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Factors Associated With Exacerbation of Heart Failure Include Treatment Adherence and Health Literacy Skills

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Abstract

We determined the factors associated with exacerbation of heart failure, using a cohort ($n = 192$) nested within a randomized trial at a university-affiliated ambulatory practice. Factors associated with emergency or hospital care included left ventricular ejection fraction, hematocrit and serum sodium levels, refill adherence, and the ability to read a prescription label. Refill adherence of <40% was associated with a threefold higher incidence of hospitalization for heart failure than a refill adherence of $\geq 80\%$ ($P = 0.002$). In multivariable analysis, prescription label reading skills were associated with a lower incidence of heart failure–specific emergency care (incidence rate ratio, 0.76; 95% confidence interval (CI), 0.19–0.69), and participants with adequate health literacy had a lower risk of hospitalization for heart failure (incidence rate ratio, 0.34; 95% CI, 0.15–0.76). We conclude that inadequate treatment adherence and health literacy skills are key factors in the exacerbation of heart failure. These findings emphasize the need for careful instruction of patients about their medications.

Patients with heart failure often require costly emergency or hospital care. In the United States, total annual health-care costs of the 5.3 million people with heart failure exceed \$34.8 billion.¹ These costs derive largely from exacerbations requiring expensive emergency visits and hospitalizations. In 2004, heart failure was the second most expensive disease billed to Medicare, involving 5.8% of Medicare's total hospital expenditures.² In 2005, it accounted for 59.3% of estimated direct costs, largely from more than >1 million hospital admissions.¹ Studies of factors associated with clinical exacerbation requiring urgent care services, such as emergency department visits and hospitalizations, have primarily examined either

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CONFLICT OF INTEREST

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socioeconomic or biomedical constructs but not both in the same analysis. Socioeconomic studies often include factors such as income, insurance status, marital status, and some measure of health-related quality of life.^{3,4} Biomedical studies often target clinical laboratory tests and cardiovascular-specific tests such as plasma brain natriuretic peptide concentration and assessment of left ventricular ejection fraction.^{5–8} Demographic factors (age, gender, and race) and the New York Heart Association (NYHA) class are often considered in each type of analysis. However, until recently, socioeconomic and biomedical factors have seldom been simultaneously assessed.^{9,10} In addition, assessments of treatment adherence and health literacy skills are rarely considered in any analysis, even though these patient abilities are essential for effective self-management of chronic illness and are important for improved health outcomes.^{11–13}

Guided by a framework that links the health system and patient characteristics to self-care and health outcomes,¹⁴ we measured a comprehensive set of variables in a cohort of 192 participants nested within a randomized controlled trial to ascertain patient characteristics and risk factors associated with clinical deterioration requiring emergency department visits or hospitalization. Variables included demographic classification, socioeconomic status, cardiac performance, functional status, results of laboratory tests, and treatments. We also measured treatment adherence and health literacy skills. We then simultaneously assessed the association of socioeconomic and biomedical factors, treatment adherence, and health literacy with the incidence of emergency and hospital care. In doing so, we determined factors independently associated with clinical exacerbation of heart failure, as well as the relative strengths of their associations. Factors amenable to intervention could be targeted to mitigate their impact on health outcomes.

RESULTS

Participant characteristics by health-care encounter type and for all participants are shown in Table 1. The mean age of the 192 participants was 62.6 ± 8.8 years; 127 (66.1%) participants were women and 100 (52.1%) were African Americans. The mean education level was 11 ± 3 years, and 136 participants (71%) had adequate health literacy. Income was perceived to be sufficient to “get by” for 124 (64%) of the participants. NYHA classification was as follows: I, 38 (19.8%); II, 78 (40.6%); III, 67 (34.9%); and IV, 9 (4.7%). Of the 192 participants, 59 (30.7%) had not needed either an emergency department visit or hospitalization. Among participants, 131 (68.2%) had at least one emergency department visit for any cause (mean (SD), 3.3 (5.5)), and 23 (12.0%) had at least one heart failure–specific emergency department visit (mean (SD), 0.4 (1.5)). In addition, 86 (44.8%) participants had at least one hospital admission (mean (SD), 1.2 (2.1)), and in 21 (10.9%) of these, heart failure was the primary cause for admission (mean (SD), 0.2 (0.7)).

Hypertension (in 96.9% of participants) was the most common comorbidity, followed by coronary artery disease (76.0%) and diabetes (68.2%). Depression was observed in 4.9% of the participants. Compared with participants with an all-cause utilization event (emergency visit or hospitalization), those who experienced a heart failure–specific event were more likely to be female; African American; have fewer years of formal education; be unmarried and live alone; have poorer functional status per the Kansas City Cardiomyopathy Questionnaire (KCCQ); have lower scores on the Short Test of Functional Health Literacy in Adults (STOFHLA); carry Medicaid insurance; have a lower ejection fraction and a higher amino-terminal pro-brain natriuretic peptide (NT-proBNP) concentration; have a diagnosis of diabetes, atrial fibrillation, or depression; have lower medication adherence; and be on treatment with digoxin or a loop diuretic.

The most commonly prescribed medications were angiotensin-converting enzyme inhibitors (71.4% of participants), β -adrenergic antagonists (62.5%), and loop diuretics (61.5%). The overall Medication Event Monitoring System (MEMS) “taking adherence” score indicated that on average participants took only two-thirds of their prescription cardiovascular medications (65.5% (95% confidence interval (CI) 60.8–70.2)). Taking adherence was lower in participants who experienced hospitalizations or emergency visits for heart failure (54.0 and 49.2%, respectively) as compared to those experiencing hospitalizations or emergency visits for all causes (61.1 and 63.6%, respectively). The MEMS “scheduling adherence” score, which is indicative of day-to-day variation in the timing of medication administration, was 45.4% (range 41.3–49.6%). Refill adherence for all participants was 100.1%, with means ranging from 87.8 to 122% and, consistent with MEMS taking-adherence scores, was lower in participants experiencing hospitalization or emergency department visits for heart failure (84.2 and 82.9%, respectively) as compared to all-cause hospitalization or emergency department use (92.9 and 100.0%, respectively).

Emergency department data are shown in Table 2. Using the value of the χ^2 -test, the rank order of factors associated with all-cause emergency department visits was Medicaid insurance, NYHA class, left ventricular ejection fraction, refill adherence, prescription label reading score, hematocrit level, race, health-related quality of life (per the Chronic Heart Failure Questionnaire), and serum sodium level. Factors associated with heart failure–specific emergency department visits were prescription label reading score, perceived income adequacy, NYHA class, Medicaid insurance, serum potassium level, and the functional status score from the KCCQ. Of the factors associated with emergency visits, those amenable to intervention included improving medication adherence; providing support for patients who have difficulties in interpreting prescription labels; and maintaining hematocrit and serum electrolyte homeostasis. The incidence rate ratio for heart failure–specific emergency visits was 64% lower among those who could accurately read and interpret prescription labels relative to those who had an error in label interpretation (incidence rate ratio 0.36; 95% CI 0.19–0.69).

Hospitalization data are shown in Table 3. The rank order of factors associated with all-cause hospitalizations was Medicaid insurance, perceived income adequacy, hematocrit level, prescription label reading score, refill adherence, serum sodium, age, NYHA class, ejection fraction, cognitive speed of processing, and depression. Factors associated with heart failure–specific hospitalization included depression, perceived income adequacy, NYHA class, health literacy as measured using the STOFHLA, and cognitive speed of processing. Participants with adequate health literacy had 64% fewer hospital admissions for heart failure (incidence rate ratio, 0.34; 95% CI, 0.15–0.76). The factors associated with hospitalization that were amenable to intervention were similar to those listed earlier for emergency encounters but also included treatment of depression.

We explored the univariate relationships between incidence of health-care utilization and refill adherence and the ability to read prescription labels (Figures 1 and 2). As shown in Figure 1a, the rate of emergency department visits and hospitalizations decreased as refill adherence increased. For heart failure–specific utilization (Figure 1b), the relationship between health-care utilization and refill adherence was variable for emergency department visits, but the annual rate of hospitalization for heart failure was threefold higher in those with a refill adherence of <40% than in those with adequate supplies of their medications, i.e., $\geq 80\%$ ($P = 0.002$). Figure 2 shows the relationship between health-care utilization and the ability to read and interpret a prescription label. As the ability to interpret information on the prescription label increased (Figure 2a), the rate of emergency department visits and hospitalization decreased, but this was not statistically significant. For heart failure–specific utilization of emergency or hospital services (Figure 2b), participants who accurately interpreted the entire prescription label (scored all correct responses) had 6-fold fewer emergency visits ($P < 0.001$).

and 11-fold fewer hospitalizations for heart failure than those who were unable to interpret a prescription label ($P < 0.001$).

DISCUSSION

Factors associated with clinical exacerbation of heart failure included left ventricular ejection fraction, hematocrit, serum sodium level, medication adherence, and the ability to read a prescription label. Factors uniquely associated with an emergency visit included race and health-related quality of life, and factors uniquely associated with hospitalization included perceived income adequacy, depression, age, and cognitive speed of processing. The incidence of hospitalization for heart failure was greater in participants who received inadequate supplies of their cardiovascular medications from the pharmacy and in those lacking the ability to accurately interpret a prescription label. Controlling for clinically relevant factors, participants with adequate health literacy had a lower risk of hospitalization for heart failure.

Measures of health literacy skills were retained in all four exploratory models. Health literacy is a multifaceted concept that includes core abilities related to reading, understanding, and making decisions about information needed for self-managing chronic illness.¹⁵ It has been shown to be associated with successful aspects of self-management such as medication adherence¹⁶ and health-care utilization.^{11,17,18} A recent study by Metlay and colleagues indicates important risks in poorly instructed patients who were prescribed warfarin.¹⁹ Of particular interest in our study is that a patient's ability to read and comprehend health information is more strongly associated with exacerbation of heart failure than factors such as ejection fraction or NT-proBNP, which are conventionally considered to be important in predictive biomedical models. This may reflect the fact that the self-management of complex illnesses such as congestive heart failure places heavy demands on patients' literacy skills, yet they receive inadequate support for these tasks because both written and spoken instructions are often difficult to understand.²⁰

Treatment adherence was also an important predictor of clinical deterioration. In our previous study of all 314 study participants (from both the intervention ($n = 112$) and usual care groups ($n = 192$)), we conducted a multivariable analysis controlling for participant functional class, counts of prescribed drugs, ejection fraction, and comorbidities.¹³ Taking adherence (measured electronically using MEMS) was an independent predictor of the numbers of hospitalizations for heart failure, cardiovascular reasons, and for all causes, as well as emergency department visits for cardiovascular reasons. However, in this analysis, although refill adherence was associated with the health-care utilization outcomes of interest, taking adherence was not. The greater importance of refill adherence, after controlling for key social and biomedical factors, suggests that access to chronically administered medications over the course of a year is more important than the day-to-day execution of the prescription regimen (as measured electronically).

Awareness of the determinants of exacerbation is a key component of the management of chronic diseases such as heart failure. However, the factors potentially amenable to intervention often do not have simple solutions. Bringing about changes in socioeconomic factors such as health insurance and income would require important policy changes. Increasing hematocrit and serum electrolyte levels may also involve complicated interventions aimed at the causes of these imbalances. In contrast, improvements to medication adherence and improving medication instruction for patients are more readily attainable objectives.¹³ After controlling for demographic and socioeconomic patient characteristics, ejection fraction, laboratory tests, and functional status, the factors associated with clinical exacerbation that could be targeted for intervention included improving medication adherence and making medication instructions easier for patients to understand.

Patients with heart failure are especially at risk because of the burden of concomitant chronic diseases such as hypertension, coronary artery disease, and diabetes, as well as the large number of accompanying medications that must be managed. Our study participants were further compromised by their limited social and economic resources. Indeed, even after controlling for insurance type, perceived income adequacy remained associated with clinical exacerbation resulting in heart failure–specific utilization of emergency and hospital services. The complicating effects of depression, which was associated with hospitalization for heart failure and all causes, have been observed by others as well.^{21,22} Given that medications are commonly used to treat depression, its successful treatment would also require attention to treatment adherence and careful medication instructions for the patient. Finally, the Institute of Medicine has identified issues such as medication management and health literacy that are central to improving the treatment of chronic disease.²³ In addition to their chronic disease and treatment burdens, the patients in our study often had low health literacy, which posed a further challenge to their ability to succeed at self-care.

Our study has several limitations. Participants were recruited from a health services center that serves a predominantly indigent population, making our findings less generalizable to other settings of care. Indeed, the generalizability of our study results could be affected by the selection bias that can occur in clinical trials. Therefore, the patients in this study may not be representative of the broad population of heart failure patients. In addition, although the number of cohort participants was small, we had data that were broad in scope. Finally, the numbers of events were sparse for heart failure–specific events of emergency and hospital services utilization. Future studies should confirm our results. Notwithstanding these limitations, we identified a number of important variables associated with these utilization events. We conclude that a variety of important sociodemographic and economic characteristics and clinical factors are associated with deterioration in patients with heart failure. Treatment adherence and health literacy skills are among the most relevant factors in costly health-care utilization. This argues for careful instruction of patients about adherence to their chronically administered cardiovascular medications, in terms that they can understand.

METHODS

Study population

The study population has previously been described.^{13,24} Participants were randomly assigned to the usual care arm of a randomized controlled trial conducted from February 2001 to June 2004. The study site was Wishard Health Services, a city–county health system that serves socioeconomically disadvantaged and medically vulnerable patients in Indianapolis, Indiana, and the surrounding community. The Indiana University–Purdue University and the University of North Carolina at Chapel Hill institutional review boards approved the study.

We used the electronic records from the Regenstrief Medical Records System (RMRS)²⁵ to identify clinically stable patients from the general internal medicine practice, the cardiology clinic, and the general medicine service of Wishard Health Services (prior to discharge). Patients were considered eligible for inclusion if they had received a diagnosis of heart failure that could be confirmed by their primary care physician; were age 50 years or older; planned to use Wishard Health Services for all of their care (including Wishard's pharmacy to obtain their medications); were prescribed an angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, β -adrenergic antagonist, diuretic, digoxin, or aldosterone antagonist such as spironolactone; were not planning to use a pillbox; had telephone access; and could hear in the range of normal conversation. Patients with dementia were excluded.

Study design

The cohort was the usual-care arm of a randomized trial. As designed *a priori*, we randomized a greater number of participants ($n = 192$) to the usual-care group so that it could serve as a prospective cohort with which to study risk factors associated with the clinical deterioration of heart failure. Follow-up interviews and other assessments, including body weight and blood pressure, were carried out at 6 and 12 months, and follow-up ended at 12 months. The funding source had no role in the study design, data collection, or interpretation of the results.

End points

Incidents of clinical exacerbations were assessed over 12 months using data relating to emergency department visits and hospital admissions from the RMRS and from participants' charts. Data were verified by research assistants during participant visits. We examined heart failure-specific and all-cause emergency department visits and hospitalizations. These end points were adjudicated by a registered nurse as the abstractor, using a previously validated methodology.²⁶

Independent variables

We examined a broad array of independent variables, including demographic and socioeconomic characteristics, health insurance, functional performance, cardiac function, vital signs, hematology, serum chemistry, health-related quality of life, health literacy skills, comorbidities, and medication adherence. Demographic variables (age, sex, self-reported race, and marital status) and socioeconomic variables (health insurance status, education, and income), body mass index, blood pressure, cardiac and functional performance, health-related quality of life, and health literacy skills assessment were obtained at baseline interviews. Diagnoses, prescription medications, and hematology and serum chemistry data were extracted from the RMRS.

Socioeconomic variables included health insurance, years of formal education, and perceived income adequacy. We have found it difficult to accurately measure actual annual household income by patient report in our indigent patient care setting for two primary reasons. First, patients with a household income exceeding the service limit for indigent care at Wishard Health Services could disqualify themselves from receiving subsidized care. Second, low-income patients often have a mixture of taxable and nontaxable jobs that account for their income. We therefore used perceived income adequacy, asking participants whether their annual household income was sufficient, just enough to get by, or not enough to get by. This subjective method has previously been used, with results that are consistent with objective measures of income.^{27,28}

Cardiac performance was measured using Doppler echocardiography performed at the baseline functional assessment, along with NYHA classification. Transthoracic two-dimensional and Doppler echocardiogram was performed using commercially available echograph ATL 5000 or Agilent 5500 with a phased-array, broadband transducer with a frequency range of 3–5 MHz. NT-proBNP concentrations were assessed at baseline (Elecsys NT-proBNP; Roche Diagnostics, Indianapolis, IN). Serum sodium, potassium, albumin, and creatinine; urea nitrogen; and hematocrit were measured at baseline by the laboratories of Wishard Health Services.

Disease-specific quality of life was analyzed using the Chronic Heart Failure Questionnaire.²⁹ This 16-item instrument has four dimensions: fatigue, dyspnea, emotion, and mastery. Scores on each question, ranging from 1 (worst function) to 7 (best function), were summed to form scales. Because we wished to determine symptom burden on a patient's function, we also used the KCCQ.³⁰ The KCCQ is a 23-item instrument that measures the physical

limitations, symptoms, self-efficacy, quality of life, and social limitations due to congestive heart failure. Depression was assessed using the short form of the Geriatric Depression Rating Scale, which is a validated 15-item screening test for depression in older adults.³¹ This instrument has been used in numerous studies to screen for depression in older adult outpatients.³² We used a score of 5 as the cutoff point for depression on this 15-point scale.³³

Health literacy was measured in two ways. First, we used the STOFHLA, the scores for which range from 0 to 36 (0–16 = inadequate health literacy, 17–22 = marginal literacy, and 23–36 = adequate literacy).³⁴ Second, literacy directly related to comprehension of medication instruction was measured by the prescription label reading test that we have used previously.³⁵ This test assesses the participant's ability to accurately interpret text and numerical information using a standardized prescription label. Scores range from 0 (no correct responses) to 2 (accurately read and interpreted prescription instructions), with 1 point awarded for partially correct responses. Correlation between the STOFHLA and the prescription label reading test was good ($r = 0.51$).³⁶ Given that health literacy is affected by cognitive performance;³⁷ we also assessed the speed of cognitive processing, using letter- and pattern-comparison tests at baseline. These timed written tests requested that participants rapidly determine the similarity of letters and patterns.³⁸ Because the letter comparison (maximum score = 42) and pattern comparison (maximum score = 30) are correlated ($r = 0.79$), we used the mean of these scores.³⁹

Prescription medication acquisition was ascertained using data from the RMRS and was verified by self-report at baseline interviews. We assessed adherence to all cardiovascular medications for 12 months, using electronic monitoring of medication with MEMS V prescription container lids (AARDEX, Untermüli, Switzerland). Refill adherence was measured for 12 months as the medication possession ratio, using prescription records from the RMRS to determine supplies of medications received by patients from the pharmacy relative to the amount prescribed by their physicians.^{40,41} Values of refill adherence generally range from 0 to 100% of prescribed quantities obtained at the pharmacy but may exceed 100% when patients obtain medications from multiple sources, including drug samples (which were considered). Patients obtaining at least 80% of their medications are considered to have received an adequate supply for chronic cardiovascular treatment regimens. The correlation between refill adherence and MEMS taking adherence was weak ($r = 0.12$).

Analysis

We considered factors known to be associated with clinical exacerbation of heart failure and also those for which we believed that an association was plausible. Based on data relating to the use of emergency and hospital services, we formed four groups of dependent variables: (i) all-cause emergency department visits, (ii) heart failure-specific emergency department visits, (iii) all-cause hospitalizations, and (iv) heart failure-specific hospitalizations. For each of the four dependent variables, over a period of 12 months, we then compared patients who experienced an emergency visit or hospitalization with those who did not, using *t*-tests for continuous variables and chi-square tests for categorical variables. We also compared electronic and refill adherence for overall cardiovascular drug use.

Incidents of clinical exacerbations leading to emergency department visits and hospitalizations were analyzed using log-linear regression to model the individual and overall counts of emergency department visits and hospital admissions. To accommodate the unequal durations of follow-up of study participants, we incorporated the logarithmic duration of follow-up into the log-linear model as an offset parameter. After examining the model fit, we determined that the Poisson distribution best fit the hospitalization data, but a negative binomial distribution best fit the emergency department data. Independent variables were selected using a stepwise model selection process. For highly correlated variables ($r > 0.2$), we selected the variable with

the highest χ^2 value. Regression parameters and standard errors were obtained from the final models. Incidence rate ratios were calculated by exponentiating the parameter estimates. Because our analysis was exploratory, we retained in each of the four models those variables with $P < 0.1$. Variables associated with each of the four dependent variables at $P < 0.1$ were ranked by χ^2 value to show their relative importance. The analysis was performed using SAS PROC GENMOD, version 9.1 (SAS Institute, Cary, NC).

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Figure 1. The effect of refill adherence on the annual rate of (a) all-cause and (b) heart failure (HF)-specific emergency department (ED) visits and hospitalizations.

Figure 2. The effect of the ability to accurately read and interpret a standard prescription container label on the annual rate of (a) all-cause and (b) heart failure (HF)-specific emergency department (ED) visits and hospitalizations.

Table 1

Baseline comparison of participant characteristics by utilization type

Variable	All-cause hospitalizations (<i>n</i> = 86)	Heart failure-specific hospitalizations (<i>n</i> = 21)	All-cause emergency department visits (<i>n</i> = 131)	Heart failure-specific emergency department visits (<i>n</i> = 23)	All participants (<i>n</i> = 192)
Age, mean (SD), years	64.2 (9.1)	65.2 (10.4)	63.5 (9.0)	66.6 (10.5)	63.2 (8.9)
<i>Sex, no. (%)</i>					
Women	60 (69.8)	16 (76.2)	91 (69.5)	19 (82.6)	128 (66.7)
Men	26 (30.2)	5 (23.8)	40 (30.5)	4 (17.4)	64 (33.3)
<i>Race, no. (%)</i>					
Black	48 (55.8)	14 (66.7)	72 (55.0)	17 (73.9)	99 (51.6)
White	35 (40.7)	6 (28.6)	56 (42.8)	5 (21.7)	90 (46.9)
Other	3 (3.5)	1 (4.8)	3 (2.3)	1 (4.4)	3 (1.6)
Adequate income, no. (%) ^a	61 (70.9)	18 (85.7)	87 (66.4)	20 (87.0)	122 (63.5)
Education, mean (SD), years	9.9 (2.6)	9.7 (2.3)	10.4 (2.6)	9.9 (2.2)	10.6 (2.7)
Married, no. (%)	24 (27.9)	4 (19.0)	37 (28.2)	5 (21.7)	52 (27.1)
Live alone, no. (%)	31 (36.9)	9 (45.0)	45 (35.2)	11 (47.8)	72 (38.5)
CHQ total score ^b	3.7 (1.2)	3.7 (1.3)	3.8 (1.3)	3.6 (1.3)	3.9 (1.2)
KCCQ functional status score ^c	51.4 (22.9)	47.3 (21.2)	55.1 (23.2)	48.6 (20.1)	57.9 (22.7)
STOFHLA, no. (%) ^d	54 (66.7)	7 (36.8)	85 (67.5)	8 (38.1)	131 (70.8)
Prescription label reading score ^e	1.4 (0.7)	0.9 (0.8)	1.5 (0.7)	1.0 (0.8)	1.5 (0.7)
Comparison task score ^f	16.3 (5.2)	13.7 (5.3)	16.9 (5.3)	14.0 (5.3)	17.1 (5.5)
<i>Insurance type, no. (%)</i>					
Medicare	56 (65.1)	16 (76.2)	82 (62.6)	16 (69.6)	109 (56.8)
Medicaid	41 (47.7)	13 (61.9)	54 (41.2)	14 (60.9)	70 (36.5)
<i>NYHA class, no. (%)</i>					
I	11 (12.8)	0 (0.0)	23 (17.6)	0 (0.0)	38 (19.8)
II	29 (33.7)	9 (42.9)	50 (38.2)	8 (34.8)	78 (40.6)
III	39 (45.4)	10 (47.6)	50 (38.2)	12 (52.2)	67 (34.9)
IV	7 (8.1)	2 (9.5)	8 (6.1)	3 (13.0)	9 (4.7)

Variable	All-cause hospitalizations (<i>n</i> = 86)	Heart failure-specific hospitalizations (<i>n</i> = 21)	All-cause emergency department visits (<i>n</i> = 131)	Heart failure-specific emergency department visits (<i>n</i> = 23)	All participants (<i>n</i> = 192)
Ejection fraction, (SD)	0.51 (0.16)	0.44 (0.18)	0.51 (0.16)	0.48 (0.19)	50 (16)
NT-proBNP, mean (SD), pg/ml	1,270 (2,591)	1,566 (1,994)	1,214 (2,375)	2,264 (4,448)	1,406 (3,486)
Log-transformed proBNP, mean (SD), pg/ ml	6.2 (1.4)	6.8 (1.1)	6.0 (1.6)	6.7 (1.4)	6.0 (1.6)
Weight, mean (SD), kg	90.0 (24.5)	95.8 (29.4)	91.6 (24.3)	92.7 (26.5)	92.4 (24.4)
Body mass index, mean (SD), kg/m ²	33.0 (8.7)	36.3 (10.9)	34.3 (10.6)	35.5 (10.1)	34.1 (10.2)
Systolic blood pressure, mean (SD), mm Hg	135.4 (22.9)	135.8 (25.8)	134.7 (25.6)	138.3 (23.8)	135.4 (25.2)
Diastolic blood pressure, mean (SD), mm Hg	69.4 (14.5)	69.9 (14.2)	70.5 (16.0)	69.5 (13.8)	70.5 (15.6)
Hematocrit, mean (SD), %	37.0 (5.9)	36.8 (5.8)	37.1 (5.7)	38.7 (7.0)	37.6 (5.7)
Hemoglobin, mean (SD), g	12.2 (1.9)	12.0 (1.9)	12.2 (1.9)	12.6 (2.2)	12.4 (1.9)
Serum creatinine, mean (SD), mg/dl	1.3 (0.8)	1.2 (0.2)	1.3 (0.8)	1.2 (0.2)	1.2 (0.7)
Blood urea nitrogen, mean (SD), mg/dl	22.0 (14.5)	24.1 (13.2)	21.3 (13.8)	24.8 (12.0)	20.6 (13.0)
Serum albumin, mean (SD), g/dl	3.7 (0.4)	3.6 (0.5)	3.7 (0.4)	3.6 (0.5)	3.7 (0.4)
Serum sodium, mean (SD), mEq/dl	139.4 (3.0)	139.1 (2.7)	139.1 (3.3)	138.5 (3.9)	139.3 (3.5)
Serum potassium, mean (SD), mEq/dl	4.3 (0.5)	4.2 (0.4)	4.3 (0.5)	4.2 (0.5)	4.3 (0.5)
Hypertension, no. (%)	84 (97.7)	21 (100)	128 (97.7)	23 (100)	186 (96.9)
Coronary artery disease, no. (%)	69 (80.2)	18 (85.7)	98 (74.8)	19 (82.6)	146 (76.0)
Diabetes, no. (%)	69 (80.2)	19 (90.5)	98 (74.8)	22 (95.6)	131 (68.2)
Stroke, no. (%)	13 (15.1)	3 (14.3)	24 (18.3)	2 (8.7)	29 (15.1)
COPD, no. (%)	39 (45.4)	10 (47.6)	55 (42.0)	11 (47.8)	67 (34.9)
Atrial fibrillation, no. (%)	13 (15.1)	5 (23.8)	18 (13.7)	6 (26.1)	27 (14.0)
Hyperlipidemia, no. (%)	22 (25.6)	6 (28.6)	33 (25.2)	6 (26.1)	47 (24.5)
Depression, mean (SD)	5.3 (4.0)	6.4 (4.4)	5.2 (3.9)	6.1 (4.4)	4.9 (3.7)
Emergency department visits, 1 year, mean (SD)	6.2 (7.1)	8.7 (8.6)	4.8 (6.1)	10.0 (10.3)	3.3 (5.5)
Hospital admissions, 1 year, mean (SD)	2.8 (2.3)	3.8 (2.8)	1.8 (2.3)	3.7 (2.9)	1.3 (2.1)
Chronic medications, <i>n</i> (SD)	12 (4.3)	11 (3.4)	12 (4.5)	11 (4.4)	11 (4.5)
MEMS taking adherence, % (95% CI) ^g	61.1 (54.5–68.8)	54.0 (38.7–69.4)	63.6 (57.7–69.5)	49.2 (35.0–63.5)	65.5 (60.8–70.2)

Variable	All-cause hospitalizations (<i>n</i> = 86)	Heart failure-specific hospitalizations (<i>n</i> = 21)	All-cause emergency department visits (<i>n</i> = 131)	Heart failure-specific emergency department visits (<i>n</i> = 23)	All participants (<i>n</i> = 192)
MEMS scheduling adherence, % (95% CI) ^g	42.5 (36.0–49.0)	40.3 (27.2–53.3)	44.3 (39.2–49.4)	34.5 (23.2–45.9)	45.4 (41.3–49.6)
Refill adherence, % (95% CI) ^h	92.9 (75.3–111)	84.2 (69.2–99.2)	100.0 (80.8–122)	82.9 (69.4–96.3)	100.1 (87.8–122)
<i>Medication type, no. (%)</i>					
ACE inhibitor	63 (73.3)	16 (76.2)	93 (71.0)	17 (73.9)	137 (71.4)
ARB	13 (15.1)	2 (9.5)	17 (13.0)	2 (8.7)	22 (11.5)
β-Blocker	51 (59.3)	12 (57.1)	82 (62.6)	13 (56.5)	120 (62.5)
Digoxin	24 (27.9)	8 (38.1)	36 (27.5)	8 (34.8)	52 (27.1)
Loop diuretic	57 (66.3)	17 (81.0)	84 (64.1)	17 (73.9)	118 (61.5)
Thiazide diuretic	14 (16.3)	4 (19.1)	20 (15.3)	4 (17.4)	29 (15.1)
Spironolactone	16 (18.6)	3 (14.3)	23 (17.6)	2 (8.7)	31 (16.2)

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CHQ, Chronic Heart Failure Questionnaire; CI, confidence interval; COPD, chronic obstructive pulmonary disease; KCCQ, Kansas City Cardiomyopathy Questionnaire; MEMS, Medication Event Monitoring System; NT-proBNP, amino-terminal pro-brain natriuretic peptide; NYHA, New York Heart Association; STOFHLA, Short Test of Functional Health Literacy in Adults.

^aPerceived income adequacy assessed by asking whether participant has an income that is comfortable, just enough to get by, or not even enough to get by.^{27,28}

^bFrom the CHQ.²⁹

^cFrom the KCCQ.³⁰

^dHealth literacy measured using the STOFHLA.³⁴

^eAbility to read text on a prescription medication container label.³⁵

^fSpeed of cognitive process as the mean of letter and pattern comparison task scores.³⁸

^gAssessment of MEMS adherence was performed over the 12-month study period for all cardiovascular medications.

^hAssessment of refill adherence performed over the 12-month study period for all cardiovascular medications.

Table 2

Baseline factors associated with emergency department visits

Variable ^a	χ^2	P value	Incidence rate ratio	95% CI
<i>All-cause</i>				
Medicaid insurance	7.06	0.008	1.67	1.14–2.44
NYHA class				
III vs. I and II	0.00	0.984	1.00	0.66–1.49
IV vs. I and II	5.73	0.017	2.55	1.18–5.50
Left ventricular ejection fraction, 0.1-point increment	5.36	0.021	1.15	1.02–1.30
Refill adherence, 10-point increment	4.89	0.027	0.07	0.01–0.74
Prescription label reading score, 1-point increment ^b	4.84	0.028	0.76	0.59–0.97
Hematocrit, 5-point increment	4.07	0.044	0.85	0.72–0.99
Race, African American	3.79	0.051	1.51	1.00–2.29
CHQ total score, 2-point increment ^c	3.56	0.059	0.71	0.50–1.01
Serum sodium, 10-point increment	3.11	0.078	0.49	0.22–1.08
<i>Heart failure-specific</i>				
Prescription label reading score, 1-point increment ^b	9.70	0.002	0.36	0.19–0.69
Income adequacy ^d				
Just enough vs. sufficient	0.08	0.778	1.23	0.30–5.06
Not enough vs. sufficient	6.07	0.014	0.09	0.01–0.61
NYHA class				
III vs. I and II	4.49	0.034	3.60	1.10–11.74
IV vs. I and II	5.21	0.022	7.83	1.34–45.81
Medicaid insurance	4.82	0.028	3.29	1.14–9.51
Serum potassium, 0.5-point increment	3.82	0.051	0.54	0.29–1.00
KCCQ functional status score, 20-point increment ^e	3.30	0.069	0.62	0.37–1.04

CHQ, Chronic Heart failure Questionnaire; CI, confidence interval; KCCQ, Kansas City Cardiomyopathy Questionnaire; NYHA, New York Heart Association.

^aFactors were assessed at baseline with the exception of treatment adherence, which was assessed over 12 months.

^bAbility to read text on a prescription medication container label.³⁵

^cFrom the CHQ.²⁹

^dPerceived income adequacy assessed by asking whether participant has an income that is comfortable, just enough to get by, or not even enough to get by.^{27,28}

^eFrom the KCCQ.³⁰

Table 3

Baseline factors associated with hospitalizations

Variable ^a	χ^2	P value	Incidence rate ratio	95% CI
<i>All-cause</i>				
Medicaid insurance, yes	21.28	<0.001	1.99	1.48–2.66
Income adequacy ^b				
Just enough vs. sufficient	3.02	0.082	0.70	0.48–1.05
Not enough vs. sufficient	16.56	<0.001	0.41	0.27–0.63
Hematocrit, 5-point increment	14.77	<0.001	0.76	0.66–0.87
Prescription label reading score, 1-point increment ^c	10.76	0.001	0.68	0.54–0.86
Refill adherence, 10-point increment	7.63	0.005	0.05	0.01–0.41
Serum sodium, 10-point increment	7.26	0.007	0.48	0.28–0.82
Age, 10-year increment	5.98	0.014	1.28	1.05–1.55
NYHA class				
III vs. I and II	0.10	0.753	1.06	0.75–1.49
IV vs. I and II	5.70	0.017	1.82	1.11–2.97
Left ventricular ejection fraction, 0.1-point increment	4.75	0.029	1.12	1.01–1.23
Comparison task score, 1-point increment ^d	4.40	0.036	1.04	1.00–1.07
Depression	3.99	0.046	1.05	1.00–1.10
<i>Heart failure-specific</i>				
Depression	25.28	<0.001	1.27	1.16–1.40
Income adequacy				
Just enough vs. sufficient	0.15	0.694	0.83	0.32–2.09
Not enough vs. sufficient	13.27	0.003	0.05	0.01–0.25
NYHA class				
III vs. I and II	0.29	0.589	0.81	0.37–1.76
IV vs. I and II	11.60	<0.001	4.99	1.98–12.60
STOFHLA score, adequate health literacy ^e	6.88	0.008	0.34	0.15–0.76
Comparison task score, 1-point increment ^d	4.62	0.032	0.92	0.85–0.99

CI, confidence interval; NYHA, New York Heart Association; STOFHLA, Short Test of Functional Health Literacy in Adults.

^aFactors were assessed at baseline, with the exception of treatment adherence, which was assessed over 12 months.^bPerceived income adequacy assessed by asking whether participant has an income that is comfortable, just enough to get by, or not even enough to get by.^{27,28}^cAbility to read text on a prescription medication container label.³⁵^dSpeed of cognitive processing as the mean of letter and pattern comparison task scores.³⁸^eHealth literacy measured using the STOFHLA.³⁴