12 months of screening 0 2,173 (62.2) 1 886 (25.4) 2 435 (12.4) Vital signs on enrollment Systolic pressure, mm Hg 120 (110, 131) Diastolic pressure, mm Hg 72 (64, 80) Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % 30 (23, 35) NT-proBNP, pg/ml 2,013 (794, 5,490) HebA1c, % 6.4 (5.8, 7.6) Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² <30 122 (3.5) 30-45 304 (8.7) 45-60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	Hypertension	2,872 (82.2)
NYHA functional classification I	VT/VF	661 (18.9)
II 1,914 (54.8) III 1,914 (54.8) III 1,004 (28.7) IV 87 (2.5) Unknown 145 (4.1) Number of prior hospitalizations within 12 months of screening 0 2,173 (62.2) 1 886 (25.4) 2 435 (12.4) Vital signs on enrollment Systolic pressure, mm Hg 120 (110, 131) Diastolic pressure, mm Hg 72 (64, 80) Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % 30 (23, 35) NT-proBNP, pg/ml 2,013 (794, 5,490) HbA1c, % 6.4 (5.8, 7.6) Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² <30 122 (3.5) 30-45 304 (8.7) 45-60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	CRT therapy	234 (6.7)
II 1,914 (54.8) III 1,004 (28.7) IV 87 (2.5) Unknown 145 (4.1) Number of prior hospitalizations within 12 months of screening 0 2,173 (62.2) 1 886 (25.4) 2 435 (12.4) Vital signs on enrollment Systolic pressure, mm Hg 120 (110, 131) Diastolic pressure, mm Hg 72 (64, 80) Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % 30 (23, 35) NT-proBNP, pg/ml 2,013 (794, 5,490) HbA1c, % 6.4 (5.8, 7.6) Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² <30 122 (3.5) 30-45 304 (8.7) 45-60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	NYHA functional classification	
III 1,004 (28.7) IV 87 (2.5) Unknown 145 (4.1) Number of prior hospitalizations within 12 months of screening 0 2,173 (62.2) 1 886 (25.4) 2 435 (12.4) Vital signs on enrollment Systolic pressure, mm Hg 120 (110, 131) Diastolic pressure, mm Hg 72 (64, 80) Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % 30 (23, 35) NT-proBNP, pg/ml 2,013 (794, 5,490) Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² <30 122 (3.5) 30–45 304 (8.7) 45–60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	I	344 (9.8)
IV 87 (2.5) Unknown 145 (4.1) Number of prior hospitalizations within 12 months of screening 0 2,173 (62.2) 1 886 (25.4) 2 435 (12.4) Vital signs on enrollment Systolic pressure, mm Hg 120 (110, 131) Diastolic pressure, mm Hg 72 (64, 80) Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % 30 (23, 35) NT-proBNP, pg/ml 2,013 (794, 5,490) HbA1c, % 6.4 (5.8, 7.6) 4.540 Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² 430 (3.2) 45 (3.2) 491 (14.1) 460 491 (14.1) 460 491 (14.1) 460 491 (14.1) 460 491 (14.1) 460 491 (14.1) 460 491 (14.1) 460 491 (14.1) 460 461 (2.2) 461 (2.2) 461 (2.2) 461 (2.2) 461 (2.2) 461 (2.2) 461 (2.2) 461 (2.2) 461 (2.2) 461 (2.2) 461 (2.2) 461 (2.2)	II	1,914 (54.8)
Unknown 145 (4.1) Number of prior hospitalizations within 12 months of screening 0 2,173 (62.2) 1 886 (25.4) 2 2 435 (12.4) Vital signs on enrollment Systolic pressure, mm Hg 120 (110, 131) Diastolic pressure, mm Hg 72 (64, 80) Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % 30 (23, 35) NT-proBNP, pg/ml 2,013 (794, 5,490 HbA1c, % 6.4 (5.8, 7.6) Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² 30 (3.5) 45-60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	III	1,004 (28.7)
Number of prior hospitalizations within 12 months of screening 0	IV	87 (2.5)
0 2,173 (62.2) 1 886 (25.4) 2 435 (12.4) Vital signs on enrollment Systolic pressure, mm Hg 120 (110, 131) Diastolic pressure, mm Hg 72 (64, 80) Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % 30 (23, 35) NT-proBNP, pg/ml 2,013 (794, 5,490 Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² 30 <30	Unknown	145 (4.1)
1 886 (25.4) 2 435 (12.4) Vital signs on enrollment Systolic pressure, mm Hg 120 (110, 131) Diastolic pressure, mm Hg 72 (64, 80) Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % 30 (23, 35) NT-proBNP, pg/ml 2,013 (794, 5,490) Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² <30 122 (3.5) 30-45 304 (8.7) 45-60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	Number of prior hospitalizations within 12 m	onths of screening
2 435 (12.4) Vital signs on enrollment Systolic pressure, mm Hg 120 (110, 131) Diastolic pressure, mm Hg 72 (64, 80) Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % 30 (23, 35) NT-proBNP, pg/ml 2,013 (794, 5,490) HbA1c, % 6.4 (5.8, 7.6) Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² <30 122 (3.5) 30-45 304 (8.7) 45-60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	0	2,173 (62.2)
Vital signs on enrollment 120 (110, 131) Diastolic pressure, mm Hg 72 (64, 80) Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % 30 (23, 35) NT-proBNP, pg/ml 2,013 (794, 5,490 Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² 30 <30	1	886 (25.4)
Systolic pressure, mm Hg 120 (110, 131) Diastolic pressure, mm Hg 72 (64, 80) Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % 30 (23, 35) NT-proBNP, pg/ml 2,013 (794, 5,490 HebA1c, % 6.4 (5.8, 7.6) Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² 304 (8.7) 45-60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	2	435 (12.4)
Diastolic pressure, mm Hg 72 (64, 80) Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % LVEF, % 30 (23, 35) NT-proBNP, pg/ml 2,013 (794, 5,490) HbA1c, % 6.4 (5.8, 7.6) Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² <30	Vital signs on enrollment	
Heart rate, beats/min 72 (66, 81) Clinical measurements and laboratory results LVEF, % 30 (23, 35) NT-proBNP, pg/ml 2,013 (794, 5,490 HbA1c, % 6.4 (5.8, 7.6) Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² <30 122 (3.5) 30-45 304 (8.7) 45-60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	Systolic pressure, mm Hg	120 (110, 131)
Clinical measurements and laboratory results LVEF, % NT-proBNP, pg/ml HbA1c, % 6.4 (5.8, 7.6) Hemoglobin, g/dl Serum creatinine, mg/dl BUN, mg/dl Sodium, mmol eGFR, ml/min/m² <30 122 (3.5) 30-45 45-60 491 (14.1) >60 1,200 (34.3) Missing Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	Diastolic pressure, mm Hg	72 (64, 80)
LVEF, % 30 (23, 35) NT-proBNP, pg/ml 2,013 (794, 5,490) HbA1c, % 6.4 (5.8, 7.6) Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² <30 122 (3.5) 30-45 304 (8.7) 45-60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	Heart rate, beats/min	72 (66, 81)
NT-proBNP, pg/ml HbA1c, % 6.4 (5.8, 7.6) Hemoglobin, g/dl Serum creatinine, mg/dl BUN, mg/dl Sodium, mmol eGFR, ml/min/m² <30 122 (3.5) 30–45 45–60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	Clinical measurements and laboratory results	
HbA1c, % Hemoglobin, g/dl Serum creatinine, mg/dl BUN, mg/dl Sodium, mmol eGFR, ml/min/m² <30 30-45 45-60 491 (14.1) >60 1,200 (34.3) Missing Medication on enrollment ACE inhibitor/ARB 13.2 (11.8, 14.4) 13.2 (11.8, 14.4) 20.0 (16.0, 28.0) 139 (137, 141) 212 (3.5) 304 (8.7) 491 (14.1) ACE inhibitor/ARB 2,102 (60.2)	LVEF, %	30 (23, 35)
Hemoglobin, g/dl 13.2 (11.8, 14.4) Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² <30 122 (3.5) 30-45 304 (8.7) 45-60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	NT-proBNP, pg/ml	2,013 (794, 5,490
Serum creatinine, mg/dl 1.1 (0.9, 1.4) BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² 30 4 (8.7) 45-60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	HbA1c, %	6.4 (5.8, 7.6)
BUN, mg/dl 20.0 (16.0, 28.0) Sodium, mmol 139 (137, 141) eGFR, ml/min/m² <30 122 (3.5) 30-45 304 (8.7) 45-60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	Hemoglobin, g/dl	13.2 (11.8, 14.4)
Sodium, mmol 139 (137, 141) eGFR, ml/min/m² 30 30-45 304 (8.7) 45-60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	Serum creatinine, mg/dl	1.1 (0.9, 1.4)
eGFR, ml/min/m ² <30 122 (3.5) 30-45 304 (8.7) 45-60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	BUN, mg/dl	20.0 (16.0, 28.0)
<30	Sodium, mmol	139 (137, 141)
30–45 304 (8.7) 45–60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	eGFR, ml/min/m ²	
45–60 491 (14.1) >60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	<30	122 (3.5)
>60 1,200 (34.3) Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	30–45	304 (8.7)
Missing 1,377 (39.4) Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	45–60	491 (14.1)
Medication on enrollment ACE inhibitor/ARB 2,102 (60.2)	>60	1,200 (34.3)
ACE inhibitor/ARB 2,102 (60.2)	Missing	1,377 (39.4)
	Medication on enrollment	
Beta-blocker 2,894 (82.8)	ACE inhibitor/ARB	2,102 (60.2)
	Beta-blocker	2,894 (82.8)

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MRA 1,161 (33.2) ARNI 451 (12.9) Loop diuretic agent 2,139 (61.2) Hydralazine 193 (5.5) 475 (13.6) Digoxin Ivabradine 42 (1.2) Inotrope 14 (0.4) Number of medications 3.0 (2.0, 4.0) Site characteristics Physician specialty Family practice 219 (6.3) Internal medicine 266 (7.6) HF specialist 718 (20.5) Other cardiologist 2,086 (59.7) Number of HF patients managed annually 1,200 (480, 3,000)

Values are median (Q1, Q3) or n (%).

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ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; ARNI = angiotensin-receptor neprilysin inhibitor; BMI = body mass index; BUN = blood urea nitrogen; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; CRT = cardiac resynchronization therapy; eGFR = estimated glomerular filtration rate; HbA1c = Hemoglobin A1c; HF = heart failure; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid antagonist; VT/VF = ventricular tachycardia/ventricular fibrillation.

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 $\label{eq:TABLE 2} \textbf{Distribution of KCCQ-os Score by Patient Subgroup (N = 3,494)}$

Age, yrs		
<40	61.2 ± 26.1	62.5 (40.1, 85.9)
40–64	61.9 ± 25.0	63.9 (43.8, 83.3)
65–80	66.5 ± 22.6	68.8 (50.0, 84.9)
>80	63.4 ± 23.7	64.6 (44.8, 83.9)
Sex		
Male	65.9 ± 23.7	68.8 (47.9, 85.4)
Female	60.3 ± 23.8	61.5 (43.8, 80.2)
Race		
White	64.9 ± 23.4	67.7 (47.9, 84.4)
Black	60.5 ± 25.2	61.2 (41.7, 82.3)
Hispanic	59.1 ± 21.0	58.3 (43.8, 75.0)
Insurance status		
Managed care	68.2 ± 24.1	71.9 (51.6, 88.5)
Private insurance	70.2 ± 22.1	73.4 (55.7, 88.5)
Medicare	63.7 ± 23.3	65.1 (46.4, 82.3)
Medicaid	56.1 ± 24.6	54.2 (38.5, 76.6)
Highest level of education		
Less than high school	58.3 ± 23.2	57.3 (41.7, 76.6)
High school	62.5 ± 24.0	64.6 (44.8, 81.8)
Some college	65.3 ± 24.2	67.7 (46.9, 85.9)
4-yr college	67.8 ± 22.9	71.1 (51.3, 87.5)
Graduate or other professional degree	69.8 ± 22.2	75.0 (53.4, 87.5)
Total household income		
<\$25,000	57.1 ± 23.2	56.3 (40.6, 75.0)
\$25,000-\$49,999	63.1 ± 24.2	66.1 (44.3, 83.3)
\$50,000-\$74,999	68.8 ± 22.6	71.9 (53.1, 87.5)
\$75,000-\$99,999	69.9 ± 22.6	75.0 (56.3, 87.5)
\$100,000-\$149,999	73.5 ± 20.9	77.1 (58.9, 92.2)
\$150,00 or More	74.6 ± 21.0	83.3 (62.5, 89.6)
Employment status		
Working full-time	74.6 ± 21.9	80.2 (62.5, 91.7)
Working part-time	70.7 ± 22.6	77.1 (57.3, 88.5)
Disability for medical reasons	52.9 ± 23.7	52.1 (34.9, 70.8)
Not employed for other reasons	65.9 ± 22.6	68.8 (49.0, 84.4)

Values are mean \pm SD and median (Q1, Q3).

 $\label{eq:kccq-os} KCCQ\text{-}os = Kansas\ City\ Cardiomyopathy\ Questionnaire-overall\ summary\ score.$

TABLE 3

Model 2: Unadjusted and Adjusted Association Between Patient Characteristics and Medications at Enrollment with KCCQ-os (N = 3,494)

	Unadjusted Effect (95% CI)	p Value	Adjusted Effect (95% CI)	p Value
Age, 10-yr increments				
70 yrs	1.2 (0.5 to 1.8)	< 0.001	1.6 (0.6 to 2.6)	0.002
70 yrs	-0.2 (-1.7 to 1.3)	0.765	-5.5 (-7.5 to -3.4)	< 0.001
Female (ref: male)	-4.8 (-6.5 to -3.1)	< 0.001	-2.2 (-3.8 to -0.6)	0.007
Race/ethnicity (ref: white)				
Black	-4.5 (-6.7 to -2.2)	< 0.001	-0.4 (-2.5 to 1.8)	0.736
Other	0.1 (-2.8 to 3.1)	0.930	3.1 (0.3 to 5.9)	0.031
Hispanic (ref: non-Hispanic)	-3.4 (-6.1 to -0.6)	0.016	-4.0 (-6.6 to -1.3)	0.003
BMI to per 7.2 U	-3.3 (-4.0 to -2.5)	< 0.001	-2.5 (-3.3 to -1.8)	< 0.001
Total household income (ref: <\$25,000)				
\$25,000–\$49,999	4.8 (2.6 to 7.1)	< 0.001	0.7 (-1.4 to 2.8)	0.505
\$50,000-\$74,999	10.1 (7.5 to 12.7)	< 0.001	3.2 (0.7 to 5.7)	0.013
\$75,000–\$99,999	10.8 (7.4 to 14.2)	< 0.001	3.8 (0.6 to 7.0)	0.019
\$100,000-\$149,999	14.2 (10.6 to 17.8)	< 0.001	4.7 (1.3 to 8.1)	0.007
\$150,000 or more	15.3 (10.4 to 20.1)	< 0.001	4.7 (0.1 to 9.2)	0.045
Prefer not to answer	-0.9 (-2.6 to 0.7)	0.267	-1.8 (-3.3 to -0.2)	0.029
Employment status (ref: working full-time)				
Working part-time	-2.8 (-6.1 to 0.6)	0.107	-1.3 (-4.5 to 1.9)	0.417
Disability for medical reasons	-20.4 (-22.8 to -17.9)	< 0.001	-14.3 (-16.8 to -11.8)	< 0.001
Not employed for other reasons	-7.4 (-9.6 to -5.2)	< 0.001	-5.0 (-7.4 to -2.5)	< 0.001
COPD	-10.4 (-12.1 to -8.7)	< 0.001	-6.2 (-7.7 to -4.6)	< 0.001
Chronic kidney disease	-6.4 (-8.3 to -4.4)	< 0.001	-2.6 (-4.4 to -0.8)	0.005
Depression	-10.5 (-12.3 to -8.7)	< 0.001	-7.3 (-9.0 to -5.7)	< 0.001
Atrial fibrillation	-2.0 (-3.6 to -0.4)	0.015	-2.0 (-3.5 to -0.5)	0.011
Coronary artery disease	-0.9 (-2.6 to 0.7)	0.267	-1.8 (-3.3 to -0.2)	0.029
Prior HF hospitalization in past year (ref: 0)				
1	-5.2 (-7.1 to -3.4)	< 0.001	-2.8 (-4.5 to -1.2)	0.001
2	-13.2 (-15.6 to -10.7)	< 0.001	-6.6 (-8.9 to -4.3)	< 0.001
Pulse, per 12.5 beats/min	-4.0 (-4.8 to -3.2)	< 0.001	-2.4 (-3.1 to -1.7)	<0.001
LVEF, per 8%	2.2 (1.5 to 3.0)	< 0.001	1.1 (0.4 to 1.9)	0.003
ARNI	1.2 (-1.3 to 3.6)	0.3474	3.9 (1.5 to 6.4)	0.002

Unadjusted Effect (95% CI) Adjusted Effect (95% CI) p Value p Value ACEi/ARB 3.6 (2.0 to 5.2) 3.6 (2.0 to 5.3) < 0.001 < 0.001 Loop diuretic agent -8.2 (-9.8 to -6.6) < 0.001 -4.4 (-6.0 to -2.9) < 0.001 0.033 Ivabradine -10.2 (-17.2 to -3.2) 0.004 -6.9 (-13.2 to -0.6) Inotrope -25.8 (-37.9 to -13.6) < 0.001 -17.0 (-27.9 to -6.1) 0.002 Page 20

Abbreviations as in Table 1.

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