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A Single-Item Self-Report Medication Adherence Question Predicts Hospitalization and Death in Patients with Heart Failure

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Abstract

Aims and objectives—To determine whether a single-item self-report medication adherence question predicts hospitalization and death in patients with heart failure (HF).

Background—Poor medication adherence is associated with increased morbidity and mortality. Having a simple means of identifying sub-optimal medication adherence could help identify atrisk patients for interventions.

Design—We performed a prospective cohort study in 592 participants with HF within a 4-site randomized trial.

Methods—Self-report medication adherence was assessed at baseline using a single-item question: "Over the past 7 days, how many times did you miss a dose of any of your heart medication?" Participants who reported no missing doses were defined as fully adherent; those missing 1 dose were considered less than fully adherent. The primary outcome was combined all-cause hospitalization or death over 1 year; the secondary endpoint was HF hospitalization. Outcomes were assessed with blinded chart reviews and HF outcomes were determined by a blinded adjudication committee. We used negative binomial regression to examine the relationship between medication adherence and outcomes.

Results—Participants were 52% male, mean age was 61 years, and 31% were NYHA III/IV at enrollment; 72% of participants reported full adherence to their heart medicine at baseline. Participants with full medication adherence had a lower rate of all-cause hospitalization and death (0.71 events/year) compared with those with any non-adherence (0.86 events/year): adjusted for site incidence rate ratio (IRR) was 0.83, fully adjusted IRR 0.68. IRRs were similar for HF hospitalizations.

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Author Contributions

The authors have confirmed that all authors meet the ICMJE criteria for authorship credit (www.icmje.org/ethical_lauthor.html), as follows:

- 1. substantial contributions to conception and design of, or acquisition of data or analysis and interpretation of data,
- 2. drafting the article or revising it critically for important intellectual content, and
- 3. final approval of the version to be published.

Conclusion—A single medication adherence question at baseline predicts hospitalization and death over 1 year in HF patients.

Relevance to clinical practice—Medication adherence is associated with all-cause and HF-related hospitalization and death in HF. It is important for clinicians to assess patients' medication adherence on a regular basis at their clinical follow-ups.

Keywords

h	ieart	failu	ıre;	outcome	es; me	edication	adh	erence;	self-rep	port		

Introduction

Heart failure (HF) is a chronic condition manifested in high morbidity and mortality and poor quality of life (Go et al., 2013; Riegel et al., 2009). Heart failure is characterized by episodes of instability that commonly require hospitalization (Opasich et al., 1996). Rehospitalization rates in patients with HF are high (Go, et al., 2013; Lloyd-Jones et al., 2010; Stewart et al., 2001): with 50% of patients readmitted within six months of discharge from a hospitalization for exacerbation of HF (Go, et al., 2013; Hamner & Ellison, 2005; Krumholz et al., 2000; Smith et al., 2000).

Patients with HF need to adhere to their prescribed medications to prevent and control symptoms and decrease the need for hospital admission (Hauptman, 2008; Hodges, 2009). However, medication adherence rates in patients with HF are sub-optimal, about 40-60% (Wu, Moser, Lennie, & Burkhart, 2008). Prior studies have shown that poor medication adherence is associated with increased all-cause emergency department (ED) visits (Esposito, Bagchi, Verdier, Bencio, & Kim, 2009; Murray et al., 2009), cardiovascular (CV)-related ED visits (Hope, Wu, Tu, Young, & Murray, 2004; Murray et al., 2007), allcause hospitalizations (Esposito, et al., 2009; Li, Morrow-Howell, & Proctor, 2004; Murray, et al., 2009; Murray, et al., 2007; Sun, Ye, Lee, Dupclay, & Plauschinat, 2008), CV-related hospitalizations (Chui et al., 2003; Murray, et al., 2007), HF hospitalizations (Ambardekar et al., 2009; Annema, Luttik, & Jaarsma, 2009; Chui, et al., 2003; Cole, Norman, Weatherby, & Walker, 2006; Murray, et al., 2007), mortality (Granger et al., 2005; Miura et al., 2001; Wu, Moser, Chung, & Lennie, 2008), longer length of stay in hospital (Esposito, et al., 2009; Miura, et al., 2001), high healthcare cost (Cole, et al., 2006; Esposito, et al., 2009; Sun, et al., 2008), and poor health status (Morgan et al., 2006) in patients with HF. Interventions to improve medication adherence can reduce clinical events and reduce costs (Murray, et al., 2007).

There are many methods to measure the extent of medication adherence: patient self-report; estimates by physicians, other health care providers, and/or family members; pill counts; pharmacy refill data; biological assays of blood, urine or saliva; and electronic pill caps such as the Medication Event Monitoring System (MEMS). All current measures have strengths and weaknesses (Wu, et al., 2008). Any measurement of medication adherence that is complicated, expensive, intrusive, or time-consuming is not ideal in clinical settings. Having a simple means of identifying sub-optimal adherence could help identify at-risk patients for interventions. Accordingly, the purpose of this study was to determine whether a single-item

self-report medication adherence question predicts hospitalization and death in patients with HF.

Methods

Study Design

This investigation was a secondary analysis of data from a prospective cohort study conducted within a 1-year, 4-site randomized controlled trial (RCT) comparing different levels of self-care training (single-session vs. multisession). All participants were interviewed at baseline to collect data on demographic and clinical variables and to complete baseline questionnaires (including single-item self-report medication adherence). Participants randomized to the single session group received a 40-minute in-person self-care training; those in the multisession group received the same initial training and then ongoing phone-based support. Outcome data were collected at 6 months and 12 months through phone interviews followed by medical record reviews.

The funding agent, National Heart, Lung, And Blood Institute had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Sample and Setting

Detailed eligibility criteria, recruitment methods, and data collection processes have been published previously (Dewalt et al., 2012). In short, participants were recruited from March 2007 to December 2009 from university-affiliated General Internal Medicine and Cardiology outpatient clinics at 4 sites: University of North Carolina at Chapel Hill; Feinberg School of Medicine, Northwestern University; University of California, San Francisco- San Francisco General Hospital; and Olive View-UCLA Medical Center. Participants who had a confirmed diagnosis of chronic HF, New York Heart Association (NYHA) class II-IV symptoms in the past 6 months, current use of a loop diuretic medication, and no cognitive impairment were enrolled in this study.

Measurement

Medication Adherence—Medication adherence was measured by patient self-report at baseline using a single item question that is commonly and widely used in the clinical settings: "Over the past 7 days, how many times did you miss a dose of any of your heart medication?" Participants who reported no missing doses were defined as fully adherent; those missing 1 dose were considered less than fully adherent.

Outcomes—The primary end-point for this study was all-cause hospitalization and death. The secondary end-point was HF-related hospitalization.

A detailed description of our outcome measures has been published elsewhere (DeWalt et al., 2009; Dewalt, et al., 2012). In short, the UNC Survey Research Unit interviewed participants by telephone at 6 and 12 months to collect data on any hospitalizations that had occurred in the previous time period and/or any reports of death. Initial data were obtained

by patient interview. Records were requested for the full study period from any hospitals in which the patient reported having had a hospital admission. We obtained admission and discharge summaries, key reports, and for deaths we also obtained death certificates when possible. During data collection, the date and reasons for hospitalization and death were noted. To determine whether a hospitalization was HF-related, one member of the 3-member adjudication committee, masked to study arm assignment and adherence, reviewed the admission and discharge summaries to determine if the hospitalization was heart failure-related. A second reviewer examined the same data for ambiguous cases; if the first two reviewers disagreed, a third reviewer helped resolve discrepancies (DeWalt, et al., 2009; Dewalt, et al., 2012).

Demographic variables—Age, gender, ethnicity, income, education level, health literacy socioeconomic status, and insurance were collected from patient interview as demographic variables. Socioeconomic status is the participant's subjective assessment of his or her position in society relative to others based on wealth. Health literacy was measured using the short Test of Functional Health Literacy in Adults (S-TOFHLA). Each participant's literacy level is categorized as low (0–22) or higher literacy (23–36) (Gazmararian et al., 1999). This instrument is one of the most commonly used instruments in research. It has been validated in several thousand patients, including patients with cardiovascular-related diseases and other chronic diseases (Gazmararian et al., 2006; Kalichman et al., 2008).

Clinical variables—New York Heart Association (NYHA) class, systolic dysfunction (ejection fraction < 45%), systolic and diastolic blood pressure (BP), body mass index (BMI), creatinine level, presence of diabetes, hypertension, atrial fibrillation, previous myocardial infarction, chronic kidney disease, smoking status, depressive symptoms, HF medication prescriptions, and HF symptoms (Baker, Brown, Chan, Dracup, & Keeler, 2005) were collected from patient interview and medication record review as clinical variables. Depressive symptoms were measured using the Patient Health Questionnaire-9 (PHQ-9) (Ackermann et al., 2005; Kroenke, Spitzer, & Williams, 2001). The PHQ-9 is a reliable (Kroenke, et al., 2001) and valid (Ackermann, et al., 2005; Kroenke, et al., 2001) scale that has been used to measure depressive symptoms in patients with HF (Ackermann, et al., 2005). HF-related symptoms were measured using a 7-item Heart Failure Symptom Scale (HFSS)(Baker, et al., 2005). The HFSS is a reliable and validated instrument to measure HF symptoms in patients with HF (Baker, et al., 2005; Macabasco-O'Connell et al., 2011).

Knowledge and behavioral variables—We also assessed HF general knowledge, salt knowledge, HF self-efficacy and HF self-care behaviors. HF general knowledge, salt knowledge, and HF self-care behaviors were measured using an adapted version of the Improving Chronic Illness Care Evaluation (ICICE) telephone survey (Baker, et al., 2005). HF general knowledge questions included general HF knowledge such as definition of HF, with a total score ranging 0–8, higher scores indicate greater knowledge. Salt knowledge questions included which foods contain a lot of salt, with a total score ranging 0–10. Self-care behaviors included weight monitoring, following a low salt diet, and exercising. Participants' self-efficacy was assessed using a 10-item Self-Efficacy Scale to measure their perceived confidence in managing their HF symptoms and performing self-care behaviors

(Macabasco-O'Connell, et al., 2011). These scales are reliable and valid instruments that have been used to measure knowledge, self-care behaviors, and self-efficacy in patients with HF (Baker, et al., 2005).

Procedure

Permission for the conduct of the study was obtained from the Institutional Review Board (IRB) for all sites. Patient eligibility was confirmed by a trained research assistant. The research assistant explained study requirements to the eligible participants and obtained informed, written consent. All data included medication adherence, demographic, clinical, knowledge and behavioral variables were collected by interview at baseline. Outcome data were collected for 12 months for each participant.

Data Management and Analysis

All data analyses were performed using Stata 12 (College Station, TX); a significance level of .05 was used throughout. Data analysis began with a descriptive examination of all variables, including frequency distributions, percent, means, and standard deviations, as appropriate to the level of measurement of the variables.

We initially compared differences in demographic and clinical factors between fully adherent and less than fully adherent participants using chi-square and t-tests. We then compared differences in the incidence rates of the primary and secondary outcomes between adherence groups using negative binomial regression. We first examined differences adjusted for site. Next, we repeated the models adjusting for demographics, clinical factors, and intervention status that were statistically significantly different between groups or that might have an impact on the outcomes from the literature (partially adjusted). Finally, we repeated the analysis adding knowledge and behavioral factors to the model (fully adjusted). In each multiple regression, data examination showed no problems with collinearity. Standard errors were adjusted for clustering by site. We also examined the effect of defining adherence using a different cutpoint (0–1 missing dose vs. >1 missing dose) as a sensitivity analysis. We conducted two additional sensitivity analyses by including total number of HF medications in the fully adjusted models and exploring the relationship between medication adherence and events with a shorter follow-up period (6 months).

Results

Patient Characteristics

We approached 1842 patients for enrollment: 682 did not meet inclusion criteria and 555 refused to participate. The remaining 605 met the inclusion criteria, agreed to participate, their physician allowed participation, and they were enrolled. 592 participants in the trial with no missing data from medication adherence, hospitalization and death, and covariates were included in this prospective cohort study (Table 1). The mean age was 61 ± 13 years. Fifty-eight percent had systolic dysfunction, 52% were male, 38% were white, 39% African American, and 16% Hispanic, and English was the preferred language for 86%. There were 51% who reported an income below \$15,000/year, only 21% reported an income above \$40,000, and 63% had adequate health literacy level. Compared to the general HF

population (Felker et al., 2004; O'Connor, Stough, Gallup, Hasselblad, & Gheorghiade, 2005; Pfeffer et al., 2003), participants in this study were younger and more likely to be African-Americans.

Fully Medication Adherent vs. Less than Fully Adherent

429 participants (72%) reported full adherence to their heart medicine (0 missed) at baseline. 163 participants (28%) were less than fully adherent (80 with 1 missed dose, 62 with 2–3 missed doses, and 21 with 4+ missed doses). Compared to participants who were less than fully adherent, fully adherent participants were older, were more likely to have medical insurance, to have history of hypertension or chronic kidney disease, were less likely to be current smoker or depressed, reported higher subjective socioeconomic status, had lower diastolic BP, scored higher on self-efficacy, and performed more self-care behaviors (Table 1). No other demographic and clinical characteristic differed between these two groups.

Medication Adherence and Hospitalization and Death

Table 2 shows differences in clinical outcomes by medication adherence. For all-cause hospitalization and death, participants who reported full medication adherence had a lower rate of events (0.71 events / year) compared with those with any non-adherence (0.86 event / year). For HF-related hospitalization, participants with full medication adherence also had a lower rate of events (0.28 event / year) compared with their less than fully adherent counterparts (0.33 event / year). There were no differences in all-cause hospitalization/death or HF hospitalization between participants who reported full medication adherence or less than full adherence (p=0.99 and 0.92, respectively). After adjusting for site, for participants who were fully adherent had fewer events of all-cause hospitalization or death and HF hospitalization: the incidence rate ratio (IRR) was 0.83 (95% CI: 0.69-1.00, p = 0.05) for allcause hospitalization or death, and 0.84 (95% CI: 0.77-0.92, p < 0.001) for HF hospitalization. When adding demographics, clinical factors, and intervention status to the model, the partially adjusted IRR for all-cause hospitalization and death = 0.71 (95% CI: 0.58-0.88, p < 0.001) and for HF hospitalization = 0.71 (95% CI: 0.56-0.89, p < 0.001). When we repeated the analysis adding knowledge and behavioral factors to the model, the fully adjusted IRR for all-cause hospitalization and death = 0.68 (95% CI: 0.53-0.86, p < 0.001) and for HF hospitalization = 0.64 (95% CI: 0.43-0.96, p = 0.03) (Table 2).

Sensitivity analysis

When full adherence was defined as 0–1 missing dose (vs. >1 dose), we found similar results for the models in which we adjust for characteristics beyond site only. When adjusting for site, adherent participants had an IRR of 0.68 (95% CI: 0.48-0.98, p = 0.04) for all-cause hospitalization or death, and 0.66 (95% CI: 0.39-1.12, p = 0.13) for HF hospitalization. In the partially adjusted model, the IRR was 0.66 (95% CI: 0.47-0.93, p = 0.02) and 0.62 (95% CI: 0.43-0.90, p = 0.01) for all-cause and HF hospitalization, respectively. In the fully adjusted model, IRR was 0.61 (95% CI: 0.46-0.82, p < 0.001) and 0.49 (95% CI: 0.38-0.64, p < 0.001) for all-cause and HF hospitalization, respectively.

Adjusting for number of HF medications did not change the results, IRRs changed from 0.68 to 0.69 for all-cause events and from 0.64 to 0.65 for HF hospitalization. The relationship

between medication adherence and all-cause events was similar when we used a shorter followup period for outcome assessment: the point estimate for the six month fully adjusted all-cause model changed from 0.68 to 0.74.

Discussion

In this study, a single question on medication adherence measured at baseline predicted hospitalization and death over 1 year in participants with HF. Fully adherent participants had a lower rate of events compared with less than fully adherent participants before and after adjusting for site, demographic, clinical, knowledge, and behavioral factors.

Consistent with prior investigators' findings, participants who had higher adherence to prescribed medications had a lower risk of events (hospitalizations, or death) compared with those who had lower adherence (Ambardekar, et al., 2009; Annema, et al., 2009; Chin & Goldman, 1997; Chui, et al., 2003; Cole, et al., 2006; Esposito, et al., 2009; Ghali, Kadakia, Cooper, & Ferlinz, 1988; Granger, et al., 2005; Hope, et al., 2004; Li, et al., 2004; Miura, et al., 2001; Murray, et al., 2009; Murray, et al., 2007; Nelson, Reid, Ryan, Willson, & Yelland, 2006; Sokol, McGuigan, Verbrugge, & Epstein, 2005; Sun, et al., 2008). In these studies, medication adherence was measured by self-report methods in six studies (Ambardekar, et al., 2009; Annema, et al., 2009; Chin & Goldman, 1997; Ghali, et al., 1988; Li, et al., 2004; Nelson, et al., 2006), by physician estimate in one study (Granger, et al., 2005), by pharmacy refill in five studies (Cole, et al., 2006; Esposito, et al., 2009; Murray, et al., 2009; Sokol, et al., 2005; Sun, et al., 2008), by MEMS in four studies (Chui, et al., 2003; Hope, et al., 2004; Murray, et al., 2007; Wu, et al., 2008), and by serum digoxin levels in one study (Miura, et al., 2001). The finding of these prior studies and our study emphasize the importance of medication adherence on health outcomes in HF.

It is important to use reliable, valid, and accurate methods to measure medication adherence. In research settings, investigators tend to choose objective measures, such as MEMS, to measure medication adherence. Self-reported adherence, a subjective method, has often been criticized because of the potential for sub-optimal accuracy due to recall bias, social desirability, and may lead to over-estimated medication adherence. However, in clinical settings, it is important to find a way to measure medication adherence feasibly. Self-report is the most frequently used method to assess medication adherence clinically because it is simple, inexpensive, feasible, and may provide a gross indicator of adherence (Morisky, Ang, Krousel-Wood, & Ward, 2008; Morisky, Green, & Levine, 1986).

One author (JRW) of this paper previously reported that a one-item self-reported measure of adherence did not predict clinical outcomes in 134 patients with HF (Wu, et al., 2008). In that study (Wu, et al., 2008), patients were asked to rate "how often did you take medication as prescribed (on time without skipping doses) in the past four weeks?" on a scale from 0 (none of the time) to 5 (all of the time). Patients who self-reported taking medication as prescribed "all of the time" and "most of the time" were categorized as adherent, and those who reported "a good bit of the time", "some of the time", "a little of the time", and "none of the time" were categorized as non-adherent. The findings between these 2 self-reported studies most likely differ because of the different self-report instruments used. In our current

study, we asked participants to recall their medication taking behavior over the past 7 days rather than over the past 4 weeks. Cognitive deficits and memory impairment are common in older people with many other chronic conditions, as well as HF (Bennett & Sauve, 2003; Bennett, Sauve, & Shaw, 2005; Harkness, Demers, Heckman, & McKelvie, 2011; Pressler et al., 2010; Sloan & Pressler, 2009). Recalling whether they missed taking their medications over the past 7 days is easier than recalling whether they missed taking their medications over the past 4 weeks for elderly participants with HF. This suggests that the self-report instrument used in this study may be a better self-report measure of medication adherence, but this should be confirmed in future studies.

Voils and colleagues (2012) recently conducted cognitive interviews in 30 hypertensive patients to develop a new self-reported measure of medication nonadherence. In terms of recall period, most patients reported "the last 7 days" was more easily and accurately recalled and a more sensitive reflection of their medication adherence. This data further supports our use of the "past 7 days" recall period.

Voils and colleagues 3-item scale (Voils, et al., 2012) assesses the extent of medication adherence. The 3 items assessed whether individuals "took all doses", "missed or skipped doses", or "were not able to take doses of their medications" over the past 7 days, using 4 response options. The 3-item scale had evidence for reliability and validity and may reduce measurement error in patients with hypertension. However, our single item measure may be more feasible for clinical use, and also appears to have good predictive validity. Neither measure has been compared or validated with other objective measures, such as pill count, pharmacy refill record, or electronic monitoring. Future studies are needed to examine both the single item measure and the Voils 3-item scale in a range of conditions and patient populations.

The mechanisms by which reported adherence influences outcomes are complex. Patients with high adherence may differ from those with lower adherence in multiple ways. In a randomized controlled trial (Granger, et al., 2005), 7,599 participants with HF were assigned to either an angiotensin receptor blocker group or a placebo group and were followed for a median of 38 months on mortality. In Cox regressions, participants with good adherence had lower all-cause mortality compared with those with low adherence, even in the placebo group. The investigators suggested that adherence may be mainly a marker for adherence to other self-care behaviors (e.g., low sodium diet, exercise, weight monitoring, and follow-up appointments). In this study, medication adherence was associated with other HF self-care behaviors. However, when we controlled for self-care behaviors in our model, the effect of medication adherence on hospitalization and death remained strong, suggesting that adherence was not simply a marker for other self-care.

There were other differences between participants who were fully adherent and less than fully adherent in this study, such as age, ethnicity, socioeconomic status, insurance, history of hypertension or chronic kidney disease, depression, and self-efficacy. When these factors were entered into the model, participants with full adherence still had reduced incidence of all-cause and HF-related hospitalizations or mortality, suggesting that the observed relationship between adherence and outcomes was not simply a result of confounding;

however, we cannot rule out the possibility of unmeasured confounding in this type of observational cohort study.

Our study has several other limitations. First, medication adherence was measured only by self-report method and only at baseline. Use of both objective and self-report measures may increase accuracy of assessment (Cassidy, Rabinovitch, Schmitz, Joober, & Malla, 2010; Liu et al., 2001). Our data, which demonstrates a strong relationship between adherence and outcomes, suggests that adherence was accurately reflected by the self-report measure in this study. Second, our findings are from only one study; thus, we need additional studies to test its validity. Third, we did not collect some clinical data that might have an impact on hospitalizations or death, such as serum sodium, B-type Natriuretic Peptide, or diuretic dose. However, this analysis was undertaken to examine the specific relationship between selfreported adherence and HF outcomes, not to be a general analysis of prognostic factors in HF. Fourth, although we included HF symptoms to represent disease severity in the statistical analysis, we acknowledge that patients with HF might have other concurrent conditions that impact health outcomes that were not collected and controlled in our study. Finally, even though we collected outcome data from patient/family interview and requested for admission and discharge summaries from all hospitals in which the patient reported having had a hospital admission for all the full study period, it is possible that participants may have not recalled all hospitalized events. However, we have no reason to believe this recall would be differential between adherence groups.

Conclusion

This study had two important findings: 1) medication adherence is associated with all-cause and HF-related hospitalization and death in HF; 2) self-reported adherence, a simple one-item question predicts health outcomes. The finding (if confirmed) provides clinicians with valuable information regarding how to easily screen patients who might be non-adherent to medication.

Implications for practice

Based on the results of this study, and of others, we recommend that clinicians consider assessing patients' medication adherence on a regular basis at their clinical follow-ups. Our single-item question may be a clinically feasible method of doing so.

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Reference

Ackermann RT, Rosenman MB, Downs SM, Holmes AM, Katz BP, Li J, et al. Telephonic case-finding of major depression in a Medicaid chronic disease management program for diabetes and heart failure. General Hospital Psychiatry. 2005; 27(5):338–343. [PubMed: 16168794]

Ambardekar AV, Fonarow GC, Hernandez AF, Pan W, Yancy CW, Krantz MJ. Characteristics and inhospital outcomes for nonadherent patients with heart failure: findings from Get With The Guidelines-Heart Failure (GWTG-HF). American Heart Journal. 2009; 158(4):644–652. [PubMed: 19781426]

- Annema C, Luttik ML, Jaarsma T. Reasons for readmission in heart failure: Perspectives of patients, caregivers, cardiologists, and heart failure nurses. Heart & Lung. 2009; 38(5):427–434. [PubMed: 19755193]
- Baker DW, Brown J, Chan KS, Dracup KA, Keeler EB. A telephone survey to measure communication, education, self-management, and health status for patients with heart failure: the Improving Chronic Illness Care Evaluation (ICICE). Journal of Cardiac Failure. 2005; 11(1):36–42. [PubMed: 15704062]
- Bennett SJ, Sauve MJ. Cognitive deficits in patients with heart failure: a review of the literature. Journal of Cardiovascular Nursing. 2003; 18(3):219–242. [PubMed: 12837012]
- Bennett SJ, Sauve MJ, Shaw RM. A conceptual model of cognitive deficits in chronic heart failure. J Nurs Scholarsh. 2005; 37(3):222–228. [PubMed: 16235862]
- Cassidy CM, Rabinovitch M, Schmitz N, Joober R, Malla A. A comparison study of multiple measures of adherence to antipsychotic medication in first-episode psychosis. Journal of Clinical Psychopharmacology. 2010; 30(1):64–67. [PubMed: 20075650]
- Chin MH, Goldman L. Factors contributing to the hospitalization of patients with congestive heart failure. American Journal of Public Health. 1997; 87(4):643–648. [PubMed: 9146445]
- Chui MA, Deer M, Bennett SJ, Tu W, Oury S, Brater DC, et al. Association between adherence to diuretic therapy and health care utilization in patients with heart failure. Pharmacotherapy. 2003; 23(3):326–332. [PubMed: 12627931]
- Cole JA, Norman H, Weatherby LB, Walker AM. Drug copayment and adherence in chronic heart failure: effect on cost and outcomes. Pharmacotherapy. 2006; 26(8):1157–1164. [PubMed: 16863491]
- DeWalt DA, Broucksou KA, Hawk V, Baker DW, Schillinger D, Ruo B, et al. Comparison of a onetime educational intervention to a teach-to-goal educational intervention for self-management of heart failure: design of a randomized controlled trial. BMC Health Serv Res. 2009; 9:99. [PubMed: 19519904]
- Dewalt DA, Schillinger D, Ruo B, Bibbins-Domingo K, Baker DW, Holmes GM, et al. Multisite randomized trial of a single-session versus multisession literacysensitive self-care intervention for patients with heart failure. Circulation. 2012; 125(23):2854–2862. [PubMed: 22572916]
- Esposito D, Bagchi AD, Verdier JM, Bencio DS, Kim MS. Medicaid beneficiaries with congestive heart failure: association of medication adherence with healthcare use and costs. American Journal of Managed Care. 2009; 15(7):437–445. [PubMed: 19589011]
- Felker GM, Leimberger JD, Califf RM, Cuffe MS, Massie BM, Adams KF Jr, et al. Risk stratification after hospitalization for decompensated heart failure. Journal of Cardiac Failure. 2004; 10(6):460–466. [PubMed: 15599835]
- Gazmararian JA, Baker DW, Williams MV, Parker RM, Scott TL, Green DC, et al. Health literacy among Medicare enrollees in a managed care organization. Jama. 1999; 281(6):545–551. [PubMed: 10022111]
- Gazmararian JA, Kripalani S, Miller MJ, Echt KV, Ren J, Rask K. Factors associated with medication refill adherence in cardiovascular-related diseases: a focus on health literacy. Journal of General Internal Medicine. 2006; 21(12):1215–1221. [PubMed: 17105519]
- Ghali JK, Kadakia S, Cooper R, Ferlinz J. Precipitating factors leading to decompensation of heart failure. Traits among urban blacks. Archives of Internal Medicine. 1988; 148(9):2013–2016. [PubMed: 3046541]
- Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, et al. Heart disease and stroke statistics--2013 update: a report from the american heart association. Circulation. 2013; 127(1):e6–e245. [PubMed: 23239837]
- Granger BB, Swedberg K, Ekman I, Granger CB, Olofsson B, McMurray JJ, et al. Adherence to candesartan and placebo and outcomes in chronic heart failure in the CHARM programme:

- Double-blind, randomised, controlled clinical trial. Lancet. 2005; 366(9502):2005–2011. [PubMed: 16338449]
- Hamner JB, Ellison KJ. Predictors of hospital readmission after discharge in patients with congestive heart failure. Heart & Lung. 2005; 34(4):231–239. [PubMed: 16027642]
- Harkness K, Demers C, Heckman GA, McKelvie RS. Screening for cognitive deficits using the Montreal cognitive assessment tool in outpatients >/=65 years of age with heart failure. American Journal of Cardiology. 2011; 107(8):1203–1207. [PubMed: 21310371]
- Hauptman PJ. Medication adherence in heart failure. Heart Fail Rev. 2008; 13(1):99–106. [PubMed: 17479364]
- Hodges P. Heart failure: epidemiologic update. Critical Care Nursing Quarterly. 2009; 32(1):24–32. [PubMed: 19077806]
- Hope CJ, Wu J, Tu W, Young J, Murray MD. Association of medication adherence, knowledge, and skills with emergency department visits by adults 50 years or older with congestive heart failure. American Journal of Health-System Pharmacy. 2004; 61(19):2043–2049. [PubMed: 15509127]
- Kalichman SC, Pope H, White D, Cherry C, Amaral CM, Swetzes C, et al. Association between health literacy and HIV treatment adherence: further evidence from objectively measured medication adherence. J Int Assoc Physicians AIDS Care (Chic III). 2008; 7(6):317–323.
- Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. Journal of General Internal Medicine. 2001; 16(9):606–613. [PubMed: 11556941]
- Krumholz HM, Chen YT, Wang Y, Vaccarino V, Radford MJ, Horwitz RI. Predictors of readmission among elderly survivors of admission with heart failure. American Heart Journal. 2000; 139(1 Pt 1):72–77. [PubMed: 10618565]
- Li H, Morrow-Howell N, Proctor EK. Post-acute home care and hospital readmission of elderly patients with congestive heart failure. Health & Social Work. 2004; 29(4):275–285. [PubMed: 15575455]
- Liu H, Golin CE, Miller LG, Hays RD, Beck CK, Sanandaji S, et al. A comparison study of multiple measures of adherence to HIV protease inhibitors. Annals of Internal Medicine. 2001; 134(10): 968–977. [PubMed: 11352698]
- Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G, et al. Heart disease and stroke statistics--2010 update: a report from the American Heart Association. Circulation. 2010; 121(7):e46–e215. [PubMed: 20019324]
- Macabasco-O'Connell A, Dewalt DA, Broucksou KA, Hawk V, Baker DW, Schillinger D, et al. Relationship Between Literacy, Knowledge, Self-Care Behaviors, and Heart Failure-Related Quality of Life Among Patients With Heart Failure. Journal of General Internal Medicine. 2011
- Miura T, Kojima R, Mizutani M, Shiga Y, Takatsu F, Suzuki Y. Effect of digoxin noncompliance on hospitalization and mortality in patients with heart failure in long-term therapy: A prospective cohort study. European Journal of Clinical Pharmacology. 2001; 57(1):77–83. [PubMed: 11372597]
- Morgan AL, Masoudi FA, Havranek EP, Jones PG, Peterson PN, Krumholz HM, et al. Difficulty taking medications, depression, and health status in heart failure patients. Journal of Cardiac Failure. 2006; 12(1):54–60. [PubMed: 16500581]
- Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypertens (Greenwich). 2008; 10(5):348–354. [PubMed: 18453793]
- Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Medical Care. 1986; 24(1):67–74. [PubMed: 3945130]
- Murray MD, Tu W, Wu J, Morrow D, Smith F, Brater DC. Factors associated with exacerbation of heart failure include treatment adherence and health literacy skills. Clinical Pharmacology and Therapeutics. 2009; 85(6):651–658. [PubMed: 19262464]
- Murray MD, Young J, Hoke S, Tu W, Weiner M, Morrow D, et al. Pharmacist intervention to improve medication adherence in heart failure: a randomized trial. Annals of Internal Medicine. 2007; 146(10):714–725. [PubMed: 17502632]

Nelson MR, Reid CM, Ryan P, Willson K, Yelland L. Self-reported adherence with medication and cardiovascular disease outcomes in the Second Australian National Blood Pressure Study (ANBP2). Medical Journal of Australia. 2006; 185(9):487–489. [PubMed: 17137452]

- O'Connor CM, Stough WG, Gallup DS, Hasselblad V, Gheorghiade M. Demographics, clinical characteristics, and outcomes of patients hospitalized for decompensated heart failure: observations from the IMPACT-HF registry. Journal of Cardiac Failure. 2005; 11(3):200–205. [PubMed: 15812748]
- Opasich C, Febo O, Riccardi PG, Traversi E, Forni G, Pinna G, et al. Concomitant factors of decompensation in chronic heart failure. American Journal of Cardiology. 1996; 78(3):354–357. [PubMed: 8759821]
- Pfeffer MA, Swedberg K, Granger CB, Held P, McMurray JJ, Michelson EL, et al. Effects of candesartan on mortality and morbidity in patients with chronic heart failure: the CHARM-Overall programme. Lancet. 2003; 362(9386):759–766. [PubMed: 13678868]
- Pressler SJ, Subramanian U, Kareken D, Perkins SM, Gradus-Pizlo I, Sauve MJ, et al. Cognitive deficits in chronic heart failure. Nursing Research. 2010; 59(2):127–139. [PubMed: 20216015]
- Riegel B, Moser DK, Anker SD, Appel LJ, Dunbar SB, Grady KL, et al. State of the science: promoting self-care in persons with heart failure: a scientific statement from the American Heart Association. Circulation. 2009; 120(12):1141–1163. [PubMed: 19720935]
- Sloan RS, Pressler SJ. Cognitive deficits in heart failure: Re-cognition of vulnerability as a strange new world. Journal of Cardiovascular Nursing. 2009; 24(3):241–248. [PubMed: 19390342]
- Smith DM, Giobbie-Hurder A, Weinberger M, Oddone EZ, Henderson WG, Asch DA, et al. Predicting non-elective hospital readmissions: A multi-site study. Department of Veterans Affairs Cooperative Study Group on Primary Care and Readmissions. Journal of Clinical Epidemiology. 2000; 53(11):1113–1118. [PubMed: 11106884]
- Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. Medical Care. 2005; 43(6):521–530. [PubMed: 15908846]
- Stewart S, MacIntyre K, MacLeod MM, Bailey AE, Capewell S, McMurray JJ. Trends in hospitalization for heart failure in Scotland 1990–1996. An epidemic that has reached its peak? European Heart Journal. 2001; 22(3):209–217. [PubMed: 11161932]
- Sun SX, Ye X, Lee KY, Dupclay L Jr, Plauschinat C. Retrospective claims database analysis to determine relationship between renin-angiotensin system agents, rehospitalization, and health care costs in patients with heart failure or myocardial infarction. Clinical Therapeutics. 2008; 30(Pt 2): 2217–2227. [PubMed: 19281916]
- Voils CI, Maciejewski ML, Hoyle RH, Reeve BB, Gallagher P, Bryson CL, et al. Initial validation of a self-report measure of the extent of and reasons for medication nonadherence. Medical Care. 2012; 50(12):1013–1019. [PubMed: 22922431]
- Wu JR, Moser DK, Chung ML, Lennie TA. Objectively measured, but not self-reported, medication adherence independently predicts event-free survival in patients with heart failure. Journal of Cardiac Failure. 2008; 14(3):203–210. [PubMed: 18381183]
- Wu JR, Moser DK, Lennie TA, Burkhart PV. Medication adherence in patients who have heart failure: a review of the literature. Nursing Clinics of North America. 2008; 43(1):133–153. [PubMed: 18249229]

What does this paper contribute to the wider global clinical community?

- Medication adherence is associated with all-cause and HF-related hospitalization and death in HF.
- Self-reported adherence, a simple one-item question predicts health outcomes.
- It is important for clinicians to assess patients' medication adherence on a regular basis at their clinical follow-ups.

Table 1

Demographic, Clinical, and Behavioral Characteristics of Participants (N=592)

	Overall Sample N(%) or Mean±SD	Non-Adherent N(%) or Mean±SD	Adherent N(%) or Mean±SD	P
Size	592	163 (28)	429 (72)	
Demographics				
Site				P=0.039
UNC	208 (35)	45 (28)	163 (38)	
NU	162 (27)	56 (34)	106 (25)	
UCSF	148 (25)	44 (27)	104 (24)	
UCLA	74 (13)	18 (11)	56 (13)	
TOFHLA: Adequate	375 (63)	113 (69)	262 (61)	P=0.063
Age	60.6±13.1	56.7±12.7	62.1±12.9	P<0.001
Race/Ethnicity				P=0.064
White NH	226 (38)	51 (31)	175 (41)	
Hispanic	96 (16)	23 (14)	73 (17)	
African American	230 (39)	78 (48)	152 (35)	
Other	40 (7)	11 (7)	29 (7)	
Gender: Male	308 (52)	88 (54)	220 (51)	P=0.556
Language: English	510 (86)	146 (90)	364 (85)	P=0.137
Income Level, \$				P=0.819
<15,000	300 (51)	82 (50)	218 (51)	
15,000–24,999	88 (15)	27 (17)	61 (14)	
25,000–40,000	65 (11)	16 (10)	49 (11)	
>40,000	124 (21)	34 (21)	90 (21)	
Education Level				P=0.255
<12th grade	157 (27)	35 (22)	122 (28)	
High School	174 (29)	56 (34)	118 (28)	
Some college	136 (23)	38 (23)	98 (23)	
College graduate or Greater	125 (21)	34 (21)	91 (21)	
Subjective Socioeconomic Status	4.77±2.51	4.23±2.37	4.97±2.53	P=0.001
Insurance				P<0.001
Medicaid	149 (25)	48 (29)	101 (24)	
Medicare Only	62 (11)	7 (4)	55 (13)	
Private Only	77 (13)	34 (21)	43 (10)	
Uninsured	77 (13)	28 (17)	49 (11)	
Medicare & Medicaid	101 (17)	24 (15)	77 (18)	
Medicare & Private	126 (21)	22 (14)	104 (24)	
Clinical characteristics				
HFSS	60.9±22.0	59.4±22.0	61.4±22.0	P=0.316

	Overall Sample N(%) or Mean±SD	Non-Adherent N(%) or Mean±SD	Adherent N(%) or Mean±SD	P
NYHA Class				P=0.937
I	112 (19)	29 (18)	83 (19)	
II	297 (50)	83 (51)	214 (50)	
Ш	117 (20)	34 (21)	83 (19)	
IV	66 (11)	17 (10)	49 (11)	
Systolic Dysfunction: Ejection fraction <0.45	346 (58)	95 (58)	251 (59)	P=0.960
Systolic BP (mm/Hg)	125±22.7	125±25.0	125±21.8	P=0.944
Diastolic BP (mm/Hg)	71.3±12.9	73.1±14.1	70.6±12.4	P=0.041
Body Mass index	33.2±8.86	33.6±8.77	33.1±8.89	P=0.574
Creatinine level	1.26±0.548	1.21±0.521	1.28±0.558	P=0.191
Diabetes	284 (48)	76 (47)	208 (49)	P=0.686
Hypertension	502 (85)	129 (79)	373 (87)	P=0.018
Atrial Fibrillation	282 (48)	70 (43)	212 (49)	P=0.159
Previous MI or angina	241 (41)	57 (35)	184 (43)	P=0.080
Chronic Kidney Disease	247 (42)	55 (34)	192 (45)	P=0.015
Depressed PHQ>=10	193 (33)	69 (42)	124 (29)	P=0.002
Current smoker	95 (16)	37 (23)	58 (14)	P=0.007
Medication History				
ACE-I	383 (65)	111 (68)	272 (63)	P=0.286
ARB	118 (20)	29 (18)	89 (21)	P=0.422
ACE-I or ARB	487 (82)	136 (83)	351 (82)	P=0.645
Beta blocker	482 (81)	136 (83)	346 (81)	P=0.437
Intervention status	298 (50)	88 (54)	210 (49%)	P=0.274
Knowledge and behavioral factors		_		
HF general knowledge	6.16±1.75	6.02±1.74	6.21±1.76	P=0.230
Salt knowledge	7.55±1.52	7.50±1.68	7.56±1.46	P=0.631
Self-efficacy	78.3±14.4	74.1±16.3	79.9±13.3	P<0.001
Self-care behaviors	4.61±2.04	3.99±1.94	4.85±2.03	P<0.001

ACE-I = Angiotensin Converting Enzyme Inhibitor; ARB = Angiotensin Receptor Blocker; HF = heart failure; HFSS = Heart Failure Symptom Scale; NYHA = New York Heart Association functional classification; PHQ = Patient Health Questionnaire; TOFHLA = Test of Functional Health Literacy in Adults.

Table 2

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All-cause and heart failure related hospitalization.

		Non-adherent Adherent $(n = 163)$ $(n = 429)$	Adherent (n = 429)			
	Z	Event Rate/ Year	Event Rate/Year Adjusted for Site Incidence Ratio	Adjusted for Site Incidence Rate Ratio	Partially Adjusted Incidence Rate Ratio [†]	Fully Adjusted Incidence Rate Ratio ^{††}
All-cause Hospitalization or death 592 0.86	592	0.86	0.71	0.83* (0.69,1.00)	0.71*** (0.58,0.88)	0.68*** (0.53,0.86)
HF-Related Hospitalization	592 0.33	0.33	0.28	0.84*** (0.77,0.92)	0.71*** (0.56,0.89)	0.64* (0.43,0.96)

HF=heart failure

† Adjusted for site, age, gender, ethnicity, socioeconomic status, insurance, systolic dysfunction, diastolic blood pressure, beta-blocker use, current smoker, hypertension, history of CVD, chronic kidney disease, HF symptoms, depression, and intervention status. † Adjusted for site, age, gender, ethnicity, socioeconomic status, insurance, systolic dysfunction, diastolic blood pressure, beta-blocker use, current smoker, hypertension, history of CVD, chronic kidney disease, HF symptoms, depression, intervention status, HF general knowledge, salt knowledge, self-efficacy, and self-care behaviors. Page 16

^{*} significant at 5%;

^{**} significant at 1%;

^{***} significant at 0.1%