Published in final edited form as:

J Card Fail. 2008 September ; 14(7): 603–614. doi:10.1016/j.cardfail.2008.02.011.

Predictors of Medication Adherence Using a Multidimensional Adherence Model in Patients with Heart F

Jia-Rong Wu, Debra K. Moser, Misook L. Chung, and Terry A. Lennie

Introduction

Heart failure (HF) is one of the many chronic conditions that require patients to adhere to a lifelong therapeutic regimen in order to achieve optimal outcomes.^{1–3} Patients with HF require multiple medications to decrease morbidity and mortality.^{1, 2} Estimates of medication adherence rates in patients with HF range from 7% to 90%, depending on definition and how adherence is measured.^{4–16} Adherence rates decrease the longer patients live with a condition.^{17, 18} Medication nonadherence is thought to be the most common cause of HF exacerbation and subsequent hospital readmission in patients with HF.^{19–22} Available data suggest that as many as one-half to two-thirds of hospitalizations for HF could be prevented and that poor adherence may play a major role in preventable rehospitalizations.²³

Medication adherence in HF is a complex and poorly understood phenomenon.²⁴ Because of the importance of medication adherence in managing HF, full understanding of the factors associated with medication adherence in patients with HF is needed so that effective interventions that improve medication adherence can be developed. Medication adherence is a behavioral problem observed in patients; however, poor adherence is not only caused by patient-related factors, but also by other factors external to the patients (e.g., financial problems, poor communication with health care providers, health care system issues).^{24–26}

Most studies of medication adherence in patients with HF have a number of limitations that reduce the usefulness of their findings. These limitations include failure to use multivariate analytic methods to study medication adherence.^{8, 9, 27–29} Investigators commonly have tested only bivariate relationships between a limited number of variables and medication adherence.^{8, 9, 27–29} Using such an approach, it is difficult to determine independent predictors of medication adherence. Even those investigators who tested multivariate models commonly failed to use a theoretical model for selection of variables,^{10, 22, 30–39} highlighting another limitation of HF adherence research.⁴⁰ Without use of rationale conceptual or theoretical models, systematic investigation of the most relevant variables predicting adherence is not possible.

In attempting to clarify the role of the many potential variables influencing medication adherence, the World Health Organization's multidimensional adherence model (MAM) has been proposed, but this model has not been validated in patients with HF. It is imperative that medication adherence be studied using an appropriate model and multivariate approach in order to obtain comprehensive information about factors associated with medication adherence. Once this information is obtained, it can be used to identify those patients at risk for

nonadherence and to develop interventions to enhance adherence thereby reducing morbidity and mortality in patients with HF. Accordingly, the purpose of this study was to determine factors contributing to medication adherence based on the MAM. The five dimensions of the MAM are: 1) socioeconomic factors, 2) health care system-related factors, 3) condition-related factors, 4) treatment-related factors, and 5) patient-related factors (Figure 1).

The specific aim of this study was to test, in a multivariate model, potential predictors selected from the MAM of medication adherence in patients with HF.

Hypothesis 1

Medication adherence in patients with HF can be predicted by the component variables of the MAM.

In this study, we used an objective measure of adherence, the Medication Event Monitoring System (MEMS), to provide information about patients' medication taking behavior.^{41, 42} Using the MEMS, it is possible to obtain the following indicators of adherence: 1) dose-count, the percentage of prescribed doses taken; 2) dose-days, the percentage of days the correct number of doses taken; and 3) dose-time, the percentage of doses taken on schedule.

Methods

Study Design

This study was conducted in the context of a prospective study in which we determined the role of medication adherence determining outcomes in patients with HF.⁴³ In the current analysis we determined whether factors making up the five dimensions of the MAM predicted medication adherence. At baseline, patients completed questionnaires and started medication adherence monitoring. Medication adherence was monitored for 3 months and outcomes were tracked for six months.

Sample and Settings

Patients were enrolled in this study from outpatient cardiology clinics in Central Kentucky. Patients enrolled in this study met the following inclusion criteria: (1) diagnosis of chronic HF confirmed by the patient's cardiologist or primary care provider; (2) undergone evaluation of HF by a cardiologist and optimization of medical therapy, defined as being on stable doses of HF medications for one month with no plans to add HF medications or titrate further in the immediate future as confirmed by patient's health care provider; and (3) are able to read and speak English. Patients had no obvious cognitive impairment (i.e., unable to give informed consent or participate in an interview) and no co-existing terminal illness (i.e., cancer).

Measures (Table 1)

Medication Adherence—Medication adherence was defined as the extent to which the patient's medication taking behavior corresponded with the prescribed medication regimen.^{24, 44, 45} Medication adherence was measured objectively using an unobtrusive microelectronic monitoring device in the caps of medication bottles, the MEMS. The MEMS registers the date and time of each opening bottle.^{46, 47} Real-time data were collected and later transferred to a computer. Data were collected on one HF medication (e.g., angiotensin-converting-enzyme [ACE] inhibitor, diuretic, β -blocker, digoxin) for each patient as it is impractical and may be burdensome to patients to use multiple MEMS. Prior research has demonstrated that monitoring one medication with the MEMS provided a valid indicator that patients took all of their medications even when they are prescribed multiple medications per day.^{46, 48} In addition, our prior research confirms that adherence in HF patients measured using only one medication in the MEMS independently predicted rehospitalization and

mortality, thus providing further evidence that using only one medication in the MEMS will accurately reflect medication adherence even in those on multiple medications.⁴³ Three indicators of adherence were assessed by the MEMS: 1) dose-count, defined as the percentage of prescribed number of doses taken; 2) dose-days, defined as the percentage of days the correct number of doses taken; and 3) dose-time, defined as the percentage of doses taken on schedule (within 25% of expected time interval [i.e., 24 ± 6 hours for once-a-day and 12 ± 3 hours for twice-a-day doses]).^{46, 47}

The MEMS is a valid instrument that has been used to measure medication adherence with high sensitivity for detecting non-adherent patients with cardiovascular diseases^{46–49} and HF.^{12, 48, 50} Although there is no universally accepted gold standard for medication adherence measure, the MEMS was chosen as the measurement of medication adherence in this study for the following reasons. First, the MEMS is an objective measure and has been used as the “new reference standard” for medication adherence.^{41, 51–53} Evidence from validation studies of the MEMS confirms that patients rarely remove a pill without taking it. For example, in Cheng et al.’s study,⁴⁶ serum low density lipoprotein (LDL) cholesterol was correlated with medication adherence using the MEMS. Second, using the MEMS, detailed and real-time information about how patients adhere to their medication can be collected.^{46, 47} Finally, using electronic monitoring caps to measure medication adherence does not alter adherence.⁵⁴ For example, in one study, HIV patients were randomly assigned to one of the following three groups in order to determine the impact of surveillance methods on adherence: MEMS, medication diary, and a no surveillance control group. After four weeks, there were no differences in adherence between the three groups, demonstrating that there is no Hawthorne effect associated with using the MEMS.⁵⁴ Moreover, in many comparison studies, the MEMS yielded the lowest adherence rates compared to other adherence measures. In one study,⁵⁵ patient self-report and the MEMS were used to compare medication adherence in a 3-month study. Medication adherence measured by the MEMS was lower than that measured by the self-report method from month 1 to month 3. In another study,⁵⁶ investigators compared medication adherence rates by self-report, pill count, physician-rating and the MEMS, and found that medication adherence was the lowest using the MEMS. In this study, medication adherence measured by the MEMS identified the greatest number of nonadherent patients, followed by pill count, physician-rating and self-report. Therefore, using the MEMS to measure medication adherence does not suffer from a Hawthorne effect bias and is considered the best method to measure medication adherence by many investigators in adherence research.^{42, 52–54, 56–61}

Patient-related factors—Patient-related factors are defined as patients’ demographic characteristics, knowledge, beliefs, and attitudes.^{24, 40} In this study, patient’s gender, age, attitudes toward medication adherence and knowledge of medication were included. Patient’s gender and age were collected by a patient interview. Attitude about medication taking was defined as patient’s attitudes toward medication adherence. Attitudes toward medication adherence were measured using the Attitude subscale of the medication adherence scale (MAS).⁶² The Attitude subscale has three items. Patients were instructed to rate how much they agree or disagree with each item on a scale from 0 (strongly disagree) to 10 (strongly agree). One negatively worded item is reverse scored. The scores on this subscale range from 0 to 30; higher scores indicate a more positive attitude toward medication adherence. Knowledge of medication was defined as patient’s knowledge of their prescribed medication. Knowledge of medication was measured using the Knowledge subscale of the MAS. The Knowledge subscale consists of three items that are self-rated on a scale from 0 (strongly disagree) to 10 (strongly agree). The Knowledge subscale item ratings are summed for a total score that can range from 0 to 30; higher scores indicate more knowledge of prescribed medication. Based on our prior study,⁶² the MAS is both reliable (Cronbach’s $\alpha = .75$)

and a valid reflection of attitudes and knowledge related to medication adherence in patients with HF.

Condition-related factors—Condition-related factors were defined as patients' clinical condition.^{24, 40} In this study, condition-related factors included symptom severity, comorbidity, and depression. Symptom severity was operationalized as New York Heart Association (NYHA) functional class.^{63–65} NYHA were determined by careful patient interview.⁶⁶ Based on patients' reports of how they are able to perform their usual activities, they were assigned a NYHA classification of I (ordinary physical activity causes no symptoms of fatigue, dyspnea, angina or palpitations), II (symptoms with ordinary physical activity that slightly limit physical activity), III (symptoms occur with less than ordinary physical activity and markedly limit activity) or IV (symptoms occur even at rest). Reproducibility both among different raters (inter-rater reliability) and across the same rater (intra-rater reliability) were insured by training raters and testing them in sample patients until inter-rater agreement was >95%.

Comorbidity was measured using the interview format of the Charlson Comorbidity Index (CCI).^{67–69} At enrollment, patients were queried about preexisting diseases (e.g., ulcer disease, diabetes). Most conditions are scored with 1 point although some (e.g., hemiplegia, cirrhosis) are assigned >1 point. Scores can range from 0 to 34 but because each subject has HF they will have a score ≥ 1 . Validity of the CCI as an appropriate measure of comorbidity was supported when comorbidity predicted mortality, complications, health care resource use, length of hospital stay, and discharge disposition.^{67–69}

Patients' depression level was measured by the Patient Health Questionnaire (PHQ).^{70, 71} The PHQ consists of nine items that are self-rated on a scale from 0 (not at all) to 3 (nearly every day). The PHQ item ratings are summed for a total score that can range from 0 to 27; higher scores indicate a greater level of depression. Scores between 10 to 14 indicate a moderate level of depressive symptoms, scores between 15 and 19 indicate moderately severe major depression, and scores 20 and above indicate severe major depression.⁷⁰ The PHQ is a reliable (Cronbach's $\alpha = .89$)⁷⁰ and valid scale that has been used to measure depression level in patients with HF.⁷¹

Treatment-related factors—Treatment-related factors are defined as factors associated with treatments that are received by patients and that influence patients' willingness to receive treatment.^{24, 40} Treatment-related factors in this study included complexity of treatment and patient's barriers to medication adherence. Complexity of the treatment is operationalized in this study as the number of pills taken per day and the medication frequency. The number of pills taken per day and medication frequency were collected by patient interview. Barriers to medication adherence were measured using the Barriers subscale of the MAS.⁶² The Barriers subscale consists of 11 items that are rated on a 10-point scale that is scored from 10 (very important cause) to 0 (not important cause). The total score can range from 0 to 110 with a higher score reflecting more barriers to adhering to prescribed medication. Based on our prior study,⁶² the Barriers subscale of the MAS is a reliable (Cronbach's $\alpha = .94$) and valid reflection of patient identified barriers to medication adherence.

Health care system-related factors—Health care system-related factors are defined as systems or persons who provide health care to patients.^{24, 40} In this study, the health care system-related factor was the patient-provider relationship. The Interpersonal Trust in a Physician (ITP) scale was used to measure patient-provider relationship. This scale includes 10 items, scored on a Likert scale from 5 (strongly agree) to 1 (strongly disagree). Negatively worded items (2, 3, 8) are reverse scored. In a national sample of 959 adults with primary care relationships (including non-physicians), the internal consistency reliability using Cronbach's

alpha was .93.^{72, 73} The validity has been supported by strongly correlating with satisfaction, desire to remain with a physician, willingness to recommend a physician to friends, and not seeking second opinions.^{72, 73} The total score can range from 10 to 50 with a higher score reflecting more positive patient-provider relationship.

Socio-economic factors—Socio-economic factors are defined as patients' social and economic status.^{24, 40} In this study, socio-economic factors were ethnicity, level of education, financial status, and social support. Ethnicity, level of education, and financial status were collected by a patient/family interview. Social support was measured by the Perceived Social Support Scale (PSSS). The PSSS is a reliable and valid questionnaire.^{74, 75} The PSSS consists of 12 items rated by patients using a 7-point Likert scale from 1 (very strongly disagree) to 7 (very strongly agree). The instrument is scored by adding the item ratings. The total score can range from 7 to 84 with a higher score reflecting better social support.

Other covariates—To characterize subjects and obtain data on potential confounding variables, information concerning the following additional variables were collected from the medical record, or patient interview: left ventricular ejection fraction (LVEF), etiology of HF, medication regimen (ACE inhibitors [yes/no], β blockers [yes/no]), and whether or not patients normally took their medications using a pill box. If data from patient interview and the medical records were different, we carefully reviewed the medical record to confirm the data, and called the patient to clarify. In all cases, conflicting data between patient report and medical records were resolved.

Procedures

Permission for the conduct of the study was obtained from the University of Kentucky (UK) Institutional Review Board (IRB). Patients were referred by nurse practitioners in the HF clinic. Patient eligibility was confirmed by a trained research associate. The research associate explained study requirements to the eligible patients and obtained informed, written consent.

At enrollment, patients visited the General Clinical Research Center of the UK Medical Center for data collection. Patient's demographic and clinical characteristics were collected by interview and medical record review. Patients completed the questionnaires and were provided detailed written and verbal instructions on use of the MEMS bottle. The investigator chose the medication to be monitored based on the following criteria. If the patient was taking a medication twice a day, this medication was chosen for monitoring using the MEMS. If all medications were taken only once per day, then the beta-blocking agent was chosen unless the patient was not prescribed one. In that case, the ACE inhibitor or angiotensin receptor blocker was chosen. Patients took that medication from the MEMS bottle for the next three months. The cap was replaced on the bottle after each use. Patients recorded time and date of unscheduled cap openings (i.e., opening to refill the bottle, check on supply, or accidentally openings) in a medication diary. These events were excluded when data were downloaded. Patients who used a pill box kept the MEMS bottle beside their pill box and took the medicine from the MEMS bottle when they took their other medications from the pill box.

Patients used the MEMS bottle daily for three months. The bottle was then returned to investigators and the data were downloaded onto a personal computer using manufacturer-supplied communicator and software.

Data Management and Analysis

Before conducting analyses, data were cleaned and multiple item scales were scored and tested for reliability. Scale reliability was acceptable if Cronbach's alpha is ≥ 0.7 . All data analyses were done using SPSS, version 14.0. Data analysis began with a descriptive examination of

all variables, including frequency distributions, means, standard deviations, medians, and interquartile ranges, as appropriate to the level of measurement of the variables. An alpha of .05 was set a priori.

The initial step in analysis was determination of the bivariate relationships between medication adherence and the components of the MAM using Spearman's rho. Hierarchical multiple linear regression with backward variable entry was used to determine predictors of medication adherence from the dimensions of the MAM. Hierarchical methods were used in order to identify the additive effects of introducing each dimension of the MAM. Patient-related factors were entered first into the model followed by condition-related factors, treatment-related factors, health care system-related factors, and socio-economic factors. The adjusted R^2 was used to determine the variance explained in medication adherence.

Results

Sample Characteristics

A total of 134 patients with HF were included in this study. The mean age of patients in the sample was 61 ± 11 years. The most common HF etiology was ischemic heart disease. The sample consisted largely of patients with advanced HF as reflected by their NYHA functional class. The average LVEF reflected the enrollment of patients with and without systolic dysfunction. Only 9% of patients had no comorbidities, while the remainder has one or more, with 44% of patients having a CCI score of 4 and greater. Full sample characteristics are presented in Table 2.

Data examination showed no problems with multicollinearity (i.e., in each regression model, all variance inflation factors [VIF] were < 8 , indicating no multicollinearity problems). Examination of the scatterplots of pairs of independent and dependent variables revealed no violation of the linearity assumption and examination of the partial regression plots revealed no violation of the assumption of homoscedasticity. Because medication adherence rates measured by the MEMS were skewed toward low scores, the nonparametric Spearman's rho test was used to examine the bivariate relationships between medication adherence and the variables tested. In each multiple regression, the MEMS data were transformed using a log transformation to approximate normality.

Description of Medication Adherence

Figure 2 illustrates medication adherence rates for each of the three indicators used in this study. The mean percentage of prescribed doses taken was 89%, the mean percentage of days the correct number of doses was taken was 81%, and the mean percentage of doses taken on schedule was 67%. There were no differences in medication adherence rates between patients who regularly used a pill box and patients who did not use a pill box ($p = .30, .29$ and $.99$, respectively for dose-time, dose-day and dose-time).

Bivariate Relationships

The bivariate correlations of each indicator of the MEMS with each variable tested are shown in Table 3.

Multivariate Predictors of Adherence

Hierarchical multiple regression with backward entry was conducted to examine the multivariate relationships between medication adherence and the variables outlined previously. The models for each indicator of medication adherence are shown in Table 4–7. Table 4 illustrates variables in the final models of each indicator of the MEMS. Tables 5–7 illustrate all variables tested of each indicator of the MEMS.

Barriers to medication adherence, ethnicity, and perceived social support composed the best group of variables associated with the first indicator of the MEMS, dose-count ($F = 7.253$, $P < .001$), explaining 20% of the variance. NYHA, barriers to medication adherence, financial status, and perceived social support were the best model associated with the second indicator of the MEMS, dose-day ($F = 6.293$, $P < .001$), explaining 21% of the variance. Barriers to medication adherence and financial status were the best group of predictors associated with the third indicator of the MEMS, dose-time ($F = 3.606$, $P = .005$), explaining 11% of the variance.

Based on different indicators of the MEMS, variance explained by each dimension of the MAM is shown in Table 8. Patient-related factors explained 6% to 10% of the variance in medication adherence; condition-related factors contributed to another 3% to 4% of variance explained; treatment-related factors contributed to 6% to 10%; health care system-related factors contributed none to the variance explained (0%); and socio-economic factors contributed to 5% to 7% of the variance explained.

Discussion

This is the first study in patients with HF in which the factors hypothesized to contribute to adherence hypothesized in the MAM, a multivariate medication adherence model, were tested.⁴⁰ The findings of this study supported some, but not all, of the relationships hypothesized in the MAM. In multivariate analyses, worse NYHA functional class, more barriers to medication adherence, minority ethnicity, lower financial status, and lack of perceived social support were related to objectively measured medication adherence, whereas health care system-related factors, such as the patient-provider relationship, were not. Despite the relative complexity of the MAM and the number of variables tested, only 11–21% of the variance in adherence was explained, demonstrating the complexity of the phenomenon of adherence.

Among the many factors proposed by the model to predict medication adherence, the most important and consistent predictor for all of the indicators of adherence was patient perception of barriers to medication adherence. Our study demonstrated that even after controlling for many other relevant variables, perceived barriers are fundamental to poor adherence. Five barriers that patients most frequently reported in this study were “forgetting the time of medication”, “not carrying my medication when I am out”, “cost of medication”, “amount of pills that I need to take a day”, and “belief that I’ll be fine even though I skip one dose of medication”. These results were consistent with previous studies, but expand those findings by demonstrating that perceived barriers are independent predictors of adherence. In prior studies, investigators have demonstrated that perceived barriers to medication taking are correlated to poor medication adherence.^{76–78} Barriers that have been studied included forgetting to take medications, cost, too many pills taken per day, and a too frequent medication schedule. Patients who had any of these barriers were less likely to adhere to medications.^{9, 27, 28, 30, 77–87} It is important to identify and help patients overcome these barriers to taking prescribed medication. Methods such as use of environmental cues (e.g., weekly drug dispensers, posting reminders in a place that the patient goes to everyday at the same time such as the bathroom mirror or refrigerator) may combat forgetfulness. In addition, healthcare providers should simplify the medication regimen and consider patients’ financial status when prescribing in order to increase medication adherence. Thus, assessment of patient’s perceived barriers to adhering to prescribed medications should be the first step in implementing any intervention to improve medication adherence.

We demonstrated that ethnicity and financial status were predictors of medication adherence in multivariate analysis. Those who were minority were more often less adherent, a finding that has been demonstrated in two prior studies in patients with HF,^{13, 88} two studies in

hypertensive,^{89, 90} three studies in coronary heart disease,^{91–93} and one study in chronic disease (i.e., diabetes, hypertension, and hypercholesterolemia)⁹⁴ patients. There is, however, considerable inconsistency in findings and a number of other investigators have demonstrated no differences based on race/ethnicity.^{4, 13, 16, 48} It is unclear why minorities might have lower adherence, but most have postulated that it is not race, but the interaction of race and income that is related to adherence. For example, Akincigil et al.⁹⁵ studied long-term adherence to pharmacotherapy after acute myocardial infarction and reported the risk of discontinuation was highest among patients from low-income neighborhoods. In our study, we asked patients their perception of their financial status and did not find a relationship between financial status and adherence nor financial status and race/ethnicity. It should be noted that the percentage of low-income minority patients was low in this study. In another study, African Americans had a higher odds ratio (OR = 1.81) of being nonadherent to their medication and more often had inadequate blood pressure control (OR = 1.70) than whites.⁹⁰ The investigators found African Americans were more likely to experience side effects of taking medication compared with whites.⁹⁰ Side effects could counterbalance the patient's motivation and lead to poor adherence. Thus, the association between medication nonadherence and ethnicity could be confounded by side effects of medication. Our results suggest the need for collecting such data to investigate medication side effects in improving adherence. However, given the inconsistencies in the literature, more comprehensive study of this aspect of adherence is needed.

Patients who reported not having enough money to make ends meet had poorer adherence. When patients do not have enough to make ends meet, they report cutting down on food to pay for drugs.⁸⁶ As many as 42% in one study did not fill their prescriptions when their medication costs exceeded the limits of the Medicaid prescription cap, slightly fewer changed the way medication was taken (37%) while some took other people's medication (11%).⁸⁴ Hsu, et al.⁹⁶ compared clinical and economic outcomes in a sample of 199,179 Medicare beneficiaries whose annual drug benefits were either capped or unlimited. These investigators found that patients whose benefits were capped took fewer of their prescribed medication, and had poorer clinical outcomes, and increased hospital and emergency department costs. In another study, patients without a prescription benefit had worse medication adherence than patients with a prescription benefit,³⁰ resulting in increased rehospitalization rates and overall healthcare costs.^{33, 97} When drug copayments increased, patient's medication adherence decreased and their risk of hospitalization increased.⁹⁸ Thus, it is not surprising that better financial status facilitates medication adherence.⁴⁸ Healthcare providers should consider affordability as a clinical factor when prescribing. Policy makers should facilitate pharmaceutical company support of vulnerable patient population like patients with HF. In the long run, the cost of medications is lower than rehospitalization costs.⁹⁶

One of the major predictors of adherence in this study was perceived social support. Patients who felt that they received adequate social support from family members and others were more adherent. Patients need practical and emotional support from their family members to assist them to take their medications.⁸⁶ Without enough social support, it is difficult for this group of patients to adhere to their medications.^{5, 80, 85, 86, 99}

A number of factors thought to influence medication adherence did not. For example, gender,^{6, 8, 14, 100} age,^{6, 8, 10, 13, 14, 16, 100} comorbidity,¹⁰⁰ number of pills taken per day,^{13, 79, 81} frequency of medication,^{48, 101} and education^{6, 16, 102, 103} were not related to medication adherence and these findings contradict results from earlier studies. One of the possible explanations for this discordance is use of different measures of medication adherence. Most of these studies used self-report measures of adherence and did not consider multivariate predictors. Gender and comorbidity were correlated to medication adherence in bivariate analysis; but not in multivariate analysis. When some more important predictors were in the

multivariate model, these factors became non-significant. Although others have found education not to be related to adherence,^{93, 104} this finding is somewhat puzzling. In our sample, however, the majority of patients (73.4%) had at least a high school education. If we had a larger proportion of poorly educated patients we may have found a relationship between education level and adherence.

The patient-provider relationship has been shown by others to be related to medication adherence,^{86, 105, 106} but was unrelated to medication adherence in this study. In our study, the mean score for patient-provider relationship was very high, demonstrating that patients in this group had high level of trust on their health care providers. This lack of variability in scores may be one reason for our failure to find a relationship between patient-provider relationship and adherence. Our finding is similar to Simpson et al.'s study.⁸⁵ They failed to find a significant relationship between patient-provider relationship and medication adherence because of patients' high level of trust in health care provider.⁸⁵

In contrast to prior studies, we demonstrated that symptom severity as reflected by worse NYHA function class was related to poor medication adherence.^{10, 100} Despite the importance of the factor, the relationship between medication adherence and NYHA functional class had only rarely been investigated.^{10, 100} Patients with poor functional status commonly have increased physical disability that produce limitations in their ability to perform common activities of daily living. In our study, about two thirds of the patients were NYHA functional class III/IV, and almost half had a high comorbidity burden. Under these circumstances, it is not surprising that poor functional class compromised medication adherence.

This study differed from previous studies in that the association of medication adherence with predictors was examined based on a conceptual framework. A sound conceptual framework can make sense of the multitude of possible variables associated with adherence. Researchers and clinicians can work more efficiently to improve medication adherence if they know which factors are associated with medication adherence and which factors are less important to medication adherence. For example, many clinicians believe that a patient's medication adherence is largely determined by number of pills taken per day and medication frequency. However, number of pills taken per day and medication frequency was not associated with medication adherence, demonstrating the potential for making errors if assumptions go untested when developing interventions to enhance medication adherence. The model tested in this study explained up to 21% of the variance in medication adherence. This compares to prior studies in which 6.8% to 33%,^{94, 104, 107–109} of the variance in medication adherence was explained. Thus, to date, even with the use of complex multidimensional models, most the variance in adherence remains unexplained. Given the importance of adherence to outcomes, it is essential that further studies be conducted to determine the important modifiable predictors of adherence.

Limitations

Although we had sufficient power to demonstrate significant differences, a larger sample size and more heterogeneous sample may be needed more thoroughly investigate predictors of adherence and to generalize the result to a larger population.

Conclusion

Although patient adherence is often quite difficult for a variety of patient, provider and healthcare system-related factors, it is essential to optimal patient outcomes. Thus, health care providers and researchers must identify ways to enhance medication adherence. One important way is to identify the factors that contribute to poor adherence.

Barriers to medication adherence were the only significant predictor of all of the three indicators of objectively measured adherence. In addition to barriers to medication adherence, condition-related factors (i.e., NYHA) and socio-economic factors (i.e., ethnicity, financial status, and social support) were related to at least one indicator of adherence. The MAM has been proposed as a model of medication adherence in HF although it has not been previously tested in this sample. This study provides a first step in testing the model and demonstrates that some of the conceptual relationships proposed by the MAM are valid, whereas others are not. Further studies are needed to fully investigate the relationships among variables in the MAM. These findings have important implications for clinicians caring for patients with HF. Assessing patients' barriers to taking prescribed medications should be the first step in implementing any intervention to improve medication adherence. Minorities and those who had more severe symptoms as reflected by NYHA functional class, lower income, and less social support should be considered at high risk for medication nonadherence. The findings of this study provide clinicians and researchers a theoretical basis for effective interventions to improve medication adherence and in turn clinical outcomes in patients with HF.

References

1. Stanley M, Prasun M. Heart failure in older adults: Keys to successful management. *AACN Clin Issues* 2002;13:94–102. [PubMed: 11852727]
2. Cleland JG, Clark A. Has the survival of the heart failure population changed? Lessons from trials *Am J Cardiol* 1999;83:112D–119D.
3. De Geest S. Another perspective in understanding adherence: qualitative research in unraveling the behavioral dimension of heart failure management. *J Cardiopulm Rehabil* 2005;25:164–165. [PubMed: 15931020]
4. Rich MW, Gray DB, Beckham V, Wittenberg C, Luther P. Effect of a multidisciplinary intervention on medication compliance in elderly patients with congestive heart failure. *Am J Med* 1996;101:270–276. [PubMed: 8873488]
5. Col N, Fanale JE, Kronholm P. The role of medication noncompliance and adverse drug reactions in hospitalizations of the elderly. *Arch Intern Med* 1990;150:841–845. [PubMed: 2327844]
6. Huang LH. Medication-taking behavior of the elderly. *Kaohsiung J Med Sci* 1996;12:423–433. [PubMed: 8753145]
7. Cline CM, Bjorck-Linne AK, Israelsson BY, Willenheimer RB, Erhardt LR. Non-compliance and knowledge of prescribed medication in elderly patients with heart failure. *Eur J Heart Fail* 1999;1:145–149. [PubMed: 10937924]
8. Gonzalez B, Lupon J, Parajon T, Urrutia A, Altimir S, Coll R, et al. Nurse evaluation of patients in a new multidisciplinary Heart Failure Unit in Spain. *Eur J Cardiovasc Nurs* 2004;3:61–69. [PubMed: 15053889]
9. Blenkiron P. The elderly and their medication: Understanding and compliance in a family practice. *Postgrad Med J* 1996;72:671–676. [PubMed: 8944209]
10. Rodgers PT, Ruffin DM. Medication nonadherence: Part II--A pilot study in patients with congestive heart failure. *Manag Care Interface* 1998;11:67–69. 75. [PubMed: 10187590]
11. Bonner CJ, Carr B. Medication compliance problems in general practice: Detection and intervention by pharmacists and doctors. *Aust J Rural Health* 2002;10:33–38. [PubMed: 11952520]
12. Bohachick P, Burke LE, Sereika S, Murali S, Dunbar-Jacob J. Adherence to angiotensin-converting enzyme inhibitor therapy for heart failure. *Prog Cardiovasc Nurs* 2002;17:160–166. [PubMed: 12417831]
13. Graveley EA, Oseasohn CS. Multiple drug regimens: Medication compliance among veterans 65 years and older. *Res Nurs Health* 1991;14:51–58. [PubMed: 2017581]
14. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Avorn J. Noncompliance with congestive heart failure therapy in the elderly. *Arch Intern Med* 1994;154:433–437. [PubMed: 8117176]

15. Artinian NT, Harden JK, Kronenberg MW, Vander Wal JS, Daher E, Stephens Q, et al. Pilot study of a Web-based compliance monitoring device for patients with congestive heart failure. *Heart Lung* 2003;32:226–233. [PubMed: 12891162]
16. Evangelista LS, Berg J, Dracup K. Relationship between psychosocial variables and compliance in patients with heart failure. *Heart Lung* 2001;30:294–301. [PubMed: 11449216]
17. Butler J, Arbogast PG, Daugherty J, Jain MK, Ray WA, Griffin MR. Outpatient utilization of angiotensin-converting enzyme inhibitors among heart failure patients after hospital discharge. *J Am Coll Cardiol* 2004;43:2036–2043. [PubMed: 15172409]
18. DiMatteo MR, Sherbourne CD, Hays RD, Ordway L, Kravitz RL, McGlynn EA, et al. Physicians' characteristics influence patients' adherence to medical treatment: Results from the Medical Outcomes Study. *Health Psychol* 1993;12:93–102. [PubMed: 8500445]
19. Chin MH, Goldman L. Factors contributing to the hospitalization of patients with congestive heart failure. *Am J Public Health* 1997;87:643–648. [PubMed: 9146445]
20. Li H, Morrow-Howell N, Proctor EK. Post-acute home care and hospital readmission of elderly patients with congestive heart failure. *Health Soc Work* 2004;29:275–285. [PubMed: 15575455]
21. 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. *Eur J Clin Pharmacol* 2001;57:77–83. [PubMed: 11372597]
22. 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. *Am J Health Syst Pharm* 2004;61:2043–2049. [PubMed: 15509127]
23. Rich MW, Beckham V, Wittenberg C, Leven CL, Freedland KE, Carney RM. A multidisciplinary intervention to prevent the readmission of elderly patients with congestive heart failure. *N Engl J Med* 1995;333:1190–1195. [PubMed: 7565975]
24. De Geest S, Sabate E. Adherence to long-term therapies: Evidence for action. *Eur J Cardiovasc Nurs* 2003;2:323. [PubMed: 14667488]
25. Miller NH, Hill M, Kottke T, Ockene IS. The multilevel compliance challenge: Recommendations for a call to action. A statement for healthcare professionals. *Circulation* 1997;95:1085–1090. [PubMed: 9054774]
26. Miller NH. Compliance with treatment regimens in chronic asymptomatic diseases. *Am J Med* 1997;102:43–49. [PubMed: 9217586]
27. Evangelista L, Doering LV, Dracup K, Westlake C, Hamilton M, Fonarow GC. Compliance behaviors of elderly patients with advanced heart failure. *J Cardiovasc Nurs* 2003;18:197–206. 208. [PubMed: 12837010]
28. Lainscak M, Keber I. Patient's view of heart failure: From the understanding to the quality of life. *Eur J Cardiovasc Nurs* 2003;2:275–281. [PubMed: 14667483]
29. Taylor AA, Shoheiber O. Adherence to antihypertensive therapy with fixed-dose amlodipine besylate/benazepril HCl versus comparable component-based therapy. *Congest Heart Fail* 2003;9:324–332. [PubMed: 14688505]
30. Jackson JE, Doescher MP, Saver BG, Fishman P. Prescription drug coverage, health, and medication acquisition among seniors with one or more chronic conditions. *Med Care* 2004;42:1056–1065. [PubMed: 15586832]
31. Struthers AD, Anderson G, MacFadyen RJ, Fraser C, MacDonald TM. Non-adherence with ACE inhibitor treatment is common in heart failure and can be detected by routine serum ACE activity assays. *Heart* 1999;82:584–588. [PubMed: 10525514]
32. Murray MD, Morrow DG, Weiner M, Clark DO, Tu W, Deer MM, et al. A conceptual framework to study medication adherence in older adults. *Am J Geriatr Pharmacother* 2004;2:36–43. [PubMed: 15555477]
33. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care* 2005;43:521–530. [PubMed: 15908846]
34. Clark DO, Tu W, Weiner M, Murray MD. Correlates of health-related quality of life among lower-income, urban adults with congestive heart failure. *Heart Lung* 2003;32:391–401. [PubMed: 14652531]

35. 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;366:2005–2011. [PubMed: 16338449]
36. Ilksoy N, Moore RH, Easley K, Jacobson TA. Quality of care in African-American patients admitted for congestive heart failure at a university teaching hospital. *Am J Cardiol* 2006;97:690–693. [PubMed: 16490439]
37. 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. *J Card Fail* 2006;12:54–60. [PubMed: 16500581]
38. Tu W, Morris AB, Li J, Wu J, Young J, Brater DC, et al. Association between adherence measurements of metoprolol and health care utilization in older patients with heart failure. *Clin Pharmacol Ther* 2005;77:189–201. [PubMed: 15735613]
39. 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). *Med J Aust* 2006;185:487–489. [PubMed: 17137452]
40. Leventhal MJ, Riegel B, Carlson B, De Geest S. Negotiating compliance in heart failure: Remaining issues and questions. *Eur J Cardiovasc Nurs* 2005;4:298–307. [PubMed: 15893959]
41. Farmer KC. Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. *Clin Ther* 1999;21:1074–1090. 1073. [PubMed: 10440628]
42. Cramer JA. Microelectronic systems for monitoring and enhancing patient compliance with medication regimens. *Drugs* 1995;49:321–327. [PubMed: 7774509]
43. Wu J, Moser DK, Chung M, Lennie TA. Objectively measured, but not self-reported, medication adherence independently predicts event-free survival in patients with heart failure. *J Card Fail.* (in press)
44. Evangelista LS, Dracup K. A closer look at compliance research in heart failure patients in the last decade. *Prog Cardiovasc Nurs* 2000;15:97–103. [PubMed: 10951951]
45. Haynes RB, McDonald HP, Garg AX. Helping patients follow prescribed treatment: Clinical applications. *Journal of the American Medical Association* 2002;288:2880–2883. [PubMed: 12472330]
46. Cheng CW, Woo KS, Chan JC, Tomlinson B, You JH. Association between adherence to statin therapy and lipid control in Hong Kong Chinese patients at high risk of coronary heart disease. *Br J Clin Pharmacol* 2004;58:528–535. [PubMed: 15521901]
47. Dobbels F, De Geest S, van Cleemput J, Droogne W, Vanhaecke J. Effect of late medication non-compliance on outcome after heart transplantation: A 5-year follow-up. *J Heart Lung Transplant* 2004;23:1245–1251. [PubMed: 15539122]
48. Dunbar-Jacob J, Bohachick P, Mortimer MK, Sereika SM, Foley SM. Medication adherence in persons with cardiovascular disease. *J Cardiovasc Nurs* 2003;18:209–218. [PubMed: 12837011]
49. Carney RM, Freedland KE, Eisen SA, Rich MW, Jaffe AS. Major depression and medication adherence in elderly patients with coronary artery disease. *Health Psychol* 1995;14:88–90. [PubMed: 7737079]
50. Bouvy ML, Heerdink ER, Urquhart J, Grobbee DE, Hoes AW, Leufkens HG. Effect of a pharmacist-led intervention on diuretic compliance in heart failure patients: A randomized controlled study. *J Card Fail* 2003;9:404–411. [PubMed: 14583903]
51. Dunbar-Jacob J, Mortimer-Stephens MK. Treatment adherence in chronic disease. *J Clin Epidemiol* 2001;54(Suppl 1):S57–60. [PubMed: 11750211]
52. Claxton AJ, Cramer J, Pierce C. A systematic review of the associations between dose regimens and medication compliance. *Clin Ther* 2001;23:1296–1310. [PubMed: 11558866]
53. Choo PW, Rand CS, Inui TS, Lee ML, Cain E, Cordeiro-Breault M, et al. Validation of patient reports, automated pharmacy records, and pill counts with electronic monitoring of adherence to antihypertensive therapy. *Med Care* 1999;37:846–857. [PubMed: 10493464]
54. Wagner GJ, Ghosh-Dastidar B. Electronic monitoring: adherence assessment or intervention? *HIV Clin Trials* 2002;3:45–51. [PubMed: 11819185]

55. Melbourne KM, Geletko SM, Brown SL, Willey-Lessne C, Chase S, Fisher A. Medication adherence in patients with HIV infection: a comparison of two measurement methods. *AIDS Read* 1999;9:329–338. [PubMed: 12737122]
56. Velligan DI, Wang M, Diamond P, Glahn DC, Castillo D, Bendle S, et al. Relationships among subjective and objective measures of adherence to oral antipsychotic medications. *Psychiatr Serv* 2007;58:1187–1192. [PubMed: 17766564]
57. Cramer JA, Mattson RH, Prevey ML, Scheyer RD, Ouellette VL. How often is medication taken as prescribed? A novel assessment technique *Jama* 1989;261:3273–3277.
58. Funk M, Krumholz HM. Epidemiologic and economic impact of advanced heart failure. *J Cardiovasc Nurs* 1996;10:1–10. [PubMed: 8656234]
59. Grosset KA, Bone I, Reid JL, Grosset D. Measuring therapy adherence in Parkinson's disease: a comparison of methods. *J Neurol Neurosurg Psychiatry* 2006;77:249–251. [PubMed: 16421131]
60. Schwed A, Fallab CL, Burnier M, Waeber B, Kappenberger L, Burnand B, et al. Electronic monitoring of compliance to lipid-lowering therapy in clinical practice. *J Clin Pharmacol* 1999;39:402–409. [PubMed: 10197299]
61. De Geest S, Schafer-Keller P, Denhaerynck K, Thannberger N, Kofer S, Bock A, et al. Supporting medication adherence in renal transplantation (SMART): a pilot RCT to improve adherence to immunosuppressive regimens. *Clin Transplant* 2006;20:359–368. [PubMed: 16824155]
62. Wu J, Chung M, Lennie TA, Hall LA, Moser DK. Testing the psychometric properties of the medication adherence scale in patients with heart failure. *Heart Lung*. (in press)
63. Maron BJ, Tholakanahalli VN, Zenovich AG, Casey SA, Duprez D, Aeppli DM, et al. Usefulness of B-type natriuretic peptide assay in the assessment of symptomatic state in hypertrophic cardiomyopathy. *Circulation* 2004;109:984–989. [PubMed: 14967727]
64. Obisesan TO, Toth MJ, Poehlman ET. Prediction of resting energy needs in older men with heart failure. *Eur J Clin Nutr* 1997;51:678–681. [PubMed: 9347288]
65. Schwarz KA, Elman CS. Identification of factors predictive of hospital readmissions for patients with heart failure. *Heart Lung* 2003;32:88–99. [PubMed: 12734531]
66. Mills RM Jr, Haught WH. Evaluation of heart failure patients: Objective parameters to assess functional capacity. *Clin Cardiol* 1996;19:455–460. [PubMed: 8790948]
67. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J Chronic Dis* 1987;40:373–383. [PubMed: 3558716]
68. Charlson ME, Sax FL, MacKenzie CR, Braham RL, Fields SD, Douglas RG Jr. Morbidity during hospitalization: Can we predict it? *J Chronic Dis* 1987;40:705–712. [PubMed: 3110198]
69. Katz JN, Chang LC, Sangha O, Fossel AH, Bates DW. Can comorbidity be measured by questionnaire rather than medical record review? *Med Care* 1996;34:73–84. [PubMed: 8551813]
70. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;16:606–613. [PubMed: 11556941]
71. 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. *Gen Hosp Psychiatry* 2005;27:338–343. [PubMed: 16168794]
72. Balkrishnan R, Dugan E, Camacho FT, Hall MA. Trust and satisfaction with physicians, insurers, and the medical profession. *Med Care* 2003;41:1058–1064. [PubMed: 12972845]
73. Hall MA, Zheng B, Dugan E, Camacho F, Kidd KE, Mishra A, et al. Measuring patients' trust in their primary care providers. *Med Care Res Rev* 2002;59:293–318. [PubMed: 12205830]
74. Canty-Mitchell J, Zimet GD. Psychometric properties of the Multidimensional Scale of Perceived Social Support in urban adolescents. *Am J Community Psychol* 2000;28:391–400. [PubMed: 10945123]
75. Picardi A, Mazzotti E, Gaetano P, Cattaruzza MS, Baliva G, Melchi CF, et al. Stress, social support, emotional regulation, and exacerbation of diffuse plaque psoriasis. *Psychosomatics* 2005;46:556–564. [PubMed: 16288135]
76. Bennett SJ, Cordes DK, Westmoreland G, Castro R, Donnelly E. Self-care strategies for symptom management in patients with chronic heart failure. *Nurs Res* 2000;49:139–145. [PubMed: 10882318]

77. Bennett SJ, Milgrom LB, Champion V, Huster GA. Beliefs about medication and dietary compliance in people with heart failure: an instrument development study. *Heart Lung* 1997;26:273–279. [PubMed: 9257137]
78. Richardson MA, Simons-Morton B, Annegers JF. Effect of perceived barriers on compliance with antihypertensive medication. *Health Educ Q* 1993;20:489–503. [PubMed: 8307768]
79. Nikolaus T, Kruse W, Bach M, Specht-Leible N, Oster P, Schlierf G. Elderly patients' problems with medication. An in-hospital and follow-up study. *Eur J Clin Pharmacol* 1996;49:255–259. [PubMed: 8857069]
80. Welsh JD, Heiser RM, Schooler MP, Brockopp DY, Parshall MB, Cassidy KB, et al. Characteristics and treatment of patients with heart failure in the emergency department. *J Emerg Nurs* 2002;28:126–131. [PubMed: 11960124]
81. Riegel B, Carlson B. Facilitators and barriers to heart failure self-care. *Patient Educ Couns* 2002;46:287–295. [PubMed: 11932128]
82. Hussey LC, Hardin S, Blanchette C. Outpatient costs of medications for patients with chronic heart failure. *Am J Crit Care* 2002;11:474–478. [PubMed: 12233973]
83. Ohene Buabeng K, Matowe L, Plange-Rhule J. Unaffordable drug prices: The major cause of non-compliance with hypertension medication in Ghana. *J Pharm Pharm Sci* 2004;7:350–352. [PubMed: 15576016]
84. Schulz RM, Lingle EW, Chubon SJ, Coster-Schulz MA. Drug use behavior under the constraints of a Medicaid prescription cap. *Clin Ther* 1995;17:330–340. [PubMed: 7614533]
85. Simpson SH, Johnson JA, Farris KB, Tsuyuki RT. Development and validation of a survey to assess barriers to drug use in patients with chronic heart failure. *Pharmacotherapy* 2002;22:1163–1172. [PubMed: 12222552]
86. Simpson SH, Farris KB, Johnson JA, Tsuyuki RT. Using focus groups to identify barriers to drug use in patients with congestive heart failure. *Pharmacotherapy* 2000;20:823–829. [PubMed: 10907972]
87. Wu JR, Moser DK, Lennie TA, Peden AR, Chen YC, Heo S. Factors influencing medication adherence in patients with heart failure. *Heart Lung* 2008;37:8–16. [PubMed: 18206522]
88. Bagchi AD, Esposito D, Kim M, Verdier J, Bencio D. Utilization of, and adherence to, drug therapy among medicaid beneficiaries with congestive heart failure. *Clin Ther* 2007;29:1771–1783. [PubMed: 17919558]
89. Hyre AD, Krousel-Wood MA, Muntner P, Kawasaki L, DeSalvo KB. Prevalence and predictors of poor antihypertensive medication adherence in an urban health clinic setting. *J Clin Hypertens (Greenwich)* 2007;9:179–186. [PubMed: 17344769]
90. Bosworth HB, Dudley T, Olsen MK, Voils CI, Powers B, Goldstein MK, et al. Racial differences in blood pressure control: potential explanatory factors. *Am J Med* 2006;119:70:e79–15.
91. Gehi AK, Ali S, Na B, Whooley MA. Self-reported medication adherence and cardiovascular events in patients with stable coronary heart disease: the heart and soul study. *Arch Intern Med* 2007;167:1798–1803. [PubMed: 17846400]
92. Benner JS, Glynn RJ, Mogun H, Neumann PJ, Weinstein MC, Avorn J. Long-term persistence in use of statin therapy in elderly patients. *Jama* 2002;288:455–461. [PubMed: 12132975]
93. Mann DM, Allegrante JP, Natarajan S, Halm EA, Charlson M. Predictors of adherence to statins for primary prevention. *Cardiovasc Drugs Ther* 2007;21:311–316. [PubMed: 17665294]
94. Schectman JM, Bovbjerg VE, Voss JD. Predictors of medication-refill adherence in an indigent rural population. *Med Care* 2002;40:1294–1300. [PubMed: 12458310]
95. Akincigil A, Bowblis JR, Levin C, Jan S, Patel M, Crystal S. Long-Term Adherence to Evidence Based Secondary Prevention Therapies after Acute Myocardial Infarction. *J Gen Intern Med*. 2007
96. Hsu J, Price M, Huang J, Brand R, Fung V, Hui R, et al. Unintended consequences of caps on Medicare drug benefits. *N Engl J Med* 2006;354:2349–2359. [PubMed: 16738271]
97. Kane S, Shaya F. Medication Non-adherence is Associated with Increased Medical Health Care Costs. *Dig Dis Sci*. 2007
98. Cole JA, Norman H, Weatherby LB, Walker AM. Drug copayment and adherence in chronic heart failure: effect on cost and outcomes. *Pharmacotherapy* 2006;26:1157–1164. [PubMed: 16863491]

99. Happ MB, Naylor MD, Roe-Prior P. Factors contributing to rehospitalization of elderly patients with heart failure. *J Cardiovasc Nurs* 1997;11:75–84. [PubMed: 9200021]
100. Roe CM, Motheral BR, Teitelbaum F, Rich MW. Angiotensin-converting enzyme inhibitor compliance and dosing among patients with heart failure. *Am Heart J* 1999;138:818–825. [PubMed: 10539811]
101. Sung JC, Nichol MB, Venturini F, Bailey KL, McCombs JS, Cody M. Factors affecting patient compliance with antihyperlipidemic medications in an HMO population. *Am J Manag Care* 1998;4:1421–1430. [PubMed: 10338735]
102. 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;23:326–332. [PubMed: 12627931]
103. Rockwell JM, Riegel B. Predictors of self-care in persons with heart failure. *Heart Lung* 2001;30:18–25. [PubMed: 11174364]
104. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res* 1999;47:555–567. [PubMed: 10661603]
105. Tolmie EP, Lindsay GM, Kerr SM, Brown MR, Ford I, Gaw A. Patients' perspectives on statin therapy for treatment of hypercholesterolaemia: A qualitative study. *Eur J Cardiovasc Nurs* 2003;2:141–149. [PubMed: 14622639]
106. Wiseman IC, Miller R. Quantifying non-compliance in patients receiving digoxin--a pharmacokinetic approach. *S Afr Med J* 1991;79:155–157. [PubMed: 1994486]
107. Byrne M, Walsh J, Murphy AW. Secondary prevention of coronary heart disease: Patient beliefs and health-related behaviour. *J Psychosom Res* 2005;58:403–415. [PubMed: 16026655]
108. Chisholm MA, Williamson GM, Lance CE, Mulloy LL. Predicting adherence to immunosuppressant therapy: a prospective analysis of the theory of planned behaviour. *Nephrol Dial Transplant* 2007;22:2339–2348. [PubMed: 17442741]
109. Phatak HM, Thomas J 3rd. Relationships between beliefs about medications and nonadherence to prescribed chronic medications. *Ann Pharmacother* 2006;40:1737–1742. [PubMed: 16985088]

Figure 1.
The Measurement Adherence Model

* Range of medication adherence for dose-count: 12-102%

** Range of medication adherence for dose-day: 0-100%

† Range of medication adherence for dose-time: 0-100%

MEMS, Medication Event Monitoring System

Dose-count: % of prescribed number of doses taken

Dose-day: % of days the correct number of doses taken

Dose-time: % of doses taken on schedule

Figure 2.

Medication adherence rates for three indicators of the MEMS

* Range of medication adherence for dose-count: 12-102%

** Range of medication adherence for dose-day: 0-100%

† Range of medication adherence for dose-time: 0-100%

MEMS, Medication Event Monitoring System

Dose-count: % of prescribed number of doses taken

Dose-day: % of days the correct number of doses taken

Dose-time: % of doses taken on schedule

Table 1

Measurement of variables

Variables	Measurement	Time Measure
Medication adherence	•Medication Event Monitoring System (MEMS) caps	Continually for 3 months from baseline
1. Patient-related factors	• Patient interview	Baseline (recruitment)
• Gender	• Patient interview	
• Age	• Attitudes subscale of the MAS	
• Attitudes	• Knowledge subscale of the MAS	
• Knowledge		
2. Condition-related factors	• Patient interview	
• Symptom severity (NYHA)	• Patient interview	
• Comorbidity	• Patient Health Questionnaire (PHQ)	
• Depression		
3. Treatment-related factors	• Patient interview	
• Complexity	• Barriers subscale of the Medication Adherence Scale (MAS)	
• Barriers to medication adherence		
4. Health care system-related factor	• Interpersonal Trust in a Physician Scale (ITP)	
• Patient-provider relationship		
5. Socio-economic factors:	• Patient interview	
• Level of education	• Patient interview	
• Ethnicity	• Patient interview	
• Financial status	• Perceived Social Support Scale (PSSS)	
• Social support		

Table 2

Demographic and clinical characteristics of participants (N=134)

Characteristics Age (Mean $\pm$ SD)	Range (Mean $\pm$ SD) or Number (%) 24–87 y/o (61.2 $\pm$ 11.5)
Gender (Male/Female)	103/44 (70%/30%)
Race	
Caucasian	130 (88%)
African American	16 (11%)
Hispanic	1 (1%)
Education (Mean $\pm$ SD)	0–22 yrs (12.5 $\pm$ 3.5)
< 12 yrs	38 (26.6%)
High school	38 (26.6%)
College	51 (35.6%)
Graduate school	16 (11.2%)
Marital status	
Married/cohabitate	90 (61%)
Single/divorce/widow	57 (39%)
Financial status	
Comfortable	37 (25%)
Enough to make ends meet	75 (52%)
Not enough to make ends meet	33 (23%)
^a Patient-provider relationship (Mean $\pm$ SD)	37–50 (43.5 $\pm$ 6.5)
Etiology	
Ischemic	87 (60%)
Idiopathic	29 (20%)
Hypertensive	10 (7%)
Other (e.g., alcoholic)	19 (13%)
LVEF (Mean $\pm$ SD), %	7–70 (34.6 $\pm$ 14)
NYHA	
Class I/II	56 (39%)
Class III/IV	87 (61%)
^b Charlson Comorbidity Index (Mean $\pm$ SD)	1–10 (3.4 $\pm$ 1.8)
Attitudes score	9–30 (28 $\pm$ 3.5)
Knowledge score	0–30 (21 $\pm$ 8.6)
Barrier score	0–110 (18 $\pm$ 29)

SD, standard deviation.

LVEF = Left Ventricular Ejection Fraction.

NYHA = New York Heart Association functional classification

^a Patient-provider relationship: higher score reflecting more positive patient-provider relationship^b Charlson Comorbidity Index: higher score reflecting more comorbidity burden

Table 3Correlation Coefficients Between Medication Adherence and Variables from the MAM[†]

Medication Adherence Variables	Dose-count ^a	Dose-day ^b	Dose-time ^c
Gender	-.173 [*]	-.123	-.124
Age	.101	.107	.135
Attitudes	.186 [*]	.158	.125
Knowledge	.065	.088	.067
NYHA	-.166	-.184 [*]	-.172 [*]
Comorbidity	-.184 [*]	-.231 ^{**}	-.191 [*]
Depression	-.260 ^{**}	-.210 [*]	-.156
# of pills taken	-.096	-.132	-.141
Frequency of med.	.045	-.011	-.046
Barriers	-.257 ^{**}	-.200 [*]	-.149
Patient-provider relationship	.039	.022	-.043
Ethnicity	.134	.118	.196 [*]
Education	-.051	-.009	-.051
Financial status	-.035	.020	.028
Perceived social support	.208 [*]	.200 [*]	.114

[†] Spearman's rho was used^{*} = p < .05^{**} = p < .01 MEMS, Medication Event Monitoring System^a MEMS data, dose-count: % of prescribed number of doses taken^b MEMS data, dose-day: % of days the correct number of doses taken^c MEMS data, dose-time: % of doses taken on schedule

Table 4

Variables Associated With Medication Adherence

Indicator of the MEMS	Significant predictors	P value	R ² (adj. R ²)
* Dose-count ^a	Barriers	< .001	.23 (.20)
	Ethnicity	.025	
	Perceived social support	.014	
** Dose-day ^b	NYHA	.049	.25 (.21)
	Barriers	< .001	
	Financial status	.036	
† Dose-time ^c	Perceived social support	.026	.16 (.11)
	Barriers	.008	
	Financial status	.039	

adj. = adjusted

NYHA = New York Heart Association functional class

MEMS, Medication Event Monitoring System

^a MEMS data, dose-count: % of prescribed number of doses taken^b MEMS data, dose-day: % of days the correct number of doses taken^c MEMS data, dose-time: % of doses taken on schedule

* F = 7.253, P < .001

** F = 6.293 P < .001

† F = 3.606 P = .005

Table 5Full Multiple Regression Model of Dose-Count ^a

Dimension	Variables	Beta	P
Patient-related	Gender	.114	.229
	Age	-.042	.658
	Attitudes	-.062	.504
	Knowledge	-.063	.492
Condition-related	NYHA	.165	.072
	Comorbidity	.073	.422
	Depression	.099	.311
Treatment-related	# of pills taken per day	.145	.113
	Medication frequency	.048	.602
	Barriers	.352	< .001 *
Health care system-related	Patient-provider relationship	.001	.991
Socio-economic	Ethnicity	-.208	.025 *
	Education	.118	.200
	Financial status	-.183	.064 *
	Social support	-.241	.014 *

MEMS, Medication Event Monitoring System

^a MEMS data, dose-count: % of prescribed number of doses taken

F = 7.253, P < .001

* P < .05

Table 6Full Multiple Regression Model of Dose-Day ^a

Dimension	Variables	Beta	P
Patient-related	Gender	.056	.558
	Age	-.065	.493
	Attitudes	-.042	.650
	Knowledge	-.047	.611
Condition-related	NYHA	.181	.049 *
	Comorbidity	.020	.835
	Depression	.028	.790
Treatment-related	# of pills taken per day	.139	.137
	Medication frequency	.071	.432
	Barriers	.349	<.001 *
Health care system-related	Patient-provider relationship	-.002	.981
Socio-economic	Ethnicity	-.166	.071
	Education	-.002	.278
	Financial status	.208	.036 *
	Social support	-.221	.026 *

MEMS, Medication Event Monitoring System

^a MEMS data, dose-day: % of days the correct number of doses taken

F = 6.293, P < .001

* P < .05

Table 7Full Multiple Regression Model of Dose-Day ^a

Dimension	Variables	Beta	P
Patient-related	Gender	.065	.517
	Age	-.127	.205
	Attitudes	-.033	.735
	Knowledge	-.028	.768
Condition-related	NYHA	.128	.199
	Comorbidity	.051	.601
	Depression	.055	.601
Treatment-related	# of pills taken per day	.181	.062
	Medication frequency	.012	.906
	Barriers	.268	.008 *
Health care system-related	Patient-provider relationship	.012	.902
Socio-economic	Ethnicity	-.136	.165
	Education	.066	.497
	Financial status	.216	.039 *
	Social support	.195	.057

MEMS, Medication Event Monitoring System

^a MEMS data, dose-time: % of doses taken on schedule

F = 3.606, P = .005

* P < .05

Table 8
Variance of Medication Adherence Explained by Each Dimension

	Patient-related	Condition-	Treatment	Healthcare system	Socio-economic
Dose-count ^a	.10	.03	.10	.00	.06
Dose-day ^b	.08	.04	.09	.00	.07
Dose-time ^c	.06	.03	.06	.00	.05

MEMS, Medication Event Monitoring System

^a MEMS data, dose-count: % of prescribed number of doses taken

^b MEMS data, dose-day: % of days the correct number of doses taken

^c MEMS data, dose-time: % of doses taken on schedule