HEART FAILURE PATIENTS'

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PRIMARY CAREGIVERS' EMOTIONS

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By

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ABSTRACT

Background: There is strong evidence to suggest that emotional distress, particularly depression, is common in patients with heart failure (HF). Caregivers of patients with HF play a pivotal role in improving HF patient outcomes; however, these caregivers are at risk for caregiver burden and emotional distress. *Objectives*: The objectives of this study were to explore potential relationships among patient and caregiver emotional status, uncertainty and caregiver appraisal. For the purposes of this study, emotional distress is defined as the presence of symptoms of anxiety or depression. *Methods*: Using a longitudinal exploratory design, 48 HF patient-caregiver pairs were recruited. Patients and caregivers completed the Hospital Anxiety and Depression Scale, Mishel Uncertainty in Illness Scale (MUIS) and caregivers also completed the Caregiver Reaction Assessment at baseline, 2 months and 4 months. *Results*: Patients had advanced HF symptoms and were older than caregivers (mean age 72.6 years, 54% male versus mean age 58.4 years, 54% female). The majority of caregivers were spouses (58%) but many were adult children (42%). There were significant relationships between: a) HF patient and caregiver uncertainty, and b) caregiver emotional distress and caregiver burden. There were no significant relationships between: a) patient and caregiver symptoms of anxiety and depression, b) emotional distress and uncertainty, or c) patient emotional distress and caregiver burden. Over time, there was a trend for a decrease in: a) patient symptoms of depression, b) caregiver symptoms of anxiety, and c) patient and caregiver uncertainty. *Conclusions*: Contrary to findings in other studies, there was no significant relationship between symptoms of anxiety and depression in patients and their primary caregivers. There was no relationship between emotional distress and uncertainty; however, this is one of the first studies using the MUIS in HF patients and caregivers and further research with this tool is needed. Finally, this study supports findings from other studies suggesting a strong relationship between caregiver emotional distress and caregiver burden.

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CHAPTER 1

INTRODUCTION

There is strong evidence to suggest that emotional distress, particularly depression, is common in patients with heart failure (HF). Rapidly emerging literature, both empirical and theoretical, identifies potential mechanisms to explain the relationship between HF and depression. Caregivers of patients with HF play a pivotal role in improving HF patient outcomes; however, these caregivers are at risk for caregiver burden and emotional distress. The primary goal of this research was to explore potential relationships between the emotional status of HF patients and that of their primary caregivers. For the purposes of this research, emotional distress is identified as including either symptoms of depression or symptoms of anxiety.

Organization of Thesis

This thesis is organized in 5 chapters. In this first chapter, background information is summarized and discussed in order to provide the context and rationale for the purpose of the study. Specifically, the epidemiology of HF and of depression and anxiety in the HF population is reviewed. The remaining chapters are as follows:

Chapter 2. Theoretical Foundation and Review of Literature

An overview of the Adaptation Potential Assessment Model (APAM) is introduced and discussed (Leidy et al., 1990). This model provides a conceptual framework for identifying key psychosocial constructs that theoretically mediate the relationship between HF and emotional distress. Empirical literature exploring the relationship between HF, depression and anxiety is reviewed in detail. Information related to the experience of primary caregivers for HF patients will be reviewed in the context of the APAM. The latter part of this chapter will outline the study purpose, research questions and hypotheses.

Chapter 3. Study Methods.

The first part of this chapter describes sample selection which includes: a) inclusion and exclusion criteria, b) screening and recruitment procedures and c) a description of the study protocol. Patient and caregiver demographic variables and instruments are outlined in the middle section. This chapter concludes with a description of data management and statistical analysis.

Chapter 4. Study Results.

The study results are presented in five main sections. The first section presents information regarding the study sample that includes: a) recruitment and flow of participants through the study, b) a description of participants who completed versus those who withdrew from the study, and c) a description of the study sample. Results of analyses conducted on baseline data relevant to the primary study objective are presented in the second section. The third section presents baseline data analyses associated with the secondary objectives. Exploratory analyses related to changes in test scores and the strength of correlations between key variables between baseline and 2 and 4 months follow up are presented in the fourth section. The fifth and final section of this chapter summarizes the results based on study hypotheses.

Chapter 5. Discussion and Future Directions

This final chapter is divided into four main sections. The first section discusses the results for the primary study objective. Secondary objectives that involve the measurement of uncertainty and caregiver appraisal at baseline are presented in the second section. The third section discusses the results from exploratory analyses involving longitudinal data. The strengths, limitations, implications for clinical practice and future research endeavors are discussed in the fourth and final section of this chapter.

Background

Epidemiology of Heart Failure

HF is a complex pathophysiological syndrome that occurs when the heart is unable to pump sufficient blood to meet the metabolic demands of the body. Hallmark clinical features include fatigue, shortness of breath and dependent edema (Arnold et al., 2006). As a result of an aging population and improved treatment for hypertension and myocardial infarction, the incidence and prevalence of HF are reaching epidemic proportions in Canada, USA and the United Kingdom (Curtis et al., 2008; Fang et al., 2008; Rich, 1999; Ho et al., 1993). Population-based studies have shown the annual incidence of HF to range from 1-5% in people aged 50-59 years and 10-23% in those over 80 years of age (Miller, 2008; Abdelhafiz, 2002; Albert, 1999; Chen et al., 1999; Burns et al., 1997). In the Framingham cohort, the mean (±SD) age at the initial diagnosis of HF was 62.7 (±8.8) years in the time period between 1950-1969 and increased to 80.0 (±10.1) years in the period between 1990-1999 (Levy et al., 2002). In the USA, approximately 5.3 million people have HF with more than 500,000 newly diagnosed cases each year. The annual incidence is expected to rise to over 700,000 cases by the year 2040 (Velgaleti &Vasan, 2007).

Despite major advances in cardiovascular disease management over the past three decades, the mortality rate for HF has not improved significantly (Hellermann et al., 2002). One to two year mortality rates range from 7.6% in younger, low risk groups to 67% in high risk populations (Hellermann et al., 2002;

Jong et al., 2002; Rozzini et al., 2002; Jiang et al., 2001; Burns et al., 1997). In a cohort of over 9000 patients who were hospitalized in Ontario, Canada with newly diagnosed HF (mean age 75.8 years, 50.4% female), median survival was 2.4 years (Ko et al., 2008). One-year mortality was 33.1% and 5-year mortality was 68% in patients with depressed left ventricular function (Ko et al., 2008). In this cohort, patients were assigned a mortality risk score, otherwise known as the EFFECT HF risk score, which was based on based on age, admission characteristics and co-morbid conditions. Using the EFFECT HF risk score to determine patient risk, median survival in the very high risk group (EFFECT risk score > 150 points) was 3 months (95% CI: 2-4 months) and a median survival of 8 months (95% CI: 7-9 months) was reported for those in the high risk group (EFFECT risk score 121-150 points). Participants with a low EFFECT risk score (61-90 points) had a median survival of approximately 5 years (95% CI: 55-62 months) (Ko et al., 2008).

In addition to significant mortality rates, HF is also associated with frequent hospitalization. HF is the most common diagnosis for patients over 65 years old admitted to hospital (Fang et al., 2008; Jong et al., 2002). In Canada, hospitalization rates increased from 1651 per 100,000 in adults aged 65-74 years to 8156 per 100,000 in adults ≥ 85 years of age (Hospital Morbidity Database, CIHI 1996/7). In Ontario, Canada, there were over 75,000 hospital admissions for HF between 1994-1997 and approximately half of these admissions (38,072) were newly diagnosed cases (Jong et al., 2002). The number of hospitalizations in the USA that included HF as either a primary or secondary diagnosis increased from 1,274,000 in 1979 to 3,860,000 in 2004 (Fang et al., 2008). Readmission rates range from 25% within 6 weeks to 33-50% within 6 months following admission to hospital with HF (Butler & Kalogeropoulos, 2008; Jiang et al, 2001; Burns et al, 1997).

Finally, HF also places a heavy financial burden on the health care system and is one of the most costly chronic diseases in developed countries (Liao et al., 2008). Estimates of the cost of HF are that it consumes between 1.1% and 1.9% of total healthcare spending in developed countries with 50%-74% of the HF costs attributed to hospitalization or long term institutional care (Liao et al., 2008).

There is a pressing need to identify important psychosocial risk factors associated with the negative outcomes for both individuals with HF and the health care system in order to effectively manage this chronic disease. After an extensive review of the literature, Jiang and colleagues (2005) concluded that depression and/or depressive symptomatology is one of the strongest psychosocial variables influencing prognosis in patients with established heart disease.

Epidemiology of Depression in Heart Failure

The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) classifies (unipolar) depression as a mood disorder characterized by one or more major depressive episodes (APA, 1994). A depressive episode is associated with symptoms of feeling sad or having no interest in previously enjoyed activities, for most of the day, nearly every day for at least two weeks. Additional psychological symptoms can include a loss of concentration and attention, feelings of guilt or worthlessness, pessimism or hopelessness about the future (Barraclough, 1997). Somatic symptoms overlap with symptoms of HF or other medical illness and can include fatigue and reduced energy, disturbed sleep, poor appetite and psychomotor agitation or retardation (Barraclough, 1997). For a major depressive disorder, five of the following symptoms must be present including depressed mood, and the symptoms should be present for at least two weeks and impair daily functioning (APA, 1994). Specifically, symptoms include:

- Depressed mood,
- Markedly diminished interest or pleasure in activities,
- Weight loss or weight gain (more than 5%),
- Insomnia or hypersomnia,
- Psychomotor retardation or agitation,
- Fatigue or loss of energy,
- Feelings of worthlessness or guilt,
- Diminished ability to concentrate or think,
- Recurrent thoughts of death.

In milder forms of depression, one of the above symptoms must be present most of the day, occurring almost daily for at least two weeks and result in some change in function or impairment in activities of daily living. A formal diagnosis of depression requires application of the DSM-IV criteria using a structured clinical interview by specially trained personnel.

Dysthymia is a chronic, milder level of depression that is characterized by having a depressed mood, for most of the day, almost every day, and for at least two years plus any two more of the following symptoms: poor appetite or overeating, insomnia or hypersomnia, low energy, low self-esteem, poor concentration or difficulty making decisions, or feelings of hopelessness.

People with HF have an increased risk of suffering from depression. The lifetime risk of developing depression in the general population ranges from 6% to 9% with a point prevalence rate of 10.6% in adults over 60 years of age (Kessler et al., 2005). Prevalence rates for depression in HF range from 13-77% (Thomas et al., 2003). This wide range is a result of variations in study populations, methodologies, measurement tools and criteria for defining depression in reported studies (Johansson et al., 2006).

The prevalence of depression in HF using established diagnostic methods has ranged from 18% (n=83; mean age 69 years; 49% male) in a sample of HF patients living in the community (Turvey et al., 2006) to 29% in a cohort attending an outpatient HF clinic (n= 100; mean age 67 years; 83% male) (Haworth et al., 2005). In a population study of community living older people (n=6125; mean age 76 (SD ±6), syndromal depression, as defined as the presence of five or more symptoms on the short form of the Composite International Diagnostic Interview (CIDI), was present in 11% of people with self-reported HF versus 3.2% of respondents with no self-reported heart disease (Turvey et al., 2002).

The majority of studies examining depression in patients with HF have used validated questionnaires that screen for symptoms of depression (Johansson et al., 2006). Prevalence rates in these studies vary considerably due to variations in the nature of items included in different screening tools and patient location at the time of testing. For example, there is a strong overlap between symptoms of HF and somatic symptoms of depression such as fatigue, trouble sleeping, and change in weight or appetite. Screening instruments may have difficulty discriminating between these different clinical syndromes and yield false positive results for the presence of depressive symptomatology. Prevalence rates of depression using screening instruments have yielded values ranging from 22% to 51%, with higher rates reported in hospitalized versus outpatient patient samples (Johansson et al., 2006). Patients hospitalized with HF have a prevalence rate of 43% to 51% for depressive symptoms while outpatient rates are slightly lower, ranging from 22-42% (Johansson et al., 2006).

The course of depressive symptoms in HF is poorly understood. The majority of longitudinal studies exploring effects of depression on negative outcomes only measure depression at baseline. Symptoms of depression may change over time but the natural course of these symptoms and predictors of the resolution or persistence of depression need to be identified. In a study of hospitalized patients with HF and depression (n=473), 64% of those with minor depression (n=246) experienced remission; mean time to remission was 5.4 (SD 2.7) weeks (Koenig, 2006). Multivariate predictors of remission were depression severity and medical co-morbidity. In the group of patients with major depression at baseline, only 29% experienced remission within 3 months following hospitalization with the mean time to remission of 11.7 (SD± 6.5) weeks.

Conversely, results reported from a population-based prospective study revealed that patients diagnosed with HF experienced higher levels of depression symptoms 6 and 12 months after the initial hospitalization for HF (vanJaarsveld et al., 2001).

Although there is considerable range in the prevalence of depression in HF patients, study findings consistently report higher rates of depression in this cohort than depression rates in the age-matched general population (Konstam et al., 2005; Rutledge et al., 2006). For the purposes of this research, the term 'depression' represents both the likelihood of depression and depressive symptomatology as defined by valid and reliable screening instruments used in the HF literature.

A rapidly growing body of evidence suggests that the combination of depression and HF can increase mortality, hospitalization rates, health care costs and further impair quality of life (QOL) compared to HF without depression (Johansson et al., 2006; Rutledge et al., 2006; Jiang et al., 2005; MacMohon & Lip, 2002; Thomas et al., 2003). In the Psychosocial Factors Outcome Study (PFOS), a sub study within the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), symptoms of depression (Beck Depression Inventory-II ≥ 13) were evident in 36% of outpatients with HF (n=153; mean age 60.9± 10.9 years; 83% male) (Friedmann et al., 2006). Using Cox regression, depression was found to be an independent predictor of mortality (HR 1.81; p=0.04), even after controlling for demographics, clinical predictors and treatment (Friedmann et al., 2006).

Similar results were found in the aggregated risk estimate from 8 studies where the presence of depression in HF patients was associated with a 2-fold risk of death or associated clinical events (RR 2.1; 95% CI 1.7-2.6) (Rutledge et al., 2006). In a meta-analysis of 6 studies comparing rates of rehospitalization, HF patients with depression versus non-depressed HF patients had more than a 2-fold risk of emergency room visits and a trend for an increase in outpatient medical appointments (Rutledge et al., 2006). Finally, in a study of older patients with HF (n=58; mean age 67.7 ± 11.8 years; 57% men), a diminished physical and emotional quality of life was significantly associated with depression (Carels, 2004).

Anxiety and Heart Failure

Even though depression is the most common form of emotional distress in patients with HF reported in the literature, emotional distress can also be manifested through symptoms of anxiety rather than depression. According to DSM-IV diagnostic criteria, a generalized anxiety disorder is classified as excessive anxiety or worry (apprehensive expectation), about a number of events or activities, that is difficult to control. At least 3 of the following symptoms must be present for a minimum of 6 months: restlessness/mental tension, fatigue, poor concentration, irritability, muscle tension, or sleep disturbance (Rickels & Rynn, 2001).

In the population study by van Jaaarsveld and colleagues (2001), 30% of patients who developed HF reported significantly higher levels of anxiety after diagnosis as compared to premorbid levels and these levels remained elevated at 12 months. In the SCD-HeFT study, 45% of the patients reported significant anxiety on the State Trait Anxiety Inventory (Spielberger, 1983), while 36% reported at least mild depression (Friedmann et al., 2006). In a sample of HF patients attending an outpatient HF clinic (n=221; mean age 67 SD 11; 78% male), 18% had at least one type of an anxiety disorder as detected in a Structured Clinical Interview (Haworth et al., 2005). Independent predictors of anxiety included a previous mental health history (OR 11.7; 95% CI 3.1-44.1), diabetes (OR 2.1; 95% CI: 1.0-4.3), angina (OR 3.87; 95% CI 1.3-18.8) and functional class (OR 1.9; 95% CI: 1.1-3.8); together these predictors explained 29% of the variance of anxiety (Haworth et al., 2005). In a qualitative phenomenographic study of women with HF, feelings of anxiety related to their life situation emerged as one of the five major themes (Martensson et al., 1998).

Similar to the epidemiology of depression in HF, the prevalence of anxiety in the HF population reported in the scientific literature varies considerably. In the SCD-HeFT trial, patients had been randomized to either receive an implantable defibrillator (ICD), pharmacological therapy or placebo for the prevention of sudden cardiac death. Anxiety levels may be relatively higher in this cohort due to treatment options compared to a cohort of patients with chronic HF receiving medical management. High levels of anxiety have been reported in the population with an ICD (Groeneveld et al., 2006). Low levels of anxiety in the sample attending the HF clinic could be due to responder bias (55% response rate), the exclusion of people with implantable defibrillators, or diagnosis of anxiety using a structured interview versus questionnaire method (Haworth et al., 2005). Thus, information regarding the epidemiology of anxiety in HF is extremely sparse and not well understood.

Even though patients with HF appear to have symptoms of anxiety, clinical outcomes associated with the coexistence of anxiety and HF are relatively unknown. In the SCD-HeFT study, while both anxiety and depression correlated with functional impairment, anxiety, unlike depression, was not an independent predictor of mortality (Friedmann et al., 2006). The presence of anxiety is associated with poorer outcomes in the population with coronary artery disease (Woldecherkos et al., 2007), but similar information in the HF population is lacking.

Summary

The high mortality, morbidity, hospitalization rates and poor QOL for people with HF is further complicated by the co-existence of depression. There is a desperate need to identify the possible physical and psychosocial risk factors associated with these negative outcomes in order to effectively and comprehensively treat this morbid condition. Currently, no definite conclusions can be made regarding the epidemiology of anxiety in HF and its effect on outcomes in this population. Although the primary objective of this study was to explore depressive symptoms in HF patients, anxiety was also measured in an effort to gain a better understanding of this manifestation of emotional distress.

Chapter 2

THEORETICAL FOUNDATION AND LITERATURE REVIEW

This chapter has three major sections. The first section describes the theoretical model used to provide the rationale for key variables included in this study. In the second section of this chapter, literature describing the psychosocial variables relevant to the relationship between emotional distress in HF patients and their caregivers is reviewed in detail. The chapter concludes with a summary of the study objectives, questions and hypotheses.

Section 2.1

Theoretical Foundation

The Adaptation Potential Assessment Model

Despite the significant health risks associated with the coexistence of HF and depression, the nature of this association is not fully understood. There is a pressing need to understand the relationship among risk factors associated with negative outcomes in HF. The majority of studies examining HF and depression have been cross-sectional, leaving unanswered questions about the underlying relationships that potentiate adverse outcomes when HF and depression coexist (Lane et al., 2006). To help explore the potential mechanisms within this relationship, psychosocial concepts described in the Adaptation Potential Assessment Model (APAM) (Leidy et al., 1990) were used to guide hypothesis generation and variable selection for this study. The APAM is derived from

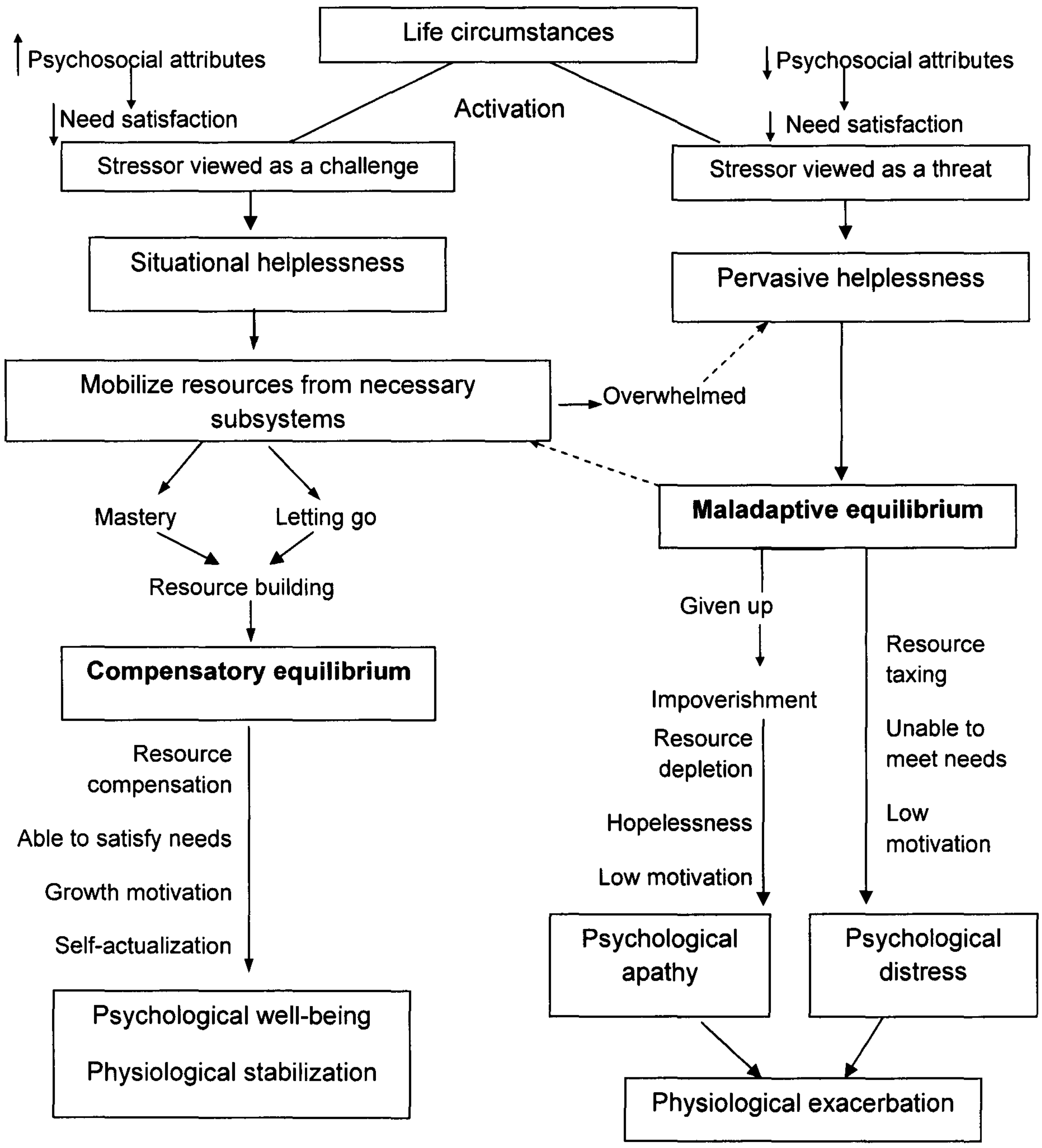
Lazarus and Folkman's meta-theory of stress, appraisal and coping and principles integral to this model are consistent with and relevant to the management of individuals who are coping with chronic illness (Leidy et al.,1990; Lazarus & Folkman, 1984). The APAM describes how individuals need to cope with stressors associated with chronic disease and ultimately re-establish a state of health. It has also been used to describe psychosocial adaptation in other cardiac populations (Delunas & Potempa, 1999; Livneh, 1999; Buetwo et al., 2001).

The APAM is a holistic model based on the theoretical stress adaptation framework for describing and classifying an individual's potential to adapt to perceived stressors through mobilization of internal and external resources. *Stressors* are defined as environmental stimuli or challenges that stimulate the mobilization of resources to ultimately master the stimuli. A stressor becomes a *distressor,* or threat, when individuals do not perceive that they have sufficient resources to master the stimuli. When this occurs, they are said to be in a state of *impoverishment*. Impoverished individuals are at risk for experiencing the negative physiological and psychological consequences of distress such as fatigue, anxiety or depression.

In the APAM, health represents a state of holistic well-being, rather than just the absence of disease. Health is characterized by a dynamic equilibrium between the *biophysical, psychological, cognitive and social subsystems* within an individual. When balance is maintained among the four subsystems, the individual is able to meet his/her basic needs and have adequate resources for participating in activities that promote growth and development. This is known as a state of *adaptive equilibrium*. If the individual senses the existence of a stressor, there is a temporary period of arousal followed by mobilization of coping resources and then a return to the state of adaptive equilibrium.

An individual's capacity for coping with stressors is influenced by the integrity of each of the four subsystems and the relationships between them. When this dynamic equilibrium is upset due to a loss of integrity in any one of the subsystems, the individual's resources for coping with stressors may become jeopardized and successful adaptation may not be possible. An individual will attempt to cope with the stressors in one subsystem by 'drawing energies' from another subsystem, or subsystems, and ultimately return to a state of adaptive equilibrium. However, with an ongoing loss of integrity in one subsystem, an individual is at an increased risk for entering into a state of impoverishment or *maladaptive equilibrium*. Basic needs may not be met and personal growth has been stagnated. Conversely, if an individual is able to meet his/her basic needs and find opportunity for personal growth, despite ongoing stressors in one subsystem (through use of resources from the other subsystems), then a state of *compensating equilibrium* has been achieved (Figure 1).

Figure 1. Psychophysiological Processes of Stress in People with a Chronic Physical Illness



In the context of the APAM, individuals living with HF can be either in a state of compensatory equilibrium or maladaptive equilibrium. A redefined balance between the biological, psychological, social and cognitive subsystems within individuals characterizes compensatory equilibrium. Thus, despite the stressors associated with HF, these individuals can meet their basic needs and find opportunities for personal growth and development. Some patients describe adaptation to HF as a process of finding meaning in their condition and a process of taking on a new identity (Stull et al., 1999). Conversely, individuals living with HF who are in a state of maladaptive equilibrium have not been able to achieve a healthy balance among their four subsystems and are at risk for negative consequences such as anxiety or depression.

Section 2.2

Literature Review

In the following section, the relationship between HF and depression and HF and anxiety are discussed using the framework from the Adaptation Potential Assessment Model (Leidy et al., 1990). Following a brief summary of the search strategy, literature describing the potential stressors imposed by HF on each of the four subsystems and how these stressors may predispose individuals to symptoms of anxiety or depression are reviewed in detail.

Search strategy

The following databases (2000-2006) were searched using Medicine Subjects Headings (MeSH)- heart failure, congestive heart failure, depression, emotional adjustment, coping, uncertainty, social support, caregiver burden, caregiving: PubMed; Medline; CINHAL; the Cochrane Collaboration; PsycINFO. Quantitative and qualitative studies from peer reviewed English journals were reviewed if they:

- Used an instrument with established psychometric properties measuring symptoms of depression, symptoms of anxiety, uncertainty, caregiver burden or caregiver appraisal in quantitative studies;
- Provided insight into the proposed relationships explored in this study using qualitative research methods.

Articles were critically appraised using techniques described by DiCenso et al. (2005). Articles were excluded if there were any major methodological flaws.

The Effect of Heart Failure on the Biophysical Subsystem

Shortness of breath, effort intolerance, fatigue, and weakness are cardinal HF symptoms. Patients with HF experience progressive functional decline over time punctuated by acute exacerbations, often requiring hospitalization (Bosworth et al., 2004). As management of symptoms becomes a daily struggle, the ability to fulfill social and occupational roles and responsibilities, and participate in hobbies, is progressively eroded. It is known that as a patient's functional class deteriorates, morbidity and mortality increase (Hunt et al., 2001). Empirical evidence also suggests a direct relationship between increased functional impairment, poorer QOL and symptoms of depression (De Jonge et al., 2006; Gott et al., 2006; Haworth et al., 2005; Carels, 2004; Jiang et al., 2004; Sullivan et al., 2004; Rumsfeld et al., 2003; Turvey et al., 2003; Faris et al., 2002; Friedman & Griffen, 2001; Vaccarino et al., 2002; Freedland & Carney, 2000; Majani et al., 1999; Glass et al., 1997; Gorkin et al., 1993). In a prospective cohort of patients with HF, 21% developed symptoms of depression within one year (Havranek et al., 2004). Quality of life was an independent predictor of developing symptoms of depression and a 10-point deterioration in the score on the Kansas City Cardiomyopathy Questionnaire (Green et al., 2000) was associated with an approximate 60% increase in the odds of developing depression (OR 1.61; 95% CI 1.2-2.3). In a longitudinal study of older patients hospitalized with HF (n=391; 51% male), baseline symptoms of depression as measured with the Geriatric Depression Scale (GDS) (Yesavage et al., 1983) were predictive of 6-month functional capacity (Vaccarino et al., 2002). Functional status was measured by means of the Katz ADL scale (Katz et al., 1970) and the Dyspnea Index (Mahler et al., 1984). There was a linear relationship between baseline GDS scores and functional decline in ADL activities among 6-month survivors. In the cohort with normal or mild symptoms of depression at baseline (n=193), 22% experienced a functional decline while 34%-46% of patients with moderate to severe depressive symptoms (n= 128) experienced functional decline over 6 months. Mortality was also significantly increased in the latter cohort, however after multivariate analysis, the association between depression and mortality was no longer significant.

A longitudinal study by vanJaarsveld et al. (2001) explored changes in QOL from pre-morbid scores to values measured 6 weeks, 6 months and 12 months after first time hospitalization for HF (n=119). Physical scores, as measured by the Groningen Activity Restriction Scale (Kempen et al., 1996), at 6 weeks were significantly worse than pre-morbid scores and continued to deteriorate significantly over the next 12 months (effect size 0.90). In addition, there was an increase in depressive symptoms on the Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983) (effect size 0.11) at 6 and 12 months and a significant decline in scores on the MOS social and role functioning subscales (effect size 0.37 each). These data suggest that functional capacity and depressive symptoms are not static and longitudinal studies with repeat testing are needed to accurately understand the trajectory and apparent relationship between these variables.

Most of the studies in the current literature describe the relationship between depression and functional status and its negative effect on patient outcomes; however, the direction of the relationship is not fully understood because of the limitations in study designs. In the study by Havranek et al. (2004), it appears that functional decline precedes depression. Conversely, findings by Vaccarino et al. (2002) suggest that pre-existing depression leads to further functional decline. The lack of repeated measures of depression and functional capacity over time significantly limits our ability to understand the natural course of depressive symptoms and the direction of the relationship between depression and functional status. In the present study, a longitudinal design with repeated measures of both depression and functional capacity in patients with HF was conducted in order to gain further insight into this relationship.

According to the stress-adaptation theory, the high symptom burden of HF imposes stress on the integrity of the biophysical subsystem, leading to functional impairment, inability to participate in valued activities, impaired QOL and ultimately contributes to feelings of uselessness and hopelessness (Leidy et al., 1990). Patients with HF must mobilize resources from their other subsystems to compensate for disruption to the biophysical subsystem while attempting to achieve a compensatory equilibrium. If these individuals are unable to effectively mobilize the necessary resources, they enter a state of maladaptive equilibrium that can be manifested as depression or anxiety. Attempts to mobilize resources from the other subsystems in order to cope with biophysical stressors may be overwhelming for some individuals since HF also has the ability to impose further stressors that independently disrupt the integrity of the other subsystems.

The Effect of Heart Failure on the Social Subsystem

Social support is a construct that has a variety of definitions (Luttik et al., 2005); however, for the purposes of this study, the definition of support system was limited to assistance from primary caregivers of the patients with HF. Thus, the patient's social subsystem is represented by the person identified by the patient who helps him/her the most with the day-to-day needs.

Because of a high symptom burden, patients with HF may require assistance when completing activities of daily living (ADL), following complex medication regimens, making significant dietary changes, participating in risk reduction behaviours and actively participating in daily self-management strategies to help avoid decompensation requiring hospitalization. Previous research has identified that many patients with HF have difficulty executing self-care behaviours, and assistance from an informal caregiver is often recommended (Leventhal et al., 2005; Molloy et al., 2005; Clark et al., 2003).

However, there is emerging evidence to suggest that caring for someone with HF imposes significant physical and emotional demands on primary caregivers (Molloy et al., 2006; Aldred et al., 2005; Fried et al., 2005; Luttik et al., 2005; Molloy et al., 2005; Brostrom et al., 2003; Meagher-Stewart & Hart, 2002; Murray et al., 2002; Mahoney, 2001; Martensson et al., 2001; Nieboer et al., 1998). In a sample of family caregivers of HF patients attending an outpatient HF clinic (patient n=20; mean age 63 years; 95% male), over 45% of caregivers reported at least moderate difficulty performing household tasks and over 25%

reported at least moderate difficulty regarding transportation assistance, finances, and dealing with patient behavior problems (Bakas et al., 2006). In one of the first studies to report outcomes for caregivers of patients with HF, Karmlovich (1994) reported that over 50% of female and 33% of male caregivers did not know if they would be able to handle their spouse's care in the future and 33% of women reported restrictions in their social/recreational activities because of caregiving responsibilities.

In a qualitative study of patients with advanced HF, patients commented on the key role their partners played in helping them manage their disease by providing emotional support and assistance with daily tasks (Aldred et al., 2005). At the same time, patients were also concerned about the strain this put on their partners, who also had health problems of their own (Aldred et al., 2005). Other studies have revealed that primary caregivers of patients with HF are at an increased risk of suffering from emotional distress or impaired quality of life, sometimes even worse than levels reported by the patients themselves (Luttik et al., 2005; Martensson et al., 2003).

Caregivers may experience anxiety related to the seriousness of their loved one's illness (MacMohon & Lip, 2002). To date, there are very few quantitative studies that specifically measured symptoms of anxiety in caregivers of patients with HF; even though 'feelings of anxiety, stress and uncertainty' from caregivers have been reported in qualitative research findings. Worrying about the health of a family member with HF was the first ranked stressor of 48 caregivers for patients living with HF (Meagher-Stewart & Hart, 2002). In a qualitative study, caregivers described significant sleep disturbance as a result of anxiety related to the patient's disease (Brostrom et al., 2003). Due to fear of deterioration in the patient's condition, they would often keep constant vigilance of the patient's heart and breathing status and be on guard for signs that would require returning to the hospital.

Even though the majority of literature has described strain or burden related to caregiving for people with HF, positive caregiving experiences have also been described. In a study of 18 caregivers (mean age 63.0 years; SD 12.25; 89% female) of 20 end-stage HF patients receiving community-based inotrope therapy (mean age 69.3 years; SD 9.0), the majority of caregivers felt positive about their role as a caregiver (Scott, 2000). Caregivers' mental health was assessed with the Mental Health Inventory-5 (MHI-5), a subscale of the Medical Outcomes Study Health Questionnaire Short Form (Ware et al., 1993), and positive aspects of caregiving were measured with the caregiver esteem subscale of the Caregiver Reaction Assessment (Given et al., 1992). All of the caregivers indicated a desire to provide care, even though 78% also described burden that affected their daily activities, health and finances as a result of caregiving responsibilities (Scott, 2000). Caregivers also experienced symptoms of anxiety (50%) and depression (45%) with 89% of the caregivers having mental health scores below the established age norm for the MHI-5. In a simple regression analysis, the mental health scores and caregiver esteem accounted for 49% of the variance in caregiver health-related quality of life. Caregiver esteem was also found to account for 30% of the variance in HF patients' health-related quality of life (Scott, 2000). Thus, to better understand the impact of caregiving for patients with HF, both the positive and negative caregiver experiences need to be examined.

In summary, it seems clear that patients with HF require assistance from informal caregivers to help achieve compensatory equilibrium and avoid emotional distress that results from ineffective coping. Caregivers' appraisal of the caregiving experience encompasses both negative and positive components. We do not know if there is a relationship between caregiver appraisal (the negative and positive components of the caregiving experience) and the emotional status of HF patients or caregivers. Even though it appears that informal caregivers of HF patients are at risk for caregiver burden and emotional distress, we do not fully understand the role of caregiver esteem in this relationship. Furthermore, we do not know if the emotional status of patients with HF correlates with caregiver burden, esteem or caregiver emotional distress. An innovative Canadian study found that there was a small, but significant correlation ($r=0.28$; $p<0.045$) between patient symptoms of depression and caregiver symptoms of depression in fifty patients attending a HF clinic (Hooley et al., 2005). Caregiver depressive symptoms were highly correlated ($r=0.61$; $p<0.001$) with caregiver burden. As well, increased caregiver burden was associated with a significant increase in 6-month rehospitalization and death in patients with HF. Although speculative, patients who have HF, complicated by symptoms of depression or anxiety, may require additional caregiver physical and emotional support which could contribute to feelings of emotional distress in caregivers. In this context, caregiver burden may represent an exhausted support system that can no longer provide necessary assistance. Patients then are at higher risk for developing the negative outcomes associated with the coexistence of HF and emotional distress. Patients without caregiver support may be at risk for developing symptoms of depression or anxiety when they can no longer utilize their social subsystem for re-establishing a state of health. Future research needs to build on the findings of Hooley and colleagues by measuring both the positive and negative components of the caregiver experience. Longitudinal designs are also needed to determine if patient and caregiver symptoms of depression and anxiety change over time and what factors moderate or mediate any observed changes.

The Effect of Heart Failure on Psychological Subsystem

The illness trajectory associated with HF is highly individual and decompensation that foretells mortality and morbidity is difficult to predict (Goodlin et al., 2004). Patients with HF report feelings of uncertainty related to their illness trajectory, in addition to self- identity, social roles and daily management strategies for symptom control (Artinian, 2003; Boyd et al., 2004). In a mixed methods study of community dwelling HF patients (n=22; mean age 70 years; 68% male), uncertainty was primarily related to symptom fluctuation, the ability to stay well and 'how bad their symptoms would become' (Winters, 1999). Patient strategies used to decrease uncertainty included; learning how to monitor and respond to their symptoms, developing a relationship with primary health care providers, and reframing their view of quality of life (Winters, 1999). In HF patients being assessed for cardiac transplantation (n=222; mean age 56.7 ± 12.5 years; 82% male), perceived control was associated with less emotional distress and better functional capacity (Dracup et al., 2003). Using a regression model, the addition of perceived control increased the explained variance in anxiety from 10% to 33% and from 15% to 34% for depression (Dracup et al., 2003). In a sub study of spouses (n=69; mean age 54 years; 75% female) from this HF population, lower levels of perceived control in caregivers, as measured on the Control Attitudes Scale- Family Version (Moser & Dracup, 2000), were also associated with poorer emotional well-being (Dracup et al., 2004). Emotional well-being was measured using the mental health (5 items) and health perceptions (5 items) from the Medical Outcomes Study Short For Health Survey (SF-36) (Ware et al., 1993). Spouses with higher perceived control scored significantly higher on the SF-36 subscales versus spouses with lower perceived control (77.6 vs. 63.3, respectively; p=0.003) (Dracup et al., 2004).

According to the Model of Perceived Uncertainty in Illness by Mishel, feelings of uncertainty occur when a person is unable to structure meaning or form a cognitive schema for an illness event. These events can encompass issues related to the diagnosis, symptoms, treatments or prognosis associated with the illness (Neville, 2003; Mishel, 1988). Subsequently, uncertainty can be appraised as an opportunity or as a threat. When uncertainty related to an illness event is appraised as a threat, coping strategies are mobilized to reduce the uncertainty (Mishel, 1988). In the setting of chronic illness, uncertainty can remain constant and individuals must shift their perspective of life and find a new sense of order within this context. This new outlook on life allows the appraisal of uncertainty to be changed from negative to a neutral or positive experience (Mishel, 1990). In the context of the APAM, compensatory equilibrium is restored by finding meaning in chronic illness, learning how to modify expectation and lifestyle, and gaining a sense of control over the illness trajectory. Failure to achieve such feelings of acceptance and adjustment may lead to symptoms of depression.

Even though uncertainty has been associated with feelings of emotional distress in a variety of populations (Mishel, 1997), there have not been any published quantitative studies exploring the relationship between levels of uncertainty and emotional status in older HF patients or HF patients who are not being considered for cardiac transplantation. Because emerging evidence suggests that feelings of uncertainty exist in these study populations, this study explores this construct in both patients with HF and their primary caregivers to determine whether uncertainty is associated with feelings of anxiety and depression.

The Effect of Heart Failure on the Cognitive Subsystem

Living with HF imposes a high cognitive demand in order to overcome symptom burden and feelings of uncertainty. For example, the ability to follow complex medication schedules and dietary changes, participating in risk factor reduction behaviours, and executing daily problem solving skills to manage variations in fluid status are required to help avoid clinical deterioration and repeat hospitalization (Carlson et al., 2001; Frantz, 2004; Duffy et al., 2004, Jurgens, 2006). Furthermore, an intact cognitive subsystem is necessary for executing active coping behaviours that are associated with lower levels of depression in patients with HF (Carels, 2004; Doering et al., 2004). However, HF patients are at an increased risk for cognitive impairment (Riegel et al., 2002; Bennett & Suave., 2003). Cognitive deficits include memory loss, difficulty concentrating and problem solving, and impaired learning, and thus have the potential to interfere with self-care capability and adaptive coping behaviours (Bennett et al., 2000; Evangelista et al., 2003). Subsequently, HF patients may be at an increased risk of developing depression because they lack the high level of cognitive integrity needed to successfully cope with stressors imposed by HF.

Summary

In order to successfully cope with HF, patients must rely on the relative integrity of their *biophysical, social, psychological* and *cognitive* subsystems. However, HF has the potential to adversely affect each subsystem and impair the ability of individuals to effectively utilize coping strategies needed to achieve compensatory equilibrium (Dixon et al., 2000; Costello & Boblin, 2001; Zambroski, 2003; Barnes et al., 2006; Rector et al., 2006). Patients who are unable to mobilize necessary resources to re-establish a healthy state in the presence of a chronic disease enter a state of maladaptive equilibrium and, as a result, may experience emotional distress such as depression or anxiety.

Section 2.3

Study Purpose, Objectives, and Questions

The prevalence of emotional distress in HF patients, especially manifested by symptoms of depression, is higher than the general healthy population and the effects of these symptoms are associated with poor clinical outcomes. Within the context of the APAM model, this study aimed to determine if there is a relationship between HF patients' adaptation and the integrity of their social subsystem. Ineffective adaptation is represented by symptoms of depression or anxiety in HF patients and the integrity of the social subsystem is primarily represented by the emotional status of the primary caregiver. Hence, the primary purpose of this study was to determine if there is a relationship between the emotional status of HF patients and their primary caregivers.

Based on the review of the literature in the context of the APAM theoretical framework, there was an opportunity within this research to gain a more comprehensive understanding of psychosocial adaptation in HF patients. In addition to caregiver emotional status, variables that were measured include disease severity (biophysical subsystem), feelings of uncertainty (psychological subsystem) and caregiver appraisal (another component of the social subsystem) and these variables were represented in the secondary objectives of this research project. Representation of the cognitive subsystem would require measurement of cognitive function in HF patients. This type of measurement can be quite complex and could significantly increase respondent burden and was therefore not included in this research. Although the relationship between symptoms of depression and other variables, such as uncertainty and caregiver appraisal, are explored in this study, these relationships are not the primary focus of this study because pilot data from the writer's previous Master's research suggested that the relationship between patient and caregiver emotions should be explored in depth. The potential relationships between HF patient emotional status and variables representing disease severity, uncertainty and caregiver appraisal were explored in this research as secondary outcomes.

Study Purpose

The primary purpose of this research was to explore potential relationships between the emotional status of HF patients and their primary caregivers.

Study Objectives

The primary objective of this study was to determine if there is a relationship between symptoms of depression and anxiety in HF patients and symptoms of depression and anxiety in their primary caregivers.

Secondary objectives of this study were to determine if there is a relationship between:

- Patients' emotional status and levels of uncertainty
- Primary caregivers' emotional status and levels of uncertainty
- Patients' emotional status and caregiver appraisal
- Primary caregivers' emotional status and caregiver appraisal

The final objective of this study was to explore whether the patients' emotional reactions and feelings of uncertainty as well as caregiver appraisal change over time.

Research Questions and Hypotheses

Research Questions Related to Primary Objective

- Is there a relationship between depression scores of both HF patients and their primary caregivers?
- Is there a relationship between anxiety scores of both HF patients and their primary caregivers?

Research Questions Related to Secondary Objectives

- Is there a relationship between symptoms of anxiety and depression and uncertainty in HF patients?
- Is there a relationship between symptoms of anxiety and depression and uncertainty in primary caregivers of HF patients?
- Is there a relationship between symptoms of anxiety and depression in HF patients and caregiver appraisal?
- Is there a relationship between symptoms of anxiety and depression in primary caregivers of HF patients and caregiver appraisal?

Research Questions Related to Secondary Objectives Exploring Change Scores

- Do symptoms of anxiety or depression in patients and their primary caregivers change over time?
- Do levels of uncertainty in patients and caregiver change over time?
- Do levels of caregiver burden and caregiver esteem change over time?
- Does the strength of the relationship between patient and caregiver emotions change over time?
- Does the strength of the relationship between patient and caregiver emotions and uncertainty change over time?
- Does the strength of the relationship between caregiver emotional status and caregiver appraisal change over time?

Hypotheses

1. There is a direct, positive relationship between:

- Symptoms of depression in patients with HF and their primary caregivers
- Symptoms of anxiety in patients with HF and their primary caregivers
- Uncertainty and symptoms of anxiety or depression in HF patients.
- Uncertainty and symptoms of anxiety or depression in primary caregivers of HF patients.

- Symptoms of anxiety and depression in patients and perceived caregiver burden.
- Symptoms of anxiety and depression in primary caregivers and perceived caregiver burden.

2. There is a negative relationship between symptoms of anxiety and depression in primary caregivers and caregiver esteem

CHAPTER 3

STUDY METHODS

A longitudinal exploratory design was used to determine if correlations existed between selected patient and caregiver variables. The following chapter has 4 major sections that include:

Section 3.1. Target population

A description of inclusion and exclusion criteria are outlined.

Section 3.2. Study procedures

Screening, recruitment and the study protocol are described.

Section 3.3. Variables and Instruments

Patient and caregiver demographic and health history variables of interest in addition to instruments used to measure emotional status, uncertainty and caregiver appraisal are described.

Section 3.4. Data management

Analytical strategies for determining statistical power, handling of missing data, and data analysis are presented and conclude this chapter.

Section 3.1

Target Population

Consecutive patients attending their initial or follow up appointment to the Heart Function Clinic (HFC) were screened for eligibility. Inclusion and exclusion criteria include:

Inclusion Criteria

- Age greater than 45 years
- Confirmed diagnosis of HF documented on patient medical chart based on Framingham Criteria outlined in Ho et al., 1993 (See Appendix A)
- Functional ability for communication (written and oral) in the English language
- Able to identify a consistent primary caregiver

Exclusion Criteria

- Coronary revascularization o***r valve surgery w***ithin the last 6 months
- Acute myocardial infarction within the last 6 months
- Planned coronary revascularization or valve surgery within the next 6 months
- Documented cognitive impairment or psychiatric illness
- Life expectancy less than 12 months due to terminal illness other than HF
- Residing in a long term care facility
- Patient-identified primary caregiver did not accompany patient to HFC appointment

Study Site

The HFC is located in the outpatient department of the Hamilton Health Sciences, McMaster Site. The Hamilton Health Sciences (HHS) is comprised of three, tertiary, acute care hospitals located in Hamilton, Ontario, Canada. The HFC was founded in November 1999 and provides regional services for patients with advanced HF with an average of 130 new patient visits annually. Currently there are approximately 300 active patients followed in the HFC. Patients are referred to the HFC from both inpatient and outpatient locations. The HFC team consists of 4 cardiologists, a geriatrician, 2 HF nurse specialists and a dietitian.

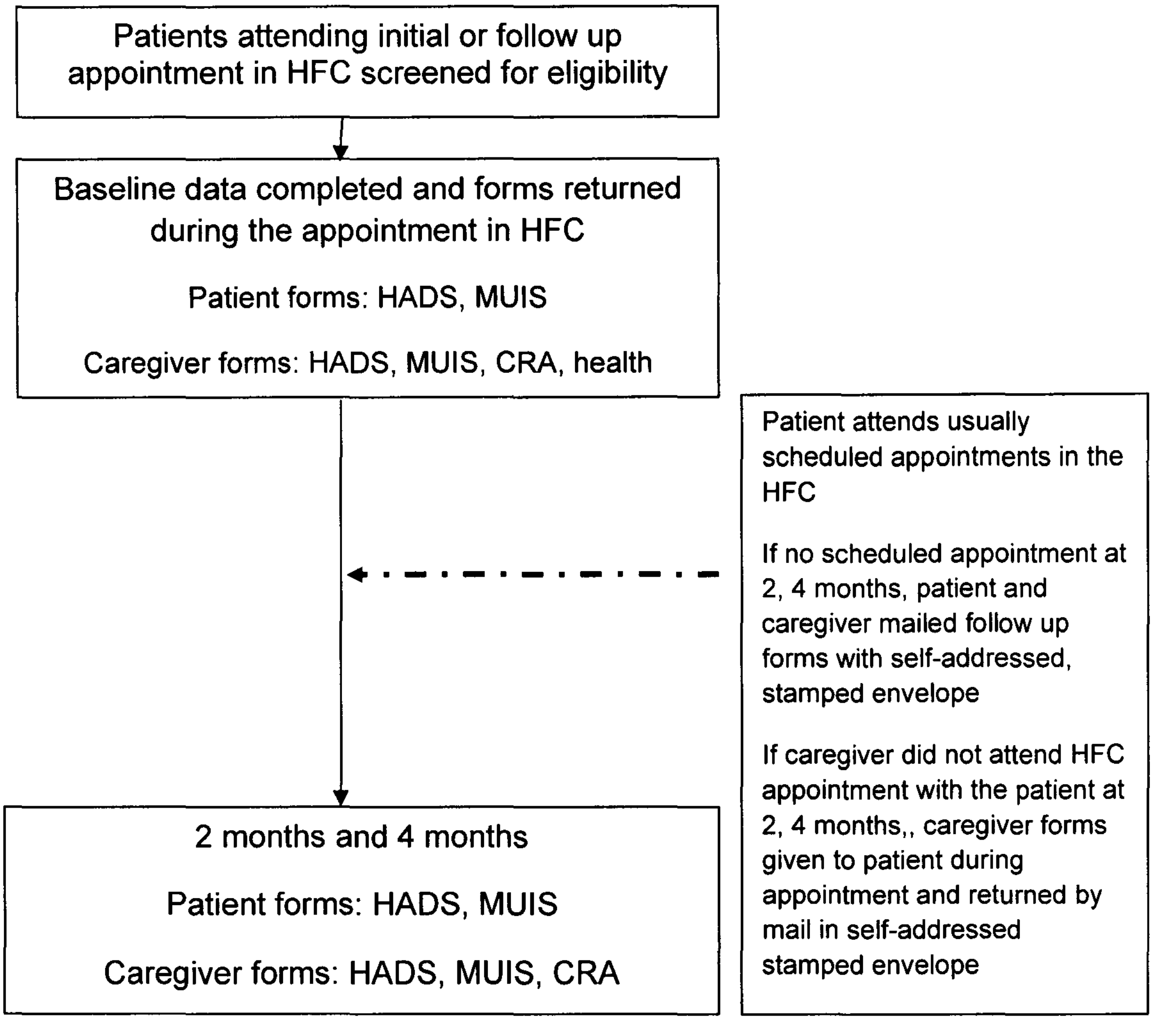
Section 3.2

Procedures

Screening and Recruitment

Following approval by the Research Ethics Board, health records in the HFC office were searched for patients attending their first appointment in the HFC. Initial plans were to only recruit patients attending their first appointment in the HFC, however recruitment was unexpectedly slow and after 12 months of recruitment, eligibility was extended to patients already followed in the HFC and who consistently brought their primary caregiver to follow up appointments. Potential patient-caregiver pairs identified by the primary investigator were approached by a research assistant (RA) during their regularly scheduled new or follow up appointment in the HFC. Study information was reviewed and informed written consent was obtained by the RA (See Appendix B for a copy of the information sheet and consent forms). All participants received a copy of the study information and signed consents. Figure 2 depicts a summary of the study procedures.

Figure 2. Summary of Study Procedures



Patients attending initial or follow up appointment in HFC screened for eligibility

Baseline data completed and forms returned during the appointment in HFC

Patient forms: HADS, MUIS

Caregiver forms: HADS, MUIS, CRA, health

Patient attends usually scheduled appointments in the HFC

If no scheduled appointment at 2, 4 months, patient and caregiver mailed follow up forms with self-addressed, stamped envelope

If caregiver did not attend HFC appointment with the patient at 2, 4 months,, caregiver forms given to patient during appointment and returned by mail in self-addressed stamped envelope

2 months and 4 months

Patient forms: HADS, MUIS

Caregiver forms: HADS, MUIS, CRA

HADS- Hospital Anxiety and Depression Scale; MUIS- Mishel Uncertainty in Illness Community Form; CRA- Caregiver Reaction Assessment

Study Protocol

Consenting patients and the patient-identified primary caregivers completed questionnaires measuring emotional status and uncertainty at baseline, and at 2 and 4 month follow up periods. Primary caregivers also completed a survey measuring the caregiving experience at each time point. Whenever possible, two and four-month follow up questionnaires were completed at subsequent appointments in the HFC. No extra appointments were needed for the purposes of completing follow up data collection. If either patients or caregivers were unable to complete forms during the scheduled appointments, they were provided with a self-addressed stamped envelope to return to the primary investigator. On rare occasions (less than 6), patient appointment scheduling did not align with study follow up measurement points and patient-caregiver pairs were mailed questionnaires with a self-addressed stamped return envelope.

Section 3.3

Variables and Instruments

Patient and Caregiver Variables

Patient demographic and health history data were collected by the primary investigator from the patient's health record located in the HF clinic office using a study-designed case report form. Caregiver demographic and health history data were collected using a self-administered, study-designed questionnaire that was completed by caregivers at baseline. Demographic data from both patients and caregivers included: age, sex, caregiver and patient relationship (e.g. spouse, adult child), living arrangement (same or separate location), employment status, and highest level of formal education. Additional patient health variables included baseline left ventricular ejection fraction (LVEF), duration of HF, time since most recent hospitalization, history of myocardial infarction (MI), atrial fibrillation (AFib), implantable defibrillator (ICD), cardiac resynchronization therapy(CRT), coronary artery bypass surgery (CABG) or valvular surgery, and percutaneous coronary intervention (PCI). New York Heart Association (NYHA) classification was recorded at each time period and was based on the assessment by the HF clinic physician or specialized HF nurse during the patient's HFC appointment. For the patients who completed follow up measurements outside of a HFC appointment, NYHA from the previous HFC appointment was used. Other patient medical data included cardiac risk factors, arthritis, chronic obstructive pulmonary disease (COPD), past or present cancer, previous cerebral vascular event (CVA) or transient ischemic attack (TIA) and chronic renal failure (patient's baseline creatinine >130 µmol/L). Caregiver medical history included self report of heart disease, COPD, diabetes, cancer, arthritis and stroke (See Appendix C for a copy of the patient and caregiver tools).

Number of patient HFC visits, hospitalizations, reason for hospitalization and other clinical events were collected from patient electronic health records, HFC health records and patient history at 2 and 4 month follow up by the primary investigator.

Instruments

The Hospital Anxiety and Depression Scale (HADS)

The HADS is a self administered questionnaire composed of 14 items, with 7 items each for the anxiety and depression subscales (Zigmond & Snaith, 1983). It is generally well accepted by individuals and can be completed in 2-6 minutes (Herrmann, 1997). The HADS is used internationally and is available in many languages (Herrmann, 1997). Items were constructed with particular attention to avoiding somatic symptoms associated with medical illness that potentially yield false positive results on other screening questionnaires for anxiety or depression (Herrmann, 1997).

All items are scored on a four-point scale ranging from 0-3. Higher scores indicate higher levels of emotional distress. A cut off point of 8+ for each subscale provides an optimal balance between sensitivity and specificity for use of the HADS as a screening instrument for anxiety or depression in a variety of medical conditions (Bjelland et al., 2002).

Psychometric testing in multiple populations has demonstrated the validity of the HADS and a strong factor structure. Internal consistency reliability is also strong with Cronbach's alpha consistently greater than 0.80 (Bjelland et al., 2002; Herrmann, 1997). The HADS is able to discriminate between individuals with high, moderate or low levels of anxiety or depressive symptomatology

(Herrmann, 1997). In a post-MI population (n=179), the HADS was found to be a reliable and valid instrument when compared to DSM-IV criteria assessed by a structured clinical interview (Strik et al., 2001) (See Appendix D for a copy of the HADS instrument).

Mishel's Uncertainty in Illness Scale- Community Version (MUIS-C)

The Uncertainty in Illness Scale –Community version is a uni-dimensional instrument used to measure uncertainty about the meaning of illness events in patients or families of chronically ill patients (Mishel, 1997). The patient version has 23 items and the caregiver version has 31 items that use a Likert-style response format from 'strongly agree'- to 'strongly disagree' with each item statement. Scores for each item range from 0-5, with higher scores representing higher levels of uncertainty. Mean scores have been shown to increase with higher levels of education (mean score of 52.7 in patients with <7 years education; mean score 62.7 in people with 7-12 years education; mean score 61.8 in patients with greater than 12 years of education) and thus scores may need to be adjusted for level of education (Mishel, 1997). In the general cardiac population, the MUIS-C has moderate to high levels of internal consistency reliability (Cronbach's alpha 0.78-0.86) (Mishel, 1997) and in a population with HF, Cronbach's alpha was 0.78 (Jurgens, 2006).

According to the MUIS-C author's guidelines, the word "illness" was replaced with "heart failure" for this study population (Mishel, 1997). For example, items on the patient MUIS-C are; "I am unsure if my heart failure is getting better or worse", "My heart failure treatment is too complex to figure out" and "the seriousness of my heart failure has been determined". Some examples from items from the MUIS-C caregiver version are;" I don't know what is wrong with him/her" and "The explanations they give about his/her heart failure seem hazy to me" (See Appendix E for a copy of the patient and caregiver versions of the MUIS-C).

Caregiver Reaction Assessment (CRA)

The CRA is a multidimensional tool to assess the negative and positive reactions of caregivers. Initial development and extensive psychometric testing were conducted in caregivers of elderly patients with physical limitations, dementia, Alzheimer's disease or cancer (Given et al., 1992). The CRA is comprised of 24-items representing 5 domains (lack of family support, impact on finances, impact of schedule, impact on caregiver health, care-derived self-esteem). Using a self-administered questionnaire format, each item is answered using a 5-point Likert scale with responses ranging from 1 (strongly agree) to 5 (strongly disagree). Composite scores are computed as averages of the items within each dimension, ranging from 1.0 to 5.0. Lower scores on the 4 negative dimensions represent lower levels of perceived burden and a lower score on the one positive dimension represents a lower level of self-esteem related to the caregiving role. Some authors have calculated the total score on each subscale and used the top quartile of the distributions as representative of a high level of caregiver burden (Brazil et al., 2003).

Each of the 5 dimensions of caregiver reactions on the CRA have consistently exhibited highly stable factor structures across a variety of caregiver populations in cross- sectional and longitudinal studies (Given et al., 1992; Nieober et al., 1999; Jacobi et al., 2003). Moreover, CRA subscores have been shown to significantly correlate with objective burden (Luttik et al., 2007; Jacobi et al., 2003; Brazil et al., 2003; Given et al., 1992); caregiver depression (Luttik et al., 2007; Kurtz et al., 1995; Given et al., 1992); caregiver mental health (De Frais et al., 2005) and caregiver health related quality of life (Scott, 2000).

Adequate internal consistency, measured by Cronbach's alpha, has been demonstrated for the CRA across a variety of caregiver populations. Reliability coefficients ranged from 0.56 (caregiver health) to 0.84 (impact on finances) for CRA scores in 18 caregivers of end stage HF patients receiving home intravenous inotrope therapy (Scott, 2000).

In summary, the CRA is a multidimensional tool that measures both the positive and negative components of the caregiving experience and has performed well in psychometric testing for a variety of populations. Even though its use in caregivers for patients with HF is rather sparse, its ease of administration, strong psychometric properties and attention to both the positive and negative experiences associated with caregiving make it an optimal choice for a generic tool to measure the subjective caregiver experience in this population. The CRA was completed by caregivers at all time periods (See Appendix F for a copy of the CRA).

Section 3.4

Data Management

Statistical Power and Missing Data

Sample size was calculated to have sufficient power to answer the primary research question; that is, to determine if there is a statistically significant relationship between anxiety and depression (as measured by the HADS) in patients and their caregivers. In order to detect a correlation of 0.40, using two continuous variables, 50 patient-caregiver dyads were needed (Norman & Streiner, 2008). A correlation of 0.40 using the Pearson product-moment correlation coefficient, *r*, represents a medium to large effect size for a relationship between two variables in behavioural science (Cohen, 1992). For the purposes of this study, a relationship represents a correlation that is clinically meaningful. According to Cohen (1992), a correlation between two key variables in behaviour science is considered clinically meaningful when the correlation coefficient is at least 0.30.

Based on pilot study data, the required sample to detect a significant change in HADS-depression scores over time (with 80% power), was 235 patient-caregiver dyads (mean change 0.87, SD 4.55). Similarly, the required sample size to detect a significant change over time in HADS-anxiety scores (mean change 0.70, SD 2.98) was 142 patient-caregiver dyads. Therefore, in order to have adequate power to determine if there is a significant change in symptoms of depression or anxiety in HF patients over time in this PhD study, 235 patient-caregiver dyads would have been needed. Adding in a 30% drop out rate (due to high event rates in this population) we would have needed to recruit 305 dyads. Due to time constraints associated with PhD research, and the fact that a relationship between patient and caregiver depression was the main outcome of interest, the target sample was 60 pairs (50 + 20% drop out rate). Although the study was not powered to detect a significant change in feelings of depression or anxiety over time, trends in change scores are reported. Because recruitment was unexpectedly slow, recruitment was terminated after 50 pairs, the minimum number needed for the primary outcome.

Missing data

For any questionnaires with less than 10% missing data, the 'last observation carried forward' imputation method was used (Norman & Streiner, 2008). This method consists of using the last valid response to replace the missing item and is a common imputation method in longitudinal studies (Norman & Streiner, 2008). Missing data were analyzed for patterns of 'missingness' as described by El-Masri & Fox-Wasylyshyn (2005). For example, examination of systematic patterns of missing data, such as specific questionnaires or items within a questionnaire, was conducted.

Data analysis

Data were analyzed using the SPSS software statistical package (SPSS v.12 for Windows, Chicago, Ill.) An alpha of $p \leq 0.05$ was considered statistically significant.

Descriptive Statistics

- Demographic variables are described using frequencies for categorical variables and mean (± standard deviation) for continuous variables.
- Instrument scores (HADS, CRA, MUIS) from each measurement time were analyzed for normality using the Shapiro-Wilk W test. Mean (normally distributed) or median scores (skewed distribution) were calculated for instrument scores for each measurement time.
- HADS- anxiety and depression scores were also dichotomized; scores of ≥8 on the HADS-anxiety and HADS-depression scales were considered to indicate symptoms of anxiety or depression respectively. The number of patients and caregivers scoring above (and below) the cut-off score at each measurement time in addition to the median score were used in all data analyses involving the HADS.
- Because recruitment involved patient-caregiver dyads, analysis was conducted on the assumption that dyad responses are interrelated. Thus, comparison between patient and caregiver characteristics and responses was based on matched-pairs statistical analysis techniques (Kraemer & Jacklin, 1979). For example, differences between patients and caregivers for continuous variables were compared using paired t-tests for normally distributed data and Wilcoxon signed-ranks test for skewed data. Chi-square analysis (χ^2) was used for categorical variables.

Associations

Bivariate correlations between continuous or interval data (HADS, MUIS, CRAS) were calculated using Spearman's rho. If continuous data were normally distributed, Pearson's correlation coefficient was used. The Phi coefficient was used when analyzing association between HADS anxiety and depression and patient and caregiver dichotomous scores.

Changes over Time

Changes between baseline, 2 months and 4 month HADS, MUIS and CRA scores that were normally distributed were analyzed using analysis of variance (ANOVA). The Kendall's W test was used to explore trends in changes HADS, MUIS and CRA scores between baseline, 2 months and 4 months if scores were not normally distributed.

CHAPTER 4

RESULTS

The following chapter is divided into five main sections as follows:

Section 4.1. Study Sample

The first section presents information regarding recruitment and flow of patient-caregiver dyads through the study. Baseline data from pairs that completed versus those that withdrew from the study are compared. This section concludes with a description of the study population.

Section 4.2. Baseline Data Analyses for Primary Objective

The second section presents the results from baseline HADS patient and caregiver scores. Correlational analyses between the emotional status of the patient and caregiver (using baseline scores only) are also presented in this section since they refer to the primary objective of this study.

Section 4.3. Baseline Data Analyses for Secondary Objectives

Secondary study objectives involve baseline data from patient and caregiver uncertainty (MUIS scores) and caregiver appraisal (CRA scores) are presented. This section begins with a summary of baseline patient and caregiver MUIS scores and then presents correlational analyses between patient and caregiver emotional status (HADS) and uncertainty (MUIS). The latter part of this section presents baseline data from caregiver CRA scores followed by analyses exploring correlations among CRA scores in caregivers, patient and caregiver emotional status (HADS) and uncertainty (MUIS).

Section 4.4. Exploratory Analyses

The fifth section presents results in the context of the secondary objectives exploring change scores. Exploratory analyses examining changes in HADS, MUIS and CRA scores at baseline, 2 months and 4 months are presented. Correlations conducted between baseline HADS, MUIS and CRA are repeated for values at 2 months and 4 months to explore if the strength of correlations between these variables changes over time.

Section 4.5. Summary of Findings Based on Study Hypotheses

The sixth and final section summarizes the study findings according to each study hypothesis.

Section 4.1a

Description of the Study Sample

Study Recruitment

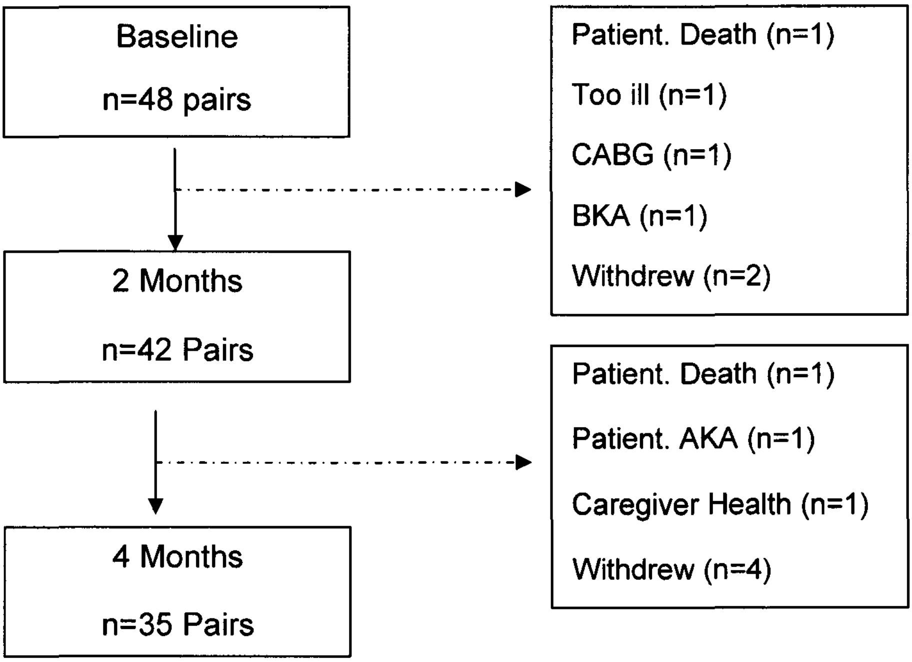
Between January 1, 2007 and May 31, 2008, a total of 266 patients were screened and 62 patient-caregiver pairs were eligible. Reasons for exclusion included caregiver unavailable (n=39); patient or caregiver language barrier (n=25), documented patient cognitive impairment (n=22), patient significant morbidity other than HF (n=20), patient history did not meet criteria for HF (n=19), cardiac surgery or myocardial infarction in the previous 6 months (n=19), documented patient psychiatric history (n=17), missed opportunity (n=12), patient resides in a long term care facility (n=7), patient age <45 years (n=7) and 'other' (n=17). From the 62 eligible patient-caregiver pairs, 12 pairs declined and 50 pairs were recruited.

Study Flow

After signing written consent, two pairs withdrew because one member from each pair found completing the questionnaires too burdensome. Thus, complete baseline data are available for 48 patient-caregiver pairs.

Between baseline and 2-month follow-up, 6 pairs withdrew due to: patient death (n=1), planned patient coronary artery bypass surgery (CABG) (n=1), urgent patient below knee amputation surgery (BKA) (n=1), illness related to competing co-morbidities (severe lung disease, West Nile virus) (n=1), and caregiver withdrawal (n=2). Between 2 and 4-month follow-up, 7 pairs withdrew due to: patient death (n=1), patient urgent above knee amputation surgery (AKA) (n=1), caregiver health problems (n=1) and no specific reason (n=4). Thus, after completing baseline data (n=48), 35 patient-caregiver pairs (73%) completed the study and 13 pairs (27%) withdrew (Figure 3).

Figure 3. Study Flow of Patient-Caregiver Pairs between Baseline, 2 months and 4 months



CABG-Coronary Artery Bypass Surgery; BKA- Below Knee Amputation; AKA- Above Knee Amputation

Section 4.1b

Description of the Study Sample

Comparisons Between Participants who Completed versus Withdrew

There were no significant differences between pairs that withdrew either after baseline (n=6) or after 2 months (n=7). Thus, these groups were collapsed into 1 cohort (n=13) for statistical analyses when comparing the patient-caregiver pairs that withdrew to the cohort of pairs that completed the study (n=35). Using Chi-square analysis, there were no significant differences in baseline patient and caregiver age, gender, living arrangement, employment status or education, patient and caregiver medical variables.

Both patients and caregivers with significantly higher baseline MUIS scores (indicating a higher level of uncertainty) were more likely to withdraw than complete the study. There was a trend for more patients with symptoms of depression (HADS depression score≥8) to withdraw versus complete the study (50% versus 29% respectively; p=.104) and more caregivers with symptoms of anxiety (HADS- anxiety score ≥ 8) to withdraw (64% versus 41%; p=.072). Caregivers who withdrew were more likely to have higher perceived caregiver burden related to feeling abandoned by their family for help with caregiving (median 2.6 (IQR 1.7) vs. median 2.1 (IQR 1.4) respectively; p=.135) and have higher perceived caregiver esteem related to caregiving (median 4.4 (IQR 1.6) vs. median 3.8 (IQR 0.8) respectively; p=.052) than caregivers who completed the study (Table 1). (Please see Appendix G for a full summary of demographic data comparing patient-caregiver pairs that completed and withdrew from the study.)

Table 1. Comparison of Baseline Questionnaire Results for Participants who Completed versus Withdrew

	Completed (n=35 pairs)	**Withdrew** (n=13 pairs)	p value
Hospital Anxiety and Depression Scale- Patient			
Anxiety **	5.0 (4)	6.0 (10)	.187
Score ≥ 8: % within group (n)***	24% (7)	29% (5)	.189
Depression**	5.0 (5)	8.0 (6)	.239
Score ≥ 8: % within group (n)***	29% (10)	50% (7)	.104
Hospital Anxiety and Depression Scale- Caregiver			
Anxiety **	6.0 (7)	10 (5)	.081
Score ≥ 8: % within group (n)***	41% (14)	64% (9)	.072
Depression*	4.0 (5)	4.0 (4)	.833
Score ≥ 8: % within group (n)***	21% (8)	14% (1)	.232
Mishel Uncertainty in Illness* – Patient and Caregiver			
Patient : mean (SD)	60.5 (11.9)	72.5 (12.1)	.002*
Caregiver: mean (SD)	80.2 (13.6)	96.2 (14.3)	.002*
Caregiver Reaction Assessment - Caregiver**			
Caregiver Schedule	2.8 (1.2)	3.2 (2.0)	.545
Financial Problems	2.0 (1.3)	2.3 (1.2)	.535
Family Abandonment	2.0 (1.4)	2.6 (1.7)	.135
Caregiver Health Problems	2.3 (1.5)	3.0 (1.6)	.220
Total Burden	2.0 (1.0)	2.2 (1.3)	.227
Self Esteem (Positive)	3.8 (0.8)	4.4 (1.6)	.052

Values expressed as median (Interquartile range) unless otherwise indicated

*Analyzed using Student's independent t-test

**Analyzed using Mann-Whitney U test

***Chi-square analysis for Hospital Anxiety and Depression Scale cut off scores

Section 4.1c

Description of the Study Sample

Patient and Caregiver Demographic Information

Patient Sample

Patients tended to represent a relatively older group (mean age 72.6 SD 11.6) with an almost balanced representation of males (54%) and females (46%). The majority of patients were retired (73%), living with their primary caregiver (63%) and had at least a high school education (70%) (Table 2). Most patients had advanced HF with 79% classified as NYHA III-IV at baseline, 69% had at least one hospitalization in the past year and 65% were diagnosed with HF for over 1 year. Over 50% of patients had an ischemic cardiomyopathy and decreased left ventricular function. The most common co-morbidities were hypertension (60%), atrial fibrillation (54%), diabetes (44%), myocardial infarction (42%) and chronic renal failure (38%). There were no significant sex differences for baseline demographic and health history variables except for the presence of diabetes. Women were more likely to have diabetes (59%) versus men (31%) ($p=0.049$) (Table 3).

Caregiver Sample

Caregivers were younger than patients with a mean age of 58.4 (± 13.2) years with 60% female and 40% male representation. Caregivers were mainly patient spouses (58%) or daughters (31%) with 35% working either full or part time and 46% retired. Only 25% did not have a high school education (Table 2).

Finally, 35% of caregivers had at least one major co-morbidity that included heart disease, diabetes, lung disease, cerebral vascular disease or cancer; 21% had arthritis. There were no significant sex differences in caregiver demographic data. However, significantly more female caregivers reported arthritis (90% woman vs. 63% men; p=0.027) and more male caregivers reported at least one major co-morbidity (47% men vs. 28% women; p=0.026).

Table 2. Patient and Caregiver Demographics

Demographic Variables		**Study Sample** (n=48 pairs)
Age: mean (SD)	Patient	72.6 (11.6)
Age: mean (SD)	Caregiver	58.4 (13.2)
Patient sex	Male	54 (26)
	Female	46 (22)
Caregiver sex	Male	40 (19)
	Female	54 (26)
Caregiver relationship	Spouse	58 (28)
	Adult Child	42 (20)
Living arrangements	Patient lives with caregiver	63 (30)
	Patient lives alone	27 (18)
Patient education	< High school	25 (12)
	≥ High school	60 (29)
Caregiver education	< High school	13 (6)
	≥ High school	75 (36)
Patient employment	Retired	73 (35)
	Homemaker/other	27 (13)
Caregiver employment	Retired	46 (22)
	Employed- full/ part time	35 (17)
	Homemaker/other	19 (9)

Values expressed as % within group (n) unless otherwise specified

Table 3. Patient Cardiac and Medical History

Patient Cardiac and Medical History Values expressed as % within group (n)	n=48
Cardiac History	
New York Heart Association Classification	
I-II	21 (10)
III-IV	79 (38)
Left Ventricular Ejection Fraction	
≥35%	48 (23)
<35%	52 (25)
Duration of Heart Failure	
< 1 year	35 (17)
1-2.5 years	27 (13)
>2.5 years	38 (18)
Time since last hospitalization	
< 2 months	52 (25)
2-6 months	17 (8)
>6 months	31 (15)
Type of Heart Failure –Ischemic	56 (27)
Attended Heart Function Clinic prior to baseline	27 (13)
Myocardial Infarction	42 (20)
Implantable Defibrillator	29 (14)
Cardiac Resynchronization Therapy	8 (4)
Coronary Artery Bypass Surgery or Valve Surgery	38 (18)
Percutaneous Coronary Intervention	13 (6)
Atrial Fibrillation	54 (26)
Cardiac Risk Factors	
Hypertension	60 (29)
Hyperlipidemia	48 (23)
Smoking history	44 (21)
Diabetes	44 (21)
Obesity	17 (8)
Family History of Premature Coronary Disease	31 (15)
Medical History	
Chronic Renal Failure (Baseline Creatinine>130umol/L)	38 (18)
Arthritis	38 (18)
Chronic Obstructive Lung Disease	23 (11)
Cancer	23 (11)
Previous Stroke or Transient Ischemic Attack	17 (8)

Section 4.2a

Baseline Data Analyses for Primary Objective

Patient and Caregiver Anxiety and Depression Raw Scores

The primary objective of this study was to determine if there was a relationship between the emotional status of HF patients and their primary caregivers. To recall, for the purposes of this study, symptoms of anxiety and depression (as measured on the Hospital Anxiety and Depression Scale) are used to represent the emotional status of study participants. Thus, the primary study objective required two research questions. The first research question involved the HADS- depression subscale and the second research question involved the HADS- anxiety subscale. The research questions related to the primary study objective are presented together in the following section since each research question related to this objective represents a different subscale of the Hospital Anxiety and Depression Scale. Specifically, the research questions were as follows:

- *Is there a relationship between depression scores in both HF patients and their primary caregivers?*
- *Is there a relationship between anxiety scores in both HF patients and their primary caregivers?*

This section begins with a summary of the baseline results for each HADS subscale (HADS- anxiety and HADS- depression) for patients and caregivers. Scores ≥8 on the specific subscale represent symptoms of either anxiety or depression and were used as the cut off scores. Baseline demographic and patient cardiac history variables were compared within patient and caregiver cohorts that scored above and below the cut off in order to describe patient and caregiver groups that had symptoms of anxiety or depression. The prevalence of symptoms of depression and anxiety between patients and caregivers were compared using the HADS cut off scores. Comparisons between patient and caregivers HADS scores were also analyzed using the median scores for each of the HADS-depression and HADS-anxiety scales.

To address the primary research questions listed above, the results from correlational analyses between patient and caregiver HADS scores is presented in the latter part of this section. Correlational analyses is conducted using both HADS cut off scores and also HADS median scores from the HADS- depression and HADS- anxiety subscales for patients and caregivers.

For this study population, Cronbach's alpha ranged between 0.835 (patient HADS scores) and 0.867 (caregiver HADS scores). Anxiety and depression scores were skewed and thus non-parametric tests were used in the analyses. To view the distribution of baseline HADS scores for patients and caregivers, please refer to Appendix H- Table H1 and H2.

Patient Baseline HADS-Depression Cut off Scores

At baseline, 35% of patients (n=17) scored above the cut off score, indicating symptoms of depression. Within this group, 6/17 patients scored above 10, indicating at least moderate symptoms of depression. Patients with symptoms of depression (HADS-depression ≥8) were more likely to be younger (mean age 69.2 years vs. 74.4; years; p=.144), not retired (47% not retired vs. 16% not retired; p=.070), have a male caregiver (53% vs. 32%; p=.161), heart failure due to coronary ischemia (71% vs. 48%; p=.138) and a history of a myocardial infarction (59% vs. 32%; p=.074) when compared to patients with normal HADS –depression scores at baseline (Table 4). For a summary comparing all baseline demographic and cardiac history variables between patients with HADS- depression scores ≥8 and patients with normal HADS-depression scores at baseline, please refer to Appendix H- Tables H3 and H4.

Table 4. Comparison of Demographic Variables in Patients (n=48) with Baseline Normal (n=31) and Abnormal (n=17) HADS-Depression Cut off scores (with a p-value ≤ 0.20)

Demographic Variables Values expressed as % within group (n)	Entire Patient group (n=48)	HADS Depression Normal (n=31)	HADS Depression ≥ 8 (n=17)	p value
Patient Age mean (SD)	72.6 (11.6)	74.4 (11)	69.2 (12.2)	.144
Patient- Retired - Other	73 (35) 27 (13)	74 (26) 16 (5)	53 (9) 47 (8)	.070
Caregiver – Male - Female	40 (19) 54 (26)	32 (10) 68 (21)	53 (9) 48 (8)	.161
Etiology of HF –Ischemic	56 (27)	48 (5)	71 (12)	.138
Previous Myocardial Infarction	42 (20)	32 (10)	59 (10)	.074

HF- Heart Failure

Patient Baseline HADS-Anxiety Cut off Scores

At baseline, 12 patients (25%) scored above the cut off HADS- Anxiety score ≥ 8, indicating at least mild symptoms of anxiety. Within this group, 7/12 scored above the cut off of 10, indicating at least moderate symptoms of anxiety. Because of the relatively small number of patients in this cohort, similar comparisons between patients with normal HADS-anxiety scores and HADS-anxiety scores ≥8 should be interpreted with extreme caution. However, for the purposes of being consistent with the analysis for patient depression scores, such comparisons were completed and a summary of these data is available in Appendix H- Tables H5 and H6. Patients with a history of myocardial infarction (42%, n=20) had statically significant higher symptoms of anxiety (67% HADS-anxiety ≥8 vs. 33% HADS-anxiety <8; p=.043) than those without such a prior history. Unlike the findings with HADS-depression scores, there was no effect of patient age on anxiety scores.

Caregiver Baseline HADS-Anxiety Cut off Scores

At baseline, 48% of caregivers reported symptoms of anxiety (HADS-anxiety score ≥ 8; n=23), with over half of this cohort scoring above 10 (n=13/23), indicating at least moderate symptoms of anxiety. Caregivers with HADS-anxiety scores ≥8 were more likely to be younger than caregivers with normal HADS anxiety scores (mean age 55.8 (± 12.7) vs. mean age 60.9 (SD± 13.5) respectively; p=.185). There were no caregiver demographic variables that were significantly different between caregivers scoring below and above the HADS-anxiety cut off score. Conversely, significantly more caregivers of male patients, younger patients and patients who were not retired had HADS- anxiety scores ≥8. There was a trend for caregivers of patients with an implantable defibrillator or attending an initial versus follow up appointment in the Heart Function Clinic to report HADS-anxiety scores ≥8 (Table 5). For a full summary comparing demographic and cardiac history variables in caregivers with normal and abnormal HADS-anxiety cut off scores, please refer to Appendix H- Tables H7 and H8.

Caregiver Baseline HADS-Depression Cut off Scores

At baseline, only nine (19%) caregivers had HADS- Depression scores ≥8, indicating symptoms of depression. Thus, comparisons between caregivers with normal HADS-depression and HADS-depression score ≥ 8 were not conducted.

Table 5. Comparison of Demographic Variables between Caregivers (n=48) with Baseline Normal (n=25) and Abnormal (n=23) HADS-Anxiety Cut off Scores (with a p value of <0.20)

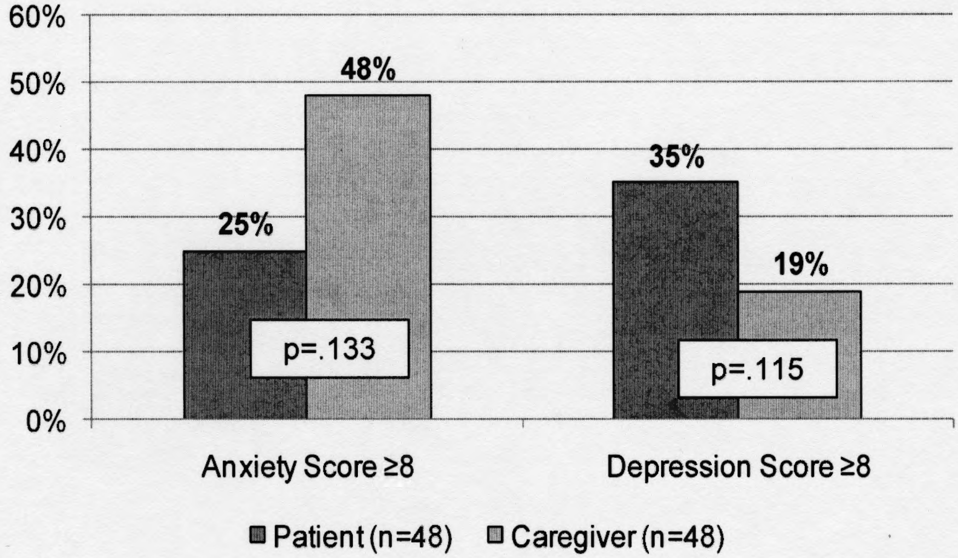
Demographic Variables Values expressed as % within group (n)		Entire Caregiver group (n=48)	HADS Anxiety Normal (n=25)	HADS Anxiety ≥ 8 (n=23)	p value
Caregiver Variables					
Age: mean (SD)	Caregiver	58.4 (13.2)	60.9 (13.5)	55.8 (12.7)	.185
Patient Variables					
Age: mean (SD)	Patient	72.6 (11.6)	76.6 (9.6)	68.2 (12.3)	.011
Patient sex	Male Female	54 (26) 46 (22)	40 (10) 60 (15)	70 (16) 30 (7)	.040
Patient employment	Retired Other	73 (35) 27 (13)	84 (21) 16 (4)	61 (14) 39 (9)	.049
Patient Cardiac History					
Heart Function Clinic prior to baseline	Yes No	27 (13) 73 (35)	36 (9) 64 (16)	17 (4) 83 (19)	.147
Implantable Defibrillator	Yes No	29 (14) 71 (34)	20 (5) 80 (20)	39 (9) 61 (14)	.190

Comparison of Patient and Caregiver Baseline HADS Scores

Baseline Hospital Anxiety and Depression Cut off Scores

At baseline, caregivers reported more symptoms of anxiety than patients (48% vs. 25% respectively; p=0.133) and patients reported more depressive symptoms than caregivers (35% vs. 19% respectively; p=0.115) ; however, these results did not reach statistical significance (Figure 4).

Figure 4. Percent of Patients and Caregivers who had Hospital Anxiety and Depression Scores ≥ 8 at Baseline



Baseline Hospital Anxiety and Depression Raw Scores

Using the Wilcoxon-sign rank test, median baseline patient and caregiver HADS anxiety scores were compared. There was a trend for patients to report higher HADS- depression median scores than caregivers at baseline while caregivers reported significantly higher HADS- anxiety median scores than patients at baseline (Table 6)

Table 6. Baseline Hospital Anxiety and Depression Median Scores in Patients and Caregivers (n=48 pairs)

	Patients	**Caregivers**	**p value**
Baseline			
Anxiety	6.0 (5.0)	7.0 (7.0)	.074
Depression	5.0 (6.0)	4.0 (5.0)	.026

Values expressed as median (Interquartile range)

Section 4.2b

Baseline Data Analyses

Correlations between Patient and Caregiver Hospital Anxiety and Depression Scores

Correlations between patient and caregiver HADS scores were calculated using two methods. First, correlations between patient and caregiver raw HADS scores were compared using Spearman's rho (Table 7) . Secondly, the correlation between the proportion of patients and caregivers who scored above and below the cut off score were calculated using the Phi-coefficient (Table 8).

Patient and Caregiver Depression

At baseline there was a non-significant positive correlation between patient and caregiver depression raw scores (rho (48) = .248; p=.089). However, when using cut-off HADS-depression scores, there was no relationship between patient and caregiver depression (Phi correlation coefficient = -.021; p=.885).

Patient and Caregiver Anxiety

There were no significant correlations between patient and caregiver HADS-anxiety raw or cut off scores. However, there was a weak, positive correlation between patient and caregiver HADS-anxiety cut off scores using the Phi correlation coefficient of .217 (p=.133).

Table 7. Bivariate Correlations between Baseline Hospital Anxiety and Depression Scores in Patient and Caregiver Pairs (n=48) using Spearman's rho

Spearman's rho correlation coefficient	Patient Anxiety	Patient Depression
Caregiver Anxiety	.168 (p =.25)	
Caregiver Depression		.248 (p =.089)

Table 8. Bivariate Correlation between Baseline Hospital Anxiety and Depression Cut off Scores in Patient and Caregiver Pairs (n=48) using the Phi Coefficient

Phi correlation coefficient	Patient Anxiety	Patient Depression
Caregiver Anxiety	.217 (p=.133)	
Caregiver Depression		-.021 (p=.885)

Section 4.2

Baseline Data Analyses for Primary Objective

Summary

Primary research question: Is there a relationship between depression scores of both HF patients and their primary caregivers?

At baseline, 35% of patients had HADS- depression cut off scores ≥ 8, indicating symptoms of depression. Higher levels of depressive symptoms were found in younger patients with an ischemic cardiomyopathy, history of myocardial infarction and support from a male caregiver. Caregivers had significantly lower median HADS-depression scores when compared to patients while only 19% of caregivers scored ≥ 8 on the HADS- depression scale, indicating symptoms of depression.

There was a weak, non-significant, positive correlation between patient and caregiver raw HADS-depression scores, but not cut-off scores at baseline. Because the correlation coefficients were < 0.30, there was no evidence of a clinically meaningful relationship between patient and caregiver symptoms of depression.

Primary research question: Is there a relationship between anxiety scores of both HF patients and their primary caregivers?

At baseline, 48% of caregivers scored above the HADS- anxiety cut off score, indicating symptoms of anxiety. Higher levels of anxiety were associated with caregivers of patients who had an implantable defibrillator or did not attend the Heart Function Clinic prior to baseline measurement. Caregivers had higher HADS- anxiety median scores and more caregivers scored above the cut off score when compared to patients; however these results did not reach statistical significance. There was a weak, positive correlation between patient and caregiver HADS- anxiety cut off scores, but not HADS-anxiety raw scores, at baseline. Thus, there was no evidence to suggest a clinically meaningful relationship between patient and caregiver symptoms of anxiety.

Section 4.3a

Baseline Data Analyses for Secondary Objectives

Patient and Caregiver Uncertainty

The first two secondary study objectives involved exploring relationships between the emotional status, as measured by the HADS, and feelings of uncertainty, as measured by the Mishel Uncertainty in Illness Scale, in both patients and caregivers. Specifically, the research questions related to these objectives were as follows:

- *Is there a relationship between the emotional status of HF patients and uncertainty?*
- *Is there a relationship between the emotional status of primary caregivers and uncertainty?*

To begin this section, the patient and caregiver baseline Mishel Uncertainty in Illness (MUIS) results are presented. Patient and caregiver baseline HADS results were presented in the previous section (Results for the Primary Study Objective) and are not repeated below. In the latter part of this section, bivariate correlations between baseline MUIS and HADS scores are presented.

In general, patients and caregivers expressed a fair amount of respondent burden when completing the MUIS. They found the 'double negative' wording and response format for some items difficult to interpret at times. For example, choosing "strongly disagree" for an item "the effectiveness of my heart failure treatment is undetermined" means that there is a low level of uncertainty for this item. Often patients and caregivers asked for clarification from the research assistant for understanding items during baseline testing. Minimal assistance was needed for follow up measurements, although participants still voiced extra time needed to complete this form, and 3 pairs did not complete the MUIS at 4 months due to respondent burden. In this study sample, Cronbach's alpha was 0.877 patients and 0.879 for patients and caregivers respectively. The following section presents the baseline MUIS scores followed by bivariate correlation analyses.

Mishel Uncertainty in Illness- Community Version (MUIS) Baseline Scores

Baseline Patient MUIS Scores

Baseline patient scores ranged between 23-100 with a mean score of 63.75 (± 13.01). Values were normally distributed (Shapiro-Wilk statistic 0.965 *df* (48); p=.164).

Over 65% of patients were uncertain about the course of their heart failure since they continued to experience good and bad days. At least 50% of patients were unsure about what is going to happen to them and 'how bad their heart failure would be'. Only 21% of patients felt certain that 'they would not find anything else wrong' with them. However; over 50% of patients felt the seriousness of their HF had been determined and the treatment they were receiving has a known probably for success. For a summary of each item response, please see Appendix I- Table I1.

Using independent t-tests, mean MUIS scores between demographic and cardiac history categorical variables were analyzed to describe the cohort of patients with higher and lower levels of uncertainty. There was a non-significant trend for higher levels of uncertainty in female versus male patients, and in patients living alone versus with their primary caregiver. Patients who were retired, or had a spousal versus adult child caregiver, had lower levels of uncertainty. Finally, patients who had been attending the HF clinic prior to baseline, or had HF for at least one year, had lower levels of uncertainty than patients who were attending their first appointment at the HFC or had HF for over one year. The above comparisons represent differences between MUIS scores with a p-value of <0.20 and are presented below in Table 9; however, please refer to Appendix I – Table I2 and I3 for a full list of demographic and cardiac history variables that were analyzed.

Table 9. Comparison of Baseline Patient MUIS Scores according to Patient and Caregiver Demographic Variables and Patient Cardiac History (p value <0.20)

Patient Variables		**n**	**Patient MUIS**	**p value**
Patient Sex	Male	26	60.7 (13.4)	.080
	Female	22	67.3 (11.8)	
Patient Employment	Retired	35	61.5 (11.4)	.053
	Other	13	69.7 (15.6)	
Living Arrangements	With caregiver	30	61.6 (12.9)	.141
	Alone	18	67.3 (12.7)	
Caregiver Variables				
Caregiver Relationship	Spouse	28	61.6 (12.6)	.180
	Adult Child	20	66.8 (13.3)	
Caregiver Employment	Retired	22	61.8 (11.9)	.189
	Employed	17	62.5 (11.6)	
	Other	9	70.9 (16.8)	
Patient Cardiac History				
Duration of Heart Failure	< 1 year	17	68.5 (12.5)	.119
	1-2.5 years	13	58.9 (16.0)	
	>2.5 years	18	62.8 (9.9)	
Attended Heart Function Clinic prior to baseline	Yes	13	59.7 (13.7)	.191
	No	35	65.3 (10.3)	

Values expressed as mean (standard deviation)
Statistical tests- independent t-test (2 variables) or ANOVA (>2 variables)

Baseline Caregiver MUIS Scores

Caregiver baseline MUIS scores ranged from 67-115 with a mean score of 84.5 (± 15.40). Responses were normally distributed (Shapiro-Wilk statistic 0.987, *df* =48; p=.870). The majority of caregivers were uncertain as to how long the HF would last. Over 50% of caregivers reported that they felt the course of HF kept changing unpredictably and they couldn't determine if patients were going to have a good or bad day. Even though most caregivers stated they understood everything explained to them, 27% felt that the HF treatment was too complex to figure out. For a summary of each item response, please refer to Appendix I- Table I4.

Using independent t-tests, mean baseline caregiver MUIS scores were compared using caregiver and patient demographic categorical variables and patient cardiac history categorical variables to describe the cohort of caregivers with higher and lower levels of uncertainty. At baseline, male caregivers had significantly higher levels of uncertainty than female caregivers (male caregiver 91.4 (± 14.8) versus female caregiver 80.1 (± 14.3); t=2.639 *df* =46; p=0.011). Also, caregivers with an education level greater than high school had significantly higher levels of uncertainty when compared to caregivers with less than a high school education (≥ high school 98.0 (± 9.9) vs. < high school 81.3 (± 15.5); t=.253 *df* =40; p=.015). There was a non-significant trend for caregivers of patients who had had HF for less than 1 year, had been hospitalized in the past 2 months or had not attended the HF clinic prior to baseline to report higher levels of uncertainty. Caregivers of male versus female patients had lower levels of uncertainty. Finally, caregivers of patients who were retired versus caregivers of patients who were not retired had lower levels of uncertainty. Please see Table 10 below for a summary of these specific comparisons. For a full summary of comparisons between baseline caregiver MUIS scores based on caregiver and demographic variables and patient cardiac history, please see Appendix I-Table I5 and I6.

Table 10. Comparison of Baseline Caregiver MUIS Scores according to Caregiver and Patient Demographic Variables and Patient Cardiac History (with a p value <0.20)

Caregiver Variables		**n**	**Caregiver MUIS**	**p value**
Caregiver Sex	Male	19	91.4 (14.8)	.011
	Female	26	80.1 (14.3)	
Caregiver Employment	Retired	22	82.4 (13.9)	.074
	Employed	17	81.8 (16.5)	
	Other	9	95.0 (13.7)	
Caregiver Education	< High school	6	81.3 (15.5)	.015
	≥ High school	36	98.0 (9.9)	
Patient Variables				
Patient Sex	Male	26	80.6 (13.4)	.054
	Female	22	89.2 (16.6)	
Patient Employment	Retired	35	82.3 (16.0)	.101
	Other	13	90.5 (12.1)	
Patient Cardiac History				
Duration of Heart Failure	< 1 year	17	90.8 (17.1)	.111
	1-2.5 years	13	81.1 (17.2)	
	>2.5 years	18	81.1 (10.4)	
Time since Hospitalization	< 2 months	25	87.8 (15.9)	.192
	2-6 months	8	85.4 (14.5)	
	>6 months	15	78.7 (14.3)	
Attended HFC prior to baseline	Yes	13	78.2 (14.0)	.083
	No	35	86.9 (15.4)	

Values expressed as mean (standard deviation); HFC- Heart Function Clinic
Statistical tests- independent t-test (2 variables) or ANOVA (>2 variables)

Of note, caregiver total MUIS raw scores appear higher than patient total MUIS raw scores; however, this difference is due to the different number of items for the caregiver and patient MUIS surveys. Specifically, the patient MUIS has 23 items and the caregiver version had 31 items. To determine if there were any significant differences between patient and caregiver MUIS scores, average total MUIS scores were calculated and then compared using a paired-t-test. Based on these calculations, there were no significant differences between patient and caregiver MUIS scores at baseline.

Section 4.3b

Baseline Data Analyses for Secondary Objectives

Correlations between Patient and Caregiver Uncertainty and Hospital Anxiety and Depression Baseline Scores

Bivariate correlations between MUIS and HADS were calculated separately for patients and caregivers. Correlation analysis was also conducted using the HADS-anxiety and HADS-depression subscale raw scores with the total MUIS scores for patients and caregivers. Because HADS scores were not normally distributed, Spearman's rho was used for determining the correlation coefficient.

There were no significant correlations between the emotional status of patients or caregivers and uncertainty; however, there was a trend for a correlation between symptoms of depression and uncertainty in patients and caregivers. Specifically, there was a trend for a positive correlation between HADS-depression and MUIS scores in patients (rho=.252; p=.085) and caregivers (rho= .251; p=.085) at baseline. There was no evidence of a correlation between symptoms of anxiety and uncertainty. Of note, there was a significant positive correlation between patient and caregiver MUIS scores (rho=.387; p=.007) (Table 11).

Table 11. Bivariate Correlations between Patient and Caregiver Baseline HADS and MUIS Scores using Spearman's rho.

	Patient (n=48)			**Caregiver** (n=48)		
	HAD-A	HAD-D	MUIS	HAD-A	HAD-D	MUIS
Patient. MUIS	.037	.252	--	.068	.018	.387*
Caregiver. MUIS	.008	.143	.387*	.202	.251	--

*p<0.05
HAD-A: Hospital Anxiety and Depression- anxiety subscale
HAD-D: Hospital Anxiety and Depression- depression subscale
MUIS-Mishel Uncertainty in Illness Scale

Section 4.3c

Baseline Data Analyses for Secondary Objectives

Caregiver Appraisal

Secondary study objectives 3 and 4 explore potential relationships between the emotional status of patients and caregivers and the positive and negative components of the subjective caregiver experience, also identified as caregiver appraisal. Specifically, the research questions were as follows:

- *Is there a relationship between patient emotional status and caregiver appraisal?*
- *Is there a relationship between primary caregiver emotional status and caregiver appraisal?*

Caregiver Reaction Assessment (CRA) results from caregivers at baseline are summarized for each of the 5 subscales on the CRA. To recall, patients did not complete the CRA. Patient and caregiver baseline HADS results were presented in the previous section (Section 4.2a) and are not repeated below. Bivariate analysis with baseline caregiver CRA scores and baseline patient and caregiver HADS-anxiety and HADS- depression scores are presented in the latter part of this section.

For this study sample, Cronbach's alpha for the entire CRA scale was 0.77 and the subscales as follows; Schedule (0.84), Financial Burden (0.83), Lack of Family Support (0.77), and Health Problems (0.74). Internal consistency reliability, based on Cronbach's alpha, was suboptimal (0.44) for the subscale Self Esteem, which measures the positive aspect of caregiving. Inter-item correlation analysis exploring each item on this 7-item subscale revealed that CRA item # 15 (I resent having to provide care for my partner/ loved one) and CRA item #21 (I will never be able to do enough caregiving to repay my partner) did not significantly correlate with any of the other items on this subscale. When these two items were removed, internal consistency improved to a Cronbach's alpha value=0.81. Thus, all further analyses using the Self-Esteem subscale from the CRA did not include item #15 or item #21.

Baseline Caregiver Reaction Assessment Scores

The highest burden subscore reported by caregivers was 'disruptions to their daily schedule'. Over 60% of caregivers stated that their daily activities are centred on caring for the person with HF. Nevertheless, all caregivers felt that caregiving was important to them and over 60% enjoyed caring for the person with HF. For a full summary of CRA item responses, please refer to Appendix J-Table J1.

Distributions of the scores for each CRA subscale, with the exception of the 'Schedule Disruption' and the 'Total Negative' subscales were skewed. Both median and mean values for each subscale are reported below in Table 12. The highest burden subscale was related to schedule disruptions (mean 2.92) followed by a negative impact on caregiver health as a result of caregiving (mean 2.42).

Table 12. Caregiver Reaction Assessment Subscale Baseline Scores (n=48 Caregivers)

Baseline CRA scores	Mean (standard deviation)	Median (Interquartile range)
Schedule Disruption	2.92 (.92)	3.0 (1.2)
Financial Burden	2.12 (.86)	2.0 (1.3)
Family Abandonment	2.13 (.89)	2.0 (1.6)
Health Problems	2.42 (.88)	2.5 (.88)
Total Negative	2.17 (.68)	2.1 (1.1)
Self Esteem (Positive)	4.13 (.56)	4.0 (.95)

Using the Mann-Whitney U tests and the Kruskal-Wallis H test, median CRA total negative and positive scores were compared using caregiver and patient demographic variables and patient cardiac history variables to describe the cohort of caregivers with higher and lower levels of caregiver burden and esteem.

Lower levels of caregiver burden were reported by the following individuals: a) caregivers who are retired, b) female, c) caregivers of patients who were retired, and d) caregivers of patients with higher physical functioning (Table 13).

Table 13. Baseline Caregiver Total Negative CRA Score based on Caregiver and Patient Demographic and Patient Cardiac History Variables (n=48 pairs)
(p value <.20)

		n	Caregiver Total Negative CRA Score at Baseline	p value
Caregiver Variables				
Caregiver Employment	Retired	22	1.97 (.55)	.138
	Employed	17	2.27 (.82)	
	Other	9	2.47 (.63)	
Patient Variables				
Patient Sex	Male	26	2.00 (.65)	.106
	Female	22	2.32 (.68)	
Patient Employment	Retired	35	2.00 (.66)	.004
	Other	13	2.63 (.54)	
Patient Cardiac History				
New York Heart Association	I-II	10	1.89 (.68)	.145
	III-IV	38	2.25 (.67)	
Left Ventricular Ejection Fraction	≥ 35%	23	2.32 (.78)	.148
	< 35%	25	2.03 (.56)	

Variables expressed as mean (standard deviation) CRA- Caregiver Reaction Assessment

Because there was a highly significant difference between total caregiver burden in caregivers of patients who were retired versus not retired, further analysis was conducted with each caregiver burden subscale. Significant differences were detected in CRA schedule, financial and caregiver health burden scores between caregivers of patients who were retired versus not retired (Table 14).

Table 14. Comparison of CRA burden Subscale Scores for Caregivers of Patients who are Retired (n=35) versus not Retired (n=13).

Baseline CRA Scores	Entire Group (n=48)	Patient Retired (n=35)	Patient Not Retired (n=13)	p value
Schedule Disruption	2.92 (.92)	2.74 (.90)	3.40 (.83)	.019
Financial Burden	2.12 (.86)	1.83 (.65)	2.92 (.88)	.001
Family Abandonment	2.13 (.89)	2.00 (.94)	2.47 (.68)	.078
Health Problems	2.42 (.88)	2.21 (.88)	2.96 (.94)	.009

Mann-Whitney U test

There were no significant differences in caregiver esteem, which represents the positive aspect of caregiving, in relation to any of the baseline caregiver or patient demographic variables or patient cardiac history variables. Adult children, versus spouses of patients with HF, and caregivers who lived in a separate residence reported non-significant higher levels of esteem related to caregiving (Table 15).

Table 15. Baseline Caregiver Esteem CRA Score according to Caregiver and Patient Demographic and Patient Cardiac History Variables (n=48 pairs)
(p value <.20)

		n	**Caregiver Esteem**	**p value** parametric (non-parametric)
Caregiver Variables				
Caregiver Relationship	Spouse	28	4.01 (.54)	.074 (.092)
	Adult Child	20	4.30 (.56)	
Patient Variables				
Living Arrangements	With caregiver	30	4.02 (.56)	.102 (.107)
	Alone	18	4.30 (.54)	

Variables expressed as mean (standard deviation)
Independent t-tests (Mann-Whitney U)

For a full summary of comparisons between baseline caregiver Total negative and Esteem scores based on caregiver and demographic variables and patient cardiac history, please see Appendix J- Tables J2 and J3.

Section 4.3d

Baseline Data Analyses for Secondary Objectives

Correlations between Caregiver Appraisal (CRA) and Hospital Anxiety and Depression Baseline Scores

Bivariate correlation between patient and caregiver HADS-anxiety and HADS- depression scores with each of the CRA subscale scores was conducted using Spearman's rho.

Correlations between Baseline Patient HADS and Caregiver CRA Scores

There were no significant correlations between baseline patient HADS-anxiety and HADS- depression scores and CRA scores. There was a trend for a positive correlation between patient HADS-depression and caregiver health burden subscore at baseline (rho=.257; p=.077).

Correlations between Baseline Caregiver HADS and Caregiver CRA Scores

There was a strong, positive correlation between baseline caregiver anxiety scores and a) CRA schedule (rho=.523; p<0.01) and b) CRA health subscores (rho=.454; p<0.01). A relatively weaker, but significant, correlation existed between caregiver anxiety scores and caregiver burden with regard to family abandonment (rho=.314; p<0.05).

There was a strong, positive correlation between caregiver depression scores and caregiver burden in the subscales of a) schedule disruption (rho=.636; p<0.01), b) caregiver health problems (rho=.519; p<0.01) and c) finances (rho=.417; p<0.01). There was a weaker, but significant, bivariate correlation between caregiver depression scores and caregiver burden related to family abandonment (rho=.335; p<0.05) Caregiver anxiety and depression scores did not correlate with caregiver esteem. Please see Table 16 below for a summary of the correlations between baseline Caregiver HADS and CRA subscales. Thus, there was a statistically significant relationship between caregiver symptoms of depression and all caregiver burden scores. Furthermore, there was a relationship between caregiver symptoms of anxiety and caregiver burden related to a) schedule, b) family abandonment and c) caregiver health burden.

Table 16. Bivariate Correlations between Caregiver HADS and CRA Subscales at Baseline (n=48)

Spearman's rho	Caregiver HADS-Anxiety	Caregiver HADS-Depression
CRA-Schedule	.523**	.636**
CRA-Financial	.198	.417**
CRA-Family	.314*	.335*
CRA-Health	.454**	.519**
CRA- Esteem (Positive)	.134	-.041

** p= 0.01 (2-tailed).
* p= 0.05 (2-tailed).
CRA- Caregiver Reaction Assessment; HADS- Hospital Anxiety and Depression Scale

Section 4.4

Exploratory Analyses

This study was not powered to detect significant changes over time. Thus, research questions related to change reflect exploratory analyses that will guide hypothesis generation rather than hypothesis confirmation. Any conclusions that are drawn from the analyses within this section are purely for hypothesis generation and must be interpreted with caution.

The main objective for this part of the study was to explore whether emotional reactions (HADS), uncertainty (MUIS) and caregiver appraisal (CRA) scores changed between baseline, 2 months and 4 months.

Also, baseline *correlations* between HADS, MUIS and CRA scores were repeated at 2 months and 4 months to determine if there were any trends indicating that the strength of the correlation increased, decreased, or stayed the same over time.

The first part of the section provides an overview of the HADS, MUIS and CRA scores at 2 months and 4 months. The latter part of this section reports *correlations* between HADS, MUIS and CRA scores at 2 months and 4 months.

Section 4.4a

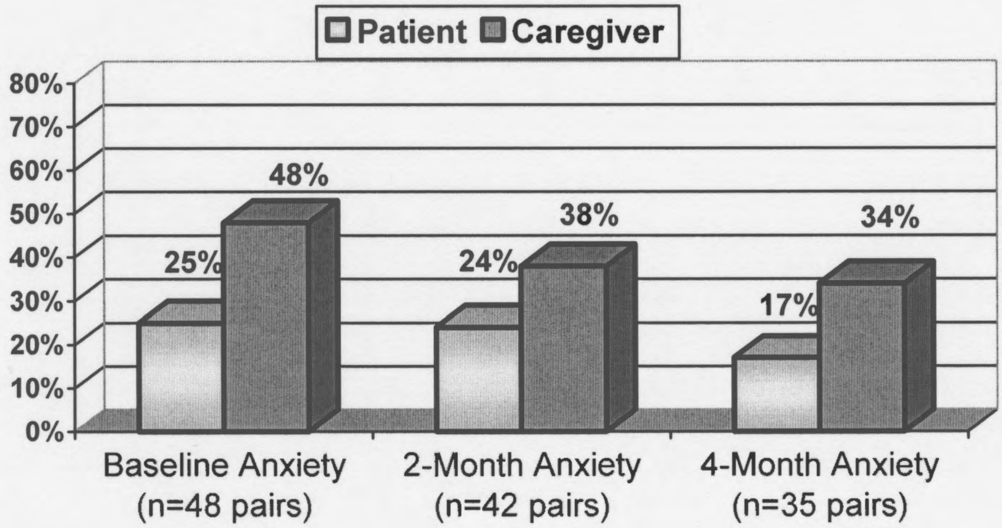
Exploratory Analyses- Change in Scores

Hospital Anxiety and Depression Scale

HADS- Anxiety Cut off Scores in Patients and Caregivers at Baseline, 2 Months and 4 Months

In general, the percentage of *patients* with symptoms of anxiety did not change between baseline and 2 months, and there was a small decrease in the percentage of patients indicating symptoms of anxiety (from 24% to 17%) between 2 and 4 months. There was a relatively larger decrease in *caregiver* symptoms of anxiety between baseline and 4 months (48% baseline to 34% at 4 months). The following graph (Figure 5) presents the percent of patients and caregivers who had HADS-anxiety scores ≥ 8, at each measurement period.

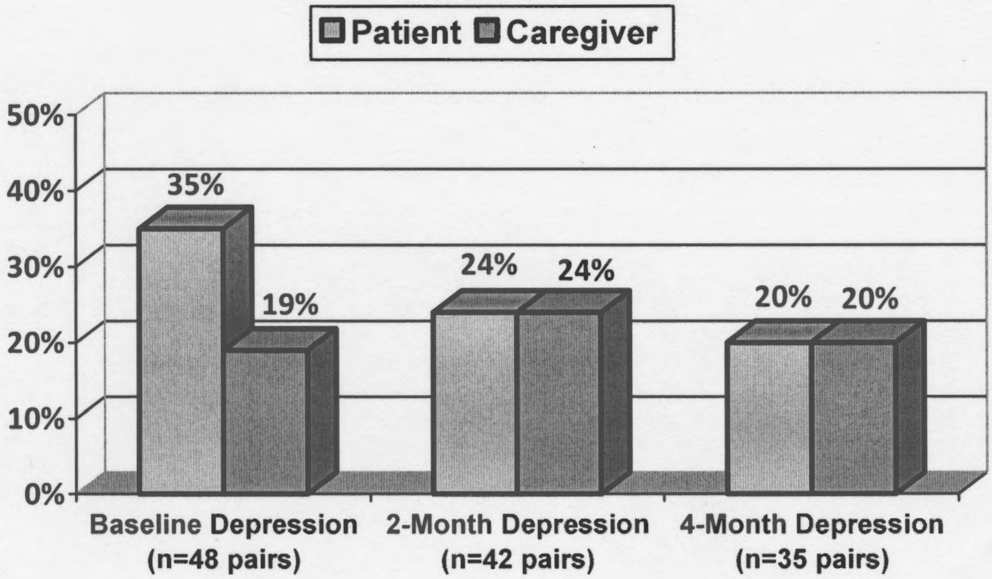
Figure 5. Percent of Patients and Caregivers who Scored above the HADS-Anxiety Cut off (≥8) at Baseline, 2 Months and 4 Months.



HADS- Depression Cut off Scores at Baseline, 2 Months and 4 Months

Between baseline, 2 months and 4 months, there was a trend for a decrease in the percent of *patients* reporting symptoms of depression (HADS-depression ≥8) (X^2=2.797 *df* (2); p=.247). This decrease occurred mainly between baseline and 2 months (35% at baseline vs. 24% at 2 months), rather than between 2 and 4 months (24% at 2 months vs. 20% at 4 months). No trends for changes in the percentage of *caregivers* who had symptoms of depression (HADS-depression ≥8) between baseline and 4 months were detected (Figure 6).

Figure 6. Percent of Patients and Caregivers who Scored above the HADS-Depression Cut off (≥8) at Baseline, 2 Months and 4 Months.



Changes in Patient and Caregiver HADS Raw Scores at Baseline, 2 Months and 4 Months.

Changes in raw HADS scores between baseline, 2 months and 4 months were also analyzed using the median and Kendall's W non-parametric statistical test. Similar to findings using HADS cut off scores, there was a trend for patient HADS-depression and anxiety median scores as well as caregiver HADS-anxiety median scores to decrease over time. There were no trends for a change in the caregiver HADS-depression scores between baseline and 2 and 4 months (Figures 7-10).

Figure 7. Box Plots of Patient HADS-Anxiety Scores at Baseline, 2 Months and 4 Months

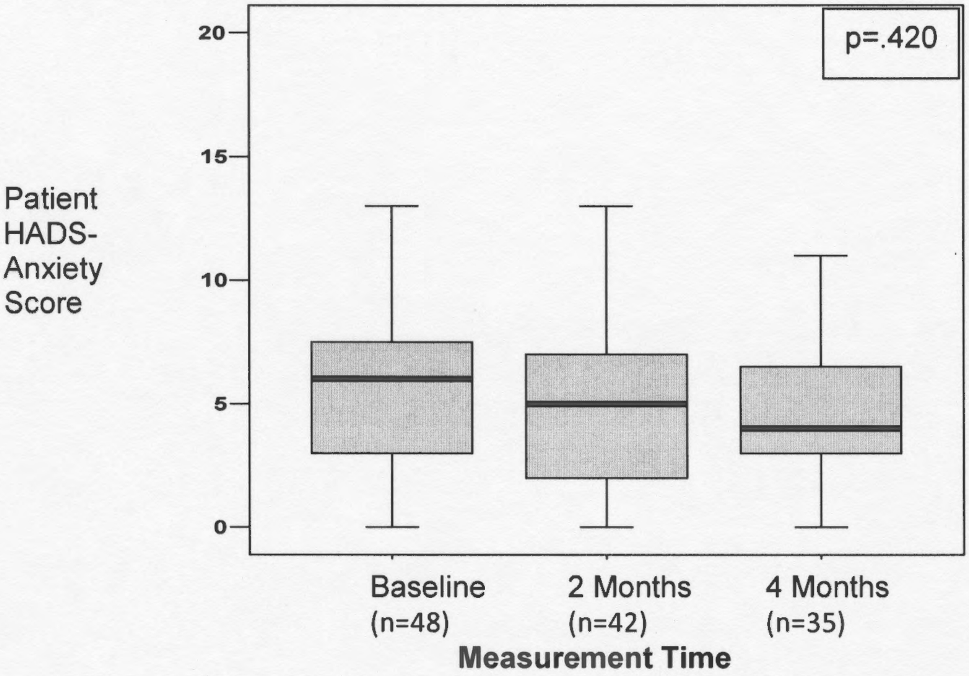


Figure 8. Box Plots of Patient HADS-Depression Scores at Baseline, 2 Months and 4 Months

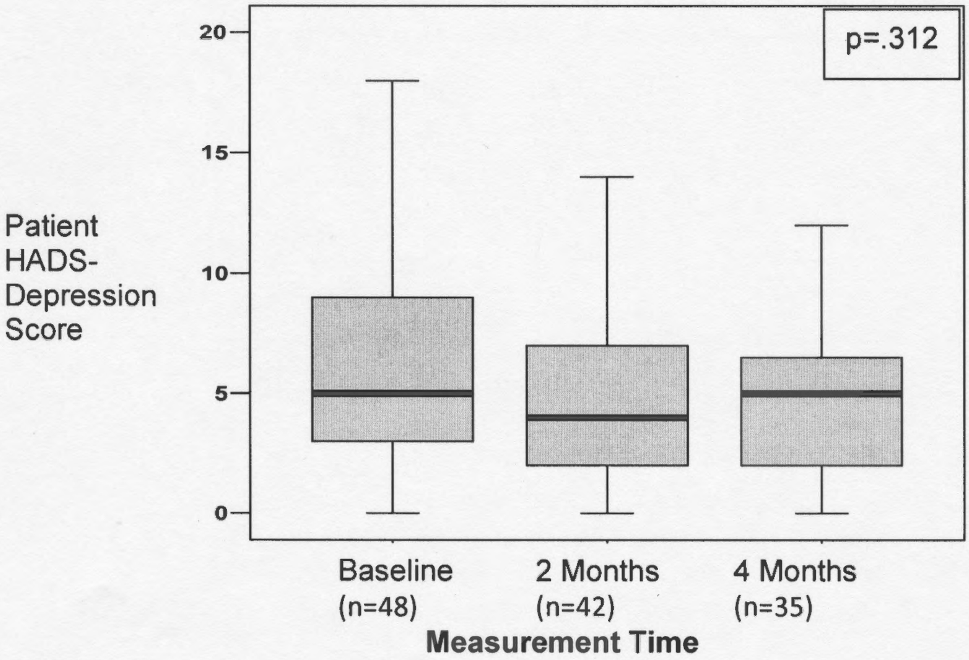


Figure 9. Box Plots of Caregiver HADS-Anxiety Scores at Baseline, 2 Months and 4 Months

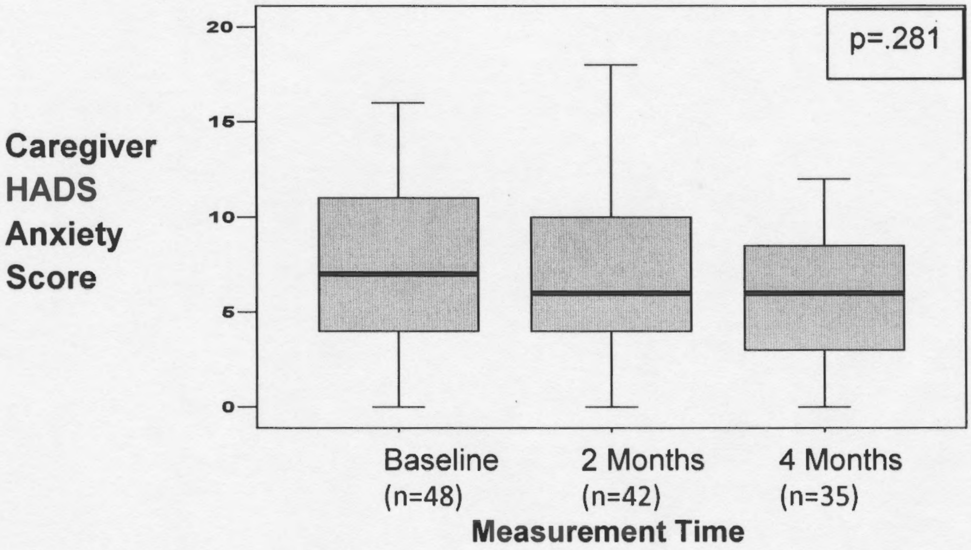
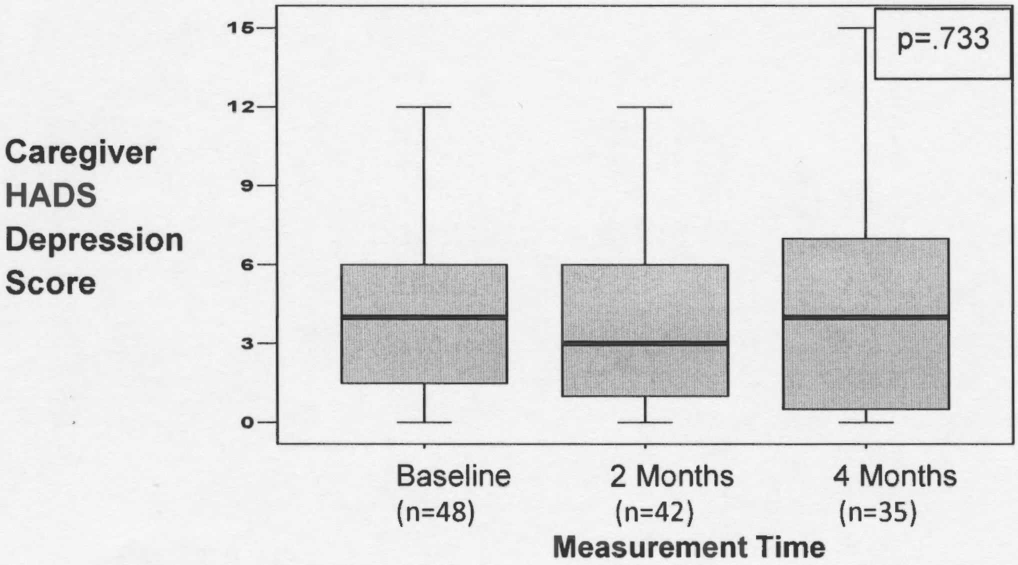


Figure 10. Box Plots of Caregiver HADS-Depression Scores at Baseline, 2 Months and 4 Months



Section 4.4b

Exploratory Analyses- Change in Scores

Mishel Uncertainty in Illness Scale

The MUIS was completed by patients and caregivers at baseline, 2 months and 4 months. Between baseline and 4 months, there was a significant decrease in uncertainty in patients (mean 63.8 (±13.0) vs. mean 55.3 (±10.7) respectively; p=.004) and a trend for a decrease in uncertainty in caregivers (mean 84.5 (±15.4) vs. mean 75.3 (±18.7); p=.077). For a summary of changes in individual item scores, please see Appendix I- Tables I1 and I2

At baseline, male **caregivers** had significantly higher uncertainty than female **caregivers** (mean 98.0 (±9.9) vs. mean 81.3 (±15.5) respectively, p=0.015). There was also a trend for female **patients** to have higher levels of uncertainty than male **patients** (mean 67.3 (±11.8) vs. mean 60.7 (±13.4) respectively; p=.08). Thus, the above analysis was repeated to determine if there was a sex by time interaction between MUIS scores from baseline to 4 months. This analysis is presented in Table 17 below.

Table 17. Changes in MUIS Scores in Male and Female Patients and Caregivers between Baseline, 2 Months and 4 Months

	Patient MUIS Scores				p value
	Male		Female		
Baseline	n=26	60.73 (13.4)	n=22	67.32 (11.8)	.080⁺
2-Month	n=25	54.00 (10.1)	n=17	61.00 (12.1)	.048⁺
4-Month	n=21	51.76 (14.4)	n=14	56.43 (13.1)	.340⁺
	p=.118*		p=.035*		
	Caregiver MUIS Scores				
	Male		Female		
Baseline	n=18	91.37 (14.8)	n=30	80.07 (14.3)	.011⁺
2-Month	n=16	85.56 (20.0)	n=26	76.42 (18.7)	.142⁺
4-Month	n=12	78.33 (24.9)	n=23	73.74 (15.0)	.500⁺
	p=.240*		p=.361*		

*ANOVA; ⁺ Paired-t-test
MUIS- Mishel Uncertainty in Illness Scale

There was a significant sex by time effect in levels of uncertainty in patients but not in caregivers. Specifically, only female patients had a significant decrease in uncertainty between baseline and 4 months (mean 67.32 (±11.8) vs. 56.43 (±13.1) respectively; p=.035).

Authors of the MUIS state there is a positive correlation between level of education and MUIS scores, with higher MUIS scores present in people with higher levels of education (Mishel, 1988). In this sample, baseline MUIS scores were significantly higher in caregivers with ≥ high school education versus caregivers with < high school education (mean 98.0 (±9.9) vs. mean 81.3 (±15.5) respectively; p=.015) but not in patients (63.3 (±12.1) vs. mean 58.8 (±15.2) respectively; p=.320).

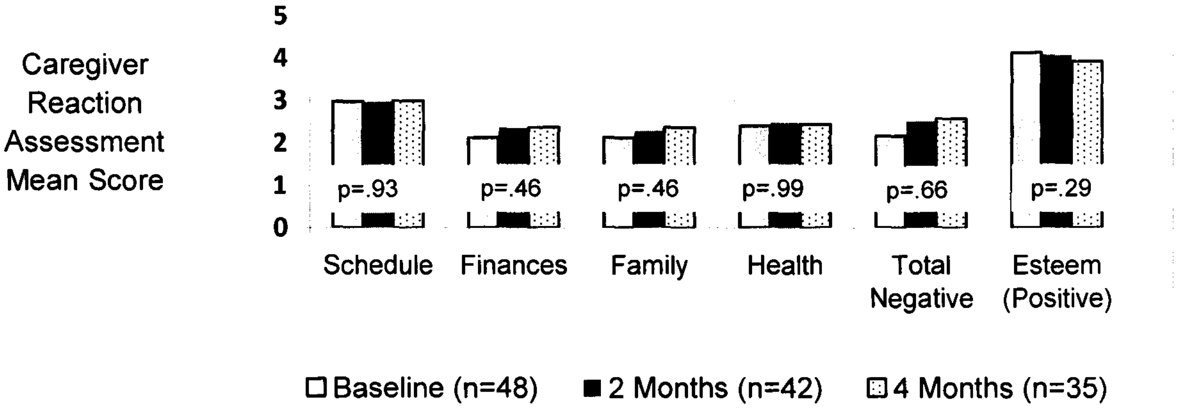
Section 4.4c

Exploratory Analyses- Change in Scores

Caregiver Reaction Assessment

The CRA was completed by caregivers at baseline, 2 months and 4 months. In general, most CRA subscale scores did not change over time. There was a trend for a decrease in caregiver esteem over time with a mean baseline score of 4.13 (±.56) compared to 3.92 (±.62) at 4 months (p=.287). Please see Figure 11 for a summary of the CRA subscale mean scores at each time period.

Figure 11. Caregiver Reaction Assessment Subscale Mean Scores at Baseline, 2 Months and 4 Months



Section 4.4d

Exploratory Analyses- Change in Scores

Summary

Do symptoms of anxiety or depression in patients and their primary caregivers change over time?

There was a trend for a decrease in *patient* symptoms of depression and *caregivers* symptoms of anxiety over time. A smaller decrease in *patient* symptoms of anxiety was evident between baseline and 4 months. Symptoms of depression in *caregivers* did not change over time.

Do levels of uncertainty in patients and caregivers change over time?

There was a significant decrease in *patient* uncertainty over time, especially for female patients. There was a trend for a decrease in *caregiver* levels of uncertainty over time.

Do levels of caregiver burden and caregiver esteem change over time?

There were no changes in any of the negative subscales of the caregiver reaction assessment between baseline and 4 months. However, caregiver esteem (positive subscale) tended to decrease over time.

Section 4.4e

Exploratory Analyses- Change in Correlations

Correlations between HADS, MUIS and CRA at 2 and 4 Months

Even though there was no evidence of significant correlations between some of the key variables of interest at baseline, correlation coefficients were calculated using values at 2 and 4 months as part of the exploratory analysis.

Correlations between Patient and Caregiver Emotions

Correlations between patient and caregiver HADS-anxiety and HADS-depression scores at baseline were calculated by using cut off scores and raw scores. These analyses were repeated for values at 2 and 4 months and presented below in Table 18 and 19.

Table 18. Bivariate Correlations between Patient and Caregiver Hospital Anxiety and Depression Scores at Baseline, 2 Months and 4 Months using Spearman's rho

		Patient Scores					
Spearman's rho		Baseline (n=48 pairs)		2 Months (n=42 pairs)		4 Months (n=35 pairs)	
		HAD-A	HAD-D	HAD-A	HAD-D	HAD-A	HAD-D
Caregiver Baseline	HAD-A	.168	.113				
	HAD-D	.157	.248				
Caregiver 2 Months	HAD-A			.218	-.077		
	HAD-D			.132	-.007		
Caregiver 4 Months	HAD-A					.329	.295
	HAD-D					.410*	.443**

*p<0.05; **p<.01
HAD-A Hospital Anxiety and Depression- Anxiety Subscale
HAD-D Hospital Anxiety and Depression – Depression Subscale

Table 19. Bivariate Correlations between Patient and Caregiver Hospital Anxiety and Depression Cut off Scores at Baseline, 2 Months and 4 Months using the Phi Correlation Coefficient

		Patient Scores					
Phi Coefficient		Baseline (n=48 pairs)		2 Months (n=42 pairs)		4 Months (n=35 pairs)	
		HAD-A	HAD-D	HAD-A	HAD-D	HAD-A	HAD-D
Caregiver Baseline	HAD-A	.217	.074				
	HAD-D	.092	-.021				
Caregiver 2 Months	HAD-A			.313*	.022		
	HAD-D			.176	.213		
Caregiver 4 Months	HAD-A					.310	.180
	HAD-D					.341*	.408*

*p<0.05
HAD-A Hospital Anxiety and Depression- Anxiety SubscaleHAD-D Hospital Anxiety and Depression – Depression Subscale

The strength of the correlation between patient and caregiver HADS scores appeared to increase over time. Thus, analysis was repeated to determine if duration of HF was a mediator in this relationship. The correlation between patient and caregiver baseline HADS in patients with HF ≤ 1 year (n=17) was compared to the cohort of patients with HF >1year (n=31) (Table20).

Table 20. Comparison of the Correlation between Patient and Caregiver Hospital Anxiety and Depression Scores in Patients with HF≤ 1 Year vs. Patients with HF> 1 Year using Spearman's rho

	HF ≤1 year (n=17)		HF > 1 year (n=31)	
Baseline	Patient Anxiety	Patient Depression	Patient Anxiety	Patient Depression
Caregiver Anxiety	.241	.159	.135	.097
Caregiver Depression	.268	.120	.097	.403*

*p<0.05

Correlations between Patient and Caregiver Uncertainty

At baseline, there was a significant positive correlation between patient and caregiver scores on the MUIS (r=.337; p=0.019). However, the strength of this correlation decreased over time and became statistically non-significant (Table 21).

Table 21. Bivariate Correlation between Patient and Caregiver Mishel Uncertainty in Illness Scores at Baseline, 2 Months and 4 Months using Pearson's Correlation Coefficient.

		Patient Mishel Uncertainty in Illness		
Pearson Correlation Coefficient		Baseline (n=48 pairs)	2 Months (n=42 pairs)	4 Months (n=35 pairs)
Caregiver Mishel Uncertainty in Illness	Baseline	.337*		
	2 Months		.299	
	4 Months			.148

*p<0.05

Contrary to the findings in the correlations between patient and caregiver emotions, the strength of the correlation between patient and caregiver MUIS scores appeared to decrease. Thus, analysis was repeated to determine if duration of HF was a mediator in this relationship. The correlation between patient and caregiver baseline MUIS in patients with HF ≤ 1 year (n=17) was compared to patients with HF >1year (n=31) (Table 22).

Table 22. Bivariate Correlation between Patient and Caregiver Mishel Uncertainty in Illness Scores using Pearson's Correlation Coefficient in Patients with Heart Failure ≤ 1 Year vs. Patients with Heart Failure > 1 Year

Pearson's Correlation Coefficient	Heart Failure ≤ 1 Year (n=17 Pairs)	Heart Failure > 1 Year (n=31 Pairs)
	Patient MUIS	Patient MUIS
Caregiver MUIS	.434	.176

MUIS- Mishel Uncertainty in Illness

Correlations between Patient and Caregiver Uncertainty and Emotions

At baseline, there was a trend for a positive relationship between *patient* symptoms of depression and patient uncertainty (Spearman's rho .252, p=.085) and, although this correlation strengthened at 2 months (Spearman's rho .325, p=.036), it weakened by 4 months and became non-significant once again (Spearman's rho =.170). The baseline correlation between patient symptoms of anxiety and uncertainty remained non-significant and the strength of this correlation did not change over time (Spearman's rho .211 (2 months) and .031 (4 months).

Similar to findings described in the patient sample, at baseline, there was a trend for a positive relationship between *caregiver* symptoms of depression and *caregiver* uncertainty (Spearman's rho =.251, p=.085). This correlation strengthened at 2 months (Spearman's rho =.489, p=.001), but became non-significant at 4 months (Spearman's rho =.273, p=.113). The strength of the correlation between *caregiver* uncertainty and *caregiver* symptoms of anxiety remained non-significant and did not change between baseline (Spearman's rho=.202), 2 months (Spearman's rho=.175) and 4 months (Spearman's rho=.101)

Correlations between Emotional Status and Caregiver Appraisal

Bivariate correlations between patient and caregiver HADS-anxiety and HADS- depression scores with each of the CRA subscale scores (which were conducted on baseline data) were repeated for 2 month and 4 month scores and are presented in Table 22. Spearman's rho was used for all calculations.

To recall, there were no significant correlations to suggest a relationship between patient HADS scores and CRA scores at baseline. However, over time, significant correlations did emerge. Specifically, the correlation between patient HADS-depression scores and caregiver health burden CRA subscale scores increased from baseline (rho=.257; p=.077) to rho=.314 (p=.042) at 2 months and rho=.371 (p=.028) at 4 months. Furthermore, significant correlations between patient HADS-anxiety scores and three caregiver burden subscale scores emerged by the 4 month measurement period. Please refer to Table 23 for a summary of bivariate correlations between patient HADS scores and caregiver CRA scores at baseline, 2 and 4 months.

Table 23. Bivariate Correlations between Patient Emotional Status and Caregiver Appraisal at Baseline, 2 Months and 4 Months using Spearman's rho

Caregiver Reaction Assessment	Patient Hospital Anxiety and Depression Scale					
	Baseline (n=48)		**2 Months** (n=42)		**4 Months** (n=35)	
	Anxiety	Depression	Anxiety	Depression	Anxiety	Depression
Schedule	.072	.150	.487**	.311	.487**	.311
Financial	.152	.229	.233	.064	.233	.064
Family	.036	.139	.337*	.229	.337*	.229
Health	.096	.257	.366*	.371*	.366*	.371*
Esteem	.116	-.205	-.200	-.009	-.200	-.009

*p<.05; **p<.01

At all measurement times, there was a strong positive correlation (rho>0.40 and p<0.01) between caregiver symptoms of depression and caregiver burden with respect to schedule disruption and effects on caregiver health. The correlation between caregiver symptoms of depression and caregiver burden related to finances and family abandonment remained significant with a Spearman's rho>0.30 at all three measurement times. Caregiver health burden and caregiver schedule burden continued to correlate with caregiver symptoms of depression and the strength of the correlation changed minimally over time. There were no correlations between caregiver esteem and caregiver emotional status at any of the measurement times (Table 24).

Table 24. Bivariate Correlations between Caregiver Emotional Status and Caregiver Appraisal at Baseline, 2 Months and 4 Months using Spearman's rho

	Caregiver Hospital Anxiety and Depression Scale					
Caregiver Reaction Assessment	**Baseline** (n=48)		**2 Months** (n=42)		**4 Months** (n=35)	
	Anxiety	Depression	Anxiety	Depression	Anxiety	Depression
Schedule	.523**	.636**	.394*	.515**	.637**	.663**
Financial	.198	.417**	.350*	.444**	.242	.333*
Family	.314*	.335*	.254	.388*	.160	.385*
Health	.454**	.519**	.418**	.416**	.496**	.679**
Esteem	.134	-.041	.155	-.161	-.053	-.102

*p<.05; **p<.01

Section 4.4f

Exploratory Analyses- Change in Correlations

Correlations between HADS, MUIS and CRA at 2 and 4 Months

Summary

Does the strength of the correlation between patient and caregiver emotions change over time?

Bivariate correlations between the emotional status of patients and caregivers appeared to strengthen over time. Further analysis revealed that the correlation between symptoms of depression in patients and caregivers was stronger in patient-caregiver dyads where patients had HF for over a year versus dyads where patients had HF for ≤ 1 year. Thus, initially there was no relationship between patient and caregiver emotions; however, duration of HF appeared to affect this relationship.

Does the strength of the correlation between patient and caregiver uncertainty change over time?

Bivariate correlations between patient and caregiver MUIS scores at baseline, 2 months and 4 months suggested that the strength of this relationship decreased over time. There was an initial, significant, positive correlation between patient and caregiver uncertainty that was no longer present at 2 and 4 months. Thus, the relationship that was present between patient and caregiver feelings of uncertainty at baseline was no longer present at 2 and 4 month follow up. It appears that the relationship between patient and caregiver feelings of uncertainty may be mediated by the duration of HF.

Does the strength of the correlation between patient and caregiver emotional status and caregiver appraisal change over time?

Bivariate correlations between *patient* HADS anxiety and caregiver CRA scores appeared to strengthen over time and reached statistical significance by 4 months. Bivariate correlations between *patient* HADS-depression scores and caregiver health burden CRA scores also strengthened over time and were statistically significant by 2 months. Thus, while there was no relationship between patient emotional status and caregiver burden at baseline, a relationship between these variables did emerge over time.

Bivariate correlations between *caregiver* HADS scores and CRA scores did not appear to change over time except for one CRA subscale. The strength of the correlation between *caregiver* symptoms of anxiety and caregiver burden, with respect to family abandonment, decreased between baseline and 4 months. The strong positive correlation between symptoms of *caregiver* depression and caregiver burden, with respect to schedule disruption and impact on caregiver health, were present at all measurement times. Thus, the relationship between *caregiver* emotions and caregiver burden was present at baseline and the strength of this relationship did not change significantly over time.

Section 4.5

Summary of Results Based on Study Hypotheses

Hypotheses

1. There is a direct, positive relationship between:

   a) Symptoms of depression in HF patients and their primary caregivers

   This hypothesis was supported only in the subgroup of patients who had HF for at least one year.

   b) *Symptoms of anxiety in HF patients and their primary caregivers*

   This hypothesis was not supported.

c) *Uncertainty and symptoms of anxiety or depression in HF patients.*

This hypothesis was not supported.

d) Uncertainty and symptoms of anxiety or depression in primary caregivers.

This hypothesis was not supported.

e) Symptoms of anxiety and depression in patients and perceived caregiver burden.

There were no relationships between symptoms of anxiety and depression in patients and perceived caregiver burden at baseline. Exploratory analysis did suggest that a significant correlation emerged over time.

c) *Symptoms of anxiety and depression in caregivers and perceived caregiver burden.*

There was a relationship between baseline caregiver symptoms of anxiety and depression and caregiver burden. This hypothesis was supported.

2. *There is a negative relationship between symptoms of anxiety and depression in primary caregivers and caregiver esteem*

This hypothesis was not supported.

CHAPTER 5

DISCUSSION

This chapter is divided into the following sections:

Section 5.1. Results for Primary Objectives.

In section 5.1, baseline patient and caregiver HADS scores are discussed followed by discussion about the relationship between these variables.

Section 5.2. Results for Secondary Objectives.

Secondary objectives required measurement of uncertainty (MUIS) and measurement of caregiver appraisal (CRA). This section begins with a discussion about MUIS scores and the relationships between HADS and MUIS scores for both patients and caregivers. The latter part of this section discusses the CRA scores and relationships between HADS and CRA scores.

Section 5.3. Longitudinal Data

Exploratory analyses using data collected at 2 months and 4 months are discussed in this section of the chapter. Comparison of the scores from HADS, MUIS and CRA instruments between baseline, 2 months and 4 months are initially discussed. Changes in the strength of the correlations between key variables calculated at baseline, 2 months and 4 months are discussed in the latter part of this section.

Section 5.4. Strengths and Limitations and implications for clinical practice and future research are discussed.

The chapter concludes with a summary of the findings from this PhD study.

Section 5.1
Discussion of Study Results
Primary Objective- Emotional Status in Patients and Caregivers

The primary objective of the study was to determine if there was a relationship between the emotional status of HF patients and their primary caregivers. Symptoms of depression and anxiety, as measured by the HADS, were used to represent emotional status in this PhD study. Analyses were conducted using Spearman's rho to determine correlation coefficients between key variables and HADS scores at baseline in HF patients and caregivers. This section begins with a discussion about the baseline HADS scores for patients and caregivers followed by a discussion exploring the relationship between patient and caregiver symptoms of anxiety and depression measured at baseline.

Baseline Patient Emotional Status

Symptoms of anxiety and depression in this sample were higher than population norms. In the general population, 7% have HADS-anxiety >10, 5% have HADS-depression ≥8 and 10% will have an abnormal HADS-anxiety or HADS-depression score (Hermann et al., 1997). The population mean for

HADS-anxiety has been reported as 3.9 (±3.6) and HADS-depression as 4.3 (±3.5) in 4,802 people living in the community (mean age 69.2 ±7.9) (van Jaarsveld et al., 2001).

When comparing symptoms of anxiety and depression in this PhD sample to values reported in other HF populations, studies that used the HADS were reviewed since findings can vary depending on the instrument and method used to measure these symptoms (Delville & McDougall, 2008). The HADS has been used in 12 studies with HF patients. Six studies were excluded from comparison with this study for the following reasons: a) reporting of the HADS scores was incomplete (Pelle et al., 2009; Haworth et al., 2007; Baxter et al., 2002), b) study populations were mixed and authors did not report HADS scores for the subgroup of HF patients (Zwisler et al., 2008; Johansen et al., 2008), and c) the study sample was not fully described to allow for comparison with this PhD study sample (Reynolds et al., 2007) Thus, the HADS results from this PhD study are compared to the 6 remaining studies.

Baseline Patient Depression

The proportion of patients reporting symptoms of depression at baseline was slightly lower in this PhD study sample compared to rates reported by studies that recruited patients while hospitalized with HF (Falk et al., 2008 in press; Yu et al., 2004; Yu et al., 2008; Johansson et al., 2006). For example, 13% of patients reported a HADS –depression score of >10 in this PhD study while 18% of patients hospitalized with HF (n=112; mean age 77 SD 10 years) had a HAD- depression score >10 (Falk et al, 2008, in press). Instruments measuring symptoms of depression typically include items that measure somatic symptoms that overlap with HF. Thus, symptoms of depression may be falsely elevated in patients hospitalized with HF because they have a higher HF symptom burden at the time of testing. However, the HADS only contains one somatic item, and therefore higher symptoms of depression, as measured by the HADS during hospitalization for HF, are not due to the measurement of overlapping symptoms of HF and depression.

Age and Symptoms of Depression

Higher symptoms of depression have also been reported in younger HF patients and could explain the difference in symptoms of depression between this PhD study sample and the younger study sample in Hofer et al. (2008). In the study sample by Hofer et al. (2008), (n=49, mean age 62; SD 11.5 years) 18% of HF patients had a HADS- depression score >10. Conversely, lower symptoms of depression (mean HADS-depression score 4.8; SD 2.7) were reported in a study with an older population (mean age 81; SD 5 years) (Witham et al., 2006) when compared to this PhD sample (mean HADS-depression score 6.1; SD 4.0). Significantly higher symptoms of depression have also been found in patients <60 years of age versus >60 years of age among those hospitalized for HF (Freedland et al., 2003) and among community-based HF patients respectively (Rumsfeld et al., 2003). Only 6 patients in this PHD study were ≤ 60 years of age, so comparison of depression scores, based on age as calculated by Freedland et al. (2003) and Rumsfeld et al. (2003), could not be conducted.

Mechanisms by which symptoms of depression may be higher in younger, rather than older, HF patients are poorly understood. According to the APAM theoretical model, and findings from this PhD study, adaptation for younger HF patients may be more difficult than older HF patients due to uncertainty related to employment status. In this PhD sample, there was a trend for higher levels of depressive symptoms and uncertainty reported by HF patients who were not retired versus retired. Furthermore, there was a trend for a positive correlation between uncertainty and symptoms of depression in HF patients at baseline (rho=.252; p=.08). In a qualitative study exploring the experiences of men living with HF, some men were retired and others were forced to leave their work because of HF (Thornhill et al., 2008). Men who were forced to retire and had several potential remaining years of employment expressed sadness and frustration about their situation because they were unable to perform expected roles in family and work life (Thornhill et al., 2008). In a study comparing functional capacity and quality of life in younger (age <65 years; n=328) versus older (age ≥65; n=218) HF patients, younger HF patients reported a worse quality of life, even though they had a better functional capacity than the older HF patients (Masoudi et al., 2004). After adjusting for baseline differences, older age remained a significant predictor of a better health-related quality of life in a multivariate model (Masoudi et al., 2004). Thus, younger versus older HF patients may report higher symptoms of depression as a result of a poorer health-related quality of life. Further qualitative studies exploring the lived experience of younger versus older HF patients, with and without symptoms of depression, would help generate hypotheses that could be then tested to better understand the psychosocial mechanisms underlying the relationship between age and symptoms of depression in male and female HF patients.

Functional Status and Symptoms of Depression

Many studies have reported higher rates of depression in HF patients who have more functional limitations than HF patients who are not as limited by their HF symptoms (Delville & McDougall, 2008). In this PhD study, a high number of patients reported moderate limitations in physical functional capacity (79% NYHA III-IV) when compared to other outpatient HF samples (range 24 %-44% NYHA III-IV) (Hofer et al., 2008; Witham et al., 2006; and van Jaarsveld et al., 2001). Thus, one would expect relatively higher levels of depression in this PhD sample when compared to other outpatient HF study samples. However, such findings were not supported Symptoms of depression were lower and HF patients reported a higher functional capacity in the studies by Witham et al.(2006) and van Jaarsveld et al.(2001), than in the current study population. Even though only 24% of participants in the study by Hofer et al.(2008) reported NYHA III-IV symptoms, this number represents the entire study population (n=89) and not the subgroup(n=49) that completed the HADS. Thus, direct comparison of the findings of the current study and those of Hofer et al. (2008) may not be accurate.

Unlike the findings in most studies, there was no correlation between functional capacity, as measured by the NYHA classification, and symptoms of depression reported by patients at baseline in this PHD study. There are a few possible explanations for this finding. The NYHA functional classification system has been used for almost 80 years and was developed to allow physicians to describe and communicate major changes in illness severity in HF patients (Bennett et al., 2002). Health care professionals assign the specific NYHA classification based on the patient description of the extent to which HF symptoms limit physical activity. The NYHA has been used in many clinical trials and found to be a strong predictor of survival, hospitalization and quality of life in the HF population (Pulignano et al., 2002; Pocock et al., 2006). Despite the known strengths of the NYHA classification system, it is based on clinical judgment and is therefore subject to limitations. For example, low inter-rater reliability has been reported in the literature and it has been recommended that, because of this limitation, NYHA classification should not be the sole indicator of functional capacity in HF patients (Raphael et al., 2007; Bennett et al., 2002). In this PhD study, NYHA classification was assigned by a small team of physicians (n=5) and two nurses who specialize in HF management and have practiced together for almost 10 years. Even though no formal evaluation of inter-rater reliability regarding NYHA classification by these individuals and been conducted, they represent a small team that has worked closely with the HF population and in the setting where recruitment for this study was conducted. Thus, the possibility for inter-rater variability as the underlying reason for the lack of a relationship between NYHA and symptoms of depression is likely to be low. Nevertheless, future research studies exploring the relationship between symptoms of depression and functional capacity should include additional measures to the NYHA classification system.

Another limitation of the NYHA classification system in identifying the functional status of HF patients is related to the presence of non-cardiac reasons for limitations in physical activity. Such limitations are not incorporated into the NYHA classification system and may affect the validity of this measurement. For example, in this study sample, 38% of HF patients reported arthritis and 23% had COPD, conditions that potentially limit their functional capacity, either alone or in addition to HF symptoms. Other measures of functional capacity that account for physical limitations from co-morbidities should be added to future study designs. The 6 minute walk test is a simple, objective test and has been extensively used to evaluate functional capacity in HF populations and could be used in addition to NYHA classification in future research endeavors (Rostagno & Gensini, 2008; Peeters & Mets, 1996).

Finally, another explanation for the lack of a correlation between the NYHA and symptoms of depression in this PhD study population may be due to the limited amount of variability in the functional capacity of the participants, with

79% classified as NYHA III-IV at baseline. The correlation coefficient reflects the amount of variability that is shared between two variables, and if the variability is constrained, as in the NYHA status, the correlation coefficient between NYHA and symptoms of depression will be lower than expected.

Ischemic Etiology of HF and Symptoms of Depression

In this PhD study sample, there was a trend for patients with an ischemic etiology of HF to report higher symptoms of depression than patients with a non-ischemic etiology of HF. Because these numbers are small, caution is needed when interpreting these findings; however, there is a growing body of evidence suggesting a physiological relationship between vascular disease and depression in older populations (Alexopoulos et al., 1997; Mast, 2004; Newberg et al., 2006). Patients with an ischemic etiology of HF may suffer from symptoms of depression through physiological mechanisms. Depression arises from either a single ischemic lesion disrupting critical pathways within the prefrontal system or by an accumulation of diffuse or multi-focal cerebrovascular ischemic lesions surpassing a threshold (Alexopoulos et al., 1997; Steffans et al., 1999; Newberg et al., 2006). Other cardiovascular lesions such as white matter hyperdensities and abnormalities in the hippocampus, amygdala and frontostriatal systems have been associated with depression (Alexopoulos et al., 2005; Newberg et al., 2006). While other studies exploring the vascular depression hypothesis have yielded conflicting results (Versluis et al., 2006), this pathophysiological concept continues to be an active area of inquiry (Newberg et al., 2006).

Patient Sex and Symptoms of Depression

Although the incidence of HF is higher in males than females in all age groups (Thomas & Rice, 2007), some studies report the prevalence of depression is higher in females with HF than males (Stromberg & Martensson 2003). Because this PhD study patient sample had an almost balanced representation of males and females, exploring sex differences between symptoms of depression was possible. Results revealed that female HF patients did not report higher symptoms of depression than male HF patients. However, male and female HF patients with male caregivers reported higher symptoms of depression. Perhaps the type of support (for example, tangible or emotional) from a male versus female caregiver is different and therefore different patient needs are met, based on the type of support provided. This finding is quite interesting and has not been described in the literature to date.

Baseline Patient Symptoms of Anxiety

Even though HF patients have reported symptoms of anxiety in the qualitative literature (Martensson et al., 1998), the measurement of this construct is extremely sparse in the overall HF literature. Patients' symptoms of *anxiety* were lower than symptoms of *depression* in this PhD study sample but anxiety scores were generally higher than those reported in other studies using the HADS in HF patients. While 15% of patients had a HADS-anxiety score >10 at baseline in this PhD study, 11% of patients scored above this threshold in two studies of patients hospitalized with HF (Yu et al., 2007 in press, Falk et al., 2008 in press). Conversely 18% of patients in the study by Hofer et al. (2008) had a HADS- anxiety score >10. Of note, the subgroup of HF patients who actually completed the HADS was not described, which makes comparison with the study by Hofer et al. (2008) difficult.

There was a non-significant trend for HF patients who were younger and not retired to report higher symptoms of anxiety. The two studies that recruited HF patients in an outpatient setting had older patients (mean age between 74 and 81 years) and lower mean HADS-anxiety scores (mean scores between 3.0 and 3.9) (Witham et al., 2008; van Jaarsveld et al., 2001) than this PhD sample (mean age 73 years and HADS-anxiety mean 5.9) . These findings support the possibility that there is a relationship among symptoms of anxiety, age and employment status. Younger HF patients who are not retired appear to have higher symptoms of anxiety compared to older, retired HF patients.

In this PhD sample, HF patients with a history of myocardial infarction (MI) reported higher levels of anxiety than HF patients without a previous MI. However, these numbers are extremely small and need to be interpreted with caution. Anxiety is common among patients recovering from an MI and persists over the long term in 20-25% patients (Moser, 2007). In patients following MI (n=89) mean levels of HADS-anxiety were 4.6 within 6 weeks after the clinical event and increased to 5.2 at the 12-month follow up assessment (van Jaarsveld et al., 2001). Thus, symptoms of anxiety in the HF population may represent a reaction to the combination of a myocardial infarction and HF, rather than strictly HF. Future studies measuring anxiety in HF need to ensure information regarding previous cardiac events, such as MI, need to be included in data collection.

Caregiver Emotional Status

Baseline Caregiver Symptoms of Anxiety

Caregiver studies have measured depression, emotional distress and caregiver mental health, but, an extensive literature review of family caregiving in HF found only one study that measured symptoms of anxiety (Molloy et al., 2005). Anxiety and caregiver burden were measured in 60 caregivers of older HF patients randomized to either a supervised hospital based cardiac rehabilitation program or usual care (Molloy et al., 2006). Patients in the intervention group attended seated exercise classes twice a week for 3 months while patients in the control group were encouraged to remain physically active. Anxiety and caregiver burden were measured in caregivers at baseline, 3 and 6 months. At baseline, 18% of caregivers (n=57; mean age 63 years, 65% female) had HADS-anxiety scores ≥8 (Molloy et al., 2006). Thus, caregivers in this PhD study reported higher levels of anxiety (48% HADS-anxiety ≥8) at baseline when compared to levels of anxiety at baseline in caregivers in the study by Molloy et al., 2006.

There is a possibility that differences in patient and caregiver age may have contributed to the differences between levels of caregiver anxiety in the study by Molloy et al., (2006) and these PhD study findings. Both patients and caregivers in this study were younger than patient and caregivers in the study by Molloy et al., (2006). Caregivers of younger versus older HF *patients* reported significantly higher levels of anxiety in this PhD study. Furthermore, there was a trend for younger versus older *caregivers* to report higher levels of anxiety in this PhD study.

Although hypothetical at this time, it is possible that the relationship between younger patient and caregiver age and increased symptoms of caregiver anxiety may be mediated by patient employment status. Caregivers of HF patients who were not retired versus those who were retired also reported significantly higher levels of anxiety. Although patient employment status was not reported by Molloy et al., (2006), there is a strong possibility that the majority of the patient sample were retired because all of them were over 65 years of age. Thus, there is a possibility that younger patient age, younger caregiver age and patient employment status contribute to feelings of anxiety in caregivers of HF patients. However, these three variables are often co-related and the unique contribution of each variable to the level of caregiver anxiety is unknown.

Baseline Caregiver Symptoms of Depression

Even though 48% of caregivers reported symptoms of anxiety at baseline, only 8% of caregivers in this study sample reported symptoms of depression and thus discussion around demographic variables that may have correlated with the presence of depressive symptomatology is not feasible. Caregiver symptoms of depression will be explored in the context of caregiver burden later in this chapter.

Relationship between Patient and Caregiver Emotional Status

There were no significant relationships between HADS-depression scores or HADS-anxiety scores in HF patients and their caregivers at baseline. In the study by Molloy et al. (2006), both HF patients and caregivers completed the HADS; however, correlation analyses were not conducted. Contrary to the findings in this PhD study, significant relationships between the emotional status of patients and their caregivers have been found in other studies. A significant relationship was found between the emotional well-being of patients and their caregivers, as measured by the mental component summary score (MCS) from the 12-item short form health survey (SF-12) in 103 patient-caregiver dyads (Evangelista et al., 2002). There was also a significant relationship between the MCS and depressive symptoms (Zung Self-rating Depression Scale) in HF patients and their spouses (Pihl et al., 2005). Finally, depression scores, as measured by the Beck Depression Inventory (BDI-II) were significantly correlated between HF patients and caregivers attending a heart function clinic (Hooley et al., 2005).

It appears that there is a higher representation of spousal caregivers and female caregivers in other studies (compared to this one) showing a significant relationship between patient and caregiver emotional status. However, none of the studies conducted analyses to determine possible mediators in the relationship between patient and caregiver emotional status.

Section 5.1
Discussion of Study Results
Primary Objective- Emotional Status in Patients and Caregivers
Summary

In summary, HF patients appear to have higher symptoms of depression than their caregivers, while caregivers appear to have higher levels of anxiety than the patients. Contrary to findings in other studies, there were no significant relationships between the emotional status of patients and their primary caregivers at baseline. Of note, to answer the primary objective of this study, only baseline patient and caregiver HADS were used in correlational analyses. As part of secondary analyses that explored HADS scores at 2 and 4 months, the correlation between the relationship between patient depression and caregiver depression appeared to strengthen over time. Thus, hypothetically speaking, duration of HF, or duration of caregiving, could mediate the relationship between patient and caregiver symptoms of depression. Variables that influence the strength of the correlation between patient and caregiver emotions have not been reported in the literature. Thus, ongoing research is needed to better understand the relationship, if any, between the emotional status of HF patients and their primary caregivers and is further explored in Section 5.4 of this chapter that outlines future research implications of this study.

The construct of 'emotional status' also needs further clarification. For the purposes of this study, emotional status was defined with HADS-anxiety and HADS-depression subscores. The decision to assess symptoms of depression was made because HF patients who also experience symptoms of depression have worse clinical outcomes than HF patients without symptoms of depression. Two studies that measured symptoms of depression found a significant correlation between patient and caregiver scores (Pihl et al., 2005; Hooley et al., 2005) and in one study, higher symptoms of depression were associated with increased caregiver burden and 6-month patient hospitalization (Hooley et al., 2005). It would appear that specifically measuring 'symptoms of depression and depression', in addition to a more global measurement of 'emotional status' may provide insight into the relationship between patient and caregiver emotions and also provide clinical relevance.

Section 5.2a
Discussion of Study Results
Secondary Objective- Patient and Caregiver Uncertainty

Feelings of uncertainty have frequently been described by HF patients and their caregivers in qualitative studies; however, these feelings but have only been measured quantitatively in two studies of HF patients. This is the first study, based on reported literature, to measure uncertainty in caregivers of HF patients.

Thus, one of the secondary objectives of this study was to measure uncertainty in HF patients and their caregivers, and to determine if uncertainty correlates with symptoms of depression or anxiety.

Patient Uncertainty

In this PhD study, baseline patient MUIS scores were higher than MUIS mean values from pooled data of 20 studies of adults (age ≥60; n=276) with multiple medical conditions (Mishel, 1997). Patient MUIS scores in this PhD study (mean 63.8) were slightly lower than scores reported by a sample of patients hospitalized with HF (n=201, mean MUIS 71.4) (Jurgens, 2006), but higher than a group of HF patients attending a follow up outpatient visit in a cardiologist's office (n=22, mean MUIS 54.9) (Winters, 1999). There was a trend for female versus male HF patients to have higher levels of uncertainty at baseline. No sex differences in MUIS sores were detected by Jurgens (2006) or Winters (1999). Moreover, there were no differences in MUIS scores in relation to age; however, there was a trend in this PhD study for retired versus not retired HF patients to report lower levels of uncertainty at baseline. Employment status was not reported in the studies by Jurgens (2006) and Winters (1999). Hypothetically speaking, it is possible that HF patients who are not retired are uncertain about their finances and their ability to perform previous roles related to employment responsibilities.

Higher levels of uncertainty were reported for similar items in this PhD study sample and the HF patients in Winters (1999). Ranking of individual item scores was not reported by Jurgens (2006). When ranking individual item scores, higher levels of uncertainty were reported for items, " I am certain they will not find anything else wrong with me" and " It is unclear on how bad my heart failure will be" in both this PhD sample and the sample by Winters (1999). Furthermore, both study samples ranked the item "I don't know what is wrong with me" as the item with the lowest level of uncertainty.

Interpretation of findings related to the ranking of uncertainty items is rather interesting and suggests that HF patients may experience different intensities of uncertainty. It appears that the source of uncertainty is related to illness progression or new illness, neither of which health care professionals can determine. The illness trajectory of HF is highly individual and difficult to predict, which naturally contributes to feelings of uncertainty in these patients.

There was a trend for HF patients who lived alone versus with their caregiver and HF patients who were cared for by an adult child versus a spouse to report higher levels of uncertainty. These HF patients may have more uncertainty about coping with the daily management of their disease because of either a lack of support when living alone, or the nature of the patient-caregiver relationship when cared for by an adult child versus spouse.

Correlation between Patient Uncertainty and Emotional Status

In this PhD study, there was a trend for HF patients with higher levels of uncertainty to also report higher symptoms of depression. One method to better understand the correlation between uncertainty and symptoms of depression would be to determine if interventions aimed at reducing uncertainty would improve symptoms of depression. However, if feelings of uncertainty in this population arise from an unknown illness trajectory, strategies to decrease uncertainty would be difficult to develop. Nevertheless, in this sample, there was a significant decrease in levels of uncertainty between baseline and 4-month follow-up, suggesting that a certain amount of adjustment and/or adaptation may occur over time.

Challenges in understanding the relationship between uncertainty and depression in this PhD study may be related to psychometric limitations of the MUIS. For example, the community version of the MUIS (MUIS-C) used for this study provided a unidimensional measurement of uncertainty. Uncertainty may actually be a more heterogeneous construct and a multidimensional tool may be a more valid measurement approach. Many items from the MUIS-C are also used in the version of the MUIS for hospitalized patients (MUIS-A) (Mishel, 1997). The MUIS-A has yielded a 4-factor structure when tested in populations that experience symptoms related to their chronic disease. These MUIS factors were: a) ambiguity concerning the meaning of symptoms, b) complexity regarding the effect of treatment upon symptoms, c) deficient information concerning diagnosis and d) unpredictability concerning outcome/ the course of illness (Mishel, 1997). Thus, the MUIS-C may need further psychometric testing to ensure it has adequate construct validity for measuring uncertainty in an outpatient HF population.

Baseline Caregiver Uncertainty

To our knowledge, this was the first study to describe uncertainty using the MUIS-C in primary caregivers of HF patients. The mean MUIS score in this sample was higher than the mean MUIS score from analysis of caregivers of patients with mixed medical conditions, as reported in the MUIS manual (Mishel, 1997). Direct comparison between mean MUIS scores is difficult because the mean scores reported in the MUIS manual are from a 30-item family member form. The family member form provided by Mishel to this author for this study contained 31 items and instructions did not indicate which item was added to the current MUIS-C version. These limitations need to be considered when trying to interpret the levels of uncertainty reported by the caregivers of HF patients in this study.

To gain some perspective, an average item score of caregivers in this study (84.5 / 31= 2.73) was compared to the average item score reported in the MUIS manual (Mishel, 1997). Similar levels of uncertainty were reported in caregivers of patients with mixed types of cancer (81.9/ 30= 2.73). Three studies of caregivers for patients post MI reported relatively lower levels of uncertainty (2.44) while caregivers for patients with dementia reported higher levels of uncertainty (2.83) (Mishel, 1997). Thus, it appears that caregivers of HF patients report higher levels of uncertainty that may be similar to caregivers of patients with cancer, but less than levels of caregivers for patients with dementia.

One possible explanation for high levels of uncertainty in this PhD study population may be due to the timing of recruitment, since most patient-caregiver pairs were recruited during their first appointment at the HFC. This possible explanation is also supported by the finding of a trend for caregivers of patients who were already enrolled in the HFC at the time of recruitment, versus caregivers of patients recruited during their initial HFC appointment, to report lower levels of uncertainty. Thus, levels of uncertainty may be transiently elevated because of the uncertainty associated with the initial HFC visit, rather than the general level of uncertainty associated with the illness.

Finally, there was a trend for male versus female caregivers to report higher levels of uncertainty. This finding is inconsistent with results of a pooled analysis from studies of caregivers for patients with a variety of illnesses, where the mean MUIS score was 57.6 ±18 for males (n=499) and 55.9±17 for females (n=514). Thus, further analysis is needed to determine if there is a sex difference in levels of uncertainty among caregivers. It is possible that the levels of uncertainty are related to norms about caregiving and caregivers within a Western culture. For example, in Western culture, more women than men tend to take on the role of caregiver and may feel less uncertain about the roles and responsibilities associated with caregiving for a HF patient.

Similar to the patient MUIS-C instrument, the community version of the MUIS for caregivers also yields a unidimensional measurement of uncertainty. However, there seemed to be an underlying theme related to items that have relatively higher scores than other scale items. All of the items that had the word 'predict' yielded an uncertainty score of >3. These items were as follows: a) His/her symptoms seem to change unpredictably, b) I cannot predict how long his/her heart failure will last, c) I can usually predict the course of his/her heart failure, d) His/her physical distress is predictable: I know when it is getting better or worse, e) Because of the unpredictability of his/her heart failure, I cannot plan for the future. These findings suggest that caregivers were uncertain about the course of HF symptoms, both on a daily and on a more long-term basis. Since the MUIS scale represents a unidimensional construct, item responses cannot be separated into possible themes and factor analysis has not been reported.

Relationship between Caregiver Uncertainty and Emotional Status

There was a trend for a relationship between uncertainty and symptoms of depression (rho= .251; p=.085) in caregivers of HF patients. Intuitively, a relationship between uncertainty and depression is sensible and it is possible that a study with a larger sample size would yield a statistically significant correlation. According to Mishel (1990), feelings of uncertainty can be appraised as either opportunity or danger. If aspects of uncertainty were strong enough to disrupt an ongoing life pattern, a state of stability is disrupted and coping strategies are mobilized. The situation is cognitively reworked through assimilation and accommodation until a new state of equilibrium is established (Mishel, 1990). Caregivers who adopt a problem-solving versus mechanistic approach to overcoming feelings of uncertainty will re-establish a state of equilibrium. In this setting, uncertainty is then viewed as a 'normal' part of life and newly developed problem solving skills will provide caregivers with the ability to re-establish a state of equilibrium. Although intuitively possible, this theoretical explanation needs to be empirically tested.

In the context of uncertainty theory as described by Mishel (1990), caregivers with symptom of depression may represent those who are unable to re-establish a new state of equilibrium while trying to overcome feelings of uncertainty related to the patient's illness. Empirical testing of this theory would involve evaluating the effect of interventions that help caregivers utilize a problem-solving approach for overcoming uncertainty on outcomes such as caregiver depression. Qualitative research exploring experiences of uncertainty and strategies to overcome such feelings in caregivers with and without symptoms of depression would provide valuable insight in to this poorly understood phenomenon.

Section 5.2a
Discussion of Study Results
Secondary Objective- Patient and Caregiver Uncertainty
Summary

This was the first study to measure levels of uncertainty in both HF patients and their caregivers. Although the MUIS scores provided new insight into these phenomena, limitations of the measurement tool created difficulties regarding interpretation of the findings. The unidimensional nature of the community-based version of the tool limits exploration of different types of uncertainty, which is possible with the acute version of the MUIS. Further testing of the construct validity of the community version of the MUIS in the HF population, as well as other populations, is needed. MUIS scores for other populations were available in the MUIS manual (Mishel, 1997), however, details about each population were not provided and thus limit the interpretation and generalizability of these study findings.

Another limitation of the MUIS was related to respondent burden and was previously described in the results section of this thesis. Patients and caregivers found the MUIS lengthy and cognitively challenging. Instructions for administration of the MUIS do encourage the person presenting the MUIS to give the participant an example of how to proceed; however, wording on items often changes because of the reverse scoring. This double negative presentation was difficult for responders to comprehend. Thus, further research with the MUIS in this study population should test a modified version that avoids double negative questions and limits the number of items as much as possible.

From a more positive perspective, there was a significant decrease in levels of patient uncertainty over time as detected by the MUIS. The responsiveness of this tool was quite good and therefore sample sizes using the MUIS may not need to be so large that feasibility becomes a major limitation. Based on MUIS-C change scores from a sample of patients undergoing insertion of an implantable defibrillator (mean change 3.87, SD 9.57; unpublished data from Master's thesis), a sample size of 30 individuals was needed to detect a significant change in levels of uncertainty. Further testing with the MUIS also needs to determine a clinically meaningful change score so that levels of uncertainty can be understood and discussed in the context of relevant HF patient and caregiver clinical outcomes.

Section 5.2b
Discussion of Study Results
Secondary Objective- Caregiver Appraisal
Caregiver Burden Subscales

Secondary study objectives also explored the relationships between the emotional status of patients and caregivers and the positive and negative components of the caregiver experience, also identified as caregiver appraisal. This section begins with a discussion about the variables associated with caregiver burden, including patient and caregiver emotional status followed by a similar discussion about the positive aspects of caregiving as per the CRA self-esteem results.

The CRA has been used in two other relevant studies measuring the caregiver experience in caregivers of HF patients. Both of these studies were cross-sectional, descriptive studies that recruited caregivers of HF patients living in the community (Saunders, 2008; Luttik et al., 2007a).

Patient Variables associated with Caregiver Burden Scores on the CRA

Caregiver burden related to schedule disruption was the highest burden reported in all studies publishing CRA scores of caregivers for HF patients. Higher scores related to schedule disruption were found in this PhD study when compared to caregivers in the study by Luttik et al. (2007a), however, patients in this PhD study were more functionally impaired than those in the study by Luttik et al. (2007a) and this may account for the difference in findings. Patients who are less active due to HF symptoms may require more assistance with activities of daily living than HF patients who are not limited by symptoms. In the study by Luttik et al. (2007a), the patients' physical functioning was an independent predictor of caregiver burden related to a disrupted schedule.

Conversely, caregivers in this PhD study reported lower levels of schedule disruption than caregivers in a study by Saunders (2008), even though 79% of patients in this study were NYHA III-IV and 57% of patients were classified as NYHA III-IV in the study by Saunders (2008). This observation must be interpreted with caution because NYHA classification was assigned based on caregivers' interpretations of the patients' functional capacity in the study by Saunders (2008). This method of determining NYHA has never been validated in the literature and may not be accurate.

In the current PhD study, caregivers of HF patients who were not retired reported significantly higher levels of total caregiver burden related to schedule disruption, finances, and caregiver health problems compared to those of patients who were retired. One explanation for this finding could be due a significant correlation between patient age and employment status (rho=-.760; p<0.001). In this PhD study, the correlation between total caregiver burden and patient employment status was no longer significant when controlling for patient age. Thus, it appears that age mediates the relationship between employment status and total caregiver burden. On the other hand, the correlation between patient employment status and caregiver burden related to finances remained significant when controlling for patient age (rho=.305; p=.037). It is possible that, HF patients who are employed at the time of HF diagnosis increase caregiver burden because of financial concerns. Younger HF patients may have children who are supported by their employment income, while older HF patients may have children who are financially independent. In addition to a loss of usual employment income, younger, unemployed HF patients my have additional financial challenges related to the cost of multiple medications, health care appointments or specific assistive devices needed for optimal HF management

(Pattenden et al., 2007). In Ontario, people ≥65 years of age have financial support for most prescription medications and do not experience the same financial burden for medications as do younger HF patients.

Even though age did not mediate the relationship between patient employment status and *financial* caregiver burden, younger HF patient age did mediate the relationship between caregiver burden related to *schedule* disruption and caregiver health problems. Hypothetically speaking, it appears that caregivers of younger HF patients experience higher levels of burden related to the demand of caregiving on their schedule and impact on their own health. One possible explanation for this finding could be related to the larger variety of physically active roles a younger versus older person may normally undertake, but can no longer perform due to HF symptoms. For example, older people may have delegated physically demanding roles, such as heavier household repairs, snow shoveling, lawn and garden care to younger individuals, due to the healthy aging process and prior to experiencing HF. Younger HF patients, who participated in physically active roles prior to experiencing HF, did not need to delegate such activities prior to experiencing HF and now the primary caregiver may have been forced to assume these roles (Luttik et al., 2007b; Barnes et al., 2006). Furthermore, a reduced financial income in HF patients who are not retired may preclude paying someone to help with such activities. As a result of assuming the roles once associated with younger pre-HF patients, caregivers of younger HF patients experience higher levels of caregiver burden.

Thus, it appears that increased caregiver burden is associated with *patient* variables that include a) physical limitations due to HF symptoms, b) a younger age, and c) an employment status other than retirement. There were no other demographic or clinical variables that were associated with increased caregiver burden in this PhD sample. However, as previously mentioned, a secondary objective was to determine if the emotional status of HF patients correlated with caregiver burden.

Relationship between Caregiver Burden and Patient Emotional Status

There was a trend for caregivers of HF patients with symptoms of depression to report higher levels of caregiver burden as a result of health problems related to caregiving compared to caregivers of HF patients with normal HADS-depression scores. It is possible that HF patients with symptoms of depression demand more emotional support from their caregivers, and as a result, caregivers experience emotional burden and distress that ultimately compromises their health. HF patients with symptoms of depression may lack the motivation to perform the necessary self-care activities and require extra psychosocial support to assist them in engaging in such behaviours (Kodiath & Shively, 2005). In a study of female spouses of HF patients (n=20), 33% of the caregivers reported moderate to extreme difficulty when dealing with patient moodiness and irritability (Bakas, 2006). Lack of motivation associated with symptoms of depression may further impair HF patients from participating in their regular social networks. In a sample of HF patients, those with symptoms of depression versus no symptoms of depression had significantly lower social functioning scores than those with no symptoms of depression (Skotzko et al., 2000). Caregivers of HF patients with symptoms of depression may experience increased caregiver burden due to the effect of the patient's emotional distress on further impairing their social network. In a qualitative study of 16 HF patients and their spouses, many discussed their loss or reduction in their social life, resulting in a reduced social support network (Barnes et al., 2006).

In order to determine mediators within a relationship, there first needs to be a significant relationship between the two variables of interest (Kraemer, 2008). The only other study measuring HF symptoms of depression and caregiver burden in HF patients detected a significant relationship between these two variables (Hooley et al., 2005). However, the tool used to measure caregiver burden was unidimensional, and therefore unable to describe the specific domains of the caregiving experience that were affected by symptoms of depression in the HF patient. Unlike the findings by Hooely et al., (2005), this PhD study did not show a significant correlation between symptoms of depression in HF patients and caregiver burden. Thus, further research is necessary to better understand the impact of HF patient symptoms of depression on caregiver burden while exploring possible mediators within these relationships.

Caregiver Variables associated with Caregiver Burden Scores on the CRA

The majority of caregiver demographic variables measured in this study did not correlate with caregiver burden. These PhD study findings were similar to findings by Saunders (2008) and Luttik et al. (2007a), where caregiver sex, age, and relationship to patient (spouse or adult child) did not affect total caregiver burden. In the study by Luttik et al. (2007a), caregivers with a lower versus higher physical health component score on the SF-36 also reported higher levels of caregiver burden. Measurement of caregiver health in this PhD study was based on a simple, self-report questionnaire and may not have yielded an accurate representation of caregiver health. Future research with caregivers needs to include a more accurate measurement of caregiver health than the questionnaire used in this study. The SF-36 appears to be an acceptable alternative for representing this construct and also prevents the need for collecting personal medical information from caregivers.

In the study by Saunders (2008), caregivers who provided care for another relative in addition to a HF patient versus only the HF patient had higher scores all CRA burden subscales. Additional caregiver responsibilities for other individuals were not collected in this PhD study or in the study by Luttik et al. (2007a). In this PhD study, there was a trend for caregivers who were not retired, versus those who were retired, to report higher levels of caregiver burden. These PhD study findings, and the findings of Saunders suggest that caregivers who have competing responsibilities, such as caring for another relative or employment, have higher levels of caregiver burden than caregivers who are not responsible for the care of another individual or are retired. Caregivers with competing responsibilities may find it difficult to find time to provide tangible support and may need to organize time away from their workplace to help the HF patient attend multiple health care appointments. In a study of older HF patients attending a 12-week cardiac rehabilitation program, there was an increase in caregiver burden for caregivers of HF patients who attended exercise sessions versus caregivers for HF patients in the control group who received 'usual care' (Molloy et al.,2006). Attending the CR program may improve HF patient outcomes, but, the added transportation responsibilities for caregivers can ultimately increase caregiver burden. Thus, interventions aimed at improving outcomes in HF patients also need to consider and measure the impact of the intervention on caregiver outcomes.

Relationships between Caregiver Burden and Caregiver Emotional Status

The strongest factors correlating with caregiver burden were caregiver symptoms of anxiety and depression. Even though the direction of these relationships is unknown, it is possible that increased feelings of anxiety may lead to increased caregiver burden because of caregiver worries about the HF patient. In a qualitative study of 13 spouses of HF patients, almost all caregivers mentioned worries about leaving the HF patient alone and therefore restricted their own activities outside the home (Luttik et al, 2007b). Thus, caregivers who experience symptoms of anxiety may restrict their own support network because they are too worried to leave the HF patient alone. Caregivers also described poor sleep habits because they were worried about the HF patient's breathing patterns at night and would stay awake listening (Luttik et al., 2007b). Caregivers who are sleep deprived may experience higher levels of burden because they do not have the energy to perform the necessary roles and responsibilities associated with their caregiving role. Caregivers often reported that family was the most important source of practical and emotional support for them (Luttik et al., 2007b). Therefore, caregivers who have higher symptoms of anxiety may be worried because they do not have the necessary family support to help them meet the HF patient's caregiving needs and provide some respite for them.

In addition to caregiver symptoms of anxiety, caregiver symptoms of depression also correlated with caregiver burden. Strong correlations between symptoms of depression and caregiver burden were also reported in the study by Saunders (2008). Furthermore, Luttik et al. (2007a) measured caregiver mental health using the MCS from the SF-36 and found that the MCS was a significant, independent predictor of caregiver burden.

The strongest correlations identified in this PhD study were between a) caregiver schedule burden and caregiver symptoms of depression and b) caregiver health burden and caregiver symptoms of depression. Perhaps caregivers who are overwhelmed with schedule demands associated with their caregiver roles sacrifice their own health in efforts to meet these demands. As their own health fails and the demand for their time continues, they develop symptoms of depression as a reaction to the overwhelming and never ending situation. Or, as caregivers face demands on their schedule because of caregiving, they do not have the same opportunities to access their social support network for help in coping with these demands. These possibilities suggest that increased caregiver burden leads to increased caregiver symptoms of depression. Although longitudinal studies are needed to test these possibilities; no studies were found for caregivers of HF patients in the published literature to date. In a longitudinal study of family caregivers for women with advanced cancer, although patient factors predicted caregiver distress, caregiver burden was the strongest predictor of caregiver anxiety and depression (Grunfeld et al., 2004).

One must consider that the opposite direction in the relationship between caregiver symptoms of depression and caregiver burden may be possible, where caregiver symptoms of depression lead to increased caregiver burden. For example, caregivers may develop symptoms of depression because they experience a change in the relationship with the HF patient due to the patient's reactions to their illness. Caregivers may not be able to share their own concerns and feelings with the HF patient because the patient is experiencing emotional distress, and caregivers have lost the intimacy and emotional support they may have shared with the HF patient prior to the illness. Symptoms of depression may develop in caregivers as a response to the loss they have experienced with the personal and unique components they once had with the patient. As a result, symptoms of depression in the caregiver develop and then deplete the physical and emotional energy necessary to fulfill caregiving roles and responsibilities, resulting in caregiver burden.

There is some evidence to suggest that the quality of the marriage for patient-spousal caregiver pairs is negatively correlated with psychological distress (Rohrbaugh et al., 2002). The majority of caregiver studies have been limited to exploring the experiences of partners or spouses of HF patients and do not describe possible differences in the caregiver experience based on the type of relationship (for example partner/spouse versus adult child versus close friend). Such information would help to provide insight into the experiences of caregivers for HF patients and provide valuable information for developing strategies to improve patient and caregiver outcomes.

In summary, it appears that there are no sex differences in perceived caregiver burden and evidence exploring the effect of caregiver age on caregiver burden is mixed. Caregivers who have other responsibilities such as care for another individual or employment report higher levels of caregiver burden. Increased caregiver burden related to finances appears to be higher for caregivers of HF patients who are not retired. However, caregiver feelings of anxiety and depression appear to have the strongest relationship with perceived caregiver burden.

Section 5.2c
Discussion of Study Results
Secondary Objective- Caregiver Appraisal
Positive Caregiver Subscale

The ability of the CRA to measure both the negative and positive experiences of caregivers was one of the primary reasons for choosing the CRA for this study. While the majority of studies have focused on the negative aspects of caregiving, positive experiences have been described by caregivers of HF patients (Scott, 2000). More recently, the positive aspects of caregiving were measured using the CRA in a similar population to this PhD study (Saunders, 2008). In both the study by Saunders (2008) and this PhD study, very few variables correlated with caregiver esteem; however both studies identified a trend for adult child caregivers to have higher levels of caregiver self-esteem than spousal caregivers. One might conjecture that adult child caregivers feel more positive about their caregiving role than spouses of HF patients because it provides adult children with an opportunity to provide care for someone who has provided care for them in the past. Obviously, very little is known about the positive aspects of caregiving and what factors contribute to and are affected by caregiver esteem. Qualitative studies are needed to help develop hypotheses that can then be tested in larger samples. The relationship between HF patients and their caregivers is not well understood and ideas for qualitative studies that can lead to hypothesis generation are discussed later in this chapter, in the section for 'implications for future research'.

Section 5.2 b, c
Discussion of Study Results
Secondary Objective- Caregiver Appraisal
Summary

In summary, caregiver support is extremely important for helping HF patients live with their chronic disease. This study supports previous findings that suggest caregivers experience daily demands on their time and energy in order to fulfill caregiving responsibilities. These demands are similar to caregivers of patients with advanced cancer living at home or patients who are frail and elderly (Grov & Eklund, 2008) but lower than demands for caregivers of people with dementia awaiting longer term care placement (Meiland et al., 2001). There is a strong relationship between caregiver emotional status and caregiver burden; however the direction of this relationship is unknown. Finally, many common demographic and medical variables collected in studies of caregivers for HF patients, in addition to the emotional status of patient and caregivers measured in this study; did not contribute to the positive aspects of caregiving. There is a dearth of literature examining the possible contributors to positive aspects of caregiving.

Section 5.3a
Discussion of Study Results
Exploratory Analysis – Longitudinal Data
HADS, MUIS, CRA Scores

Hospital Anxiety and Depression Scores- Changes between Baseline, 2 Months, 4 Months

There were minimal changes in symptoms of anxiety and depression in HF patients between baseline and 4 months. Patients with higher levels of depression at baseline were more likely to withdraw from the study than patients with no symptoms of depression and may have influenced the results. Of note, between baseline, 2 months and 4 months, the functional class of patients improved, where 28/35 (80%) of patients were NYHA III-IV at baseline and only 20/35 (57%) by 4 months. Thus, even though there was an improvement in the functional capacity of patients between baseline and 4 months, symptoms of depression did not improve to the same magnitude. These study findings were similar to those of Koenig et al. (2006) where symptoms of depression remain unchanged while physical symptoms improved when measured in hospital and 12 weeks later. Thus, it appears that symptoms of depression can change over time, but changes are relatively small and do not always follow in the same direction as physical capacity. Future studies will require large sample sizes to determine if there is a significant change in symptoms of depression over time and what factors contribute to these changes. As mentioned earlier, initial power calculations for this PhD study determined that a sample size of 235 patient-caregiver pairs would be needed to detect a significant change in HADS-depression scores.

Caregivers experienced higher symptoms of anxiety than patients at baseline and there was a trend for these values to decrease over time. Perhaps caregivers' feelings of anxiety decreased as they became more comfortable with the caregiver role. Spousal caregivers have been reported to experience feelings of anxiety, especially after HF was diagnosed (Luttik et al., 2007b). Even though many of the HF patients in this PhD study had advanced symptoms of HF, 35% had been diagnosed with HF in the last year and over 50% had been admitted for HF in the 2 months prior to baseline testing. Perhaps caregivers felt increased anxiety when HF patients first came home from a recent hospital admission and some of this anxiety was detected in baseline caregiver HADS-anxiety scores. Increased anxiety has been reported by caregivers of elderly patients immediately following hospital discharge (Grimmer et al., 2000), in the first six weeks following hospital discharge for cardiac surgery (Davies, 2000) and in the first 4-5 months following an MI or coronary artery bypass surgery (Moser et al., 1993). Finally, education and reassurance from the HF clinic staff may have also alleviated some of the worries and concerns caregivers were initially experiencing.

In summary, symptoms of depression in patients decreased over time, but the change was very small, even though there was an overall improvement in functional capacity by 4 months. Symptoms of anxiety decreased over time, and although this change did not reach statistical significance, this value represented the largest change in the HADS scores in patients and caregivers over time.

Uncertainty in Illness Scores- Changes between Baseline, 2 Months and 4 Months

This is the first study to measure levels of uncertainty in patients attending a HF clinic. There is a possibility that the significant decrease in uncertainty between baseline and 4 months could have been a result of education received from the health care team in the HF clinic. HF clinics, in general, have been shown to improve outcomes in HF patients and one of the key nursing interventions has been patient education (McAlister et al., 2004). The MUIS appears to be responsive to the change in patient knowledge about their disease. Relevance to clinical outcomes associated with a significant decrease in MUIS scores still needs to be determined.

This is the first study to measure levels of uncertainty in caregivers of HF patients attending a HF clinic. Mean scores in male caregivers (of male or female HF patients) decreased over 10 points between baseline and 4 months, however, due to small numbers this did not reach statistical significance. All caregivers accompanied the patient to the HF clinic appointment at baseline, but not all caregivers attended patient follow up visits. Thus, caregivers may not have received the same 'dose' of education as patients and therefore no significant changes were detected over time. Information regarding caregiver attendance to HF clinic patient appointments was not collected. Because uncertainty levels did not correlate with caregiver symptoms of anxiety, the decrease in caregiver MUIS scores was not mediated by a decrease in caregiver HADS-anxiety scores between baseline, 2 months and 4 months.

In summary, female *patients* and male *caregivers* appeared to experience the largest decrease in uncertainty scores between baseline and 4 months. This decrease in levels of uncertainty may have been a result of participation in the HF clinic. There is a potential role for individual item scores on the uncertainty scale items to help guide health care professionals about areas for education and clarification to decrease uncertainty in HF patients and their caregivers. Decreases in uncertainty scores may be a reasonable outcome measurement for HF clinic program evaluation; however further testing with the MUIS to decrease respondent burden is needed.

Caregiver Reaction Assessment Scores- Changes between Baseline, 2 Months and 4 Months

There was a very small amount of change in CRA scores between baseline, 2 months and 4 months. Even though the tool has strong psychometric properties, it has been primarily used in cross-sectional studies, and its responsiveness is not fully understood. Furthermore, this generic tool may not be sensitive enough to detect changes in the caregiver experience and a disease specific tool is needed. Another possibility is that significant changes in the caregiver experience take longer than 4 months to become apparent and a longer follow up period is needed.

Section 5.3b
Discussion of Study Results
Exploratory Analysis – Longitudinal Data
HADS, MUIS, CRA Correlations

Relationships between Patient and Caregiver Emotional Status

The strength of the correlation between patients and their caregivers' emotions which, over time became clinically meaningful, highlights the fact that living successfully with HF often demands the help of a caregiver and that management of the disease is a 'team approach'. It also suggests that helping patients and caregivers cope with HF needs to address both patient and caregiver emotions. In a small intervention study, an advanced practice nurse used the Calgary Family Systems Nursing Approach (CFSNA) to help support HF patients and their spouses (Duhamel et al., 2007). Participants felt that this approach helped them better understand each other's experience and gain a new perspective on each other's behaviour. Couples felt this intervention improved their adjustment to the impact of HF on their lives.

Relationships between Uncertainty and Emotional Status

Contrary to the findings related to patients and caregiver emotions, the relationship between uncertainty in patients and caregivers weakened and no longer existed over time. Even though caregivers are encouraged to attend clinic appointments with the HF patient, this was not always feasible for caregivers and therefore HF patients' levels of uncertainty decreased more than caregivers.

Relationships between caregiver burden and patient and caregiver emotional status

Baseline relationships between *caregiver* emotions and caregiver burden were quite strong at all measurement times. Although no relationships between symptoms of anxiety and depression in *patients* and caregiver burden existed at baseline, significant correlations did emerge between symptoms of anxiety and depression in patients and caregiver burden at 2 months and 4 months. Caution must be applied when interpreting these results since the number of patient-caregiver pairs was quite small by the 4-month follow-up (n=35 pairs). One possibility for these findings could be that HF patients who continue to have symptoms of anxiety or depression beyond a few months may contribute to caregiver burden. Another possibility is that there is a change in the variability of HADS and CRA scores between baseline and 4 months and thus, relationships between these scores became statistically easier to detect. Even with a small sample size, it is important to realize that these correlations are not static and longitudinal study designs would be extremely helpful in understanding the dynamics of these relationships.

Summary

In summary, it is important to highlight that examination of the correlations among patient and caregiver HADS, MUIS and CRA scores over time was strictly for exploratory purposes and hypothesis generation and no definite conclusions can be made from these data. Although some baseline correlations strengthened over time, some weakened and others did not change. Interpretation of these observations is limited by the study sample size; however, it is obvious that the presence of relationships between patient and caregiver emotions, levels of uncertainty and caregiver burden are not static and a longer period of observation is needed.

Section 5.4a

Strengths and Limitations

Strengths

The demographic profile of patients is one of the strengths of this study. The patient sample was older, had a good representation of female patients, included many patients with advanced symptoms of HF and therefore was similar to the HF population that is hospitalized with HF. In the sample of 48,612 patients enrolled in the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure (OPTIMIZE-HF), the mean (SD) age of patients admitted to hospital with HF was 73.1 (±14.0) years and 52% were female (Abraham et al., 2008). In Canada, the mean age of patients admitted to hospital for the fiscal year 2000 was 75.9 years and 50.3% were female (Tsuyuki et al., 2003).

The demographic profile of caregivers is another strength. A relatively larger proportion of caregivers who were male or were adult children of patients with HF were enrolled in this study when compared to similar studies in the literature. Thus, new insight into sex and relationship differences in caregiver outcomes was possible and provides excellent ground work for future research.

To our knowledge, this is one of the first studies to measure symptoms of anxiety and levels of uncertainty in caregivers of HF patients. Findings from these two variables provided valuable information and the opportunity for hypothesis generation to guide future research. Symptoms of anxiety were prevalent in this study and associated with caregiver burden. Feelings of uncertainty in this study were as high as feelings of uncertainty reported in caregivers of patients with cancer.

Limitations

The drop out rate in this study (30%) was higher than the estimated drop out rate (10%) and limited the statistical power of baseline data analyses. However, participants in this study had advanced heart failure and event rates are known to be high. Six patients withdrew from the study because of significant health problems that required hospitalization. Furthermore, drop out rates may be higher in pairs research because once either member of the pair could no longer continue in the study; *both* members of the pair were excluded from further study participation.

The generalizability of study findings may be limited because patients in this study were recruited from a HFC located in a tertiary care centre. These patients may not be representative of HF patients living in the community who do not attend the HFC. To date, there are no published studies exploring referral patterns to outpatient HF clinics; however, the CCS guidelines suggest that all patients with HF should be referred to a specialized HFC when available and accessible (Arnold et al., 2008).

Patients and caregivers in this study were exposed to a team of highly specialized nurses and physicians that have worked closely together in the HFC for over five years. Thus, patient-caregiver pairs tend to receive a consistent approach to management of their disease and application of supportive-educational strategies. Findings from this study may not be relevant to patient-caregiver pairs who interact with different health care professionals, such as members of family health care teams. Variables such as patient-caregiver relationships with the team of health care professionals, content and delivery of information provided for patient-caregiver pairs, or consistency of the approach to management of the HF may be different between these clinical settings and potentially influence outcomes measured in this PhD study. Although such information is not published in the HF literature, these variables have been identified as relevant to principles of adult education, (Knowles, 1970).

The generalizability of this PhD study is also limited to patient-caregiver pairs that are fluent in the English language and live in a Western society. The dynamics of the patient-caregiver relationship may be quite different in other ethnic groups who have different cultural norms and results from this PhD study cannot be generalized to these populations. Future research is needed in culturally diverse population and discussed in the 'implications for future research' within this thesis.

The lack of internal consistency in the CRA esteem subscale was a limitation of this study. This was unexpected since other studies using the CRA have not reported this finding and the CRA has undergone extensive psychometric testing in many populations (Harkness & Tranmer, 2007). In this study, item #21 (I can never do enough caregiving to repay my partner) was removed to improve the internal consistency. In the study of caregivers of patients with colorectal cancer (Nijboer et al., 1999), internal consistency of the self-esteem subscale using Cronbach's alpha improved from 0.73 to 0.83 when the same item was removed. Thus, future studies using the CRA should construct an inter-item correlation matrix and reliability coefficient for each subscale to ensure adequate reliability of the instrument scores. Factor analysis would also help to determine if these items can be removed without sacrificing the validity of the subscale.

Section 5.4b

Implications for Clinical Practice and Future Research

Clinical Practice

Symptoms of Anxiety and Depression- Implications for Clinical Practice

The prevalence of symptoms of depression in HF patients and symptoms of anxiety in their caregivers was quite high and demand the attention of clinicians caring for HF patients. Clinicians need to screen for emotional distress, such as anxiety and depression in HF patients and their caregivers and recognize the presence of these feelings when interacting with HF patients and their caregivers. Results from this study suggested a trend in the relationship between patient and caregiver emotions. Thus, if a HF patient presents with symptoms of depression, clinicians need to carefully screen for symptoms of anxiety or depression in their primary caregiver. If there is a strong possibility that this caregiver may have symptoms of anxiety or depression, clinicians must also carefully explore the possibility of co-existing caregiver burden.

Common emotions, including symptoms of anxiety and depression and caregiver burden experienced by HF patients and caregivers needs to be included in patient and caregiver education and education for health care professionals interacting with this patient population. Currently, the majority of education resources regarding living successfully with HF include information such as diet, medications, exercise and daily weight behaviours and do not include the emotional reactions of patients and caregivers. Health care professionals interacting with this patient population need to be educated on the common emotional reactions. Clinicians need to acknowledge that emotional distress is common and help HF patients and their primary caregivers explore their feelings and help them develop strategies to overcome these negative emotions.

There was a trend for younger patients with HF, or those who were not retired, to report higher levels of depression than older HF patients and those who were retired. Furthermore, caregivers of younger patients who were not retired reported higher levels of caregiver financial burden. In the clinical setting, clinicians may need to be more attentive to the financial implications of living with HF in younger HF patients and those who are not retired. For example, pharmacological management of HF often involves multiple medications and clinicians may need to be creative in ensuring medication regimens are evidence-guided while requiring the lowest possible financial cost for the HF patient. Younger HF patients and their caregivers may also require assistance from clinicians to clarify the impact of HF on their ability to return to previous employment and alternative employment strategies may need to be explored. These patients and their caregivers may require referral to a social worker for assistance with current financial difficulties or for assistance with employment strategies such as return-to-work or applying for disability programs.

Patient and Caregiver Uncertainty- Implications for Clinical Practice

Even though uncertainty scores from patients and their caregivers were mainly for exploratory analyses, there are some clinical implications that can be extrapolated from these results. Findings from this study suggest that feelings of uncertainty in HF patients and their caregivers are common and clinicians need to better understand factors contributing to these feelings. Education strategies need to target information that will help both patients and caregivers overcome their feelings of uncertainty. For example, education regarding self-care and self-management may help patients and caregivers better understand the daily management and course of HF. With this information, they may be better able to predict the ability of the HF patient or caregiver when participating in daily activities and special events such as holidays. Information regarding details of prognosis is not fully understood by clinicians and decreasing uncertainty regarding the prognosis for an individual HF patient may be rather difficult. When discussing uncertainty related to prognosis, clinicians need to simply acknowledge the limited current information and challenges when trying to provide an accurate prognosis. In this situation, the approach of 'preparing for the worse, but hoping for the best' has been recommended in palliative care for patients with cancer (Evans et al., 2006).

Results from this study also suggested that more patients versus caregivers experienced a larger decrease in uncertainty over time. The usual care practices in the HFC *encourage versus require* caregivers to attend patient HFC appointments. Even though caregivers needed to be present during the patient HFC appointment at baseline, this was mainly due to recruitment strategies outlined in this study protocol versus usual practices within the HFC. The study protocol did not require primary caregivers to attend follow up appointments with the HF patient and often data from caregivers at 2 and 4 months was obtained through the postal system. As a result of these situations, patients, rather than caregivers, may have been exposed to more interactions with the HFC team, which contributed to a larger decrease in patient versus caregiver uncertainty over time. This finding has relevance to the clinicians working in the HFC setting.

Clinicians working in an outpatient HFC setting need to better understand the barriers and facilitators of caregivers attending the HFC and determine if caregiver uncertainty is not being resolved because of the caregiver's inability to attend patient HFC appointments. Furthermore, clinicians in a HFC setting need to better understand methods to target caregiver uncertainty that extend beyond the usual care practices within the HFC. For example, caregivers could be encouraged to contact the HFC nurses through telephone or electronic mail if they have questions or concerns. Clinicians can provide a written summary of highlights from the HFC visit (reason for change in medication, follow up blood tests or diagnostic tests) that the patient can share with their primary caregiver. This practice has been recently implemented in the HFC and has had a favourable response from patients and caregivers to date.

Caregiver Burden- Implications for Clinical Practice

Finally, results from this study highlight the presence of caregiver burden experienced by caregivers of HF patients, even in the presence of caregiver self-esteem. Caregivers play key roles in helping patients live with HF, and yet, this may come at the expense of caregiver outcomes. Chronic disease management strategies claim that interventions that help develop self-care skills in HF patients are necessary for improving patient outcomes. However, clinicians need to be aware of the impact of such strategies on primary caregivers. For example, dietary changes may require challenges for caregivers who buy the groceries and prepare meals. Time is required to learn label reading or cooking meals versus using ready-made, prepared foods and caregivers may have difficulty with the time commitment needed for these changes that are part of HF self-management. Transportation to patient appointments may be burdensome for caregivers because of conflicting responsibilities, such as child care or employment, and clinicians need to find creative methods to closely monitor unstable HF patients in an outpatient setting while minimizing multiple visits to the HFC. Finally, clinicians also need to be sensitive to the challenges that caregivers may experience with their caregiving roles and ensure psycho-educational support for caregivers is part of their routine care when interacting with primary caregivers.

Implications for Research

The trends in relationships in patient and caregiver emotions, feelings of uncertainty and caregiver burden from this study suggest that further research needs to recruit HF patient-caregiver pairs. When conducting research with dyads, there is an underlying assumption that the interdependence between each member of the pair contributes to the responses (West et al., 2008). Studies recruiting patient-caregiver dyads in the HF population are subject to many challenges- both logistically and statistically. In this study, even when the patient met all the inclusion criteria, 19% of those excluded were due to caregiver variables. Also, drop out rates may be higher than in studies that recruit patients or caregivers separately. Finally, statistical procedures needs to assume that both members of the pair are interdependent and adhere to guidelines for dyadic research analysis, which is quite complex.

The main purpose of this study was to determine if there was a relationship between the emotions of HF patients and their primary caregivers. Although a significant correlation between these variables was not detected in this study, the results revealed that the correlation between the emotional status of patients and their caregivers strengthened over time. This finding suggests that future research needs to focus on determining the variables that affect the strength of the correlation between patient and caregiver emotional status. In such a study design, the *strength* of the correlation between patient and caregiver emotions becomes the outcome of interest. Theoretical underpinnings for such a study could be based on family systems theory (Wright & Leahey, 1990) and use structural equation models to help describe these inter-related variables and their influence on patient and caregiver outcomes.

Another possibility for future research would be to explore the contextual and perceptual variables in the relationship between HF patients and caregivers in qualitative research designs and described in the context of social exchange theory. This theory has been used to describe the dynamics of the relationship between family members caring for frail elders living at home (Phillips &

Rempusheski, 1986 and has been applied to findings describing the differences between the caregiving experience in younger versus older spousal caregivers for adults with functional limitations (Lima et al., 2008). Because this theory is situated in a social context, variables such as ethnicity and cultural norms are embedded in the contextual landscape in which patients and caregivers interact. This type of research inquiry would provide an excellent opportunity for a transdisciplinary research team that could be comprised of nurses, sociologists, anthropologists and psychologists.

In this PhD study, and in the study by Saunders (2008), caregivers who were adult children reported higher levels of caregiver esteem than spousal caregivers. Future research striving to better understand this finding could explore dimensions of the quality of the interaction and exchanges between HF patients and their caregivers using a newly developed Caregiver Reciprocity Scale (Carruth, 1996). Although identification of important moderators and mediators in the relationship between patient and caregiver outcomes is necessary for future intervention studies, there is a dearth of information exploring potential variables and future research needs to stress qualitative methodologies for hypothesis generation that can then be used to guide hypothesis testing.

The measurement of uncertainty in HF patients and their caregivers needs further development. To date, the MUIS-C is the only tool available to measure this construct, but challenges in the response format and unidimensional nature of this tool are significant limitations. Conversely, the responsiveness of the tool in this study was evident in the patient and caregiver samples. Alternative versions of the current MUIS-C that minimize respondent burden and provide a multidimensional representation of the construct are needed.

Future research aiming to clarify the relationship between uncertainty and clinical outcomes in the HF population may need to also measure perceived control. Using the stress-adaptation theoretical approach to understanding emotional reactions of HF patients and their caregivers, this study explored the construct of uncertainty; however the concept of perceived control has also been described in the HF literature in the context of a similar theoretical approach. Perceived control in HF patients was associated with lower levels of anxiety and depression (Moser et al., 2009) and perceived control was an independent predictor of emotional well being for spouses of patients with advanced HF (Dracup et al., 2004). Future research could explore the relationships amongst patient and caregiver emotional status, uncertainty and perceived control to further understand psychosocial adaptation to either living with HF or caring for someone with HF.

When designing this study, choosing an instrument that measured both the negative *and* positive aspects of caregiving was important to the study design. However, few variables correlated with positive subscale of the CRA. The positive aspects of caregiving and the effect on patient and caregiver outcomes continue to be poorly understood. Even though the positive scale of the CRA did not have sufficient internal consistency in this study, this tool has performed well in other studies. Furthermore, the only other scale that measured the positive aspects of caregiving for caregivers of HF patients does not have superior psychometric properties to the CRA (Harkness & Tranmer, 2007; Schwartz & Elman, 2003). A new disease-specific tool for caregivers of HF patients does not include a positive domain (Luttik et al., 2008) and therefore the CRA continues to be the best instrument to measure positive aspects of caregiving for caregivers of HF patients to date. Future research measuring the positive aspect of caregiving in similar studies should use the CRA, but psychometric evaluation of the positive subscale should be part of the study analyses.

Chapter 5. Summary

Patients living with HF experience symptoms of depression and their caregivers experience symptoms of anxiety. There was a trend for a relationship between HF patient and caregiver symptoms of depression and further research with a larger sample size is needed to verify that this relationship exists and subsequently identify variables that are mediators. Feelings of uncertainty have been described by HF patients and their caregivers in qualitative studies and this was the first study to measure uncertainty in HF patient-caregiver pairs. Even though there was a significant relationship in HF patient and caregiver feelings of uncertainty, surprisingly, there was no relationship between HF patient and caregiver emotions and feelings of uncertainty. Limitations with the instrument measuring uncertainty may have contributed to the negative findings and further testing of this tool, with possible refinement to increase the validity and decrease responded burden, is needed. Finally, this study supports findings from other studies suggesting a strong relationship between caregiver emotions and caregiver burden. Many variables did not correlate with the positive aspects of caregiving and there continues to be a dearth of information in this area. Results from this study have provided new insight into the areas of patient and caregiver emotions, feelings of uncertainty and caregiver burden and have also provided evidence to help inform clinical practice and future research endeavors.

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APPENDIX A

Diagnostic Criteria for Heart Failure

Appendix A. Diagnostic Criteria for Heart Failure

The patient must have at least one subjective and one objective finding documented in the health record.

Subjective:
Decrease in effort tolerance due to dyspnea
Orthopnea
Paroxysmal nocturnal Dyspnea (PND)
Bilateral peripheral edema

Objective:
Rales
Pulmonary congestion on chest x-ray
Jugular venous pressure >4cm above the sternal angle
Positive hepatojugular reflux
Abdominal tenderness secondary to liver congestion
S3 gallop
Bilateral pitting edema

(Adapted from the Framingham Criteria for Congestive Heart Failure as printed in Ho et al. (1993))

APPENDIX B

Patient and Caregiver Information Forms and Consents

Appendix B. Patient and Caregiver Information Forms and Consents

University and Hospital Letterhead

" Patients with Heart Failure and their Primary Caregivers' Emotions"
Principal Investigator: Karen Harkness RN BScN

You are being invited to participate in a research project that is hoping to help us learn more about some of the emotions that both people with heart failure and their primary caregiver may experience.

One of you has been treated for heart failure. We know that heart failure is a chronic condition that can lower quality of life for some people. In addition, patient's caregivers may become worried or depressed.

The purpose of this project is to find out if there is a link between the feelings or emotions of someone with heart failure and their caregiver.

What happens if we join the project?

Each of you will be asked to complete two surveys about your feelings and emotions and again in two and four months. If you are caregiver of the person with heart failure, you will have one additional survey to complete each time. It will probably take each of you less than 20 minutes to complete the surveys each time.

The two-month and four-month follow-up surveys can be completed during a regular appointment in the Heart Function Clinic or they will be mailed to your home.

Are there any benefits for us by joining this project?

Not directly. You will be helping us learn more about the feelings and emotions people with heart failure and their caregivers' experiences. We can then learn how to better treat people with heart failure and help their caregivers as well. If your survey answers show that you may need medical treatment for your emotions, Karen Harkness will contact your family doctor with your permission.

Are there any risks for us joining this project?

There are no expected risks to your participation.

Appendix B. Patient and Caregiver Information Forms and Consents (continued)

Who is funding this project?

Karen Harkness is a registered nurse who is presently working on her Doctorate degree in Clinical Health Sciences at McMaster University. She is being supported by a student fellowship award from the Heart and Stroke Foundation of Canada.

Do we get paid for joining this project?

You will not be paid for participating in this research project.

What happens to the information on the surveys we complete?

All information that is collected in this study will be confidential and carefully protected in a locked office in the Heart Function Clinic at McMaster Hospital. Only Karen Harkness will have a key to this cupboard. You will be given a special study code number and not be identified by name on any research documents.

Joining this research project is completely voluntary. You may refuse to participate and may withdraw from the project at any time without your care being affected.

If you would like to know the results of this project, you may contact Karen Harkness or her supervisor. The names and phone numbers are listed below.

Who do we talk to if we have any questions or concerns about this project?

If you have any questions or concerns about this project, please feel free to call:

Karen Harkness (Investigator) 905-521-2100, Ext. 76219
Dr. Heather Arthur (Supervisor) 905-525-9140, Ext. 22270

You may also contact the Hamilton Health Sciences Patient Relations Specialist at 905-521-2100, Ext.75420

Appendix B. Patient and Caregiver Information Forms and Consents (continued)

University and Hospital Letterhead

" Patients with Heart Failure and their Primary Caregivers' Emotions"
Principal Investigator: Karen Harkness RN BScN
Patient Consent Form

I have read the information on pages 1 and 2 of the Information Sheet for the research project " Patients with Heart Failure and their Primary Caregivers' Emotions" and it has been explained to me by

____________________________________.

I have had the chance to have my questions answered and I agree to participate in this project. I will receive a signed copy of the form and the information sheet.

Patient Signature: ____

Date: _______________

Patient name: (please print) __________________________________

Primary Caregiver Name (please print) ____________________________

Witness Signature: ______________________________

Date: ______________

Witness name: (please print) __________________________________

Appendix B. Patient and Caregiver Information Forms and Consents (continued)

University and Hospital Letterhead

" Patients with Heart Failure and their Primary Caregivers' Emotions"
Principal Investigator: Karen Harkness RN BScN
Primary Caregiver Consent Form

I have read the information on pages 1 and 2 of the Information Sheet for the research project " Patients with Heart Failure and their Primary Caregivers' Emotions" and it has been explained to me by

______________________________________.

I have had the chance to have my questions answered and I agree to participate in this project. I will receive a signed copy the form and the information sheet.

Primary Caregiver Signature: ______________________________

Date: ____________________

Primary Caregiver Name (please print): ______________________________

Patient Name (please print): ______________________________

Witness Signature: ______________________________

Date: ____________________

Witness name (please print): ______________________________

APPENDIX C

Patient and Caregiver Demographic and Health History Forms

Appendix C. Patient Case Record

DOB(mm/dd/yr) ______________________Age_______Sex______
HCN____
Highest Education: Grade school____ High school____ >Highschool____

Cardiac History:
Type : ☐ ischemic ☐ non-ischemic
Onset of HF: YR______________
LVEF______date______________

Attended HFC prior to study ______

Cardiac History: (mm/dd/yy/)
___MI date______________
___ICD date:_____________
___CRT: _______________
___Pacemaker: ____________
___CABG/Valve date: _______
___PCI date: _____________
Atrial fibrillation

Cardiac Risk Factors:
Family History___Current Smoking____ History Smoking____
Cholesterol____Hypertension____Diabetes____Obesity____ETOH____

Major health comorbidities
Cancer ____(past/present)CVA ____PVD ____Arthritis ____COPD ____
Chronic renal failure (baseline >130)____

Baseline (mm/dd/yy)___________________
Most recent Hospitalization: Discharge date_____________
Diagnosis HF _____ other cardiac_________ other ___________

Events between baseline, T2, T3 (mm/dd/yy)
Date T2:___________________ Date: T3__________________
Visits to HF clinic:
Date: _______________Date:_____________ Date:_____________
Date: _______________Date:_____________ Date:_____________
Hospitalizations:
Date adm____________date Dch______________LOS ______
Diagnosis________________elective ____
Date adm______++_____date Dch______________LOS ______-
Diagnosis________________ elective ____
Death
Date: ____________________ Cause of death: HF ________

Withdrawal: Reason ______________________________________

Appendix C. Caregiver Demographic Questionnaire

Please complete the following questions

Age______years

Male_____ Female______

Relationship to the person with heart failure: (please check one)

Spouse/Partner___ Daughter____ Son___ Daughter in-law____ Son in-law____

Friend_____ Other________________

Living Arrangements: (please check one)

With patient______ Separate residence_____

Employment: (please check one)

Full time____ Part time_____ Retired______other____________________

Do you have any of the following health problems?

	Yes	No
Heart disease		
Cancer (past or present)		
Stroke		
Arthritis		
COPD		
Diabetes		

APPENDIX D

Hospital Anxiety and Depression Scale
(Zigmond and Snaith, 1983)

Appendix D. Hospital Anxiety and Depression Scale

Doctors and nurses are aware that emotions play an important part in most illnesses. If your doctor or nurse knows about these feelings, they will be able to help you more. This questionnaire is designed to help your doctor or nurse know how you feel. Read each item and place a firm tick in the box beside the reply that comes closest to **how you have been feeling in the past week**.

Don't take too long over your replies; your immediate reaction to each item will probably be more accurate than a long thought out response.

I feel tense or 'wound up':

☐ Most of the time
☐ A lot of the time
☐ Time to time, Occasionally
☐ Not at all

I still enjoy the things I used to enjoy

☐ Definitely not as much
☐ Not quite so much
☐ Only a little
☐ Hardly at all

I get a sort of frightened feeling as if something awful is about to happen:

☐ Very definitely and quite badly
☐ Yes, but not too badly
☐ A little, but it doesn't worry me
☐ Not at all
☐

I can laugh and see the funny side of things:

☐ As much as I always could
☐ Not quite so much now
☐ Definitely not so much
☐ Not at all
☐

Worrying thoughts go through my mind:

☐ A great deal of the time
☐ A lot of the time
☐ From time to time, but not too often
☐ Only occasionally

Appendix D. Hospital Anxiety and Depression Scale (continued)

I feel cheerful:

- ☐ Not at all
- ☐ Not often
- ☐ Sometimes
- ☐ Most of the time

I can sit at ease and feel relaxed:

- ☐ Definitely
- ☐ Usually
- ☐ Not often
- ☐ Not at all

I feel as if I am slowed down:

- ☐ Nearly all of the time
- ☐ Very often
- ☐ Sometimes
- ☐ Not at all

I get a sort of frightened feeling like 'butterflies' in the stomach:

- ☐ Not at all
- ☐ Occasionally
- ☐ Quite often
- ☐ Very often

I have lost interest in my appearance:

- ☐ Definitely
- ☐ I don't take so much care as I should
- ☐ I may not take quite as much care
- ☐ I take just as much care as ever

I feel restless as if I have to be on the move:

- ☐ Very much indeed
- ☐ Quite a lot
- ☐ Not very much
- ☐ Not at all

Appendix D. Hospital Anxiety and Depression Scale (continued)

I look forward with enjoyment to things:

- ☐ As much as I ever did
- ☐ Rather less than I used to
- ☐ Definitely less than I used
- ☐ Hardly at all

I get sudden feelings of panic:

- ☐ Very often indeed
- ☐ Quite often
- ☐ Not very often
- ☐ Not at all

I can enjoy a good book or radio or TV show:

- ☐ Often
- ☐ Sometimes
- ☐ Not often
- ☐ Very seldom

APPENDIX E

Mishel Uncertainty In Illness Scale- Community Version (Mishel, 1997)

Appendix E. Mishel Uncertainty in Illness Scale- Community Version (Patient Form)

Please read each statement. Take your time and think about what each statement says. Then place an 'X' under that column that most closely measures how you are feeling **TODAY.**
If you agree with a statement, then you would mark under either "Strongly Agree" or "Agree".
If you disagree with a statement, then you would mark under either "Strongly Disagree" or "Disagree".
If you are undecided about how you feel, then make under 'Undecided' for that statement
Please respond to every statement.

1. I don't know what is wrong with me.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

2. I have a lot of questions without answers.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

3. I am unsure if my heart failure is getting better or worse.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

4. It is unclear on how bad my heart failure will be.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

5. The explanations they give about my heart failure seem hazy to me.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

6. The purpose of my heart failure treatment is clear to me.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

Appendix E. Mishel Uncertainty in Illness Scale- Community Version (Patient Form) (continued)

7. My symptoms of heart failure continue to change unpredictably.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

8. I understand everything explained to me.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

9. The doctors say things to me that could have many meanings.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

10. My heart failure treatment is too complex to figure out.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

11. It is difficult to know if the treatments or medications I am getting are helping.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

12. Because of the unpredictability of my heart failure, I cannot plan for the future.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

13 The course of my heart failure keeps changing. I have good days and bad days.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

Appendix E. Mishel Uncertainty in Illness Scale- Community Version (Patient Form) (continued)

14. I have been given many differing opinions on what is wrong with me.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	_____	_____	_____	_____

15. It is not clear what is going to happen to me.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	_____	_____	_____	_____

16. The results of my heart tests are inconsistent.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	_____	_____	_____	_____

17. The effectiveness of my heart failure treatment is undetermined.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	_____	_____	_____	_____

18. Because of my heart failure treatment, what I can and cannot do keeps changing.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	_____	_____	_____	_____

19. I am certain they will not find anything else wrong with me.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	_____	_____	_____	_____

20. The treatment for my heart failure that I am receiving has a known probability to success.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	_____	_____	_____	_____

Appendix E. Mishel Uncertainty in Illness Scale- Community Version (Patient Form) (continued)

21. They have not given me a specific diagnosis.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	_____	_____	_____	_____

22. The serious of my heart failure has been determined.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	_____	_____	_____	_____

23. The doctors and nurses use everyday language so I can understand what they are saying.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	_____	_____	_____	_____

Appendix E. Mishel Uncertainty in Illness Scale- Community Version (Family Member Form)

Instructions
Please read each statement. Take your time and think about what each statement says. Then place an 'X' under that column that most closely measures how you are feeling **TODAY.** If you agree with a statement, then you would mark under either "Strongly Agree" or "Agree".
If you disagree with a statement, then you would mark under either "Strongly Disagree" or "Disagree".
If you are undecided about how you feel, then make under 'Undecided' for that statement
Please respond to every statement.

1. I don't know what is wrong with him/her.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	_____	_____	_____	_____

2. I have a lot of questions without answers.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	_____	_____	_____	_____

3. I am unsure if his/her heart failure is getting better or worse.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	_____	_____	_____	_____

4. It is unclear on how bad his/her heart failure will be.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	_____	_____	_____	_____

5. The explanations they give about his/her heart failure seem hazy to me.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	_____	_____	_____	_____

6. The purpose of each treatment for him/her is clear to me.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	_____	_____	_____	_____

7. I do not know when to expect things will be done to him/her.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	_____	_____	_____	_____

Appendix E. Mishel Uncertainty in Illness Scale- Community Version (Family Member Form) (continued)

8. His/her symptoms continue to change unpredictably

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	______	______	______	______

9. I understand everything explained to me.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	______	______	______	______

10. The doctors say things to me that could have many meanings.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	______	______	______	______

11. I cannot predict how long his/her heart failure will last.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	______	______	______	______

12. His/her treatment is too complex to figure out.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	______	______	______	______

13. It is difficult to know if the treatments or medications he/she is getting are helping.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	______	______	______	______

14. There are so many different types of staff; it's unclear who is responsible for what.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	______	______	______	______

15. Because of the unpredictability of his/her heart failure, I cannot plan for the future.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	______	______	______	______

16.The course of his/her heart failure keeps changing. I have good days and bad days.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
______	______	______	______	______

Appendix E. Mishel Uncertainty in Illness Scale- Community Version (Family Member Form) (continued)

17. It's vague to me how I will manage the care of him/her after he/she leaves the hospital.

Strongly Agree Agree Undecided Disagree Strongly Disagree
______ ______ ______ ______ ______

18. It is not clear what is going to happen to him/her.

Strongly Agree Agree Undecided Disagree Strongly Disagree
______ ______ ______ ______ ______

19. I usually know if he/she is going to have a good or bad day.

Strongly Agree Agree Undecided Disagree Strongly Disagree
______ ______ ______ ______ ______

20. The results of his/her heart tests are inconsistent.

Strongly Agree Agree Undecided Disagree Strongly Disagree
______ ______ ______ ______ ______

21. The effectiveness of his/her heart failure treatment is undetermined.

Strongly Agree Agree Undecided Disagree Strongly Disagree
______ ______ ______ ______ ______

22. It is difficult to determine how long it will be before I can care for him/her by myself.

Strongly Agree Agree Undecided Disagree Strongly Disagree
______ ______ ______ ______ ______

23. I can generally predict the course of his/her heart failure.

Strongly Agree Agree Undecided Disagree Strongly Disagree
______ ______ ______ ______ ______

24. Because of the heart failure treatment, what he/she can and cannot do keeps changing.

Strongly Agree Agree Undecided Disagree Strongly Disagree
______ ______ ______ ______ ______

25. I am certain they will not find anything else wrong with him/her.

Strongly Agree Agree Undecided Disagree Strongly Disagree
______ ______ ______ ______ ______

Appendix E. Mishel Uncertainty in Illness Scale- Community Version
(Family Member Form) (continued)

26. They have not given him/her a specific diagnosis.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

27. His/her physical distress is predictable: I know when it is going to get better or worse.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

28. His/her diagnosis is definite and will not change

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

29. I can depend on the nurses to be there when I need them.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

30. The seriousness of his/her illness has been determined.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

31. The doctors and nurses use everyday language so I can understand what they are saying.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
_______	_____	_____	_____	_____

APPENDIX F

Caregiver Reaction Assessment
Given et al., 1992

Appendix F. Caregiver Reaction Assessment

This questionnaire is designed to help us know about your experience with helping take care of your loved one or close friend who has heart failure. Read each question and place a tick in the box beside the reply that comes closest to your experiences with caregiving **over the past month.**

My activities are centred around care for my loved one or partner.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

I am healthy enough to take care of my loved one or partner.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

My family works together at caring for my loved one or partner.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

Caring for my loved one or partner is important for me.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

It takes all my physical strength to care for my loved one or partner.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

I enjoy caring for my partner
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

I have to stop in the middle of my work or activities to provide care.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

My health has gotten worse since I've been caring for my loved one or partner.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

Since caring for my loved one or partner, I feel my family has abandoned me.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

Caring for my loved one or partner makes me feel good.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

It is very difficult to get help from my family in taking care of my loved one or partner.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

I feel privileged to care for my loved one or partner.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

Appendix F. Caregiver Reaction Assessment (continued)

Others have dumped caring for my loved one or partner onto me.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

I have eliminated things from my schedule since caring for my loved one or partner.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

I resent having to care for my loved one or partner.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

The constant interruptions make it difficult for me to find time for relaxation.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

My family (brothers, sisters, children) left me alone to care for my loved one or partner.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

Since caring for my loved one or partner, it seems like I am tired all the time.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

I really want to care for my loved one or partner.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

I visit family and friends less since I have been caring for my loved one or partner.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

I will never be able to do enough caregiving to repay my loved one or partner.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

Financial resources are adequate.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

It is difficult to pay for my loved one or partner.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

Caring for my loved one or partner puts a financial strain on me.
☐Strongly disagree ☐ Disagree ☐ Do not agree nor disagree ☐ Agree ☐ Strongly agree

APPENDIX G

Results Comparing Participants Who Completed versus Withdrew

Appendix G. Completed versus Withdrew

Table G1. Comparison of Demographic Variables for Participants who Completed versus Withdrew

		Completed (n=35 pairs)	**Withdrew** (n=13 pairs)	p value
Age :mean (SD)	Patient	73.5 (11.7)	70.8 (11.5)	.373
	Caregiver	60.6 (12.2)	54.1 (15.4)	.166
Patient sex	Male	60 (21)	38 (5)	.183
	Female	40 (14)	62 (8)	
Caregiver sex	Male	34 (12)	54 (7)	.218
	Female	66 (23)	46 (6)	
Caregiver relationship	Spouse	63 (22)	46 (6)	.327
	Adult Child	37 (13)	54 (7)	
Living arrangement	Patient lives with caregiver	69 (24)	46 (6)	.154
	Patient lives alone	31 (11)	54 (7)	
Patient education (n=42)	< High school	31 (10)	20 (2)	.845
	≥ High school	69 (22)	80 (8)	
Caregiver education (n=42)	< High school	15 (5)	11 (1)	.845
	≥ High school	85 (28)	88 (8)	
Patient employment	Retired	77 (27)	62 (8)	.215
	Homemaker/other	23 (8)	38 (5)	
Caregiver employment	Retired	51 (18)	31 (4)	.158
	Employed- full/ part time	37 (13)	31 (4)	
	Homemaker/other	11 (4)	38 (5)	

Categorical variables expressed as % within group (n)

Appendix G. Completed versus Withdrew (continued)

Table G2. Comparison of Patient Cardiac History for Participants who Completed versus Withdrew

Values expressed as % within group (n)	**Completed** (n=35)	**Withdrew** (n=13)	p value
NYHA : I-II NYHA: III-IV	20 (7) 80 (28)	23 (3) 77 (10)	.816
LVEF: ≥35% LVEF: <35%	50 (17) 50 (17)	38 (5) 62 (8)	.424
Duration Heart Failure < 1 year 1-2.5 years >2.5 years	 31 (11) 29 (10) 40 (14)	 46 (6) 23 (3) 31 (4)	.637
Time since last hospitalization < 2 months 2-6 months >6 months	 51 (18) 17 (6) 31 (11)	 54 (7) 15 (2) 31 (4)	.985
Etiology of Heart Failure-Ischemic	51 (18)	69 (9)	.269
Attended Heart Function Clinic prior to baseline	31 (11)	15 (2)	.266
Myocardial Infarction	43 (15)	38 (5)	.784
Implantable defibrillator	31 (11)	23 (3)	.572
Cardiac resynchronization therapy	6 (2)	15 (2)	.281
CABG/Valve replacement surgery	46 (16)	15 (2)	.054
Percutaneous Coronary Intervention	11 (4)	15 (2)	.794
Atrial Fibrillation	57 (20)	46 (6)	.313

NYHA- New York Heart Association Classification; CABG- Coronary Artery Bypass Surgery

Appendix G. Completed versus Withdrew (continued)

Table G3. Comparison of Patient Medical History for Participants who Completed versus Withdrew

Values expressed as % within group (n)	**Completed** (n=35 pairs)	**Withdrew** (n=13 pairs)	p value
Patient Medical History			
Chronic renal failure (Baseline Creatinine>130umol/L)	41 (13)	29 (5)	.933
Arthritis	38 (12)	50 (6)	.480
COPD	21 (7)	29 (4)	.430
Previous Stroke or TIA	21 (7)	7 (1)	.309
Cancer (past)	23 (8)	21 (3)	.987
Patient Cardiac Risk Factors			
Hyperlipidemia	41 (15)	64 (8)	.250
Hypertension	56 (19)	71 (10)	.254
Smoking history	41 (15)	50 (6)	.390
Diabetes	47 (16)	36 (5)	.653
Obesity	18 (6)	14 (2)	.885
Excessive Alcohol Intake	6 (2)	7 (1)	.801
Family history	38 (13)	14 (2)	.346
Caregiver Medical History			
At least one co-morbidity present (Diabetes, heart disease, lung disease, cancer, stroke or TIA, arthritis)	31 (11)	39 (5)	.646

COPD- Chronic Obstructive Lung Disease; TIA- Transient Ischemic Attack

Appendix G. Completed versus Withdrew (continued)

Table G4. Comparison of Baseline Questionnaire Results for Participants who Completed versus Withdrew

	Completed (n=35 pairs)	**Withdrew** (n=13 pairs)	P value
Hospital Anxiety and Depression Scale- Patient			
Anxiety	5.0 (4)	6.0 (10)	.187
Score ≥ 8: % within group (n)	24% (7)	29% (5)	.189
Depression	5.0 (5)	8.0 (6)	.239
Score ≥ 8: % within group (n)	29% (10)	50% (7)	.104
Hospital Anxiety and Depression Scale- Caregiver			
Anxiety	6.0 (7)	10 (5)	.081
Score ≥ 8: % within group (n)	41% (14)	64% (9)	.072
Depression	4.0 (5)	4.0 (4)	.833
Score ≥ 8: % within group (n)	21% (8)	14% (1)	.232
Mishel Uncertainty in Illness – Patient and Caregiver			
Patient : mean (SD)	60.5 (11.9)	72.5 (12.1)	.002
Caregiver: mean (SD)	80.2 (13.6)	96.2 (14.3)	.002
Caregiver Reaction Assessment - Caregiver			
Caregiver Schedule	2.8 (1.2)	3.2 (2.0)	.545
Financial Problems	2.0 (1.3)	2.3 (1.2)	.535
Family Abandonment	2.0 (1.4)	2.6 (1.7)	.135
Caregiver Health Problems	2.3 (1.5)	3.0 (1.6)	.220
Total Burden	2.0 (1.0)	2.2 (1.3)	.227
Self Esteem (Positive)	3.8 (0.8)	4.4 (1.6)	.052

Values expressed as median (IQR) unless otherwise indicated.

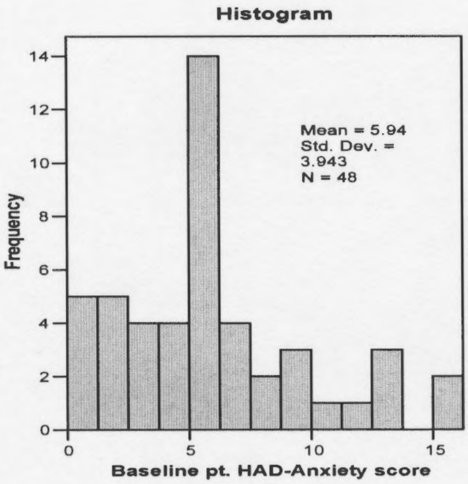
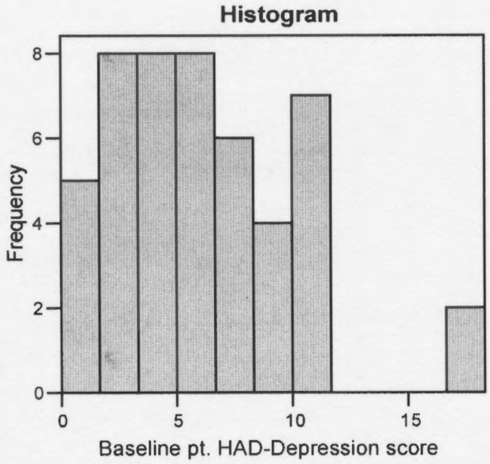
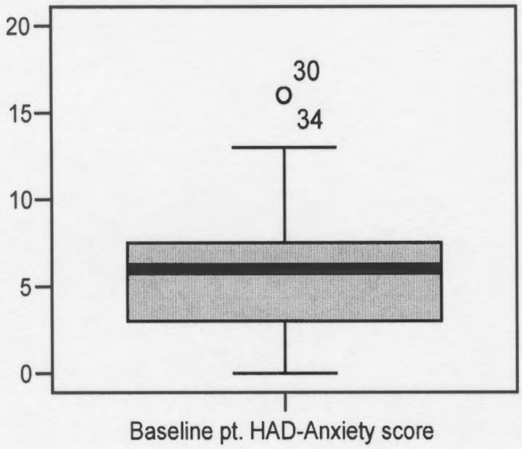
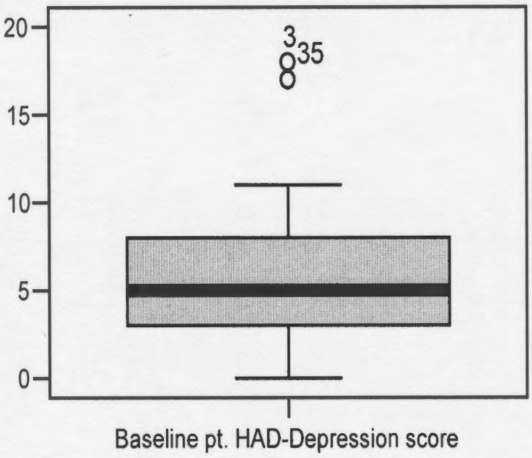
Mann-Whitney U (HADS, CRA); χ^2 (HADS cut off scores); Independent Student's t-test (MUIS)

APPENDIX H

Hospital Anxiety and Depression Scale Further Analyses

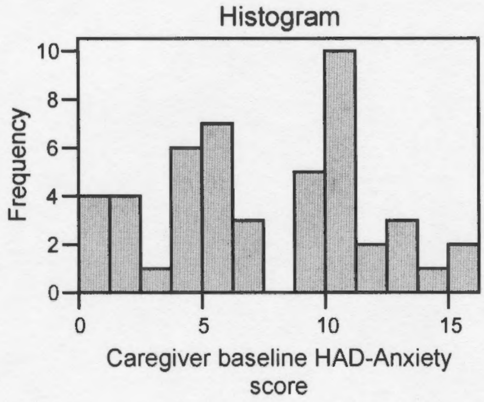
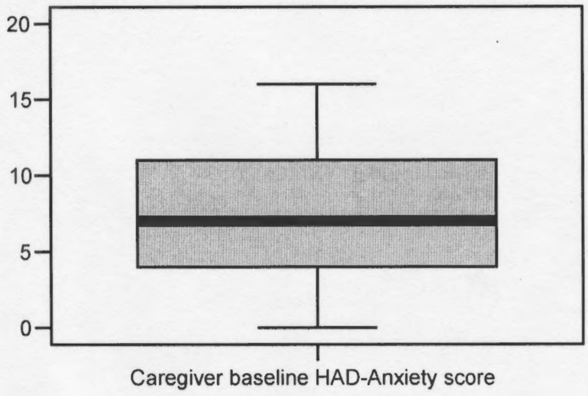
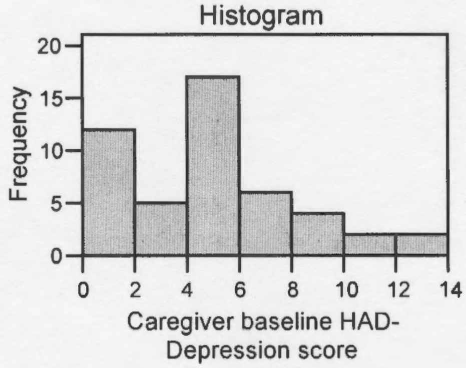
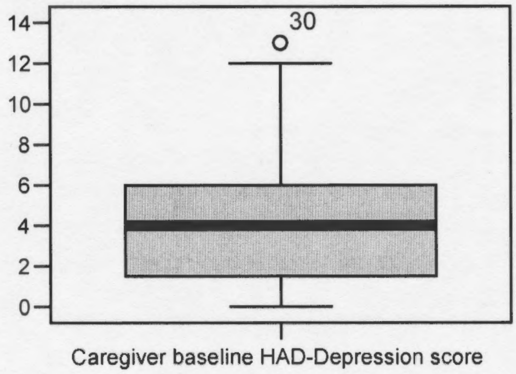
Appendix H. Hospital Anxiety and Depression Scale- Further Analyses

Table H1. Distribution of Patient Baseline HADS Scores

Anxiety	**Depression**
	
	
Baseline Patient Anxiety (n=48) Mean: 5.94 (3.94) Median: 6.00 (5.0) 95% CI: 4.1-69 ≥8: n=12 (25%) Shapiro-Wilks test for normality: p=.007 Skewness : .846 (SE .343) Kurtosis: .409 (SE .674)	Baseline Patient Depression (n=48) Mean: 6.04 (3.99) Median: 5.00 (6.0) 95% CI: 4.88-7.20 ≥8: n=17 (35%) Shapiro-Wilks test for normality: p=.010 Skewness : .892 (SE .343) Kurtosis: 1.029 (SE .674)

Appendix H. Hospital Anxiety and Depression Scale- Further Analyses (continued)

Table H2. Distribution of Caregiver Baseline HADS Scores

Anxiety	**Depression**
	
	
Baseline Caregiver Anxiety (n=48) Mean: 7.42 (4.23) Median: 7.00 (7.0) 95% CI: 6.19-8.65 ≥8: n=23 (48%) Shapiro-Wilks test for normality: p=.175 Skewness.017 (SE .343) Kurtosis: -0.965 (SE .175)	Baseline Caregiver Depression (n=48) Mean: 4.40 (3.17) Median: 4.00 (5.0) 95% CI: 3.47-5.32 ≥8: n=9 (19%) Shapiro-Wilks test for normality: p=.007 Skewness: .741 (.343) Kurtosis .403 (SE .674)

Appendix H. Hospital Anxiety and Depression Scale- Further Analyses (continued)

Table H3. Comparison of Demographic Variables in Patients (n=48) with Normal (n=31) and Abnormal (n=17) Baseline HADS Depression Cut off Scores

Demographic Variables Values expressed as % within group (n)		Entire patient group (n=48)	HADS Depression Normal (n=31)	HADS Depression ≥ 8 (n=17)	p value
Patient Variables					
Age: mean (SD)	Patient	72.6 (11.6)	74.4 (11)	69.2 (12.2)	.144
Patient sex	Male Female	54 (26) 46 (22)	58 (18) 42 (13)	47 (8) 53 (9)	.464
Patient education (n=41)	< High school ≥ High school	25 (12) 60 (29)	33 (9) 67 (18)	21 (3) 79 (11)	.725
Patient employment	Retired Other	73 (35) 27 (13)	74 (26) 16 (5)	53 (9) 47 (8)	.070
Living arrangements	With caregiver Alone	63 (30) 27 (18)	68 (21) 32 (10)	53 (9) 47 (8)	.311
Caregiver Variables					
Age: mean (SD)	Caregiver	58.4 (13.2)	59.7 (13.9)	56.2 (12.1)	.399
Caregiver sex	Male Female	40 (19) 54 (26)	32 (10) 68 (21)	53 (9) 48 (8)	.161
Caregiver relationship	Spouse Adult Child	58 (28) 42 (20)	61 (19) 39 (12)	53 (9) 47 (8)	.575
Caregiver education (n=42)	< High school ≥ High school	13 (6) 75 (36)	17 (5) 83 (24)	8 (1) 92 (12)	.642
Caregiver employment	Retired Employed Other	46 (22) 35 (17) 19 (9)	48 (15) 36 (11) 16 (5)	41 (7) 35 (6) 24 (4)	.433

Appendix H. Hospital Anxiety and Depression Scale- Further Analyses (continued)

Table H4. Comparison of Medical Variables in Patients (n=48) with Normal (n=31) and Abnormal (n=17) Baseline HADS Depression Cut off Scores

Cardiac and Medical History Values expressed as % within group (n)	Entire patient group (n=48)	HADS Depression Normal (n=31)	HADS Depression ≥ 8 (n=17)	p value
Cardiac History				
NYHA: I-II	21 (10)	19 (6)	24 (4)	.733
III-IV	79 (38)	81 (25)	76 (13)	
LVEF: ≥35%	48 (23)	42 (13)	59 (10)	.263
<35%	52 (25)	58 (18)	41 (7)	
Duration of HF: < 1 year	35 (17)	42 (13)	24 (4)	.418
1-2.5 years	27 (13)	26 (8)	29 (5)	
>2.5 years	38 (18)	32 (10)	47 (8)	
Time since last hospitalization				
< 2 months	52 (25)	52 (16)	53 (9)	.771
2-6 months	17 (8)	19 (6)	12 (2)	
>6 months	31 (15)	29 (9)	35 (6)	
Etiology of HF –Ischemic	56 (27)	48 (5)	71 (12)	.138
Attended HFC prior to baseline	27 (13)	23 (7)	35 (6)	.343
Myocardial Infarction	42 (20)	32 (10)	59 (10)	.074
Implantable Defibrillator	29 (14)	26 (8)	35 (6)	.489
CABG or Valve Surgery	38 (18)	35 (11)	41 (7)	.697
Atrial Fibrillation	54 (26)	58 (18)	47 (8)	.464
Cardiac Risk Factors				
Hypertension	60 (29)	61 (19)	59 (10)	.867
Hyperlipidemia	48 (23)	48 (15)	47 (8)	.930
Smoking history	44 (21)	42 (13)	47 (8)	.732
Diabetes	44 (21)	42 (13)	47 (8)	.732
Family History of CAD	31 (15)	26 (8)	41 (7)	.272
Medical History				
Chronic Renal Failure (Baseline Creatinine>130umol/L)	38 (18)	42 (13)	29 (5)	.391
Arthritis	38 (18)	42 (13)	29 (5)	.391
COPD	23 (11)	23 (7)	24 (4)	.940
Cancer	23 (11)	28 (8)	18 (3)	.520
Previous Stroke or TIA	17 (8)	13 (4)	24 (4)	.345

NYHA- New York Heart Association; LVEF- Left Ventricular Ejection Fraction; HF- Heart Failure; HFC- Heart Function Clinic; CABG- Coronary Artery Bypass Surgery; CAD- Coronary Artery Disease; COPD- Chronic Obstructive Pulmonary Disease; TIA- Transient Ischemic Attack

Appendix H. Hospital Anxiety and Depression Scale- Further Analyses (continued)

Table H5. Comparison of Demographic Variables in Patients (n=48) with Normal (n=36) and Abnormal (n=12) Baseline HADS Anxiety Cut off Scores

Demographic Variables Values expressed as % within group (n)		Entire patient group (n=48)	HADS Anxiety Normal (n=36)	HADS Anxiety ≥ 8 (n=12)	p value
Patient Variables					
Age: mean (SD)	Patient	72.6 (11.6)	73.1 (11.2)	70.1 (13.2)	.439
Patient sex	Male Female	54 (26) 46 (22)	53 (19) 47 (17)	58 (7) 42 (5)	.738
Patient education (n=41)	< High school ≥ High school	25 (12) 60 (29)	32 (10 68 (21)	20 (2) 80 (8)	.692
Patient employment	Retired Other	73 (35) 27 (13)	81 (29) 19 (7)	50 (6) 50 (6)	.110
Living arrangements	With caregiver Alone	63 (30) 27 (18)	67 (24) 33 (12)	50 (6) 50 (6)	.302
Caregiver Variables					
Age: mean (SD)	Caregiver	58.4 (13.2)	59.5 (14.0)	55.3 (10.4)	.248
Caregiver sex	Male Female	40 (19) 54 (26)	33 (12) 67 (24)	58 (7) 42 (5)	.125
Caregiver relationship	Spouse Adult Child	58 (28) 42 (20)	61 (22) 39 (14)	50 (6) 50 (6)	.499
Caregiver education (n=42)	< High school ≥ High school	13 (6) 75 (36)	16 (5) 84 (27)	10 (1) 90 (9)	.547
Caregiver employment	Retired Employed Other	46 (22) 35 (17) 19 (9)	47 (17) 33 (12) 20 (7)	42 (5) 42 (5) 16 (2)	.631

Appendix H. Hospital Anxiety and Depression Scale- Further Analyses (continued)

Table H6. Comparison of Medical Variables in Patients (n= 48) with Normal (n=36) and Abnormal (n=12) Baseline HADS Anxiety Cut off Scores

Cardiac and Medical History Values expressed as % within group (n)	Entire patient group (n=48)	HADS Anxiety Normal (n=36)	HADS Anxiety≥ 8 (n=12)	p value
Cardiac History				
NYHA: I-II III-IV	21 (10) 79 (38)	22 (8) 78 (28)	17 (2) 83 (10)	.682
LVEF: ≥35% <35%	48 (23) 52 (25)	50 (18) 50 (18)	42 (5) 58 (7)	.617
Duration of HF: < 1 year 1-2.5 years >2.5 years	35 (17) 27 (13) 38 (18)	39 (14) 28 (10) 33 (12)	25 (3) 25 (3) 50 (6)	.554
Time since last hospitalization < 2 months 2-6 months >6 months	 52 (25) 17 (8) 31 (15)	 44 (17) 22 (8) 31 (11)	 67 (8) 0 33 (4)	.188
Etiology of HF –Ischemic	56 (27)	47 (17)	33 (4)	.401
Attended HFC prior to baseline	27 (13)	22 (8)	42 (5)	.189
Myocardial Infarction	42 (20)	33 (12)	67 (8)	.043
Implantable Defibrillator	29 (14)	28 (10)	33 (4)	.714
CABG or Valve Surgery	38 (18)	44 (16)	17 (2)	.085
Atrial Fibrillation	54 (26)	56 (20)	50 (6)	.751
Cardiac Risk Factors				
Hypertension	60 (29)	55 (20)	75 (9)	.233
Hyperlipidemia	48 (23)	47 (17)	50 (6)	.868
Smoking history	44 (21)	47 (17)	33 (4)	.401
Diabetes	44 (21)	44 (16)	42 (5)	.867
Family History of CAD	31 (15)	28 (10)	42 (5)	.369
Medical History				
Chronic Renal Failure (Baseline Creatinine>130umol/L)	38 (18)	33 (12)	50 (6)	.302
Arthritis	38 (18)	33 (12)	50 (6)	.302
COPD	23 (11)	25 (9)	17 (2)	.552
Cancer	23 (11)	25 (9)	17 (2)	.552
Previous Stroke or TIA	17 (8)	22 (8)	0	.074

NYHA- New York Heart Association; LVEF- Left Ventricular Ejection Fraction; HF- Heart Failure; HFC- Heart Function Clinic; CABG- Coronary Artery Bypass Surgery; CAD- Coronary Artery Disease; COPD- Chronic Obstructive Pulmonary Disease; TIA- Transient Ischemic Attack

Appendix H. Hospital Anxiety and Depression Scale- Further Analyses (continued)

Table H7. Comparison of Demographic Variables between Caregivers (n=48) with Normal (n=25) and Abnormal (n=23) Baseline HADS Anxiety Cut off Scores

Demographic Variables Values expressed as % within group (n)		Entire caregiver group (n=48)	HADS Anxiety Normal (n=25)	HADS Anxiety≥ 8 (n=23)	p value
Caregiver Variables					
Age: mean (SD)	Caregiver	58.4 (13.2)	60.9 (13.5)	55.8 (12.7)	.185
Caregiver sex	Male Female	40 (19) 54 (26)	44 (11) 56 (14)	35 (8) 65 (15)	.514
Caregiver relationship to Patient	Spouse Adult Child	58 (28) 42 (20)	52 (13) 48 (12)	65 (15) 35 (8)	.353
Living arrangements	With patient Not with patient	63 (30) 27 (18)	56 (14) 44 (11)	70 (16) 30 (7)	.332
Caregiver education (n=42)	< High school ≥ High school	13 (6) 75 (36)	14 (3) 86 (19)	15 (3) 85 (17)	.879
Caregiver employment	Retired Employed Other	46 (22) 35 (17) 19 (9)	56 (14) 13 (8) 12 (3)	35 (8) 39 (9) 26 (6)	.376
Number of caregiver co-morbidities	None At least one	65 (31) 35 (17)	64(16) 36 (9)	65 (15) 35 (8)	.868
Patient Variables					
Age: mean (SD)	Patient	72.6 (11.6)	76.6 (9.6)	68.2 (12.3)	.011
Patient sex	Male Female	54 (26) 46 (22)	40 (10) 60 (15)	70 (16) 30 (7)	.040
Patient education (n=41)	< High school ≥ High school	25 (12) 60 (29)	29 (6) 71 (17)	33 (6) 67 (12)	.575
Patient employment	Retired Other	73 (35) 27 (13)	84 (21) 16 (4)	61 (14) 39 (9)	.049

Appendix H. Hospital Anxiety and Depression Scale- Further Analyses (continued)

Table H8. Comparison of Patient Cardiac History Variables in Caregivers (n=48) with Normal (n=25) and Abnormal (n=23) Baseline HADS-Anxiety Cut off scores

Patient Cardiac I History Values expressed as % within group (n)	Entire caregiver group (n=48)	HADS Anxiety Normal (n=25)	HADS Anxiety≥ 8 (n=23)	p value
Cardiac History				
NYHA				
I-II	21 (10)	24 (6)	17 (4)	.573
III-IV	79 (38)	76 (19)	83 (19)	
LVEF				
≥35%	48 (23)	48 (12)	48 (11)	.990
<35%	52 (25)	52 (13)	52 (12)	
Duration of HF				
< 1 year	35 (17)	28 (7)	43 (10)	.305
1-2.5 years	27 (13)	36 (9)	17 (4)	
>2.5 years	38 (18)	36 (9)	3 (9)	
Time since last hospitalization				
< 2 months	52 (25)	56 (14)	48 (11)	.655
2-6 months	17 (8)	12 (3)	22 (5)	
>6 months	31 (15)	32 (8)	30 (7)	
Etiology of HF –Ischemic	56 (27)	60 (15)	52 (12)	.585
HFC prior to baseline- Yes	27 (13)	36 (9)	17 (4)	.147
No	73 (35)	64 (16)	83 (19)	
Myocardial Infarction	42 (20)	44 (11)	39 (9)	.732
Implantable Defibrillator	29 (14)	20 (5)	39 (9)	.190
CABG or Valve Surgery	38 (18)	40 (10)	35 (8)	.709
Atrial Fibrillation	54 (26)	56 (14)	52 (12)	.790

NYHA- New York Heart Association Classification; LVEF- Left Ventricular Ejection Fraction; HF- Heart Failure; HFC- Heart Function Clinic; CABG- Coronary Artery Bypass Surgery

APPENDIX I

Mishel Uncertainty in Illness Scale Further Analyses

Appendix I. Mishel Uncertainty in Illness Further Analyses

Table I1. Patient MUIS Item Scores at Baseline (n=48)

	Values expressed at % (n) who 'agree' or 'strongly agree' with the statement	Baseline n=48
1	I don't know what is wrong with me.	17 (8)
2	I have a lot of questions without answers.	29 (14)
3	I am unsure if my heart failure is getting better or worse	33 (16)
4	It is unclear how bad my heart failure will be.	52 (25)
5	The explanations they give about my heart failure seem hazy to me.	33 (16)
6	The purpose of my heart failure treatment is clear to me.	79 (38)
7	My symptoms of heart failure continue to change unpredictably.	33 (16)
8	I understand everything explained to me.	69 (33)
9	The doctors say things to me that could have many meanings.	33 (16)
10	My heart failure treatment is too complex to figure out.	29 (14)
11	It is difficult to know if the treatments or medications I am getting are helping.	38 (18)
12	Because of the unpredictability of my heart failure, I cannot plan for the future.	46 (22)
13	The course of my heart failure keeps changing. I have good days and bad days.	65 (31)
14	I have been given many differing opinions on what is wrong with me.	27 (13)
15	It is not clear what is going to happen to me.	50 (24)
16	The results of my heart tests are inconsistent.	17 (8)
17	The effectiveness of my heart failure treatment is undetermined.	33 (16)
18	Because of my heart failure treatment, what I can and cannot do keeps changing.	48 (23)
19	I am certain they will not find anything else wrong with me.	21 (10)
20	The treatment for my heart failure that I am receiving has a known probability to success.	54 (26)
21	They have not given me a specific diagnosis.	40 (19)
22	The seriousness of my heart failure has been determined.	69 (33)
23	The doctors and nurses use everyday language so I can understand what they are saying.	85 (41)

Appendix I. Mishel Uncertainty in Illness Further Analyses (continued)

Table I2. Comparison of Patient Baseline MUIS Scores according to Demographic Variables

Patient Variables		n	**Patient MUIS**	**p value**
Patient Sex	Male	26	60.7 (13.4)	.080
	Female	22	67.3 (11.8)	
Patient Education	< High school	12	58.8 (15.2)	.320
	≥ High school	29	63.3 (12.1)	
Patient Employment	Retired	35	61.5 (11.4)	.053
	Other	13	69.7 (15.6)	
Living Arrangements	With caregiver	30	61.6 (12.9)	.141
	Alone	18	67.3 (12.7)	
Caregiver Variables				
Caregiver Sex	Male	19	64.0 (10.7)	.916
	Female	26	63.6 (14.5)	
Caregiver Relationship	Spouse	28	61.6 (12.6)	.180
	Adult Child	20	66.8 (13.3)	
Caregiver Employment	Retired	22	61.8 (11.9)	.189
	Employed	17	62.5 (11.6)	
	Other	9	70.9 (16.8)	
Caregiver Education	< High school	6	66.5 (9.3)	.381
	≥ High school	36	61.4 (13.5)	

Values expressed as mean (standard deviation)
Statistical tests- independent t-test (2 variables) or ANOVA (>2 variables)

Appendix I. Mishel Uncertainty in Illness Further Analyses (continued)

Table I3. Comparison of Baseline Patient MUIS Scores according to Patient Cardiac History

Cardiac History Variable		n	Patient MUIS Score	p value
New York Heart Association	I-II	10	61.1 (10.6)	.475
	III-IV	38	64.4 (13.6)	
Left Ventricular Ejection Fraction	≥ 35%	23	61.6 (13.5)	.289
	< 35%	25	65.7 (12.5)	
Duration of Heart Failure	< 1 year	17	68.5 (12.5)	.119
	1-2.5 years	13	58.9 (16.0)	
	>2.5 years	18	62.8 (9.9)	
Time since Hospitalization	< 2 months	25	63.6 (12.7)	.766
	2-6 months	8	66.6 (10.6)	
	>6 months	15	62.4 (15.2)	
Ischemic Origin on Heart Failure	Yes	27	63.1 (13.8)	.632
	No	21	62.7 (11.0)	
Myocardial Infarction	Yes	20	62.2 (15.9)	.505
	No	28	64.8 (10.7)	
Implantable Defibrillator	Yes	14	63.1 (13.8)	.838
	No	34	64.0 (12.9)	
CABG or Valve Surgery	Yes	18	60.1 (14.3)	.129
	No	30	66.0 (11.8)	
Atrial Fibrillation	Yes	26	62.8 (9.8)	.622
	No	22	64.8 (16.2)	
Attended HFC prior to baseline	Yes	13	59.7 (13.7)	.191
	No	35	65.3 (10.3)	

Values expressed as mean (standard deviation)
Statistical tests- independent t-test (2 variables) or ANOVA (>2 variables)
CABG- Coronary Artery Bypass Surgery; HFC- Heart Function Clinic

Appendix I. Mishel Uncertainty in Illness Further Analyses (continued)

Table I4. Caregiver MUIS Item Scores at Baseline (n=48)

	Values expressed at % (n) who 'agree' or 'strongly agree' with the statement	Baseline (n=48)
1	I don't know what is wrong with him/her	17 (8)
2	I have a lot of questions without answers	31 (15)
3	I am unsure if HF is getting better or worse	35 (17)
4	It is unclear how bad HF will be	42 (20)
5	The explanations about HF seem hazy to me	23 (11)
6	The purpose of treatment is clear	67 (32)
7	I don't know when to expect things to be done to ..	31 (15)
8	Symptoms continue to change unpredictably	50 (24)
9	Understand everything explained to me	79 (38)
10	Doctors say things that could have many meanings	23 (11)
11	Cannot predict how long HF will last	73 (35)
12	Treatment too complex to figure out	27 (13)
13	Difficult to know if treatments/ medications working	25 (12)
14	So may types of staff- unclear who is responsible	24 (12)
15	Because HF unpredictable, cannot plan for future	50 (24)
16	Course of HF changing. I have good and bad days	54 (26)
17	Vague to me how I'll manage HF care after leave hospital	29 (14)
18	Not clear what is going to happen to..	52 (25)
19	Usually know when he/she going to have a good or bad day	48 (23)
20	Results of heart tests are inconsistent	18 (9)
21	Effectiveness of HF treatment is undetermined	25 (12)
22	Difficult to determine how long I can provide care	17 (8)
23	I can generally predict the course of HF	21 (10)
24	Because of HF, what he/she can/cannot do keeping changing	40 (19)
25	Certain they will not find anything else wrong	23 (11)
26	They have not given him/her a specific diagnosis	10 (5)
27	HF is predictable- I know when getting better/worse	33 (16)
28	Diagnosis is definite and will not change	50 (24)
29	Can depend on nurses to be there when needed	69 (33)
30	Seriousness of illness has been determined	75 (23)
31	Doctors and nurses use everyday language to I can understand them	83 (40)

Appendix I. Mishel Uncertainty in Illness Further Analyses (continued)

Table I5. Comparison of Caregiver MUIS Scores according to Caregiver and Patient Demographic Variables and Patient Cardiac History

Caregiver Variables		**n**	**Caregiver MUIS**	**p value**
Caregiver Sex	Male	19	91.4 (14.8)	.011
	Female	26	80.1 (14.3)	
Caregiver Relationship	Spouse	28	85.9 (14.6)	.490
	Adult Child	20	82.7 (16.6)	
Caregiver Employment	Retired	22	82.4 (13.9)	.074
	Employed	17	81.8 (16.5)	
	Other	9	95.0 (13.7)	
Caregiver Education	< High school	6	81.3 (15.5)	.015
	≥ High school	36	98.0 (9.9)	
Patient Variables				
Patient Sex	Male	26	80.6 (13.4)	.054
	Female	22	89.2 (16.6)	
Patient Education	< High school	12	86.6 (13.6)	.388
	≥ High school	29	82.1 (15.6)	
Patient Employment	Retired	35	82.3 (16.0)	.101
	Other	13	90.5 (12.1)	
Living Arrangements	With caregiver	30	84.1 (15.1)	.815
	Alone	8	85.2 (16.3)	

Values expressed as mean (standard deviation)
Statistical tests- independent t-test (2 variables) or ANOVA (>2 variables)

Appendix I. Mishel Uncertainty in Illness Further Analyses (continued)

Table I6. Comparison of Caregiver MUIS Scores according to Patient Cardiac History

Cardiac History Variable		**n**	**Caregiver MUIS**	**p value**
New York Heart Association	I-II	10	84.1 (16.5)	.920
	III-IV	38	84.7 (15.3)	
Left Ventricular Ejection Fraction	≥ 35%	23	86.1 (16.9)	.511
	< 35%	25	83.1 (14.1)	
Duration of Heart Failure	< 1 year	17	90.8 (17.1)	.111
	1-2.5 years	13	81.1 (17.2)	
	>2.5 years	18	81.1 (10.4)	
Time since Hospitalization	< 2 months	25	87.8 (15.9)	.192
	2-6 months	8	85.4 (14.5)	
	>6 months	15	78.7 (14.3)	
Myocardial Infarction	Yes	20	81.9 (14.2)	.320
	No	28	86.4 (16.2)	
Implantable Defibrillator	Yes	14	86.0 (17.4)	.322
	No	34	81.1 (8.5)	
CABG or Valve Surgery	Yes	18	84.5 (15.5)	.989
	No	30	84.6 (15.6)	
Attended HFC prior to baseline	Yes	13	78.2 (14.0)	.083
	No	35	86.9 (15.4)	

Values expressed as mean (standard deviation)
Statistical tests- independent t-test (2 variables) or ANOVA (>2 variables)
CABG- Coronary Artery Bypass Surgery; HFC- Heart Function Clinic

Appendix I. Mishel Uncertainty in Illness Further Analyses (continued)

Table I7. Patient MUIS Item Responses at Baseline, 2 months and 4 Months

	Values expressed at % (n) who 'agree' or 'strongly agree' with the statement	Baseline n=48	2 months n=42	4 months n=35
1	I don't know what is wrong with me.	17 (8)	12 (5)	15 (5)
2	I have a lot of questions without answers.	29 (14)	19 (8)	20 (7)
3	I am unsure if my heart failure is getting better or worse	33 (16)	21 (9)	14 (5)
4	It is unclear how bad my heart failure will be.	52 (25)	33 (14)	37 (13)
5	The explanations they give about my heart failure seem hazy to me.	33 (16)	21 (9)	11 (4)
6	The purpose of my heart failure treatment is clear to me.	79 (38)	86 (36)	94 (33)
7	My symptoms of heart failure continue to change unpredictably.	33 (16)	19 (8)	23 (8)
8	I understand everything explained to me.	69 (33)	69 (29)	74 (26)
9	The doctors say things to me that could have many meanings.	33 (16)	26 (11)	20 (7)
10	My heart failure treatment is too complex to figure out.	29 (14)	19 (8)	20 (7)
11	It is difficult to know if the treatments or medications I am getting are helping.	38 (18)	31 (13)	17 (6)
12	Because of the unpredictability of my heart failure, I cannot plan for the future.	46 (22)	45 (19)	26 (9)
13	The course of my heart failure keeps changing. I have good days and bad days.	65 (31)	60 (25)	54 (19)
14	I have been given many differing opinions on what is wrong with me.	27 (13)	5 (2)	11 (4)
15	It is not clear what is going to happen to me.	50 (24)	24 (10)	31 (11)
16	The results of my heart tests are inconsistent.	17 (8)	7 (3)	6 (2)
17	The effectiveness of my heart failure treatment is undetermined.	33 (16)	21 (9)	17 (6)
18	Because of my heart failure treatment, what I can and cannot do keeps changing.	48 (23)	37 (13)	31 (11)
19	I am certain they will not find anything else wrong with me.	21 (10)	40 (17)	20 (7)
20	The treatment for my heart failure that I am receiving has a known probability to success.	54 (26)	64 (27)	63 (22)
21	They have not given me a specific diagnosis.	40 (19)	7 (3)	9 (3)
22	The seriousness of my heart failure has been determined.	69 (33)	79 (33)	74 (26)
23	The doctors and nurses use everyday language so I can understand what they are saying.	85 (41)	98 (41)	89 (31)

Appendix I. Mishel Uncertainty in Illness Further Analyses (continued)

Table I8. Caregiver MUIS Item Responses at Baseline, 2 Months and 4 Months

	Values expressed at % (n) who 'agree' or 'strongly agree' with the statement	Baseline (n=48)	2 months (n=42)	4 months (n=35)
1	I don't know what is wrong with him/her	17 (8)	12 (5)	3 (1)
2	I have a lot of questions without answers	31 (15)	21 (9)	9 (3)
3	I am unsure if HF is getting better or worse	35 (17)	26 (11)	14 (5)
4	It is unclear how bad HF will be	42 (20)	26 (11)	37 (13)
5	The explanations about HF seem hazy to me	23 (11)	21 (9)	9 (3)
6	The purpose of treatment is clear	67 (32)	78 (33)	83 (29)
7	I don't know when to expect things to be done to ..	31 (15)	19 (8)	14 (5)
8	Symptoms continue to change unpredictably	50 (24)	31 (13)	20 (7)
9	Understand everything explained to me	79 (38)	83 (35)	89 (31)
10	Doctors say things that could have many meanings	23 (11)	24 (10)	24 (8)
11	Cannot predict how long HF will last	73 (35)	74 (31)	51 (19)
12	Treatment too complex to figure out	27 (13)	19 (8)	14 (5)
13	Difficult to know if treatments/ medications working	25 (12)	21 (9)	11 (4)
14	So may types of staff- unclear who is responsible	24 (12)	26 (11)	20 (7)
15	Because HF unpredictable, cannot plan for future	50 (24)	45 (19)	20 (7)
16	Course of HF changing. I have good and bad days	54 (26)	36 (15)	34 (12)
17	Vague to me how I'll manage HF care after leave hospital	29 (14)	19 (8)	11 (4)
18	Not clear what is going to happen to..	52 (25)	45 (19)	23 (8)
19	Usually know when he/she going to have a good or bad day	48 (23)	52 (22)	51 (18)
20	Results of heart tests are inconsistent	18 (9)	12 (5)	6 (2)
21	Effectiveness of HF treatment is undetermined	25 (12)	14 (6)	14 (5)
22	Difficult to determine how long I can provide care	17 (8)	19 (8)	20 (7)
23	I can generally predict the course of HF	21 (10)	36 (15)	20 (7)
24	Because of HF, what he/she can/cannot do keeping changing	40 (19)	31 (13)	37 (13)
25	Certain they will not find anything else wrong	23 (11)	24 (10)	17 (6)
26	They have not given him/her a specific diagnosis	10 (5)	14 (6)	9 (3)
27	HF is predictable- I know when getting better/worse	33 (16)	31 (13)	37 (13)
28	Diagnosis is definite and will not change	50 (24)	36 (15)	51 (18)
29	Can depend on nurses to be there when needed	69 (33)	81 (34)	89 (31)
30	Seriousness of illness has been determined	75 (23)	67 (28)	71 (25)
31	Doctors and nurses use everyday language to I can understand them	83 (40)	88 (37)	89 (31)

APPENDIX J

Caregiver Reaction Assessment
Further Analyses

Appendix J. Caregiver Reaction Assessment – Further Analyses

Table J1. Baseline CRA Item Responses (n=48)

% that agree or strongly agree	**Baseline** (n=48)
Schedule Disruption	
Activities centered around care	65 (31)
Have to stop in the middle of my activities or work to provide care	23 (11)
Eliminated things from my schedule	38 (18)
Constant interruptions make it hard to find time to relax	25 (12)
I visit family and friend less	35 (17)
Financial Burden	
Financial resources are not adequate	15 (7)
Difficult to pay for my partner	8 (4)
Caring puts a financial strain on me	13 (6)
Lack of Family Support	
My family does not work together at caring	23 (11)
Since caring, I feel my family has abandoned me	6 (3)
Very difficult to get help from my family	21 (10)
Others have dumped care onto me	13 (6)
My family left me alone to care	17 (8)
Health Problems	
I am not healthy enough to provide care	13 (6)
It takes all my physical strength to provide care	27 (13)
My health has gotten worse since providing care	19 (9)
It seems like I am tired all the time	27 (13)
Self Esteem (Positive)	
Caring is important to me	100 (48)
I enjoy caring	73 (35)
Caring makes me feel good	81 (39)
I do not resent caring	81 (39)
I really want to care	89 (43)

Responses expressed as % within group (n)

Appendix J. Caregiver Reaction Assessment – Further Analyses (continued)

Table J2. Baseline Caregiver Total Negative CRA Score according to Caregiver and Patient Demographic and Patient Cardiac History Variables (n=48 pairs)

		n	**Caregiver Total Negative**	**p value**
Caregiver Variables				
Caregiver Sex	Male	19	2.29 (.62)	.331
	Female	26	2.09 (.72)	
Caregiver Relationship	Spouse	28	2.26 (.66)	.315
	Adult Child	20	2.05 (.71)	
Number of caregiver Co-morbidities	None	32	2.22 (.68)	.485
	At least 1	16	2.07 (.70)	
Caregiver Employment	Retired	22	1.97 (.55)	.138
	Employed	17	2.27 (.82)	
	Other	9	2.47 (.63)	
Patient Variables				
Patient Sex	Male	26	2.00 (.65)	.106
	Female	22	2.32 (.68)	
Patient Employment	Retired	35	2.00 (.66)	.004
	Other	13	2.63 (.54)	
Living Arrangements	With caregiver	30	2.50 (.80)	.348
	Alone	18	2.26 (1.0)	
Patient Cardiac History				
New York Heart Association	I-II	10	1.89 (.68)	.145
	III-IV	38	2.25 (.67)	
Left Ventricular Ejection Fraction	≥ 35%	23	2.32 (.78)	.148
	< 35%	25	2.03 (.56)	
Duration of Heart Failure	< 1 year	17	2.20 (.73)	.872
	1-2.5 years	13	2.09 (.68)	
	>2.5 years	18	2.17 (.68)	
Time since last hospitalization	< 2 months	25	2.14 (.60)	.930
	2-6 months	8	2.24 (.68)	
	>6 months	15	2.19 (.84)	
Attended Heart Function Clinic prior to baseline	Yes	13	2.23 (.73)	.716
	No	35	2.15 (.67)	

Independent t-tests and ANOVA

Appendix J. Caregiver Reaction Assessment – Further Analyses (continued)

Table J3. Baseline Caregiver Esteem CRA Score according to Caregiver and Patient Demographic and Patient Cardiac History Variables (n=48 pairs)

		n	**Caregiver Esteem**	**p value** parametric (non-parametric)
Caregiver Variables				
Caregiver Sex	Male	19	4.17 (.57)	.699 (.832)
	Female	26	4.10 (.56)	
Caregiver Relationship	Spouse	28	4.01 (.54)	.074 (.092)
	Adult Child	20	4.30 (.56)	
Number of caregiver Co-morbidities	None	32	4.14 (.54)	.886 (.956)
	At least 1	16	4.11 (.61)	
Caregiver Employment	Retired	22	3.98 (.55)	.234 (.250)
	Employed	17	4.28 (.52)	
	Other	9	4.20 (.62)	
Patient Variables				
Patient Sex	Male	26	4.04 (.58)	.353 (.353)
	Female	22	4.21 (.54)	
Patient Employment	Retired	35	4.09 (.58)	.450 (.426)
	Other	13	4.23 (.52)	
Living Arrangements	With caregiver	30	4.02 (.56)	.102 (.107)
	Alone	18	4.30 (.54)	
Patient Cardiac History				
New York Heart Association	I-II	10	4.28 (.58)	.344 (.347)
	III-IV	38	4.09 (.58)	
Left Ventricular Ejection Fraction	≥ 35%	23	4.03 (.57)	.225 (.190)
	< 35%	25	4.22 (.55)	
Duration of Heart Failure	< 1 year	17	4.31 (.60)	.204 (.299)
	1-2.5 years	13	4.12 (.62)	
	>2.5 years	18	3.97 (.45)	
Time since last hospitalization	< 2 months	25	4.15 (.48)	.276 (.238)
	2-6 months	8	3.85 (.71)	
	>6 months	15	4.24 (.59)	
Attended Heart Function Clinic prior to baseline	Yes	13	4.12 (.57)	.964 (.879)
	No	35	4.13 (.56)	