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# Rurality and Event-Free Survival in Patients With Heart Failure

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# Rurality and Event-Free Survival in Patients With Heart Failure

**Abstract**

**Background**

Evidence of health disparities between urban and rural populations usually favors urban dwellers. The impact of rurality on heart failure (HF) outcomes is unknown.

**Objective**

We compared event-free survival between HF patients living in urban and rural areas.

**Methods**

In this longitudinal study, 136 patients with HF (male, 70%; age, mean ± SD 61 ± 11 years; New York Heart Association class III/IV, 60%) were enrolled. Patients' emergency department visits for HF exacerbation and rehospitalization during follow-up were identified. Rural status was determined by rural-urban commuting area code. Survival analysis was used to determine the effect of rurality on outcomes while controlling for relevant demographic, clinical, and psychosocial variables.

**Results**

Rural patients (64%) had longer event-free survival than urban patients ($P = .015$). Rurality ($P = .04$) predicted event-free survival after controlling for age, marital status, New York Heart Association class, medications, adherence to medications, depressive symptoms, and social support.

**Conclusions**

Rural patients were less likely than their urban counterparts to experience an event. Further research is needed to identify protective factors that may be unique to rural settings.

**Disciplines**

Cardiology | Cardiovascular Diseases | Community-Based Research | Demography, Population, and Ecology

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# Rurality and Event-free Survival in Patients with Heart Failure

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## Abstract

**Background—**Evidence of health disparities between urban and rural populations usually favors urban dwellers. Unknown is the impact of rurality on heart failure (HF) outcomes.

**Objective—**To compare event-free survival between HF patients living in urban and rural areas.

**Methods—**In this longitudinal study, 136 pts with HF (male 70%, age 61±11 yrs, NYHA III/IV 60%) were enrolled. Patient emergency department visits for HF exacerbation and rehospitalization during follow-up were identified. Rural status was determined by rural-urban commuting area code. Survival analysis was used to determine the effect of rurality on outcomes while controlling for relevant demographic, clinical and psychosocial variables.

**Results—**Rural patients (64%) had longer event-free survival than urban patients ($p = .015$). Rurality ($p = .04$) predicted event-free survival after controlling for age, marital status, NYHA class, medications, medication adherence, depressive symptoms, and social support.

**Conclusion—**Rural patients were less likely than their urban counterparts to experience an event. Further research is needed to identify protective factors that may be unique to rural settings.

### Keywords

rurality; heart failure; outcomes; Medication Event Monitoring System; medication adherence

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**Disclaimer Statement**

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## INTRODUCTION

Health disparities between individuals living in rural and urban regions have been reported in many studies and usually favor those living in urban areas. Patients with a variety of chronic illnesses living in rural areas often have less access to healthcare,[1] have lower incomes,2, 3 and are less likely to have private insurance.3 Shortages of medical personnel are more common in rural than urban areas.4 Moreover, rural residents are less likely to receive recommended cardiac treatments, such as fibrinolytics or percutaneous coronary intervention (PCI) compared with their urban counterparts.[5] As a consequence, rural residents with cardiac conditions are more likely than urban residents to visit the emergency department (ED)3 and their mortality is higher.6, 7

Despite these data, there is conflicting evidence about the relationship between rurality and health outcomes. In one study, investigators reported that mortality from myocardial infarction in rural hospitals was similar to that in urban hospitals.[8] In other studies, rurality was associated with better mental health,[9] lower hospitalization rates for depression,10 and higher survival rates.11 Patients living in rural areas had lower stress levels9 and were more likely to be married, a factor that has been associated with better health.[11] However, possible factors (e.g., access to health care facilities, patient income, education) related to known disparities were not measured in these studies.[8-11]

Heart failure is one of the most common and costly discharge medical diagnoses in the United States (US) and worldwide.[12-14] Due to an aging population and improved treatment for cardiac conditions, the number of patients with heart failure is expected to increase. The estimated direct and indirect costs of heart failure in the US for 2009 is expected to be $37.2 billion, with hospital care accounting for about 54% of the total cost.15 Many patients with heart failure live in rural areas and the association of rurality with heart failure outcomes is unknown. Accordingly, the purpose of this study was to compare event-free survival between heart failure patients living in urban and rural areas, controlling for demographic, clinical, and psychosocial factors known to be related to outcomes.

## METHODS

### Study Design

This was secondary data analysis of a prospective, longitudinal study in which patients with heart failure were followed for an average of 393 days to obtain event-free survival.[16] In the current study, we compared event-free survival between patients with heart failure living in urban and rural areas. At baseline, patients' demographic, clinical, and psychosocial data were collected by patient interview or medical record review. Medication adherence was assessed with the Medication Event Monitoring System (MEMS) during the beginning 3 months. Hospitalizations or ED visits data were assessed monthly by patient/family interview and hospital administrative record.

### Samples and Setting

Detailed eligibility criteria and recruitment methods have been published.[16, 17] Patients with a confirmed diagnosis of chronic heart failure were recruited from outpatient cardiology clinics in Central Kentucky in this study. Patients were excluded if they had a serious terminal illness or obvious cognitive impairment.

## Measurement of Variables

### Independent variable

**Rurality:** There is no universally agreed upon definition of rurality. In this study, patient's rural status was determined by linking the patient ZIP code to its rural-urban commuting area code (RUCA).[1, 5, 18, 19] A RUCA code is assigned to each U.S. zip code based on factors that include standard U.S. Census definitions of urbanization (based on population density) and work commuting data to assess the functional relationship between population centers and surrounding communities. The RUCA taxonomy includes codes from 1.0 to 10.6. The RUCA designations were aggregated into 4 categories: urban (i.e., an urbanized area of population 50,000 or greater), large rural city (i.e. a large rural city of 10,000-49,999), small rural town (i.e., a rural town of 2,500-9,999), and isolated rural town (i.e., a town of less than 2,500 populations). These groups reflect centers with similar population characteristics and population density. In this study, 2 independent RUCA groups were defined prior to data analysis: urban (i.e., urban category) and rural (i.e., 3 types of rural locations: large rural city, small rural town and isolated rural town). The RUCA taxonomy has been used in health services research and now provides the basis for categorizing rurality in many research studies.[1, 5, 18, 19]

**Dependent variable:** The dependent variable was event-free survival. Events were defined as ED visits for symptoms of heart failure exacerbation or all-cause rehospitalizations. There were only two deaths in this sample during the follow-up period, one among the urban patients and one among the rural patients, thus, death was not included as an end-point and these patients were censored when their death occurred. Data on event-free survival were obtained by patient/family interview, log book review, and hospital data base review. During data collection, the date and reasons for ED visits and hospitalization were noted. If there was a difference between patient/family report and the hospital records, we carefully reviewed the medical record to confirm the visit date and reason, and discussed the discrepancy with the patient or family. If the patient was admitted to a hospital or visited an ED outside of the university system a patient release was obtained and the medical record was reviewed. In this study, mortality data were also collected by a combination of discussion with family, medical record review and review of death certificates and records.

**Covariates:** Age, marital status, ethnicity, NYHA functional class, prescribed medications, comorbidity, medication adherence, perceived social support, and depression were collected as covariates. Patients' age, marital status, ethnicity, and medication regimen (i.e., angiotensin-converting-enzyme inhibitors, beta-adrenergic blockers, diuretics, digoxin, aldosterone antagonist) were collected from the medical record and patient interview. Patients' NYHA functional class was determined by patient interview based on how patients are able to perform their usual activities.[20]

Medication adherence was measured for 3 months using the MEMS, a microelectronic monitoring device, which is housed in the cap of a medication vial. The MEMS records the date and time that the patient opens and closes the cap from the medication bottle.[21, 22] Data were collected on one HF medication (e.g., angiotensin-converting-enzyme [ACE] inhibitor, diuretic, β-blocker, digoxin) for each patient. If patients normally used a pill box for their medicine, patients were asked to keep MEMS bottle beside their pill box and take this one medicine from the MEMS bottle. The MEMS is a valid measure of medication adherence in patients with HF.[23-25] Medication adherence from the MEMS was defined as the dose-count which is the percentage of prescribed doses taken during the monitoring period.16

Perceived social support was measured by the Perceived Social Support Scale (PSSS). The PSSS is a 12-item self-report instrument. Patient rate their agreement with each item using a scale that ranges from 1 (very strongly disagree) to 7 (very strongly agree). The total score can range from 7 to 84 with a higher score reflecting better social support. The PSSS is a reliable (Cronbach's α = .93−.94)[26, 27] and valid questionnaire.[26-28] In this study, the Cronbach α coefficient was 0.95.

Patients' depressive symptoms were measured by the Patient Health Questionnaire-9 (PHQ-9).[29, 30] The PHQ-9 consists of nine items that are self-rated on a scale from 0 (not at all) to 3 (nearly every day). The PHQ-9 item ratings are summed for a total score that can range from 0 to 27; higher scores indicate a greater level of depression. Patients were divided into depressive symptoms or non-depressive symptoms groups using the cut point of 10.[29] The PHQ-9 is a reliable (Cronbach's α = .89)[29] and valid scale that has been used to measure depression in heart failure patients.[30] In this study, the Cronbach α coefficient was 0.84.

## Procedure

Permission to conduct the study was obtained from the University of Kentucky (UK) Institutional Review Board (IRB). Patients' sociodemographic and clinical data were collected by interview and medical record review at baseline. After interview, patients completed the PSSS, PHQ-9 questionnaires and were given detailed written and verbal instructions on how to use the MEMS bottle. A medication diary was given to each patient to record unscheduled cap opening. At 3 months from baseline, patients returned the MEMS bottle. The data from the MEMS cap were downloaded to a personal computer. Unscheduled cap openings as documented in the patient's medication diary were excluded from analysis.

## Data Management and Analysis

All data analyses were done using SPSS, version 16.0; a significance level of .05 was used throughout. 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.

Patients were divided into urban and rural groups based on their RUCA code. Because patients in urban and rural areas may differ on some demographic (e.g., age, gender) and clinical (e.g., left ventricular ejection fraction, comorbidity, prescribed medications) variables, baseline difference between urban and rural groups first were examined using two-sample t-test (for continuous variables), Mann-Whitney U tests (for ordinal variables), or chi-square tests (for nominal variables), as appropriate. The variables that were significantly different in both groups were adjusted in the Cox regression model.

To compare time to the composite end-point of ED visits for heart failure exacerbation or rehospitalization, the log-rank test was used to compare the time to event-free survival between urban and rural groups. Kaplan-Meier plots were used to graphically depict group differences in event-free survival. Cox proportional hazards regression modeling was used to determine the effect of rurality on time to the first event, while controlling for the following potential covariates: age, marital status, ethnicity, baseline NYHA, ACE inhibitor use, medication adherence, perceived social support, and depression.

# RESULTS

## Patient Characteristics

Of the 301 eligible heart failure patients approached for the study; we recruited 147 patients and the remainder declined to participate due to long travel distance, no interest in research participation, or lack of energy. In this study, we included data from the 136 patients for whom we have full MEMS data (Table 1). MEMS data were missing in 11 patients because of technical failures (n = 6) or loss of the MEMS cap by the patient (n = 5). Using the RUCA code, 36% of patients lived in urban areas and 64% of patients lived in rural areas. Patients who were white and married or cohabitating were more likely to live in rural areas.

Patients living in rural areas were more likely than their urban counterparts to have an ACE inhibitor prescribed and were more adherent to prescribed medication. No other sociodemographic and clinical variables differed between patients living in urban and rural areas. Full sample characteristics and comparison of patients living in urban and rural groups are presented in Table 1.

## Event-Free Survival Analyses

A Kaplan-Meier plot with the log-rank test demonstrated that event-free survival was better in patients living in rural areas than those in urban areas (p = .01) (Figure 1). Patients living in rural areas had a longer time to the first event than their urban counterparts. Patients living in rural areas were less likely to visit the ED for heart failure exacerbation or be hospitalized compared to those living in urban areas (37% vs 57%). No difference in death rate between these two groups was found (p = .49), as there was only one death in each group during our follow-up period.

In Cox regression modeling (Table 2), rurality (p = .04) predicted event-free survival after controlling age, marital status, NYHA class, ACE inhibitor use, medication adherence, depressive symptoms, and perceived social support. Patients living in rural areas were about half as likely to experience an event as those who lived in urban areas. When ethnicity and all other covariates were entered in the model (Table 3), rurality (p = .05) but not ethnicity (p = .98) predicted event-free survival. The only other independent predictor of outcomes was depression. Patients with higher levels of depression have worse outcomes.

# DISCUSSION

Results from this study indicate that compared to urban dwellers, patients living in rural areas were less likely to visit the ED for symptoms of heart failure or be hospitalized. This is the first study in which the relationship between rurality and outcomes in patients with heart failure was examined. Patients with heart failure who lived in rural areas had better outcomes than their urban counterparts even after controlling for risk factors related to event-free survival and personal characteristics that differed between the two groups. Patients living in rural areas were about half as likely to have ED visits for heart failure exacerbation or hospital admissions as those living in urban areas.

Our result is in direct contrast to the findings of previous investigators as most, although not all, have found that patients living in rural settings have worse outcomes. Inconsistent results have been reported in previous studies in which the relationship between rurality and outcomes has been examined in other health conditions.[2, 3, 5-11, 18, 31] In most studies, patients living in rural areas had worse outcomes.[2, 3, 5-7, 18, 31] For example, patients in rural hospitals had higher adjusted 30-day post-acute myocardial infarction (MI) death rates from all causes than those in urban hospitals.5 In one study,7 the relative risk of ischemic heart disease (IHD) mortality in rural areas was similar to that in urban areas. The relative

risk of a hospital stay was significantly lower in rural patients. However, the relative risk of mortality within 28 days of discharge was higher in rural patients. Axelrod and colleages18 found that patients living in rural areas were 8-15% less likely to be wait-listed and 10-20% less likely to undergo heart, liver, and kidney transplantation than patients living in urban areas. In a cancer survey,31 rural residents were less likely to be screened for cervical carcinoma, and, therefore, had a higher invasive cervical carcinoma incidence rate compared to their urban counterparts.

Many mechanisms have been explored to explain health disparities based on rurality. Poorer outcomes for certain health conditions in rural or remote populations have been attributed to greater prevalence of socioeconomic disadvantage,[2, 3, 32] poorer access to health services,[1] and less opportunity to receive recommended treatments.[5] For example, investigators have demonstrated that patients living in rural areas must travel 2 to 3 times farther to see medical and surgical specialists than those living in urban areas.[1, 31] Rural patients typically rely on generalists.[1] In a large retrospective study using the February 1994-July 1995 Cooperative Cardiovascular Project and the 1995 American Hospital Association's Annual Survey of Hospitals database, Medicare patients in rural hospitals were less likely than those in urban hospitals to receive aspirin, intravenous nitroglycerin, heparin, fibrinolytics, or PCI.[5] Furthermore, there are more non-physician clinicians as well as more vacant family physicians and registered nurses full-time positions in rural health centers compared with urban health centers.[4]

Poorer health outcomes in rural areas have not been consistently observed across studies. James et al.[8] found no association between rurality and outcomes. In other studies,[9-11] rural residents had better outcomes than urban residents. Myocardial infarction patients living in rural areas had a lower post-MI mortality rate than those in urban areas.[11] Rural patients in that study were more often married, but had lower levels of education, lower employment rates and less income compared to those in urban areas. PCI and coronary artery bypass graft surgery rates were higher in urban areas in this study. The investigators postulated that the low post-MI death in rural patients despite these factors might be related to high pre-hospital fatality rates for MI due to longer delay before starting reperfusion because of the greater distance from rural areas to hospitals.

In our study, patients living in rural areas had fewer events compared with patients in urban areas. One possible explanation for these findings could be that our rural patients went to the ED or hospital less often despite the need to do so. In that case, we would expect to see more deaths compared to urban patients. However, the rates of death were very low in both the rural and urban groups. Therefore, a longer prospective study examining the relationship between rurality and mortality is needed to examine this possibility.

In a recent study,[2] investigators used path analysis to examine the relationships among rurality, hospitalization, and other possible predictors of hospitalization and found that although rurality did not have a direct effect on hospitalization, there was an indirect effect of rurality on hospitalization through service use. Rurality influenced the number of home health care service uses. There was a positive association between the number of home health visits and hospitalization. Rural patients had lower home health care service uses and therefore had fewer hospitalizations. The investigators suggested that the lack of available health providers in rural areas resulted in rural patients receiving less home health care service. The result of this study provides another possible explanation for our finding. Rural patients may have been less likely to go to the ED or hospital because of lack of adequate professional health staff in rural areas. Rural patients may have had less access to health care and therefore had fewer documented events in our study.

Rurality has been shown to be associated with better mental health,[9] and patients in rural counties have lower hospitalization rates compared with patients in urban counties.[10] The hospitalization rate for depression in rural areas was 49% lower than in most urban areas.[10] The finding of our study is consistent with these two studies. However, the investigators of these two studies did not explore reasons for the difference between urban and rural patients.

In another study, investigators found better quality of care in rural areas than in urban areas.[33] Better quality of care might be one reason for that heart failure patients living in rural areas have better health outcomes. In this study, patients living in rural areas were more likely to receive ACE inhibitors than their urban counterparts in bivariate analysis; but not multivariate analysis. No difference was found in beta-blocker prescription between groups. However, we did not collect all information on quality of care (e.g., discharge instructions, distance to health care facility). Future studies of urban/rural differences in outcomes would benefit from assessing quality of care.

Our study demonstrated that even after controlling for many other relevant covariates, patients living in rural areas were less likely to experience an event than those in urban areas. However, reasons for the decreased risk for hospitalization in rural heart failure patients compared to urban heart failure patients are unclear. Some researchers have reported that differences in rehospitalizations may be related to difference in socioeconomic factors (e.g., age, race, access to care),[34, 35] psychological factors (e.g., depression),[36] and adherence to diet and prescribed medication.[37] These studies have shown that patients who are older, in a minority ethnic group, have more limited access to health care, have greater depressive symptoms, or are less adherent to low sodium diet or to prescribed medications are more likely to visit the ED, be hospitalized or die. In our study, more black patients lived in urban areas, while patients living in rural areas were more likely to be white, married, having an ACE inhibitor prescription and had higher medication adherence rates compared to patients living in urban areas. However, when these urban/rural differences were controlled for in Cox regression model, none predicted event-free survival, and, rurality remained a protective factor.

There is no universally agreed upon definition of rurality. This may be one of the reasons for the different results found in the rurality literature. Different investigators have used different methods to define rurality, which makes it difficult to compare results between studies.[11] Many studies of rurality were conducted without a clear definition of rurality.[11] Theoretical and operational definitions guide the direction of investigation, choice of appropriate instruments and the interpretation of findings. Future research will benefit from a common definition of rurality.

Rurality may be a proxy measure for a group of unmeasured risk (or protective) factors that affect health outcomes.[10] Our results suggest further research is needed to identify factors such as access to healthcare facilities, income, stress level, environmental and cultural factors that are important to rurality and health outcomes.

In addition to rurality, we demonstrated that depression predicted of event-free survival. These data are consistent with data from multiple studies that have demonstrated higher mortality and rehospitalization rates in depressed compared with non-depressed heart failure patients.[38-41] This result also demonstrates that depressive symptoms predict outcomes independent of urban/rural status.

## LIMITATIONS

Although we had sufficient power to demonstrate significant differences, a larger and more heterogeneous sample is needed to more thoroughly investigate the possible mechanisms

explaining differences in event-free survival between rural and urban patients. We did not include all possible factors that might be related to rurality and outcomes in this study. For example, we did not collect information on access to health care facilities or quality of health care received. However, in the final model we controlled for all demographic, clinical and psychosocial variables that differed between the urban and rural groups.

## CONCLUSION

Controlling for differences in demographic, disease-specific, and social support factors, patients who lived in rural areas were far less likely than their urban counterparts to experience an adverse event. These results are striking because the two groups were similar on most characteristics and the demographic and disease-specific variables for which they did differ were included as covariates in the Cox regression. Further research is needed to identify protective factors that may be unique to rural settings.

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Because this study was funded from the NIH/NINR, I also would like to inform the publishers of *Heart & Lung* about a new NIH Public access policy as below.

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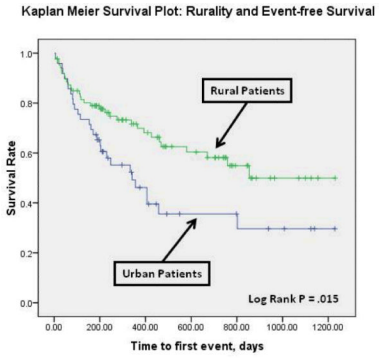


**Figure 1.**
Rurality and Time to First Event of Emergency Department Visits, Rehospitalization, or Mortality (Event-free Survival)

## Table 1

Total Sample Characteristics and Comparison of Patients in Urban and Rural areas*

| Characteristics | Total Sample N = 136 | Urban n = 49 | Rural n = 87 | *P* Value* |
|---|---|---|---|---|
| Age, years | 61 ± 11 | 62 ± 12 | 60 ± 11 | .323 |
| Female | 41 (30.1) | 19 (38.8) | 22 (25.3) | .074 |
| Minority race | 14 (10.3) | 11 (22.4) | 3 (3.4) | .001 |
| Education, years | 12.6 ± 3.3 | 13.0 ± 3.4 | 12.4 ± 3.1 | .287 |
| Marital status | | | | .001 |
| Single/Divorced/Widowed | 52 (38.2) | 28 (57.1) | 24 (27.6) | |
| Married/Co-habitate | 84 (61.8) | 21 (42.9) | 63 (72.4) | |
| Living alone | 41 (30.1) | 19 (38.8) | 25.3 (29.3) | .074 |
| Financial status | | | | .943 |
| Comfortable | 33 (24.6) | 11 (22.9) | 22 (25.6) | |
| Enough to make ends meet | 71 (53.0) | 26 (54.2) | 45 (52.3) | |
| Not enough to make ends meet | 30 (22.4) | 11 (22.9) | 19 (22.1) | |
| LVEF, % | 34.6 ± 14.2 | 37.3 ± 16.5 | 33.0 ± 12.5 | .122 |
| NYHA functional class | | | | .306 |
| I/II | 54 (39.7) | 25 (47.2) | 33 (35.1) | |
| III | 63 (46.3) | 20 (37.7) | 47 (50.0) | |
| IV | 19 (14.0) | 8 (15.1) | 14 (14.9) | |
| Charlson comorbidity index | 3.3 ± 1.7 | 3.7 ± 1.9 | 3.2 ± 1.5 | .092 |
| Taking ACEI | 97 (71.3) | 27 (55.1) | 70 (80.5) | .002 |
| Taking BB | 121 (89.0) | 43 (87.8) | 78 (89.7) | .470 |
| Medication adherence | 88.7 ± 15.6 | 83.4 ± 20.4 | 91.6 ± 11.3 | .011 |
| Perceived social support | 66.3 ± 18.4 | 63.9 ± 19.3 | 67.6 ± 17.9 | .274 |
| Depression | 42 (31) | 14 (29.8) | 28 (32.2) | .467 |

* P value for comparison of patients in urban and rural areas

Data are presented as means ± SD, or N (%); LVEF = Left Ventricular Ejection Fraction; NYHA = New York Heart Association; ACEI = angiotensin-converting-enzyme inhibitor; BB = beta blocker

**Table 2**

Cox Regression Modeling: Rurality Regressed on Event-free Survival

| Variables | Hazard ratio | Wald | Significance |
|---|---|---|---|
| Rurality | .563 | 3.968 | .04 |
| Age | 1.005 | .143 | .70 |
| Marital status | 1.037 | .0874 | .77 |
| NYHA | 1.244 | 1.383 | .24 |
| Taking ACEI | .660 | 1.806 | .17 |
| Medication adherence | .998 | .075 | .78 |
| Perceived social support | 1.004 | .250 | .61 |
| Depression | 1.978 | 4.952 | .02 |

* $\chi^2 = 20.627$, $p<.01$

**Table 3**

Cox Regression Modeling: Rurality (with ethnicity) Regressed on Event-free Survival

| Variables | Hazard ratio | Wald | Significance |
|---|---|---|---|
| Rurality | .5674 | 3.669 | .05 |
| Age | 1.005 | .143 | .70 |
| Marital status | 1.036 | .081 | .77 |
| Ethnicity | 1.011 | .001 | .98 |
| NYHA | 1.245 | 1.369 | .24 |
| Taking ACEI | .660 | 1.799 | .18 |
| Medication adherence | .998 | .075 | .78 |
| Perceived social support | 1.004 | .242 | .62 |
| Depression | 1.977 | 4.887 | .02 |

* $\chi^2 = 20.636$, $p = .01$