## Title

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# Health Literacy Mediates the Relationship between Age and Health Outcomes in Patients with Heart Failure

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## Abstract

**BACKGROUND—**Prior studies have linked frequent rehospitalizations for heart failure (HF) and increased mortality with older age, higher severity of HF, lack of an evidence-based medication regimen, and inadequate health literacy. However, the pathway between age and health outcomes in patients with HF remains unknown. Therefore, the purpose of this study was to test whether the association between age and health outcomes can be explained by severity of HF, evidence-based medication use, and health literacy in patients with HF.

**METHODS AND RESULTS—**This was a longitudinal study of 575 rural patients with HF recruited from outpatient clinics and hospitals. Demographics, clinical data, and health literacy were collected at baseline. HF readmissions and cardiac mortality were followed for 2 years. 57% of patients were 65 years or older. Older HF patients were more likely to have low health literacy and less likely to be prescribed angiotensin-converting-enzyme inhibitors or beta-blockers. Using Kaplan-Meier survival curves with log-rank tests, health outcomes were significantly worse in patients who were 65 years or older and in those with low health literacy. Separate Cox regressions revealed that age and health literacy predicted worse health outcomes ($p$ =.006 and <.001, respectively). When health literacy was entered into the model, the hazard ratio for age changed from 1.49 to 1.29 (a 41% reduction); age was no longer a significant predictor of health outcomes, but health literacy remained significant (p < .001), demonstrating mediation.

**CONCLUSIONS—**Health literacy mediates the relationship between age and health outcomes in adults with HF.

**CLINICAL TRIAL REGISTRATION—**URL: http://www.ClinicalTrials.gov. Unique identifier: NCT00415545.

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**DISCLOSURES**

None.

## Keywords

health literacy; heart failure; health outcomes; aging; mediator

An estimated 5.7 million Americans have heart failure (HF), and that figure is expected to increase 46% from 2012 to 2030, resulting in more than 8 million Americans with this chronic condition.[1, 2] Heart failure incidence and prevalence rates increase with advancing age making it the leading cause of hospitalizations for adults aged 65 and older.[1] High hospitalization rates lead to high total costs for HF; costs were estimated to be 30.7 billion in the United States in 2012.[1]

Although older age predicts worse HF outcomes,[3–7] the literature does not explain the pathways for this relationship. One hypothesis is a difference in the severity of HF or a difference in medication regimen. Using New York Heart Association (NYHA) and B-natriuretic peptide (BNP) as indicators of HF severity,[7, 8] researchers have found that older HF patients tend to have worse NYHA, higher BNP, and worse health outcomes compared with younger patients.[7, 8] In addition, some evidence-based medications (e.g., angiotensin-converting-enzyme inhibitors [ACEI], beta-blockers) were less likely to be prescribed for older patients with HF.[9, 10]

Health literacy, the capacity to obtain, read, understand, and process health-related information, is essential for making health-related decisions.[11] Unfortunately, inadequate literacy—the primary component of health literacy, is quite common, especially for adults 65 and older.[12] In 2003, the National Assessment of Adult Literacy reported that 43 percent of American adults had below basic or basic literacy levels; among the subgroup aged 65 and older, 61% had below basic or basic levels.[12]

It is well-known that old age is associated with low health literacy, and in turn, low health literacy is related to poor health outcomes.[13] Two groups of researchers who systematically reviewed studies of health literacy published from 1980 to 2003[14] and from 2003 to 2010[15] reported low health literacy was associated with adverse health outcomes, including increased hospitalization and increased mortality. The purpose of this study was to explore the possible pathways between age and health outcomes in patients with HF. We tested whether the association between age and the composite endpoint of cardiac event-free survival of HF hospitalizations or cardiac mortality could be explained by severity of HF, evidence-based medication use (i.e., ACEI use and beta-blocker use), and health literacy in patients with HF.

# METHODS

## Study Design

The study was conducted within the context of the randomized controlled trial, Rural Education to Improve Outcomes in Heart Failure (REMOTE-HF).[16] In brief, we tested an education and counseling intervention on detection and management of escalating symptoms among rural heart failure patients to improve self-care abilities and decrease preventable readmissions. In REMOTE-HF, patients were followed for 2 years. At baseline, patients' demographic and clinical data (including age, NYHA, BNP, medication regimen, and health literacy) were collected by patient interview or medical record review. Outcome data were assessed monthly by telephone interviews, examination of the hospital administrative database, and review of the hospital discharge summary.

## Samples and Setting

Detailed eligibility criteria and recruitment methods have been published previously.[16] Patients living in rural areas of California, Nevada, and Kentucky were recruited from outpatient clinics and hospitals after referral to the study by healthcare providers working at these sites. Enrolled patients were 18 years or older with stable heart failure at the time of enrollment, were living independently (i.e., not institutionalized), had experienced heart failure hospitalization in the past 12 months, and could read and write English. Patients were excluded if they were diagnosed with major disruptive psychiatric illness such as schizophrenia, were referred for heart transplantation, had a co-existing serious life-limiting illness (e.g., terminal cancer), or had cognitive impairment. Cognitive screening using the Mini-Cog, which is a global measure of cognitive status,[17] was performed to identify cognitive dysfunction; a word recall score <3 or an abnormal clock drawing precluded participation.

## Measurement of Variables

**Independent variable—**Patient's age was collected during patient interview.

**Mediating variables—**Severity of HF, medication regimen, and health literacy were tested as potential mediating variables in the study.

**Severity of HF:** NYHA and BNP were collected as indicators of HF severity.[7, 8] NYHA was determined during standardized patient interview by trained cardiovascular research nurses.[18] BNP was measured at the time of enrollment using point-of-care testing equipment.

**Use of ACEIs and beta-blockers:** Patients' medication prescription (i.e., ACEIs [yes/no], β-blockers [yes/no]) was collected during patient interview and confirmed by medical record review.

Health literacy was measured by the 36-item Short Test of Functional Health Literacy in Adults (S-TOFHLA).[19] Patients were scored on the number of items they answered correctly in seven minutes. The S-TOFHLA measures the patient's ability to read and understand health-related passages using a section on preparation for an x-ray procedure and a Medicaid application. This instrument has been validated with several thousand patients, including those with cardiovascular-related diseases and other chronic diseases.[20, 21] Each participant's health literacy was categorized into one of three levels: 1) inadequate (0–16 correct answers); 2) marginal (17–22 correct answers); and 3) adequate (23–36 correct answers).[22] In this study, when not using the continuous version of this measure, we grouped participants by literacy level into lower (i.e., inadequate and marginal) and higher (i.e., adequate) groups. Cronbach's alpha for this instrument in this study was 0.76.

**Outcome variable—**The outcome variable was the composite end-point of time to the following events: HF hospitalizations and cardiac mortality (i.e., cardiac event-free survival). Data on cardiac event-free survival were obtained by patient/family interview and review of hospital database and death certificates. During data collection, the dates/reasons for hospitalization and death were noted.

**Covariates—**Gender, ethnicity, income, marital status, employment status, and left ventricular ejection fraction (LVEF) were collected as covariates from the medical record and patient interview.

## Procedure

We obtained IRB approval from all sites. Trained research nurses confirmed patients' eligibility, explained study requirements to eligible patients, and obtained informed consent. At baseline, patients' sociodemographic, health literacy, and clinical characteristics were collected by questionnaires and medical record review. Patients were followed for 2 years to collect data regarding hospitalizations and death.

## Data Management and Analysis

All data analyses were performed using SPSS, version 23; a significance level of .05 was used throughout. All study variables were summarized descriptively, including means and standard deviations or frequency distributions and quartiles, as appropriate to the level of measurement.

Patients were divided into younger (age<65) or older (age≥65) subgroups. Kaplan-Meier survival curve with log-rank test was used to compare time to the composite end-point of HF hospitalization or cardiac death between the two age groups. Cox proportional hazards regression modeling was used to assess the time to the composite end-point between the two age groups, while controlling for potential covariates: gender, ethnicity, income, marital status, employment status, LVEF, NYHA, BNP, ACEI use, beta-blocker use, and health literacy. To account for the effect of educational intervention on the outcome, we controlled for REMOTE study group (intervention vs. control group) in the analyses.

A series of linear, logistic and Cox regression models were conducted (Figure 1) to test for mediation following the steps outlined by Baron et al.[23, 24] For each potential mediator, up to four regression models were run to test for the mediator effect. The first series of models tested whether the independent variable (age) predicted each of the potential mediators (i.e., severity of HF, medication use, or health literacy) using either linear (e.g., age and BNP) or logistic regression (e.g., age and NYHA [I/II vs. III/IV]), depending on the level of measurement of potential mediator. The second series of models tested whether the potential mediator predicted cardiac event-free survival. The third model tested age as a predictor of cardiac event-free survival. In the fourth model, both age and the potential mediator were entered simultaneously as predictors of the outcome. The following conditions are required for a mediator effect to be present: 1) the results of the first, second, and the third models should be significant; and 2) the significance level of the coefficient for the independent variable (i.e., age) in the fourth model is either less significant (partial mediation) or nonsignificant (full mediation) compared to the third model.[23, 24] We initially investigated the mediator effects with age and health literacy as continuous variables; a secondary analysis was based on binary versions of these variables to test the robustness of the findings determined from the initial models. We assessed variance inflation factors to verify multicollinearity was not distorting regression parameters.

# RESULTS

## Patient Characteristics

A total of 575 patients with HF were recruited for the study. The mean age of patients in the sample was 66 (±13) years. The mean health literacy score was 25.6 ± 8.8 (median 28; 25$^{th}$ and 75$^{th}$ percentiles: 19 and 34). The average LVEF reflected enrollment of patients with and without systolic dysfunction: about half of the participants (49%) had HF with preserved systolic function (HFpEF, LVEF≥40%). The most common cause of HF was ischemic heart disease (48%). Forty percent of patients were female. About one-sixth of the patients did not complete high school (16%). Most patients had high comorbidity burden (64% had a Charlson score >2), an annual household income of less than $40,000 (73%), and were unemployed (85%).

Comparison of the two age groups was presented in Table 1.

More than half of the patients were 65 years and older (57%). Health literacy, ethnicity, employment status, LVEF, ACEI use, beta-blocker use were different between the two age groups (see Table 1). In the total sample, 36% patients were classified as having low health literacy. Older patients (47%) were more likely to have low health literacy compared with younger patients (21%). There was a greater percentage of Caucasians in the older group (91%) than in the younger group (86%). Older patients had a higher mean LVEF, more HFpEF, and were less likely to use ACEIs or beta-blockers. There were no age group differences in patients' gender, income, education, marital status, NYHA, BNP, comorbidity, or study group.

## Age and cardiac event-free survival

There were 202 cardiac events (72 cardiac deaths and 130 HF-hospitalizations) during the follow-up period, with 131 events in older patients and 71 events in younger patients. There was a significant difference in the prevalence of composite end-point of HF-hospitalization or cardiac mortality between older and younger patients (40.2% vs. 28.5%, respectively; $\chi^2$=8.4, $p$=.004). Similarly, the prevalence of cardiac mortality was higher in older patients than younger patients (16.9% vs. 6.8%, respectively; $\chi^2$=13.0, $p$<.001). Since 92.3% of the sample was followed for 750 days or less, the comparison of survival distributions between the age groups was accomplished using only those in this subset so that there would be a reasonable number of at-risk patients throughout. In the Kaplan-Meier survival curve analysis (Figure 2), the 2-year event-free survival rate was 63.9% (95% confidence interval [CI]: 56.6%–70.2%) in the younger group, compared to 53.0% (95%CI: 46.9%–58.8%) in the older group ($\chi^2$=4.2, $p$=.04).

### Mediation analysis

**Potential mediators (i.e., severity of HF, medication regimen, health literacy) between age and cardiac event-free survival, with age and health literacy as continuous variables—**The first step of testing for mediation explored whether age predicted any of the potential mediators (i.e., severity of HF, medication use, and health literacy). We found no association between age and severity of HF (for either NYHA or BNP). There were significant associations between age and a) medication regimen (ACEI use [odds ratio (OR) =.962, 95% confidence interval (CI): .949–.976, *p*<.001]; and b) beta-blocker use [OR=.978, 95%CI: .961–.994, *p*=.008]). There was also an association between age and health literacy (standardized beta (β)= −.406, 95%CI: −.327– −.225, *p*<.001). So, we tested ACEI use, beta-blocker use, and health literacy in the second step of mediation assessment.

In this step, we explored whether any potential mediator predicted cardiac event-free survival. In Kaplan-Meier survival curves with log-rank tests, there were no differences in cardiac events between patients who used and who did not use ACEI and between patients who used and who did not use beta-blocker (*p*>.05 for both). In Cox proportional hazards modeling, patients with higher health literacy scores had lower risk to experience a cardiac event (HR=.968, *p*<.001). Therefore, we tested whether health literacy was a mediator between age and cardiac event-free survival.

In the third mediation model, older age was associated with higher risk of experiencing a cardiac event (HR:1.016, 95% CI [1.005, 1.028], *p*=.006). In the final model that included both age and health literacy, age was no longer a significant predictor of cardiac event-free survival (HR: 1.007, 95% CI [.995, 1.019], *p*=.28) with and without adjustment for all covariates (Table 2, Figure 1); this indicates complete mediation by health literacy.

### Assessment of mediation, with age and health literacy as dichotomous variables

In the first model (Path A; see Figure 3), age independently predicted binary health literacy status. Compared with younger patients (<65 years), older patients were 3.3 times more likely to be in the lower health literacy group (*p* <.001). For the second model (Path B), patients with lower health literacy had 1.8 times greater risk of experiencing a cardiac event than those with higher health literacy (HR:1.842, 95% CI:1.395–2.432, *p*<.001). In the third model (Path C), older HF patients had 1.5 times greater risk of experiencing a cardiac event than younger patients (HR:1.491, 95%CI:1.116–1.990, *p*=.007). In the final model, with age and health literacy as predictors (Path D), age was no longer a significant predictor of cardiac event-free survival (HR:1.292, 95%CI:.957–1.745, *p*=.095), with and without adjustment for all covariates (Table 3). This confirms complete mediation by health literacy, whether continuous or binary.

In the adjusted model with all covariates, whether age and health literacy were included as continuous or binary, NYHA classification was a predictor of cardiac event-free survival. Patients with NYHA III/IV had more than twice the risk a cardiac event than those with NYHA I/II (*p*<.001 in both models). No significant relationship was found between following variables and cardiac event-free survival: gender, ethnicity, income, marital status, employment status, LVEF, BNP, ACEI use, and beta-blocker use (see Tables 2 & 3). In each adjusted regression model, all variance inflation factors were <1.4, suggesting no parameter distortion due to multicollinearity.

## DISCUSSION

In this study we examined the mediating role of severity of HF, medication use, and health literacy in the relationship between age and health outcomes. Similar to prior studies,[3–7] we found that older age was associated with worse health outcomes (i.e., frequent HF-hospitalizations and more cardiac mortality). We demonstrated that health literacy, but not severity of HF (i.e., NYHA, BNP) or medications (i.e., ACEI use, or beta-blocker use), mediated the effects of age on cardiac event-free survival.

This finding is consistent with prior research.[25, 26] In one study,[26] the investigators examined whether health literacy explained the relationship between education and health outcomes in 395 patients with diabetes. Higher educational attainment was associated with better glycemic control and health literacy mediated the effects of education on glycemic control.[26] In another study,[25] the investigators examined whether patient-centered instructions for HF medications increased comprehension and memory for medication information in older adults with HF. They found that age was a significant predictor of recall of instructions, but when health literacy was added to the model the impact of age on recall was eliminated ($p$>.05), indicating the mediating role of health literacy between age and recall. These results support our findings that in rural adults with HF, health literacy at least partially explains the relationship between older age and worse health outcomes.

In line with prior studies, including our own previous work,[27–29] participants with low literacy were more likely to experience a cardiac event than those with adequate literacy. Three investigative groups who studied patients with HF reported that patients with lower health literacy had worse health outcomes than those with adequate health literacy.[27–29] These results emphasize the importance of considering participants' health literacy level when healthcare professionals deliver health-related information.

It is worth noting that in the final mediation model when both age and health literacy were entered as dichotomous variables, the hazard ratios for age changed from 1.49 to 1.29 (41% reduction). Consistent with this, when age and health literacy were analyzed as continuous variables, the hazard ratios decreased from 1.016 to 1.007 (56% reduction). Our findings from both models underscore the mediation effect of health literacy in this relationship, which is the first time this relationship has been reported. In most studies,[27–29] standard cutpoints have been used to group subjects into lower (inadequate and marginal) and higher level of health literacy, and investigators found significant relationship between literacy and outcomes. However, Wolf and colleagues studied 3,260 U.S. community-dwelling elderly and found the relationship between health literacy and physical functioning was continuous and graded; but this did not characterize the relationship between health literacy and mental health.[30] Therefore, it is clear that HF patients with low health literacy are at risk for poor health outcomes, but more research may be needed to verify whether there is a threshold between health literacy and outcomes.

Some interventional studies[22,31,32] in the HF population have shown that patients with low health literacy benefit more[22,32] or at least the same[31] from educational counseling on self-care training compared with those at higher literacy levels. Patients in an intervention group of education counseling had better medication adherence,[31] more HF-related knowledge and HF self-efficacy,[32] higher rates of daily weight monitoring,[32] lower health care utilization (ED visits and hospitalizations),[31,32] lower costs[31] and greater patient satisfaction[31] compared with the patients in the usual care group. Our findings suggest an opportunity to reduce age-related disparities in outcomes by simplifying health-related information to better accommodate patients' level of health literacy.

In addition to health literacy, it is also important to explore whether there are other factors in the causal pathway that can explain the relationship between age and health outcomes. Socio-demographic differences between the two age groups and/or differences in clinical factors may play a role on different outcomes. In the current HF literature, some socio-demographic factors, such as African-American ethnicity,[33] unmarried status,[34] and low socio-economic status[35] are associated with worse outcomes. When we compared socio-demographic variables between older and younger groups, only ethnicity and employment status were different between these two age groups. We adjusted for ethnicity and employment status in the Cox regression and neither predicted cardiac event-free survival.

Differences between age groups in health outcomes may be related to differences in the severity of HF, and in the effectiveness of treatment. Older HF patients tend to have worse NYHA and higher BNP as markers of worse HF severity.[7,8] In addition, older patients with HF are less likely to be prescribed some evidence-based medications (i.e., ACEI, beta-blockers) than younger patients.[9,10] In this study, we examined whether NYHA, BNP, ACEI use, and beta-blocker use mediated the relationship between age and outcomes; our finding did not support these factors as mediators of the relationship between age and outcomes. In the Cox regression, we controlled for NYHA, BNP, ACEI use, and beta-blocker use as potential confounders, and still found that health literacy mediates age and outcomes.

The prevalence of comorbid conditions may play a role in differences between age groups in health outcomes. Older adults with HF tend to have greater comorbidity burden than younger adults.[36] When we ran an additional analysis to include comorbidity burden in the Cox regression model, our findings were unchanged.

The role of health literacy as a mediator between age and outcomes raises the question of whether health literacy is a marker for other factors that are associated with aging. In a large study, Baker and colleagues[13] examined the association between age and health literacy among elderly adults. Health literacy was measured at baseline using the S-TOFHLA and mean health literacy scores declined 1.4 points for every year increase in age.[13] Older age is associated with lower education,[13] poorer cognitive function,[13] lower frequency of reading a newspaper,[13] impaired memory and recall.[37] Health literacy is associated with years of education completed,[13,38–40] ethnicity,[38] economic condition,[39,40] cognitive function,[13,37] perceived health status,[41] comorbidity,[38,41] and frequency of reading a newspaper.[13] It is possible that cognitive function or other factors might play a role in the link between older age and low health literacy. Therefore, the paths by which age is related to health literacy require further elucidation.

Our study has several limitations. First, we cannot rule out unmeasured confounding factors, such as access to primary care that might link the relationship between old age and worse health outcomes. However, we controlled for many potential confounders that were reported in HF literature. Second, the concept of health literacy is complex and multifaceted. It includes multiple elements (e.g., reading, numeracy skill, communication).[42] We measured reading ability with the S-TOFHLA at baseline without considering the multiple literacy elements. However, the S-TOFHLA is one of the most commonly used health literacy assessments in the published literature and has been a strong predictor of health outcomes.[27–29]

## CONCLUSION

Among rural patients with HF, we demonstrated that low health literacy was prevalent in older compared with younger patients (47% vs. 21%) and was associated with 1.8 times risk of cardiac events. The major finding of this study was that health literacy mediates the relationship between age and health outcomes. Interventions intended to improve health outcomes in elderly adults with HF need to take into account patients' level of health literacy.

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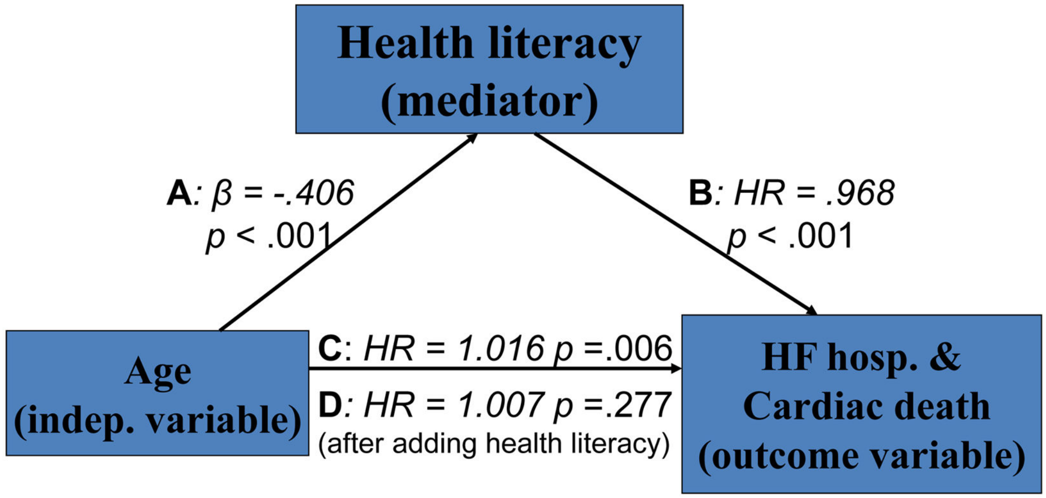
### Clinical Perspective

Heart failure (HF) rehospitalizations and mortality are associated with older age, higher severity of HF, lack of an evidence-based medication regimen, and inadequate health literacy. In a longitudinal study of 575 rural patients with HF, we found that older HF patients were more likely to have low health literacy and less likely to be prescribed an evidence-based medication regimen, such as angiotensin-converting-enzyme inhibitors or beta-blockers. Older age and low health literacy were more likely to have worse health outcomes. Health literacy, but not severity of HF or medication regimen, is one possible reason by which older age contributed to worse health outcomes for adults with HF. Therefore, information or education intended to improve health outcomes in elderly adults with HF should consider patients' level of health literacy.




**Path A: Test of whether age is a predictor of health literacy.**

**Path B: Test of whether health literacy is a predictor of cardiac event-free survival.**

**Path C: Test of whether age is a predictor of cardiac event-free survival.**

**Path D: Test of whether age and health literacy together are predictors of cardiac event-free survival.**

**Figure 1.**

Test of health literacy as a mediator of the relationship between age and cardiac-free survival; age and health literacy are included in the models as continuous variables. The results of the four regression models specified in Paths A–D demonstrate that health literacy completely mediates this relationship, as evidenced by a significant association between age and event-free survival until health literacy is added to the model.

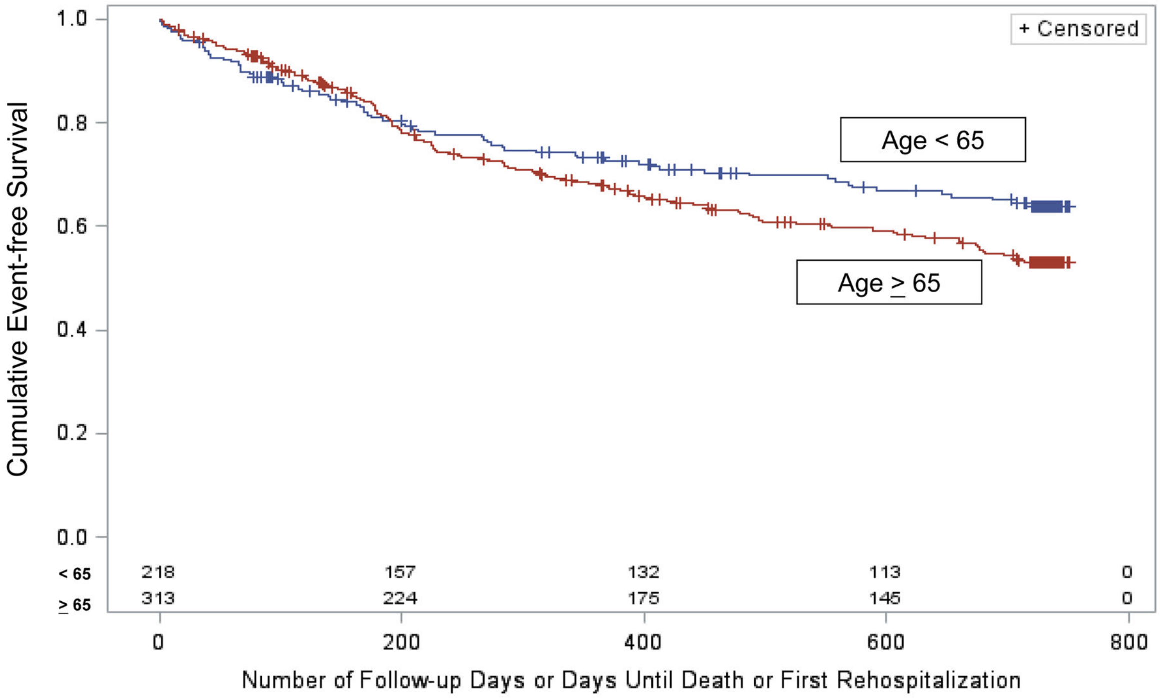
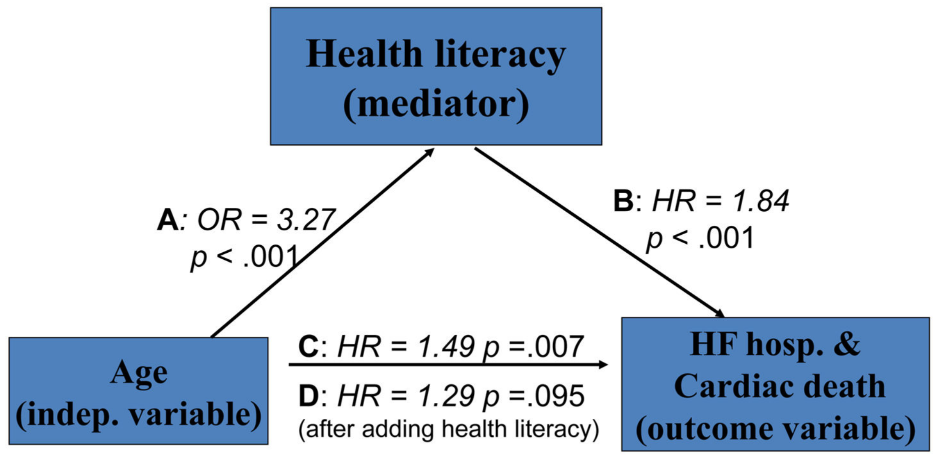



**Figure 2.**

Kaplan-Meier survival curves for patient age groups consisting of those less than 65 (blue line) versus 65 and above (red line); each censored observation appears as a plus. With 93% of the sample followed for 750 days or less, the Kaplan-Meier curves excluded those followed for a longer time; the number of patients at risk for each 200-day period is shown by age group at the base of the graph. The group comparison of event-free survival is significant ($\chi^2$ = 4.2; *p* = .04).




**Path A: Test of whether age (< 65 vs. ≥ 65) is a predictor of health literacy (lower vs. higher).**
**Path B: Test of whether health literacy (lower vs. higher) is a predictor of cardiac event-free survival.**
**Path C: Test of whether age (< 65 vs. ≥ 65) is a predictor of cardiac event-free survival.**
**Path D: Test of whether age (< 65 vs. ≥ 65) and health literacy (lower vs. higher) together are predictors of cardiac event-free survival**.

**Figure 3.**

Test of health literacy as a mediator of the relationship between age and cardiac-free survival; age and health literacy are included in the models as dichotomous variables. The results of the four regression models specified in Paths A–D demonstrate that health literacy completely mediates this relationship, as evidenced by a significant association between age and event-free survival until health literacy is added to the model.

**Table 1**

Sample Characteristics

| **Characteristics** | **Younger group (*n*=249)** ***Mean* ± *SD* or *n* (%)** | **Older group (*n*=326)** ***Mean* ± *SD* or *n* (%)** | ***p*** |
|---|---|---|---|
| Age | 54±8.7 | 75±6.7 | - |
| Female | 96(39) | 138(42) | .392 |
| Ethnicity: white | 213(86) | 298(91) | .032 |
| Income: = < 40,000/yr | 161(71) | 214(75) | .269 |
| Education: < high school | 38(15) | 56(17) | .571 |
| Marital status: married | 141(57) | 181(58) | .865 |
| Employment status: employed | 60(24) | 25(8) | <.001 |
| LVEF, % | 36.7±15.2 | 41.8±15.2 | <.001 |
| LVEF ≥ 40% | 98(40) | 178(56) | <.001 |
| NYHA functional class | | | .132 |
| III/IV | 77(31) | 121(37) | |
| BNP | 330.8±1006.5 | 482.2±977.1 | .077 |
| Charlson comorbidity index | 3.3±1.7 | 3.4±1.8 | .575 |
| Study group: | | | |
| Control group | 90(36) | 110(34) | .596 |
| Intervention group | 159(64) | 216(66) | |
| Taking ACEI | 159(64) | 160(50) | .001 |
| Taking beta-blocker | 210(84) | 247(76) | .016 |
| Health literacy score | 29±7.1 | 23±9.0 | <.001 |
| Health literacy level: | | | <.001 |
| Low (inadequate/marginal) | 53(21) | 153(47) | |

ACEI=angiotensin-converting-enzyme inhibitor; LVEF=left ventricular ejection fraction; MI=myocardial infarction; NYHA=New York Heart Association

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## Table 2

Cox Regression: Age and Health Literacy[§] on Event-free Survival (N=575)

| Variable | Hazard Ratio | 95%CI | Significance |
|---|---|---|---|
| Without covariate adjustment | | | |
| **Step 1* | | | |
| **Age (years)** | **1.016** | **1.005–1.028** | **.006** |
| ***Step 2* | | | |
| Age (years) | 1.007 | .995–1.019 | .277 |
| **Health literacy score** | **.972** | **.956–.988** | **<.001** |
| *** With covariate adjustment | | | |
| ****Step 1* | | | |
| **Age (years)** | **1.015** | **1.002–1.028** | **.027** |
| *****Step 2* | | | |
| Age (years) | 1.006 | .992–1.020 | .383 |
| Female | 1.381 | .979–1.949 | .066 |
| Black | .972 | .596–1.584 | .909 |
| Income ≤$40,000 | 1.272 | .846–1.914 | .248 |
| Married | 1.212 | .865–1.698 | .264 |
| Employed | .995 | .611–1.620 | .984 |
| Left ventricular ejection fraction (%) | .996 | .985–1.007 | .447 |
| **NYHA III/IV** | **2.136** | **1.569–2.908** | **<.001** |
| BNP (per pg/ml point) | 1.000 | 1.000–1.000 | .638 |
| ACEI user | 1.164 | .843–1.607 | .356 |
| Beta-blocker user | 1.071 | .703–1.632 | .749 |
| Intervention group | 1.042 | .755–1.438 | .805 |
| **Health literacy score** | **.972** | **.953–.990** | **.003** |

CI=confidence interval; ACEI=angiotensin-converting-enzyme inhibitor; NYHA=New York Heart Association; BNP=B-type Natriuretic Peptide

[§] Age and health literacy were analyzed as a continuous variable;

[*] $\chi^2$=7.531, *p*=.006;

[**] $\chi^2$=20.767, *p*<.001;

[***] $\chi^2$=40.667, *p*<.001;

[****] $\chi^2$=51.088, *p*<.001

## Table 3

Cox Regression: Age and Health Literacy[§] on Event-free Survival (N=575)

| Variable | Hazard Ratio | 95%CI | Significance |
|---|---|---|---|
| Without covariate adjustment | | | |
| *Step 1 | | | |
| **Age (≥65 years)** | **1.491** | **1.116–1.990** | **.007** |
| **Step 2 | | | |
| Age (≥65 years) | 1.292 | .957–1.745 | .095 |
| **Low health literacy** | **1.718** | **1.287–2.293** | **<.001** |
| With covariate adjustment | | | |
| ***Step 1 | | | |
| **Age (≥65 years)** | **1.418** | **1.027–1.958** | **.034** |
| ****Step 2 | | | |
| Age (≥65 years) | 1.237 | .887–1.726 | .211 |
| Female | 1.410 | .998–1.990 | .051 |
| Black | .960 | .588–1.566 | .870 |
| Income ≤$40,000 | 1.223 | .812–1.843 | .334 |
| Married | 1.158 | .826–1.623 | .396 |
| Employed | .971 | .597–1.577 | .905 |
| Left ventricular ejection fraction (%) | .996 | .985–1.007 | .429 |
| **NYHA III/IV** | **2.104** | **1.544–2.868** | **<.001** |
| BNP (per pg/ml point) | 1.000 | 1.000–1.000 | .440 |
| ACEI user | 1.162 | .844–1.601 | .358 |
| Beta-blocker user | 1.078 | .708–1.642 | .727 |
| Intervention group | 1.035 | .750–1.428 | .834 |
| **Low health literacy** | **1.797** | **1.291–2.502** | **.001** |

CI=confidence interval; ACEI=angiotensin-converting-enzyme inhibitor; NYHA=New York Heart Association; BNP=B-type Natriuretic Peptide

[§] Age and health literacy were analyzed as a dichotomous variable;

[*] $\chi^2$=7.426, $p$<.001;

[**] $\chi^2$=21.823, $p$<.001;

[***] $\chi^2$=40.183, $p$<.001;

[****] $\chi^2$=53.718, $p$<.001