2016

Biobehavioral Influences of Anxiety, Depression, and Hostility Symptoms on Health-Related Outcomes in Patients with Heart Failure

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Digital Object Identifier: https://doi.org/10.13023/ETD.2016.479

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BIOBEHAVIORAL INFLUENCES OF ANXIETY, DEPRESSION, AND HOSTILITY SYMPTOMS ON HEALTH-RELATED OUTCOMES IN PATIENTS WITH HEART FAILURE

DISSERTATION

A dissertation submitted in partial fulfillment of the
requirements for the degree of Doctor of Philosophy in the
College of Nursing at the University of Kentucky

By
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ABSTRACT OF DISSERTATION

BIOBEHAVIORAL INFLUENCES OF ANXIETY, DEPRESSION, AND HOSTILITY SYMPTOMS ON HEALTH-RELATED OUTCOMES IN PATIENTS WITH HEART FAILURE

The incidence of heart failure (HF) has increased each year as more people are living longer with heart disease and other chronic conditions. Recently, there has been much interest in the psychological dimensions of HF and the influence psychological symptoms have on the health outcomes (e.g., self-care, rehospitalization, mortality and quality of life) of patients living with HF. Patients with HF frequently experience symptoms of anxiety, depression, and hostility that may be associated with poor health outcomes. The purpose of this dissertation was to examine how psychological variables influence health outcomes of patients with HF, how psychological variables change over time, and whether different trajectories of psychological variables are associated with health outcomes. The specific aims of this dissertation were to: (1) evaluate the psychometric properties of the Brief Symptom Inventory (BSI) Hostility subscale in patients with HF; (2) determine whether anxiety, depression, and hostility predict self-reported self-care behaviors in patients with HF; and (3) describe trajectories of anxiety and depressive symptoms among patients with HF at baseline and 3 and 12 months post-baseline, and explore whether these symptom trajectories predict 1-year cardiac event-free survival and physical health-related quality of life (P-HRQOL).

Secondary analyses of longitudinal data from a large, multi-region registry representing the Midwest, Southwest, Southeast, Northwest and Northeast United States (Heart Failure Quality of Life Trialists Collaborative) were conducted. Data from three subsets of participants enrolled in the Collaborative with complete data on the variables of interest comprised the samples for the three studies in this dissertation. In the first study, a psychometric evaluation of the BSI Hostility subscale was conducted using data from 345 patients with HF. The subscale demonstrated adequate internal consistency reliability (Cronbach's alpha = .77) and construct validity. In the second longitudinal study of 214 patients with HF, baseline anxiety, depression, and hostility did not predict self-reported self-care at 12 months; however, higher perceived social support predicted greater levels of self-reported self-care. In the third study, baseline, 3-month, and 12-month data from 597 patients with HF were used to examine the association of anxiety and depression trajectories with one-year cardiac event-free survival and P-HRQOL in

patients with HF. Distinct trajectories of anxiety and depression predicted mortality, hospital readmission, and P-HRQOL.

The findings of these studies filled some gaps in our understanding regarding how anxiety, depression, and hostility influence health outcomes of patients with HF. The findings suggest how a measure of hostility may be improved to assess hostility in patients with HF and the importance of assessing psychological symptoms routinely in order to identify changes in these symptoms. Results showed that psychological variables did not predict self-reported self-care, a component of risk reduction in improving health outcomes among patients with HF, but that social support, an important psychosocial variable, was a strong predictor of self-reported self-care. Trajectories of psychological variables were significant predictors of health outcomes in patients with HF at 1-year follow-up. Implications include the importance of monitoring psychological symptoms over time. A better understanding of how psychological symptoms change is meaningful, as it affords clinicians the opportunity for timely interventions designed to reduce the risk of adverse events and improve health outcomes. Even though numerous studies exist which examine psychological symptoms and health outcomes in patients with HF, there are very few longitudinal studies investigating trajectories of psychological symptoms in this population. Subsequently, more research is needed to investigate psychological symptom trajectories and identify high risk groups. In addition, the design and testing of interventions aimed at reducing psychological symptoms is critical to improve health outcomes in patients with HF.

KEYWORDS: heart failure, anxiety, depression, hostility, trajectories, psychological symptoms

Lynn P. Roser

November 29, 2016

BIOBEHAVIORAL INFLUENCES OF ANXIETY, DEPRESSION, AND HOSTILITY SYMPTOMS ON HEALTH-RELATED OUTCOMES IN PATIENTS WITH HEART FAILURE

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November 29, 2016
Date

Dedication
To my husband, Thomas,
and my children, Tommy, and Mimi,
the loves of my life

and

To the memory of my parents,
Thomas Jackson Price III and Betty Morford Price

Each of us will know or love someone suffering from heart failure. Such is the case with me. I lost both my parents to complications from heart failure after acquiring bacterial endocarditis. I can only hope my knowledge made their last journey a little easier.
I love and miss them every day.

Acknowledgements

No one advances in any profession without the encouragement and support of other individuals. I have many people that have helped me fulfill my goals and dreams of earning my PhD so that my knowledge might benefit the care and health of patients suffering from heart failure. First and foremost, I would like to thank my chair, Dr. Debra Moser, who has been the most influential person in my career. Little did I know the first day I met her that she would be the individual who inspired me the most to be best I can be. She has guided me, encouraged me, uplifted me, talked with me, laughed with me, and of course, taught me the intricacies and nuances of research. I consider her my mentor and my friend and will be forever grateful that our paths crossed and I had the wonderful opportunity to study under her guidance.

I would like to thank Dr. Lynne Hall who has supported me and helped guide me. When I was struggling, she helped me find the path back to my goals. I also want to thank Dr. Mary Kay Rayens with whom I had several enjoyable statistics classes and helped me find assistance with my last research project. Dr. Rayens was instrumental in facilitating my introduction to Dr. Christopher Lee who guided me and provided expert consulting in the analysis of my most challenging project utilizing latent growth modeling. Dr. Lee availed himself to me whenever I needed him and helped me complete a research project that is one of the first to appear in the literature surrounding my thesis topic. My gratitude does not stop with these individuals as my entire committee has been committed to helping me with my dissertation and offered support, guidance, encouragement, and, when needed, humor. My committee members are dedicated, wonderful faculty who have helped me see this project to its conclusion: Dr.

Susan Frazier, Dr. Terry Lennie, Dr. Stephen Fleming, and Dr. Michael Andrykowski, my outside examiner. I cannot thank them enough for their flexibility and support.

My gratitude and thankfulness would not be complete without acknowledging the love and support of friends and family. I would like to thank Andrea Flinchum for allowing me time off to write. I know this was not always convenient, but Andrea wanted to see me succeed and I appreciate her consideration of my needs probably more than she realizes. My sister, Mary McCray, and my brother, Thomas Price, have both understood when my time commitments would not allow me to participate in family events and loved me anyway. Many thanks and much gratefulness go to my husband, Thomas, and my children, Tommy and Mimi, who have always encouraged me to persevere and continue to strive for my dreams. Collectively, they arranged and did things for me and our family when I could not. Their love and support carried me through when times seemed bleak. I also want to thank my parents, Thomas and Betty Price, who provided me with unconditional love and a home that nourished inquisitiveness, compassion, courage, and confidence. Most importantly, I want to thank my Lord and Savior, Jesus Christ, who has blessed me with so many things. Never a day goes by that I don't give thanks to Him for all of His many blessings. I have experienced much happiness and success in my life; however, through my faith and love for Christ, I know that when I am faced with challenges, disappointments, and failures, there will be an end to the trials and joy will be waiting for me on the other side.

This work was supported by: The National Institutes of Health and the National Heart Lung and Blood Institute, 1R01HL083176; and The National Institutes of Health and the National Institute of Nursing Research, R01 NR008567.

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Chapter One: Introduction

For over 2000 years people have written about the connection between emotions and physical health.[1,2] Since antiquity strong negative emotions have been associated with cardiopulmonary symptoms to the extent that many believed the heart was the center of emotions.[3] Egyptians believed the heart was the seat of human wisdom, emotions, and life itself - a place where the soul resided - and when the dead were judged, the heart was weighed against the feather of truth to determine if the deceased could enter the afterlife.[4] While the heart is not the center of emotions as once believed, it is clearly affected by psychological conditions. Studies have shown that negative emotions, such as anxiety, depressive symptoms, and hostility, increase the risk of the development and progression of cardiovascular disease[5-7] and subsequent heart failure (HF).[8-13]

Currently more than 5,700,000 people in the United States suffer from HF, and an estimated 870,000 new cases are diagnosed each year.[14] The prevalence of HF has continued to increase annually as more people survive longer with cardiovascular disease. It is estimated that the prevalence of HF will increase 46% from 2012 to 2030.[14] This steady rise in HF has important implications for healthcare. In addition to a variety of physical symptoms, patients with HF suffer from psychological distress that impacts survival and quality of life.[15] The relationships between these negative emotions and HF are multidimensional, complex, and poorly understood. However, research suggests negative emotions affect health outcomes of patients of living with HF. [9,16-19]

Patients with HF experience higher levels of anxiety, depressive symptoms, and hostility than their healthy elder counterparts or patients with other cardiac conditions.[20] Negative emotions may lead to pathophysiological changes that subsequently increase

risk of clinical events[21] and can complicate cardiovascular disease in general.[22] The clinical risks associated with negative emotional states in cardiac patients may be equal to or greater than those associated with traditional risk factors such as diabetes and smoking. Heart failure patients who have negative emotional states have poorer health-related quality of life (HRQOL),[23-25] decreased adherence to treatment regimens,[26-29] and higher rates of hospitalization[30] and mortality.[31-33,34]

However, research concerning the incidence, prevalence, and health outcomes associated with symptoms of anxiety, depression, and hostility among patients with cardiovascular disease and HF has yielded varying results.[20,35] This may be attributed to the different ways these negative emotional states have been defined, heterogeneity of patients in subgroups of cardiac disease, and the methods used to screen for their presence.[36,37]

Conceptual Dimensions of Anxiety, Depressive Symptoms, and Hostility

Anxiety. Anxiety is a negative affective state; however, it is often used as an umbrella term for a variety of disorders.[38] It has been difficult to define the conceptual dimensions of anxiety, as researchers often use the term loosely to describe various psychiatric conditions (i.e. panic disorder, post-traumatic stress disorder, generalized anxiety disorder, obsessive compulsive disorders, and specific phobias)[39] as well as a normal transient emotional experience.[40] Additional ambiguity exists in defining anxiety, as anxiety has often been studied as either trait anxiety or state anxiety[41,42]

Trait anxiety refers to the predisposition of an individual to experience anxiety, and state anxiety refers to the actual experience of anxiety that is manifested by a transitory emotional reaction to a situation that is accompanied by a physiological

response.[43,44] Therefore, trait anxiety is considered a personality dimension of neuroticism rather than emotional stability[45] and is suggestive of an enduring predisposition of an individual to respond to many threatening situations in a relatively consistent manner.[44]

Despite the different conceptual definitions of anxiety, a shared characteristic of all anxiety disorders is that anxiety is a complex subjective human experience in response to a foreboding dread or perceived threat that has physiological, behavioral, affective, and cognitive symptoms.[46,47,48] A majority of the symptoms of anxiety are physical in nature and occur as a result of activation of the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS), of which activation of the SNS is the predominate physiological response.[48] Physical symptoms of anxiety include increased heart rate, palpitations, nausea, sweating, shaking, breathlessness, hyperventilation, diarrhea, and tingling and numbness in the mouth and arms, and may result in behaviors that include agitation, avoidance, and withdrawal.[40,48] The affective and cognitive reactions of anxiety include symptoms of restlessness, agitation, fearfulness, feelings of helplessness and of being overwhelmed as well as worrying, recurrent unpleasant thoughts, poor concentration, confusion, narrowing of attention, hypervigilance for any threat, poor memory, and difficulty in reasoning.[40,48]

The severity of anxiety symptoms exists on a continuum ranging from normal to pathological depending on subjective perception, intensity, duration, sense of control, and subsequent dysfunction or interference with life activities.[48-50] Some symptoms of anxiety serve a useful purpose insofar as the physiological changes often seen in anxiety are responses that prepare the body both mentally and physically to react to situations that are

perceived as dangerous. The perception of danger elicits a fear response that results in autonomic arousal and the subsequent ability and motivation to respond to or confront that danger.[40,48] Therefore, both fear and anxiety are considered adaptive processes to threats of danger.

Although fear and anxiety are adaptive states which function to preserve life, some researchers use these terms interchangeably.[51] Part of the confusion lies in the fact that the physiological responses to fear and anxiety are similar with SNS arousal and subsequent symptoms. Fear and anxiety have been differentiated by some[52] with fear being defined as the intellectual appraisal of danger and anxiety being defined as the emotional response to that appraisal. However, a growing body of evidence supports the premise that fear and anxiety are different emotions and constructs conceptually.[51] The neuroscience literature suggests fear is a response to a perception of a specific threat,[53] while anxiety is viewed as a prolonged hypervigilance in response to a diffuse threat that is not specific or clearly imminent.[54]

Anxiety and specific anxiety disorders are commonly diagnosed by a medical health professional from an interview process. However, many studies use symptoms of state or trait anxiety as determined by self-report scales such as the Brief Symptom Inventory (BSI) Anxiety Subscale,[55,56] the Spielberger State-Trait Anxiety Inventory (STAI),[57] Beck Anxiety Inventory (BAI),[58] and the Hospital Anxiety and Depression Scale-Anxiety (HADS-A).[59] I chose to measure state anxiety with the BSI Anxiety Subscale in the three studies included in this dissertation. The BSI Anxiety Subscale is a short 6-item self-report questionnaire[55] that can be used to assess symptoms of anxiety. The self-report questionnaire is easy to administer and does not create undue burden on

patients with HF who may experience symptoms such as fatigue. The BSI has been used in numerous populations[56,60] and has good internal consistency and excellent validity in several samples of patients with HF.[26,61,62]

Depressive symptoms. Depression has resulted in more human suffering than any other disease affecting mankind.[63,64] It is considered a disorder of mood characterized by the presence of a number of symptoms which interfere with a person's ability to carry out activities of daily living as outlined in *The ICD-10 Classification of Mental and Behavioral Disorders: Clinical Descriptions and Diagnostic Guidelines (ICD 10)*[65] and the *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition.*[66] In order to meet the definition for a major depressive disorder, a person must experience at least five of the following nine symptoms over a two-week period of time: 1) depressed mood most of the day; 2) markedly diminished interest or pleasure in most activities; 3) significant weight loss or weight gain; 4) inability to sleep or oversleeping most days; 5) fatigue or loss of energy; 6) psychomotor agitation or retardation; 7) feelings of worthlessness or excessive or inappropriate guilt; 8) decreased ability to think or concentrate, or indecisiveness; or 9) recurrent thoughts of death. For a diagnosis of clinical depression, one of the symptoms must include either depressed mood or loss of interest or pleasure in activities.[39] Together, these symptoms represent the core symptoms of depression.[67]

However, there is some controversy as to how depression should be conceptualized apart from a clinical diagnosis. Individuals with depression often complain of an unpleasant emotional state, a changed attitude toward life and loss of interest in activities, somatic symptoms typical of depression (e.g. fatigue, leaden paralysis, loss of appetite), and somatic symptoms not typical of depression (e.g.

headache, constipation).[39,68] An interesting phenomenon in depression is that a majority of patients experience a disturbance in self-concept and negative view of themselves that is in stark contrast from the objective assessment a clinician may make.[64] This has led to the belief that depression is primarily an affective disorder. However, researchers have demonstrated that depressed patients often complain of physical symptoms regardless of whether they have a mental or physical illness.[64,68,69] The variety of symptoms seen in depression as well as the various semantics used have resulted in difficulty conceptualizing depression.

From time to time many individuals complain of feeling 'depressed' without any low mood, sadness, or clinical diagnosis.[64] Loose use of the term depression in everyday language as well as the use of the term to describe symptoms or a psychopathology makes conceptualizing depression challenging as depression is used to describe numerous feelings or symptoms, a symptom-complex (syndrome), or a specific disease entity.[64] Symptoms of depression may range from transitory feelings of 'being down' to a specific psychopathology such as major depressive disorder (MDD) or bipolar disorder. However, deviations in feelings, cognition, and behavior are seen most often when the term depression is used.[64,69]

Thus, depression is best described as the presence of symptoms that are syndromal in nature, implying that there is cluster of symptoms that occur together ranging in intensity.[64,67] These depressive symptoms occur along a spectrum of increasing severity of symptoms which range from non-specific symptoms that are not indicative of a disorder to a diagnosis of major clinical depression.[70-73] In fact, patients can have very distressful depressive symptoms without having an actual diagnosis of MDD.[74] Screening

for depressive symptoms allows for greater understanding of subclinical depression[70] as well as residual depression where patients have been treated but still have symptoms of depression. This is important for improving health outcomes as residual depression may represent persistence of a milder form of depression or signal increased risk of relapse.[75]

Depressive symptoms may be screened through a clinical interview, review of a patient's medical record, or depression symptom inventories which include self-report measures.[19] Self-report measures have been criticized as they depend on patient memory, honesty, and potential desire of the patient to be viewed favorably. However, in a meta-analysis of 27 studies reporting depression rates among patients with HF, Rutledge et al.[19] found prevalence rates for depression varied from 10% to 54% depending on the method of assessment used. Those studies using self-report had substantially higher prevalence rates than those studies that utilized clinical interview combined with self-report or clinical interview alone. This would suggest that self-report measures might be more sensitive in identifying depressive symptoms that are troublesome to patients.

Several self-report questionnaires are available for assessing depressive symptoms including the Beck Depression Inventory (BDI),[76] Center for Epidemiological Studies-Depression Scale,[77] BSI Depression Scale,[55,56] and the Patient Health Questionnaire-9 (PHQ-9).[78,79] I chose to use the PHQ-9 to measure depressive symptoms in all three studies comprising this dissertation. The PHQ-9 is a self-report measure composed of nine Likert scale items that reflect the symptom criteria outlined for depressive disorders.[73,78] The PHQ-9 is short, easy to administer, and has excellent reliability and validity in numerous patient populations[79,80] as well as in samples of patients with HF.[62,81]

Hostility. Hostility is a multidimensional construct that has cognitive, affective, and behavioral components. It has been defined as a negative attitude or personality trait that is directed toward others[37] and characterized by a belief that others are unworthy, underserving,[82] and immoral.[83] The concept of hostility has been confusing to define as it is associated with other phenomenon such as anger and aggression.[37] These constructs are closely related negative psychological constructs that are often thought of as being one and the same and sometimes used interchangeably in research.[37,84,85] While several studies have demonstrated strong correlations between hostility scales and trait anger[86] and aggression scales, these constructs are different. However, defining and differentiating these constructs can be challenging as some of the personality factors related to hostility, anger, and aggression are similar.[37,87]

The constructs of hostility, anger, and aggression are best understood by examining the emphases on components of cognition, affect, and behavior.[88] The cognitive component of hostility entails a negative attitude toward others consisting of ill will, enmity, and denigration.[89] Hostility also includes components of cynicism, mistrust, and a biased attributional style[83,89,90] This sense of mistrust results in an expectancy that people will not fulfill obligations and are frequent sources of provocation, mistreatment, and even harm.[89] The cynicism of hostile individuals makes them more likely to believe that others are motivated by selfish concerns rather than by a genuine concern for others.[89] Together, these beliefs produce a biased attributional style leading hostile individuals to interpret the actions of others as antagonistic or threatening, thus making the hostile individual more likely to respond to others in an aggressive or antagonistic manner.[91]

In addition, the affective component of hostility includes numerous emotions such as anger, annoyance, resentment, disgust, and contempt.[83,92-94] The behavioral component of hostility may include acts of overt aggression, subtle aggression, and verbal aggression.[83] Thus, a hostile individual may respond to the acts of others with frustration and anger and behave in a physically aggressive manner or exhibit verbal aggression through hateful insults, opposition to others, rudeness, sarcasm, or argumentativeness.[89,95] Therefore, as a general trait, hostility involves a devaluation of the worth of others and interpersonal suspicion and mistrust of the motives of others. These beliefs result in an expectation that others are likely sources of wrongdoing, and there is also a desire to inflict harm or see others harmed.[89,96]

Anger, on the other hand, is an affective construct that is characterized by an unpleasant emotion that may range in intensity from irritation or annoyance to fury or rage.[97,98] It can be defined as either a state or a trait. The state of or experiential component of this emotion is usually accompanied by physiological arousal and activation of tendencies toward aggression.[97] Anger is also characterized by a relational theme whereby the angry individual has the perception of being subjected to illegitimate or unfair interference or harm.[50,99] Therefore, the experience of anger is a subjective process with related emotions of contempt and resentment similar to hostility.[89,98] Anger, as a trait, is the tendency of an individual to experience states of anger with greater frequency, over a wider range of situations, and over longer periods of time.[87,91,100] The behavioral component of anger includes concepts of anger expression and anger-coping styles and refers to the extent to which people express or display feelings of anger. Anger-out is the tendency an individual possesses to openly express anger and typically

involves some type of aggression while anger-in is tendency to suppress or deny anger.[91,101]

Both hostility and anger share traits of aggression in terms of behavioral components. However, aggression is usually associated with behaviors directed to harm another and may range from verbal to physical attacks. Physical aggression can be direct, indirect, or passive.[89] Common behaviors associated with aggression include demeaning remarks, sarcasm, intimidating glares, rolling of eyes, hateful insults, rudeness, and confrontation.[89,91] Thus, aggression can be viewed as an antagonistic behavior that is one aspect of the behavioral component of hostility.[83]

Hostility, however, involves a more complex cognitive component than anger or aggression. The prominent characteristic in hostility is one of cynicism. While anger has a cognitive component, the more overriding component is the affective or emotional component, and aggression's most prominent feature is that of behavior. Therefore, in conceptualizing hostility, the three attributes of cynicism, anger, and aggression may be present together with hostility or in the absence of the other two constructs.[83]

Hostility has been measured using an assortment of self-report measures such as the Cook-Medley Hostility Subscale,[90,102] the Buss-Durkee Hostility Inventory,[92,103] and the BSI Hostility Subscale.[55,56,60] I used the BSI Hostility Subscale in two of the studies in this dissertation as it is a short 5-item self-report survey that asks questions about symptoms of hostility experienced by patients in the last two weeks that occur within the three dimensions associated with the concept of hostility: thoughts, feelings, and behavior.[60] While hostility is a concept frequently measured in the cardiac population, it is not routinely measured in patients with HF. Part of the problem may be the issue of

conceptualizations of hostility versus anger and aggression. In addition, most measures of hostility have greater than 50 items that may create undue fatigue among patients with HF. The BSI Hostility Subscale is the briefest hostility measure available and is very easy for clinicians to administer;[104] therefore, its use and application in studies of patients with HF is ideal. The BSI Hostility Subscale has been used in many populations,[60] and has good internal consistency and validity in patients with HF.[105,106]

Influence of Symptoms of Anxiety, Depression, and Hostility on Health Outcomes

Numerous studies have demonstrated a strong association between negative emotional states and the development and progression of cardiovascular disease.[2,107-110] However, the mechanisms linking anxiety, depressive symptoms, and hostility with adverse health outcomes in patients with HF are not well established. Negative emotional states may worsen or be a risk factor for HF, or HF may exacerbate symptoms of anxiety, depression, or hostility, or these negative emotions may interact with HF.[16] However, several mechanisms through which negative emotional states may convey increased cardiovascular risk and worsening of HF have been proposed. Currently, there are two primary potential pathways by which negative emotions increase the risk of adverse cardiovascular outcomes: (1) physiological hyperreactivity and (2) behavioral factors such as non-adherence to medical regimes, engagement of risky behaviors, and limited use of appropriate health-related resources (Figure 1.1).[26,109,111-123] The extent to which symptoms of anxiety, depression and hostility influence the two potential pathways can be mediated or moderated by individual vulnerability factors such as age, sex, comorbidities, perceived social support, education, and functional ability (Figure 1.1).

Potential physiological hyperreactivity. Negative emotions have been associated with the development of cardiovascular disease through a direct physiologic effect that results in dysregulation of the autonomic nervous system (ANS) that initiates a cascade of events that confer increased risk.[7,124,125] The influence of negative emotions may cause a similar physiological hyperreactivity in patients with HF which results in worsening HF, decreased physical health-related quality of life (P-HRQOL), increased hospitalizations, and increased mortality (Figure 1.1).[126]

Dysregulation of the autonomic nervous system. The ANS is responsible for regulating cardiovascular homeostasis through the SNS and the PNS. Negative emotional states produce alterations in ANS modulation causing activation of the SNS and inhibition or withdrawal of the PNS.[126] These negative emotions produce physiological reactions that are excessive and prolonged and may explain the association of these emotions to poor health outcomes.[2,110,127,128] Dysregulation of the ANS results in alteration of neurohumoral function and increased circulating levels of norepinephrine (NE) and epinephrine (E).[18] Autonomic nervous system dysregulation has been shown to worsen HF and is a strong predictor HF progression,[18] mortality, and sudden cardiac death.[129]

Increased SNS activation from negative emotions in patients with HF can result in electrical instability of the myocardium that subsequently increases risk of ventricular arrhythmias due to inadequate opposition of SNS.[130] Approximately 50% of patients with advanced HF experience sudden death thought to be attributable to ventricular dysrhythmias.[131] Negative emotions are also associated with decreased heart rate variability (HRV) in patients with heart disease.[132,133,134] Higher heart rate variability

reflects better balance between the SNS and the PNS and is a healthier state. The heart rate (HR) of healthy individuals varies in response to respiration and to changes in the physical demands of the body; however, negative emotions are associated with decreased HRV.[135,136] Heart rate variability is considered a measure of cardiac autonomic innervation; therefore, decreased HRV is an indication of abnormal ANS modulation of HR, excessive sympathetic stimulation, and reduced vagal activity.[132] Decreased PNS innervation exposes the heart to unopposed stimulation by the SNS and has been shown to be an independent predictor of morbidity and mortality in patients with HF.[137]

Alteration of neurohormonal function. The ANS response to emotions differs according to the state of emotion.[138,139] Positive emotion states increase PNS activity whereas negative emotional states result in activation of the SNS and subsequent inhibition or withdrawal of the PSN.[138,140] When the SNS is activated, there are immediate changes in the neurohumoral, hematologic, endocrine, and vascular systems.[3] The subsequent hemodynamic and neurohumoral responses caused by the release of catecholamines, NE, and E, and further increases SNS activity.[141-143] This initially results in increased HR, cardiac output, and blood pressure.[141] However, patients with HF may have decreased clearance of NE due to compromised cardiac output resulting in further increased levels of NE.[144] The presence of increased levels of NE and E may exacerbate HF symptoms as these catecholamines increase HR, increase contractility, and increase cardiac workload in patients with HF whose cardiac reserve is already compromised. Researchers have demonstrated that increased levels of NE and E are associated with adverse HF prognosis[144,145] and predict mortality in patients with HF.[146]

Norepinephrine plays a determinate role in executive function such as regulating

intellect, cognition, and motivation, and influences the ability to have social relationships[147] while E helps to regulate cognition, attention, mental focus, and arousal. Executive functions are fundamental to problem-solving capacity in ways that are acceptable to the individual as well as society.[147] These functions include the ability to suppress nonpertinent information, inhibit unacceptable behavior, and self-regulate affect, motivation, and arousal.[147] Patients with negative emotional states have elevated serum and urinary levels of NE[128,148-150] and E.[135] The increased levels of NE and E may be associated with increased stimulation from the SNS and the stress response.[128,151] Negative moods may interfere with cognitive processes. Further, chronic stimulation of the stress response by the SNS leads to structural changes in the pre-frontal cortex (PFC) of the brain, where executive function is controlled.[152] Highly elevated levels of NE can suppress neuronal firing in the brain and impair spatial working memory[152] as well as leading to a relapse of maladaptive behaviors such as smoking, overeating, drinking alcohol, and drug addiction.[153] The balance of neurotransmitters in the PFC is sensitive to change and may influence the behavioral pathway through its influence on self-care and maladaptive behaviors.

Activation of the hypothalamic-pituitary-adrenal (HPA) axis. Negative emotional states are associated with reduced feedback control of the HPA axis with subsequent increased HPA activity.[18,154,155] Increased HPA axis activity results in a sequence of events including signaling the hypothalamus to release corticotropin-releasing factor. Release of corticotropin-releasing factor increases corticotropin release from the pituitary and reduces adrenocorticotropin response to corticotropin resulting in increased cortisol levels and aldosterone from the adrenal cortex.[156] This cascade of responses results in a

failure of the body's normal feedback inhibition system such that cortisol levels remain high.[157]

Increased cortisol levels are associated with hypertension,[158] insulin resistance,[159] abdominal obesity,[160] oxidative stress,[161] altered endothelial function,[162] vasoconstriction,[162] and inflammation.[163] Increased cortisol levels may be associated with progression of HF and worse health outcomes.[164,165] Increased cortisol levels may imitate the effects of aldosterone by binding with aldosterone's receptor, the mineralocorticoid receptor and stimulating the effects of aldosterone. The subsequent increase in aldosterone conserves sodium, secretes potassium, and promotes water reabsorption thereby increasing blood volume and subsequent blood pressure adding to workload on the heart.[166] Activation of the HPA axis by a failing ventricle in the presence of increased workload produces more cortisol and aldosterone which leads to further cardiac remodeling, thereby increasing the severity of HF.[164]

Stimulation of the SNS, along with renal hypotension and decreased amounts of sodium delivered to the renal tubules, stimulates the release of renin and the further release of aldosterone by the renin-aldosterone-system (RAAS). Renin activates the conversion of angiotensin I to angiotensin II which causes vasoconstriction resulting in increased blood pressure as well as inhibition of the release and reuptake of NE. The increase in NE increases levels of antidiuretic hormone which also inhibits water excretion and further vasoconstriction, further contributing to myocardial remodeling.[167] In addition, cytokines, macrophages, and neutrophils are released due to the activation of RAAS. This results in the deposition of fibroblasts and collagen leading to ventricular hypertrophy, fibrosis, and heart remodeling.[168] Negative mood states activate RAAS

through stimulation of SNS.[168,169]

Increased activation of the HPA axis by negative emotions may contribute to decreased cognitive function observed in HF patients. Depressed patients have increased cortisol levels as studies indicate there is diminished negative feedback in the HPA axis.[170] Extended exposure to elevated levels of cortisol has been shown to have adverse effects on verbal memory,[171,172] and impaired performance in declarative memory and spatial thinking tasks[173] among patients with depressive symptoms.

Woo and colleagues[174] examined magnetic resonance images (MRIs) of 9 patients with HF and 27 controls. Compared to the controls, patients with HF had reduced grey matter in areas associated with ANS control, areas essential for mediating pain, areas associated with autonomic regulation (important for multiple fluid, thermoregulatory, and sleep maintenance functions as well as ANS control), areas associated with depressive symptoms and mood regulation, and areas associated with cognition, behavioral performance, and mediating expressive aphasia. Woo et al.[174] suggest mechanisms of injury to the brain may be ischemic, hypoxic, or inflammatory processes. The investigators suggest that patients with HF have structural changes in the brain that may compromise their ability to understand and adhere to medical regimens and the changes in brain structure may also have a role in the subsequent development of depressive symptoms.[174] Almeida et al. examined the MRIs of 35 patients with HF and 56 patients with ischemic heart disease against 64 healthy individuals and found the patients with HF had evidence of loss of grey matter in various areas of brain and lower scores than the control group on immediate memory, long delay recall and digit coding.[175] These studies illuminate the possibility that brain changes found in heart failure may influence the

ability of patients with HF ability to care for themselves, take medications, and keep medical appointments.

Activation of cytokine cascade. Inflammation and changes in the immune system occur through activation of the HPA axis and the ANS via the outflow pathways of the central nervous system. Increased release of corticotropin hormone occurs in response to negative emotions that results in the release of pro-inflammatory cytokines.[176] Numerous studies have documented the effects anxiety, depressive symptoms, and hostility have on the activation of pro-inflammatory cytokines, specifically tumor necrosis factor-*a* (TNF-a) and interleukin-6 (IL-6).[7,177-181] Inflammation is characterized by an interaction between pro-inflammatory cytokines and anti-inflammatory cytokines. Usually anti-inflammatory cytokines counteract the toxic effects of pro-inflammatory cytokines; however, patients with HF[182] as well as negative emotions[176] have increased levels of pro-inflammatory cytokines. Cytokines activate macrophages and increase the growth of fibroblasts and collagen leading to myocardial wall fibrosis and wall-motion abnormalities resulting in myocardial remodeling and decreased left ventricular ejection fraction.[114,183] Elevated levels of TNF-*a* is associated with worsening and more severe HF.[184] In concert with other neurohumoral processes, proinflammatory cytokines suppress cardiac contractility,[185] increase apoptosis,[185] increase HF symptoms,[182] facilitate myocardial remodeling,[186] and result in adverse health outcomes in patients with HF.[187] In addition, IL-6 is implicated in the development of future HF.[188]

Heart failure is usually the end result of cardiovascular disease. Negative emotional states increase the levels of circulating proinflammatory cytokines which may be involved in the pathogenesis of atherosclerosis and resulting cardiovascular

disease.[18,189] Damage to the endothelium lining in the coronary vessels stimulates the release of proinflammatory cytokines such as interleukin (IL)-1, IL-6, and tissue necrosis factor alpha (TNF-α). The release of cytokines encourage adhesion of inflammatory cells to the endothelium which then further activate more cytokine and growth factor release.[190] Intimal smooth muscle cells then proliferate and accelerate the atherosclerotic process. In a study of healthy adult volunteers, Gianaros[7] found those individuals exposed to situations generating negative emotions had the greatest levels of IL-6 as well as greater carotid artery intima-media thickness and inter-adventitial diameter, indicating preclinical atherosclerosis. The same inflammatory process is also implicated in the development of vascular depression due to the endothelial damage to the cerebral arteries.[18]

Change in platelet receptors and function. Studies suggest negative emotional states produce changes in the clotting process including increased platelet aggregation,[191] vasoconstriction, and subsequent plaque rupture.[192,193] Increased SNS activation provides a pathway for thrombogenesis.[194] Findings of studies examining the role of negative emotions and platelet reactivity have been inconsistent. Depression and platelet reactivity have been studied to a greater extent than anxiety and hostility.[195] In a study[191] of 153 individuals without a history of cardiovascular disease (108 were depressed, 45 were controls), investigators found that depression was significantly associated with platelet activation and when depression resolved, platelet activation was reduced. However, in a study[196] of 83 stable cardiac patients, investigators found anxiety was a better predictor of platelet reactivity than depression. Further, in a study[197] of hypertensive patients without a history of cardiovascular disease, researchers found that hostility was significantly

associated with platelet reactivity and did not diminish when controlling for other risk factors. While the role of negative emotions and platelet reactivity may not be fully understood, negative emotions have been shown to be predictive of poor health outcomes such as acute myocardial infarction[198,199] and subsequent cardiovascular mortality.

Cardiac remodeling. Cardiac remodeling occurs as a compensatory mechanism for a failing left ventricle which results in changes in the size, shape, and function of the myocardium.[200] The process of cardiac remodeling and subsequent HF occurs as a result of damage or injury to the heart and are influenced by autonomic dysregulation[201,202] and neurohumoral activation[203] as well as activation the HPA axis and RAAS.[200] While these compensatory changes are in response to falling cardiac output in the face of increased cardiac workload, these changes are also responsible for deterioration in cardiac function and physiologic cardiac remodeling and progression of HF.[200,204] Elevated circulating levels of angiotensin II, aldosterone, NE, E, and proinflammatory cytokines result in dilation of the left ventricle and increased inotropic and chronitropic effects on the myocardium to adapt to increased volume.[204] After the ventricle wall is chronically stretched, myocytes decrease in number (apoptosis)[205,206] and become elongated and hypertrophied as an adaptive process. The LV will hypertrophy, and fibroblasts will proliferate[207] and increase collagen synthesis[208] which leads to fibrosis[209] and further hypertrophy of the LV. As compensatory changes continue, the heart will actually change shape, becoming less elliptical and more spherical.[200,210,211]

Symptoms of anxiety, depression, and hostility complicate and hasten the remodeling process of the myocardium in patients with HF as negative emotions are associated with further increases in autonomic dysregulation, neurohumoral and immune

system changes, and activation of the HPA axis and RAAS.[35] The heart must work harder to overcome increased hemodynamic load and changes resulting from physiological hyperreactivity of systems that are activated to maintain cardiac output. Wall-motion abnormalities and decreased left ventricular ejection fraction from impaired ventricular function are associated with negative emotions.[212,213] While not all patients with HF experience symptoms of anxiety, depression, and hostility, these negative emotions have been strongly implicated in hastening and progression of HF by exacerbating common biological compensatory processes[18] and contribute to increased mortality in this population.[32]

Summary of potential physiological hyperreactivity. The potential physiological hyperreactivity is a plausible pathway through which negative emotions may confer increased risk of poor health outcomes in patients with HF. Heart failure is a progressive adaptation and remodeling due to injury and cardiac demand. Negative emotions elicit further autonomic system dysregulation, neurohumoral changes, increased activation of the HPA axis, RAAS, and cytokine cascade, changes in platelet receptors and function, and remodeling of the myocardium resulting in hastening and progression of HF. Patients with HF who experience negative emotions may be at greater risk of disease progression and poor outcomes than those patients with HF who do not experience negative emotional states.[35]

Potential behavioral pathways. In addition to the proposed physiological hyperreactivity pathway, another possible pathway linking symptoms of anxiety, depression, and hostility with poor health outcomes is the manner in which symptoms of anxiety, depression, and hostility can produce certain behaviors in patients with HF that

result in worse health outcomes. Patients with negative emotions often fail to adhere to medical treatment regimens such as medications, [26,27,113,214-217] continue or adopt risky lifestyles such as smoking or a sedentary lifestyle,[116,217,218] and often do not utilize appropriate resources (e.g., cardiac rehabilitation, clinic appointments, counseling) that can assist them achieve better health outcomes.[219-221]

Nonadherence. Negative emotions impact rehospitalization, P-HRQOL, and mortality of patients with HF due to their influence on patient adherence to treatment regimens. After discharge from the hospital for HF, approximately 23% to 28.9% of Medicare beneficiaries are rehospitalized within 30 days.[222-224] O'Connor and colleagues found that rehospitalization rates for HF patients increased to 57.9% after 60 days from discharge after initial hospitalization.[225] However, as many as 44% to 82% of patients with HF are readmitted to a hospital within 90 days to one year following hospitalization for decompensated HF.[226,227] One of the key factors in prevention of hospital readmissions among patients with HF is poor self-care, which includes adherence to treatment regimens and monitoring of symptoms.

Nonadherence to treatment regimens is associated with poor health outcomes and worse HF symptoms as well as increased rates of emergency department visits and rehospitalizations.[228-230] It is estimated that one-half to two-thirds of HF related hospitalizations could be prevented by better patient adherence.[215,216,231] The average rate of nonadherence in HF patients is approximately 40% to 60%; however, rates of adherence have been reported in the literature ranging from 10% to 98% depending on the methods used to measure adherence.[232]

Evidence suggests that negative emotions may be an important contributor to

nonadherence among patients with HF.[233] In the cardiovascular population, patients with depression are more likely to have poor adherence with prescribed medications, diet, and exercise regimens.[234,235] Tang et al.[27] found that patients with HF who were depressed were 2.3 times more likely to report nonadherence to prescribed medications than those patients who were not depressed. Farrell and colleagues[29] examined whether depression, hostility, social support, and personality traits known to influence medication adherence would be predictive of patient adherence to HF medications. These authors reported that both depression and hostility were predictive of medication adherence among patients with HF. In addition, DeJong and colleagues[26] found anxiety independently predicted medication adherence among 147 patients with HF and suggested anxiety mediated the relationship between nonadherence and event-free survival.

Depressive symptoms such as fatigue, lack of motivation, problems with concentration, social withdrawal, and feelings of worthlessness may hinder the ability of patients to adequately follow prescribed treatment plans.[236] Anxiety may hinder adherence to treatment regimens due to the need for lifestyle changes which may overwhelm their coping ability as anxious individuals have fewer coping responses needed to deal with change.[17,237] In a study of patients hospitalized for a myocardial infarction, Moser et al.[238] found patients with high levels of anxiety had feelings of a low sense of control leading to feelings of powerlessness. Cynicism and a basic mistrust of others are characteristic of hostile individuals who are more likely to have poor adherence with medications[238] as well as diet and exercise.[217,240]

Negative emotions also contribute to impairments in attention, memory, and executive function such as problem solving.[241] Rosenberg et al.[242] reported depression

predicted impairment in cognitive functioning including episodic, immediate, and delayed memory as well as impaired psychomotor speed and executive functioning. In a study of patients with HF and depression, Garcia et al. reported depression was found to be predictive of cognitive impairments to executive function, memory, language, and motor function even after controlling for sex, cardiac fitness, and presence of a comorbidity such as hypertension.[243] An impairment in memory, attention, or decision-making, often seen in negative emotional states, can interfere with many aspects of daily life and the ability to care for oneself.[244] Depressed patients have more errors of attention when compared to nondepressed patients as well as performance deficits in working memory and attention that worsen with severity of illness.[245,246] Depressive thoughts (e.g. intrusive thoughts) limit working memory and impairs a patient's ability to learn and retain new information.[247] Subsequently, negative emotional states decrease the speed with which patients with HF can learn, synthesize, and recall information about their condition and their prescribed medical regimen.

Several meta-analyses describe the complex relationships between negative emotions and cognitive performance. In a meta-analysis of the effects of depression and anxiety on memory performance, Kizilbash et al.[248] found comorbid depression and anxiety had an adverse effect on immediate recall and amount of acquisition of new knowledge as well as on the ability of patients to retrieve the newly learned information. In addition, Zaninotto and colleagues[249] demonstrated that patients with negative emotional states (e.g. melancholic) not only had worse cognitive performance in attention, working memory, and visual learning, but also in reasoning and problem-solving than those patients without symptoms. While hostility is often viewed as a

relatively stable personality trait and shown to be predictive of CAD[250,251] and worsening of HF,[217,252] it is also shown to be independently associated with cognitive impairment.[253,254] Studies suggest hostility may influence cognition through exaggerated cardiovascular or neuroendrocrine responses[255] as well as a vulnerability to experience increased levels of stress than non-hostile individuals,[256] both of which impair memory and recall.[253] These studies suggest that negative emotions contribute to cognitive dysfunction in patients with HF resulting in problems with learning appropriate self-care about the disease. Heart failure self-care requires understanding of a relatively complex medical regimen, being able to detect significant changes in symptoms, and evaluating changes in symptoms and needed actions to prevent worsening of symptoms.

In a meta-analysis of studies on brain changes in clinically depressed patients without HF, Palmer and colleagues[257] reported there were consistent changes in the brains and affecting integrated pathways linking select cortical, subcortical and limbic sites. The meta-analyses reported that demand of the task would determine what network would be activated and depression would dampen the efficiency of functions of the network.[257] This would suggest that clinically depressed patients would need to apply greater conscious effort in completing the same task than nondepressed indviduals.[257] The cognitive impairments found in the changes of the brains of depressed patients interfere with learning and understanding treatment regimens, particularly remembering to take medications, maintaining follow-up appointments and check-ups, as well as continuing appropriate diet and exercise. Therefore, adherence to medical regimens would be especially difficult for patients with HF whose medical regimen is very complex.

In addition, symptom awareness and subsequent management of those symptoms

also influence adherence to the recommended HF regimen and optimal self-care. Symptom awareness is influenced by cognitive appraisal of a patient's perception of that threat. Smith and Lazarus[258] proposed six domains of cognitive appraisal: (a) motivational relevance; (b) motivational congruence related to one's goals; (c) accountability related to placement of blame (self versus others); (d) problem solving related to coping potential; (e) emotion-focused potential (how an individual perceives coping ability should the situation not change); and (f) perception of how likely the situation is to change. Negative emotional states, as with symptoms of anxiety, depression, and hostility, are associated with a dysfunctional cognitive appraisal.[52,64,259 260] Often individuals with negative emotions interpret information in a negative manner and have problems in cognitive control in the processing of negative material as they have an enhanced memory for negative material.[261]

Individuals with symptoms of anxiety, depression, and hostility all appraise situations according to motivational relevance and motivational congruence related to their goals.[193] However, individuals with specific negative emotional states may view events and respond differently to events due to dysfunctional cognitive appraisal. Individuals experiencing symptoms of sadness and guilt, as in depression, appraise situations in a way that results in low expectations for their abilities to effect change.[193,262] Anxious individuals have low or uncertain emotional focused potential within the cognitive appraisal domains which influences how they view their ability to handle a situation psychologically and often use avoidant coping.[258] Hostile individuals often have attributional bias and are not motivated to change as they do not see their behavior as the cause of any problem.[259] Subsequently, faulty cognitive appraisals associated with

negative emotional states influence an individual's ability to perceive the situation correctly as well as their subsequent behavioral and coping responses.[258]

Risky behaviors. Emotions may affect behaviors or adherence to medical treatment regimens[124] that may in turn influence the health outcomes of patients with HF. Patients with HF often have bothersome physical symptoms as well negative emotional states and often adopt risky behaviors to alleviate or cope with these symptoms. Anxious and depressed individuals are more likely to eat unhealthy diets, gain weight, adopt sedentary lifestyles, and fail to quit smoking.[17,263,264,265] In studies of patients having an acute myocardial infarction, those individuals with higher anxiety and depressive symptoms were more likely to resist smoking cessation[17,266] and were more likely to be heavy smokers.[267] Wong et al.[217] reported hostility was significantly associated with poor health behaviors, physical inactivity, and smoking. In addition negative emotions were associated with higher intake of alcohol in an attempt to cope; however, intake of alcohol was also associated with greater anxiety, depressive, and hostility symptoms.[268,269] Clearly, negative states put patients with HF at greater risk for adopting or maintaining unhealthy lifestyles that may lead to exacerbations of HF.

*Limited use of appropriate healthcare resources***.** Negative emotions hinder a patient's ability utilize appropriate resources to maintain optimal health. Coping style is viewed as an important predictor of the course of HF progression and health outcomes.[16] Patients with higher levels of anxiety and depressive symptoms frequently utilize avoidant coping[18,270] which includes denial, behavior disengagement, self-blame and substance abuse.[271] Patients with higher levels of hostility have poorer physical health, a pessimistic attitude, unrealistic expectations of self and others, a desire to avoid

difficulties, and are more likely to utilize escape-avoidance, and confrontive coping styles.[268] In addition, hostile individuals often have attributional bias, which influences their ability to take responsibility for their actions. Negative emotional states may produce behaviors that are not proactive resulting in behavioral disengagement that can manifest itself by missed clinic appointments, lack of participation in cardiac rehabilitation, and lack of utilization of medical and counseling services. Behavioral disengagement is viewed as a self-destructive behavior that can significantly affect health. Murburg and Bru[272] reported behavioral disengagement was a significant predictor of mortality risk among patients with HF who were followed for a 2-year period. Avoidance coping is maladaptive and predisposes a patient to ignore medical advice and symptoms that may signify the need to seek medical attention for early intervention.[273] Conversely, adaptive coping promotes active engagement to encourage patients to monitor symptoms, seek medical attention, and adequately manage HF symptoms and progression of the disease.[274]

Summary of potential behavioral pathways. The potential behavioral pathway of negative emotions in patients with HF is a plausible mechanism for poor health-related outcomes such as disease progression, poor quality of life (QOL), increased hospitalizations, and mortality.[16-18] The behavioral pathway may also influence the physiological pathway through nonadherence to medical regimens, adoption of maladaptive or risky behaviors (e.g. smoking, weight gain, eating a diet high in fat and sodium, and excess alcohol intake), and limited use of appropriate resources. Nonadherence to medical regimens is common in patients with negative mood states. The association between the physiological and behavioral pathway is bi-directional as

illustrated in Figure 1.1. The physiological pathway provides for a mechanism that may adversely affect HF progression, impair cognition, and the ability of patients to adhere to medical regimens.[117] Conversely, the behavioral pathway provides a mechanism that influences the physiological response to negative emotions through inadequate self-care behaviors such as nonadherence, adoption of risky behaviors, and failure to utilize appropriate health resources to prevent exacerbations of HF symptoms.

Aims of Dissertation

Most of the research surrounding negative emotional states and their associations with health outcomes has traditionally occurred within the literature related to the development of coronary artery disease (CAD), risk of myocardial infarction, or development and progression of cardiovascular disease. However, in the last several decades there has been an increase in interest related to exploration of negative emotional states and how they influence the health-related outcomes in HF. The interaction of negative emotional states with other aspects of the lives of patients with HF impact the progression of HF, mortality, readmission, as well as physical HRQOL.[24,275] Negative emotions in patients with HF are associated with increased cardiovascular risk and worse health-related outcomes.[9-12,16,17,20,21,23-26,34,36,37,49,96,107,112,114,116,141,198,217,251,252,264,276]

This dissertation will fill some of the gaps in the literature more fully through increasing our understanding of how symptoms of anxiety, depression, and hostility influence health outcomes of patients with HF. Symptoms of depression and anxiety[16] have been studied more often than hostility in patients with HF. Part of the issue may be that most hostility measures are long and cumbersome, creating an undue burden on patients. The BSI Hostility Subscale[60] is a short self-report measure of hostility

commonly used in patients with HF; however, the psychometric properties have not been examined in this patient population.

In exploring the influence of negative emotions on poor health outcomes, my dissertation proposes two potential pathways moderating the relationships between negative emotional states and poor P-HRQOL, hospital readmissions, and mortality. Potential pathways proposed are biological hyperreactivity and behavioral pathways, similar to what has appeared previously in the literature.[16,17,124] In addition to examining the relationship of negative emotions on future health-related outcomes, the study described in Chapter 2 of this dissertation also examines the influence of negative emotions on self-care. Self-care has been identified as the single most important variable in preventing or limiting exacerbations of HF symptoms.[277]

Many of the studies in the literature examining the relationships between negative mood states and poor health outcomes have utilized cross-sectional data measuring negative emotional states and their relationship to health-related outcomes at one point in time. Of the longitudinal studies examining trajectories of negative emotional states at different points in time, pre-set cut-points on negative emotional states were used to determine how patients would be grouped.[24] While this method of analysis provides valuable information on the effects of negative emotional states and health outcomes, studies utilizing this method cannot fully describe the extent to which negative mood states may change and fluctuate over the course of time and how these patterns of change influence the health of patients with HF. The study in Chapter 4 is the first to utilize latent growth modeling to determine naturally occurring trajectories of anxiety and depressive symptoms without pre-determined groupings and examine their relationship to

cardiac related events and P-HRQOL.

Therefore, the purpose of this dissertation was to examine how symptoms of anxiety, depression, and hostility influence health outcomes of patients with HF as well as describe how these psychological variables change over time, and whether different trajectories of these variables are associated with different health outcomes. Thus, the primary aims of this dissertation are threefold: 1) provide evidence of the psychometric properties of the BSI Hostility Subscale as a valid and reliable instrument to assess the hostility symptoms of patients with HF; 2) determine whether symptoms of anxiety, depression, and hostility at baseline predict better self-reported self-care at one-year among patients with HF; and 3) describe trajectories of anxiety and depressive symptoms among patients with HF across three points in time (baseline, 3 months and 12 months) and explore whether these symptom trajectories predict one-year cardiac event-free survival and P-HRQOL.

Summary of Subsequent Chapters

Chapter 2 is an analysis of the psychometric properties of the BSI Hostility Subscale. The BSI Hostility Subscale is widely used to assess symptoms of hostility in many populations,[56,60,278] including patients with HF.[105] However, reliability and validity of the subscale have not been evaluated in this population. Cross-sectional data of a subset of 345 patients enrolled in a larger longitudinal study of 1,136 patients were used for this analysis. The primary aims of this study were to (1) explore the dimensionality of the subscale in patients with HF; (2) assess the internal consistency of the subscale; and (3) evaluate the construct validity of this subscale. The hypotheses were that levels of hostility would be positively associated with measures of anxiety and depressive

symptoms and negatively associated with perceived social support.

In Chapter 3 I present findings from a secondary analysis of data in which I examined whether anxiety, depressive symptoms, and hostility were predictive of self-care and P-HRQOL at 12 months in patients with HF. The conceptual framework for the relationship of negative emotions and self-care is outlined in Figure 1.2. Data analyzed in this study were collected as part of larger longitudinal studies of patients. A subset of 214 patients with complete data on the variables of interest was used in this analysis.

In Chapter 4 I present results from a study I conducted to identify trajectories of depressive and anxiety symptoms in patients with HF over 12 months and determine whether changes in these symptoms were predictive of subsequent P-HRQOL and event-free survival at one year. Little is known about trajectories of depressive and anxiety symptoms in patients with HF and how these influence health outcomes over time. This study was a secondary data analysis of data collected as part of a larger longitudinal study of patients enrolled in the Heart Failure Quality of Life Trialists Collaborative contributed to by investigators at eight different sites in the United States. The design, procedures, and results of the primary studies have been previously reported.[276,279] The study sample consisted of a subset of 597 patients with HF enrolled in the larger longitudinal studies. Baseline, 3-month, and 12-month data on the variables of interest were used in the analysis. Latent growth mixture modeling was used to identify distinct trajectories of change in depressive and anxiety symptoms.

In Chapter 5 I present an integrated summary, discussion, and conclusion. Included in this chapter is a discussion of the implications from these studies as well as recommendation for future research to advance our understanding of the relationship of

symptoms of anxiety, depression, and hostility and their influence on self-care and health-related outcomes.

Figure 1.1 Overarching Framework for Conceptualizing the Biobehavioral Influences of Anxiety, Depressive, and Hostility Symptoms on Health Care Outcomes in Patients with Heart Failure

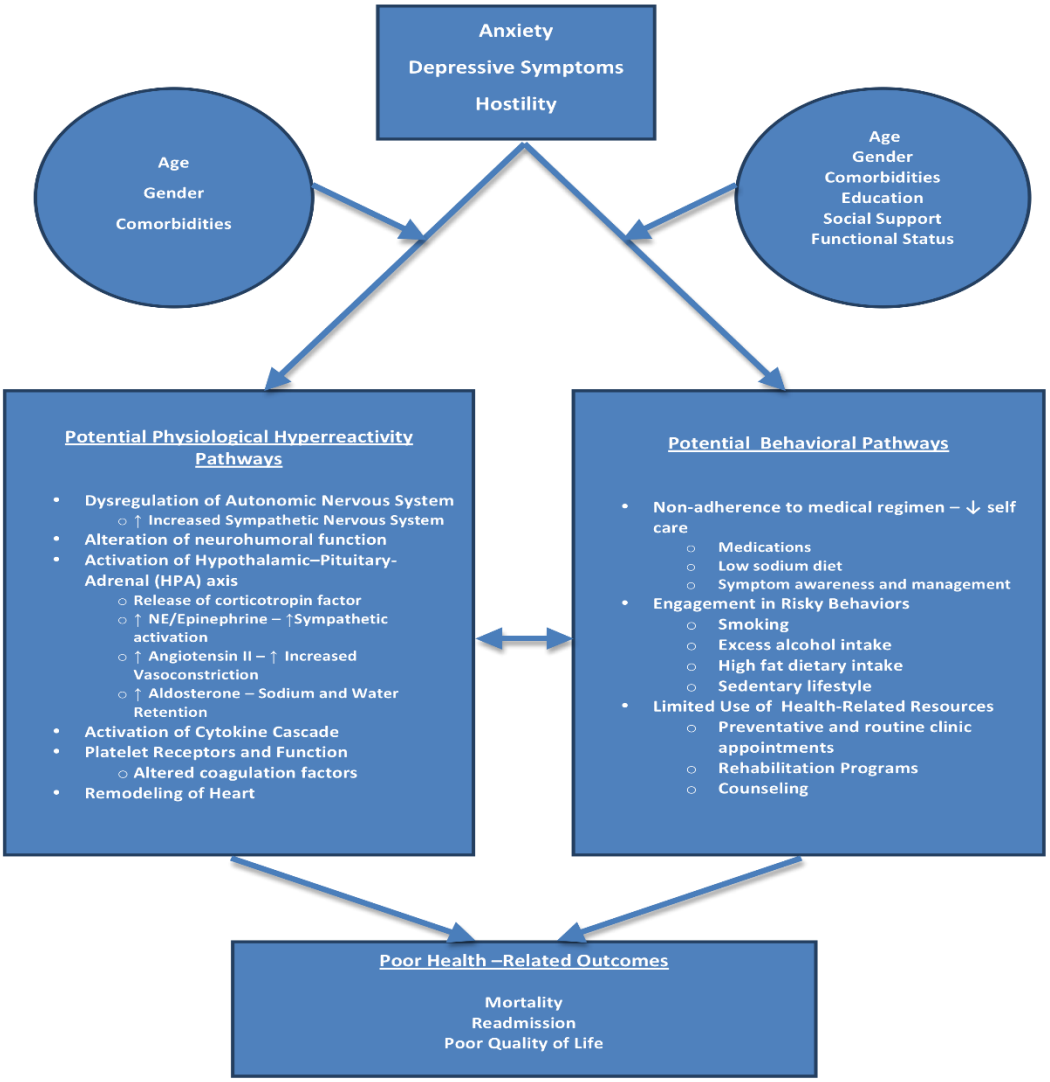
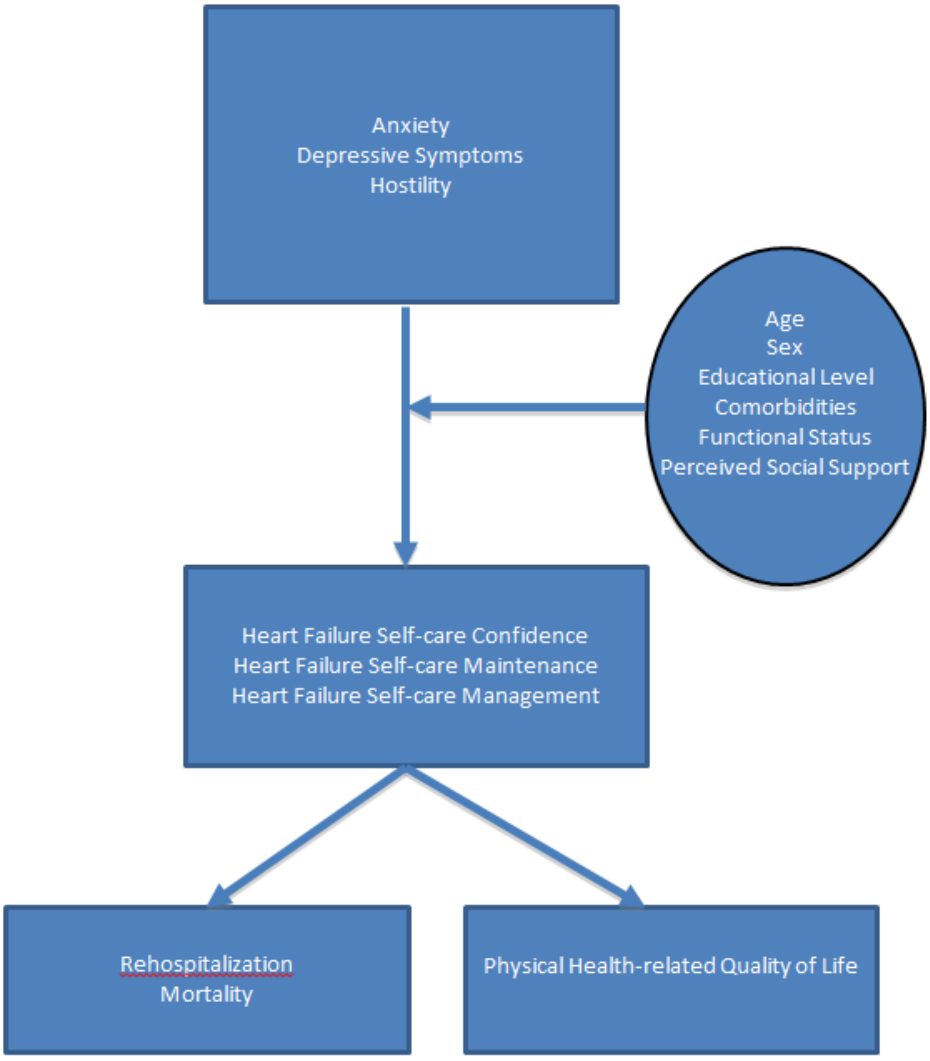


Figure 1.2 Conceptual Framework of Relationship of Anxiety, Depressive, and Hostility Symptoms to Self-Care and Subsequent Health Outcomes



Chapter Two: Psychometric Properties of the Brief Symptom Inventory Hostility Subscale in Patients with Heart Failure

Introduction

The purpose of the study was to investigate the psychometric properties of the Hostility Subscale of the Brief Symptom Inventory (BSI) in adult patients diagnosed with heart failure (HF). More than 5.7 million Americans suffer from HF which is associated with high rates of morbidity and mortality, poor health outcomes, and repeated hospitalizations.[1] Heart failure is a progressive and deteriorating condition characterized by multiple distressing physical and psychological symptoms. Subsequently, patients with HF experience greater levels of psychological distress and hostility when compared to their healthy counterparts or those with other cardiac conditions.[2] Hostility is an independent risk factor for poor health outcomes and is associated with increased risk for repeat hospitalizations for cardiovascular events such as HF.[3] Consequently, reliable and valid instruments that measure hostility in patients with HF are needed to adequately understand the relationship between hostility and HF and how hostility influences health outcomes.

Background and Conceptual Framework

The concept of hostility typically is defined as a negative attitude toward others accompanied by mistrust, cynicism, aggressive behaviors, and feelings of anger.[4,5] Although hostility has been associated with the development of cardiovascular disease (CVD) for many years, the results of existing research are inconsistent related to the mechanisms by which hostility influences CVD or other cardiovascular related events.[6,7,8] One mechanism may be that hostility exerts a toxic effect on the cardiovascular system

through a physiological pathway which activates potentially harmful neural, endocrine, and inflammatory responses.[9,10] Another mechanism may be that hostility promotes poor health and self-care behaviors such as physical inactivity and nonadherence with medications.[8,11] The inconsistencies may be because of the multidimensional nature of hostility which has been challenging to define and difficult to capture,[12] because hostility includes complex emotional, cognitive, and behavioral processes.[13,14] In addition, most studies investigating the associations of hostility with CVD and HF used diverse hostility measures that include not only self-report measures but also structured interviews.[4] Although the BSI Hostility Subscale is commonly used with many populations, its use in patients with HF is limited.

Despite a large body of research investigating the role of hostility in developing CVD or its influence on the progression of heart disease, there is limited research on the relationship of hostility to health outcomes in patients with HF. More importantly, there is even less research available about interventions to decrease levels of hostility with the goal of improving health outcomes. Some cardiac rehabilitation programs address negative emotional states such as hostility to improve risk factor profiles for recurrent events, increase adherence to medication regimens, and support lifestyle changes to improve overall quality of life.[15] However, to understand hostility and its influence on outcomes in patients with cardiac problems and HF, clinicians need a brief, psychometrically sound measure of hostility that does not increase patient burden—one that can be easily scored and interpreted by clinicians.

The specific aims of this study were to: (1) assess the internal consistency and reliability of the BSI Hostility Subscale; (2) explore the dimensionality of the BSI

Anxiety, Depression, and Hostility Subscales through principal component and exploratory factor analyses to determine whether the Hostility Subscale is a distinct dimension of the BSI in a sample of patients with HF; and (3) evaluate the construct validity of the BSI Hostility Subscale by testing the following hypotheses:

H_1: The higher the Hostility Subscale score, the greater the levels of depression measured by the Patient Health Questionnaire-9 (PHQ-9) and the BSI Depression Subscale.

H_2: The higher the Hostility Subscale score, the greater the BSI Anxiety Subscale score.

H_3: Greater hostility will be associated with lower perceived social support as measured by the Multidimensional Scale of Perceived Social Support (MSPSS).

Construct validity is an important part of psychometric testing concerning the validity of an instrument and includes both convergent and discriminant validity. Our hypotheses reflect how the BSI Hostility Subscale should or should not correlate with other measures.

Methods

Research Design. The cross-sectional data for this secondary data analysis were collected as part of a larger longitudinal study of 1,136 patients who participated in nine clinical trials at eight sites representing the Midwest, Southwest, Southeast, Northwest, and Northeast regions of the United States.[16,17]

Sample. A subset of 345 patients with complete data on the variables of interest comprised the sample for this study. Patients who did not have complete data were excluded. There were no sociodemographic differences between those who did and did

not have complete data. Incomplete data was the result of some sites not collecting on the variables of interest. Eligibility criteria were similar at all sites: (1) documented diagnosis of HF associated with preserved or nonpreserved left-ventricular systolic function, and (2) ability to read and write English. Patients were excluded if they had an acute myocardial infarction (MI), unstable angina, cognitive impairment, or severe psychiatric problems requiring acute treatment. In addition, patients discharged to an extended care or skilled nursing facility and those who were homeless were excluded.

Measures.

Hostility. Hostility was defined as an emotional, cognitive, and behavioral dimension that involves negative beliefs and attitudes about people and human nature.[18] Although it is associated with anger and aggression, hostility is characterized by a negative cognitive and behavioral style that affects an individual's expectations, perceptions, and responses to others. Hostility was measured using the Hostility Subscale of the BSI. The Hostility Subscale consists of five items from the original BSI, a 53-item self-report inventory describing nine primary dimensions: Somatization, Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation, and Psychoticism.[19] Patients respond to the stem, "…circle the number to the right that best describes how much the problem has distressed or bothered you recently, including today." Each item is rated on a 5-point scale of distress ranging from 0 (not at all) to 4 (extremely). A total score is calculated by summing the values for each item and dividing by 5 resulting in scores ranging from 0 to 4. The threshold norm for adult non-patients is .35 ± .42.[19]

Items for the Hostility Subscale of the BSI were selected based on a factor

analysis of the Symptom Checklist-90-Revised (SCL-90-R); those items with the strongest loadings on the hostility dimension were selected to form this subscale.[20] In a sample of 1002 psychiatric outpatients, Derogatis and Melisaratos[19] confirmed the nine primary symptom dimensions of the BSI through principal component analysis which included the Hostility Subscale. The subscale has good internal consistency. Cronbach's alpha was .78 in a study of 1,002 adult psychiatric outpatients, and in a sample of 60 non-patients who were tested across a 2-week period, the test-retest reliability coefficient was .81.[19] Several studies support the internal consistency of the BSI Hostility Subscale in samples of patients with HF with Cronbach's alpha of .80 and .79.[21,22]

Depressive symptoms. Depression was defined as a negative affective state associated with a range of depressive symptoms related to dysphoric mood and affect that influence an individual's view of self, the world, and the future.[7] Depressive symptoms were measured using the PHQ-9 and BSI Depression Subscale.

Patient Health Questionnaire-9. The PHQ-9[23] is a self-administered measure of the presence and severity of depressive symptoms. It was developed from the full PHQ according to criteria for clinical depression outlined in the *Diagnostic and Statistical Manual of Mental Disorders (4th ed., DSM-IV)* and includes emotion and somatic dimensions of depression.[24] The PHQ-9 is composed of nine Likert scale items. Patients are asked to rate how often in the past 2 weeks they experienced each symptom on a scale of 0 (not at all) to 3 (nearly every day); therefore, possible scores range from 0 to 27. Higher scores reflect higher levels of distress and depressive symptoms according to the following categories: 0-4 (minimal depression); 5-9 (mild depression); 10-14 (moderate depression); 15-19 (moderately severe depression), and 20-27 (severe depression). The

PHQ-9 had excellent reliability in samples of 3,000 obstetric-gynecologic patients[23] and 3,000 adult patients in a primary care setting.[25] with Cronbach's alphas of .89 and .86, respectively. Cronbach's alpha was .83 in two different samples of patients with HF[26,27] which supports the reliability of the PHQ-9 in this population. In the present sample, the Cronbach's alpha was .85**.**

Brief Symptom Inventory Depression Subscale. The BSI Depression Subscale is composed of six items selected based on factor analysis of the SCL-90-R.[28,29] Items in the scale represent a range of symptoms of clinical depression such as dysphoric mood and affect characterized by a lack of motivation and loss of interest in life. Each item is scored from 0 (not at all) to 4 (extremely). A score is derived by summing the item values and dividing by six. Scores on the subscale range from 0 to 4. Higher scores indicate higher levels of distress and severity of symptoms of depression. The mean score in a sample of 719 healthy non-patients was reported by Derogatis and Melisaratos[19] as .28 ± .46. The Depression Subscale has good internal consistency; Cronbach's alpha was .85 in a sample of 60 non-patients[19] and was stable over a 2-week period of time with a test-retest reliability coefficient of .84. The BSI Depression Subscale had good internal consistency in two studies of patients with HF with Cronbach's alphas of .78 and .82.[30,31] In our sample, Cronbach's alpha was .88.

Anxiety. Anxiety was defined as a state of uneasiness, nervousness, and restlessness. It was assessed with the six-item BSI Anxiety Subscale, derived by Derogatis[20] via factor analysis of the SCL-R-90. This subscale includes statements about symptoms of anxiety such as nervousness, tension, feelings of terror, apprehension, and spells of terror or panic. The items within the subscale are scored from 0 (not at all) to 4

(extremely). The score is obtained by summing the values of each item and dividing by six; scores range from 0 to 4. A mean score of .35 ± .45 was reported in a sample of 719 healthy non-patients.[19] Cronbach's alpha in this healthy sample was .81. In addition, the BSI Anxiety Subscale was stable across a 2-week time period with a test-retest coefficient of .79 in a sample of 60 non-patients.[19] The BSI Anxiety Subscale had good internal consistency in several samples of patients with HF[27,31,32] with Cronbach's alphas of .85, .83, and .84, respectively. In the study, the Cronbach's alpha for the Anxiety Subscale was .82.

Perceived social support. Perceived social support was defined as a subjective feeling of support, help, and comfort from family, friends, and significant others. It was assessed using the self-report MSPSS.[33] The MSPSS consists of 12 items addressing social support from three groups: family, friends, and significant other. Four items are asked for each group and are rated on a 7-point Likert scale ranging from 1 (very strongly disagree) to 7 (very strongly agree). Items are summed for a total score and subscale scores for Family, Friends, and Significant Other. Total scores range from 12 to 84; subscale scores range from 4 to 28. Higher scores indicate greater levels of perceived social support.[33] The authors reported a Cronbach's alpha of .88 in a sample of 275 undergraduate students. Dahlem et al.[34] and Riegel et al[22] reported Cronbach's alphas of .90 and .95, respectively, in samples of patients with HF. Cronbach's alpha in the present sample was .88.

Data collection. Institutional review board approval was obtained at each site. Specially trained nurse researchers explained the purpose and procedures to each participant in the study. All patients gave signed, informed consent. Data were collected

through the use of self-administered questionnaires and structured patient interviews conducted by trained cardiovascular nurses. Nurses ascertained the weight and height of each participant and interviewed patients in order to complete sociodemographic data. Subsequently, participants were given a packet of self-administered questionnaires with instructions regarding how to complete each questionnaire. The nurse researcher examined all questionnaires to make sure participants did not inadvertently leave any items unanswered; however, participants were free to leave items unanswered.

Data analysis. Statistical analyses were performed using the SPSS for Windows (version 18.0, SPSS, Inc., Chicago, IL). Descriptive statistics were computed for sociodemographic and clinical data as well as the BSI and its subscales, the PHQ-9, and the MSPSS. Potential differences in proportions by gender of the participant were tested by using χ^2 for categorical variables; differences in means of continuous variables by gender were evaluated using the independent samples *t* test. Bivariate relationships were evaluated using the Pearson product moment correlation coefficient for continuous variables; the Spearman rank order correlation was used for ordinal data. After ensuring there were no violations of the assumptions of normality, linearity, and homoscedasticity, the internal consistency reliabilities of the BSI Hostility and Anxiety Subscales were assessed using Cronbach's alpha. Coefficients greater than .70 were deemed to represent good internal consistency. The 17 items of the three BSI subscales were subjected to PCA followed by exploratory factor analysis (EFA).

Results

Characteristics of the patients with HF are shown in Tables 2.1 and 2.2. Age was similar for both males and females (61 ± 12 years and 59 ± 12 years, respectively). There

was no significant difference in proportions for NYHA classification by sex of the patient. Males and females did not differ on mean scores on the BSI Hostility, Depression, and Anxiety Subscales. However, participants' scores on the BSI Hostility, Depression, and Anxiety Subscales were elevated relative to published norms for adult nonpatients,[28] reflecting greater hostility, depression, and anxiety symptoms for the patients with HF in our study.

Reliability. The Cronbach's alpha for the Hostility Subscale was .77, indicating good internal consistency for a subscale composed of only five items. Inter-item correlations between .30 and .80 were considered acceptable. Items with coefficients of .80 or greater indicate possible item redundancy.[35] The inter-item correlation coefficients for the BSI Hostility Subscale ranged from .30 to .78.

Dimensionality. Prior to performing the PCA, we determined the data were suitable for analysis through inspection of the inter-item correlation matrix of the BSI which revealed numerous coefficients of .30 and above as recommended by Kaiser.[36,37] In addition, the Kaiser-Meyer-Olkin value was .91, exceeding the value of .6 or above as recommended by Kaiser.[36,37] The Bartlett's test of sphericity[38] was also significant ($p <$ .0001).

Principal component analysis revealed two eigenvalues exceeding one. Inspection of the scree plot also supported a two-dimensional structure. Varimax rotation of the two factors using exploratory factor analysis yielded: Factor I-- Dysphoria and Factor II-- Hostility. The BSI Hostility Subscale items loaded on both factors with moderate or strong loadings of .40 or greater; however, only three of the five items (Items 12, 13, and 15) loaded on Factor II Hostility (see Table 2.3). The items that loaded on Factor II were

similar in content in that the items asked participants to rank how often they experienced urges or feelings of aggression. Although three of the five items loaded on Factor II, one item, "temper outbursts you could not control," double loaded on both Factors I and II. When this item was removed from the subscale, Cronbach's alpha for the BSI Hostility Subscale decreased from .77 to .70, and this item was retained in the subscale. Another item, "easily annoyed or irritated," loaded on Factor I moderately strong. This item may describe a restless state more similar to those associated with anxiety.

The items in the Anxiety Subscale of the BSI loaded exclusively on Factor l (see Table 2.3). Items on the Depression Subscale loaded strongly on Factor I (see Table 2.3) with the exception of Item 10, "thoughts of ending your life," which loaded moderately strong on Factor II. Thus, the BSI Hostility Subscale was not clearly distinguished from the Anxiety and Depression Subscales in this sample.

Construct Validity. *Hypothesis testing.* All hypotheses were supported thus providing evidence of construct validity of the BSI Hostility Subscale (Table 2.4). The BSI Hostility Subscale had strong, positive correlation with the BSI Depression Subscale and a moderate, positive correlation with the PHQ-9. Thus, patients with greater hostility had worse symptoms of depression. There was also a strong, positive correlation between the BSI Hostility Subscale and the BSI Anxiety Subscale. Patients who experienced more hostility also experienced more anxiety. There was a weak, negative correlation between the BSI Hostility Subscale and the MSPSS. Patients who perceived less social support reported greater hostility.

Discussion

Although studies exist on the psychometric properties of the complete nine

dimensions of the BSI, we found no studies that examined the reliability and validity of the BSI Hostility Subscale among patients with HF. The BSI and its various subscales have been used in numerous studies in patients with HF.[30,32,39,40] One study examined the psychometric properties of the BSI Anxiety and Depression Subscales in this population;[31] however, there were no prior studies of the reliability and validity of the BSI Hostility Subscale in patients with HF. The results of this study provide initial support for the psychometric soundness of the BSI Hostility Subscale as a measure of hostility in patients with HF.

The BSI Hostility Subscale demonstrated satisfactory reliability and validity in patients with HF. The Hostility Subscale demonstrated good internal consistency. The hypotheses were supported, providing evidence of construct validity.

The two-factor model reflected dimensions of dysphoria and hostility. Agitation and annoyance with others, accompanied by aggression and anger, are often cited as common emotional and behavioral components of hostility.[41,42] Three items loaded on Factor II; one item asking about temper outbursts which cannot be controlled double loaded on both Factors I and II. This item covers a broad concept influenced by personal perception or may measure different aspects of one component, namely that of temper outbursts and personal control. This item may have double loaded because of the ambiguity in defining an outburst one cannot control; individuals who have frequent temper outbursts may not perceive themselves as out of control. However, rewording of this item may produce better discrimination. Perhaps asking about frequent temper outbursts, getting mad or upset, or arguing with others without asking about control would produce a less ambiguous item. In addition, one item loaded on Factor I, rather

than Factor II, representing the dysphoric symptoms of hostility (agitation, annoyance). This is not surprising, because anger, aggression, antagonistic behavior as well as annoyance, irritation, and cynicism, are all facets of hostility and hostility measures usually assess these very different components.[41] This item may describe a restless state more similar to feelings associated with anxiety. Examination of the inter-item correlations demonstrated there was no redundancy among items of the BSI Hostility Subscale.

In addition, items in the Anxiety and Depression Subscales of the BSI loaded almost exclusively on Factor I with the exception of one item on the Depression Subscale about ending one's life which loaded on Factor II. This may be because ending one's life may be viewed as an act of hostility or aggression against oneself as suicidal acts have been correlated with self-reported hostility.[43] Lemogne et al.[44] found cognitive hostility was predictive of suicide independent of baseline depressive mood in a cohort study of 14,752 non-patients over a mean follow-up of 15.7 years.

Therefore, in this sample of patients with HF, the Hostility, Anxiety, and Depression Subscales of the BSI had two, not three, dimensions as proposed by Derogatis.[28]

The results of our study supported the hypothesis that the BSI Hostility Subscale was associated with measures of depression, anxiety, and social support. There were strong positive correlations between the BSI Hostility Subscale and the Beck Depression Inventory-II, PHQ-9, and the BSI Depression and Anxiety Subscales. This is consistent with the findings of Moser et al.[2] who demonstrated patients with HF had higher levels of hostility, depression, and anxiety compared to healthy elders. Lee and colleagues[21] also

reported that hostility was positively associated with higher levels of depression and anxiety in patients with moderate to advanced HF. In addition, results from this study indicated there was a weak, negative correlation between the BSI Hostility Subscale and the MSPSS. Patients with HF who had higher levels of hostility had lower levels of perceived social support. Numerous studies support the negative correlation between hostility and social support.[41,45] Other researchers also reported inverse relationships between hostility and perceived social support and sociability (appreciation of the company of others, cooperativeness, and responsiveness to social stimulation).[46,47] Blumenthal et al.[48] found that patients undergoing coronary angiography who were also classified as Type A behavior pattern and reported better social support had lower levels of CAD as compared to their Type A counterparts with lower levels of social support. Social support, therefore, may confer a protective effect in the face of stress.[49,50] Also, sociable individuals receive more support than unsociable individuals.[51]

Limitations

A limitation of this study is that the sample was not randomly selected; however, patients were recruited from multiple sites and the sample size was adequate for our analysis. Also worth noting is the influence of self-report bias. Patients in this study may have responded differently to the items in the BSI Hostility Subscale because of the influence of social desirability which may have more of an impact on the BSI Hostility Subscale than on other psychological measures such as depression and anxiety, as hostility is negatively viewed by society.[41] In addition, most of the participants in this study consisted of white males which limits the generalizability of our findings to other groups such as women and minorities.

Conclusion and Implications

Our study provides psychometric support for the BSI Hostility Subscale as a reliable and valid measure of hostility in patients with HF. In addition to the psychological symptoms of depression and anxiety, clinicians need to routinely assess hostility as part of follow-up visits throughout the treatment regimen to target interventions aimed at improving health. To this end, there is a distinct advantage of using a brief, five-item subscale to assess hostility levels in patients with HF without increasing respondent burden. Many hostility measures are longer and take more time to complete. Having a short, easy to use hostility measure that is reliable and valid allows clinicians to quickly assess a negative emotional state linked to poor health outcomes among patients with HF. We made recommendations for improvements in the BSI Hostility Subscale for future research. Although the link between hostility and heart disease is well established, more in-depth investigation of the relationships among hostility, HF, and poor health outcomes is needed using psychometrically sound measures of hostility.

Table 2.1. Demographic Characteristics of the Sample of Patients with Heart Failure (N = 345)

Variable	*n*	%
Sex		
Male	245	71.0
Female	100	29.0
Marital Status		
Single	43	12.5
Married	181	52.5
Divorced/Separated	63	18.3
Widowed	46	13.3
Co-habitate	12	3.5
Race		
African-American	62	18.0
Caucasian	279	80.9
Hispanic/Latino/American-Indian/Alaskan Native/Mixed	4	1.2
Educational Level		
Less than high school graduate	68	19.7
High school graduate	82	23.8
Business school or some college	82	23.7
Associate Degree or Bachelor's Degree	60	17.4
Master's Degree or higher	51	14.8

Table 2.1 (continued)

Employment Status		
Employed full or part-time outside home	79	22.9
Sick leave or disability	69	20.0
Retired due to heart failure	83	24.1
Retired not due to heart failure	87	25.2
Other	25	7.2
Smoking History		
Current Smoker	69	20.0
Recent (stopped within 1 year)	22	6.0
Former (stopped more than 1 year)	136	39.4
Never smoked	118	34.2
Drinking History		
Never	229	66.4
1 or fewer alcoholic drinks per week	66	19.1
2-7 drinks per week	37	10.7
7 or more alcoholic drinks per week	11	3.2
Exercise		
None	56	16.2
Less than 30 minutes per week	49	14.2
30-60 minutes per week	72	20.9
1 to 3 hours per week	82	23.8
More than 3 hours per week	86	24.9

Table 2.1 (continued)

Variable	*n*	%
Health Perception		
Excellent	3	0.9
Very good	39	11.3
Good	124	35.9
Fair	138	40.0
Poor	41	11.9

Table 2.2. Clinical Characteristics of the Sample of Patients with Heart Failure (N = 345)

Categorical Variables	*n*	%
Etiology of Heart Failure		
Ischemic (heart disease)	172	79.9
Idiopathic (unknown cause)	66	19.1
Hypertension	33	9.6
Valvular heart disease	2	0.6
Alcoholic	3	0.9
Postpartum	1	0.3
Other	56	16.2
NYHA Classification*		
I	29	8.4
II	154	44.6
III	132	38.3
IV	29	8.4
Missing	1	0.3

Continuous Variables	Mean ± SD
Age	61.0 ± 12.0
Left Ventricular Ejection Fraction	35.4 ± 3.9
Body Mass Index	31.8 ± 7.6
Months since Heart Failure diagnosis	78.0 ± 81.3
Months since hospitalized for Heart Failure	211.0 ± 380.4

*NYHA=New York Heart Association Classification

Table 2.3. Factor Pattern Matrix for Varimax Rotation of Two Factors for Items of the Brief Symptom Inventory (N = 345)

Item number/Item/Subscale	Factor	
	I[a]	II[b]
8. Feeling fearful (Anxiety)	**.80**	-.03
6. Feeling blue (Depression)	**.80**	.32
9. Feeling hopelessness about the future (Depression)	**.80**	.18
7. Feeling no interest in things (Depression)	**.75**	.19
5. Feeling lonely (Depression)	**.73**	.28
1. Nervousness or shakiness inside (Anxiety)	**.72**	.10
11. Feeling tense or keyed up (Anxiety)	**.68**	.26
3. Scared for no reason (Anxiety)	**.67**	.05
17. Feelings of worthlessness (Depression)	**.65**	.35
2. Easily annoyed or irritated (Hostility)	**.62**	.35
16. Feeling so restless you can't sit still (Anxiety)	**.61**	.21
4. Temper outbursts you could not control (Hostility)	**.49**	**.43**
14. Spells of terror or panic (Anxiety)	**.48**	.28
12. Urges to beat, injure, or harm someone (Hostility)	.04	**.89**
13. Urges to break or smash something (Hostility)	.12	**.87**
10. Thoughts of ending your life (Depression)	.19	**.67**
15. Getting into frequent arguments (Hostility)	.35	**.64**

[a] Component I = Dysphoria

[b] Component II = Hostility

Note. Factor loadings > .40 are in boldface. BSI = Brief Symptom Inventory.

Table 2.4. Intercorrelations of the BSI Subscales with the PHQ-9 and MSPSS in Patients with Heart Failure (N = 345)

Scale/subscale	BSI - Hostility	BSI - Depression	BSI – Anxiety	PHQ-9
BSI - Depression	.64*			
BSI - Anxiety	.60*	.75*		
PHQ-9	.47*	.66*	.58*	
MSPSS	-.24*	-.38*	-.23*	-.35*

Note. BSI – Hostility = Brief Symptom Inventory Hostility Subscale; BSI – Depression = Brief Symptom Inventory Depression Subscale; BSI – Anxiety = Brief Symptom Inventory Anxiety Subscale; PHQ-9 = Patient Health Questionnaire-9; MSPSS = Multidimensional Scale of Perceived Social Support

*$p < .0001$ (two-tailed)

Chapter Three: Symptoms of Anxiety, Depression, and Hostility as Predictors of Self-Care in Patients with Heart Failure

Introduction

Heart failure (HF) is one of the most common chronic conditions among older adults in the United States.[1] The incidence and prevalence of HF is increasing as more people live longer with cardiovascular disease.[2] Between 2012 and 2030, it is estimated that the prevalence of HF will increase by 46%.[2] Heart failure is associated with many physical and emotional symptoms and is one of the most frequent causes of readmissions to the hospital.[3] Patients with HF often experience exacerbations of symptoms and cycle in and out of hospitals and clinics for control of these symptoms.[4]

Inadequate self-care among patients with HF is the most common reason for hospitalization in this population.[5] Optimal self-care is difficult as it is a complex set of activities that involves both cognitive and behavioral elements[6] which patients with HF must learn and practice.[7] Patients must learn how to maintain hemodynamic stability through adherence behaviors, problem solving, and management of HF symptoms.[5,6] Optimal self-care involves learning how to be adherent with medications, to follow the low sodium diet, to remain active and get regular exercise, as well as being engaged in health promotion activities such as receiving annual flu immunizations. Patients with HF must know how to monitor and respond to symptoms such as weight gain, edema, and dyspnea.[4,8] While adherence to medical regimens is difficult for patients with HF, learning how to manage this chronic condition is even more difficult as patients must be actively engaged and proactive in order to make decisions concerning symptoms.[7] Patients with HF who report lower engagement in self-care have higher mortality and

hospitalization rates than those patients who report higher engagement with self-care.[9]

Inadequate self-care and inability to engage in appropriate self-care has been associated with numerous factors including increasing age, female sex, lack of knowledge about HF, previous experience and severity of HF, lower socioeconomic status, poor health literacy, social isolation and poor social support, poor functional status, impaired cognition, and the presence of other comorbidities.[10] In addition, symptoms of anxiety, depression, and hostility are viewed as potential barriers to adequate self-care, yet the data supporting the association of anxiety, depression and hostility symptoms with self-care are conflicting.

Negative emotional states may influence self-care by a number of mechanisms (Figure 1.1). For example, patients with symptoms of depression are more likely to be nonadherent with medical regimens than those without depression, although not all investigators have confirmed this association.[10,11] Patients with depressive symptoms may have impairments in cognition that interfere with the ability to learn and process information, perceive symptoms, and make decisions about their care.[5] Depressive symptoms have been shown to adversely affect functional status as well as physical activity and endurance, making it challenging to exercise or carry out other activities needed for optimal self-care.[5] Individuals with depressive symptoms may view situations with a certain degree of hopelessness which then negatively impacts their ability to see any type of change in behavior or self-care as worthwhile[12]

Anxiety symptoms may also influence a patient's ability and willingness to engage in self-care as it alters cognition, energy, and motivation[12] to learn new information.[5,13] Cynical hostility is associated with negative views of others and self-

reports of adopting unhealthy behaviors such as smoking.[14] In addition, patients with negative emotional states often report feelings of social isolation and withdrawal from those who can offer support.[12] While negative emotions have been associated with poor outcomes among HF patients,[15-18] the exact mechanism by which they influence these outcomes is not fully understood.[19] One proposed mechanism is that negative emotions negatively alter patients' self-care behaviors (Figure 1.1).

Accordingly, the primary aim of this study was to evaluate whether baseline symptoms of anxiety, depression, and hostility were predictive of self-care at 12 months in adults with HF while controlling for the effects of other covariates (i.e. age, sex, educational level, functional ability, comorbidities, and perceived social support; Figure 1.1). Our hypothesis is that negative emotional states are predictive of poorer self-reported self-care at 12 months.

Methods

Research design. This was a secondary analysis of data collected as part of a larger longitudinal study of patients who participated in the Heart Failure Quality of Life Collaborative in clinical studies at eight sites representing the Southwest, Southeast, Northwest, Northeast, and Midwest regions of the United States. The design, procedure, and results of the primary studies have been previously reported.[20-23]

Participants and setting. Approval from appropriate institutional review boards was received prior to recruitment at all sites. Participants were recruited from community hospitals, academic medical centers, and outpatient clinics. A subset of 214 patients with complete data on the variables of interest at baseline and 12 months comprised the sample for the present study. Patients who did not have complete data were excluded;

however, there were no sociodemographic differences between those who did and did not have complete data. Incomplete data was the result of some sites not collecting on the variables of interest. Eligibility criteria were similar at all sites: (1) documented diagnosis of HF associated with preserved or non-preserved left-ventricular systolic function and confirmed by a cardiologist, (2) ability to read and write English, (3) freedom from major cognitive impairment, and (4) freedom from major life-threatening co-morbidities which might result in death within 12 months. Patients were excluded if they had an acute myocardial infarction (MI) in the previous 3 months, were on a cardiac transplantation waiting list, were discharged to a skilled nursing facility, or were homeless.

Measures.

Anxiety. Anxiety was assessed with the Brief Symptom (BSI) Anxiety Subscale, a short 6-item self-report measure of anxiety.[24] The BSI Anxiety Subscale includes statements about symptoms of anxiety such as apprehension, nervousness, tension, feelings of terror, and spells of terror or panic. The items within the subscale are scored from 0 (not at all) to 4 (extremely), with scores ranging from 0-4.[25] Higher scores indicate higher levels of anxiety symptoms. The BSI Anxiety Subscale is a valid and reliable measure of anxiety[24] that is easy to administer and minimizes patient burden. The subscale has demonstrated good internal consistency in several samples of HF patients.[26-29] Cronbach's alpha for the Anxiety Subscale in this study was 0.83.

Hostility. Hostility was measured using the BSI Hostility Subscale. The BSI Hostility Subscale is a 5-item self-report of symptoms of hostility.[24] Patients respond to each of the 5 symptom-based items according to how bothersome hostility symptoms

have been during the recent past. Each item is rated on a 5-point scale of distress ranging from 0 (not at all) to 4 (extremely), with scores ranging from 0-4.[24] The BSI Hostility Subscale has good internal consistency in numerous patient populations.[29] as well as in samples of patients with HF.[30, 31] Cronbach's alpha for the BSI Hostility Subscale was 0.77 in this study.

PHQ-9. Depressive symptoms were measured using the PHQ-9.[32] The PHQ-9 is a brief self-administered measure of symptoms of depression and is composed of nine Likert scale items that include the emotional and somatic dimensions of depression,[32,33] consistent with the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV). Patients are asked to rate how often they experienced each symptom on a scale of 0 (not at all) to 3 (nearly every day) over the course of the past two weeks; therefore, possible scores range from 0 to 27.[33] Higher scores indicate higher levels of depressive symptoms and distress. The PHQ-9 has excellent reliability,[32,34] and several studies support the reliability of the PHQ-9 in samples of patients with HF.[28,35] In the present sample, the Cronbach's alpha was 0.86**.**

Perceived social support. Perceived social support was assessed using the self-report Multidimensional Scale of Perceived Social Support (MSPSS).[36] The MSPSS consists of 12 items addressing social support from three groups: family, friends, and significant other.[36,37] Each item is rated on a 7-point Likert scale ranging from 1 (very strongly disagree) to 7 (very strongly agree). Total scores range from 12 to 84 and the three subscale scores range from 4 to 28,[36] with higher scores indicating greater levels of perceived social support.[37] The MSPSS has good reliability[36-38] and has been used in samples of patients with HF.[39-41] Cronbach's alpha coefficient for the MSPSS total score

in this study was 0.94.

Self-care. Self-care was assessed using the Self-Care of Heart Failure Index (SCHFI) which is a 22-item self-report that uses a 4-point Likert scale to measure three domains of self-care: self-care maintenance, management, and confidence[42]. The self-care maintenance subscale is comprised of 10 items, which ask questions concerning self-care behaviors on living a healthy lifestyle, adhering to treatment regimens, monitoring symptoms, and weighing daily.[43] The self-care management subscale is a 6-item subscale used to assess how well patients address and respond to symptoms of HF. Asymptomatic patients do not complete this subscale as it is only appropriate for symptomatic patients.[42,43] For this reason, we did not use the self-care management subscale as we recruited both symptomatic and asymptomatic patients with HF. The self-care confidence subscale is comprised of six items concerning patients' perceived confidence in their ability to engage in each self-care activity.[42] The scales in each domain range from 1-4; the maximum score in each domain is 100 (total rating X 5), with a total possible score of 300 points on the SCHFI if all three domain are used.[42,43] Higher scores indicate better self-reported self-care behaviors.[44] Scores below 70 are indicative of inadequate self-care on all the subscales.[43] The SCHFI has good reliability in numerous samples of HF patients[39,42,43,45,46] In our study, the Cronbach's alpha for the self-care maintenance scale was 0.80, and for the self-care confidence scale it was 0.83.

Functional status. We used the New York Heart Association (NYHA) functional classification to measure functional status.[47] The NYHA functional class is based on numbers assigned to patients according to patients' reports of symptoms occurring with physical activity ranging from I (no symptoms with regular physical activity) to IV

(physical symptoms of dyspnea, chest pain, fatigue, and palpitations at rest). Trained nurses collected this data through structured patient interviews. We combined classifications I and II for one group and classifications III and IV for a second group.

Comorbid illness. We collected data on the burden of comorbid disease by using the Charlson Comorbidity Index.[48] This standardized instrument is widely used in research to reflect comorbidity burden and has well-established reliability and validity. Trained nurses collected this information from the medical records and patient interviews.

Demographic Data. Demographic data were collected on age, sex, and educational level through standard questionnaires.

Data collection. Specially trained nurse researchers explained the purpose and procedure of the study to each participant. All patients were given time to ask questions and gave signed, informed consent. Trained nurses collected data through the use of structured patient interviews and self-administered questionnaires at baseline and again at 12 months. Upon participant completion, the nurse researcher examined all questionnaires to make sure items were not inadvertently left unanswered; however, participants were free to leave items unanswered if they wished.

Data analysis. Statistical analyses were performed using IBM SPSS Statistics for Windows (version 22.0, released 2013, Armonk, NY: IBM Corp.). Descriptive statistics were computed for sociodemographic data as well as the BSI and its subscales, the PHQ-9, the MSPSS, SCHIFI, and the Physical Subscale of the LHRQ. Hierarchical multiple regression modeling was used to examine the relationships between symptoms of anxiety, depression, and hostility with self-care confidence and with self-care maintenance,

controlling for covariates. The assumptions of a linear relationship between the predictor variables and the dependent variable, no multicollinearity, no significant outliers, equal error variance and normally distributed errors were tested and no violations were found. Statistical significance was preset at 0.05.

Results

Patient characteristics. Two hundred and fourteen patients with HF were included in the analyses of this study (Table 3.1). The majority of patients in the sample were white males. There was a greater proportion of males than females in the NYHA classification group I/II (64.7% vs. 37%). The patient sample had a mean BMI of 32.41 (±8.55) and the majority of the sample either smoke (17.3%) or reported being a former smoker (42.1%). Over one-third of the patients (39.3%) reported they were retired due to HF or were disabled, while 27.6% of the patients reported they were employed full-time.

At baseline, the patients in this sample had elevated levels of anxiety (0.56 ± 0.66) and hostility symptoms (0.44 ± .50) compared to the normal mean level of 0.35 ± 0.45 and 0.35 ± 0.42, respectively.[29] The sample population also had elevated levels of depression (5.03 ± 4.90) at baseline according to scoring guidelines[49] and the perception that their level of social support was moderate (68.86 ± 18.11) at baseline as compared to suggested thresholds recommended by developers of the MSPSS.[36,38] At 12 months, sample patients reported poor self-care maintenance (55.94 ± 19.53) and self-care confidence (60.04 ± 19.58) as shown in Table 3.2.

Hierarchical regression. In the two separate hierarchical multiple regression models for self-care maintenance and self-care confidence, predictor variables were entered in four blocks. Demographic variables of age, sex, and level of education were

entered into the first block; clinical variables of NYHA functional classification and comorbidities were entered into the second block; MSPSS was entered into the third block; and the negative emotional states of anxiety, depression, and hostility symptoms were entered into the final block of each of the self-care behavior models.

Self-care maintenance. The relationships between predictor baseline variables and self-care maintenance in patients with HF are presented in Table 3.3. In the final model, only age (p = .014), level of education (p = .001), and perceived social support (p = .003) at baseline were significant predictors of self-care maintenance at 12 months. Sex, NYHA functional classification, comorbidities, and symptoms of anxiety, depression, and hostility were not predictive of self-care maintenance at 12 months. The final model of baseline predictor variables and self-care maintenance was significant (F=4.619, p< .001).

Self-care confidence. The final multiple regression model of baseline predictor variables and self-care confidence at 12 months is presented in Table 3.4. Baseline education (p=.039) and perceived social support (p<.001) were significant predictors of 12-month self-care confidence among patients with HF. The other variables of age, sex, NYHA, comorbidities, and all three negative emotional states of anxiety, depression, and hostility symptoms were not significant predictors of self-care confidence at 12 months. The final model was significantly predictive of self-care confidence at 12 months in patients with HF (F= 4.334, p<.001).

Discussion

The results of our study provide more insight into understanding the influence of negative emotions and subsequent self-reported self-care behaviors. Our patient sample

had inadequate self-care maintenance and self-care confidence as mean scores on both subscales were less than 70 which is the recommended threshold for determining adequacy in self-care. The patient sample also had elevated baseline symptoms of anxiety, depression, and hostility; however, none of the negative emotional states were predictive of self-reported self-care behaviors. Nonetheless, increasing age, higher education, and higher perceived social support were predictive of better self-care maintenance, while higher education levels and higher perceived social support were found to be predictive of better self-care confidence.

The absence of negative emotions as a significant predictor of self-care was a surprising finding in our study as negative emotions have been identified as barriers to self-care[5] and associated with poor self-care in several studies.[11,50] While the study sample had elevated baseline symptoms of anxiety, depression, and hostility, symptoms of these negative states were not severe as published norms.[29] In addition, the mean of the depressive symptom measure, PHQ-9, was elevated, but below the score of 10 often used as an indication of clinical depression.[33] This may be a contributing factor in the results of our study. Patients with HF who have symptoms of anxiety, depression, and hostility are more likely to be less adherent to medical regimens, less likely to utilize appropriate health-care resources, and more likely to adopt or maintain unhealthy lifestyles.[5,51]

The results of studies on the influence of negative emotional states on self-care have been inconsistent. Some studies have found negative emotions (e.g. depressive symptoms) were associated with various behaviors indicative of poor self-care such as poor medication adherence, poor physical activity or adherence with an exercise

program, and delay in seeking medical treatment but only weakly or not associated with general self-care.[52-54] However, Van Der Wal et al.[52] found those patients who reported fewer depressive symptoms were more adherent to the medical regimen overall. The studies by Johansson et al.[53] and Nieuwenhuis et al.[54] reported depressed patients had delays in seeking medical care despite awareness of worsening symptoms; however, the majority of patients were adherent with the regimens. These findings are interesting in that they may suggest that patients may have more social support to assist in adherence to a medical regimen overall; however, caregivers may not be able to recognize worsening symptoms being suggestive of a worsening of HF until a certain threshold of immediate need is reach. The investigators did not address this area.

In a cross-sectional study of 615 patients with HF, Hwang and colleagues[55] reported that depression and anxiety were associated with poor self-care; however, only depression was a significant predictor of self-care. In another cross-sectional study of 255 outpatients with HF, Becker et al.[51] identified depression as one of several significant predictors of poor adherence to medical regimens and self-care behavior. Conversely, Lee and colleagues[56] studied whether depressive symptoms influenced trajectories of self-care in patients with HF over the course of six months, and reported greater depressive symptoms at enrollment were associated with reduced odds (0.85, p=<0.001) of declining self-care over time. The investigators postulated the findings of their study could have resulted from the fact that those patients in the trajectory that showed improved self-care may have also had an improvement in their depression. [56]

The influence of symptoms of depression and anxiety on self-care has been studied more often in patients with HF than have symptoms of hostility. Kessing et al.[10]

conducted a meta-analysis of 65 studies similar in sample and study characteristics on psychological determinants of self-care behaviors among patients with HF and concluded depression, but not anxiety, was significantly associated with self-reported self-care. However, despite this finding, depression was not associated with objectively measured medication adherence. Self-care behaviors in the cited studies included those activities commonly associated with self-care such as medication adherence, following the recommended low-sodium diet, and regular exercise.

Further, in a longitudinal study, Bauer et al.[57] examined the effects of depression and anxiety on adherence to medication and health behaviors in cardiac patients hospitalized for acute coronary syndrome, HF, or arrhythmia. The study found that improvement in depression was associated with better self-care at 6 months; however, improvement in anxiety was not. Improvements in anxiety were associated with better self-care only at 6 weeks. The influence of hostility on self-care behaviors in cardiac patients has been studied in relation to poor health habits (e.g. risky behaviors and poor self-care). In a longitudinal study of outpatients with stable CHF, Wong et al.[58] determined that hostility was a significant predictor of adverse events and concluded much of the association was moderated by poor health habits such as sedentary lifestyle and smoking. While HF self-care is a foundational to better health-related outcomes, it is clear that long-term effects of negative emotional states on self-care of HF patients warrants more investigation in order to fully understand the impact of these psychological variables on self-care and intervene appropriately.

It is noteworthy that some of the inconsistencies reported in the literature may be due to the fact that the majority of studies investigating the influence of negative

emotions on self-care are cross-sectional in nature and only examine variables at one point in time. There are limited longitudinal studies examining the predictive ability of negative emotions on self-care over time. Our study used baseline measures of negative emotions and other covariates to predict self-care at 12 months. Using measures of negative emotional states at one point in time to predict future events do not reflect how negative emotions may change, fluctuate, or improve over time which may have influenced the outcome variable of self-care. However, a major strength to longitudinal studies is that they are more robust than cross-sectional studies and can infer causality unlike cross-sectional studies.[59]

In addition, the results in our study as compared to other studies may be partially explained by investigators using different measures of self-care and adherence to medical regimens as studies do not consistently use the same measures, making comparison difficult.[10] However, there may also be the issue of self-report bias. Patients may not remember correctly, or there may be bias in self-reporting as patients may overestimate their adherence to weight management, taking medications, dietary recommendations, and activity status. Nevertheless, our findings suggest there is clearly a need for more research in order to gain further insight and understanding of the influences of negative emotions on self-reported self-care behaviors.

Our study also demonstrates the influence of other variables on self-care. We found higher levels of perceived social support from family, friends, and significant others was a strong predictor of both self-care maintenance and self-care confidence in our regression models. This finding supports previous work suggesting social support from family and others is related to higher self-reported self-care behaviors in patients

with HF.[5,60,61] Self-care is often difficult for patients with HF as it is complex, burdensome, and sometimes difficult to understand and follow. Patients with HF are often older, may have cognitive impairment cognition, and have numerous self-care demands from other comorbidities (e.g. diabetes, chronic obstructive pulmonary disease, arthritis, and renal failure) which limits patients' abilities to engage in self-care.[7] Adequate social support may improve patients' adherence to medical regimens. Social support may influence self-care through direct support from family such as reminders to patients to take medications and keep medical appointments, and encouragement to seek medical advice when symptoms arise.[5] Sayers and colleagues[4] reported higher perceived social support was associated with better self-reported adherence to diet recommendations, medication, and daily weighing. DiMatteo et al.[62] also suggested improved health outcomes may be mediated by the influence of social support on adherence to treatment regimens. The strong predictive ability of social support to self-reported self-care behaviors in our study may be an indication of the moderating effects of social support on negative emotions and subsequent self-care; however, this relationship was not analyzed.

Our findings suggest age is predictive of self-care maintenance. This is not a surprising finding as the majority of patients with HF are elderly, and the prevalence of HF increases with the aging population.[2] While cognitive impairment was not a variable in the current study, cognitive impairment is one of the most common comorbidities among elderly people with HF.[63] Cognitive impairment interferes with self-care in that it affects decision-making ability, memory, learning, and recall,[64] and is associated with poor HF self-care.[50] In addition, elderly patients with HF often have a higher incidence of

depression and anxiety[65] which also impair memory and decision-making that negatively influences self-care further.

Results from our study provide additional support for educational level being associated with self-care maintenance and self-care confidence. The patients in our sample were relatively well educated with a mean of approximately 14 years of education, two years beyond high school. Those who had higher education had better self-care. One of the most important self-care activities important to good HF outcomes is becoming knowledgeable about the condition.[7] This entails having the basic educational preparation to be able to understand the medical regimen, be able to read and follow directions on prescription medications, understand the influence of weight gain on HF, understand what a low sodium diet entails, and being knowledgeable about HF and what symptoms mean in order make decisions and seek medical help.[5,7]

Self-care maintenance and self-care confidence are associated with how well patients with HF adhere to their medical treatment regimens and how confident patients with HF are in their ability to make decisions concerning symptom recognition and subsequent actions.[31] Chen et al [66,67] reported a strong association between patients who had at least a high school education and greater self-care confidence and subsequent overall self-care as compared to those who did not complete high school. Rockwell et al.[68] and Gonzales et al.[69] both reported that higher education levels in patients with HF were associated with better self-care and a higher likelihood of engagement in self-care behaviors when compared to those with lower education. Educational level has also been associated with health literacy which is vital for understanding as well as decision making in optimal self-care of patients with HF.[70] Individuals with high education (high

school and beyond) have higher health literacy than individuals with less education.[71] In addition, Rockwell et al.[68] suggested that education may also influence self-care in that higher education develops critical thinking skills that facilitate self-care behaviors such as setting self-care priorities and problem solving. The complex self-care regimens, often seen in patients with HF, combined with lack of education may contribute to poor self-care behaviors and subsequent poor health outcomes.

It is important to note the results of our study underscore the need to tailor education and management strategies to patients' educational levels and their abilities to understand the complexities of adequate self-care in HF. Patients need to be taught about successful self-care behaviors such as adherence to medical regimens, monitoring of symptoms, problem solving, and what resources to utilize to prevent exacerbations and complications of HF. Despite our findings concerning higher educational level and optimal self-care, our study should not be interpreted to mean that a person who is poorly educated cannot be taught self-care. Teaching self-care should not be a one-size-fits-all approach. The process needs to be individualized to patients' educational and health literacy abilities. Those with less education may need more time and practice in order to understand how to take care of themselves and be fully engaged in self-care.[68]

Our study also found that sex was not predictive of self-care at 12 months. It is interesting that in society there is a belief that women take better care of themselves than men.[72] Heo et al.[73] reported differences between the sexes in factors affecting self-care. Older males with higher perceived control and knowledge of HF had better self-care behaviors than women; while women who had poorer functional status and higher self-care confidence had better self-care behaviors than men.[73] In a longitudinal study, Chriss

and colleagues[74] reported being an older male was a significant predictor of successful self-care at three months. However, contrary to these findings, the majority of cross-sectional studies reported no differences between the sexes in various aspects of self-care.[68,75-78]

In addition to chronic HF, our sample Charlson Comorbidity Score was 2.95 (± 1.82); however, we found cormorbid disease burden was not predictive of self-reported self-care behaviors in our regression models. Besides HF, the comorbid disease burden in our sample population was similar to what is observed in the general HF population.[7,68] Having a high overall disease burden has been associated with self-care as patients with HF who have higher comorbidity scores have poorer self-care than those with a lower comorbidity scores.[79] Comorbidities such as diabetes, hypertension, liver disease, myocardial infarctions, and corpulmonale are common in patients with HF.[5,51] Patients with HF who have other chronic illnesses have complicated regimens and are less like to adhere to medical regimens due to polypharmacy, confusion over symptoms related to having several chronic illnesses, and lack of knowledge concerning the management of multiple conditions.[5,74]

We used the NYHA functional classification as a measure of HF symptom severity affecting functional status. Our model did not show that functional status was a significant predictor of HF self-care maintenance and HF self-care confidence. Intuitively, poor functional status impairs patients' abilities to engage in appropriate self-care due to activity intolerance. Activity intolerance along with dyspnea are the hallmark manifestations of HF and limit how well patients perform activities of daily living, exercise, cook appropriate diets, and attend needed provider appointments for follow-

up.[70,80] However, some studies have indicated that patients with HF who have worse symptoms and functional status perform better self-care;[68,81] others suggest that functional impairment is a barrier to self-care.[5] Over 50% of our sample had mild symptoms with activity (NYHA I/II) that may have affected the outcome of our proposed model.

Strengths and Limitations

A major strength of this study is its longitudinal design over a 12-month period as opposed to many of the existing studies on negative emotions and self-care that are cross-sectional in design. There are limitations to this study that should be considered when examining the results. The majority of patients with HF in this study were males, thus females were underrepresented in our study. In addition, we utilized self-report measures of self-care behaviors that may be influenced by memory, recall or desire to viewed positively regarding adherence to medical regimens. Self-report questionnaires may introduce a bias that could over- or underestimate the existence of symptoms of HF as well as adherence to medication, diets, and exercise. However, the SCHFI is a valid instrument and its use in the HF population is well documented.

Conclusion

Our study provides more insight into the self-reported self-care behaviors of patients with HF. While our study did not support the hypothesis that symptoms of anxiety, depression, and hostility would be predictive of self-care, the study did illuminate other variables that have an important influence on self-care. Our study does provide more evidence that self-reported self-care behaviors among patients with HF are inadequate. Also evident from our study and others is that the relationships of anxiety,

depression, and hostility symptoms on self-care are inconsistent. Negative emotions are associated with poor health outcomes. However, there is a need for further research in the area of how negative emotional states influence patients' abilities to take care of themselves. Due to the fact that self-care is one of the primary mechanisms to prevent poor health outcomes in patients with HF, a better understanding of how these negative emotions interact with self-care is needed.

Figure 3.1. Conceptual Framework of Relationships of Symptoms of Anxiety, Depression, and Hostility, Self-Care, and Poor Health-Related Outcomes

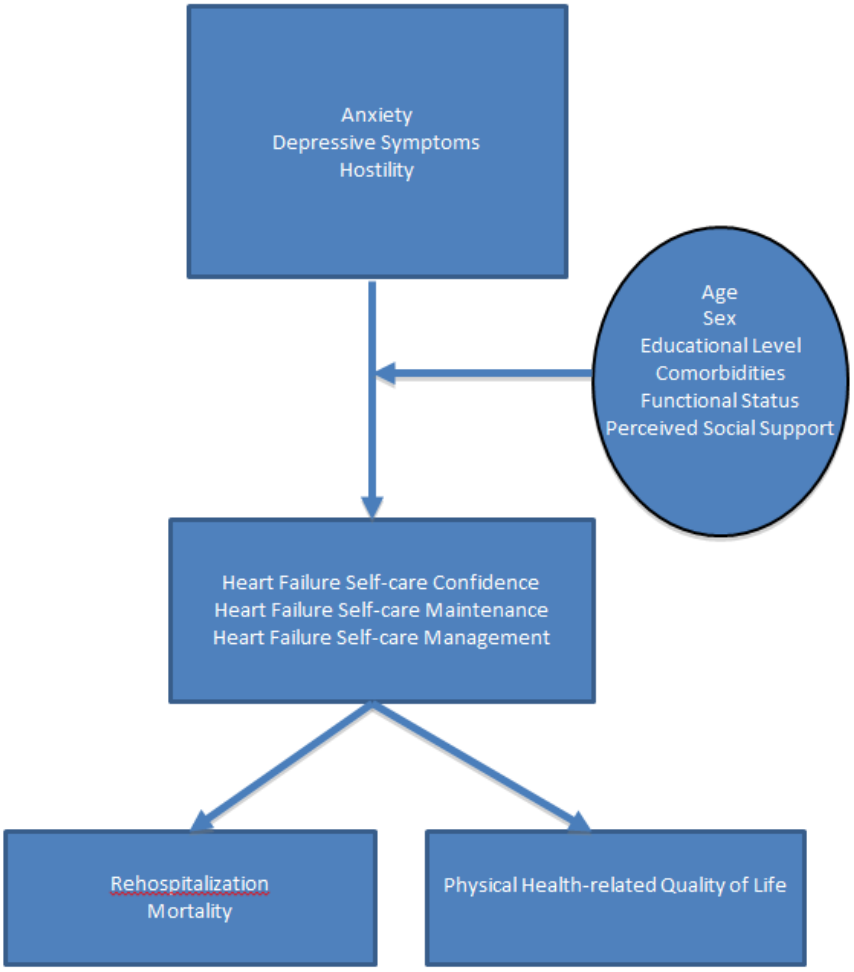


Table 3.1. Demographic and Clinical Characteristics of the Sample (N=214)

Variable	n (%)	Mean (± SD)
Demographic Characteristics		
Age		60.12 (± 12.1)
Gender		
Male	136 (63.5)	
Female	78 (36.4)	
Educational Level		14.12 (± 3.55)
Marital Status		
Single/Divorced/Widowed	83 (38.8)	
Married/Co-habitate	127 (59.3)	
Employment Status		
Employed	59 (27.6)	
Retired due to HF/disability	4 (39.3)	
Retired not due to HF/unemployed by choice	58 (27.1)	
Homemaker/other	12 (5.6)	
Smoking		
Current smoker	37 (17.3)	
Former smoker	90 (42.1)	
Never smoked	86 (40.2)	
Clinical Characteristics		
LVEF		36.74 (± 14.50)

Table 3.1 (continued)

Variable	n (%)	Mean (± SD)
NYHA Functional Classification		
Classifications I/II combined	117 (54.7)	
Classifications III/IV combined	94 (43.9)	
Body Mass Index		32.41 (± 8.55)
Charlson Comorbidity Score		2.95 (± 1.82)
Medications		
ACE Inhibitors	149 (69.6)	
ARBs	29 (13.6)	
Beta Blockers	192 (89.7)	

LVEF = Left ventricular ejection fraction
NYHA = New York Heart Association functional classification
ACE = Angiotensin converting enzyme
ARB = Angiotensin receptor blocker

Table 3.2. Mean Scores of Predictor Variables related to Symptoms of Anxiety, Depression, Hostility and Perceived Social Support and Dependent Variables of Self-Care Maintenance and Self-Care Confidence (N=214)

Variable Measure	**Possible Range**	**Mean**	**Standard Deviation**
BSI Anxiety Subscale	0 - 4	0.56	± 0.66
BSI Hostility Subscale	0 - 4	0.44	± 0.50
PHQ-9 Depression Scale	0 - 27	5.02	± 4.90
Perceived Social Support (PSS)	7 - 84	68.86	± 18.11
Self-Care Maintenance (SCHFI)	0 - 100	55.94	± 19.54
Self-Care Confidence (SCHFI)	0 - 100	60.04	± 19.58

BSI = the Brief Symptom Inventory
PHQ-9 = the Patient Health Questionnaire-9
MPSS = the Multidimensional Scale of Perceived Social Support
SCHFI = the Self-Care of Heart Failure Index

Table 3.3. Multiple Hierarchal Regression Analysis: Baseline Predictors of Self-Care Maintenance at 12 Months (N=214)

Model	Variable	Standardized β	t statistics	Variable p value	R^2	R^2 Change/ P value	F statistics	Model p value
1	Age	.189	2.881	.004	.108	.108/<.001	8.508	<.001
	Gender	-0.76	-1.156	.249				
	Education Level	.236	3.596	.000				
2	Age	.187	2.850	.005	.119	.011/.287	5.620	<.001
	Gender	-.040	-.571	.569				
	Education Level	.238	3.509	.001				
	NYHA – Two Classifications I/II and III/IV	-0.83	-1.129	.260				
	Charlson Comorbidity Index	.102	1.427	.155				
3	Age	.155	2.378	.018	.157	.038/.002	6.440	<.001
	Gender	-.044	-.648	.518				
	Education Level	.232	3.482	.001				
	NYHA – Two Classifications I/II and III/IV	-.052	-.709	.479				
	Charlson Comorbidity Index	.124	1.761	.080				
	Perceived Social Support	.203	3.066	.002				

Table 3.3 (continued)

4	Age	.167	2.469	.014	.169	.012/.403	4.619	<.001
	Gender	-.043	-.614	.540				
	Education Level	.228	3.425	.001				
	NYHA – Two Classifications I/II and III/IV	-.056	-.746	.457				
	Charlson Comorbidity Index	.133	1.862	0.64				
	Perceived Social Support	.199	2.957	.003				
	BSI Hostility Subscale	-.092	-1.028	.305				
	BSI Anxiety Subscale	.168	1.703	.090				
	PHQ-9 Score (Depressive Symptoms)	.060	-.647	.518				

NYHA = New York Heart Association functional classification

BSI = Brief Symptom Inventory

PHQ-9 = Patient Health Questionnaire-9

Table 3.4. Multiple Hierarchal Regression Analysis: Baseline Predictors of Self-Care Confidence at 12 Months (N=214)

Model	Variable	Standardized β	t statistics	Variable p value	R2	R2 Change/ p value	F Statistics	Model p value
1	Age	-.036	-.533	.594	.050	.050/.013	3.675	.013
	Gender	-.097	-1.431	.154				
	Education Level	.191	2.827	.005				
2	Age	-.025	-.367	.714	.079	.029/.039	3.572	.004
	Gender	-.076	-1.057	.292				
	Education Level	.145	2.093	.038				
	NYHA – Two Classifications I/II and III/IV	-.135	-1.798	.074				
	Charlson Comorbidity Index	-.082	-1.126	.261				
3	Age	-.066	-1.004	.317	.143	.064/<.001	5.750	<.001
	Gender	-.081	-1.177	.241				
	Education Level	.137	2.041	.042				
	NYHA – Two Classifications I/II and III/IV	-.095	-1.289	.199				
	Charlson Comorbidity Index	-.054	-.758	.450				
	Perceived Social Support	.262	3.925	<.001				

Table 3.4. (continued)

4	Age	-.102	-1.497	.136	.161	.018/.235	4.334	<.001
	Gender	-.085	-1.197	.233				
	Education Level	.139	2.077	0.39				
	NYHA – Two Classifications I/II and III/IV	-.069	-.913	.363				
	Charlson Comorbidity Index	-.045	-.621	.535				
	Perceived Social Support	.248	3.669	<.001				
	BSI Hostility Subscale	.001	.008	.994				
	BSI Anxiety Subscale	-.146	-1.469	.143				
	PHQ-9 Score (Depressive Symptoms)	.006	.061	.951				

NYHA = New York Heart Association functional classification

BSI = Brief Symptom Inventory

PHQ-9 = Patient Health Questionnaire-9

Chapter Four: Trajectories of Symptoms of Depression and Anxiety are Predictive of Mortality and Physical Health-Related Quality of Life at 1-Year Among Patients with Heart Failure

Introduction

Heart failure (HF) is associated with manifestation of a wide range of psychological symptoms, although the most common are anxiety and depression. Presence of anxiety and depression in patients with HF is associated with poor adherence to prescribed therapy, increased healthcare service utilization, higher mortality, and poorer health-related quality of life (HRQOL).[1,2] Anxiety and depression are not stable, but dynamic states that can worsen or improve over time, yet most research in this area has included only measures done at one point in time. As a consequence, little is known about the trajectory of anxiety and depression and the association of different symptom trajectories with patient outcomes.

Background and Aims

Anxiety and depressive symptoms are influenced by biological, behavioral, social, cultural, environmental, and economic factors that change over time. By exploring trajectories of anxiety and depression symptoms, clinicians can anticipate and identify those patients who are at greatest risk for adverse events, when to intervene, and whether changing these trajectories can ultimately change and improve health outcomes.[3]

Thus the primary aims of this study were (1) to determine trajectories of depressive and anxiety symptoms among patients with HF at three points in time (baseline, 3, and 12 months), and (2) explore how these trajectories influence one-year cardiac event-free survival and physical health-related quality of life (P-HRQOL). We hypothesized that a) multiple trajectories of depressive and anxiety symptoms could be

identified, and b) trajectories of depression and anxiety would be predictive of clinical events and P-HRQOL at one year.

Methods

Design. This was a secondary data analysis in which we used longitudinal data from the Heart Failure Quality of Life Collaborative contributed by investigators from eight sites representing the Southwest, Southeast, Northwest, Northeast, and Midwest regions of the United States. The design, procedures, and results of the primary studies have been previously reported.[4,5]

Participants and setting. Approval from appropriate institutional review boards was obtained at all sites and all participants gave signed, informed consent. Settings for recruitment of participants included community hospitals, academic medical centers, and outpatient clinics. Baseline, 3-month and 12-month data on 597 participants with complete data on the variables of interest comprised the sample. Patients who did not have complete data were excluded as not all sites collected data on the variables of interest. There were no sociodemographic differences between those who did and did not have complete data. Inclusion criteria were the following: 1) diagnosis of HF documented in the medical record confirmed by a cardiologist; 2) community-dwelling; 3) free of major cognitive impairment; 4) free of major life-threatening co-morbidities expected to result in death within 12 months; and 5) not on a cardiac transplantation waiting list.

Measurements.

Physical health-related quality of life. P-HRQOL was measured using the Minnesota Living with Heart Failure Questionnaire (MLHFQ) Physical Subscale. The MLHFQ is an HF-specific measure of HRQOL that is commonly used to assess patients'

psychosocial, economic, and emotional aspects of their lives.[6] This instrument has demonstrated adequate reliability and validity in a number of studies.[7-9] The MLHFQ consists of an emotional subscale (5 items) and a physical subscale (8 items) and eight additional items not included in the subscales but contributing to the total score. The emotional subscale and the total summary score of the MLHFQ were not used in this study as symptoms of depression and anxiety are components of both scores, thus only the 8-item physical subscale score (ranging from 0-40) of the MLHFQ was used as the outcome variable for P-HRQOL. Higher scores indicate worse quality of life.

Anxiety. Anxiety was assessed with the 6-item anxiety subscale of the Brief Symptom Inventory (BSI).[10] The BSI Anxiety Subscale was chosen because it is a brief, valid, reliable, and sensitive measure of anxiety that minimizes patient burden. The BSI Anxiety subscale has well-documented reliability and validity in patients with HF.[11] Higher scores indicate higher levels of anxiety.

Depressive symptoms. Depressive symptoms were assessed using the Patient Health Questionnaire-9 (PHQ-9).[12] The PHQ-9 consists of nine items,[13] each of which corresponds to one of nine symptoms of the major depressive disorder criteria in the Diagnostic and Statistical Manual of Mental Disorders-IV. The scores can range from 0 to 27 with higher scores indicating higher levels of depressive symptoms.[13] The reliability and validity of PHQ-9 have been demonstrated in numerous studies in various patient care settings[12,14] as well as in patients with HF.[15,16]

Event-free survival. Event-free survival was defined as the end point of time to first cardiac-related hospitalization or all causes of death during the 12-month follow-up period from baseline. Data on hospitalization or death were collected from medical

record review, patient/family interviews, and death certificates. In addition, patients were asked to keep a record of all hospitalizations. Trained cardiology clinicians blinded to patient status reviewed all sources of data about hospitalization and death that were then reviewed and confirmed by a second blinded cardiology clinician.

Functional status. We used the New York Heart Association (NYHA) functional classification to measure functional status of participants at baseline through an in-depth interview. Participants are assigned a classification based on symptoms occurring with physical activity ranging from I (no symptoms with regular physical activity) to IV (physical symptoms of fatigue, dyspnea, chest pain, palpitations at rest).

Comorbid illnesses. We collected data on the number of comorbid illnesses of study participants at baseline using the Charlson Comorbidity Index.[17] The data were abstracted from the medical records and patient interviews by trained nurse researchers.

Measurement of other variables. In order to completely characterize participants, data on the following demographic variables was collected: age, sex, and marital status. These data were collected during the participant interview. Clinical characteristics of left ventricular ejection fraction (LVEF), body mass index (BMI), and prescribed medications (e.g., beta blockers, angiotensin converting enzyme inhibitors [ACEI]) were collected by chart review and interview with participants at baseline.

Procedure. Specially trained research nurses explained the purpose and procedures to participants in the study as well as the risks and benefits of participation in the study. After patients completed the informed consent process, they were given a packet of self-administered questionnaires with instructions regarding how to complete each questionnaire. Participants completed these assessments at baseline and again at 3

months and 1 year. The nurse researcher was available to all participants to assist them. In addition, the nurse researcher examined all questionnaires to make sure participants did not inadvertently leave any items unanswered; however, participants were free to leave items unanswered if they so desired.

Statistical analysis. Data analyses were performed using SPSS for Windows (version 18.0, SPSS, Inc., Chicago, IL) and Mplus v6.0 (Muthén & Muthén, Los Angeles, CA). Latent growth mixture modeling (GMM) was used to identify distinct trajectories of change in depressive symptoms and anxiety. We used baseline, 3-month and 12-month measures of anxiety and depressive symptoms to develop trajectories. GMM is an approach to modeling that identifies distinct trajectories of change that vary around different means, have unique estimates of variance, and are homogenous within trajectory growth. Based on conditional probabilities and not absolute certainty, cases are assigned to the "most likely" trajectory or pattern of change over time. Changes in factors over time are modeled as random effects, and data need not be measured at evenly-spaced time intervals.[18]

Our approach to model specification in GMM was based on common procedures put forth by Ram and colleagues.[19] In each instance, we used several metrics to support the number of trajectories within the sample. The Lo-Mendell-Rubin adjusted likelihood ratio test[20] parametric bootstrapped likelihood ratio test, Bayesian Information Criterion (BIC; Schwarz, 1978), convergence (entropy closest to 1), the proportion of sample in each trajectory (≥ 5%), and posterior probabilities (average probability of belonging in "most likely" trajectory close to 1.0) were used to compare alternative models (e.g. k vs. k-1 trajectories[21]). Mplus v6.0 was used to perform all GMM. The default method of

mitigating bias due to missing data in Mplus is full-information maximum likelihood estimation (FIMLE), which effectively handles most data that are missing at random.

Among adults with HF, mixture modeling has been useful in identifying previously unobserved subgroups with respect to physical and psychological symptom burden[22] and self-care behaviors,[23] as well as medication adherence[24] and cognitive function[25] over time. An identify and associate approach to GMM was used to address specific aims. Accordingly, the first step was to develop separate growth mixture models for each symptom measure. Then GMMs that accounted for changes in both symptom measures over time were developed. The second step involved modeling associations among symptom trajectories and both 12-month event-free survival and physical health-related quality of life. Using GMM, continuous-time survival was modeled. Associations between symptom trajectories and 12-month physical health-related quality-of-life were quantified using generalized linear modeling.[26] Cox proportional hazards modeling was used in analysis of time to first event.

Results

Characteristics of the sample. Demographic and clinical characteristics of patients (N = 597) are summarized in Table 4.1. At baseline, the mean levels of depressive symptoms and anxiety symptoms were 6.42 ± 6.02 and 0.72 ± 0.84, respectively. At 3 months, mean levels of depressive and anxiety symptoms were 5.9 ± 5.8 and 0.62 ± 0.78, respectively. Mean levels of depressive and anxiety symptoms were slightly improved at 12-month follow-up (5.66 ± 5.90, and 0.60 ± 0.79, respectively). Based on repeated measures analysis of variance (ANOVA), these changes in depressive and anxiety symptoms from baseline to 12 months were statistically significant ($p <$

0.001 and p = 0.001, respectively).

Trajectories of symptoms of depression and anxiety. Using latent GMM, we identified models with 1-5 trajectories of depressive symptoms and 1-5 trajectories of anxiety. The best-fit model for depressive symptoms and anxiety included three trajectories each, allowing trajectories' membership to interact (Figure 4.1). This result was supported by the Lo-Mendell Rubin Adjusted LRT test (140.861, $p<0.001$ for depressive symptoms trajectories and 83.912, $p = 0.004$ for anxiety trajectories) and parametric bootstrapped likelihood ratio test (142.53, $p<0.001$ for depressive symptoms trajectories and 88.288, $p<0.001$ for anxiety trajectories). The trajectories were identified based on observance of naturally occurring trajectories relative to severity of symptoms within the sample. Depressive symptoms (Figure 4.2) were divided into three trajectories as follows: trajectory I ('getting better'; n=484, 81.1%), trajectory II ('bad and getting slightly worse'; n=83, 13.9%), and trajectory III ('bad and getting much worse'; n=30, 5.0%). Anxiety symptoms (Figure 4.3) were divided to three trajectories as follows: trajectory I ('getting better'; n= 398, 66.7%), trajectory II ('stable with slight improvement'; n=132, 22.1%), and trajectory III ('getting much worse'; n= 67, 11.2%).

Trajectories of depressive and anxiety symptoms and prediction of 12-month physical quality-of-life. Patients characterized as belonging to the 'bad and getting much worse,' or 'bad and getting slightly worse' in depressive symptoms had markedly worse P-HRQOL at 12 months compared with those who were 'getting better' (Table 4.2).

Patients characterized as belonging to the "stable with slight improvement' and 'getting much worse' in anxiety symptoms had poorer P-HRQOL at 12 months compared with those patients who were "getting better' (Table 4.3).

Trajectories of depressive and anxiety symptoms and event-free survival. Patients belonging to 'bad and getting worse' in depressive symptoms had a higher risk of clinical events at 12 months compared with those who were 'getting better' (Table 4.4). However, this did not hold true for those patients in the 'bad and getting much worse' in depressive symptoms, as membership in this group was not a significant predictor of event-free survival at 12 months. This indicated that relative to changes in depressive symptoms trajectory I, 'getting better,' patients in depressive symptoms trajectory III, "bad and getting much worse,' had a comparable risk of clinical event.

In adjusted analyses, with regard to prediction of event-free survival using trajectories of depressive symptoms, we controlled for age, gender, marital status, NYHA class, LVEF, BMI, use of ACEI, use of beta blockers, and Charlson comorbidity score. We found depressive symptoms trajectory II, 'bad and getting worse,' to be a significant predictor of event-free survival (Table 4.4) when compared to depressive symptoms trajectory II, 'getting better.' Depressive symptoms trajectory III, 'bad and getting much worse,' remained insignificant when compared to depressive symptoms trajectory I. The adjusted risk of clinical events for both depressive symptoms trajectories III and I were similar (Table 4.4, Figure 4.3).

Patients belonging to 'stable with slight decline' in anxiety symptoms did not have a greater risk of clinical events at 12 months when compared with those individuals whose anxiety symptoms were 'getting better' (Table 4.5). However, patients in 'getting much worse' trajectory of anxiety symptoms did have a significantly greater risk of clinical events at 12 months when compared to those patients who anxiety symptoms were 'getting better.'

In adjusted analyses with regard to prediction of event-free survival using trajectories of anxiety, we controlled for age, gender, marital status, NYHA class, LVEF, BMI, use of ACEI, use of beta blockers, and Charlson comorbidity score. We found membership in anxiety trajectory II, 'stable with slight improvement,' was not a significant predictor of event-free survival when compared to patients in trajectory I whose symptoms were getting better (Table 4.5). However, anxiety trajectory III, 'bad and getting worse,' membership was a significant predictor of event-free survival risk when compared to patients in trajectory I (Table 4.5). This indicated that those patients in anxiety trajectory III, 'bad and getting worse,' had a greater adjusted risk of clinical events when compared to those patients in trajectory I. Those patients in anxiety trajectories II and I had a comparable risk of clinical events (Table 4.5, 4.4).

Another analysis was conducted for an integrated model where depressive symptoms and anxiety were combined in one model with entropy of 0.919 that indicated a high posterior probability exceeding 90%, reflecting very low uncertainty in trajectory membership. This was supported by the Lo-Mendell Rubin Adjusted LRT test (<0.05) and the parametric bootstrap likelihood ratio test (<0.05). However, in this model the trajectory membership was not independent because there was a strong relationship between patterns of depressive symptoms and patterns of anxiety as presented earlier with the significant correlation between depressive symptoms and anxiety symptoms over time. Based on our findings, the best model is the one presented earlier with three separate trajectories for depressive symptoms and three separate trajectories for anxiety.

Discussion

The findings from this study indicate that symptoms of depression and anxiety are

dynamic and present as multiple unique trajectories over a 12-month period. There are three distinct trajectories of depressive symptoms and three distinct trajectories of anxiety. Our findings further demonstrate that distinct trajectories of depressive and anxiety symptoms over time predict P-HRQOL as well as event-free survival. This study is unique in that there are no studies to date in which trajectories of both depressive and anxiety symptoms were examined over time and the subsequent effect on health outcomes using latent GMM analyses was tested. Being able to identify depressive and anxiety symptom trajectories using a GMM approach allows investigators to discern trajectory classes that may not be evident with traditional growth modeling approaches.

In the trajectories for both depressive symptoms and anxiety with the majority of patients, it was most common for these psychological symptoms to decrease over time. This is important for both patients and clinicians to understand as it helps guide potential therapy and provides reassurance that dysphoric states most commonly resolve. There is, however, an important minority of patients whose psychological symptoms do not resolve and may even worsen. These patients have the highest risk for poor quality of life, morbidity and mortality. This finding underscores the importance of monitoring anxiety and depressive symptoms over time.

A few investigators have studied changes in depressive symptoms in patients with HF and have documented that depressive symptoms change over time as some patients may have persistent depressive symptoms while others may experience improvement in symptoms or develop depressive symptoms. In our study, we found those patients in trajectory II, 'bad and getting slightly worse,' and trajectory III, 'bad and getting much worse,' had poorer P-HRQOL. However, our study is quite different from other studies

that have examined the influence of depressive symptom trajectories on these health outcomes. Rather than using a naturalistic approach to identify symptom trajectories, most of the depressive symptom trajectory studies to date have included techniques that assign depressive symptoms trajectory according to specific trajectories determined a priori.[2,27,28] Using this approach, possible changes in depressive symptoms may not have been detected due to the deterministic approach used in the analyses. Further cross-sectional studies[29-31] provide support for the negative impact of depressive symptoms on HRQOL at one point in time; however, these studies fail to examine how depressive symptoms may change over time and make drawing conclusions about the true nature of the impact of depressive symptoms on HRQOL challenging.

We found those patients in depressive symptoms trajectory II, 'bad and getting slightly worse,' were most at risk of having a clinical event at one year. Other investigators[32-34] have also demonstrated that changes in depressive symptoms were predictive of event-free survival. However, pre-established cut-points were used to determine the presence or absence of depressive symptoms and classify patients into groups describing subsequent changes in the depressive symptoms determined a priori. Depressive symptom trajectory studies and risk of clinical events are limited; however, other non-trajectory studies[35,36] reported depressive symptoms at baseline were also associated with an increased risk of clinical events such as hospitalization or death.

An interesting and unexpected finding in our study was membership in depressive symptoms trajectory III, 'bad and getting much worse,' was not a significant predictor of event-free survival. It is difficult to evaluate this finding in light of other studies determining trajectory membership a priori. The patients in this group had depressive

symptoms at baseline, even according to cut-points of 9 or 10 commonly used with the PHQ-9; however, the symptoms grew worse over time. None of the studies which we reviewed identified a depressive symptom trajectory which was bad at baseline and grew worse over the course of a year. This finding could be attributed to the small number of patients in that trajectory (5%); however, that proportion is considered acceptable for latent GMM analysis.

Symptoms of anxiety are studied less frequently than depressive symptoms in the HF population. However, our study demonstrated that anxiety symptom trajectory II, 'stable with slight improvement,' and trajectory III, 'bad and getting worse,' were both predictive of poor P-HRQOL and event-free cardiac survival. We did not find any studies of anxiety symptom trajectories which examined the influence of the symptom trajectory on HRQOL and event-free survival. However, we did find studies[37,38] where baseline measurements of anxiety were predictive of HRQOL.

Our study is unique as GMM allowed us to investigate the symptoms of a heterogeneous condition and identify naturally occurring trajectories or homogeneous subpopulations within the larger heterogeneous population of patients with HF that may not be apparent with traditional growth modeling. Our study adds to the understanding of how trajectories of depressive and anxiety symptoms change over time and influence P-HRQOL and event-free survival as it allowed us to investigate the change in these symptom trajectories as they occurred naturally.

Strengths and Limitations

A major strength of our study is the analysis approach we used, which allowed us to examine a heterogeneous population and identify homogenous subgroups. In addition,

we had an adequate sample size for this type of analysis and controlled for major covariates. Potential limitations of our study include the use of self-reported measures for depressive and anxiety symptoms rather than diagnostic interviews for major depressive disorder or generalized anxiety disorder. Further, we did not have information on the participants' past psychiatric history. However, we utilized trained nurse researchers who adhered to a rigid protocol for administering the questionnaires. In addition, we utilized measures for depressive symptoms, anxiety, and P-HRQOL that have well-documented validity and reliability in patients with HF.

Conclusion

Although this study cannot infer causality, the findings underscore the need for clinicians to assess for the presence of depressive and anxiety symptoms in patients with HF over time as an important area to target for interventions. The psychological state of patients impacts how they are managed medically. Through understanding how depressive and anxiety symptoms change over time, clinicians are better able to evaluate the therapeutic effectiveness of treatment as well as how to assist patients in taking care of themselves and maintaining optimal health.

Table 4.1. Clinical and Demographic Characteristics of the Sample (N=597)

Variable	n (%)	Mean (± SD)
Age		64.3 (± 12.8)
Gender		
Male	372 (62.3)	
Female	225 (37.7)	
Marital status		
Never married	40 (6.7)	
Divorced/widowed/	215 (36.0)	
Married/cohabitating	342 (57.29)	
Body mass index (kg/m2)		32.44 (± 9.02)
Charlson Comorbidity Score		3.22 (± 1.76)
NYHA Functional Classification		
Class I	62 (10.4)	
Class II	329 (55.1)	
Class III	187 (31.3)	
Class IV	18 (3.0)	
Left Ventricular Ejection Fraction		38.37 (± 15.02)
Medications		
ACE*	365 (61.1)	
Beta blocker	497 (83.2)	

*Angiotensin Converting Enzyme Inhibitor

Table 4.2. Linear Regression of Depressive Symptoms Trajectories Associated with 12-Month Physical Quality of Life in Patients with Heart Failure

Predictor Variable	**β**	**CI**	**P**
Trajectory II – 'Bad and Getting Slightly Worse'	11.6	9.10 – 14.10	<0.001
Trajectory III – 'Bad and Getting Much Worse'	15.6	11.60 – 19.70	<0.001
Overall Model (Adjusted R^2 = 0.17, F= 63.6; P<0.001)			

Note: CI = confidence interval, β = adjusted regression slope coefficient; coefficients β for each trajectory are relative to Trajectory I, 'Getting Better'

Table 4.3. Linear Regression of Anxiety Symptoms Trajectories Associated with 12-Month Physical Quality-of-Life of Patients with Heart Failure

Predictor Variable	**β**	**CI**	**P**
Trajectory II – 'Stable with Slight Improvement'	12.0	10.14 – 13.95	<0.001
Trajectory III – 'Getting Much Worse'	18.7	16.16 – 21.16	<0.001
Overall Model (Adjusted R2 = 0.34, F= 155; P<0.001)			

Note: CI = confidence interval, β = adjusted regression slope coefficient; coefficients β for each trajectory are relative to Trajectory I, 'Getting Better'

Table 4.4. Adjusted Cox Proportional Hazards Regression Model of Variables Associated with Event-free Survival (Depressive Symptoms Model)

Predictor Variables	**Hazard Ratio**	**95% CI**	**P**
Age	1.02	1.01 – 1.04	0.003
Female Gender	1.13	0.78 – 1.63	0.509
Marital status			
Divorced/widowed	1.54	0.64 – 3.69	0.331
Married/cohabitating	1.64	0.70 – 3.84	0.252
NYHA class			
II compared to I	2.37	1.02 – 5.49	0.045
III compared to I	3.77	1.60 – 8.89	0.002
IV compared to I	2.52	0.74 – 8.61	0.139
LVEF	1.00	0.98 – 1.01	0.460
Use of ACE Inhibitors	1.00	0.71 – 1.42	0.987
BMI	1.00	0.98 – 1.02	0.997
Use of Beta Blockers	0.87	0.56 – 1.35	0.549
Charlson Comorbidity Score	1.14	1.05 – 1.24	0.002
Depressive Symptom Trajectories			
Trajectory II compared to Trajectory I	2.17	1.45 – 3.26	<0.001
Trajectory III compared to Trajectory I	1.83	0.91 – 3.68	0.088
Final Model Overall Model (χ^2 = 57.31, df. = 14; p <0.001)			

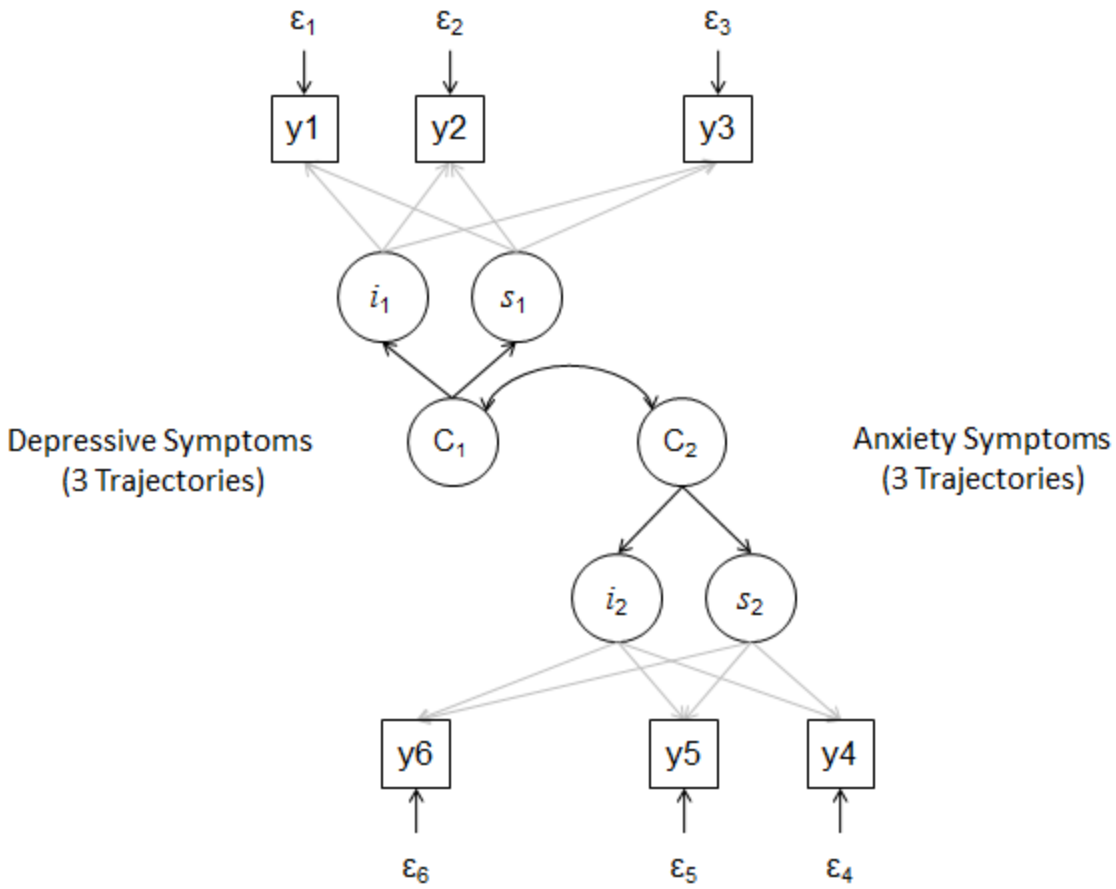
Trajectory I = 'Getting Better'
Trajectory II = 'Bad and Getting Slightly Worse'
Trajectory III = 'Bad and Getting Much Worse'

Table 4.5. Adjusted Cox Proportional Hazards Regression Model of Variables Associated with Event-free Survival (Anxiety Model)

Predictor Variables	Hazard Ratio	95% CI	P
Age	1.02	1.00 – 1.04	0.004
Female Gender	1.19	0.83 – 1.71	0.353
Marital status			
Divorced/widowed	1.45	0.61 – 3.47	0.405
Married/cohabitating	1.54	0.66 – 3.59	0.321
NYHA class			
II compared to I	2.33	1.00 – 5.41	0.049
III compared to I	3.66	1.55 – 8.62	0.003
IV compared to I	2.52	0.74 – 8.64	0.140
LVEF	1.00	0.98 – 1.01	0.430
Use of ACE Inhibitors	1.03	0.73 – 1.46	0.924
BMI	1.00	0.98 – 1.02	0.924
Use of Beta Blockers	0.85	0.55 – 1.33	0.487
Charlson Comorbidity Score	1.13	1.03 – 1.23	0.005
Anxiety Trajectories			
Trajectory II compared to Trajectory I	1.12	0.75 – 1.69	0.581
Trajectory III compared to Trajectory I	2.18	1.38 – 3.45	0.001
Final Model Overall Model (χ^2 = 53.43, df. = 14; p <0.001)			

Trajectory I = 'Getting Better'
Trajectory II = 'Stable with Slight Improvement'
Trajectory III – 'Getting Much Worse'

Figure 4.1. Final Model of Depressive and Anxiety Trajectories using Latent Growth Mixed Modeling



Final Model includes growth curves for two continuous measures (*y*, depressive symptoms and anxiety) as observed at 3 time points, each with an intercept (*i*) slope (*s*), a categorical variable indicating "most likely" trajectory (C), and ε which refers to latent variables**.** Trajectories of change in one variable (C1) were modeled to be associated with trajectories of the other (C2).

Figure 4.2. Final Model of Depressive Symptoms Trajectories

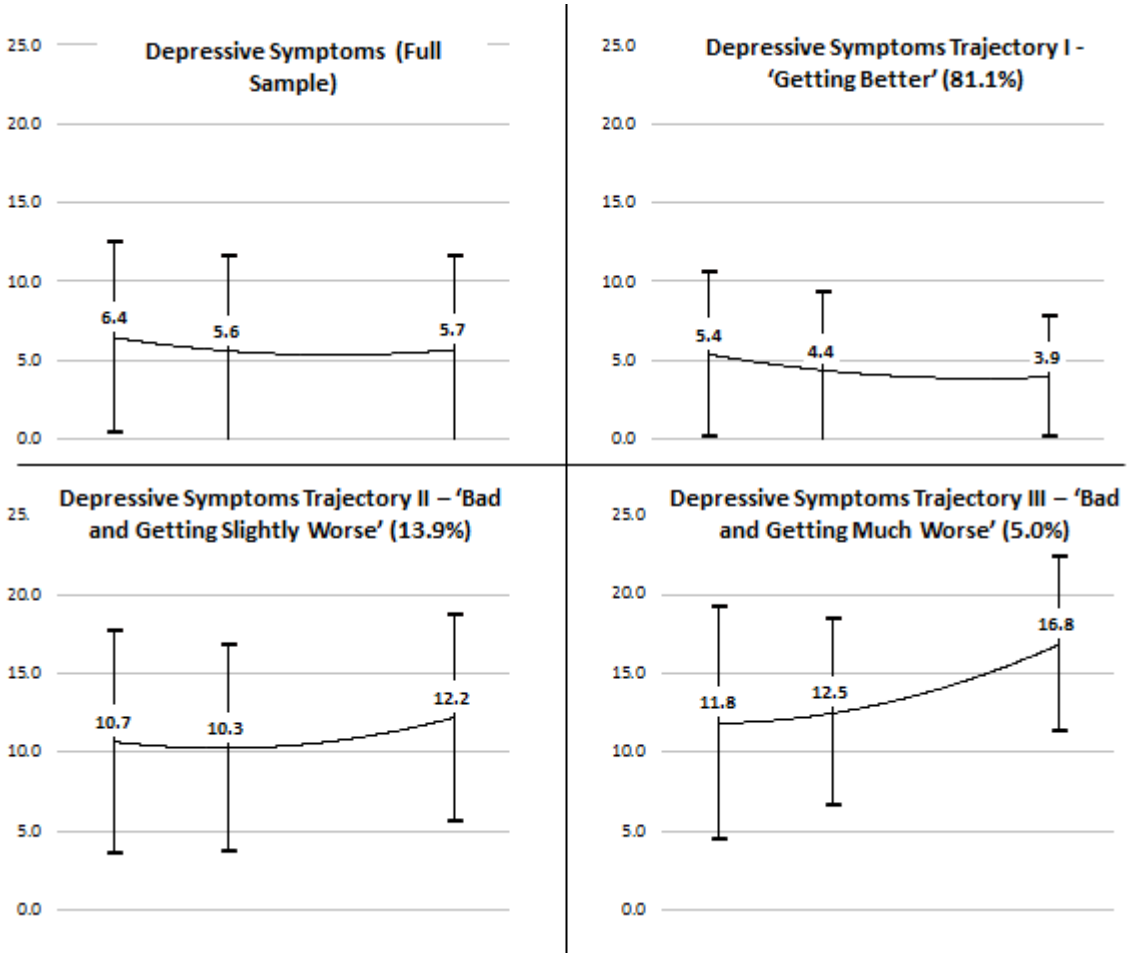
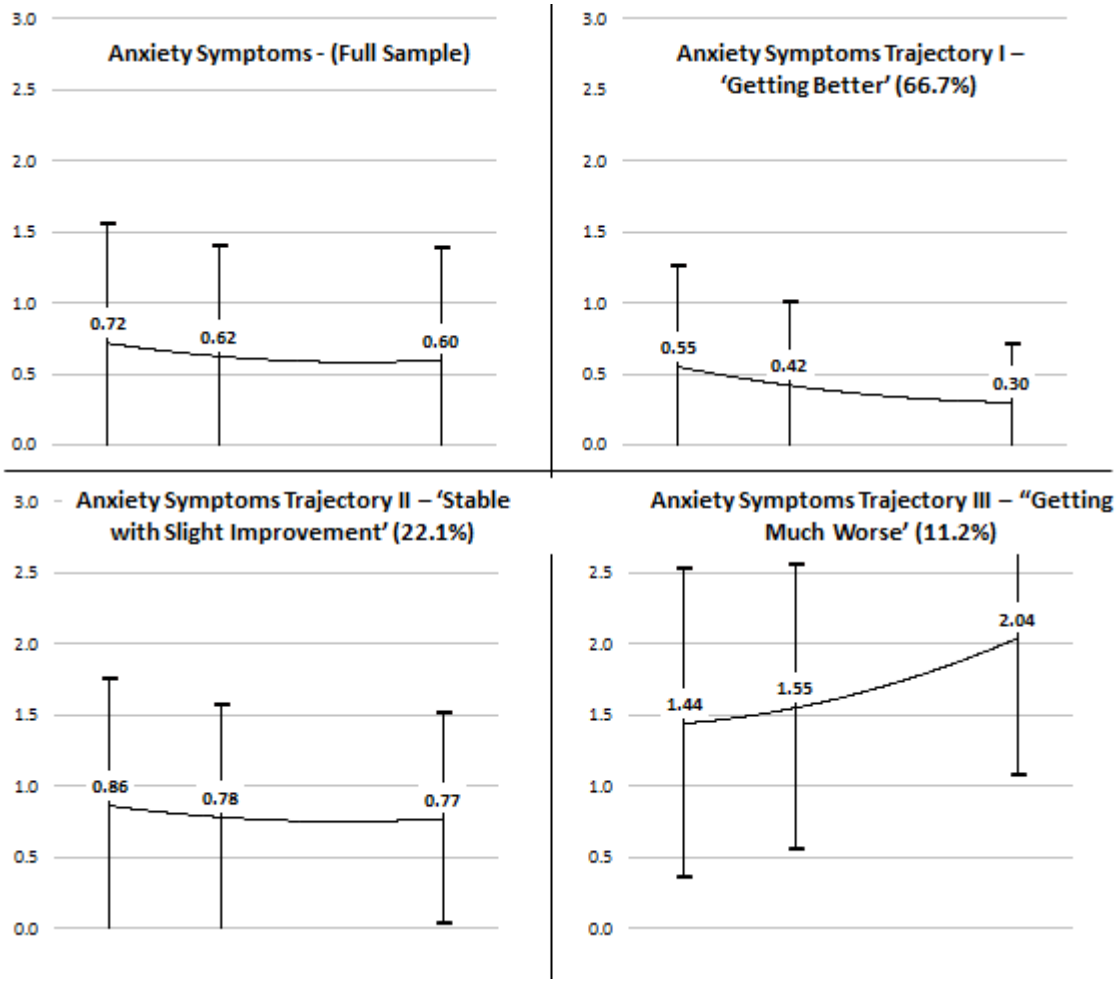


Figure 4.3. Final Model of Anxiety Symptom Trajectories



Chapter Five: Conclusions and Discussion

Summary and Integration

The overall purpose of this dissertation was to determine the influence of symptoms of anxiety, depression, and hostility on health-related outcomes. To this end, three studies were conducted for the following aims: 1) provide evidence of the psychometric properties of the Brief Symptom Inventory Hostility Subscale as a valid and reliable instrument to assess the hostility symptoms of patients with heart failure (HF); 2) determine whether symptoms of anxiety, depression, and hostility at baseline predict poorer self-reported self-care at one year among patients with HF; and 3) describe trajectories of anxiety and depressive symptoms among patients with HF across three points in time (baseline, 3 and 12 months) and explore whether these symptom trajectories predict one-year cardiac event-free survival and P-HRQOL.

Since the mid 19th century, the biomedical model (BMM) provided the traditional foundation for research on the understanding of disease and its treatment in the human body. The BMM focused on disease as a departure from a normal healthy state of the human body and therefore promoted a mechanistic approach to the treatment of disease.[1] This approach to the treatment of disease still dominates the medical practice of most providers.[1] This model works well with the treatment of an infectious disease but doesn't work as well with chronic diseases and conditions that are increasing in prevalence due to an increase in the elderly population and increase in people with chronic illnesses. The true nature of health is more than just the absence of disease as posited by the BMM.

The World Health Organization (WHO) defined health as "a state of complete physical, mental and social well-being and not merely the absence of disease or

infirmity."[2] This definition served as an impetus to develop a more integrated and holistic approach to human behavior, illness, and disease – the biopsychosocial model (BPSM).[1] The BPSM views health and illness as a consequence of the interplay of biological, psychological, and social factors and how these factors influence the course and treatment of disease and illness.[1] Subsequently, fields such as medicine, psychology, and nursing have utilized an interdisciplinary approach to patient care, especially in the care of individuals with chronic conditions such as HF. This shift in paradigm has resulted in medical providers understanding the importance of looking not only at illness and disease, but also understanding the influences of social and psychological variables such as negative emotional states on health-related outcomes in chronic conditions such as HF.

Patients with HF suffer troublesome physical and psychological symptoms which adversely affect the quality of their lives and result in poor health outcomes.[3] Negative emotions such as anxiety, depression, and hostility, are prevalent in patients with HF.[3-5] Research has demonstrated that patients with HF who have negative emotions are more likely to die or have adverse cardiac events compared to patients without negative emotional states.[6] Practitioners need to be able to recognize and treat these negative emotional states early and throughout the course of medical treatment to reduce the risk of adverse effects and optimize the health and well-being of patients with HF. Besides pharmacotherapy, recent studies have demonstrated that interventions such as cognitive behavioral therapy,[7,8] as well as stress reduction[9] and counseling,[10] have been effective in reducing negative emotional states in patients with cardiac conditions and HF and improving health-related outcomes. However, in order to design and test interventions, more research is needed to elucidate how negative emotions interact, change, and

subsequently influence health-related outcomes in patients with HF.

Symptoms of anxiety, depression, and hostility have been studied extensively in the general cardiovascular population. However, of the three negative emotional states, hostility has been studied less frequently than symptoms of anxiety and depression in patients with HF. The conceptual definition of hostility is challenging as hostility is also used interchangeably with anger and aggression, both of which are behaviors commonly seen with hostility. For example, Chida and Steptoe[11] conducted a meta-analytic review of studies examining the association between anger and hostility and coronary heart disease (CHD). The 25 studies examined by the investigators included different measures of hostility, trait anger, anger control, anger-out, anger reaction, anger temperament, anger suppression, cynical hostility, anger symptoms, behavioral hostility (interviews), and aggression. While the investigators concluded the studies examined in the meta-analysis provided support that anger and hostility are associated with CHD outcomes, their review also demonstrated how problematic and challenging the concepts of hostility or anger may be when evaluating studies and associated cardiac outcomes. It is noteworthy that some investigators[12] have begun examining both anger and hostility along with anxiety and depressive symptoms due to the overlapping effects of related affective traits. These negative emotions tend to cluster in individual patients;[13] therefore, research investigating these psychological variables may help identify patients at risk for early intervention. While there are numerous measures of hostility available for researchers, the psychometric properties of the Brief Symptom Inventory (BSI) Hostility subscale have not been examined in the HF population. I thought it important to validate this instrument as measurement burden in HF patients is a concern, and the BSI Hostility

subscale is short, easy to understand and can be completed in 1-2 minutes.

Thus, Chapter 2 is an evaluation of the psychometric properties of the BSI Hostility Subscale in patients with HF. Cross-sectional data were collected from a subset of 345 patients with HF as part of a larger longitudinal study of 1,136 patients in nine clinical trials throughout the United States. The Cronbach's alpha for the BSI Hostility Subscale was .77 indicating good internal consistency among the five items comprising the subscale. The inter-item correlation coefficients for the BSI Hostility Subscale ranged from .30 to .78, indicating adequate homogeneity. The BSI Hostility, Anxiety, and Depression Subscales were subjected to principal component analysis (PCA) followed by exploratory factor analysis (EFA). These analyses, as well as examination of the scree plot, supported a two-dimensional structure within the three subscales of the BSI: Factor I (Dysphoria) and Factor II (Hostility). I hypothesized the BSI Hostility Subscale would have a positive correlation with the BSI Depression and Anxiety Subscales and PHQ-9 as well as a negative correlation with the MSPSS, indicating patients with greater hostility levels would have greater levels of depressive and anxiety symptoms as well as poorer perceived social support. The findings of my study demonstrated there was a moderate to strong positive correlation between the BSI Hostility Subscale and the BSI Anxiety and Depression Subscales as well as the PHQ-9. In addition, there was a weak, negative correlation between the BSI Hostility Subscale and the MSPSS. These findings supported my hypotheses and initial support for the psychometric soundness of the BSI Hostility Subscale as a measure of hostility in patients with HF.

Patients with HF who have negative emotional states often have poor self-care behaviors and fail to adhere to medical treatment regimens such as taking prescribed

medications,[5,14-21] following a prescribed low-sodium diet, exercising,[22] monitoring for symptoms, and making sure they weigh themselves daily.[23] In addition, patients with symptoms of anxiety, depression, and hostility often continue or adopt risky behaviors such as smoking,[24,25] sedentary lifestyle, and poor diets.[19,25-29] Depressed, anxious, or hostile patients may not utilize available resources appropriately such as attending cardiac rehabilitation and may miss or fail to seek needed clinic appointments and follow-ups.[23] As a point of fact, inadequate self-care behavior has been shown to be the most commonly cited reason for hospital readmissions among patients with HF.[30] Subsequently, developing strong self-care behaviors in patients with HF is viewed to be the cornerstone to preventing exacerbations of symptoms and improving health-related outcomes (i.e. QOL, hospital readmissions, and mortality) in this population.[31,32]

Many of the studies examining the influence of negative emotional states on self-care are cross-sectional in design.[33,34] Studies report negative emotions are associated with poorer self-care behaviors. While cross-sectional studies are economical, allow for collection of a large amount of data over a shorter period, and are easily reproduced, investigators are limited to making observations to one point in time.[35] Cross-sectional studies do not allow investigators to make a temporal association between negative emotions and self-care behaviors; therefore investigators may be able to demonstrate association but not causality.[36]

Conversely, longitudinal studies have the advantage of inferring causal relationships that cross-sectional studies are unable to do as repeated measurements on the same individuals are gathered over a long period of time.[37] Longitudinal study designs have the ability to demonstrate progress and change in variables of interest and

show clear patterns over time.[37] Disadvantages of longitudinal studies include the possibility of drop-out of participants over time and the fact that they are more expensive and labor-intensive than cross-sectional studies.[37] Several longitudinal studies have demonstrated that negative emotions are predictive of self-care behaviors.[19,38] However, results have been inconsistent in the literature. Some studies have shown negative emotions were associated with specific self-care behaviors such as medication adherence and exercise, but not associated with general self-care.[39-41] Clearly there is a need for more longitudinal studies investigating the long-term effects of negative emotions on self-care and how providers may intervene to support adequate self-care in patients with HF.

Chapter 3 is a secondary data analysis of longitudinal data to determine whether baseline symptoms of anxiety, depression, and hostility were predictive of self-care at 12 months in patients with HF. I identified a subset of 214 patients with HF enrolled in a larger longitudinal study representing the Midwest, Southwest, Southeast, Northwest, and Northeast regions of the United States with complete data on the variables of interest. Hierarchical multiple regression was utilized in the analysis of the data. Baseline measures of anxiety, depression, and hostility symptoms were entered into the model along with covariates identified from the literature (i.e. age, sex, educational level, functional status, comorbidities, and perceived level of social support). The study did not show that baseline negative emotional states were predictive of self-reported self-care maintenance and self-reported self-care confidence at 12 months. However, baseline age, level of education, and perceived social support were significant predictors of 12-month self-reported self-care maintenance, and baseline level of education and perceived social

support were significant predictors of 12-month self-reported self-care confidence.

The results from my study may be due to the fact that a repeated measures design was not implemented and only baseline measures of anxiety, depressive, and hostility symptoms were used as predictors of self-reported self-care maintenance and self-reported self-care confidence at 12 months. The nature of negative emotions is that they are dynamic and change over time. Failure to find a significant relationship between negative emotions and self-reported self-care may be attributable to the fact that patients did not continue to have symptoms of anxiety, depression, or hostility for the duration of the study.[42] Being able to look at the trend or trajectory of negative emotional states on self-care over time may be more revealing.

Trajectory studies in patients with HF have demonstrated depression is predictive of poor health-related outcomes.[43-45] However, these studies used subgroups identified a priori in examining the predictive ability of negative emotions on health-related outcomes. In the study described in Chapter 4, I chose to use latent growth mixture modeling in order to identify distinct subgroups that may be obscured using traditional methods.

Chapter 4 is an analysis of trajectories of anxiety and depressive symptoms over 12 months and evaluation of whether these trajectories across three points in time (baseline, 3 and 12 months) were predictive of event-free survival and P-HRQOL at 12 months in patients with HF. Data from a subset of 597 patients with HF enrolled in a larger longitudinal study was used in the analysis. I used latent growth mixture modeling to identify unique trajectories of symptoms of anxiety and depression in the patient sample and Cox linear regression models to determine whether these negative emotions

were predictive of event-free survival and P-HRQOL. Results of the study demonstrated the majority of patients' anxiety and depressive symptoms got better over time. However, the study also demonstrated that unique trajectories of anxiety and depressive symptoms were predictive of event-free survival and P-HRQOL. However, an interesting finding in the study is that the worst trajectory of depressive symptoms was not predictive of event-free survival at 12 months in patients with HF. These findings may be the result of the small number of patients in that trajectory of depressive symptoms although the number was sufficient for the trajectory analysis.

Impact of Dissertation on the State of Science

The findings of this dissertation filled some gaps in understanding how anxiety, depression, and hostility symptoms influence health-related outcomes of patients with HF. Negative mood states most often studied in relation to health outcomes in patients with HF are symptoms of anxiety and depression. Hostility has been studied extensively in relation to its influence on the development and progression of CAD but not as extensively in the HF population. Patients with HF often report higher levels of multiple negative emotional states,[46] yet these states are often not recognized or treated adequately.[10,47-49] In addition, many studies examine symptoms of anxiety, depression, and hostility apart from each other; however, associations of multiple affective traits with cardiovascular disease overlap.[12] Symptoms of these negative emotional states often overlap.[23] Individuals with depressive symptoms are often anxious, individuals with anxiety often have depressive symptoms,[23,50] and individuals with symptoms of hostility often demonstrate high levels of annoyance and irritability seen in anxious states. Therefore, it is important to examine all three negative states to understand their

prevalence, how they interact and fluctuate over time, as well as their relationships to health outcomes.

In Chapter 2 I advanced the state of science in the literature by evaluating the validity and reliability of the BSI Hostility Subscale in patients with HF. Most of the measures for symptoms of hostility are lengthy[11,51] and may create an undue burden on patients with HF who often report high levels of fatigue.[52,53] The BSI Hostility subscale is a short five-item subscale, does not create undue burden on patients, and has been used in several studies in the HF population. However, there are no studies in the literature evaluating the psychometric properties of this measure in patients with HF. Thus, this study is the first to provide psychometric support for the BSI Hostility Subscale as a sound measure of hostility in HF patients.[54,55] In addition to psychometric support for the BSI Hostility Subscale, suggestions for improvement in wording on items in the Subscale were made that may be useful in future studies.

The longitudinal study described in Chapter 3 advances the state of science in evaluating how predictive baseline measures of anxiety, depression, and hostility symptoms are relative to self-care at 12 months. There are limited longitudinal studies examining the influence of negative emotions on self-care,[56] as most studies are cross-sectional and offer inconsistent results. My study did not provide evidence that baseline measures of negative emotions are predictive of self-care. However, the results do provide support for the contribution of age, educational level, and, more importantly, perceived social support in predicting self-care. These findings are consistent with other studies. In addition, the study does offer more insight into the relationship of negative emotions on self-care. The patients in my study had mild elevations of negative

emotional states, yet these states did not influence future self-care significantly. This finding provides some evidence that negative states may need to be above a certain threshold in order to be an important predictor of future self-care and provides evidence that interventions aimed at increasing social support may result in better self-care behaviors in patients with HF. Despite the lack of significant findings on the contribution of negative emotions influencing self-reported self-care behaviors, the study does underscore that patients with HF have elevated levels of negative emotional states that should be routinely assessed in order to target interventions aimed at improving self-care and health outcomes.

Lastly, in Chapter 4, I advanced the state of science by identifying and evaluating how trajectories of symptoms of anxiety and depression may predict P-HRQOL and event-free survival at 12 months. This is a very important study in several ways. First, to my knowledge, this is first study of patients with HF that has utilized latent growth mixture modeling in evaluating the predictive ability of trajectories of negative emotions and future health outcomes. In general, there are limited studies evaluating trajectories of negative emotional states on health outcomes, and those that do exist have used deterministic approaches where trajectories are pre-determined at set cut-points and patients are then grouped into those categories. Secondly, this study demonstrated how negative emotions actually fluctuate over time to influence health-outcomes. I identified three distinct trajectories of these symptoms of anxiety and symptoms of depression. While the majority of patients had improvement in symptoms of over the course of one year, those patients whose symptoms worsened over time had worse P-HRQOL and more cardiac related events. Lastly, this study adds to our understanding of how negative

emotional states truly change over time naturally and how studies using a deterministic approach may not capture how these fluctuations actually influence health outcomes. For example, if using a cut-point of 10 (commonly used for determining the presence of depression)[57] in the PHQ-9, I would not have been able to identify the two significantly distinct trajectories of depressive symptoms that worsened over time that subsequently revealed different outcomes in my study. One was predictive of event-free survival, while the very worst trajectory of depressive symptoms was not. The findings in this study demonstrate how negative emotions change over time (baseline, 3 and 12 months) and emphasize the importance of routine assessment of anxiety and depression symptoms. Through routine assessment of negative emotional states, clinicians may monitor efficacy of treatment and intervene earlier to improve symptoms, slow the progression of HF, and subsequently improve future health-related outcomes.

Recommendations for Nursing Practice and Research

Negative emotional states are important predictors of health-related outcomes in patients with HF such as poor P-HRQOL, increased hospital admission, and increased mortality. Increased levels of anxiety, depression, and hostility symptoms are more common in cardiac patients than in healthy individuals.[46] As a result, negative emotional states in patients with HF need to be assessed routinely over time to detect their presence as well as need for intervention.

In order to assess the presence of negative emotional states, clinicians need to be able to use psychometrically sound measures that are easy to administer and brief, without being burdensome to patients with HF. There are numerous tools available to measure hostility, and each vary in their psychometric properties and clinical utility.[11]

While this dissertation has provided initial support for the soundness of the BSI Hostility Subscale, more studies need to be conducted in order to replicate the results of this study and support the Subscale's reliability in the heart failure population.

Negative emotional states are a barrier to engaging in appropriate self-care behaviors.[23] Patients who have symptoms of anxiety, depression, and hostility have poor adherence to medical regimens, as well as adoption or continuance of unhealthy lifestyle practices (i.e. smoking, unhealthy diets, lack of exercise).[24,25,58-64] In addition, negative emotions are often associated with poor use of appropriate resources such as keeping scheduled clinic appointments and cardiac rehabilitation[23,65] as well as social isolation and poor social support.[23,65-68]

The study outlined in Chapter 3 did not support my hypothesis that baseline negative emotional states would be predictive of self-reported self-care at 12 months; however, results demonstrated social support was a significant predictor of self-care and a potentially strong mediator of the relationship between negative emotions and self-reported self-care behaviors. This is an important finding as social support has been shown to aid in the ability of HF patients to care for themselves[23,32] as well as act as a means to cope with the stress of having a chronic illness.[69] Patients with symptoms of anxiety, depression, and hostility often report poor social support.[70,71] The presence of negative emotional states and poor social support among HF patients has been shown to be predictive of poor outcomes and higher risk of events.[72] Most of the studies investigating the relationships between negative emotions and self-care are cross-sectional in design and present inconsistent results. The implication from my study as well as others in the literature is that more longitudinal studies need to be conducted to

examine the relationships of negative emotions on self-care behaviors.

In addition, the study described in Chapter 4 is novel in that the analyses utilized latent GMM to identify unique trajectories of anxiety and depressive symptoms that were found to be predictive of P-HRQOL and event-free survival. It is my belief that this type of analysis is more robust than using a deterministic approach. However, due to the novel application of latent GMM used in this study, more studies using this type of analysis are needed to determine whether the findings can be replicated.

The studies in this dissertation did not involve examination of any interventions aimed at improving negative emotional states, self-care, or health-related outcomes. However, the studies in this dissertation do serve as an impetus to investigate non-pharmacological interventions targeting negative emotional states and self-care behaviors. One such therapy that holds promise for improving health outcomes is cognitive behavior therapy that encourages cognitive reappraisal. Individuals with negative emotional states appraise situations according to motivational relevance and congruence related to their goals; therefore, they may view and respond to events differently.[73] Cognitive reappraisal may improve symptoms of anxiety, depression, and hostility and assist patients with HF in making behavior changes that improve self-care and health-related outcomes.

In summary, implications of this dissertation include the importance of monitoring negative emotions over time as well as the need for further longitudinal studies that examine relationships between negative emotions and health-related outcomes. A better understanding of how psychological symptoms change is meaningful, as it affords clinicians the opportunity for timely interventions designed to reduce the risk

of adverse events and improve health outcomes. In order to achieve this, further research is needed to investigate psychological symptom trajectories and identify high-risk groups. In addition, the design and testing of interventions aimed at reducing psychological symptoms is critical to improve health outcomes in patients with HF.

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PROFESSIONAL EXPERIENCE

Dates	Institution and Location	Academic Position
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2013 – present	University of Kentucky, College of Public Health, contract worker for Kentucky Department for Public Health, Healthcare Associated Infection Prevention Program, Frankfort, KY	Infection Prevention Nurse Consultant
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PUBLICATIONS:

Journal Articles:

Roser, L.P., Alhurani, A.S., Lee, C.S., Lennie, T.A., Biddle, M., Frazier, S., Fleming, S., & Moser, D.K. (2016). *Trajectories of depression and anxiety are predictive of mortality, readmission, and physical health-related quality of life at 1-year among patients with heart failure*. Submitted for publication

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Book Chapter:

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Published Abstracts:

Zambroski, C.H., Moser, D.K., **Roser, L.P**., Heo, S. & Chung, M.L. (2003). Abstract: Characteristics of heart failure patients who received hospice care at the end of life. *Journal of Cardiac Failure, 9*(5) Supplement, S103.

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HONORS AND AWARDS:

2006	Who's Who among Executives in Health Care
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1991	Academic Excellence Award, University of Kentucky College of Nursing, Lex., KY
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PROFESSIONAL MEMBERSHIPS:

2010 - present	Association for Professionals in Infection Control and Epidemiology (APIC)
2006 – present	American Heart Association
2005 – present	American Heart Failure Association of Nurses
2004 – present	Kentucky League for Nursing
2003 – present	Southern Nursing Research Society
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