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Exploring Dose Effect Of An Early Palliative Care Intervention For Advanced Heart Failure Patients

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EXPLORING DOSE EFFECT OF AN EARLY PALLIATIVE CARE INTERVENTION FOR ADVANCED HEART FAILURE PATIENTS

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ABSTRACT

Heart failure (HF), a progressive condition with reduced quality of life (QoL) and high healthcare use, affects 6.5 million US adults. Research supports positive effects of palliative care integration into HF care, but there is limited consensus about the most beneficial intervention 'dose' (e.g. amount, duration, frequency, intensity). To date, no studies examining dose in palliative care HF interventions have been completed. Therefore, we examined dose using an existing data from the ENABLE CHF-PC trial (Educate, Nurture, Advise, Before Life Ends Comprehensive Heart Care for Patients and Caregivers; NCT02505425).

Operationalizing dose as dichotomous complete/noncomplete of all intervention components (6-weekly, psychoeducational telephone sessions + one-time, in-person palliative care consultation), we examined ENABLE CHF-PC intervention dose effect on quality of life and healthcare use of advanced HF patients. We conducted an exploratory concurrent mixed methods study with 3 aims: 1) determine the relationship between ENABLE CHF-PC intervention dose and patient-reported (QoL) and healthcare use, 2) determine the relationship between ENABLE CHF-PC patients' sociodemographic and clinical characteristics and intervention completion, and 3) explore ENABLE CHF-PC patients' perspectives and experiences with intervention components, dose, and study outcomes.

Linear mixed models were used to model intervention dose effect. Correlations and logistic regressions were used to examine associations between intervention completion and sociodemographic/clinical characteristics. Constant comparative analysis of semi-structured interviews was used to identify participant themes related to the intervention dose and study outcomes.

Of 208 ENABLE CHF-PC patients randomized to receive the intervention, 127 (61.1%) did not complete all components. No significant sociodemographic and clinical differences were found between those who completed versus those who did not. Moderate, clinically significant effect size dose-related outcome differences were found at 16-weeks in QoL measures with improved QoL in those completing the intervention (between-group difference: -9.71 (3.18), *d=0.47, p=0.002*) but not healthcare use. An overarching theme of dose and study experience being filtered and influenced by disease-related, social, provider relationships, emotional, and logistical individual contexts emerged from the 45 semi-structured interviews.

These findings suggest that increased exposure to early palliative care services may be beneficial; affecting QoL of certain subgroups of advanced HF patients in the Deep South.

Keywords: advanced heart failure patients, early palliative care, psychoeducational intervention, dose effect, quality of life, mixed methods research

DEDICATION

To John and Brian

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CHAPTER ONE

Introduction

The overarching aim of Chapter 1 is to introduce a concurrent mixed methods dose analysis study of an early palliative care intervention for advanced heart failure patients. Specifically, this chapter will describe (1) the significance of studying the problem of palliative care intervention dose in heart failure, (2) the study purpose and specific aims, (3) the study design and methods, and (4) key study terms.

Problem Statement

Heart failure (HF), one of the most common cardiovascular conditions in the U.S. (Benjamin et al., 2019), is associated with high disease burden (Alpert, Smith, Hummel, & Hummel, 2017). Cardiology professional organizations recommend the integration of palliative care into traditional HF care to address symptom burden, care coordination, goal setting, and quality of life (QoL) given the promising outcomes in these areas. However, these promising palliative care interventions vary considerably in dose, which is the amount, duration, frequency, and intensity, of the services provided. It is essential to define optimal dose or "exposure" in order to make further progress in testing palliative care for HF interventions and improving patient outcomes.

Significance

Over 6.5 million people in the United States are living with HF (Benjamin et al., 2019), which is characterized by the progressive inability to pump enough blood to meet

bodily demand (National Heart, Lung, and Blood Institute, 2015). Within the next 15 years, over 8 million U.S. adults will be living with HF with healthcare-related costs estimated at over $70 billion annually, an increase of nearly $40 billion from current healthcare expenditures (Benjamin et al., 2019). In addition to patients, informal family caregivers shoulder a significant burden across all stages of illness - providing a mean of nearly 2 hours of weekly care. For African American and Hispanic caregivers, this figure exceeds 3 hours (Dunbar et al., 2018). A recent study reported that total health care costs of informal HF caregiving were $6.5 billion annual with annual costs expected to exceed $13 billion by 2035 (Dunbar et al., 2018).

In older adults, HF is a leading cause of all-cause mortality (National Center for Health Statistics, 2014) and hospitalization (Desai & Stevenson, 2012) accounting for 8.5% of all U.S. deaths (AHA, 2017). Nearly half of HF patients die within the first 5 years of diagnosis (Benjamin et al., 2019). Additionally, older adults with multiple comorbidities represent most new cases of HF (Benjamin et al., 2019). Persons with HF are generally older, overall more ill (Benjamin et al., 2019), with poor QoL, high symptom burden, and complex treatment plans (Alpert, Smith, Hummel, & Hummel, 2017; Gadoud, Jenkins, & Hogg, 2013). QoL and symptom burden in those living with HF are generally worse than with most other chronic illnesses (Bekelman et al., 2009; Juenger et al., 2002).

Background

Palliative Care in Heart Failure

Given the burden of an HF diagnosis, collaboration between cardiology and palliative care, a specialty that focuses on relief of suffering through symptom management, goals of care discussions, and holistic care coordination (Center to Advance Palliative Care (CAPC), n.d.) has been recommended (Hunt, 2005; Institute of Medicine, 2015). Recent guidelines issued by the American College of Cardiology (ACC), the American Heart Association (AHA), and the Heart Failure Society of America (HFSA) recommend introducing palliative care as soon as patients develop significant symptoms, difficult health decisions, and substantial caregiver burden (Allen et al., 2012; Yancy et al., 2013).

Despite national guidelines recommending palliative care integration, uptake remains low in advanced HF patients (Adler, Goldfinger, Kalman, Park, & Meier, 2009; Gelfman, Bakitas, Warner Stevenson, Kirkpatrick, & Goldstein, 2017), especially in comparison to oncology populations (Hupcey, 2012). However, there is little guidance about timing, duration, or amount of palliative care services for this population (Yancy et al., 2013). A positive development is the increase in the number of palliative care behavioral intervention studies being reported over the last decade (Diop, Rudolph, Zimmerman, Richter, & Skarf, 2017; Payne & Turner, 2008; Walshe, 2017). However these interventions, delivered by a variety of providers, varied in dose attributes including number, timing, and duration of visits or services (Diop et al., 2017; Kavalieratos et al., 2016).

Although interventions varied in intensity, most demonstrated positive effects in patient-report outcomes such as QoL, symptom burden, anxiety and depression (mood), quality of death, and healthcare resource use (Kavalieratos et al., 2016; Rogers et al., 2017). However, these intention-to-treat analyses did not attempt to explore the relationship between intervention dose or exposure and the study outcomes. Intention-to-treat analyses compare treatment groups as allocated after randomization regardless of intervention dose, completion, or exposure (Polit & Beck, 2017; Sedgwick, 2015). By maintaining original study allocation, confounding factors are limited in intention-to-treat analyses (Polit & Beck, 2017; Sedgwick, 2015). Additionally, intention-to-treat analyses reflect real-world clinical practice as treatment adherence varies (Sedgwick, 2015). However, given this strict maintenance of intervention allocation, intention-to-treat analyses cannot reflect per-protocol/protocol-deviation treatment differences or dose differences (Gupta, 2011). Yet, many HF palliative care intervention study investigators described difficulties in recruitment, retention, and per protocol intervention completion (Bakitas et al., 2017; Bekelman et al., 2014; Kane et al., 2017; Rogers et al., 2017).

Intervention Dose in Palliative Care Research

Reviews of palliative care studies indicate small to moderate improvements in QoL, symptom burden, mood, and resource utilization (Diop et al., 2017; Dionne-Odom et al., 2017), though side-by-side comparisons of completed studies are difficult due to paucity of intervention details, such as fidelity and dosing. Although most guidelines on trial reporting recommend reporting intervention dose (Bellg et al., 2004; Craig et al., 2008; Currow, Plummer, Kutner, Samsa, & Abernethy, 2012; Hoffmann et al., 2014),

most intervention studies provided limited descriptions of the intervention or intervention dose (Candy, Vickerstaff, Jones, & King, 2018; Glasziou, Meats, Heneghan, & Shepperd, 2008; Kavalieratos et al., 2016). Similarly, Bouça-Machado et al. (2017) found limited descriptions of intervention or intervention dose in a recent review of clinical trials in palliative care.

Intervention dose, or the amount, duration, frequency, and intensity of an intervention (Voils et al., 2014), is needed for intervention evaluation, replication, and implementation (Hobfoll, Walter, & Horsey, 2008; Hoffmann et al., 2014). Definitions of these dose attributes of amount, duration, frequency, and intensity are located at the end of the chapter. While intervention-reporting guidelines exist, study reports or papers often do not include full intervention details (Candy et al., 2018). Even in studies in which positive outcomes are apparent, many participants may not have experienced the per-protocol intervention dose. Given participants' life-limiting diagnoses and therefore shortened prognosis, palliative care studies often encounter unique recruitment and retention challenges (Ammari, Hendriksen, & Rydahl-Hansen, 2015; Currow et al., 2012; Hudson, Aranda, & McMurray, 2001; LeBlanc, Lodato, Currow, & Abernethy, 2013; White, Hardy, Gilshenan, Charles, & Pinkerton, 2008). Additionally, while less is known about factors contributing to adherence or completion of an intervention in palliative care, age (Oosterom-Calo et al., 2013), comorbidity (Guzman-Clark, van Servellen, Chang, Mentes, & Hahn, 2013; Kato et al., 2009), spirituality (Alvarez et al., 2016), personal beliefs/goals (Alvarez et al., 2016; Zhang, Dindoff, Arnold, Lane, & Swartzman, 2015), anxiety/depression (Luyster, Hughes, & Gunstad, 2009), and residence (Holmes, Hughes, & Morrison, 2014) have influenced adherence in various non-palliative care HF

studies. However, these interventions have limited features in common with palliative care interventions as most HF studies focused on medication or self-care adherence. To make further progress in care of those living with serious illnesses, therefore, it is essential to report relationships among palliative care intervention dose and other factors, such as sociodemographic and clinical factors and patient-reported outcomes.

ENABLE CHF-PC Randomized Clinical Trial

The completed study detailed in Chapters 1-5 is an embedded, ancillary concurrent mixed methods study of an ongoing palliative care intervention trial, Educate, Nurture, Advise, Before Life Ends Comprehensive Heartcare for Patients and Caregivers (ENABLE CHF-PC, ClinicalTrials.gov Identifier: NCT02505425). ENABLE CHF-PC is an early palliative care randomized controlled trial (RCT) for advanced HF patients and caregivers. In the ENABLE CHF-PC study, participants were randomized to receive usual cardiac care with or without a multi-component psychoeducational intervention. This parent study has two primary aims: (1) to determine whether ENABLE CHF-PC leads to higher advanced HF patient-reported QoL and mood and lower symptom burden and resource use at 8- and 16-weeks and (2) to determine whether ENABLE CHF-PC leads to higher caregiver-reported QoL, mood, and self-reported health and lower caregiver burden at 8- and 16- weeks after baseline.

The ENABLE CHF-PC intervention consists of an in-person palliative care consultation and 6 nurse-led, phone-based palliative care sessions. Charting Your Course, a guidebook that reinforces content on problem-solving, self-care, symptom management, communication, decision-making, life review, and legacy buildling (Bakitas et al., 2017),

frames the nurse coach phone sessions. The comprehensive in-person palliative care consultation is guided by the National Consensus Project (NCP) guidelines which includes evaluations of disease understanding, decision-making preferences, goals of care, symptoms, spirituality, advance care planning, and care coordination (NCP, 2018). Although the ENABLE CHF-PC intervention was offered to all patient participants randomized to the intervention arm, almost two-thirds of enrolled patients did not complete the intervention as outlined by the protocol in terms of frequency, duration, session content, or intensity. Figure 1 details the ENABLE CHF-PC study intervention and intervention dose.

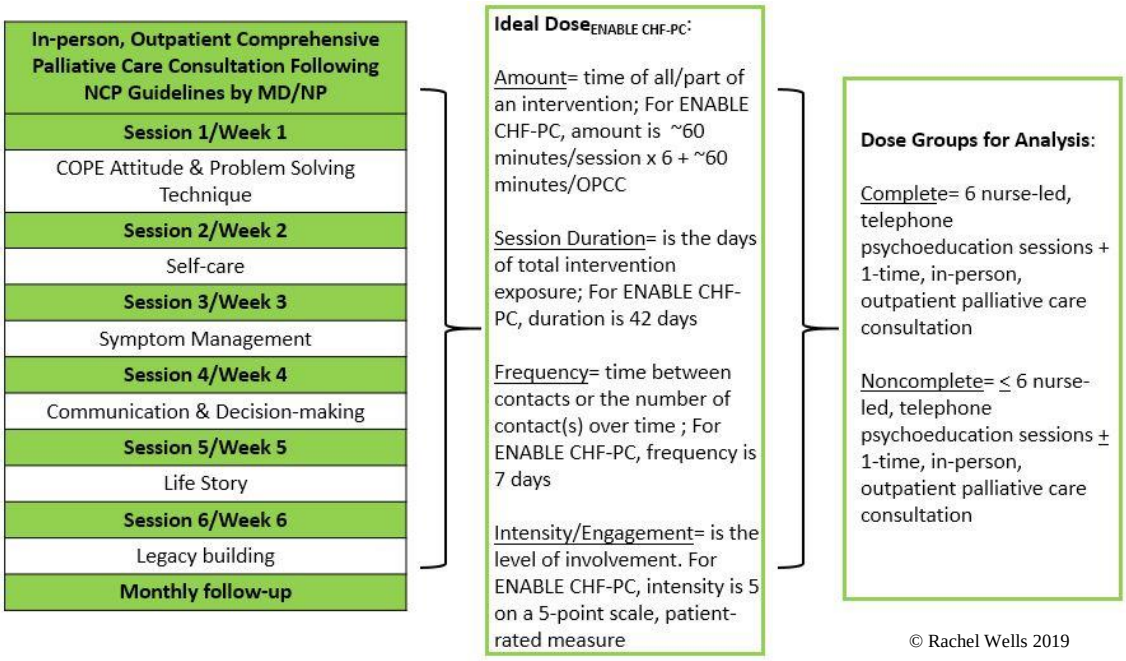


Figure 1. ENABLE CHF-PC Intervention Components. This figure illustrates intervention components and intervention dose of the ENABLE CHF-PC study.

Study Purpose

Given the lack of understanding of the relationship between palliative care dose and patient outcomes, the purpose of this study was to examine the factors that influence ENABLE CHF-PC intervention completion and dose-related intervention effects on patient-reported QoL and resource use outcomes. To address this purpose, we conducted an embedded, exploratory concurrent mixed methods study with three primary aims and one integrated aim. First, using linear mixed models, we examined relationships between dose, measured dichotomously as "complete" versus "noncomplete" for all intervention components (Figure 1), and patient-reported outcomes. Second, using bivariate tests of association and logistical regression, we examined relationships between sociodemographic/clinical characteristics and intervention dose attributes and completion. Third, concurrent with these quantitative analyses, we conducted semi-structured interviews with willing and available study participants exploring their experience with the intervention and their perspectives on dose attributes. Fourth, qualitative and quantitative outcomes were integrated using matrix diagrams to examine fully the relationship between dose and patient outcomes.

Study Aims

The specific aims of this study were:

Specific Aim #1: Determine the relationship between ENABLE CHF-PC dichotomous intervention dose and patient-reported QoL and healthcare resource use at 16- and 32-weeks after baseline.

Specific Aim #2: Determine the relationship between ENABLE CHF-PC patient characteristics (age, residence, comorbidities, HF disease severity) and intervention dose attributes and completion.

a. Determine the relationships between age, comorbidities, and HF disease severity and dose attributes of amount and frequency.
b. Determine the relationships between residence and HF disease severity and intervention completion.

Specific Aim #3: Explore ENABLE CHF-PC patients' experiences with the intervention components, intervention dose (amount, duration, frequency, intensity), and their perspectives on the intervention effects on patient-reported outcomes and trial participation in general.

Specific Aim #4 (Integrated Mixed Methods): Determine the intersection of participant intervention dose experiences with key sociodemographic, clinical, and intervention dose variables and how this intersection jointly explains the overall uptake of the ENABLE CHF-PC intervention in Deep South advanced HF patients.

Study Design and Methods

Setting

The study was an exploratory analysis of intervention dose and outcome data from the longitudinal RCT of a multi-component psychoeducational palliative care intervention for advanced HF patients and caregivers located in the Deep South, the ENABLE CHF-PC study. Recruiters approached patients and caregivers from two health care systems: (1) the University of Alabama at Birmingham Health System (UAB) and (2) the Birmingham Veterans Affairs Medical Center (BVAMC).

Recruitment and Sample

At UAB, community-based recruiters approached eligible patient participants in the outpatient cardiology clinic and an HF clinic for underinsured patients within UAB Hospital. At BVAMC, recruiters approached eligible patient participants at their outpatient cardiology clinics. The Recruitment and Retention Shared Facility (RRSF), housed within the Division of Preventive Medicine at the University of Alabama at Birmingham (UAB, n.d.) recruited all study participants. Although the parent study includes both patients and caregivers, this study only examined dose effects in patient participants. Patient inclusion criteria were: (1) New York Heart Association class III-IV or equivalent HF, (2) 50 years of age or older, (3) English speaking, and (4) reliable telephone access (Wells et al., 2018). An additional inclusion criterion for the study included participation in the ENABLE CHF-PC intervention arm. Exclusion criteria were: (1) heart transplantation or mechanical circulatory assist device, (2) active DSM-IV Axis I diagnosis (e.g. schizophrenia or bipolar disorder) excluding major depression or generalized anxiety disorder, (3) non-correctable hearing loss, and (4) dementia or significant confusion (measured by ≤3 Callahan score [Callahan, Unverzagt, Hui, Perkins, & Hendrie, 2002]) (Wells et al., 2018). The study did not use any additional exclusion criterion. All patient participants randomized to receive the ENABLE CHF-PC intervention were included in the quantitative analyses. For the qualitative strand, we attempted to interview all patient participants randomized to receive the intervention who were available for contact.

Design

This study used a mixed methods design to explore intervention dose in this study. The mixed methods research paradigm, which integrates quantitative and qualitative methods (Plano Clark & Ivankova, 2016), has become more common in palliative care (Wallen & Berger, 2004) and cardiovascular disease research (Campbell et al., 2017; Curry, Nasembhard, & Bradley, 2009). Common rationales for utilizing mixed methods in palliative care and cardiovascular research are validation, complementarity, and triangulation. In this study, a mixed methods design offsets the weaknesses of a mono-method approach. For example, a traditional quantitative analysis of dose (Tran et al., 2012) might examine the effect of the ENABLE CHF-PC intervention on patient-reported outcome measures but would not capture why participants received different intervention doses. Additionally, given the lack of dose literature in palliative care, understanding palliative behavioral intervention dose is a primary priority. By using mixed methods, a more complete understanding may be reached through complementarity as each strand enhances and clarifies palliative care intervention dose impact.

In an embedded, concurrent mixed methods design, the quantitative and qualitative strands occur simultaneously with equal or unequal priority (Plano Clark & Ivankova, 2016). For this study, given the aim for a more comprehensive understanding of dose effect, the quantitative and qualitative strands were equal. Relationships between patient-reported outcome measures from the parent ENABLE CHF-PC study and intervention completion, dose attributes, and dose were examined using bivariate analyses, logistic regression, and linear mixed models (Specific Aim #1), bivariate

analyses, and logistic regression (Specific Aim #2). In the qualitative strand, we conducted semi-structured interviews with ENABLE CHF-PC participants and analyzed the verbatim interview transcripts using a constant comparison approach (Glaser & Strauss, 1967; Lincoln & Guba, 1985; O'Connor et al., 2008). The aim of the qualitative strand was to explore patient perspectives on intervention experience including facilitators and barriers to intervention completion and their perspectives on intervention outcomes and different intervention components (Specific Aim #3). After separate analyses of the quantitative and qualitative data, we integrated the results during the interpretation phase through matrix diagrams (Specific Aim #4-Integrated Aim). The joint displays, matrix diagrams, facilitated triangulation and complementarity with side-by-side comparison of results for convergence and divergence (O'Cathain, Murphy, & Nicholl, 2010) in factors associated with intervention completion and dose effects.

Quantitative Strand Data

Quantitative data included the following patient-reported outcome measures collected as part of the parent ENABLE CHF-PC study: (1) Kansas City Cardiomyopathy Questionnaire and (2) Investigator-developed healthcare resource use questions.

Qualitative Strand Data

The qualitative strand of this study used a naturalistic approach, which emphasizes multiple context-specific realities rather than a single objective reality (Sandelowski, 2010). The assumption of multiple realities supports the potential for varying participant perspectives of dose and intervention dose experience during the

qualitative strand. Qualitative data collection included 30-40 minute semi-structured interviews conducted by telephone with ENABLE CHF-PC intervention patient participants. While data saturation was reached at 22 participants, we completed 45 interviews to reflect all possible dose levels. We stratified the patient participants into complete and noncomplete dose groups for analysis to ensure adequate representation of varying experiences with intervention dose and to facilitate comparison.

Data Analysis

We performed the quantitative analyses using R statistical software version 3.5.0 and R studio, an integrated development environment (The R Project, 2019). Prior to analysis, we created data labels and data dictionary. We also inspected the dataset for outliers. Then, we inspected the data for missingness and used multiple strategies to address missingness as needed for different analyses (Young & Johnson, 2015). We also assessed normality and heterogeneity of the dataset to determine which statistical test to perform for each planned analysis. Next, we completed all necessary variable recoding, scaling for outcome scores, and new variable creation (i.e., dichotomous dose variable, amount, frequency, and duration). After preparing the data, principal analyses included descriptive statistics, correlation, odd ratios, *t*-tests, chi-square tests, and linear mixed modeling. We reported effect sizes and *p*-values where appropriate.

We performed qualitative analyses using a constant comparative process, a common method used in descriptive qualitative studies (Kim, Sefcik, & Bradway, 2016). Constant comparative analysis aids in concept or relationship clarification, such as intervention dose, through initial cross-case comparison of inductive coding, resulting in

themes that are constantly refined throughout data collection and analysis (Goetz & LeCompte, 1981). We coded and analyzed verbatim transcripts of the semi-structured interviews using QSR NVivo 11 ©.

Definition of Terms

In the following section, we define common terms used in the study.

Amount is the length of time of a single instance of an intervention or part of an intervention

Amount $_{ENABLE\ CHF\text{-}PC}$ is 60 minutes per weekly nurse-led, telephone psychoeducational intervention session.

Behavioral psychoeducational intervention is an actions or set of actions delivered to participants designed to influence certain behaviors (Lukens & McFarlane, 2004).

Charting Your Course 'CYC' guidebook- A booklet developed for the ENABLE CHF-PC randomized controlled trial including sections divided by session content. Content in the CYC guidebook reflects content delivered and discussed by nurse coaches.

Complete Dose $_{ENABLE\ CHF\text{-}PC}$ reflects completion of all ENABLE CHF-PC intervention components: 6 nurse-led, telephone psychoeducational sessions and an in-person outpatient palliative care consultation.

Deep South is a region of the Southeastern United States including the states of Georgia, Alabama, South Carolina, Louisiana, Mississippi, and parts of the Northwest panhandle of Florida. (Fryer, n.d.).

Dose. See Intervention dose. Alternative and related terms may include "exposure'"or "adherence"(Washington et al., 2014).

Dose attributes are amount, duration, frequency, and intensity. See Amount, Duration, Frequency, and Intensity.

Dose $_{ENABLE\ CHF\text{-}PC}$ is a dichotomous variable used for analysis with "complete" and "noncomplete" as possible categories. See Complete dose and Noncomplete dose.

Dose effect refers to the change in outcome response in relation to a change in "dose" provided. An alternative or related term is dose response (pattern of response to varied dosage).

Duration is the length of time of total intervention exposure, similar to range (Voils et al., 2014). Duration may reflect study duration or intervention duration.

Duration $_{ENABLE\ CHF\text{-}PC}$ is 42 days of intervention, focused on the Charting Your Course guided, nurse-led telephone psychoeducational sessions and in-person, outpatient palliative care consultation.

Early palliative care is palliative care provided close to the onset of disease diagnosis (Howie & Peppercorn, 2013).

ENABLE CHF-PC intervention is an early palliative care intervention used in the National Institute of Nursing Research-funded randomized controlled clinical trial, ENABLE CHF-PC. The intervention consists of an in-person outpatient palliative care consultation for advanced heart failure patients and 6- (for patients) or 4- (for caregivers) nurse-led, telephone based psychoeducational sessions with monthly follow-up for the rest of the study. Also see Early palliative care, Behavioral psychoeducational intervention, Complete dose $_{ENABLE\ CHF\text{-}PC}$, and Noncomplete dose $_{ENABLE\ CHF\text{-}PC}$.

Family caregiver is someone identified by a patient as a family member or friend who helps with their medical or home needs (Bakitas et al., 2017).

Frequency is the length of time between contacts or the number of contacts over time (Voils et al., 2014).

Frequency $_{ENABLE\ CHF\text{-}PC}$ is the 7 days between successful phone contacts for Charting Your Course intervention sessions by nurse coach.

Intensity/Engagement is the level of interventionist and participant involvement (Collins, Murphy, & Strecher, 2007; Lei, Nahum-Shani, Lynch, Oslin, & Murphy, 2012; Svetkey et al., 2015).

Intensity $_{ENABLE\ CHF\text{-}PC}$ is participant description of their interaction during the course of the study. Patients were asked during the semi-structured interview to rate their engagement from 1-5 with '5' representing the highest possible engagement.

Intervention dose is overall exposure to a behavioral intervention. Dose attributes include amount, duration, frequency, and intensity (Voils et al., 2014).

Healthcare resource use is the amount of resources to create a specific healthcare product, such as a clinic visit (Agency for Healthcare Research and Quality (AHRQ), n.d.).

Healthcare resource use $_{ENABLE\ CHF\text{-}PC}$ is measured by four investigator-developed questions querying about hospital visits, hospital days, ICU days, and Emergency Department (ED) visits over the previous 8 weeks.

Mood is an individual's mental and/or emotional state and includes assessments of anxiety and depressive symptoms (U.S. Department of Health & Human Services, 2017).

Mood $_{ENABLE\ CHF\text{-}PC}$ is measured by the Hospital Anxiety and Depression Scale (HADS).

Heart failure severity is the severity classification based on presence of symptoms or physical activity limitations (Class I-IV) (AHA, 2018) or disease progression and structural alterations (Stage A-D) (Yancy et al., 2013).

Noncomplete dose $_{ENABLE\ CHF\text{-}PC}$ reflects completion of part of the ENABLE CHF-PC intervention components; either $\leq$ 6 nurse-led, telephone psychoeducational sessions and/or an in-person outpatient palliative care consultation.

Psychoeducational intervention is a type of behavioral intervention that focuses on information transfer, which is often disease-specific, within an effective therapeutic framework (Holm, et al., 2015).

Quality of Life (QoL) is the sum of patient-determined multi-factored daily living experience (Getpalliativecare.org, 2012).

Quality of Life $_{ENABLE\ CHF\text{-}PC}$ is measured by the Kansas City Cardiomyopathy Questionnaire (KCCQ).

Study duration $_{ENABLE\ CHF\text{-}PC}$ is 48 weeks of study participation.

Symptom burden is the patient-determined physiological burden related to a disease process (Gapstur, 2007).

Symptom burden $_{ENABLE\ CHF\text{-}PC}$ is the experience of the patient with physical, psychosocial, social, or spiritual symptoms or suffering and is measured by the Functional Assessment of Chronic Illness Therapy- Palliative Care (FACIT-Pal) Symptom Subscale score and the Patient-Reported Outcomes Measurement (PROMIS) Pain Intensity and Interference items.

Summary

Over 6.5 million U.S. adults are living with HF and HF-associated symptom burden, poor QoL, decreased mood, and high healthcare resource use. Although palliative care intervention studies demonstrate improved patient-reported outcomes and resource use, intervention designs vary between studies and no reported palliative care HF studies have examined intervention dose effects. Given the clinical and research implications, we aimed to explore the relationship between dose and patient-reported outcomes in the study. This chapter provided a brief review of the significance, background, conceptual model, study design, and methods of the embedded mixed methods dose study.

CHAPTER TWO

Introduction

The aim of Chapter 2 is to understand and review the current state of knowledge of palliative care for heart failure patients and its application to the concurrent mixed methods dose analysis study.

This chapter includes: (1) epidemiology of heart failure, (2) background of concepts of interest in relation to heart failure, (3) the Chronic Care Model and Conceptual Framework of Implementation Fidelity as guiding conceptual frameworks, (4) palliative care intervention literature search strategy, (5) synthesis of palliative care intervention-related literature, (6) overview of mixed methods study design and methods, and (7) ethical issues related to the palliative care and heart failure population.

Heart Failure Epidemiologic Basis and Concepts of Interest

Heart failure is a chronic, progressive condition resulting from inability of the heart to sufficiently sustain enough blood flow for metabolic demands and adequately accommodate systemic venous return (Yancy et al., 2013a). The possible etiologies of heart failure are numerous including ischemic heart disease, coronary artery disease, hypertension, diabetes, cardiomyopathy, valvular disease, myocarditis, congenital heart malformations, heart rhythm disorders, or cardiotoxic medication (Kovacs, Papp, & Nagy, 2014). After cardiac injury with resultant loss of cardiac output or the blood volume effectively expelled from the left ventricle, the heart undergoes structural, neurohumoral, cellular, and molecular changes to maintain function (Borlaug & Paulus,

2011). However, these body-wide changes result in cycle of blood volume overload, increased sympathetic activity, and myocyte remodeling (Dharmarajan & Rich, 2017). Regardless of whether this cyclical progression results in cardiac dilatation or stiffening, the pumping ability of the heart is further compromised and results in worsening heart failure.

Of those diagnosed with heart failure, approximately half are diagnosed with heart failure with preserved ejection fraction and the other half have heart failure with reduced ejection fraction (Borlaug & Paulus, 2011). Ejection fraction is the percentage of blood that leaves the left ventricle during contraction. The term of heart failure with preserved ejection fraction replaced the term, 'diastolic heart failure' whereas heart failure with reduced ejection fraction replaced 'systolic heart failure.' (Borlaug & Paulus, 2011). The use of preserved or reduced ejection fraction implies an agreed upon value for normal ejection fraction, however, there is not a consensus of the percentage value for normal, preserved, or reduced ejection fraction (Borlaug & Paulus, 2011). In general, reduced ejection fraction refers to a pumping percentage of less than 40% and preserved ejection fraction refers to a pumping percentage above 50% (Borlaug & Paulus, 2011). While there are no significant survival and symptom differences between heart failure with and without preserved ejection fraction, heart failure with preserved ejection fraction occurs more frequently in older women and patients with hypertension (Abebe, Gebreyohannes, Tefera, & Abegaz, 2016).

Heart Failure Prevalence

Over 6.5 million adults in the United States are living with heart failure (Benjamin et al., 2019) with an expected increase to over 8 million adults or 1 out of every 33 adults by 2030 (Heidenreich et al., 2013). There are 1,000,000 new cases of heart failure diagnosed annually (Benjamin et al., 2019) with incidence rates increasing with age. By the age of 65 or older, 21 out of every 1000 adults will be diagnosed with heart failure (Huffman et al., 2013). Heart failure disproportionately affects minority populations with African Americans experiencing the highest risk, 4.6 per 1000 person-years, as opposed to Chinese Americans experiencing the lowest risk, 1.0 per 1000 person-years (Bahrami, Kronmal, Bluemke, & et al., 2008). African Americans are also more likely to be diagnosed with heart failure before the age of 50 and without an incident myocardial infarction (Bibbins-Domingo et al., 2009). Other heart-failure related risks include age, gender, hypertension, obesity, smoking, and lifestyle choices such as elevated sodium intake (Huffman et al., 2013). These risk factors also represent a trend in newly-diagnosed heart failure patients of growing complexity, comorbidities, and advanced age (Benjamin et al., 2019).

The rate of heart failure attributable death has grown since 2002 by 27.7% with any-mention heart failure mortality found in 1 in every 8 deaths (Benjamin et al., 2019). Additionally, 5-year mortality rates post new heart failure diagnosis remains steady with half of newly-diagnosed heart failure patients dying within the first 5 years (Gerber, Weston, Redfield, & et al., 2015).

Heart Failure Healthcare Resource Use and Cost

Heart failure is a top-cause hospitalization in adults (Desai & Stevenson, 2012), accounting for 900,000 hospitalizations as the primary discharge diagnosis in 2014 (Benjamin et al., 2019). The number of heart failure associated hospitalization balloons to over 4 million annually when including heart failure as a secondary diagnosis (Blecker, Paul, Taksler, Ogedegbe, & Katz, 2013). In addition to hospitalizations, 2,370,000 provider visits and 459,000 emergency department visits listed heart failure as a primary diagnosis in 2014 (Benjamin et al., 2019).

In 2012, the total cost of heart failure related healthcare for the year 2010 was estimated to be $30.7 billion annually (Heidenreich et al., 2013). Given growing number of U.S. adults living with heart failure, healthcare costs are expected to exceed $69 billion annually by 2030 (Benjamin et al., 2019). In addition to patient-associated healthcare cost, there are employment and opportunity costs to family caregivers of heart failure patients. Family caregivers, or close family and friends who are not paid for professional caregiving, provide a mean of 1.95 hours of care weekly related to heart failure with higher care hour means provided by caregivers caring for minority populations (Dunbar et al., 2018). Without accounting for opportunity cost, the total cost of family caregiving hours attributed to heart failure was $6.5 billion annually (Dunbar et al., 2018). Consistent with the anticipated increase of people living with heart failure and their associated healthcare cost, informal caregiving cost related to heart failure is estimated to exceed $13 billion by 2035 (Dunbar et al., 2018).

Clinical Manifestations and Classifications of Heart Failure

Heart failure is a clinical syndrome without a single definitive test confirming the presence of heart failure. Frequently, clinicians diagnose heart failure based off the presence of symptoms in conjunction with diagnostics tests demonstrating the structural and functional changes of the heart. The classic physical symptoms of heart failure include dyspnea, fatigue, and fluid retention.

The two leading classifications for heart failure include the New York Heart Association (NYHA) Functional Classification and the American Heart Association/American College of Cardiology (AHA/ACC) Stages of Heart Failure (AHA, 2018). The NYHA classifications use physical and functional symptoms to determine the heart failure severity. In Class I, patients experience no functional limitation or fatigue, palpitations, or dyspnea with ordinary activity (AHA, 2018). With Class II, patients experience some limitations with physical activity in addition to slight fatigue, dyspnea, or palpitations (AHA, 2018). Class III and IV are characterized by severe physical limitations with dyspnea, fatigue, and palpitation with less than ordinary activity (AHA, 2018). With treatment optimization, patients may move within NYHA classes. However, classification to an earlier AHA/ACC stage is not possible. AHA/ACC staging focuses on structural and functional changes in the heart (AHA, 2018). In Stage A, patients are at risk for heart failure but have no structural changes. For example, some risks associated with Stage A classification include hypertension, diabetes, or coronary artery disease. In Stage B, patients have structural changes such as reduced ejection fraction or hypertrophy without heart failure symptoms (AHA, 2018). If heart failure symptoms develop in conjunction with the structural changes, the patient has Stage C

heart failure (AHA, 2018). The last stage, Stage D, includes patients with refractory heart failure who require more interventions such as inotropes, mechanical circulatory assist devices, or heart transplantation (AHA, 2018).

Symptom Burden in Heart Failure

Although many definitions of symptom burden exist, symptom burden is commonly operationalized as the experience of the patient with physical, psychosocial, social, or spiritual symptoms or suffering (Alpert, Smith, Hummel, & Hummel, 2017; Gill, Chakraborty, & Selby, 2012). Symptom burden may include the influence of specific symptom prevalence, frequency, and severity on the experience of living with an illness (Gapstur, 2007). Heart failure patients frequently experience multiple symptoms with studies reporting a range of 7-19 patient-reported symptoms (Bekelman et al., 2007; Blinderman, Homel, Billings, Portenoy, & Tennstedt, 2008; Ekman, Cleland, Andersson, & Swedberg, 2005; Lokker et al., 2016; Zambroski, Moser, Bhat, & Ziegler, 2005). In addition to multiple symptoms present from the point of diagnosis, heart failure patients also experience an exponential symptom increase near the end of life (Evangelista et al., 2012).

Multiple studies found the number of symptoms and symptom burden experienced by heart failure patients to be significantly higher than those experienced by patients with cancer or other progressive, chronic conditions (Bekelman et al., 2007; Bekelman et al., 2009; Solano, Gomes, & Higginson, 2006). This high symptom burden has ramifications on the day-to-day living with advanced HF. For example, symptom burden influences healthcare decisions (Stanek, Oates, McGhan, Denofrio, & Loh, 2000),

and is associated with adverse cardiac events (Lee et al., 2014), hospitalization (Ekman, Cleland, Swedberg, et al., 2005), healthcare resource use (Patel, Shafazand, Schaufelberger, & Ekman, 2007; Shafazand, Patel, Ekman, Swedberg, & Schaufelberger, 2012), and mortality (Ekman, Cleland, Swedberg, et al., 2005).

Anxiety and Depressive Symptoms in Heart Failure

Anxiety includes feelings of restlessness, difficulty concentrating, fatigue, or irritability (NIMH, 2016). Depressive symptoms includes feelings of sadness, hopelessness, irritability, or guilt in addition to anhedonia, fatigue, appetite or weight change (NIMH, 2018). Blindermen et al. (2008) reported over 40% of hospitalized heart failure patients experienced feelings of anxiety or worry and similar rates of feelings of depressive symptoms or sadness (2008). Friedmann et al. (2006) and Bekelman et al. (2007) reported similar rates of anxiety and depressive symptoms in outpatient heart failure populations.

Anxiety and depressive symptoms predict physical functioning (Shen et al., 2011), hospitalization (Ramos, Prata, Bettencourt, Goncalves, & Coelho, 2016), mortality (Ramos et al., 2016) in heart failure patients. Higher levels of depressive symptoms in heart failure patients are associated with lower medication adherence and other preventative health behaviors (Bauer et al., 2012) whereas higher levels of both anxiety and depressive symptoms are also associated with lower dietary adherence (Luyster, Hughes, & Gunstad, 2009).

Quality of Life in Heart Failure

QoL or health-related QoL refers to the sum of patient-determined multi-factored daily living experience (Dunderdale, Thompson, Beer, Furze, & Miles, 2008; S. Heo, Lennie, Okoli, & Moser, 2009; Seongkum Heo, Moser, Riegel, Hall, & Christman, 2005). QoL may include elements of physical, social, psychological, spiritual, and financial health (Heo et al., 2005). As heart failure progresses, patients experience worsening QoL (Alpert, Smith, Hummel, & Hummel, 2017; Gadoud, Jenkins, & Hogg, 2013). In comparison to other chronic illness, heart failure patients experience lower QoL, often from the point of diagnosis (Bekelman et al., 2009; Juenger et al., 2002). QoL independently predicts HF-related hospitalizations and mortality (Konstam et al., 1996).

Health-related QoL is associated with gender, social support, age, and sleep quality. HF failure patients who are older, female, with poor social support, or poor sleep quality experience lower QoL (Heo, Moser, & Widener, 2007; Johansson, Dahlström, & Broström, 2006). Self-reported QoL is associated with physical function and physical symptoms in women (Heo, Moser, & Widener, 2007). In contrast, QoL in men is more likely to be associated with depressive symptoms (Heo et al., 2007).

Heart Failure Treatment Guidelines

Since 1995, the AHA and the ACC have jointly published guidelines concerning the evaluation and management of heart failure. Starting in 2001, the HFSA and the International Society of Heart and Lung Transplantation have either jointly developed or endorsed the AHA/ACC guidelines. The most recent guideline was published in 2013

(Yancy et al., 2013a) with a pharmaceutical update in 2016 (Yancy et al., 2016) and a focused update in 2017 (Yancy et al., 2017).

Evidence-based treatment for Stage A includes lifestyle modification such as exercise and restriction of dietary sodium to less than 2000 milligrams daily (Yancy et al., 2013a). Additionally, patients diagnosed with Stage A heart failure may also start blood pressure lowering medications such as an angiotensin II-receptor blocker (ARB) or an angiotensin-converting enzyme inhibitor (ACEI) in addition to a statin to lower cholesterol (Yancy et al., 2016). For patients diagnosed with Stage B heart failure, a beta blocker may be introduced in addition to the statins and ARBs or ACEI. Depending on the structural and functional changes, a Stage B patient might receive an implantable cardioverter defibrillator (Yancy et al., 2017). In Stage C heart failure patients, diuretics may be added to the previous medications to help with fluid retention (Yancy et al., 2016). In Stage D patients, inotropes, mechanical circulatory assist devices, and heart transplantation are considered to treat refractory heart failure (Yancy et al., 2017). In addition to pharmaceutical and surgical treatment, palliative care is recommended for Stage D heart failure patients (Yancy et al., 2013; Yancy et al., 2017).

In the 2001 ACC/AHA heart failure guidelines, chronic inotrope infusion was recommended with the lowest level of support for palliation at the end of life (Hunt et al., 2001). However, in the 2009 update, the recommendation of palliative care extended beyond pharmaceutical management of symptoms to include palliative care services to address goals of care, refractory symptom management, and end of life planning (Jessup et al., 2009). Currently, the ACC/AHA/HFSA guidelines recommend palliative care integration into heart failure care (Yancy et al., 2013).

Palliative Care

Palliative care is a healthcare approach focused improving QoL and relieving suffering of those living with serious illness (World Health Organization [WHO], n.d.). Palliative care may be delivered throughout the illness trajectory and may occur concurrently with curative treatment (WHO, n.d.). Palliative care addresses patient and family distress related to physical, intellectual, emotional, social, and spiritual symptoms while maintaining patients' autonomy and choice (NCP, 2018). In 2001, national palliative care experts representing major palliative care organizations met to develop guidelines to standardize palliative care practices (NCP, 2018). These guidelines, known as the National Consensus Project for Quality Palliative Care, were revised in 2009 and 2013, and 2018 (NCP, 2018). The NCP guidelines identify the following 8 domains of care for comprehensive palliative care: structure and process, physical, psychological, social, spiritual, cultural, ethical, and end of life care.

Primary palliative care can be provided by any provider and focuses on basic pain and symptom management (Ahia & Blais, 2014; McCormick, Chai, & Meier, 2012) whereas specialty palliative care is provided by palliative care trained providers who focus on management of refractory symptoms, complex distress, and conflict resolution between patients, families, and other providers (Quill & Abernethy, 2013). Palliative care is delivered in a variety of settings including inpatient consultation services, dedicated inpatient palliative care units, patients' homes, outpatient clinics, or nursing homes (Quill & Abernethy, 2013). Although national guidelines recommend palliative care services as part of advanced heart failure patients (Allen et al., 2012; Fang et al., 2015; Feldman et al., 2013; Yancy et al., 2013), uptake of palliative care remains low in this population

(Adler, Goldfinger, Kalman, Park, & Meier, 2009; Gelfman, Bakitas, Warner Stevenson, Kirkpatrick, & Goldstein, 2017) and late (Bakitas et al., 2013; Kavalieratos et al., 2014).

ENABLE CHF-PC Early Palliative Care Randomized Clinical Trial

Like the low and slow utilization of palliative care in heart failure populations, palliative care research in heart failure is limited and only recently moved from observational to experimental studies (Gelfman, Du, & Morrison, 2013; Xie, Gelfman, Horton, & Goldstein, 2017). The ENABLE CHF-PC (Educate, Nurture, Advise Before Life Ends Comprehensive Heartcare for Patients and Caregivers ,ClinicalTrials.gov Identifier: NCT02505425), is an ongoing, National Institute of Nursing Research funded, early palliative care randomized controlled clinical trial for advanced heart failure patients and caregivers. Previously, we identified the ENABLE CHF-PC study as the parent study for the intervention dose effect study.

In the study, participants were randomized to receive a multi-component psychoeducational intervention or usual heart failure care. The ENABLE CHF-PC patient intervention consists 6 hour-long telephone-based, nurse-led palliative care sessions and a single, in-person palliative care consultation. The telephone sessions include content on problem solving, self-care, symptom management, medical decision making, legacy building, and life review (Wells et al., 2018). The comprehensive in-person palliative care consultation is guided by the NCP guidelines (NCP, 2018). All patient participants randomized to the intervention arm are offered the per protocol intervention as described previously.

The aims of the ENABLE CHF-PC study are: (1) to determine whether ENABLE CHF-PC leads to higher advanced heart failure patient-reported QoL and mood and lower symptom burden and resource use at 8- and 16-weeks and (2) to determine whether ENABLE CHF-PC leads to higher caregiver-reported QoL, mood, and self-reported health and lower caregiver burden at 8- and 16- weeks after baseline.

Conceptual Model

To explore the relationships between the concepts of interest, including dose and patient-reported outcomes, the Chronic Care Model (CCM) (Wagner et al., 2001; Wagner, Austin, & Von Korff, 1996) was used as a primary theoretical framework to identify proposed linkages between concepts. Additionally, the CCM was combined with the Conceptual Framework for Implementation Fidelity (Carroll et al., 2007; Hasson, 2010; Hasson et al., 2012) to more fully explore relationships between intervention dose and outcomes.

Chronic Care Model

Chronic illnesses such as heart failure, cancer, chronic obstructive lung disease, and diabetes, affects more than 140 million individuals in the United States (Buttorff, Ruder, & Bauman, 2017) with approximately a quarter of these individuals experiencing more than one chronic illness (Center for Disease Control and Prevention, 2018; Center for Disease Control and Prevention, 2019). Care for those with chronic illness is complex and requires frequent and collaborative healthcare services (Wagner, Austin, & Von Korff, 1996). However, the healthcare system in the U.S. prior to the mid-1990s was

designed as an acute care model with care coordination and collaboration uncommon (Wagner, Austin, & Von Korff, 1996). This acute care model focused on the immediate healthcare needs (Iyer, Reeves, Varadarajan, & Alessandrini, 2011), often related to a single illness or injury, with limited follow-up, collaboration, and preventive or disease management care.

Given the discrepancy between the needs of patients with chronic illness and the acute-care focused healthcare system, Wagner et al. (1996) developed the CCM to transform care for chronic illness. Figure 2 is a depiction of the CCM with ENABLE CHF-PC intervention components.

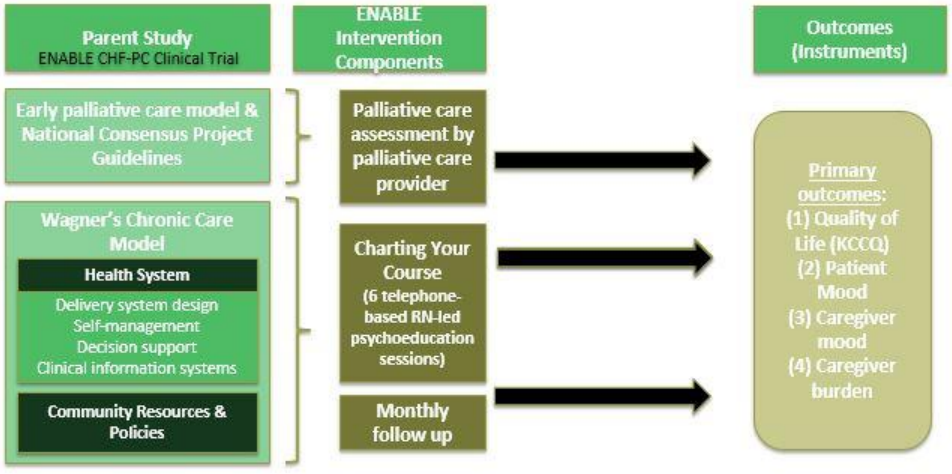


Figure 2. Chronic Care Model Applied to ENABLE CHF-PC. ENABLE CHF-PC= Educate, Nurture, Advise Before Life Ends Comprehensive Heartcare for Patients and Caregivers; RN=Registered Nurse; KCCQ=Kansas City Cardiomyopathy Questionnaire. This figure illustrates concepts presented in the Chronic Care Model.

The CCM depicts system-wide change by examining the relationships between two key areas that impact chronic illness care: (1) the health system and (2) the community (Wagner et al., 2001; Wagner et al., 1996). Ideally, the motivated, activated

patient and proactive, informed healthcare providers along with the health system and community interact together resulting in a productive interaction that leads to improved chronic care outcomes, such as better symptom control or improved health related QoL (Wagner et al., 2001; Wagner et al., 1996). Activated patients actively participate in healthcare addressing their chronic illness needs in collaboration with proactive provider team (Wagner et al., 2001; Wagner et al., 1996).

The CCM identifies the following potential areas for improvement leading to better outcomes, for community, resources and policies and for the health system, self-management support, delivery system design, decision support, and clinical information systems (Wagner et al., 2001). These areas of improvement are frequently depicted as nested ovals with a larger community oval with resources and policies and a nested smaller health system oval housing the areas of self-management support, delivery system, decision support, and clinical information systems (Institute for Healthcare Improvement [IHI], 2017).

Community

Community refers to the use of community resources, including programs or interventions, to meet patient needs (IHI, 2017). By accessing existing community-based resources, healthcare systems expand the breadth of services provided without duplicating effort (IHI, 2017).

Policies. Policies refer to national, state, and local regulations that address management of chronic illness care (IHI, 2017). Actions related to policies include advocacy and lobbying.

Resources. Resources are the materials, staff, or strategies located within a specific community (IHI, 2017). Resources may include other primary care providers, navigators, transportation systems, or senior centers. Resources may also include materials development by organizations such as the AHA or the HFSA.

The Health System

Health system is commonly defined as the organization or policies that address management of chronic diseases, such as development of lay navigator programs or the ENABLE CHF-PC study (Wagner et al., 2001; Wagner et al., 1996). With management of chronic illness, the organization of the health system includes recognition that comprehensive institutional change provides the foundation for effective care delivery (Wagner et al., 2001; Wagner et al., 1996). Collaboration across the institution is an important element in the health system and require participation from all providers from senior leadership to bedside clinicians (IHI, 2017).

Self-management support. Self-management support refers to dissemination of disease-specific knowledge and usually focuses on the patient whereas decision support refers to the use of evidence-based clinical practice guidelines, which focuses on providers (IHI, 2017).The self-management area of the CCM includes: 1) activities that

promote health; 2) interactions with healthcare providers and adherence to treatment recommendations; 3) self-assessment with medical decision making; and 4) managing the chronic illness to optimize QoL and activities of daily living (Wagner et al., 2001; Wagner et al., 1996). Self-management support includes collaborative care between the community, healthcare system, provider organizations, providers, and patients (Wagner et al., 2001; Wagner et al., 1996).

Delivery system design. Delivery system design is a team-based concept of role delineation as well as system-wide communication of the individual-patient plan (IHI, 2017). The configuration of healthcare delivery in the CCM results in the creation of prepared, proactive practice teams. The system or practice teams providing treatment are considered 'proactive' by providing evidenced-based care that shifts the focus from acute to chronic illness care, such as palliative care (Wagner et al., 2001; Wagner et al., 1996).

Decision support. Decision support refers to the use of evidence-based clinical practice guidelines, which focuses on providers (IHI, 2017).

Clinical information systems. Clinical information systems, a mode of clinical communication, can be registries, study databases, or electronic health records (Hroscikoski et al., 2006).

Relationships in the CCM

As previous indicated, these areas of improvement interact with no arrows to address directional relationships among these concepts (Wagner et al., 2001; Wagner et al., 1996). The areas for improvement influence the bracketed arrow labeled productive interactions between patients and healthcare providers (IHI, 2017; Wagner et al., 2001). A double-sided arrow between activated patients and the prepared, proactive practice team crosses through the productive interaction arrow which indicates a relationship between the patients and providers in the productive interaction with the community and health system (IHI, 2017). The productive interactions lead to improved patient outcomes such as reduced hospitalizations or improved QoL (IHI, 2017).

CCM within the Study

The CCM proposed by Wagner, was used as a guiding model for this study. The utility of the CCM is three-fold. First, the CCM informed the development of the ENABLE intervention (Bakitas et al., 2009; Dionne-Odom et al., 2014). With the parent study, the investigators use the CCM to examine potential mechanisms of reported improvement in palliative care studies (Wells et al., 2018). Specifically, the ENABLE CHF-PC parent study hypothesizes that the intervention may affect patients through the adoption of behaviors including activation, goal setting, problem solving, coordination, and decision support, which act as proximal mediators of the intervention resulting improved patient, reported outcomes (Wells et al., 2018). The study examined dose and patient outcome relationships aligned closely with both the parent study's aims and conceptual framework. Second, the fluid dynamic of the CCM and the representation of

multiple concepts of interest, including interactions or interventions, patients, providers, and outcomes, fit an exploratory analysis of dose. As little is known about palliative care intervention dose, a guiding framework that explores potential relationships should depict multiple areas of potential interaction. Third, the CCM is common in palliative care (Allen et al., 2012; Bakitas et al., 2017; Bakitas et al., 2009; Sendall, McCosker, Crossley, & Bonner, 2017). The focus of the CCM on changes in the health care system that shift the emphasis from siloed disease treatment to holistic, collaborative care fit well with a palliative care approach (Wagner et al., 2001; Wagner, Austin, & Von Korff, 1996). However, the main limitation of using the CCM in an intervention dose analysis was the lack of description of dosing and dose-related relationships between the health care system, patients, and providers.

Conceptual Framework for Implementation Fidelity

To address the lack of dose variables within the CCM model, the study expanded the CCM by combining the CCM with the Conceptual Framework for Implementation Fidelity. The Conceptual Framework of Implementation Fidelity depicts the relationships between an intervention, adherence, and outcomes (Carroll et al., 2007). Figure 3 depicts the Conceptual Framework for Implementation Fidelity.

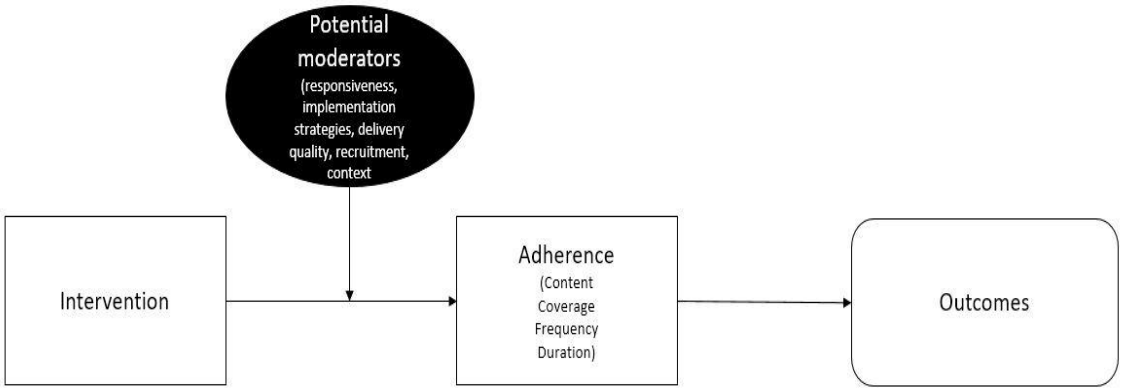


Figure 3. Modified Conceptual Framework of Implementation Fidelity. Original model described in Hasson, H. (2010). Systematic evaluation of implementation fidelity of complex interventions in health and social care. *Implementation Science,* 5(1). doi:10.1186/1748-5908-5-67

Adherence is whether a program or service is being delivered as it was designed. As defined by Carroll, adherence includes dose or 'coverage' and elements of 'dose" such as duration and frequency. The relationship between intervention and adherence is potentially moderated by policy, implementation strategies, quality of delivery, responsiveness of the participant, and context of the participant (Hasson, 2010). Within the Conceptual Framework of Implementation Fidelity, Carroll et al. (2007) operationalize adherence as "the content, frequency, duration, and coverage" of an intervention. These elements of frequency, duration, and coverage are similar to dose attributes of frequency, duration, amount, and intensity. One of the strengths of the Conceptual Framework of Implementation Fidelity is the match between Carroll et al.'s (2007) operationalization of adherence and the core elements of intervention dose. Another strength of this implementation framework is the clear depiction of adherence or dose effect on outcomes. This framework proposes that there is a relationship between

intervention adherence and outcomes and that this relationship may be modified by elements like responsiveness, implementation, delivery, and context. The authors describe a mediating relationship between adherence and outcomes (Carroll et al., 2007; Hasson, 2010). Additionally, the Conceptual Framework of Implementation Fidelity explores the roles of patient context such as sociodemographic and clinical factors, noting that these factors may influence adherence or intervention completion (Hasson, 2010; Hasson et al., 2012). While the Conceptual Framework of Implementation Fidelity introduces the elements of dose and dose attributes, the primary limitation of this framework is the incongruence with examples of intervention dose relationships in the current dose literature. While Carroll et al. (2007) do not depict adherence on the figure as a moderator, most behavioral intervention dose studies describe dose as moderating the relationship between intervention and outcomes.

In summary, the combination of the CCM and the Conceptual Framework of Implementation Fidelity address all the variables of interest. However, these frameworks do not reflect the relationships highlighted in dose, palliative care, and heart failure literature. Figure 4 is a modified combination of the CCM and Conceptual Framework of Implementation Fidelity for the analysis. Figure 5 depicts the conceptual model for the dose study.

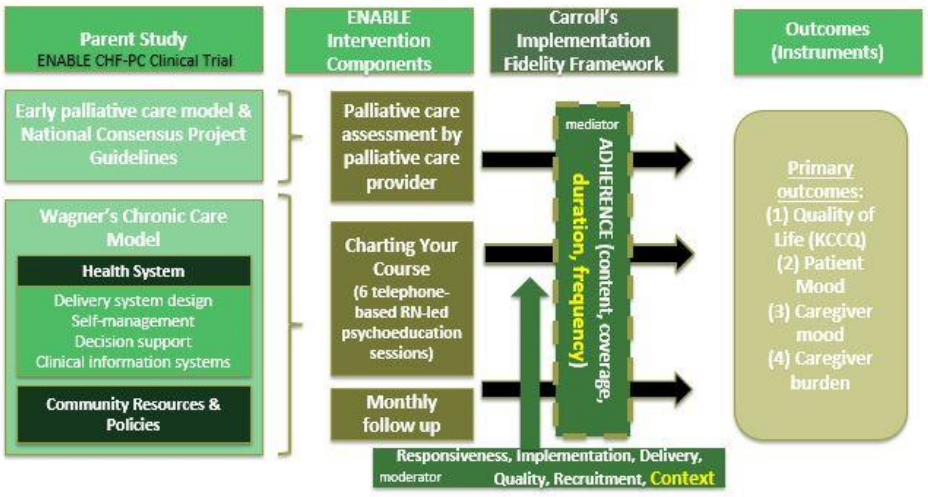


Figure 4. Combined Chronic Care Model and Conceptual Framework of Implementation Fidelity. ENABLE CHF-PC= Educate, Nurture, Advise Before Life Ends Comprehensive Heartcare for Patients and Caregivers; KCCQ=Kansas City Cardiomyopathy Questionnaire

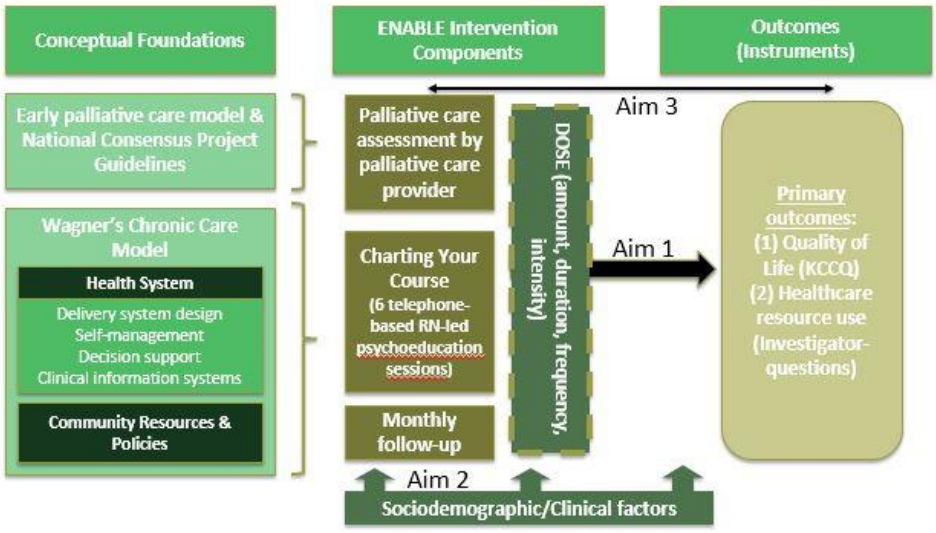


Figure 5. Conceptual Model for Intervention Dose Effects. Modeling Dose Effects of an Early Palliative Care Intervention for Advanced Heart Failure Patients. ENABLE CHF-PC= Educate, Nurture, Advise Before Life Ends Comprehensive Heartcare for Patients and Caregivers; KCCQ=Kansas City Cardiomyopathy Questionnaire

In the conceptual model for the study, dose of the ENABLE CHF-PC intervention impacts outcomes, such as QoL or healthcare resource use for patients. This conceptual model depicts context or baseline patient characteristics such as age, residence, comorbidities, or HF severity moderating dose. Given the proposed combinations and modifications, the CCM was an ideal theoretical framework to inform the conceptual model exploring dose effects of an early palliative care intervention. Guided by the combined frameworks, we examined relationships between intervention dose and QoL and healthcare resource use (Specific Aim #1) and the influence of sociodemographic and clinical characteristics on intervention dose and intervention effects (Specific Aims #2 & #3).

Behavioral Intervention Dose

Palliative care research has expanded from mostly observational and qualitative research to intervention-based design (Gelfman, Du, & Morrison, 2013; Xie, Gelfman, Horton, & Goldstein, 2017). With the transition into intervention studies, guidelines such as the Template for Intervention Description and Replication (TIDiER) checklist (Hoffmann et al., 2014) play an important role in reporting and evaluating individual interventions. The TIDiER checklist includes 12 items that should be included when reporting on interventions and intervention effects. The checklist items include name, intervention rationale, intervention materials, interventionist, mode of delivery, locations of intervention, when and how much of an intervention, intervention tailoring, modifications within study, fidelity, and adherence (Hoffmann et al., 2014). Some of these items, such as “when and how much of an intervention”, “fidelity,” and “adherence,” are related to behavioral intervention dose. Intervention dose is the amount,

duration, frequency, and intensity of an intervention (Hobfoll, Walter, & Horsey, 2008; Manojlovich & Sidani, 2008; Miller & Rollnick, 2014; Reed et al., 2017; Sidani, Manojlovich, & Covell, 2010; Voils et al., 2012; Voils et al., 2014; Washington et al., 2014). Table 1 includes dose elements described in intervention methodology literature.

Table 1

Literature Describing Behavioral Intervention Dose

Article	Dose Attributes	Recommendations for Analysis
Voils et al., 2014	Duration, Frequency, Amount	Multiple approaches detailed including descriptive and inferential strategies
Hoffmann et al., 2014	Number of times the intervention was delivered; Period of delivery time; Amount, Frequency, Duration, and Intensity	12 step checklist for intervention reporting; no recommendations for specific analysis
Manojlovich & Sidani, 2008	Purity, amount, frequency, duration	No recommendations for future analysis
Washington at al., 2014	Treatment receipt, Treatment enactment; investigator determined dose score (0-1 with 0 no attendance, 1 attendance)	Dose score, fidelity score, weighing content required for regression analyses

Despite the prevalence of reporting guidelines including the TIDiER checklist (Hoffmann et al., 2014) and the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) guidelines (Chan et al., 2013), there is limited literature exploring dose in palliative care intervention studies. Moreover, dose attributes are infrequently provided in palliative care protocol or study reports, similar to the lack of dose reporting found across all health studies (Dodd, White, & Williamson, 2012). Additionally, likely due to journal page limits, most authors rarely describe the full details of intervention dose and very few studies include additional analyses examining outcomes by intensity of intervention received. The following section synthesizes the state of the science of intervention dose literature including dose attributes found in palliative care intervention studies for advance heart failure patients.

Intervention Dose in Non-palliative Care Intervention Studies

There is limited evidence about whether the dose of the palliative care interventions for heart failure patients moderates patient outcomes in a similar manner seen in (1) pharmaceutical studies (Bleehen, Girling, Machin, & Stephens, 1993; Dicko et al., 2016; Düngen et al., 2014; Roobottom & Loader, 2016; Tran et al., 2012; Tsertsvadze et al., 2009; Webster et al., 2016), (2) psychiatric or psychological studies (Howard, Kopta, Krause, & Orlinsky, 1986; Lotfizadeh, Kazemi, Pompa-Craven, & Eldevik, 2018; Sikorskii et al., 2007; Xia et al., 2014), (3) exercise studies (Dishman, Vandenberg, Motl, Wilson, & DeJoy, 2010; Goode et al., 2011), (4) nutrition studies (Perri et al., 2014; Legrand et al., 2012; Lippke, Corbet, Lange, Parschau, & Schwarzer, 2016; Lundholm, Daneryd, Bosaeus, Korner, & Lindholm, 2004; Perri et al., 2014) or (5) non-palliative care intervention chronic disease studies (Cummings et al., 2011; Goode et al., 2011; Goode, Winkler, Reeves, & Eakin, 2015; Jonkman, Schuurmans, Groenwold, Hoes, & Trappenburg, 2016). While the previous studies reported dose-moderating outcome effects, a palliative cancer pain study (Rustoen et al., 2014) and heart failure lifestyle trial (Thomson, Zoellner, Tussing-Humphreys, & Goodman, 2016) did not find similar moderation effects. Given the lack of palliative care intervention dose effect studies for advanced heart failure patients and the prevalence of dose-response models in other health studies, 18 heart failure palliative care interventional studies were reviewed for dose analyses and dose attributes.

Search Strategy

A literature search was performed to identify palliative care interventions for heart failure. The database searches were limited to peer-reviewed, full-text English articles published from database inception to 2018. The search for palliative care intervention studies was performed in Cumulative Index to Nursing and Allied Health Literature (CINAHL) Plus and PubMed databases with key words of ("palliative care" OR "supportive care" OR "hospice" OR "end of life care" OR "pallia*") AND ("heart failure" OR "systolic dysfunction" OR "diastolic dysfunction") AND ("intervention" OR "psychoeducation"). The search term of dose or related terminology was not included based on previous poor search performance. A total of 139 articles in PubMed and 88 articles in CINAHL Plus were retrieved. The search results were combined and duplicates were removed resulting in a total of 161 records. All commentaries, editorials, non-English language, and non-full text articles were excluded yielding a total of 126 article abstracts for review.

Inclusion and Exclusion Criteria

All articles with abstracts detailing a pediatric patient sample, non-heart failure patient sample, a non-palliative care intervention using the NCP guidelines as palliative care criteria, or palliative pharmaceutical intervention or palliative surgical intervention without accompanying behavioral or psychoeducational intervention were excluded. Articles were removed that described interventions examining only transitional care, goals of care, or advance care planning unless those activities occurred specifically in a palliative care setting (n=88). Further exclusion upon full-text review included studies

with samples including other chronic disease patients such those living with cancer or chronic obstructive lung disease that did not identify heart failure-specific results (n=14). The articles were reviewed for duplication and articles were not removed if the duplication related to study protocol, design, or pilot studies. Two studies were removed due to duplication and reporting of the same results. A total of 104 articles were removed. Study protocol and design findings were combined with main outcomes in the integrative review. Systematic reviews and meta-analyses (n=4) were included. Reviews and meta-analyses were reviewed for studies not found in the results. Based on this review, one additional study was included. After full text review, a total of 18 studies and 4 reviews were included.

A total of 18 heart failure-related palliative care interventional study articles are included in the integrative review. Figure 6 shows a Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow chart of the literature search and screening process for heart failure-related palliative care interventions.

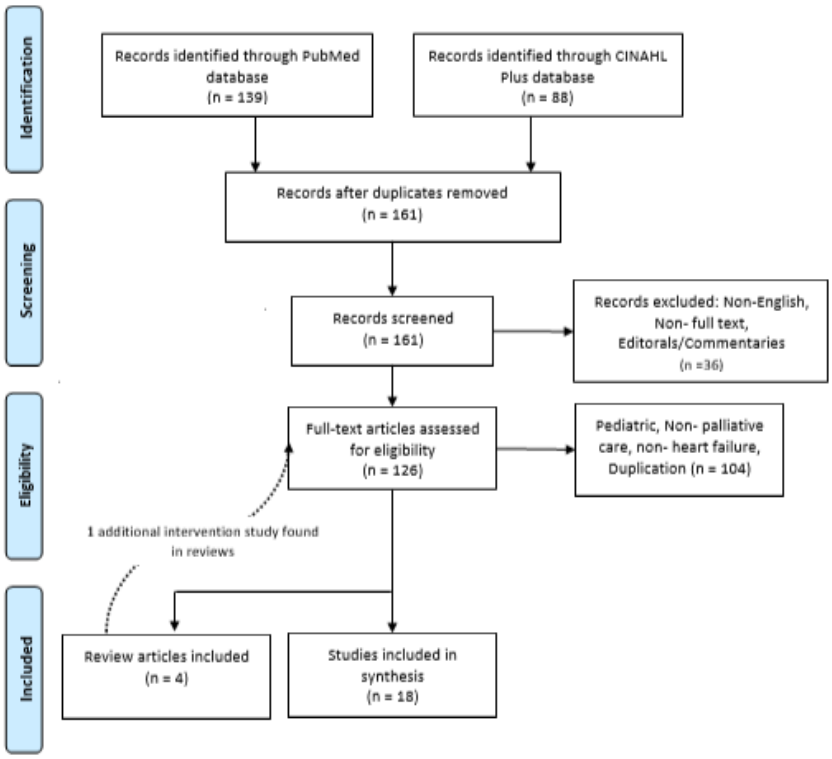


Figure 6. Palliative Care Interventions for Heart Failure PRISMA Diagram. This figure illustrates the literature search for palliative care interventions for heart failure. The diagram was adapted from the Preferred reporting items for systematic reviews and meta-analyses (PRISMA) figure detailed in Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2010). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. International Journal of Surgery, 8(5), 336-341.

Analysis of the Literature

Summary of Included Studies

When investigators perform dose analyses, they are generally completed with pre-selected dose categories in randomized control studies (MacDougall, 2012). Most studies included for review are randomized studies (Aiken et al., 2006; Bekelman et al., 2018; Brannstrom & Boman, 2014; Brumley et al., 2007; Hopp et al., 2016; Pantilat, O'Riordan, Dibble, & Landefeld, 2010; Rogers et al., 2017; Sahlen, Boman, &

Brannstrom, 2016; Sidebottom, Jorgenson, Richards, Kirven, & Sillah, 2015; Wong et al., 2016). Other studies included quasi-experimental designs (Bakitas et al., 2017; Campbell et al., 2015; Fitzpatrick, Mavissakalian, Luciani, Xu, & Mazurek, 2018; Pattenden, Mason, & Lewin, 2013; Rabow, Dibble, Pantilat, & McPhee, 2004; Schwarz et al., 2012). One article is a case control study with prospective palliative care consultation (Evangelista et al., 2012) and another article details a qualitative study (Kane et al., 2017). All studies were conducted through a healthcare system or hospital and focused on adult patients with advanced heart failure characterized either through New York Heart Association Class II-IV (Aiken et al., 2006; Bakitas et al., 2017; Brannstrom & Boman, 2014; Hopp et al., 2016; Kane et al., 2017) or other diagnostic clinical guidance found in the patient health record (Bekelman et al., 2018; Brumley et al., 2007; Evangelista et al., 2012a; Fitzpatrick et al., 2018; Pantilat et al., 2010; Sidebottom et al., 2015; Wong et al., 2016).

Study Populations

All studies required a heart failure diagnosis and some had a heart failure exacerbation or hospitalization as another inclusion criterion (Bekelman et al., 2018; Brännström & Boman, 2014; Evangelista et al., 2014; Sidebottom et al., 2015; Wong et al., 2016). Sample sizes ranged from 18 to 297; however, many studies included patients with other chronic disease diagnoses. The large heart failure-only sample study included 200 patient participants (Rogers et al., 2017). While small sample sizes are common in palliative care research, the generalizability of the included studies is limited due to selection bias concern. Additionally, most study samples reviewed were racially

homogenous and recruited from a single site (Aiken et al., 2006; Bekelman et al., 2018; Brannstrom & Boman, 2014; Brumley et al., 2007; Evangelista et al., 2012; Kane et al., 2018; Sahlen, Boman, & Brannstrom, 2016; Sidebottom, Jorgenson, Richards, Kirven, & Sillah, 2015; Wong et al.) and over 50 years old (Aiken et al., 2006; Bakitas et al., 2017; Bekelman et al., 2018; Brannstrom & Boman, 2014; Brumley et al., 2007; Campbell et al., 2015; Evangelista et al., 2012; Fitzpatrick, Mavissakalian, Luciani, Xu, & Mazurek, 2018; Hopp et al., 2016; Pantilat, O'Riordan, Dibble, & Landefeld, 2010; Pattenden, Mason, & Lewin, 2013; Rabow, Dibble, Pantilat, & McPhee, 2004; Rogers et al., 2017; Sahlen, Boman, & Brannstrom, 2016; Schwarz et al., 2012; Sidebottom, Jorgenson, Richards, Kirven, & Sillah, 2015; Wong et al., 2016). Clinical palliative care reach in diverse populations is limited (Durant et al., 2007; Jenerette et al., 2008; Steinke, 2004) even though heart failure disproportionately affects minorities (Benjamin et al., 2019). Attrition related to death is expected in palliative care research given the focus on chronic, life-limiting diseases. However, non-death attrition in some studies (Aiken et al., 2006; Bakitas et al., 2017; Brännström & Boman, 2014; Evangelista et al., 2014; Sidebottom et al., 2015; Wong et al., 2016) was a significant limitation with implications for examining dose effect. However, all quantitative studies utilized intention-to-treat analyses.

Intervention Types

All reviewed studies were prescreened to include at least 1 aspect of the National Consensus Project (NCP) palliative care domains (NCP, 2018). The NCP guidelines were used to identify key elements for an intervention to be considered

"palliative" in nature. Noted difficulties in comparison of palliative care studies include incongruence concerning what constitutes palliative care (Gaertner et al., 2015; Jan Gaertner et al., 2016; Kavalieratos et al., 2016; Stygles, Klein-Fedyshin, & Kavalieratos, 2017). The delivery of palliative care varied. A single in-person palliative care consultation was provided in 7 studies (Campbell et al., 2015; Evangelista et al., 2012a; Fitzpatrick, Mavissakalian, Luciani, Xu, & Mazurek, 2018; Hopp et al., 2016; Kane et al., 2018; Pantilat, O'Riordan, Dibble, & Landefeld, 2010; Rabow, Dibble, Pantilat, & McPhee, 2004; Sidebottom, Jorgenson, Richards, Kirven, & Sillah, 2015). A multi-component palliative care intervention that included palliative care consultation was used in 9 studies (Aiken et al., 2006; Bakitas et al., 2017; Bekelman et al., 2018; Brannstrom & Boman, 2014; Brumley et al, 2007; Pattenden, Mason, & Lewin, 2013; Rabow, Dibble, Pantilat, & McPhee, 2004; Rogers et al., 2017; Wong et al., 2016). Other studies did not report intervention details about delivery. For the randomized control studies, two articles included details about the control condition outside of 'usual' care (Bekelman et al., 2018; Wong et al., 2016). The inclusion of an attention comparison control helped reduced attention bias in those studies.

Intervention Dose Analysis and Description

While general intervention descriptions were included by all studies as indicated in the above paragraph, details about dose attributes of frequency, duration, intensity or purity, and amount varied in each study. No study included a dose analysis or as-treated analysis. While some studies included some dose details including amount (Aiken et al., 2006; Bakitas et al., 2017; Bekelman et al., 2018; Kane et al., 2018; Rogers et al., 2017)

and frequency (Sidebottom et al., 2015; Bakitas et al., 2017; Bekelman et al., 2018; Rogers et al., 2017), other studies did not include any intervention dose information. Recent pilot and randomized control studies either included some dose attributes or published protocol papers detailing the intervention (Bekelman et al., 2018; Rogers et al., 2018).

Quality of Life Outcome Measures

Most of the studies examined the effect of palliative care interventions on QoL (Aiken et al., 2006; Bakitas et al., 2017; Bekelman et al., 2018; Brannstrom & Boman, 2014; Evangelista et al., 2012; Kane et al., 2017; Pattenden, Mason, & Lewin, 2013; Rogers et al., 2017; Sidebottom, Jorgenson, Richards, Kirven, & Sillah, 2015; Wong et al., 2016) using QoL outcomes measured by the Kansas City Cardiomyopathy Questionnaire, the Minnesota Living with Heart Failure Questionnaire, or investigator-determined questions. In the studies reviewed, most reported improvement in QoL after palliative care exposure varying from small to moderate effect size change. However, Bekelman et al. (2018) reported no statistical change in QoL outcomes post intervention. Bekelman et al. (2018) attributed this lack of change to potential inadequate intervention intensity or dose and mismatch between measuring QoL with the KCCQ, which focuses on symptoms and function, and a holistic palliative care intervention with content focused on social support and emotional health. Another study reported conflicting improvement based on two different instruments used to measure QoL (Brännström & Boman, 2014). Varying instruments and data collection times are limitations for comparing results between studies. Additionally, Rogers et al. (2017) reported

statistically significant improvements in QoL in the PAL-HF study. Given the strength of the randomized controlled study design, the reported improvements in QoL may be more generalizable and should be considered stronger evidence.

Resource Use and Palliative Care for Heart Failure Systematic Reviews

Most systematic reviews reported variance in palliative care interventions for heart failure patients including number of sessions, timing of sessions, duration of sessions, and provider (Cagle et al., 2017; Diop, Rudolph, Zimmerman, Richter, & Skarf, 2017; Kavalieratos et al., 2016; Xu et al., 2018). The systematic reviews examined outcomes of QoL, symptom burden, anxiety, depression, quality of death, and healthcare resource use outcomes. Most reviews reported either narrative or statistically significant positive effects in QoL, rehospitalization or healthcare resource use, and symptom burden (Kavalieratos, Corbelli, Zhang, & et al., 2016; Diop et al., 2017; Xu et al., 2018). At the time of publication of the systematic reviews, the results of the largest randomized controlled palliative care trial of only heart failure patients was not published. The study by Rogers et al. (2017) found no statistically significant changes in rehospitalization rates between those receiving the palliative care intervention and those who received usual care. Two systematic reviews reported no significant change or mixed outcomes in quality of death outcomes (Diop et al., 2017; Xu et al., 2018).

Symptom Burden Outcomes

Most studies found improved symptom burden with palliative care intervention (Aiken et al., 2006; Bakitas et al., 2017; Brumley et al., 2007; Evangelista et al., 2012;

Rogers et al., 2017; Sahlen, Boman, & Brannstrom, 2016; Sidebottom, Jorgenson, Richards, Kirven, & Sillah, 2015; Wong et al., 2016) although no change was found in 2 studies (Bekelman et al., 2018; Brannstrom & Boman, 2014). Symptom burden outcomes were commonly measured using the Edmonton Symptom Assessment Scale, Memorial Symptom Assessment Scale, or investigator determined questions. Despite most studies reporting improved symptom burden, the two randomized controlled trials differed in outcomes; Bekelman et al. (2017) reporting no change in symptom burden whereas Wong et al. (2016) reported statistically significant change in symptom burden.

Anxiety and Depressive Symptom Outcomes

Four studies specifically evaluated anxiety and depressive symptom outcomes before and after palliative care intervention exposure. Anxiety and depressive symptoms were commonly measures by the Hospital Anxiety and Depression Scale or investigator-determined questions. All studies reported statistically significant improvement in anxiety and depressive symptoms (Bekelman et al., 2018; Evangelista et al., 2012; Sidebottom et al., 2015; Rogers et al., 2017). However, neither study reported effect size or confidence intervals.

Identified Gap and Summary

To our knowledge, associations between intervention dose and outcomes have not been examined in current palliative care intervention literature . While most palliative care intervention studies for heart failure patients reported positive change in QoL, symptom burden, anxiety, depression, and resource use outcomes, more recently

published randomized controlled trials reported mixed outcomenn changes. Additionally, all studies performed intention to treat analyses despite noted attrition limitations. With significant attrition, the determination of true intervention effects is difficult as this attrition may mask intervention effect. The study aimed to evaluate intervention dose in an ongoing palliative care clinical trial, the Educate, Nurture, Advise Before Life Ends Comprehensive Heartcare for Patients and Caregivers (ENABLE CHF-PC) study (Wells et al., 2018), addressing the gap in intervention dose analyses and mixed findings on QoL and healthcare resource use. Additionally, studies exploring the influence of sociodemographic and clinical factors in behavioral intervention adherence in current palliative care are limited. Residence, comorbidity, age, and disease severity influence adherence in medication and lifestyle behavioral interventions (Bauer et al., 2012; Beatty & Binnion, 2016; Dev et al., 2016; Dickson, Knafl, & Riegel, 2015; Faul, 2014; Hasson, Blomberg, & Duner, 2012; Luyster, Hughes, & Gunstad, 2009; Oertle & Bal, 2010; Riegel & Dickson, 2016; Ruppar, Delgado, & Temple, 2015; Strachan, Currie, Harkness, Spaling, & Clark, 2014). Similar relationships may influence adherence or intervention completion in palliative care behavioral interventions.

In summary, the study aimed to address the gap in understanding about the relationship of intervention dose and patient-reported outcomes, characteristics associated with intervention adherence, and patient experiences with intervention dose in palliative care heart failure studies. Specifically, the dose study aimed to examine intervention dose effects on advanced heart failure patient-reported outcomes of QoL and healthcare resource use (Specific Aim #1), associations between age, residence, comorbities, and HF severity and ENABLE CHF-PC intervention completion (Specific Aim #2), and patients'

perspectives and experiences with intervention dose, participation in the ENABLE CHF-PC study, and QoL and healthcare resource use change (Specific Aim #3). In exploring intervention dose both quantitatively and qualitatively, this concurrent mixed methods study aimed to more comprehensively describe palliative care intervention dose and its impact on QoL and healthcare resource use of advanced HF patients in the Deep South.

Study Design and Methods

The research study was a concurrent mixed methods design that explored dose effects of an early palliative care intervention for heart failure patients. Mixed methods designs use qualitative, quantitative, and mixed methods integrative approaches to explore and examine a proposed research topic (Plano Clark & Ivankova, 2016). Within these three approaches, the following designs were weighed and selected for use: (1) quasi-experimental design for the quantitative strand, (2) qualitative description for the qualitative strand, and (3) concurrent design for the mixed methods approach.

Quantitative Design

Traditional dose analyses require pre-determined doses of an intervention (MacDougall, 2012). Polit and Beck (2017) describe an embedded dose response design that utilizes non-protocol driven dose variation to examine outcome differences. Although ENABLE CHF-PC is designed as a non-variable intervention (Bakitas et al., 2017), variation in intervention completion is present among patient participants allocated to the intervention arm. As the duration of the intervention varied, the study design was also longitudinal to capture outcome variation in response to duration.

Using an embedded dose response design within a larger randomized controlled trial allowed for a practical, feasible approach (Handley, Schillinger, & Shiboski, 2011) while limiting group differences through the initial randomization in the larger study (Polit & Beck, 2017).

Qualitative Design

A descriptive qualitative research design (Sandelowski, 2010) was used as a framework to explore heart failure study participants' perspectives of palliative care intervention dose. Traditional dose analysis relies on a pre-determined dose of an intervention and strict adherence to the intervention protocol (MacDougall, 2012). While feasibility and acceptability studies might explore or explain some dose variation using quantitative methods, these approaches are limited in addressing how intervention dose understanding or other factors might influence intervention dose received. Strengths of qualitative methods include flexibility to meet evolving inquiry and context-seeking inquiry (Creswell & Poth, 2018; Marshall & Rossman, 2016). A qualitative approach is appropriate for exploring intervention dose due its ability to identify unexplored and underappreciated phenomena and their relationships related to the clinical trial context and the participants' varied serious illness experiences (Creswell & Poth, 2018). These unknown factors and interactions are difficult to quantify and require identification and clarification (Munday, Johnson, & Griffiths, 2003). Additionally, the utility of qualitative research in palliative care has been previously identified (Audrey, 2011; Flemming, Adamson, & Atkin, 2008; Schildmann & Higginson, 2011). However, multiple methodological approaches might be used in qualitative inquiry including

phenomenology, grounded theory, ethnography, or case study (Creswell & Poth, 2018). Some qualitative approaches emphasize theoretical frameworks or theory-generating endpoints like grounded theory (Creswell & Poth, 2018). Of the qualitative approaches, both phenomenology and descriptive qualitative design were considered as both approaches could capture the experience and patient-perceived factors associated with the ENABLE CHF-PC intervention dose received. Phenomenology focuses on the in-depth exploration of individual's lived experiences. The in-depth focus on an individual's lived experience did not match with the integrated study aim to reach a more complete understanding of palliative care intervention dose, which is a form of concept clarification. Descriptive qualitative design with its aim on concept clarifications aligns closely with the purpose of the study to examine the concept of palliative care intervention dose and dose effects. Additionally, descriptive qualitative design is pragmatic (Neergaard, Olesen, Andersen, & Sondergaard, 2009; Sandelowski, 2010) and naturalistic (Sandelowski, 2010) which allows for the dose variation found in the parent ENABLE CHF-PC study. Also, another consideration for selecting qualitative description includes the lack of tight theoretical orientation (Sandelowski, 2010) which fits with the need to borrow from non-palliative care fields for dose-response models.

Overall, the lack of detailed description of the components of complex palliative care intervention dose and participant-identified dose-moderating factors matches the data-driven, naturalistic approach of qualitative description as the primary focus is on heart failure-related palliative care dose conceptualization.

Mixed Methods Design

A concurrent mixed methods design was used to explore dose in this study. Mixed methods research integrates both quantitative and qualitative methods to address a research question (Plano Clark & Ivankova, 2016). In mixed methods, considerations of timing and priority influence the selection of different approaches. Timing refers to the occurrence of the qualitative and quantitative strand in relation to each other (Plano Clark & Ivankova, 2016). Time categories for mixed methods study include concurrent, sequential, or multiphase (Plano Clark & Ivankova, 2016). Concurrent timing was selected as quantitative data collection is still ongoing in the parent ENABLE CHF-PC trial (i.e. interviews and subsequent analysis began before quantitative data collection and analysis was complete). Priority refers to the focus and the weight of each strand in relation to the other. The study has equal priority with the results of both the quantitative and qualitative strand weighing equally in exploring dose effect. If the quantitative strand was prioritized, the outcome dose effects would frame the integration of the results and the qualitative strand would provide additional support or lack of support to the quantitative findings. Given the limited evidence and literature on palliative care intervention dose, patients' experiences and perceptions concerning dose and intervention completion provided the necessary context to the quantitative dose analysis. Some of the strengths of a mixed methods study include offsetting weaknesses in mono-methods, validation, complementarity, and triangulation of findings (Plano Clark & Ivankova, 2016). Most dose analysess use quantitative methods (Tran et al., 2012) to identify outcome changes related to a dose variable; however these analyses have not been able to explore the experiences of study participants in completing the intervention

components as could be done with qualitative designs. However, mixed methods designs may take longer to complete than traditional mono-methods, require more financial support, and overburden the research participants (Plano Clark & Ivankova, 2016).

Given the lack of dose literature in palliative care, a more complete understanding of palliative behavioral intervention dose is needed. Mixed methods research results in more robust and comprehensive inferences through its use of validation, triangulation, and complementarity. A concurrent mixed methods design was selected for the study as the benefits of robust inferences outweigh the time and financial limitations.

Ethical Considerations

Burden

Research-related burden refers to the time, effort, sensitivity, and stress experienced by a study participant (Ulrich, Wallen, Fiester, & Grady, 2005). Palliative care populations have been characterized as a 'vulnerable' population due to issues surrounding participation burden, unrealized benefit, and consent (Agar, Ko, Sheehan, Chapman, & Currow, 2013; Blum, Inauen, Binswanger, & Strasser, 2014; Pessin et al., 2008). With a chronic disease diagnosis, such as advanced heart failure, patients experience significant disease burden which may be compounded by participation in research (Emanuel, Fairclough, Wolfe, & Emanuel, 2004). The aggregate burden might alter the benefit to risk ratio (Ulrich, Wallen, Fiester, & Grady, 2005). Another consideration for participation burden is the likelihood that the illness trajectory of a seriously ill patient participant might limit his exposure to the benefits of the research study and skew the benefit to risk ratio. However, studies examining patients'

perspectives of palliative care participation show research involvement to be mostly positive with proposed benefits of helping others and transforming knowledge (Gysels, Evans, & Higginson, 2012; Higginson et al., 2013; Mackin et al, 2009).

Consent

Informed consent is a three-part process of providing adequate study information to a potential participant, ensuring the potential participant's comprehension of the study information, and ensuring the potential participant's freedom to enroll in the study (Steinke, 2004). As previously mentioned, palliative care research participants have been characterized as a 'vulnerable' population. Vulnerable palliative care populations may be at risk for poor comprehension of study information or freedom from participation coercion (Agar, Ko, Sheehan, Chapman, & Currow, 2013). Additionally, many with advanced heart failure have impaired cognition associated with cerebral hypoperfusion related to decreased cardiac output (Moises, Neil, & Adam, 2011). Another ethical consideration for consent includes health literacy. Health literacy--the ability to read, understand, and act appropriately on health-related information--is a key factor in understanding consent information (Ownby, Acevedo, Goodman, Caballero, & Waldrop-Valverde, 2015). Concerns about health literacy, which might influence informed consent, were identified during the pilot trial (Bakitas et al., 2017). While consensus has been reached that it is possible to ascertain informed consent with patients receiving palliative care (Agar et al., 2013; Davis, 2015; Duke & Bennett, 2010), these studies have not considered aggregate consent issues such as impaired cognition and health literacy.

Appropriateness of Secondary Analysis

The study was a hybrid of a secondary analysis in the quantitative strand and original data collection in the qualitative strand. Despite the identified population being selected in the parent study, one of the considerations for a study population and sample in a secondary analysis included determining whether the pre-selected population fits with the proposed study (Elia, Von Elm, Chatagner, Pöpping, & Tramèr, 2016). While the participants in the ENABLE CHF-PC dataset match the disease condition of the study as they were all diagnosed at the time of recruitment with advanced heart failure, another consideration for sample fit is fair subject selection. The parent study did use community based recruiters, a strategy identified for minority recruitment (Heller et al., 2014) and stratified patients by race during randomization to ensure equal representation. As heart failure disproportionately affects African Americans and rural residents (CDC, 2016), recruitment efforts for this population should be weighed in consideration of a secondary analysis. While traditional recruitment strategies, such as community and stakeholder involvement, provider engagement, or media publications, are valuable tools for future palliative care research, careful selection of a dataset is a key ethical consideration for a secondary dose analysis (Heller et al., 2014).

Like the consideration given to the appropriateness of the population in a collected dataset, another consideration concerning ethical risks in a secondary analysis was to review the consent and data collection process of the initial study (Elia et al., 2016). The ENABLE CHF-PC study was approved by both institutional review boards (IRBs) at the University of Alabama at Birmingham and the Birmingham Veterans Affairs Medical Center, meeting the criteria for independent review. Informed consent

was obtained from all study participants, all adults with no cognitive impairment, as evidenced by a Callahan score of greater than 4 (Callahan, Unverzagt, Hui, Perkins, & Hendrie, 2002). While informed consent was sought, it should also be reviewed given the disclosure of the dataset to a new researcher. With the parent study informed consent, the ability of participants to understand the details of the informed consent document and process should be reviewed, especially if the informed consent included a clause releasing the data for other research purposes such as the dose effect study. While the dataset was de-identified as all participants are assigned unique study identification numbers for confidentiality by the study coordinator during screening, it was not anonymous given the study PI's role as a nurse coach at study initiation. The dataset would be subject to federal protections, according to federal regulation 45 CFR 46 sub part 101 b number 4. As a de-identified but not anonymous dataset, the secondary analysis study would be subject to the institutional IRB review. Other human subject protections include data security which were addressed by the location of the dataset on a secured, firewalled server maintained by UAB in a folder that is password encrypted.

Overall, the ability to mitigate recruitment, data collection, and human subject protection issues in the existing ENABLE CHF-PC dataset is limited, an in-depth understanding of strategies and procedures used in the parent study provided ample knowledge to assess the validity of the data, a prime determinant of existing data use (Polit & Beck, 2017).

Summary

Individuals living with heart failure experience significant symptom burden, poor QoL, decreased mood, and high healthcare resource use. While most palliative care intervention studies demonstrate improved QoL and decreased healthcare resource use, intervention designs vary between studies and no reported palliative care heart failure studies have examined dose-response effects.

This chapter provided an in-depth review of the state of the science of palliative care interventions for heart failure and included the epidemiological background of heart failure, CCM and the Conceptual Framework for Implementation Fidelity, and potential research designs. The studies included in both the palliative care heart failure intervention integrative review and intervention dose review along with the foundations of the CCM shape the purpose, design, and analysis of the dose study. Based on this thorough literature review, the concurrent mixed methods study used both quantitative and qualitative strands to explore palliative care intervention dose for heart failure patients balancing the need for defining, operationalizing, and evaluating intervention dose with the time and financial constraints of a dissertation study. The lack of palliative care behavioral intervention dose analysis was highlighted as a gap in the literature. Multiple research guidelines recommend the inclusion of intervention dose as dose may affect outcomes and is requisite for implementation, replication, and effectiveness comparison.

The following chapter will build upon this in-depth review of the state of the science of palliative care interventions for heart failure patients and intervention dose by providing a detailed description of the research design and methodology of the dose study.

CHAPTER THREE

HF, a chronic, life-limiting illness affecting 6.5 million U.S. adults (Benjamin et al., 2019), is a leading cause of hospitalization in older adults (Agency for Healthcare Research and Quality, 2013), likely due to its high symptom burden and poor QoL. While recent palliative care intervention research demonstrates positive patient-reported outcome trends in QoL, symptom burden, and healthcare use, intervention elements vary widely (Diop, Rudolph, Zimmerman, Richter, & Skarf, 2017; Kavalieratos et al., 2016). Despite the identification of dose, composed of frequency, duration, timing, and intensity (Voils et al., 2014), as a fundamental component of intervention quality and success (Hobfoll, Walter, & Horsey, 2008), dose is rarely specified in palliative care interventions. Given the lack of dose response analyses, the study addressed this gap by examining the effect of a multi-component palliative care intervention dose on QoL and healthcare resource use in older adult advanced HF patients. The purpose of Chapter 3 is to describe the research methods used in the study.

Chapter 3 will start with brief overview of the specific aims, hypotheses, and research design. The next section will include a description of the sampling procedures, as well as inclusion and exclusion criteria and recruitment sites. Additionally, the recruitment strategies and recruitment protocol are included in the sampling section. The next section will describe the informed consent process for both the qualitative strand and quantitative strand. A section describing the data collection procedure for the qualitative semi-structured interviews and strategies to address rigor and credibility will follow the

informed consent section. The next section will outline the data analysis plan for the quantitative strand followed by the planned analysis for the transcribed interviews.

In summary, this chapter will review the following components: (1) sampling procedures, (2) the informed consent process, (3) data collection procedures, (4) reliability and validity strategies, and (5) data analysis plan for the concurrent dose effect mixed methods study.

Brief Overview of Study

The research study was a concurrent mixed methods study that explored dose effects of an early palliative care intervention for heart failure patients. The study was an embedded ancillary study of the ongoing Educate, Nurture, Advise Before Life Ends Comprehensive Heartcare for Patients and Caregivers (ENABLE CHF-PC, NCT02505425) early palliative care clinical trial (Wells et al., 2018).

Mixed methods designs use qualitative and quantitative integrative approaches to explore and examine a proposed research topic (Plano Clark & Ivankova, 2016). Mixed methods is an ideal approach for palliative care intervention dose inquiry as it can address the large gap concerning behavioral intervention dose by integrating the traditional quantitative dose-related intervention effect analysis with a rich qualitative description of the palliative care study context, documented non-protocol dose variability, and the complexity of palliative care itself (Audrey, 2011; Creswell & Poth, 2018; Flemming, Adamson, & Atkin, 2008; Schildmann & Higginson, 2011). Although the parent ENABLE CHF-PC intervention was designed as a non-variable intervention (Wells et al., 2018), variation in intervention completion was present among patient participants

allocated to the intervention arm. Given this variation, this study examined characteristics associated with intervention completion. As the duration of the intervention varied, the study design was longitudinal to capture outcome variation in response to duration. Mixed models were used to dose group (i.e., complete versus noncomplete) intervention effects on QoL and healthcare resource use at 16- and 32 weeks.

The qualitative strand focused on patients' perceptions of dose, dose experience, and overall intervention experience, aspects of dose that are difficult to quantify and need clarification (Munday, Johnson, & Griffiths, 2003). We used descriptive qualitative research design as the qualitative framework. Descriptive qualitative design focuses on concept clarification, which aligns with the purpose of the study to explore the concept of palliative care intervention dose and dose effects. Additionally, qualitative description does not have a specific theoretical orientation (Neergaard et al., 2009; Sandelowski, 2010), which fits with the need to borrow from non-palliative care fields.

The specific aims and hypotheses of the study were to:

Specific Aim #1: Determine the relationship between ENABLE CHF-PC dichotomous intervention dose and patient-reported QoL and healthcare resource use at 16- and 32-weeks after baseline.

Specific Aim #2: Determine the relationship between ENABLE CHF-PC patient characteristics (age, residence, comorbidities, HF disease severity) and intervention dose attributes and completion.

a. Determine the relationships between age, comorbidities, and HF disease severity and dose attributes of amount and frequency.

b. Determine the relationships between residence and HF disease severity and intervention completion.

Specific Aim #3: Explore ENABLE CHF-PC patients' experiences with the intervention components, intervention dose (amount, duration, frequency, intensity), and their perspectives on the intervention effects on patient-reported outcomes and trial participation in general.

Specific Aim #4 (Integrated Mixed Methods): Determine the intersection of participant intervention dose experiences with key sociodemographic, clinical, and intervention dose variables and how this intersection jointly explains the overall uptake of the ENABLE CHF-PC intervention in Deep South advanced HF patients.

Overview of Parent Study

The parent ENABLE CHF-PC study is an ongoing, National Institute of Nursing Research-funded, early palliative care randomized clinical intervention study for advanced HF patients and caregivers. The aims of the parent ENABLE CHF-PC study are as follows: (1) Determine whether ENABLE CHF-PC leads to higher advanced HF patient-reported QoL and mood and lower symptom burden and resource use at 8- and 16-weeks after baseline and (2) Determine whether ENABLE CHF-PC leads to higher caregiver-reported QoL, mood, and self-reported health and lower caregiver burden at 8- and 16-weeks after baseline (Wells et al., 2018). In ENABLE CHF-PC, participants randomized to the intervention arm receive a multi-component psychoeducational intervention. For patient participants, the ENABLE CHF-PC intervention consists of 6 weekly, hour-long, nurse-led, telephone-based psychoeducational sessions and a single,

in-person palliative care consultation (Wells et al., 2018). The telephone sessions include content on problem-solving, self-care, symptom management, decision-making, legacy building, and life review (Wells et al., 2018).

Sampling

Inclusion criteria for the parent ENABLE CHF-PC study include: (1) New York Heart Association stage III-IV or ACC/AHA Stage C or D or equivalent heart failure, (2) 50 years of age or older, (3) English-speaking, and (4) reliable telephone access (Wells et al., 2018). Exclusion criteria for the parent ENABLE CHF-PC study include: (1) heart transplantation or mechanical circulatory assist device, (2) active Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) Axis I diagnosis (e.g. schizophrenia or bipolar disorder) excluding major depression or generalized anxiety disorder, (3) non-correctable hearing loss, and (4) dementia or cognitive impairment determined by the Callahan Cognitive Screen (Callahan, Unverzagt, Hui, Perkins, & Hendrie, 2002). These a priori eligibility criteria fit the study population of older advanced HF patients. An additional inclusion criterion for this dissertation study included randomization to receive the palliative care intervention. We did not use any additional exclusion criteria.

Recruitment for the ongoing parent study started in December 2015 and continued until April 2018. The parent ENABLE CHF-PC study recruited from two health care systems: (1) the University of Alabama at Birmingham Health System (UAB) and (2) the Birmingham Veterans Affairs Medical Center (BVAMC) (Wells et al., 2018). Trained staff from a community-based recruitment and retention service (RRSF) reviewed and

screened cardiology clinic lists a week in advance for eligible patients. Patient records that were screened for over 5 minutes were entered into a secure, firewalled database housed on a BVAMC server. If the patient was deemed "ineligible," the reason of ineligibility was recorded. On the day of the scheduled outpatient cardiology clinic visit, community-based recruiters approached eligible patients. At UAB, eligible patient participants were approached in the outpatient cardiology clinic at Kirklin Clinic and a U.S. Health Resources and Services Administration (HRSA)-funded HF clinic within UAB Hospital. At BVAMC, eligible patient participants were approached at multiple outpatient cardiology clinics.

All patients who elected not to participate in the study were also entered into the study database along with their reason for non-participation. These data entries were used in the parent study to evaluate representativeness of the study sample as a strategy to assess selection bias (Polit & Beck, 2017). Through the parent study, 415 patient participants were recruited. After baseline outcome measures were collected, the study program manager was notified (Wells et al., 2018). Then a computer-based algorithm, accounting for stratification by recruitment site and race, computed each participant's randomization assignment (intervention versus usual care) (Wells et al., 2018). The study program manager verified the usual care or intervention arm allocation with a backup randomization table and then entered the allocation into the secure database (Wells et al., 2018). The program manager then notified the patient of their study allocation by phone (Wells et al., 2018). A total of 208 patients were randomized to the intervention arm. If the patient was randomized to receive the ENABLE intervention, a nurse coach was notified to begin the intervention within the next 3 business days.

As an embedded study in the ongoing ENABLE CHF-PC trial, access to the study sample was through a dataset created from intervention and outcome data reports and contact information found in the parent study database. The primary investigator (PI) of the study created a skeleton report that filtered participants by allocation to receive the intervention. For the dose study, all the study participants (208 patients) randomized to the intervention were included in the correlation, odds ratios, and mixed model analyses in the quantitative strand given the focus on intervention dose effect. As an exploratory study, the quantitative strand analyses were not powered for hypothesis testing.

Attrition for palliative care studies often reaches 30% (Kane et al., 2018; Zambroski, Buck, Garrison, & McMillan, 2014) which was also experienced in the parent study. The initial 208 randomized participants did not complete all outcome measures. For the qualitative strand, we attempted to reach all randomized UAB patient participants to maximize the possibility of capturing all dose experiences and perspectives. The intervention interviewee subsample was stratified into complete and noncomplete groups for analysis, mirroring the dichotomous dose groups (Chapter 1 Figure 1) from the quantitative strand.

The study used stratified purposive sampling to facilitate comparison (Marshall & Rossman, 2016) between groups. Stratified purposive sampling fits the purpose of capturing the majority of dose variation experienced by participants (Palinkas et al., 2015). This stratification aided with group comparison and integration between qualitative and quantitative strands. We also grouped participants by gender, race, and residence during analysis but did not use these stratifications during recruitment. Potential participants were contacted by study staff via telephone to gauge interest in

study participation (Newington & Metcalfe, 2014). Appendix A is a workflow document of qualitative participant recruitment and interview procedure. For data saturation, we estimated we would need sample sizes of 20 participants per dose category for a total of 40 patient participants based on palliative care qualitative descriptive studies (Epiphaniou et al., 2012; Yoong et al., 2013). We reached data saturation between 10-12 participants for each dose category (complete versus noncomplete). Also, the use of multiple cases is a form of triangulation (Marshall & Rossman, 2016), with participants acting as informants both within their dose category and all dose categories.

Overall, the study sample consisted of patients randomized to the intervention arm of the parent ENABLE CHF-PC study. A subsample of the intervention participants was recruited for the semi-structured interviews of the qualitative arm using purposeful sampling techniques.

Informed Consent

Informed consent is a multi-step process of providing adequate study information to potential participants to ensure their comprehension of the study information and freedom to enroll in the study (Steinke, 2004). As previously mentioned in Chapter 2, the potential study participants may be considered a "vulnerable" population due to their chronic, severe disease status and HF-related cognitive changes.

Concerning consent for the quantitative strand of the study, the consent process for the ENABLE CHF-PC parent study took place in person during the initial approach in the cardiology clinic. Trained community-based recruiters or study staff reviewed the details of the ENABLE CHF-PC study including study purpose, data collection

procedures, potential risks and benefits, strategies to protect confidentiality, the ability to opt out at any time, and the contact information for study PI. Recruiters also discussed with potential participants the following study aspects: (1) $10 compensation by check related to data collection for a total of $70 (2) non-participation in the study would not affect their clinical care at UAB or the BVAMC, and (3) time commitment related to study activities. All study patients randomized to the intervention arm signed the informed consent document prior to baseline data collection and baseline chart review.

Given the aims of the parent study to examine the effect of the ENABLE intervention on patient-reported outcome measures detailed in the "Overview of Parent Study" section above, the informed consent document signed in the parent study aligns with the quantitative-related specific aims of the study. We sought no additional informed consent for the qualitative strand, as the interviews were an additional data point embedded into the parent study. Study staff mailed a letter to potential participants describing the qualitative interview along with directions for an opt-out process. Then, the PI or other study staff contacted the potential participant by telephone in a secured interview room on the campus of UAB, a strategy to protect privacy. An example of the study letter and information sheet is in Appendix B. During the call, the study staff described the study, screened for exclusion through verification of study enrollment, and reaffirmed prior consent. The potential participant per the recruitment process would have received by mail a study letter and study information sheet (Appendix B). The study staff followed an UAB IRB-approved interview script (Appendix C) during the post-mailing follow-up call to conduct a review of prior consent discussions along with a detailed description of each section of the study information document. Study staff also

reviewed compensation, a $25 check, for completing the interview. Then study staff conducted an additional review of the potential participants' W-9 status and mailed W-9 forms for those interested in participating who did not complete a W-9 in the parent study or whose address had changed since enrollment in the parent study. Potential participants were encouraged to ask questions during the discussion and provide brief summaries of their understanding concerning the study, a common strategy for assuring comprehension (Agar, Ko, Sheehan, Chapman, & Currow, 2013). Potential risks associated with participation include distress related to the interview questions and confidentiality of the data. Concerning confidentiality, all study related documents were stored in a locked cabinet in a locked office only accessible by the PI.

Overall, informed consent for the dose study is two-fold. Due to the alignment of the aims of the quantitative strand with the parent study's aims, we did not seek additional consent for the embedded study. However, we did conduct a phone-based informed consent discussion along with mailed study information documents for all intervention participants who agreed to the semi-structured interviews of the qualitative strand.

Data Collection

Parent Study

The data for the parent ENABLE CHF-PC study was collected through phone-based collection with trained staff members. Study staff members underwent a week-long training that orients them to the study purpose, the data collection timeline, the study instruments, data entry, and bias. Shadowing and role-playing a data collection call was

also included in training. Patients were provided outcome measures response/answer choices in table format printed in size 14 font on yellow cardstock in their initial study mailing. Data collection calls were completed in a private room or office. Data collection call attempts were documented on a call log in the study database. The staff members read the instrument questions along with the responses for all instrument items. Participant responses were either recorded directly into the study database or recorded on paper. The study program manager performed data entry of written responses. Baseline data collection occurred after informed consent was documented. The baseline data collection lasted approximately 45 minutes. Subsequent data collection calls were approximately 40 minutes or less. If a study participant could not complete all the instruments in a single call, the data collector attempted to complete the rest of the instruments during the data collection window. If more than 7 data collection call attempts were made without success, the data collection for that time point was marked incomplete. If an intervention participant did not participate in both data collection and intervention calls after 10 weeks, the participant was considered a "passive withdrawal" and was removed from the study.

Data includes patient- and caregiver-self reported outcome measures collected every 8 weeks for 48 weeks. A schedule of data collection was available through the study database. Although the data collection schedule was set for every 8 weeks, a 2-week window before and after the designated time point was included due to patient or caregiver-related scheduling conflicts. This 4-week window is a strategy to maximize data collection at each time point. Appendix D is a table of all instruments included in the parent study. For this study, only data collection through 32 weeks was included in the

dataset. Data was limited to the time period between baseline and 32-week data collection as a reflection of Specific Aim #1 time periods. The selection of 16- and 32-week data was driven by the time period for per protocol intervention completion. The OPCC and telephone-based psychoeducational sessions were designed to be completed within 7 weeks of randomization. However, allocation notification and the introductory phone call by the nurse coach also added time to the ideal per-protocol intervention schedule. Given these factors and the ideal intervention duration, per protocol intervention completion would occur between 8- and 16- week data collection time points. Using the 16-week time point as a midpoint, we included data collected through 32-weeks to model intervention effects of the two dose groups before, during, and after the per-protocol schedule of weekly telephone sessions and OPCC.

Quantitative Strand

Identification of variables of interest in a study is linked to the specific aims or research questions (Polit & Beck, 2017). For the study, the following two specific aims guided variable selection: (1) examine the effect of dose of a palliative care intervention on QoL and healthcare resource use in older advanced HF patients and (2) determine whether patient characteristics (age, residence, comorbidities, disease severity) are associated with intervention dose attributes and completion.

The study included 14 variables for primary analyses. As mentioned in Chapters 1 and 2, the concept of dose is rarely specified in palliative care studies. Given the lack of consensus on the operationalization of intervention dose, Figure 1 (Chapter 1) and Table 1 (Chapter 2) list the common dose attributes of frequency, duration, amount, and

intensity found in other health literature (Manojlovich & Sidani, 2008; Reed et al., 2007; Voils et al., 2014). Ideal dose attribute values were also previously presented in Chapter 1, Figure 1. Table 2 includes the application of these dose attributes and definitions to the ENABLE CHF-PC study and new dose-related variables specific to the ENABLE intervention (dose, group, session count, standardized duration, and duration drift). However, the primary dose variable used in analyses was a new variable, a dichotomous variable of per-protocol intervention completion or noncompletion, a modified strategy of high/low dose categorization common in intervention dose analyses (Barry et al., 2014; Legrand et al., 2012; Reed et al., 2007). As previously noted, behavioral intervention dose is complex. By defining dose groups as complete (OPCC + 6 telephone sessions) or noncomplete ($\leq$ 6 telephone sessions $\pm$ OPCC), we aimed to sidestep issues of assigning weight to different intervention components such as the telephone sessions and the OPCC which may or may not be equivalent.

Table 2

Study Dose Variables

Dose Component Variables	**Definition**	**Unit of Measurement**
Frequency	Day(s) between contacts during CYC-guided telephone sessions	Days
Session Duration	Length of time of total telephone sessions intervention exposure (date of 1st session – date of last session)	Days
Standardized Duration	Overall days in study divided by number of telephone sessions completed	Days
Duration Drift	Day(s) difference from per-protocol telephone session date	Days
Amount	Total time of a single instance of contact	Minutes
Intensity/Engagement	Indicator for interventionist and participant involvement	Interventionist rated Likert scale (0-5)
Session Count	Number of telephone-based psychoeducational sessions completed	Whole number (0-6)
Dose Group	Completion versus non-completion of the intervention	Complete/Noncomplete (Dichotomous variable)

The duration of a behavioral intervention requiring multiple parties to agree upon a day to deliver an intervention component in a pragmatic trial is inherently difficult to measure. In essence, duration is how long a participant is exposed to an intervention or parts of an intervention. ENABLE CHF-PC was designed to be delivered as weekly sessions with a palliative care consultation within 7 weeks of randomization. Consequently, intervention duration is expected to be 7 weeks. However, difficulty in

scheduling and reaching participants by phone often led to the intervention being delivered over an extended time period that varied greatly by participant. As a result, while someone who completed all 6 sessions might complete all sessions by 80 days, another participant may have completed 3 sessions over the same period of 80 days. To normalize duration values, number of days from randomization to the completion of the last session was then divided by the total number of sessions completed, creating a session count/duration variable labeled "standardized duration." Smaller values of the standardized duration represent higher intensity and duration more closely aligned with the per-protocol duration of the intervention. Additionally, we created another duration variable, "duration drift", that reflected the difference in days between the ideal duration and frequency of the intervention (set from the date of randomization) and the date a telephone session was completed.

The study used the instruments measuring QoL and resource use from the parent study. A subset of the parent study dataset was given to the study PI. Only the study PI and UAB IRB-approved study members had access to this new dose dataset. The dose dataset is kept on a secure password-protected, firewalled server at UAB. Appendix E includes a table of definitions and measures of interest and Appendix F includes the full instruments from the parent study that were used in the proposed study.

Qualitative Strand

Recruitment for the qualitative strand began in September 2018. An amendment to the parent ENABLE CHF-PC study was approved by the UAB IRB in April 2018 (Appendix G). Once recruited, study participants were asked to participate in a semi-

structured interview by telephone with the PI or trained study staff. The trained study staff were nurse coaches in the parent study. Interviews were assigned to study staff who did not have contact with the patient during the parent study. The PI oversaw the 4-hour qualitative interview training activities with the study staff. Bi-weekly meetings with the study staff were held from October – April 2019 when interviews were being conducted to debrief and review ongoing interviews and interview procedure. The PI also reviewed all recordings and fields notes and provided feedback on interview procedure.

As indicated by Sandelowski (2000), qualitative descriptive studies usually use interviews as a source of data. The interviews lasted approximately 40 minutes and were audio recorded using a digital recorder. Appendix H includes the initial draft of the interview questions. An interview guide that includes 13 questions with prompt suggestions guided the semi-structured interview. Appendix C includes the final draft of the interview questions. The final interview guide included 14 open-ended questions and 1 investigator-created, forced choice question asking participants to rank their engagement with the intervention on a scale from 1 to 5. The interview guide was revised once based on ongoing interview question performance. Pilot testing of the semi-structured interview occurred prior to recruitment initiation to develop good interview practice (Creswell & Poth, 2018).

During the interview, the PI or study staff performing the interviews kept field notes (Marshall & Rossman, 2016) concerning the noise level, participant engagement, rapport, and question performance. Study staff also completed field notes after the completion of the interview. An example of the field note template is included in Appendix I. Journaling was used for transparency, auditability, and trustworthiness in the

study (Malagon-Maldonado, 2014), as journaling is often used for reflection of researcher's perspective and bias in qualitative studies (Munhall, 2012).

After completion of the interview, study staff notified the program manager responsible for processing incentives for the interview participants. Also after the interview, we downloaded the recording and stored it, along with the field note and memo, in a secured, firewalled drive housed and maintained by UAB. Access to the data was limited to the PI and the parent study program manager. Additional physical security included a key access-only office containing the computer used to access the university secured, firewalled, and encrypted server that housed the password-protected database. Encrypted audio recordings were sent to a transcribing service that is contracted by UAB. Recordings were transcribed verbatim. After review of the transcripts, transcripts were saved in the secured, firewalled drive at UAB. Then, recordings and transcripts were deleted from the transcribing service site.

Reliability and Validity

Quantitative Strand

Careful sampling procedures attempted to standardize the study process in the parent study and contributed to the external validity, whereas thorough staff training and use of data collection scripts may have helped minimize threats to internal validity. In addition to those previously described strategies to minimize validity threats, another consideration includes appropriate instrument selection (Polit & Beck, 2017). Other instrument considerations include availability, population appropriateness, and norms within a field (Polit & Beck, 2017). The study examined previously collected data,

addressing concerns about instrument availability and cost. Tables in Appendix D and E lists and describes the outcome measures associated with each variable. Appendix D also details the reliability of each instrument. The appropriateness and field norms of each instrument were evaluated with a rapid review of the literature as follows: (1) the Kansas City Cardiomyopathy Questionnaire (KCCQ) is a common QoL instrument in both older adults with heart failure (Green et al., 2000) and palliative care (Goodlin, 2009); (2) the Patient-Reported Outcomes Measurement (PROMIS)-Global Health 10 short form-physical and mental health only is a set of patient-centered assessments evaluating overall physical and mental health frequently used in palliative care populations (Teresi et al., 2016); (3) the Functional Assessment of Chronic Illness Therapy- Palliative Care (FACIT-PAL) has been used in a prior palliative care heart failure study (Rogers et al., 2017); (4) the Hospital Anxiety and Depression Scale (HADS) is a non-diagnostic depression measure validated in the general adult population (Bjelland et al., 2002) with established use in palliative care heart failure studies (Rogers et al., 2017); and (5) the Charlson Comorbidity Index is a measure of comorbidity severity commonly used in palliative care practice (Dickson, Buck, & Riegel, 2013).

Qualitative Strand

Trustworthiness, or the believability of findings, includes the following four elements: credibility, transferability, dependability, and confirmability (Lincoln and Guba, 1985). Triangulation or member checks are strategies to strengthen credibility or the truth value (Munhall, 2012). The study used both between-strand and within-qualitative strand triangulation. Triangulation involves multiple sources of data (Munhall,

2012), a step also detailed in the data collection section of this chapter as both audio recordings and patient-reported outcomes were used as data sources. Additionally, we performed member checking with four patient participants from the complete and noncomplete groups from the semi-structured interviews. The dissertation chair, Dr. Marie Bakitas, also provided oversight of code development and code refinement during biweekly meetings.

Data Analysis

Quantitative

Polit and Beck (2017) detail multiple steps necessary during data analysis including preanalysis, preliminary assessments of reviewing data quality, principle analyses, and interpretation. As outlined in Chapter 1 and using Polit and Beck (2017) as a guide, the data analysis plan for the quantitative strand included the following: (1) for preanalysis, using R software, we inspected data for outliers, cleaned data labels, and created a data dictionary; (2) for preliminary assessments, we inspected data for types of missingness and if appropriate, performed multiple imputations to code the missing data (Young & Johnson, 2015) and assessed dataset for heterogeneity and normality; and (3) for preliminary actions, we created new dose attribute variables and a dichotomous dose group variable. Addressing missingness in palliative care studies require careful consideration if the missingness is related to death or progression of the illness (missing not at random) (Preston et al., 2013). We approached each type of missingness differently so that outcome change was not overestimated (Higginson et al., 2013; Hussain et al., 2017). Individual-level data imputation was performed for outcome measures when

enough data were available. For example, on the KCCQ, if responses were missing for some of the 23 items, we imputed based on the other items in a subscale. Outcome data missingness was associated with not completing all of the intervention. We assessed normality and heterogenity of the data to guide the specific test to run in the next steps of analysis.

Next, we calculated descriptive statistics for dose attributes, all randomized ENABLE CHF-PC participants, and the qualitative interview subsample. Then, we performed bivariate analyses, including correlation (Spearman's Rho) and odds ratios (logistic models; multivariate models) to examine the relationship of individual sociodemographic or clinical factors with intervention completion (Outpatient palliative care consultation (OPCC) + 6 telephone-based psychoeducational sessions). We controlled for variables identified in the bivariate analyses and literature, including age (Oosterom-Calo et al., 2013), comorbidity (Guzman-Clark, van Servellen, Chang, Mentes, & Hahn, 2013; Kato et al., 2009), and residence (Holmes, Hughes, & Morrison, 2014), in the linear mixed models to examine dichotomous dose intervention effect. While linear mixed models are more robust to missing data, the relationship between missingness and the noncomplete intervention group likely led to an overestimate of effects.

Qualitative

Data analysis commenced when the interviews began, an approach common in qualitative descriptive studies (Sandelowski, 2000). A priori categories were created based on the 15 questions from the interview guide. Using NVivo 2.0 software, the study PI performed in-vivo coding of the transcripts. The study PI was supervised by her

dissertation chair, Dr. Marie Bakitas, an expert in qualitative analysis and the PI of the parent study. A debriefing strategy was employed to ensure credibility (Cooney, 2011), including reviewing and discussing the inductive code and theme generation process with the parent study PI (Marshall & Rossman, 2016). This activity was intended to support the study's credibility (Cooney, 2011). The PI also kept an audit trail for confirmability and dependability (Creswell & Poth, 2017; Lincoln & Guba, 1985) and detailed analytic memos/journal (Saldana, 2015). Following the analytic strategy of Miles, Huberman, and Saldana (2019), the first step of the analysis plan included memoing while reading the transcript, followed by reflective thinking. As the process of interviews was ongoing during analysis, findings from analysis altered some of the original interview questions. The analysis notes were then summarized into descriptive codes, which were added to a codebook used for analysis of other interviews. The a priori categories were then collapsed into 3 key areas: impressions of dose, facilitators/barriers of completion, and study outcomes. As analysis progressed, the facilitator/barrier category was then expanded and renamed "context," based on the descriptions provided by the participants. The final steps of the analysis plan included grouping and refining codes into common themes and categories, extracting all passages with a specified theme, and then interpreting the data with an emphasis on contrasts and comparisons (Miles, Huberman, & Saldana, 2019).

In addition to narrative description supported by exemplar quotes, interpretation included narrative weaving and matrix displays with the strands as columns (Miles, Huberman, & Saldana, 2019). A procedural diagram to aid with visualization of the timing of data collection, priority, and integration (Plano Clark & Ivankova, 2016) is

depicted in Appendix M. The matrix diagrams, presented in Chapter 4, includes results from the quantitative analysis and provides an interpretation of convergence and divergence concerning dose effects that addresses the integrated mixed method aim. Using the commentary by Guetterman et al. (2015) as a guide, we integrated the findings of the quantitative and qualitative strand using these matrices. The matrices includes findings related to intervention effect by dose category. The qualitative data included frequency counts for shared themes, a minimal data transformation (Happ, Dabbs, Tate, Hricik, & Erlen, 2006; Sandelowski, 2000). However, the transformation strategy was limited in order to maintain the methodological rigor of the qualitative strand (Moffatt, White, Mackintosh, & Howel, 2006). The study also used narrative weaving to explain the intersection of the qualitative and quantitative findings. Specific Aims #1-3 served as primary discussion points.

One possible outcome from the integration of the findings was discordance or incongruence between the strand results (Fetters et al., 2013). While Fetters et al. (2013) suggest examining the findings for sources of bias as well as reviewing the methods, others suggest providing potential rationales for discongruence in addition to careful examination of the study procedures and collecting additional data (Moffatt et al., 2006). Review of study procedures and identification of sources of bias were incorporated as steps for data integration during the interpretation phase. In the study, reflection on incongruence included considering these instances of incongruence as different aspects (Johnson & Schoonenboom, 2016; Moffatt et al., 2006) of the dose concept and included additional dialogue with participants and other study experts (i.e., Marie Bakitas or others as appropriate) (Farquhar, Ewing, & Booth, 2011).

Summary

Individuals living with HF experience poor QoL, significant symptom burden, high levels of anxiety and depression, and significant healthcare resource use. While patients in previous palliative care intervention studies often experienced improved QoL and resource use and lowered symptom burden, anxiety, and depression, intervention designs, including dosing, vary widely. This chapter provided a detailed description of the research design and methodology of the completed study. The concurrent mixed methods study used purposive sampling for the quantitative strand and purposive, maximum variation sampling for the qualitative strand to examine jointly palliative care intervention dose for HF patients. While the aims of the quantitative strand align with the parent ENABLE CHF-PC study purpose and fall within the confines of its informed consent process, additional consent for the semi-structured interviews was sought via detailed phone discussion. The study used both parent study data and original qualitative data collection. Additionally, the study included multiple strategies to address validity, including representative sampling, procedure fidelity, validated instruments, triangulation, and member checking. A multi-step data analysis plan concluded with the integration of quantitative analysis results with thematic analysis from the interviews.

CHAPTER FOUR

This study aimed to explore dose of the ENABLE CHF-PC intervention by describing patient participation in different components of the intervention, modeling the effect of intervention completion on QoL and resource use outcomes at 16- and 32-week time points (Specific Aim #1) and examining relationships between sociodemographic, clinical factors, and baseline patient-reported outcomes with session completion (Specific Aim #2). Concurrently, this study explored patient experiences and perspectives around dose attributes, components of the ENABLE CHF-PC intervention, and study-related QoL and healthcare resource use outcome change (Specific Aim #3). The findings of the quantitative strand (Specific Aims #1 & 2) and the qualitative strand (Specific Aim #3) were integrated to more fully understand intervention dose experience, intervention dose impact on outcomes, and overall study experience (Specific Aim #4). This chapter presents the findings from these aims.

First, descriptive statistics from intervention component completion are presented followed by the participants' sociodemographic and clinical information. Second, the participants' baseline patient reported outcomes scores are outlined. Third, addressing Aim #1, linear mixed models examining the impact of dose group on patient-reported QoL and resource use are presented. Next, addressing Specific Aim #2, correlation and odds ratios of sociodemographic and clinical characteristics with the number of intervention sessions are presented. A brief summary of the quantitative findings concludes this section. Then, addressing Specific Aim #3, the central themes of the semi-structured qualitative interviews are described and exemplar quotes are highlighted. A

brief summary of the qualitative findings concludes this section. Then the findings from the quantitative and qualitative strands are integrated. Instances of convergence and divergence between strands are highlighted and explored. This chapter concludes a short summary of the integrated findings.

Quantitative Strand Results

This section presents the results of the quantitative strand. The purpose of the quantitative strand was two-fold. First, we aimed to examine the impact of dichotomous doses groups (complete versus noncomplete, see Chapter 1 for definitions) of the ENABLE CHF-PC intervention (Specific Aim #1). Addressing Specific Aim #1, the results of the linear mixed models are detailed after descriptive statistics of the intervention and sample are presented. Second, we examined sociodemographic and clinical characteristics associated with intervention dose attributes (Specific Aim #2a) and intervention completion (Specific Aim #2b). To address Specific Aim #2, the correlation and odds ratios of patient characteristics with dose attributes and intervention completion are detailed. This section ends with a brief summary of the quantitative findings.

ENABLE CHF-PC Intervention Descriptive Statistics

A total of 208 participants of the ENABLE CHF-PC parent study were randomized to receive the intervention. Following guidelines described in the revised Consolidated Standards of Reporting Trials (CONSORT) statement (Moher, Schultz,

Altman, for the CONSORT Group, 2001), the study flow diagram for participants is illustrated in Figure 7.

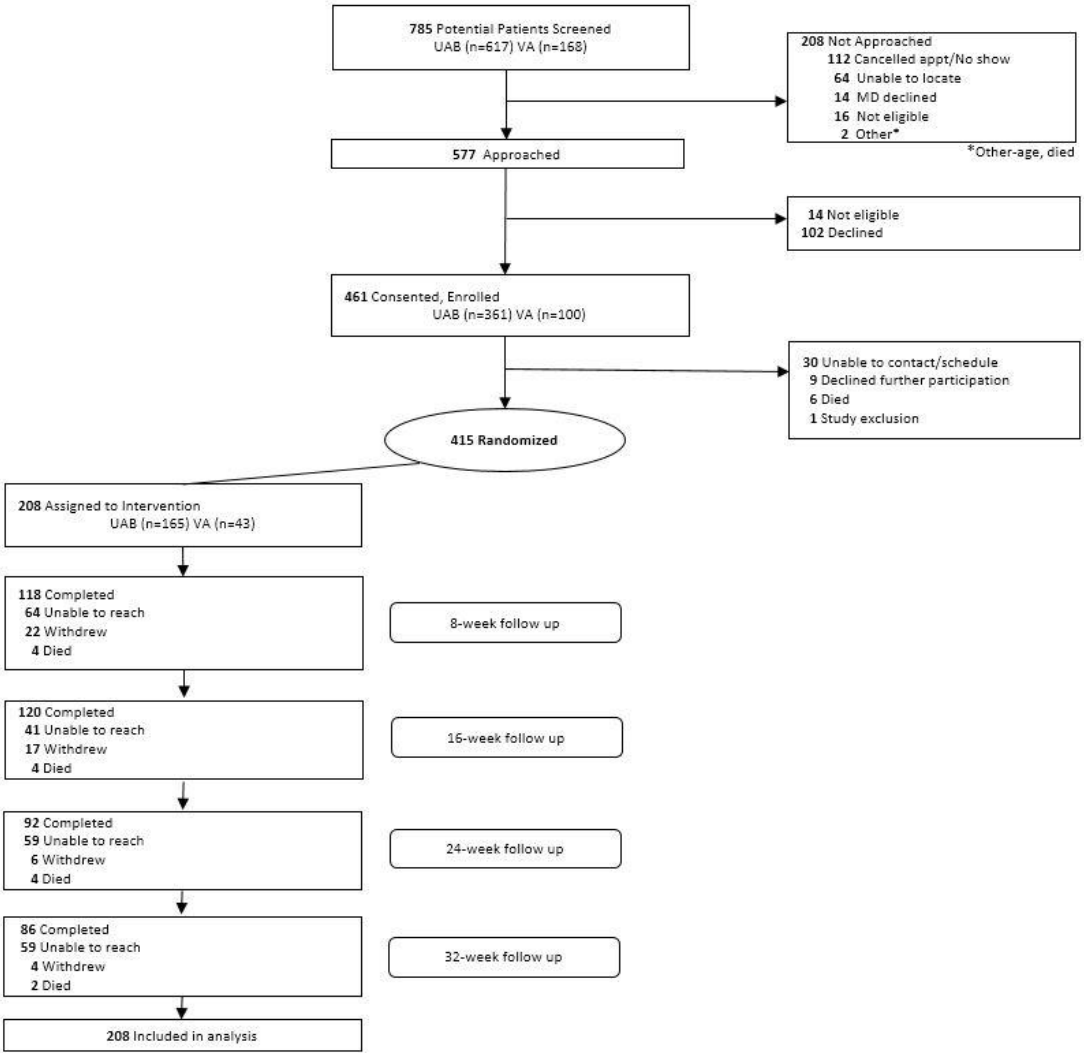


Figure 7. ENABLE CHF-PC Dose Study Consort Diagram- Quantitative Strand. From Moher, D., Schulz, K.F., & Altman, D.G. (2001) The CONSORT statement: Revised recommendations for improving the quality of reports of parallel-group randomized trials. *Annuals of Internal Medicine. 134*, 657-62.

While all intervention-arm participants were offered a total of 6 weekly sessions on topics of problem solving, self-care, symptom management, advance care planning, life review, and legacy building in addition to a single, in-person outpatient palliative care clinic visit at their primary recruitment site (UAB; BVAMC), participants completed

varying numbers of intervention components at different times. The sessions were completed in a specific order (see Chapter 1 for intervention figure; Chapter 3 for intervention session description). A total of 127 participants completed 6 Charting Your Course telephone sessions. Of those 127 participants, 81 completed the one time, in-person outpatient palliative care consultation (OPCC) (Table 3).

Table 3

ENABLE CHF-PC Intervention Session and OPCC Completion

Nurse-led, telephone-based psychoeducational sessions Completed	OPCC Completed (n=100)	OPCC Not Completed (n=108)
0 sessions	6	37
1 session (COPE & Problem-solving)	2	6
2 sessions (COPE & Problem-solving; Self-care)	4	4
3 sessions (COPE & Problem-solving; Self-care; Symptom management)	4	9
4 sessions (COPE & Problem-solving; Self-care; Symptom management; Communication & Decision-making)	3	6
5 sessions (COPE & Problem-solving; Self-care; Symptom management; Communication & Decision-making; Life review)	0	0
6 sessions (COPE & Problem-solving; Self-care; Symptom management; Communication & Decision-making; Life review; Legacy building)	81	46

The average session count, or the number of nurse-led telephone psychoeducational sessions completed, was 4.2 $\pm$ 2.5 sessions (Table 4). Overall average nurse-led telephone amount was 45.5 $\pm$ 16.1 minutes. Individual telephone session average length

in minutes are listed in Table 4. While nurse coaches attempted to contact participants within the 3 business days from the point of randomization, participants frequently did not complete the first session until 3 weeks (Mean=21.4 days; SD = 20.1 days) after randomization (Table 4). Time between telephone sessions averaged 17 days. Once the first telephone session was completed, participants averaged 70 days until all sessions were completed with the final telephone session completion occurring between the 8- and 16- week data collection time point. Of those who completed all intervention components, the first intervention telephone session was completed an average of 17.5 days from the point of randomization as opposed to 25.2 days for those who did not complete the entire intervention. The difference between these means was significant ($p=0.01$) with a moderate effect size ($d=0.4$). Mean difference in frequency, or time between completed telephone sessions, between those who completed the intervention as designed ($M=13.1$) and those who did not ($M=20.1$) was significant ($p=0.0005$) with a large effect size difference ($d=0.6$).

Table 4

ENABLE CHF-PC Intervention Participation

Variable	N	Mean	SD	Min	Max
Session Count	208	4.2	2.5	0.0	6.0
Amount of session 1 in minutes	167	49.4	19.1	13.0	129.0
Amount of session 2 in minutes	155	35.8	14.4	0.0	111.0
Amount of session 3 in minutes	149	37.8	15.0	11.0	100.0
Amount of session 4 in minutes	136	53.2	20.5	13.0	127.0
Amount of session 5 in minutes	128	46.9	26.1	6.0	250.0
Amount of session 6 in minutes	127	59.3	27.2	14.0	237.0
Individual session average in minutes	167	45.5	16.1	13.0	135.5
Average time between sessions (days)	208	17	13.0	6	106
Time from randomization to session 1 (days)	162	21.4	20.1	4.0	125.0
Session duration (days)	125	70.0	45.7	27.0	321.0
Time from randomization to session 6 (days)	125	89.4	53.8	39.0	334.0
Time from randomization to OPCC (days)	100	98.6	95.9	0.0	765.0

Note. N= number of sample represented in each variable, SD = standard deviation, Min = minimum data value in dataset, Max= maximum data value in dataset; OPCC=outpatient palliative care consultation

ENABLE CHF-PC Intervention Participant Sample Characteristics

Mean and standard deviations for continuous variables and frequency and proportions for categorical variables are displayed on Tables 5-8. Group difference effect sizes are displayed for all variables in Tables 5-8.

Sociodemographic characteristics. ENABLE CHF-PC participants randomized to receive the intervention (n=208) had a mean age of 63.5 $\pm$ 8 years with a nonsignificant difference in age between those who did and did not complete the intervention as designed. Tables 5 and 6 depict sociodemographic characteristics of ENABLE CHF-PC intervention participants. The majority of participants were recruited

from UAB (n=148, 71.2%). Most intervention-arm participants were black (n=113, 54.3%), married (n=105; 50.5%), male (n=111, 53.4%), living with others (n=165, 79.3%), and urban-dwelling (n=150, 72.1%) (Table 5).

While type of health insurance varied, most participants were well-educated with a high school education or above (n=179, 86.1%) and scored at the high school equivalent health literacy level on the Rapid Estimate of Adult Literacy in Medicine–Short Form (REALM) (n=192, 92.3%) (Arozullah et al., 2007) (Table 6). Most were retired or on disability (Table 6).

Most identified as Protestants (n=195, 93.8%) and regularly attended religious services (n=103, 49.5%) (Table 7). Most have prayed for their health (n=191, 91.8%) and reported praying for their health in the month prior to enrollment in the ENABLE CHF-PC study (n=183, 95.8%) (Table 7).

Almost all participants reported no alcoholic drink weekly intake (n=182, 87.5%) and just over half identified as current or previous smokers (n=119; 57.2%) (Table 8). Small to moderate differences were found between dose completion groups (Tables 5-8; Cohen's d: 0.22; Cramer's V: 0-0.20).

There were no statistically significant differences in baseline sociodemographic characteristics.

Table 5

ENABLE CHF-PC Sociodemographic Descriptive Statistics of Intervention Participants

Variable	All (N=208)		Complete (n= 81)		Noncomplete (n= 127)		Effect size
	n	%	n	%	n	%	d* or V
Age, M (SD)	63.5 (8)		64.6 (7.7)		62.8	(8.2)	0.22*
Gender							
Male	111	53.4	47	58.0	64	50.4	0.06
Female	97	46.6	34	42.0	63	49.6	
Hispanic/Latino							
No	207	99.5	80	98.8	127	100	0
Yes	1	0.5	1	1.2	0	0	
No response	0	0	0	0	0	0	
Race							
White	92	44.2	31	38.3	61	48.0	0
Black	113	54.3	49	60.5	64	50.4	
Other	3	1.4	1	1.2	2	1.6	
Site							0.18
UAB	148	71.2	51	63.0	97	76.4	
Birmingham VA	43	20.7	24	29.6	19	15.0	
Other clinic (HRSA)	17	8.2	6	7.4	11	8.6	
RUCA Residence							
Rural	58	27.9	22	27.2	36	28.3	0.002
Urban	150	72.1	59	72.8	91	71.7	
Marital Status							0.11
Never married	29	13.9	15	18.5	14	11.1	
Married or living with partner	105	50.5	37	45.7	68	54.0	
Divorced or separated	52	25	20	24.7	32	25.4	
Widowed	21	10.1	9	11.1	12	9.5	
Lives alone							
No	165	79.3	61	75.3	104	81.9	0.07
Yes	43	20.7	20	24.7	23	18.1	
Has caregiver enrolled in study							
No	126	60.6	44	54.3	82	64.6	0.09
Yes	82	39.4	37	45.7	45	35.4	

Note. Age range in years: 50 – 89; Cohen's d: small~0.2, medium~0.5, large~0.8; Cramer's V: .07- low, .07-.21 moderate, and >.35 is large

Table 6

ENABLE CHF-PC Sociodemographic Descriptive Statistics of Intervention Participants, continued

Variable	All (N=208)		Complete (n= 81)		Noncomplete (n= 127)		Effect size
	n	%	n	%	n	%	V
Work status							0.20
Employed	19	9.1	5	6.2	14	11.0	
Retired/Homemaker	82	39.4	40	49.4	42	33.1	
Not employed	2	1.0	1	1.2	1	0.8	
Disability	101	48.6	35	43.2	66	52.0	
Other	4	1.9	0	0	4	3.1	
Education							0.13
≤ 8th grade	3	1.4	2	2.5	1	0.8	
Some high school	26	12.5	5	6.2	21	16.5	
High school graduate or GED	82	39.4	33	40.7	49	38.6	
Some college or technical school	61	29.3	24	29.6	37	29.1	
College graduate	29	13.9	11	13.6	18	14.2	
Graduate degree	7	3.4	6	7.4	1	0.8	
Literacy in medicine (REALM-SF)							0.16
≤ 3rd grade	3	1.4	1	1.2	2	1.6	
4th to 6th grade	3	1.4	2	2.5	1	0.8	
7th to 8th grade	7	3.4	0	0	7	5.5	
≥ High school	192	92.3	77	95.1	115	90.6	
Unable to determine	3	1.4	1	1.2	2	1.6	
CAGE							0.03
0	198	95.2	79	97.6	119	93.7	
1	0	0	0	0	0	0	
2	2	1.0	0	0	2	1.6	
No response	8	3.8	2	2.4	6	4.7	
Medical insurance							
Private/commercial	44	21.2	18	8.7	26	12.5	0.15
Medicare	34	16.3	13	6.3	21	10.1	
Medicaid	23	11.1	6	2.9	17	8.2	
Military	26	12.5	14	6.7	12	5.8	
Medicare + Private	60	28.8	23	11.1	37	17.8	
Uninsured	21	10.1	7	3.4	14	6.7	

Note. Cramer's V: .07- low, .07-.21 moderate, and >.35 is large; Higher REALM-SF scores indicate higher grade equivalent

Table 7

ENABLE CHF-PC Religion Descriptive Statistics of Intervention Participants

Variable	All (N=208)		Complete (n= 81)		Noncomplete (n= 127)		Effect size
	n	%	n	%	n	%	V
Religion							0.09
Protestant	195	93.8	78	96.3	117	92.2	
Other	7	3.3	2	2.5	5	3.9	
None	6	2.9	1	1.2	5	3.9	
Attend religious services							0.16
Never	18	8.7	3	3.7	15	11.8	
Occasionally	85	40.9	35	43.2	50	39.4	
Regularly	103	49.5	43	53.1	60	47.2	
Not applicable	2	1	0	0	2	1.6	
Ever prayed for your own health							0.09
No	17	8.2	4	4.9	13	10.2	
Yes	191	91.8	77	95.1	114	89.8	
If yes, ever prayed in past month	183	95.8	72	93.5	111	97.4	

Note. Cramer's V: .07- low, .07-.21 moderate, and >.35 is large

Table 8

ENABLE CHF-PC Smoking and Alcohol Consumption Descriptive Statistics of Intervention Participants

Variable	All (N=208)		Complete (n= 81)		Noncomplete (n= 127)		Effect size
	n	%	n	%	n	%	V
Smoking							0.10
Yes	119	57.2	52	96.3	67	69.2	
No	89	42.8	29	1.2	60	1.6	
Packs per day*							
Less than ½ pack	5	27.8	2	28.6	3	27.3	
½ pack	9	50.0	4	57.1	5	45.4	
1 pack	2	11.1	0	0	2	18.2	
1 ½ packs	2	11.1	1	14.3	1	9.1	
Time since smoking*							0.15
Less than 1 month	3	3.0	1	2.2	2	3.6	
1-6 months	1	1.0	0	0	1	1.8	
6-12 months	3	3.0	1	2.2	2	3.6	
More than 12 months	92	92.0	42	93.4	50	91.0	
No response	1	1.0	1	2.2	0	0	
Range of smoking years			15-44 years		25-60 years		
Ever used other tobacco products							0.04
No	176	84.6	67	82.7	109	85.8	
Yes	32	15.4	14	17.3	18	14.2	
Alcoholic drinks per week							0.09
None	182	87.5	69	85.2	113	89.0	
1-5	22	10.6	11	13.6	11	8.6	
6-10	4	1.9	1	1.2	3	2.4	

Note. * sample size < 208; Cohen's d or d-equivalent: small~0.2, medium~0.5, large~0.8; Cramer's V: .07-low, .07-.21 moderate, and >.35 is large

Baseline clinical characteristics. Participants were diagnosed with advanced heart failure an average of 5.1 years prior to enrollment in the ENABLE CHF-PC study. The majority of participants had NYHA Class IIIa heart failure (n=168, 80.8%) with an average left ventricular ejection fraction of 40.9% and systolic blood pressure of 125.4 mmHg (Table 8). Using the Seattle Heart Failure Model, a heart failure-based prognostication tool based on a multivariate risk model that has been validated in multiple heart failure cohorts (Levy et al., 2006; Mozaffarian, et al., 2007), mean life expectancy was 7.0 $\pm$ 3.7 years with half of participants predicted to survive to 5 years (Table 9). Other disease diagnoses, like diabetes mellitus or chronic obstructive pulmonary disease, were common. Participants had an average comorbidity score of 3.2 as measured on the Charlson Comorbidity Index, a prognostic measure that incorporates aggregate disease burden (Charlson, Pompei, Ales, & MacKenzie, 1987). Exposure to palliative care services or advance care planning was low with the majority of participants not enrolled in a hospice program (n=199, 95.7%). Most had also not completed an advance directive (n=157, 75.5%) or do-not-resuscitate orders (n=177, 85.1%) (Table 9). All baseline clinical characteristics differences were not significant. Small differences were found for most variables between dose completion groups (Cramer's V: 0.01-0.27) with moderate effect size differences in left ventricular ejection fraction and systolic blood pressure. However, these differences do not have substantial clinical relevance.

Table 9

ENABLE CHF-PC Baseline Clinical Descriptive Statistics of Intervention Participants

Variable	All (N=208) Mean (SD)	Complete (n= 81) Mean (SD)	Noncomplete (n= 127) Mean (SD)	Effect size d
Years since advanced HF diagnosis	5.1 (5.1)	4.7 (4.3)	5.4 (5.5)	0.15
Weight (kg)	94.8 (24.7)	94.6 (23.6)	95.0 (25.4)	0.01
Ejection fraction	40.9 (16.4)	43.6 (16.3)	39.2 (16.4)	0.27
Systolic blood pressure	125.4 (20.6)	128.4 (19.4)	123.5 (21.1)	0.24
Charlson Comorbidity Index	3.2 (1.9)	3.0 (2.0)	3.3 (1.9)	0.12
Seattle HF Model				
Mean life expectancy (years)	7.0 (3.7)	7.1 (3.5)	6.9 (3.9)	0.03
1-year survival %	86.8 (11.3)	87.9 (10.0)	86.1 (12.1)	0.16
2-year survival %	76.3 (17.8)	78.0 (15.6)	75.2 (19.0)	0.16
5-year survival %	52.5 (24.8)	54.2 (22.2)	51.5 (26.4)	0.11
	n (%)	**n (%)**	**n (%)**	**V**
NYHA Class at baseline				
Class IIIa	168 (80.8)	69 (86.3)	99 (78.0)	0.10
Class IIIb	19 (9.1)	5 (6.2)	14 (11.0)	
Class IV	20 (9.6)	6 (7.5)	14 (11.0)	
Hospice program, last 2 months				0.02
No	199 (95.7)	77 (95.1)	122 (96.1)	
Yes	9 (4.3)	4 (4.9)	5 (3.9)	
Completed an advance directive				0.12
No	157 (75.5)	64 (79.0)	93 (73.2)	
Yes	50 (24)	16 (19.8)	34 (26.8)	
Don’t know	1 (0.5)	1 (1.2)	0 (0)	
Do-not-resuscitate order				0.07
No	177 (85.1)	68 (84.0)	109 (85.8)	
Yes	28 (13.5)	11 (13.6)	17 (13.4)	
Don't know	3 (1.4)	2 (2.4)	1 (0.8)	

Note. Cohen's d or d-equivalent: small~0.2, medium~0.5, large~0.8; Cramer’s V: .07- low, .07-.21 moderate, and >.35 is large; Higher Charlson Comorbidity Index scores indicate higher comorbidity-associated burden and lower likelihood of survival.

Baseline patient-reported outcome measures. Overall, mean scores on the KCCQ clinical summary (M=54.2 $\pm$ 20.5) and subscales indicate that participants had moderate perceived health status and QoL (M=58.3 $\pm$ 25.9) (Table 10). A majority of participants had baseline KCCQ scores above 50 (n=116, 55.7%) with several participants with scores > 90 (n=9, 4.3%). Hospital and emergency department visits were low as expected given that participants were recruited during non-acute follow up visits in cardiology outpatient clinics (Table 10). Other baseline measures indicate that participants had fair physical health status, moderate mental health status, and low anxiety and depressive symptoms. Primary coping responses included use of religion and acceptance followed by active coping, use of emotional support, use of instrumental support, and planning. Most of these strategies are problem-focused coping strategies (Litman, 2006). Small differences were found for most variables between dose completion groups (Cohen's d: 0.004-0.28). Larger, though still small, effect size differences were found in hospital days, mental health status, baseline anxiety, QoL, and coping responses of substance use, disengagement, and humor. Boxplots of the primary outcomes of the KCCQ summary scores and healthcare resource use means by dose group and data collection time points are displayed in Appendix J.

Table 10

ENABLE CHF-PC Baseline Patient-Reported Outcomes Descriptive Statistics of Intervention Participants

Variable	All (N=208) M(SD)	Complete (N=81) M(SD)	Noncomplete (N=127) M(SD)	Effect size d
KCCQ clinical summary	54.2 (20.5)	55.6 (20.8)	53.3 (20.4)	0.11
KCCQ functional status	51.5 (20.3)	53.6 (20.9)	50.2 (19.9)	0.17
KCCQ symptoms	52.2 (22.1)	53.5 (22.7)	51.4 (21.7)	0.10
KCCQ symptom frequency	52.9 (24.9)	53.8 (25.6)	52.3 (24.5)	0.06
KCCQ symptom severity	51.3 (22.0)	53.0 (22.2)	50.1 (21.8)	0.13
KCCQ QoL	58.3 (25.9)	58.2 (25.0)	58.3 (26.5)	0.004
KCCQ physical limitation	50.8 (24.0)	53.7 (24.1)	49.0 (23.9)	0.19
KCCQ social limitation	52.9 (27.3)	55.1 (26.7)	51.5 (27.6)	0.13
KCCQ self-efficacy	89.2 (16.4)	89.8 (16.3)	88.9 (16.5)	0.06
Hospital visits, last 8 weeks	0.5 (0.87)	0.43 (0.91)	0.55 (0.85)	0.13
Days in hospital, last 8 weeks	2.6 (5.23)	2.0 (4.7)	3.0 (5.5)	0.20
ICU days in hospital, last 8 weeks	0.5 (1.8)	0.23 (1.1)	0.62 (2.2)	0.21
ED visits, last 8 weeks	0.43 (0.85)	0.44 (0.99)	0.42 (0.75)	0.03
Secondary				
PROMIS Global Physical Health T	38.6 (8)	39.4 (8.4)	38.1 (7.8)	0.16
PROMIS Global Mental Health T	45.8 (8.6)	47.0 (8.7)	45.1 (8.5)	0.22
FACIT Pal 14	36.8 (9.3)	38.1 (9.4)	36.0 (9.2)	0.23
HADS Anxiety	6.6 (3.5)	6.0 (3.4)	7.0 (3.6)	0.28*
HADS Depression	5.7 (4.3)	5.3 (4.4)	6.0 (4.2)	0.17
Brief COPE- self distraction	1.5 (0.9)	1.5 (0.9)	1.5 (0.9)	0.1
Brief COPE- active coping	1.9 (0.9)	2.0 (0.9)	1.8 (1.0)	0.19
Brief COPE- denial	0.7 (0.9)	0.7 (0.9)	0.7 (0.9)	0.03
Brief COPE- substance use	0.1 (0.3)	0.05 (0.2)	0.13 (0.4)	0.22
Brief COPE- emotional support	1.9 (1.0)	2.0 (1.0)	1.9 (1.0)	0.08
Brief COPE- instrumental social support	1.8 (1.0)	1.7 (1.0)	1.6 (1.0)	0.07
Brief COPE- disengagement	0.4 (0.6)	0.4 (0.7)	0.3 (0.5)	0.27
Brief COPE- venting	1.0 (0.9)	1.0 (0.8)	1.0 (0.9)	0.003
Brief COPE- reframing	1.7 (0.9)	1.8 (0.9)	1.7 (1.0)	0.15
Brief COPE- planning	1.8 (1.0)	1.8 (1.0)	1.8 (1.0)	0.006
Brief COPE- humor	0.7 (1.0)	0.5 (0.7)	0.8 (1.0)	0.23
Brief COPE- acceptance	2.2 (0.9)	2.3 (0.9)	2.2 (0.9)	0.05
Brief COPE-religion	2.3 (0.9)	2.4 (0.9)	2.2 (1.0)	0.20
Brief COPE- self blame	0.7 (0.9)	0.7 (0.9)	0.8 (0.9)	0.03

Note. Cohen's d or d-equivalent: small~0.2, medium~0.5, large~0.8; KCCQ scores range from 0 to 100;Higher KCCQ scores indicate better perceived health status; PROMIS T scores have a mean of 50 and SD of 10 in the general US population; Higher PROMIS Global scores indicate better functioning; FACIT Pal 14 scale scores range from 0 to 56; Higher FACIT Pal 14 scores indicate better quality of life; HADS scale scores range from 0 to 21 with a cutoff score of 8 ;Higher HADS scores indicate more severe symptoms; COPE Inventory scores

* indicates $p < 0.05$

Specific Aim #1: Linear Mixed Models of Intervention Effects by Time Periods

The following section addresses Specific Aim #1, determine the relationship between ENABLE CHF-PC dichotomous intervention dose and patient-reported QoL and healthcare resource use at 16- and 32-weeks after baseline. Meeting Specific Aim #1 to examine the effect of intervention dose groups on change in patient-reported outcomes of QoL (KCCQ) and healthcare resource use, we fitted linear mixed models using dose group, data collection time points, the interaction between the group and time period and adjusted for covariates (Tables 11-14; Figures 8-13). The following covariates for the first set of linear mixed models were included based on their clinical significance in the literature: age, residence, NYHA HF classification as an indicator for disease severity, and comorbidity score. A second set of linear mixed models were fitted using dose group, data collection time points, the interaction between the group and time point, and adjusted for data-selected covariates of gender, NYHA HF classification, and baseline anxiety scores. No notable differences were found between the models fitted using the literature-based covariates and data-selected covariates. Models for hospital visits and ICU days failed to converged using R statistical software, likely due to noted issues with the glmer package and negative binomials (StackExchange, n.d.). After consultation with an expert statistician (A.A), we fitted linear mixed models in SAS statistical software with no issues of convergence. The fitted models using data-selected covariates for the KCCQ are included in Appendix K. In instances where there was complete separation between groups or collinearity, the covariate with separation was removed from the model. Random effects were added for individual participants, characterizing the

variation due to individual differences. Spaghetti plots depicting the primary outcome observations by each participants are included in Appendix L.

KCCQ change. The intra-class correlations were found to be <0.5 demonstrating there were associations on KCCQ repeated measurement within individual subject. Between-group change in KCCQ clinical summary score was significant at 16 weeks (p=0.002) with a magnitude of -9.71 and a moderate effect size (d=0.47). A mean difference of 5-points in the KCCQ clinical summary reflects a clinically significant change in HF status whereas a 10-point change has prognostic implications (Kelkar, et al., 2016). All other between group differences were not significant. Model-estimated within group change in the KCCQ of those who completed the intervention was approximately 5 points or greater starting at 16 weeks.

Healthcare resource use change. The intra-class correlations were found to be <0.5 demonstrating there were associations on healthcare resource use repeated measurement within individual subject. All between group differences were not significant.

Table 11

Model-estimated change in KCCQ and Resource Use at Week 8

	Within Group		Between Groups		
	Complete (n=81)	Non-complete (n=127)	Difference	Effect size	
	M (SE)	M (SE)	M (SE)	d	P value
KCCQ					
KCCQ clinical summary	4.20 (2.61)	0.59 (2.50)	-3.62 (3.16)	0.21	0.25
KCCQ functional summary	3.65 (2.64)	2.96 (2.53)	-0.69 (3.19)	0.03	0.83
KCCQ symptom summary	4.98 (2.83)	2.50 (2.75)	-2.48 (3.61)	0.11	0.49
Resource Use			Ratio Est. (SE)		
Days in Hospital	0.13 (0.88)	-1.65 (0.60)	-0.86 (0.77)	0.17	0.26
ER Visits in last 8 weeks	-0.06 (0.06)	-0.06 (0.06)	0.04(0.41)	0.05	0.92

Note. Change: Week 8 minus baseline; Difference: Noncomplete Intervention – Complete Intervention; Mean Ratio: Week 8 / Baseline; Ratio: Complete/Noncomplete;Linear mixed models adjusted for age, comorbidities, HF severity, and location; Cohen's d: small~0.2, medium~0.5, large~0.8, using baseline pooled SD; KCCQ scores range from 0 to 100 (baseline pooled SD=20.52 for clinical summary, SD=20.33 for functional status, SD = 22.07 for symptom status); Higher KCCQ scores indicate better perceived health status; Days in hospital baseline pooled SD=5.23; ED visits SD=0.85

Table 12

Model-estimated change in KCCQ and Resource Use at Week 16

	Within Group		Between Groups		
	Complete (n=81)	Non-complete (n=127)	Difference	Effect size	
	M (SE)	M (SE)	M (SE)	d	P value
KCCQ					
KCCQ clinical summary	9.88 (2.55)	0.17 (2.57)	9.71 (3.18)	0.47	0.002
KCCQ functional summary	7.88 (2.59)	3.51 (2.60)	4.37 (3.21)	0.22	0.17
KCCQ symptom summary	10.05 (2.77)	3.99 (2.83)	6.83 (4.14)	0.27	0.09
Resource Use			Ratio Est. (SE)		
Days in Hospital	-0.41 (0.63)	-1.53 (0.68)	1.12 (0.77)	0.09	0.54
ER Visits in last 8 weeks	-0.14 (0.04)	-0.09 (0.06)	0.35 (0.43)	0.41	0.43

Note. Change: Week 16 minus baseline; Difference: Complete Intervention – Noncomplete Intervention; Mean Ratio: Week 16 / baseline; Ratio: Complete/Noncomplete;Linear mixed models adjusted for age, comorbidities, HF severity, and location; Cohen's d: small~0.2, medium~0.5, large~0.8, using baseline pooled SD; KCCQ scores range from 0 to 100 (baseline pooled SD=20.52 for clinical summary, SD=20.33 for functional status, SD = 22.07 for symptom status); Higher KCCQ scores indicate better perceived health status; Days in hospital baseline pooled SD=5.23; ED visits SD=0.85

Table 13

Model-estimated change in KCCQ and Resource Use at Week 24

	Within Group		Between Groups		
	Complete (n=81)	Non-complete (n=127)	Difference	Effect size	
	M (SE)	M (SE)	M (SE)	d	P value
KCCQ					
KCCQ clinical summary	7.48 (2.66)	1.64 (2.96)	-5.84 (3.59)	0.28	0.10
KCCQ functional summary	4.66 (2.48)	1.00 (3.03)	-3.67 (3.65)	0.18	0.32
KCCQ symptom summary	6.77 (2.91)	-0.05 (3.34)	-6.83 (4.14)	0.31	0.10
Resource Use			Ratio Est. (SE)		
Days in Hospital	-0.53 (0.63)	-1.61 (0.81)	-0.45 (0.86)	0.09	0.58
ER Visits in last 8 weeks	-0.07 (0.06)	-0.15 (0.06)	-0.43 (0.52)	0.51	0.40

Note. Change: Week 24 minus baseline; Difference: Complete Intervention – Noncomplete Intervention; Mean Ratio: Week 24 / week 16; Ratio: Complete/Noncomplete;Linear mixed models adjusted for age, comorbidities, HF severity, and location; Cohen's d: small~0.2, medium~0.5, large~0.8, using baseline pooled SD; KCCQ scores range from 0 to 100 (baseline pooled SD=20.52 for clinical summary, SD=20.33 for functional status, SD = 22.07 for symptom status); Higher KCCQ scores indicate better perceived health status; Days in hospital baseline pooled SD=5.23; ED visits SD=0.85

Table 14

Model-estimated change in KCCQ and Resource Use at Week 32

	Within Group		Between Groups		
	Complete (n=81)	Non-complete (n=127)	Difference	Effect size	
	M (SE)	M (SE)	M (SE)	d	P value
KCCQ					
KCCQ clinical summary	6.23 (2.72)	6.37 (2.99)	0.14 (3.64)	0.01	0.97
KCCQ functional summary	4.90 (2.75)	7.73 (3.02)	2.83 (3.67)	0.14	0.44
KCCQ symptom summary	5.22 (2.97)	6.56 (3.33)	1.34 (4.16)	0.06	0.75
Resource Use			Ratio Est. (SE)		
Days in Hospital	-0.81 (0.53)	-2.07 (0.55)	-0.63 (0.88)	0.12	0.47
ER Visits in last 8 weeks	-0.08(0.06)	-0.15(0.06)	-0.36 (0.52)	0.42	0.49

Note. Change: Week 32 minus baseline; Difference: Complete Intervention – Noncomplete Intervention; Mean Ratio: Week 32 / Baseline; Ratio: Complete/Noncomplete;Linear mixed models adjusted for age, comorbidities, HF severity, and location; Cohen's d: small~0.2, medium~0.5, large~0.8, using baseline pooled SD; KCCQ scores range from 0 to 100 (baseline pooled SD=20.52 for clinical summary, SD=20.33 for functional status, SD = 22.07 for symptom status); Higher KCCQ scores indicate better perceived health status; Days in hospital baseline pooled SD=5.23; ED visits SD=0.85

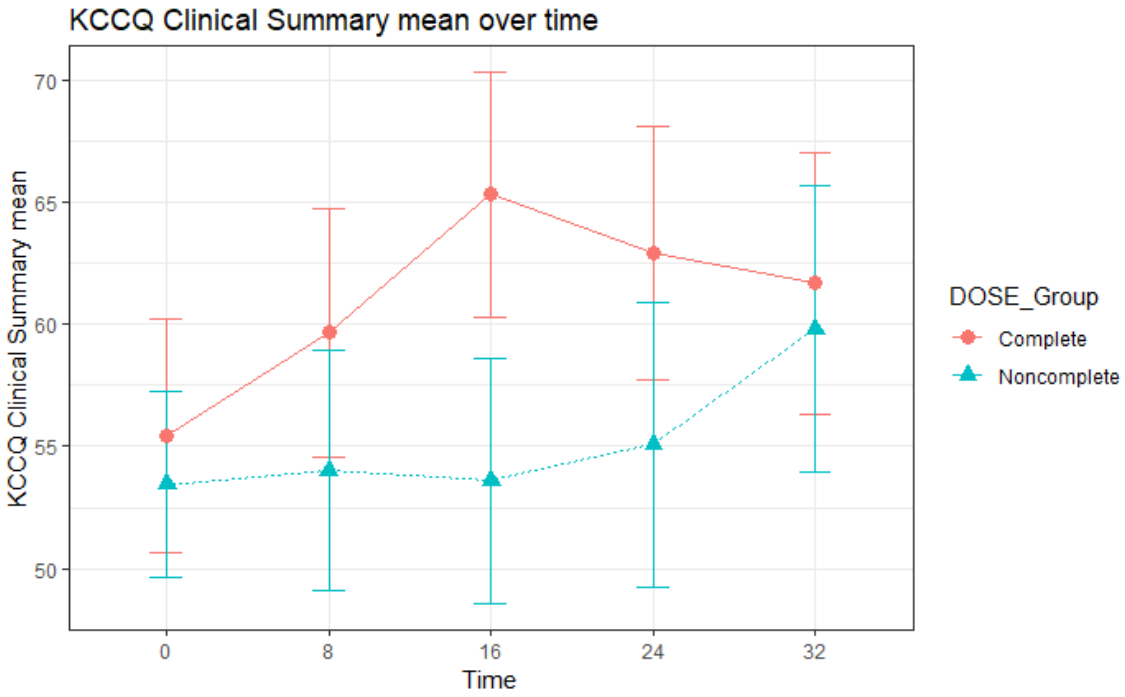


Figure 8. Modeled KCCQ Clinical Summary Means over Time by Dose Groups.

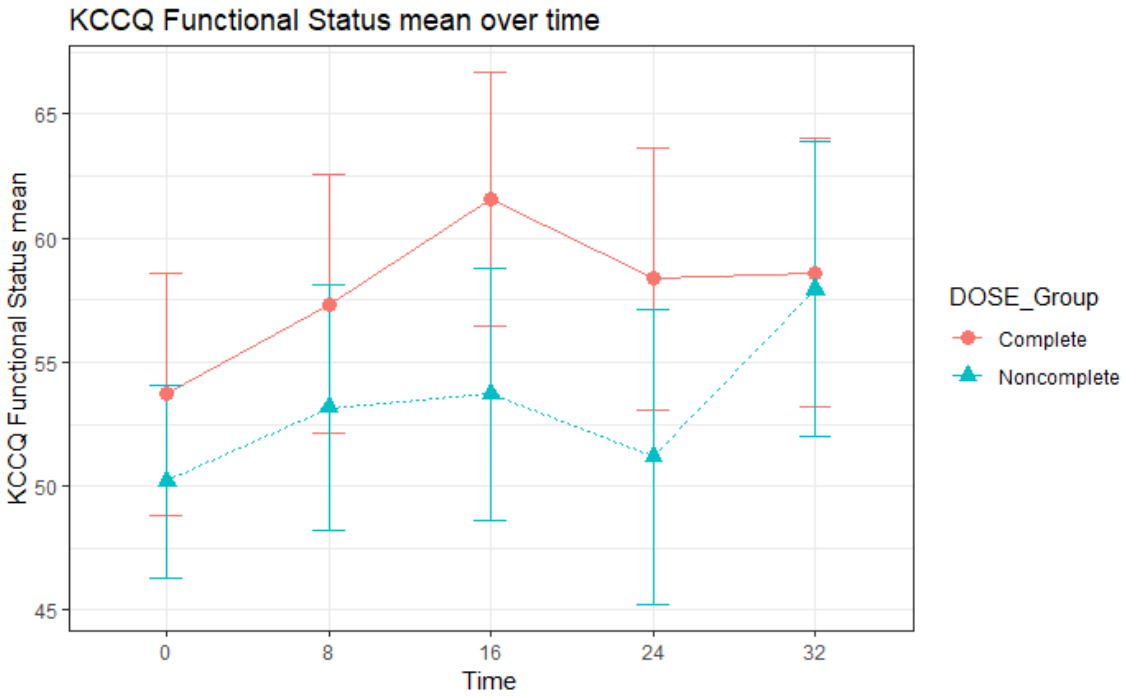


Figure 9. Modeled KCCQ Functional Status Means over Time by Dose Groups

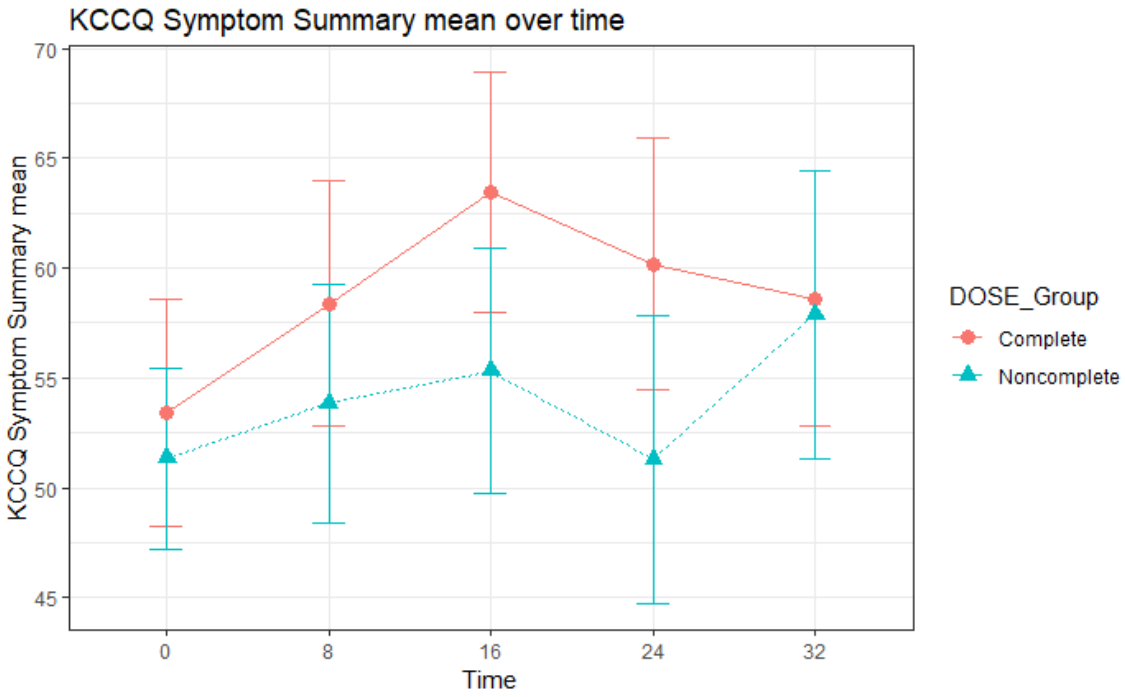


Figure 10. Modeled KCCQ Symptom Summary Means over Time by Dose Groups

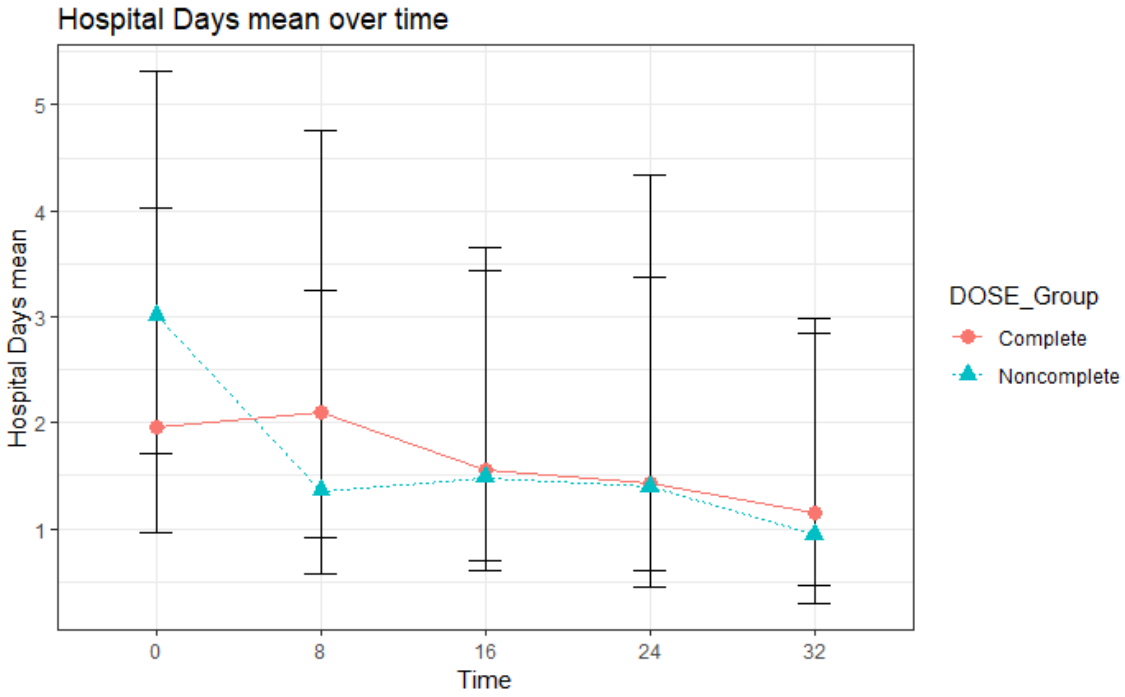


Figure 11. Modeled Hospital Days Means over Time by Dose Groups

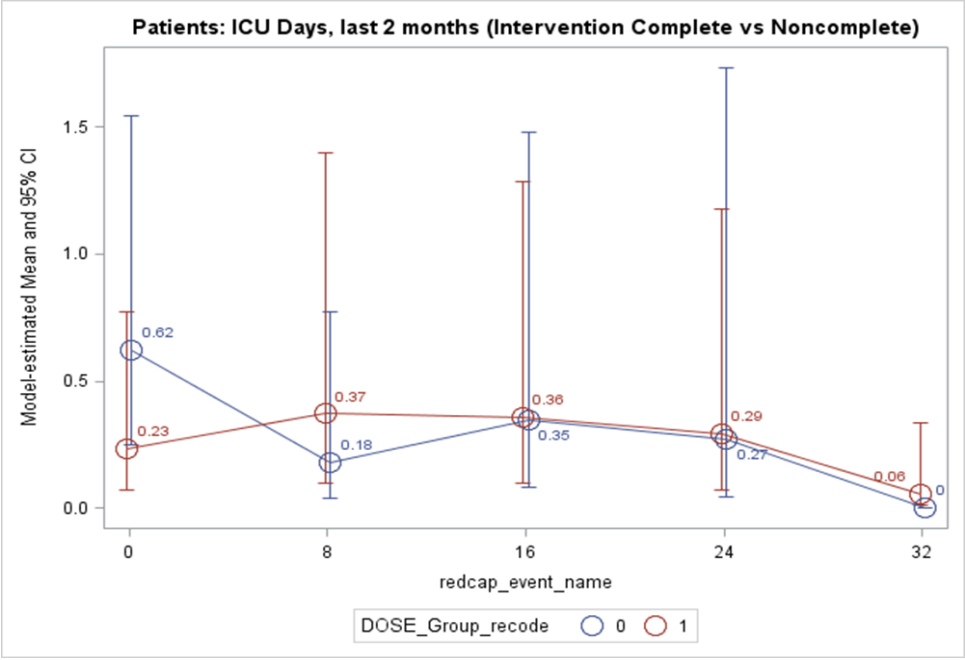


Figure 12. Modeled ICU Days over Time by Dose Groups. Modeled ICU days means over data collection time points by intervention completion groups. Blue '0' represents noncomplete group; Red '1' represents complete

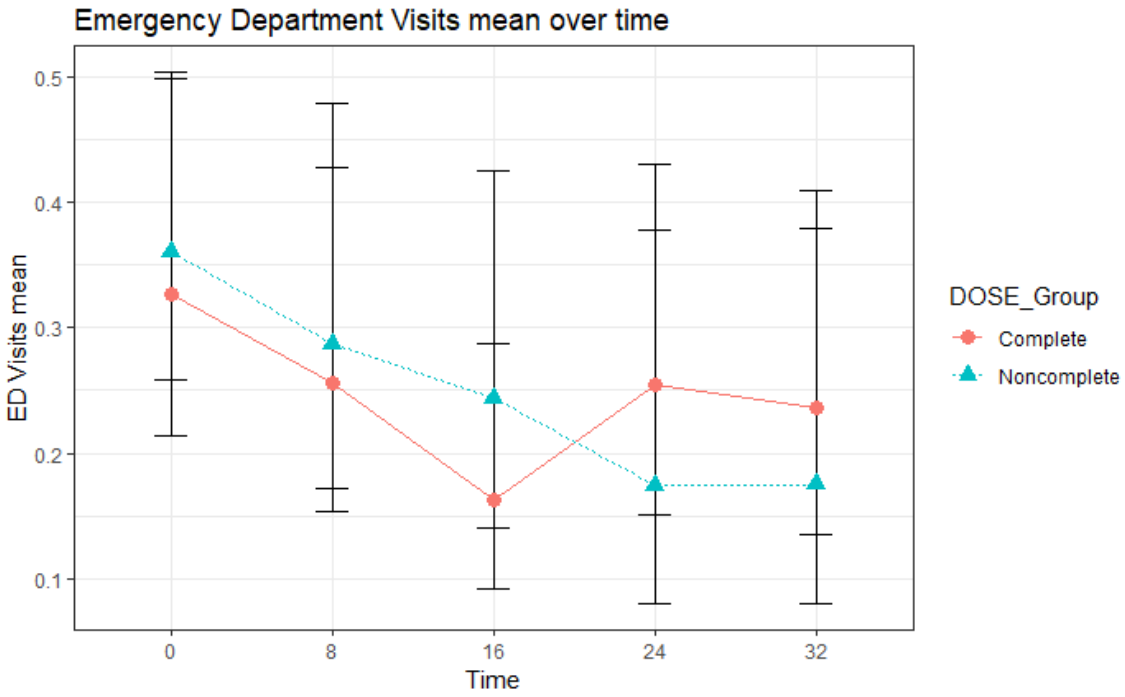


Figure 13. Modeled Emergency Department Visits Means over Time by Dose Groups

Specific Aim #2: Relationships between Dose Groups and Baseline Characteristics

The following section addresses Specific Aim #2, to determine the relationship between ENABLE CHF-PC patient characteristics (age, residence, comorbidities, HF disease severity) and intervention dose attributes and completion.

First, meeting Specific Aim #2a to determine the relationships between age, comorbidities, and HF disease severity and dose attributes of amount and frequency, we performed correlations between baseline clinical variables dose attributes of amount and frequency. As defined in Chapter 1, amount is the length of time of the intervention or intervention component and frequency is the number of days between completed intervention contacts. For the ENABLE CHF-PC intervention, amount is the number of minutes per completed nurse-led telephone session and frequency is the number of days

between completed telephone sessions. The results of these Spearman's rho correlations are listed in Table 14.

Associations between clinical characteristics and dose attributes.

While correlations were calculated between all clinical continuous variables, the focus of Specific Aim #2a was to examine the relationship between dose attributes. The strongest relationship was found between frequency and NYHA classification (r_s =0.40, $p<0.05$), indicating that as days between session completion increase so does the NYHA class (Table 15). For amount, ejection fraction, or the estimated pumping function of the left ventricle, has a positive mild association (r_s=0.17). Higher ejection fraction indicates better overall pumping function. This small association indicates that as ejection fraction increases, the average minutes per nurse-led telephone session also increases. For session count, or intervention session completion, all correlations were small to moderate ($r_s<0.37$) and most were not significant except associations with amount and frequency and a small, positive correlation with patient age. This small association indicates that as age increases so does the number of sessions completed. Additionally, while not significant, the next strongest association with session count is between NYHA HF classification and session count (r_s = -0.11) indicating that as NYHA class increases, session completion decreases. Both age and NYHA HF classification were identified in Chapter 2 as likely contributors to intervention completion and were included in the linear mixed models presented in a previous section.

Table 15

Correlations of ENABLE CHF-PC Baseline Clinical Variables with Dose Attributes

Variable	1	2	3	4	5	6	7	8	9	10	11
1.Session count	-	0.23*	-0.37*	0.13*	-0.03	-0.03	-0.03	-0.11	0.08	0.06	0.01
2.Amount	0.23*	-	-0.16*	0.07	0.00	0.00	0.03	-0.05	0.17*	0.00	0.00
3.Frequency	-0.37*	-0.16*	-	-0.11	-0.01	-0.08	-0.11	0.40*	-0.05	-0.06	-0.02
4.Patient age	0.13*	0.07	-0.11	-	0.10	-0.14*	-0.14*	0.03	0.19*	0.03	-0.12
5.Charlson comorbidity score	-0.03	0.00	-0.01	0.10	-	-0.19*	-0.23*	0.14*	-0.11	-0.08	0.02
6.SHFM mean life expectancy (years)	-0.04	0.00	-0.08	-0.14*	-0.19*	-	0.91*	-0.39*	-0.03	0.32*	-0.19*
7.SHFM 5 year mortality	0.003	0.03	-0.11	-0.14*	-0.23*	0.91*	-	-0.46*	0.03	0.34*	-0.19*
8.NYHA class (ordinal)	-0.11	-0.05	0.40*	0.03	0.14*	-0.39*	-0.46*	-	-0.04	-0.19*	0.11
9.Ejection fraction	0.08	0.17*	-0.05	0.20*	-0.11	-0.03	0.03	-0.05	-	0.28*	-0.08
10.Systolic blood pressure	0.07	0.00	-0.06	0.04	-0.08	0.31*	0.34*	-0.19*	0.28*	-	-0.11
11.Inotropes/ Vasopressors	0.01	0.00	-0.02	-0.12*	0.02	-0.19*	-0.19*	0.11	-0.09	-0.11	-

Note. Spearman's rho correlation (absolute value): small ~0.1; medium ~0.3; large ~0.5 or greater
*indicates p-values were <0.05;

Associations between baseline patient-reported outcomes and dose attributes.

Spearman's rho correlations between baseline patient-reported outcomes of QoL, physical health, mental health, anxiety, and depression, and dose attributes of amount and frequency are listed in Table 16. Frequency, or the days between session completions, had a significant moderate, positive association with anxiety scores (r_s=0.30), indicating that as the number of days between sessions increase, the scores on the HADS-anxiety, which measures anxiety symptoms, also increases. Similarly, frequency had a smaller, significant positive association with depression scores (r_s=0.21). For session count, all correlations with baseline measures were small (r_s<0.09) and nonsignificant. Large,

significant associations ($r_s > 0.5$) were found between instruments and instrument subscales measuring similar constructs such as the following: (1) physical health: KCCQ-Functional status score and PROMIS- Global physical health, (2) mental health: HADS-Depression, HADS-Anxiety, and PROMIS- Global mental health, and (3) QoL: KCCQ Clinical summary and FACIT-Pal.

Table 16

Correlations of ENABLE CHF-PC Baseline Outcome Measures with Dose Attributes

Variable	1	2	3	4	5	6	7	8	9	10	11
1.Session count	-	0.23*	-0.37*	-0.09	0.01	0.07	0.04	0.05	0.04	0.08	0.07
2.Amount	0.23*	-	-0.16*	-0.01	0.00	-0.06	-0.08	-0.08	-0.03	-0.02	-0.08
3.Frequency	-0.37*	-0.16*	-	0.30*	0.20*	-0.19*	-0.16*	-0.12*	-0.14*	-0.17*	-0.16*
4.HADS-Anxiety	-0.09	-0.01	0.30*	-	0.588	-0.62*	-0.46*	-0.42*	-0.47*	-0.62*	-0.66*
5.HADS-Depression	0.01	0.00	0.21*	0.58*	-	-0.53*	-0.39*	-0.38*	-0.39*	-0.66*	-0.62*
6.KCCQ-Clinical summary	0.07	-0.06	-0.19*	-0.62*	-0.53*	-	0.82*	0.79*	0.66*	0.55*	0.74*
7.KCCQ-Functional status	0.04	-0.08	-0.16*	-0.46*	-0.398	0.82*	-	0.87*	0.65*	0.42*	0.56*
8.KCCQ-Symptom summary	0.05	-0.08	-0.12	-0.42*	-0.38*	-0.79*	0.87*	-	0.58*	0.39*	0.59*
9.PROMIS-Global physical health	0.04	-0.03	-0.14	-0.47*	-0.39*	0.66*	0.65*	0.58*	-	0.52*	0.56*
10.PROMIS-Global mental health	0.08	-0.02	-0.17*	-0.62*	-0.66*	0.55*	0.42*	0.39*	0.52*	-	0.67*
11. FACIT-Pal	0.07	-0.08	-0.16*	-0.66*	-0.62*	0.74*	0.57*	0.59*	0.56*	0.67*	-

Note. Spearman's rho correlation (absolute value): small ~0.1; medium ~0.3; large ~0.5 or greater
* indicates p-values were <0.05

Associations between baseline healthcare resource use and dose attributes.

Spearman's rho correlations between baseline patient-reported hospital visits, hospital days, ICU days, and ED visits in the last 8 weeks and dose attributes of amount and frequency are listed in Table 17. For the dose attributes (amount, frequency), all

correlations with baseline healthcare resource use were small (r_s<0.10) and nonsignificant. Given that healthcare resource use variables were potentially measuring related constructs, most associations between healthcare resource use variables were moderate to large (r_s =0.29-0.70) and significant.

Table 17

Correlations of ENABLE CHF-PC Baseline Healthcare Resource Measures with Intervention Session Count

Variable	1	2	3	4	5	6	7
1.Session count	-	0.23*	-0.37*	0.08	-0.03	0.04	0.06
2.Amount	0.23*	-	-0.16*	-0.10	-0.06	0.06	0.06
3.Frequency	-0.37*	-0.16*	-	0.05	0.04	0.02	0.02
4.Hospital visits	0.08	-0.10	0.05	-	0.70*	0.29*	0.69*
5.Hospital days	-0.03	-0.06	0.04	0.70*	-	0.44*	0.46*
6.ICU days	0.04	0.06	0.02	0.29*	0.44*	-	0.16*
7.ED visits	0.06	0.00	0.02	0.69*	0.46*	0.16*	-

Note. Spearman's rho correlation (absolute value): small ~0.1; medium ~0.3; large ~0.5 or greater
* indicates p-values were <0.05

Associations between outcome change and dose attributes. Spearman's rho correlations between the outcome change from baseline to 16 weeks in the KCCQ clinical summary, hospital visits, days in the hospital, days in the ICU, and ED visits and dose attributes of amount and frequency are listed in Table 18. Spearman's rho correlations between the outcome change from baseline to 32 weeks in the KCCQ clinical summary, hospital visits, days in the hospital, days in the ICU, and ED visits and dose attributes of amount and frequency are listed in Table 19.

For the dose attributes, all correlations with KCCQ clinical summary and healthcare resource use outcome change at 16 weeks were small (rs<0.14) and

nonsignificant. For the dose attributes, all correlations with KCCQ clinical summary and healthcare resource use outcome change at 32 weeks were small (rs<0.22) and nonsignificant.

Given that healthcare resource use variables were potentially measuring related constructs, some associations between outcome change in healthcare resource use variables at 16- and 32-weeks were moderate to large (r_s = 0.26-0.80) and significant. Additionally, the KCCQ clinical summary is moderately negatively associated (rs= -0.34) with the change in ICU days at 32- weeks.

Table 18

Correlations of ENABLE CHF-PC Dose Attributes with Outcome Change at 16 weeks

Variable	1	2	3	4	5	6	7	8
1.Session count	-	0.23*	-0.37*	0.03	0.06	0.14	-0.06	-0.04
2.Amount	0.23*	-	-0.16*	0.07	0.03	0.04	-0.02	-0.07
3.Frequency	-0.37*	-0.16	-	0.03	0.01	0.04	-0.05	0.05
4.KCCQ-Clinical summary	0.03	0.07	0.03	-	-0.13	0.03	-0.03	0.14
5. Hospital Visits	0.06	0.03	0.01	-0.13	-	0.79*	0.41*	0.49*
6.Hospital Days	0.14	0.04	0.04	0.03	0.79*	-	0.43*	0.49*
7.ICU Days	-0.06	-0.02	-0.05	-0.03	0.41*	0.43*	-	0.80*
8. ED visits	-0.04	-0.07	0.05	0.14	0.49*	0.49*	0.80*	-

Note. Outcome change = Score at 16 weeks – Score at baseline; Spearman's rho correlation (absolute value): small ~0.1; medium ~0.3; large ~0.5 or greater; ENABLE CHF-PC = Educate, Nurture, Advise Before Life Ends Comprehensive Heartcare for Patients and Caregivers; KCCQ = Kansas City Cardiomyopathy Questionnaire; ICU= intensive care unit, ED = emergency department
* indicates p-values were <0.05

Table 19

Correlations of ENABLE CHF-PC Dose Attributes with Outcome Change at 32 weeks

Variable	1	2	3	4	5	6	7	8
1.Session count	-	0.23*	-0.37*	0.07	-0.05	-0.04	-0.06	-0.05
2.Amount	0.23*	-	-0.16*	0.22	0.05	-0.02	-0.10	-0.05
3.Frequency	-0.37*	-0.16	-	0.09	0.19	0.25	0.14	0.15
4.KCCQ-Clinical summary	0.07	0.22	0.09	-	-0.05	-0.15	-0.34*	0.06
5. Hospital Visits	-0.05	0.05	0.19	-0.05	-	0.76*	0.15	0.56*
6.Hospital Days	-0.04	-0.02	0.25	-0.15	0.76*	-	0.34*	0.56*
7.ICU Days	-0.06	-0.10	0.14	-0.34*	0.15	0.34*	-	0.20
8. ED visits	-0.05	-0.05	0.15	0.06	0.56*	0.56*	0.20	-

Note. Outcome change = Score at 32 weeks – Score at baseline; Spearman's rho correlation (absolute value): small ~0.1; medium ~0.3; large ~0.5 or greater; ENABLE CHF-PC = Educate, Nurture, Advise Before Life Ends Comprehensive Heartcare for Patients and Caregivers; KCCQ = Kansas City Cardiomyopathy Questionnaire; ICU= intensive care unit, ED = emergency department
* indicates p-values were <0.05

Odds ratios between sociodemographic and clinical characteristics and dose groups. Meeting Specific Aim #2b to determine the relationships between residence and HF disease severity and intervention completion, we performed logistic regressions between sociodemographic and clinical characteristics and intervention dose group. Table 20 depicts crude odds ratios, adjusted odds ratios, and confidence intervals calculated by logistic models for crude ratios and a single multivariate model that accommodated for an additive covariate model approach for adjusted ratios. For odds ratios, when the ratio is less than 1, it indicates a unit increase associated with the odds of completing the intervention as designed. For participants to complete the intervention and be labeled in the dose group, "complete," they completed the in-person OPCC and 6 nurse-led telephone-based psychoeducational sessions.

Black participants were 1.4 times more likely their white counterparts to complete the intervention. Similarly, those living alone (Adjusted OR=1.8), with a caregiver

enrolled in study (Adjusted OR=2.5), who attending religious services regularly (Adjusted OR=6.4), were retired (Adjusted OR=1.9), had completed college or beyond (Adjusted OR=4.3), with high school-level equivalent for health literacy (Adjusted OR=2.9) were more likely to complete the intervention. Participants who were female (Adjusted OR= 0.6), who were or previously married (Adjusted OR= 0.3-0.5), or whose HF was classified as more severe (Adjusted OR = 0.5- 0.6) were less likely to complete the entire intervention.

Table 20

Baseline Sociodemographic and Clinical Odds Ratios and Confidence Intervals for Intervention Completion

	Unadjusted		Adjusted	
Variable	**OR**	**95% CI**	**OR**	**95% CI**
Race				
White	Ref.	-	Ref.	-
Black	1.5	[0.9, 2.7]	1.4	[0.7, 2.8]
Other	1.0	[0.04, 10.7]	0.8	[0.02, 16.3]
Living Status				
With others	Ref.	-	Ref.	-
Alone	1.5	[0.7, 2.9]	1.8	[0.7, 4.8]
Caregiver				
Not in study	Ref.	-	Ref.	-
Enrolled in study	1.5	[0.9, 2.7]	2.5	[1.2, 5.3]
Gender				
Male	Ref.	-	Ref.	-
Female	0.5	[0.4, 0.7]	0.6	[0.3, 1.4]
Recruitment site				
VA Medical Center	Ref.	-	Ref.	-
Other Clinic (HRSA)	0.4	[0.1, 1.3]	0.7	[0.1, 3.4]
UAB	0.4	[0.2, 0.8]	0.3	[0.1, 0.7]
Marital Status				
Never Married	Ref.	-	Ref.	-
Married/Living with Partner	0.5	[0.2, 1.2]	0.3	[0.1, 0.8]
Divorced/Separated	0.6	[0.2, 1.5]	0.5	[0.2, 1.4]
Widowed	0.7	[0.2, 2.2]	0.4	[0.1, 1.7]
Residence				
Rural	Ref.	-	Ref.	-
Urban	1.1	[0.6, 2.0]	0.8	[0.4, 1.8]
Attends religious services				
Never	Ref.	-	Ref.	-
Occasionally	4.0	[1.2, 17.9]	4.3	[1.1, 22.0]
Regularly	4.1	[1.3, 18.2]	6.4	[1.7, 33.4]
Work status				
Disability	Ref.	-	Ref.	-
Retired/Homemaker	1.8	[1.0, 3.3]	1.9	[0.9, 4.1]
Not employed/Other	0.4	[0.02, 2.5]	0.2	[0.0, 2.0]
Employed	0.7	[0.2, 1.9]	0.5	[0.1, 1.8]
Education				
Some high school or below	Ref.	-	Ref.	-
High school/GED	2.1	[0.8, 5.9]	3.5	[1.2, 11.7]
Some college	2.0	[0.8, 5.8]	3.0	[0.9, 10.2]
College/Graduate School	2.8	[1.0, 8.6]	4.3	[1.2, 16.6]
NYHA class				
IIIa	Ref.	-	Ref.	-
IIIb	0.5	[0.2, 1.4]	0.5	[0.1, 1.6]
IV	0.6	[0.2, 1.6]	0.6	[0.2, 2.0]
Health literacy (REALM)				
$\leq$ 8th grade	Ref.	-	Ref.	-
$\geq$ High school	2.2	[0.7, 10.2]	2.9	[0.8, 14.4]

Note. OR= odds ratio; CI= confidence intervals

Summary of Quantitative Results (Specific Aim #1 & Specific Aim #2)

A total of 208 participants were randomized to receive a multi-component, early palliative care intervention with 81 participants completing all the intervention per protocol and 127 participants not completing all intervention components. Given these small sample sizes, all analyses are exploratory. The Charting Your Course-guided telephone sessions on average were 45 minutes with 2 ½ weeks between sessions. Most participants completed their last session between 8- and 16- week data collection points. No significant baseline sociodemographic or clinical differences were found between those who completed all components of the intervention versus those who did not. However, those who did complete the intervention had lower baseline HADS-anxiety scores ($p=0.05$) and shorter time to intervention initiation ($p=0.01$). Overall, participants had fair to moderate HF-related QoL and low healthcare resource use. While participants had poorer physical health status scores than the general US adult population, the average baseline mental health status scores was within 1 standard deviation of the general US population. Additionally, the majority of participants endorsed adaptive coping strategies. Black participants were more likely to complete the intervention. Other sociodemographic characteristics were associated with higher odds of completing the intervention including higher educational level, higher health literacy, living alone, having a caregiver also enrolled in the study, attending religious services regularly, and being retired. Concerning intervention effects, positive trends with moderate effect sizes were commonly seen at the 16-week data collection time point in those that completed all the intervention. However, only the between-group KCCQ clinical summary score difference was significant at 16 weeks.

Specific Aim #3: Qualitative Strand Results

The primary purpose of the qualitative strand, addressing Specific Aim #3, was to explore ENABLE CHF-PC patients' experiences with the intervention components, intervention dose (amount, duration, frequency, intensity) and their perspectives on the intervention effects on patient-reported outcomes and trial participation in general. This section includes the results of the semi-structured qualitative interviews that were conducted with 45 patient participants who were randomized to receive the ENABLE CHF-PC intervention. First, this section begins with a description of recruitment, enrollment, and data saturation. Then, a brief description of the interview participants is provided. Next, participant descriptions separated into three a priori categories, impressions of dose and dose attributes, individual context, and outcomes, are presented. Each a priori category is further divided into subcategories and themes. This section concludes with a brief summary of the qualitative findings.

Interviewee Sub-sample: Recruitment, Enrollment, and Data Saturation

Of 208 potential patient participants, 165 participants were recruited from UABMC and 43 were recruited from the BVAMC. Recruitment of participants from the BVAMC was not initiated due to ongoing delays with IRB review and approval. Of the 165 UABMC participants, 50 participants had withdrawn from the parent study and 18 participants had died prior to the start of qualitative interviews (Figure 14). We contacted 97 UABMC participants (46.6%) by mail concerning potential participation in a one-time, semi-structured telephone interview about their experiences with the ENABLE study, dose attributes of the intervention, and QoL and healthcare resource use outcomes.

Eleven mail packets were returned as undeliverable and one participant contacted the study PI to decline further contact. After initial contact by mail, participants were called by study staff about potential participation in the semi-structured interviews. Recruitment and enrollment procedures are described in Chapter 3 and detailed in Appendix A. Forty participants did not participate in the interviews for the following reasons: (1) unable to reach by phone (n=26, 65%), (2) poor health/death (n=10, 25%), (3) truncated interview due to poor recall (n=3, 7.5%), and (4) 'not interested' (n=1, 2.5%). Forty-five participants were interviewed from October 2018 to April 2019. The length of interviews ranged from 13.12 to 85 minutes with an average of 41.9 minutes. All interviews took place by telephone in private office space at UAB School of Nursing. Interviews were conducted with the PI or two trained study staff with oversight by the PI.

Data saturation was reached at 10 interviews for those who completed all the intervention and 12 for those who did not complete the intervention. Guided by the concept of 'informational redundancy' described by Sandelowski (1995), we defined data saturation as the number of interviews needed until no new concepts, themes, or codes are introduced. In particular, we used similar phrases or descriptions of intervention and overall study experiences and perceptions of dose attributes and QoL and healthcare resource use outcomes as markers of redundancy. The remaining interviews were performed to aid with rich descriptions and dose group comparisons as initial interviews in the non-complete study group included only participants who did not attend the OPCC.

For member checking, all interview participants were mailed an aggregate summary of interviews and four participants were called for follow up concerning the summary. The aggregate summary is included in Appendix N.

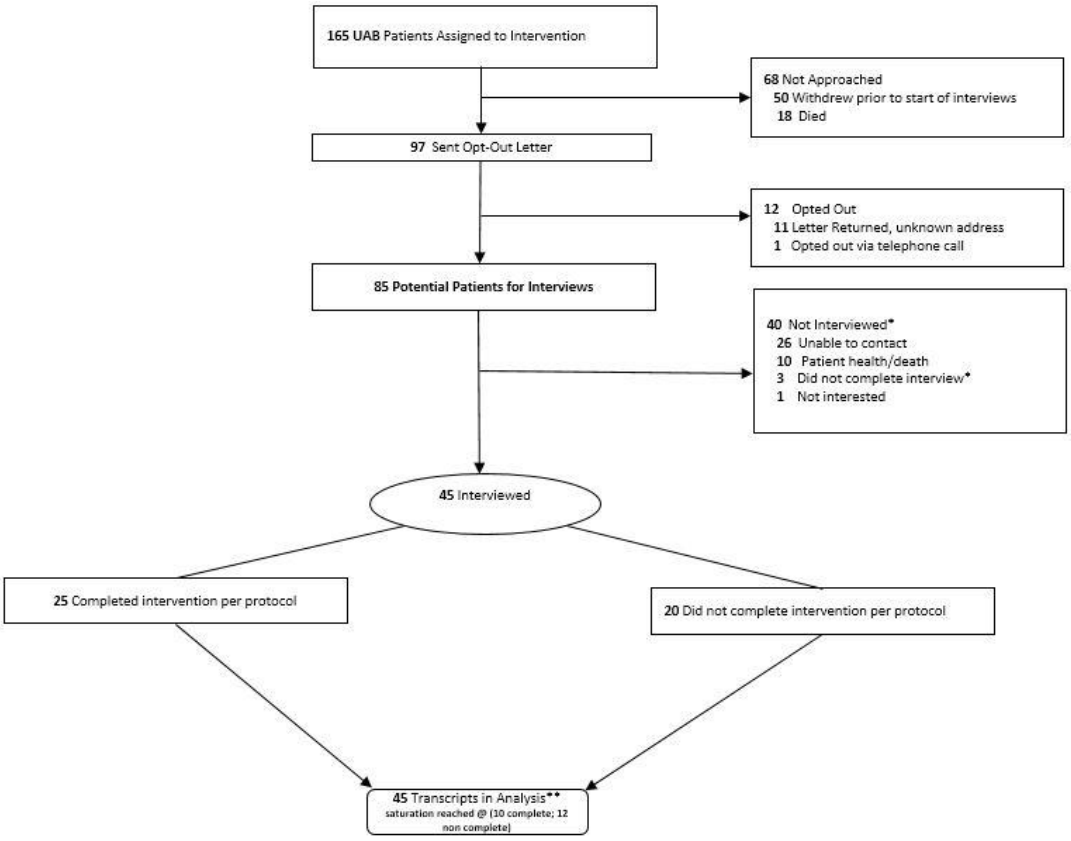


Figure 14. ENABLE CHF-PC Dose Study Consort Diagram- Qualitative Strand. Framework modified from Moher, D., Schulz, K.F., & Altman, D.G. (2001) The CONSORT statement: Revised recommendations for improving the quality of reports of parallel-group randomized trials. *Annuals of Internal Medicine. 134*, 657-62.

ENABLE CHF-PC Intervention Interviewee Sub-sample Descriptive Statistics

Sociodemographic characteristics of interviewee sub-sample. Proportions of sociodemographic characteristics of interview participants were similar to all intervention participants in the quantitative strand except in gender. The mean age of interview participants was 62.6 $\pm$ 7.3 years. Overall, interview participants were mostly female (n=33, 73.3%), black (n=28, 62.2%), living with others (n=35, 77.8%) in urban locations

(n=31, 68.9%). Sociodemographic characteristics of ENABLE CHF-PC intervention interview participants are included in Table 21.

Table 21

Interviewee Sub-sample: Sociodemographic Characteristics

Variable	All (N=208) n	%	Not Interviewed (N=163) n	%	Interviewed (N=45) n	%	Effect size (d*/V)
Age, M (SD)	63.5 (8)		63.8 (8.3)		62.6 (7.3)		0.15*
Gender							0.06
Male	111	53.4	98	60.1	13	28.9	
Female	97	46.6	65	39.9	32	71.1	
Hispanic/Latino							0
No	207	99.5	162	99.4	45	100	
Yes	1	0.5	1	0.6	0	0	
No response	0	0	0	0	0	0	
Race							0.10
White	92	44.2	77	47.2	15	33.3	
Black	113	54.3	83	50.9	30	66.7	
Other	3	1.4	3	1.8	0	0	
Site							0.29
UAB	148	71.2	108	66.3	40	88.9	
Birmingham VA	43	20.7	43	26.4	0	0	
Other clinic	17	8.2	12	7.3	5	11.1	
Residence							0.05
Rural	58	27.9	43	26.4	15	33.3	
Urban	150	72.1	120	73.6	30	66.7	
Marital Status							0.11
Never married	30	14.4	20	12.2	10	22.2	
Married or living with partner	105	50.5	85	52.2	20	44.4	
Divorced or separated	52	25	41	25.2	11	24.4	
Widowed	21	10.1	17	10.4	4	8.9	
Lives alone							0
No	165	79.3	130	79.8	35	77.8	
Yes	43	20.7	33	20.2	10	22.2	
Has caregiver enrolled in study							0.09
No	126	60.6	102	62.6	24	53.3	
Yes	82	39.4	61	37.4	21	46.7	

Note. M=mean, SD=standard deviation, UAB=University of Alabama at Birmingham, VA= Veterans Affairs Medical Center; Cohen's d or d-equivalent: small~0.2, medium~0.5, large~0.8; Cramer's V: .07-low, .07-.21 moderate, and >.35 is large; Higher Charlson Comorbidity Index scores indicate higher comorbidity-associated burden and lower likelihood of survival.

Intervention participation descriptive statistics of interviewee sub-sample. Of the 45 interview participants, 24 completed all telephone psychoeducational sessions and the one time, in-person OPCC. While most interview participants the majority of the psychoeducation sessions (> 4 sessions; n=39, 86.7%) with less attending the in-person palliative care consultation (n=28, 62.2%) (Table 22). The average amount, or length of the session telephone call, was 47.9 ± 19.6 minutes. Individual session average length in minutes are listed in Table 22. Average completion of the first session occurred two weeks after randomization (M=16 days; SD = 13 days). Overall, participants who completed the interview completed more of the intervention telephone sessions than those who were not interviewed (d=0.74, $p=7.6e^{-9}$), likely due to an association of study withdrawal with low intervention completion. Also, more interviewees completed the OPCC than those who did not complete the interview (V=0.14, p=0.04).

Table 22

Interviewee Sub-sample: ENABLE CHF-PC Intervention Participation

Variable	N	Mean	SD	Min	Max
Session Count	45	5.4	1.6	0	6
Amount of session 1 (minutes)	43	52.2	24.9	13.0	129.0
Amount of session 2 (minutes)	42	36.5	13.1	14.0	84.0
Amount of session 3 (minutes)	41	39.0	11.9	18.0	65.0
Amount of session 4 (minutes)	39	50.2	20.3	16.0	122.0
Amount of session 5 (minutes)	38	53.4	37.3	24.0	250.0
Amount of session 6 (minutes)	38	63.9	36.3	25.0	237.0
Average time per session (minutes)	43	47.9	19.6	13.0	135.5
Days to Session 1 completion	42	16.0	11.0	7.0	56.0
Session Duration	37	59.3	22.5	33.0	110.0
Days from randomization to session 6 completion	37	75.0	26.2	41.0	126.0
OPCC completed			28 (62.2%)		

Note. SD = standard deviation, Min = minimum data value in dataset, Max= maximum data value in dataset; OPCC=outpatient palliative care consultation

Clinical characteristics of interviewee sub-sample. Most interview participants had NYHA Class IIIa HF with a mean life expectancy of 7.4 ± 3.2 years. Table 23 depicts baseline clinical characteristics of interview participants. Participants who were interviewed had a statistically significant higher ejection fraction than those who were not interviewed (d=0.30, p=0.05). Tables 24 and 25 show the baseline scores and responses on the KCCQ, healthcare resource use questions, FACIT-Pal, HADS, PROMIS global and mental health, and the COPE Inventory of interview participants. There were no significant differences between average scores and on baseline measures between those who were and were not interviewed. Table 26 includes brief descriptions of all interviewee participants divided by dose category.

Table 23

Interviewee Sub-sample: Baseline Clinical Characteristics

Variable	All (N=208) M(SD)	Not Interviewed (n=163) M(SD)	Interviewed (n=45) M(SD)	Effect size (d)
SHFM				
Mean life expectancy	7.0 (3.7)	6.9 (3.9)	7.3 (3.2)	0.12
Years since HF diagnosis	5.1 (5.1)	5.4 (5.3)	4.16 (3.8)	0.08
Systolic blood pressure	125.4 (20.6)	124.6 (21.0)	128.5 (18.7)	0.19
Ejection fraction	40.9 (16.4)	39.8 (17.0)	45.8 (13.8)	0.30
Comorbidity Index	3.2 (1.9)	3.3 (2.0)	2.9 (1.8)	0.17
NYHA Class at baseline	**n (%)**			**V**
Class IIIa	167 (80.3)	133 (81.6)	36 (80.0)	0.01
Class IIIb	19 (9.1)	14 (8.6)	5 (11.1)	
Class IV	20 (9.6)	16 (9.8)	4 (9.9)	

Note. SHFM = Seattle Heart Failure Model; Comorbidity Index = Charlson Comorbidity Index- Higher Charlson Comorbidity Index scores indicate higher comorbidity-associated burden and lower likelihood of survival; NYHA= New York Heart Association HF classification; Cohen's d or d-equivalent: small~0.2, medium~0.5, large~0.8; Cramer's V: .07- low, .07-.21 moderate, and >.35 is large;

Table 24

Interviewee Sub-sample: Baseline KCCQ and Healthcare Resource Use

Variable	N	Mean	SD	Min	Max
KCCQ					
Clinical summary	45	54.2	21.0	10.3	93.1
Functional status	45	51.3	20.9	10.6	88.2
Symptom summary	45	55.6	23.5	11.7	97.1
Physical limitation	45	47.0	22.8	0	92
Symptom severity	45	53.6	23.0	13.3	93.3
Symptom frequency	45	57.1	26.7	10.4	100.0
Social limitation	45	51.7	26.5	8	100
Quality of life	45	59.6	26.8	0	100
Self-efficacy	45	86.7	20.7	25	100
Healthcare resource use in last 8 weeks					
Hospital admissions	45	0.6	1.0	0	3
Hospital days	45	2.0	3.5	0	15
ICU days	45	0.2	1.0	0	6
ER visits	45	0.4	0.8	0	3

Note. KCCQ=Kansas City Cardiomyopathy Questionnaire; KCCQ scores range from 0 to 100;Higher KCCQ scores indicate better perceived health status

Table 25

Interviewee Sub-sample: Baseline FACIT-Pal, HADS, PROMIS-Global Health, & Brief COPE

Variable	N	Mean	SD	Min	Max
FACIT-Pal	45	37.7	10.1	8	53
HADS					
Anxiety	45	6.7	4.6	0	21
Depression	45	6.0	4.5	0	16
PROMIS Global Health					
Global physical	45	38.3	8.9	20.0	58.0
Global mental	45	45.5	9.3	21.3	67.0
Brief COPE					
Self-distraction	45	1.4	0.8	0	3
Active coping	45	2.0	0.8	0	3
Denial	45	0.6	0.8	0.0	2.5
Substance abuse	45	0.1	0.2	0	2
Emotional support	45	2.0	1.0	0.0	3.0
Instrumental support	45	1.7	1.0	0	3
Disengagement	45	0.3	0.6	0.0	2.0
Venting	45	1.0	0.9	0	3
Reframing	45	1.7	0.8	0	3
Planning	45	1.9	1.0	0.0	3.0
Humor	45	0.7	0.9	0.0	3.0
Acceptance	45	2.4	0.9	0	3
Religion	45	2.3	0.8	0	3
Self-blame	45	0.5	0.8	0.0	3.0

Note. SD= standard deviation, Min= minimum, Max= Maximum; PROMIS T scores have a mean of 50 and SD of 10 in the general US population; Higher PROMIS Global scores indicate better functioning; FACIT Pal 14 scale scores range from 0 to 56; Higher FACIT Pal 14 scores indicate better quality of life; HADS scale scores range from 0 to 21 with a cutoff score of 8 ;Higher HADS scores indicate more severe symptoms; COPE Inventory scores

Table 26

Interviewee Sub-sample Attributes

Participant ID			
Complete		Noncomplete	
PT 131, 65 yo rural dwelling WF	PT 396, 73 yo urban dwelling WF	PT 007, 63 yo urban dwelling BF	PT 241, 56 yo rural dwelling BM
PT 144, 65 yo urban dwelling BF	PT 399, 58 yo urban dwelling BM	PT 043, 55 yo urban dwelling BF	PT 250, 63 yo urban dwelling WF
PT 161, 55 yo rural dwelling BF	PT 434, 53 yo urban dwelling BM	PT 068, 62 yo urban dwelling BF	PT 251, 58 yo rural dwelling BF
PT 176, 78 yo urban dwelling WF	PT 446, 62 yo urban dwelling WM	PT 102, 56 yo urban dwelling BF	PT 257, 64 yo rural dwelling WF
PT 181, 64 yo urban dwelling WF	PT 453, 63 yo urban dwelling BF	PT 104, 58 yo urban dwelling, BF	PT 273, 57 yo rural dwelling BF
PT 198, 55 yo urban dwelling BF	PT 460, 61 yo rural dwelling WM	PT 127, 53 yo rural dwelling WF	PT 333, 60 yo rural dwelling WF
PT 243, 77 yo rural dwelling BF	PT 464, 71 yo urban dwelling WF	PT 130, 54 yo urban dwelling WF	PT 356, 80 yo urban dwelling BF
PT 244, 60 yo urban dwelling BF	PT 471, 50 yo urban dwelling BM	PT 139, 58 yo rural dwelling WM	PT 414, 74 yo urban dwelling BF
PT 265, 64 yo urban dwelling BM	PT 478, 70 yo rural dwelling BF	PT 142, 62 yo urban dwelling BM	PT 444, 64 yo rural dwelling WF
PT 278, 70 yo rural dwelling BF	PT 480, 63 yo urban dwelling BF	PT 195, 68 yo urban dwelling BM	
PT 369, 67 yo urban dwelling BF	PT 487,55 yo urban dwelling BM	PT 226, 73 yo rural dwelling WF	
PT 375, 61 yo urban dwelling WM	PT 503, 63 yo urban dwelling WF		
PT 379, 59 yo urban dwelling BF			

Note. PT= patient participant; yo = year old; W= White, B= Black; F= female; M= male

Qualitative Categories and Themes

We used the following a priori categories describing patients' intervention dose experiences and perspectives of intervention dose: 1) impressions of ENABLE intervention dose and dose attributes, 2) individual context, and 3) study outcomes. Table 27 lists categories, subcategories, and themes.

Table 27

Central categories, subcategories, and themes

Category	Subcategory	Themes
I. Impressions of ENABLE intervention dose and dose attributes	a. Duration	1) "You could've shortened it" 2) "Didn't seem that long"
	b. Frequency	1) "Seemed more"- Too frequent is burdensome 2) Monthly calls not intensive enough
	c. Intensity/Engagement	1) High engagement: descriptions of participant-rated > 5 intensity 2) Low engagement: descriptions of participant-rated < 5 intensity 3) Between call preparation 4) Overall study preparation
	d. Length of calls	1) "Worth the length" 2) "Just right" 3) "A little bit too long for my patience"
	e. Sum of parts	1) "It's the combination" 2) Finding the right balance
	f. Delivery	1) Dislike of telephone 2) In-person
	g. Timing	1) "Could be earlier" 2) "Others could use it more"- match perceived health with intervention
II.Individual contexts	a. Disease-related factors	1) Perceived disease severity 2) Perceived HF related knowledge deficit 3) HF/comorbidities impact in daily life
	b. Emotions/State of mind	1) Anxiety 2) Depression 3) Optimistic disposition
	c. Social support	1) Family/friend support
	d. Logistical factors	1) Free time 2) Transportation
	e.Interactions with providers	1) Nurse coach 2) Palliative care clinician
III.Study outcomes	a.Overall study effect	1) Health promoting habits 2) HF knowledge 3) "Hope" 4) Provider communication 5) Non-healthcare relationships 6) Quality of life 7) Healthcare resource use
	b. Impressions of dose effect	1) Dose-related change 2) No impact

Impressions of ENABLE intervention dose and dose attributes

Participants were asked specifically about their perspectives on the dose attributes of duration, frequency, intensity, and amount as well as how these attributes might have contributed to their QoL and healthcare resource use outcomes. Participants often struggled to answer questions concerning dose-dependent outcome change as this concept was more abstract. Modifications to the interview guide led to specific questions about the how the levels of these dose attributes could contribute to change. For example, participants were asked if they experienced QoL change, how much did the frequency (weekly calls) contributed to the change.

Most participants found the intervention "just right" (PT 104, a 58 year old urban dwelling black female) or "the right amount of dosage" (PT 161, a 55 year old rural dwelling black female). Often participants described weighing the dose with the perceived benefit or outcome of the study:

> Well, I think it was probably just right, cuz like I said, I was receiving a lot of information during the time that we talk and all this. She [the nurse coach] would tell me a lot of things. Then she would ask questions, see that I understand what all was bein' done then. Then maybe next time she called, she would see that the thing that she had said, did it help me in any way, which it did. I think that the time that was spent was well spent. It wasn't too short, and really wasn't too long. It was about right in the middle. Everything was fine. (PT 265, a 64 year old urban dwelling black male)

There was little differences between the perspectives of participants who did complete the intervention versus those who did not complete all of the intervention when discussing dose attributes. However, a few participants preferred less of the intervention stating, "I think it [the study dose] was a little too much for my patience, you know… The only thing I have a problem with is the amount of time." (PT 127, a 53 year old rural dwelling white female) or "That [the study activities] got sort of cumbersome because the

doctor's appointments and this, and that, and the other. But it started helping me" (PT 181, a 64 years old urban dwelling white female). This comment by participant 181 highlights a common finding as participants often described their experiences and perspectives on dose and dose attributes within a certain context. Given the prevalence, these contexts were separated into another theme, individual context.

Duration. Participants infrequently described duration. Of those who described duration, they often had difficulty recalling the duration of the intervention, "It just seems like it was shorter than that" (PT 161, a 55 year old black female). We found little concordance describing the 'ideal' duration. Some participants described the duration as too short, "I didn't think it was too long, personally. In fact, when I had my last call with [my nurse coach], I truly was disappointed. I said, 'oh, man'" (PT 379, a 59 year old urban dwelling black female) whereas others felt the duration was too long, "I ain't know it was gonna last that long. I mean, that's a long time. You could've shortened it. You could've have shortened it up a little bit" (PT 434, a 53 year old urban dwelling black male who completed the intervention). Similar to descriptions of overall dose, many participants provided context when considering duration. For example, one participant (PT 161), a rural dwelling black female who completed the intervention, first expressed disbelief over the duration of the study. She continued to describe her experience with duration and talked about how the timing of intervention worked well within her life which affected her perception of the duration, "…so I'm gonna say that the length of the time [duration], the only role that it really played was it came in at a good time for me

and it could've been longer than that because once I stopped getting it, I really realized how much I missed it."

Frequency. Very few participants who did not complete all of the intervention described the frequency of the intervention other than to state that they felt that the frequency of the intervention did not contribute to study-related change. We found disparate perspectives on frequency within those who completed all the intervention. Some participants found the frequency overwhelming and suggested more time between calls, "once a month might be a better thing." (PT 131, a 65 year old white female who did not complete all of the intervention) or "I'm reckoning they're too much, too many phone calls and stuff." (PT 399, a 58 year old black male who did complete the intervention). Other participants felt the frequency fit the aim of the calls as, "it gave you a breathin' time to think and be ready to talk and be able to do the next section of it" (PT 414, a 74 year old black female who did not complete all of the intervention). One participant, a 59 year old black female who did complete the intervention, described the weekly then monthly frequency as beneficial:

> Initially, the weekly phone calls, I think, allowed me to be a lot more focused in okay, this is something weekly that I'm doing. It was a lot more focused which I appreciated … It got me more in tuned. Okay, what are we talkin' about here? Then going to monthly, I think was a good shift. I liked the six weeks initially because it allowed you to be a lot more focused. You were reminded weekly. This is the conditions, what we're doing. This is how we can work on alleviating some stresses and practice all these skills. Those kind of things, I think initially, the weekly calls were very appreciated because it didn't allow a lot of time for me to lag about oh, it's another call again. The calls every week were definitely a way to keep me focused, so that was good. (PT 379, a 59 year old black female)

The quote by PT 379 also highlighted how the weekly format helped with remembering the next session appointment, a benefit echoed by other participants, "I

think during the study, the once a week is probably the way it should go. If you do it once a month, people are gonna forget about it. Well, I read it the day I got off the phone, I'll remember it now. Once a week is good" (PT 446, a 62 year old white male who complete the intervention).

However, some participants found that the telephone-based sessions were too infrequent, "Yeah, just more time, that I get a[n] extra call from—sometimes you call twice a week sometime—be all right" (PT 434, a 53 year old black male who completed the intervention). Another participant, a 63 year old white female who completed the intervention, highlighted the differences between weekly and monthly calls and preferred the weekly format, "I think probably the intensive calls maybe could have lasted a little longer. They didn't even necessarily have to be centered on a lesson. They could've just been, "Tell me how you're doin' this week" kind of thing" (PT 503).

Similar to overall dose and duration, many participants included the role of context in describing frequency:

> It just could be an inconvenience for people done on a weekly basis. Depends on what somebody has. Even for myself, it wasn't a problem for me because, like I said, I agreed to do the study so I was gonna put my best foot forward. There were days where she may wanted to do it on a Monday and I'm like, "Oh, I can't do it Monday because I got such and such I gotta do.(PT 453, a 63 year old black female who completed the intervention)

Some participants described how their context led to setting their preferred frequency, "Yeah. I told her to call me every other week by the book. By the book, yeah" (PT 471, a 50 year old black male) and "Well, it [the frequency] don't matter. They would just call and talkin'" (PT 480, a 63 year old black female).

Intensity/Engagement. Interviewees were asked to rank their intensity with the intervention on a scale from 1 to 5 with 5 representing the most intense and engaged. They were given examples of intensity/engagement such as "5" would represent setting time aside each week to review the guidebook and work through study activities like the the problem solving worksheets whereas "1" might be watching TV or muting the phone during the nurse coach calls. All participants ranked themselves as a '4' or higher except two with one of those completing all the intervention. Most participants described their intensity in terms of the preparation they completed after the nurse coach calls, "Well, we would have somethin' maybe like maybe I'll say [coughing] some 20 minutes or more and then we would—then when some days when I'm just sittin' down lookin' I get my book and read to understand more about it" (PT 414, a 74 year old black female who did not complete all of the intervention) and "then, when it was over with, I would go back and look over some of the things that they had said, and then I got materials from them that I read and would help" (PT 161, a 55 year old black female who completed the intervention). Other participants described their interaction during the nurse coach calls:

> We were engaged and I was learnin' as we—the whole overall experience made me aware of some things—like I said, made me more aware of things that I ordinarily would not have been thinking of had I not done that study. Just givin' it my undivided attention, I don't know what more I can say towards that. (PT 453, a 63 year old black female who completed the intervention)

Similar to descriptions of overall dose and other dose attributes, many participants provided context when considering intensity/engagement, "I would rate myself a 5 because, if I was taking time out, as a heart patient, time is very important. You don't feel like you have time to waste. I didn't feel like I had time to waste" (PT 244, a 60 year old black female) and "Well, there was a day or two I didn't feel good. It's hard for me to

concentrate on those days" (PT 181, 64 year old white female). Another participant, a 61 year old urban dwelling white male, described the diminishing need for the same intensity as the study continued, "Like I said, the longer you went into it [the intervention], the less and less [you gave] because you was more knowledge about it and I figured out all the information. The longer you was in it, really, the less you was thinkin' about it, basically" (PT 375).

Amount. Participants in both complete and noncomplete groups describe the amount or the length of the telephone sessions in the intervention as too long, "it was just too long for me to be sittin' there and holding the phone to my head" (PT 127, a 53 year old white female), too short "too short. I don't think it was long enough. You could've made it longer" (PT 434, a 53 year old black male) or adequate, "it's just right. It's just right" (PT 471, a 50 year old black male). While we found descriptions of the entire range from too short to too long, most participants described the length of the telephone sessions as adequate. For example, one participant, a 58 year old urban dwelling black male who did not complete all of the intervention, first described the calls as too long but then backtracked, "they [the phone calls] were usually longer than what I wanted to be on the phone, but— [long pause] I guess, the right amount. I mean, I talked to them when they called" (PT 104). Other participants echoed a similar sentiment and often added elements about their control in participating in the length of the calls, "I can't say whether they was too long or too short because, I mean, if I wanted to make 'em short, I always coulda made 'em [the phone calls] short. I coulda not come the phone, but my thing was, when she [the nurse coach] called me, my time was hers until she finished what she was

doin'" (PT 243, a 77 year old black female). A few participants talked about reasons why they remained on what they perceived as longer calls, "they [the phone calls] just seemed sort of long sometimes, but, no, I don't mind participating in them… I think they'd [the phone calls] be better if they were more frequent but shorter" (PT 130, a 54 year old white female who did not complete all of the intervention) and "sometimes it seemed like it went a little long, but when you're talkin' about things, you don't hang up in the middle of it" (PT 181, a 64 year old white female who completed the intervention).

As with other dose attributes, context was frequently discussed by participants when considering the length of the intervention. One participant, a 63 year old urban dwelling black female who completed the intervention, highlighted why phone length should be responsive to context,

> The length of the call would depend on the person who—-and what they needed to talk about. The maintenance calls I feel like the nurse coach has a limited stuff of what she wants to talk about and, "When we're done, we hang up." I think maybe if—maybe a couple more of the intensive calls could've been structured so that—I didn't feel like I was necessarily fulfilling her checklist. (PT 480).

Delivery. A few participants discussed the mode of delivery of the intervention including the telephone based nurse coach session and *Charting Your Course* guidebook. Most discussions about how the intervention was delivered came from participants who did not complete all of the intervention. However, some participants who completed the intervention also discussed how the mode of delivery impacted their experience. For example, one participant, a 65 year old white female who completed the intervention, described how she struggled to complete the intervention due to telephone sessions, "well, it's just hard for me havin' a—even if it's not a lotta people talkin', it just annoys me so" (PT 131, a 65 years old white female who completed the intervention). Her

sentiment is also echoed by another participant who did not complete all of the intervention, “I don’t really like talkin’ on the phone” (PT 127, 53 years old white female who did not complete all of the intervention). Another participant clarified why having interactions with the study staff aided with study completion:

> Even though the person on the phone askin’ the questions—if that person was a machine, it sure didn’t sound like one and then havin’ the nurse there and also havin’ this lady there, they were actually people that I could—they could touch me and I could touch them. To me, that was the best part about it. (PT 161, a 55 year old rural dwelling black female)

Timing. Most participants who completed all the intervention felt that intervention happened at the right time in their life and in their experiences living with heart failure. One participant who completed all the intervention sums up how her introduction to palliative care came at the right time:

> When I was first approached about this thing, I took it seriously because I guess in the time that was I called to do this study and the time that I had been in the hospital when I went through my illness, I think the timeframe, that time in there, really made me be dedicated to doin’ what I need to get done. (PT 161, a 55 year old black female)

Similarly, participant 503, a 63 year old white female, used a hospitalization to determine best timing and expressed a desire to have the OPCC earlier, “yeah, I wish I had met with him [the palliative care clinician] much sooner. I wish I had met with him before I left the hospital. Then I wish that I’d met with him then and then I wished I had met with him after I got out of the hospital much sooner than in October” (PT 503).

While some participants felt like the timing coinciding with a poorer health or a HF related health event provided a needed push to engage with the study, one participant talked about how feeling well was necessary for the right timing, “it came at the right time because I was beginning to understand what I had been diagnosed with. Then I was

well enough at that time to comprehend what she was telling me" (PT 176, a 78 year old white female). Another participant used humor to discuss her perspective on the right timing for the intervention, "I guess, in timing, I guess, the right time. I'm not dead and gone so-…I don't think it's ever too late. You understand what I'm trying to say?" (PT 104, a 58 year old black female). She continued to clarify when palliative care would be appropriate, "well, I think the beginning is fine [to offer palliative care]- cuz they can always learn something to help 'em, even if they are bad off" (PT 104).

Some participants who did not complete all of the intervention described the timing as too early with many sharing sentiments similar to participant 139, a 58 year old white male:

> Well, time really made it, and I'd say the first time they need to get the information they might need, especially with their medications and whatnot, and probably—I'm 61, but I'm still pretty active. Probably people that was a little older or maybe sicker than I am could use it more. (PT 139)

Individual context

While all participants were encouraged to complete all intervention components, over half elected to complete less. Even within groups completing similar sessions and/or the OPCCs, their descriptions and impressions of the intervention and its impact on outcomes of QoL and healthcare resource use varied. All interviewee participants highlighted different factors or contexts that either augmented or dampened their 'dose' of the intervention. These individual contexts occurred at primarily two time-points. First, many of these factors played a role prior to the initiation of the intervention. At this time point, these factors affect the 'loading dose' required for outcome change. Additionally, many of these factors also played a role during the intervention. Participants described six

subthemes of these individual contexts: (1) disease-related factors, (2) emotional state factors, (3) social support, (4) logistical factors, (5) interactions with providers, and (6) impressions of palliative care.

Disease-related factors. Almost all participants described instances where HF or other disease factors impacted their engagement with the intervention. These disease factors played a role in their willingness to participate when they were initially approached during study recruitment. Some participants described how an exacerbation of their HF altered their level of engagement with the intervention,

> It wasn't before the incident [cardiac event] happened. I mean it would be great to get this stuff [the intervention] beforehand, but a lot of times, you're not gonna get an honest answer from people if they haven't gone through it, but after goin' through it, I think the time made me more interested in taking what you all had to offer me and taking it correctly and on time because I had just went through my illness and in the timeframe that you all contacted me was the best time. I don't know if you all can—I know you can't anticipate things like this but mines was at the right time. I took my medication at the right time if I could use that as a metaphor. (PT 161, a 55 year old black female who completed the intervention)

While HF exacerbations were often described as an impetus to enroll in the ENABLE CHF-PC study or to engage more with the intervention, physical symptoms were often described as a deterrent for higher engagement during the intervention:

> Well, most—I won't say most of the time, but a lot of the times, I have sickle cell. A lot of the time when I do a call, sometime I will be in a lot of pain, so I still would try to go ahead and accept her call and go through it. For some reason—not every time she called, but just about most of the time that I would be in a lot of pain, but I got through it. (PT 265, a 64 year old black male)

This impact of physical symptoms was found in both dose groups. Other participants described how their perceived good health acted as a dampening effect during the intervention, "I'm gonna say no [the intervention did not impact her quality of

life], but the reason I'm gonna say no is because I already was in a good place with my illness" (PT 453).

Some participants talked about how they perceived a need to gather information since being diagnosed and living with HF and how participation with the intervention was an opportunity to address that need,

> I said yes because I was willing to get any help available regarding my heart condition, which was a complete shock to me that I even had a heart condition. I wasn't somebody who knew for a long time that they had problems. This was just out of the blue. Anything that could help me understand my condition I wanted to do. (PT 503, a 63 year old white female)

While many participants described similar HF-related knowledge needs, some participants described how individual perceived needs might differ and impact intervention effects:

> You've got to want to know what's going to help you. I looked at it as something that was going to benefit me, with the book that the study—the information you gave me to study and to—sometimes I miss the words. I felt—I went into it as a benefit for me, not just for you, but I learned a lot about my condition and what to expect. I was interested in that. I think that depends upon the individual. (PT 244, a 60 year old, black female who completed the intervention)

Another participant, a 77 year old black female who completed all the intervention, described how a perceived need influences engagement in the study but not the perception of dose attributes, "I can't elaborate on people, but if it's me and it's somethin', for instance, that I was getting' the phone call from, it don't make a difference if it's once a month or once a week because I'm getting' information that I needed and I feel that I want. You make time for what you feel that you need or want, you know?" (PT 243). The concept of making time for what is perceived as needed was echoed by another participant who described how nurse coaches tapping into this perceived need might aid

with intervention completion, “Like I said, you guys—you gotta put that person to want it to do it. If they don’t wanna do it, they’ll say say anything” (PT 434, a 53 year old black male).

Emotions. Many participants described how their general emotional state of mind influenced how they interacted with the intervention. A few participants described how their anxiety or worry curtailed their involvement with the study. One participant, a 71 year old white female, recalled how her anxiety influenced her relationship with her nurse coach as she hesitated to complete the second session, “then, because I tend to have a lot of anxiety and to get worked up over things that I can’t make right. Hey, look, life can’t be all peaches and cream” (PT 464). Other participants described how their worry made them more receptive to the intervention, “It [the intervention] did occur at the right time because I was worried about it in the beginning, but after the conversations and everything, it calmed me down. I could ask questions, and they were answered. I could be relieved from that fear” (PT 356, a 80 year ole black female who did not complete all of the intervention).

While most participants described how their state of mind ‘primed’ them to receive or interact with the intervention, a few participants described how their general state of mind may have muted the intervention effect. One participant, a 58 year old white male, explained how his optimistic nature made him less responsive to the intervention, “well, if I had a question, most of the time they could answer very well. But as far as changes in life, I can’t say that it [the study] made much difference. I am a very optimistic person, and, well…” (PT 139).

Social support. Participants frequently described social and environmental factors or resources that influenced their interactions with the intervention. A few participants described the impact of having a loved one on their perceived need for the intervention,

> in other words, she was—a lotta people ain't gonna have a person like her [a wife who is a nurse] to follow it through, so the questions they was askin' on the coachin' would be good for the layperson, I'd say, in other words. A lotta mine that asked me, I knew a lotta the answers because, like I said, as a caregiver I had because she was on top of it (PT 375).

This 61 year old, urban-dwelling, white male participant went on to describe how having his wife lessened his perceived impact of the study. Other participants described how their family needs affected their engagement with the intervention, "with my heart failure, I do have a busy life with grandkids. I raised one, and then we got three of the other ones a lot of the time, but the oldest one, me and my wife raised, so I'm busy and all that" (PT 460, a 61 year old white male).

Logistical factors. Participants often identified the lack of time as a top barrier to completing the intervention and conversely an abundance of time as a facilitator, "I guess, I wasn't doin' anything at the time that she would call" (PT 480, a 63 year old black female) or "no, pretty much during a lot of those times, I was stuck in the house. It wuddn't nothin' else to do, you know?" (PT 375, a 61 year old white male). While time often contributed to not completing the palliative care consultation, participants also identified transportation as another top barrier to completing this part of the intervention, "Well, maybe for some people, transportation, 'cause myself, I live about an hour and a

half from Birmingham. Older people, they can't drive or whatever" (PT 241, a 56 year old rural dwelling black male who did not complete all of the intervention).

Interactions with providers. The majority of the participants described how their relationship with the nurse coaches influenced their interaction with the intervention. Many participants felt that rapport with nurse coaches had a vital role in retention during the study. One participant, a 53 year old black male, who kept referring to how nurse coaches "got to feel you," described nurse coaches as a salesperson for the intervention highlighting how nurse coaches engaging with the participants increases the likelihood of completing the next session:

> You gotta get to know them on that first call. You got to tell them—you gotta sell them. You gotta sell that to them. If you don't sell that to them to get to know—you don't get to know you, they ain't gonna open up to you. They want you to call them and tell them—and let them know what's going on. You know what's going on. You got to tell that to them (PT 434).

Another participant, a 71 year old white female who completed the intervention, described how her nurse coach getting to know her encouraged her to trust the intervention content, "One of the things she [the nurse coach] got me involved in—I love to cook. She got me back into doing that... Then she'd talk about it to me when I would call. I thought, "Goddamn." [Chuckles] She's all right. You know what I mean?" (PT 464). A few participants also described how the relationship with the nurse coach would change how frequently participants might want to be called, "If it was somebody just callin' every week just, I don't know, mighta been, you know, if it hadn't of been somebody that really seemed like they were tryin' to help, you, might not of been so great that long" (PT 131, a 65 years old white female).

Other participants described how their nurse coaches heavily influenced the outcome change they experienced related to the intervention. Often participants emphasized the importance of the nurse coach giving them time to talk about living with HF, “I think that [the nurse coach], she was doin’ a good job, and just takin’ up the time to really to help me and understand what was goin’ on.” (PT 265, a 64 year old black male). A few participants described how talking to a nurse coach impacted their symptoms, “Well, I wasn't so stressed out and nervous, and my blood pressure wasn't as high like it was before because I actually had someone to talk to and to help me through my problems that I was having as far as my health” (PT 257, a 64 year old white female). Participants also described providers ‘taking time to listen’ during the OPCCs, “I felt like he listened. He spent time. I didn’t feel like we were rushed in and out. I felt like he took time with us and really listened to what I said and really took what I said into consideration. I just felt listened to” (PT 503, a 63 year old white female).

While most participants attributed the changes they experienced during the study to the relationship they had with their nurse coach, “I wanna say with the nurse played the biggest role because she was there to answer those questions” (PT 161, a 55 years old black female), a few participants separated the support they received from the nurse coach from other health behaviors. For example, participant 241, a 56 year old rural dwelling black male who did not complete all of the intervention, described this separation, “I mean being able to talk to someone about it, I really didn’t have to do a whole lot to make things better or right, but I just had to stick with my program, far as what the doctors told me to do and don’t do and that kind of stuff, more or less.”

Study Outcomes

The intervention effect, both overall and dose-related, varied among participants in the ENABLE CHF-PC study. However, we did not find differences between the perspectives and experiences of those completing the intervention compared to those who did not complete all of the intervention. Many participants were quick to describe the intervention as helpful, "what part was helpful? Everything was helpful. Any time you can get some education, it's helpful. All of it's helpful" (PT 278, a 70 year old black female) even when the participant did not complete all of all of the intervention, "I mean it's [the intervention is] just—it's something that I feel like was helpful, and it helped me" (PT 241, a 56 year old black male). Other participants described the intervention as impacting them in more than one way, "I just have to weigh everything out. I guess it probably was helpful to me. Maybe more ways than I can even realize" (PT 131, a 65 year old white female).

However, a few participants did not find the intervention beneficial, "I really don't know if it's [the intervention has] affected it [my life] either way. It's not really doing anything besides the manner you go at things" (PT 139, a 58 year old white male). One participant singled out the OPCC as non-beneficial, "well, I remember thinking, man, this is a major waste of time. I don't need to go do this. But since they asked me, I'm gonna go do it" (PT 446, a 62 year old white male).

While most participants generalized the intervention impact as 'helpful', some participants described specific outcome change related to their participation in the study. Most outcome change centered on health behavior and living with HF, concepts that were not measured as part of the quantitative data collection. Participants were asked

specifically about QoL and healthcare resource use, as those concepts were the primary outcomes of the quantitative strand. Additionally, they were asked about how dose attributes may have contributed to outcome change. Despite specific questions, participants often focused on overall effect. The descriptions of the overall study effects were similar between complete and noncomplete intervention groups whereas participants who completed the intervention tended to describe a dose-dependent relationship with study effects.

Overall study effects.

Health-promoting habits. The majority of participants described their intervention experience as impacting health-promoting habits. Some participants felt that the intervention provided the necessary information and support to adopt a heart healthy diet such as participant 104, a 58 year old black female, “well, it’s a helpful program. I’ve learned stuff to help me to deal with the symptoms and to try to watch the salt cuz I was eating salt. I love Chinese food, but I ain’t had it in a long time.” Other participants described a change in diet and exercise as related to the study, “Well, in general, you know, I guess it [the study] 's just been a reminder that I need to watch what I eat. I need to exercise, I need to live my life, you know, the congestive heart failure way, so to speak-” (PT 446, a 71 year old white female) and “it [the intervention] played a lot because I’ve learned about my diet and everything, exercise—it played a good little bit” (PT 487, a 55 year old black male). One participant described how the intervention helped with smoking after completing the session on self-care, “they haven't got me to quit smoking, but I've cut down [laughter]” (PT 127, a 53 year old white female). Many

participants also talked about how the intervention promoted being aware of symptoms or other health concerns:

> It [the ENABLE intervention] made me listen to my body more. Now, whenever there's a pain, I just don't overlook it or whatever. I sit down and try to figure out what's going on, what I did, what did I do to influence or whatever, whenever a ache or something comes through. [Before] I would just blow it off. Well, maybe I'm tired, or maybe I overworked my chest, or something like that. (PT 487, a 55 year old black male)

Other participants described how the intervention impacted how they recognize and react to stress, "I think it has influenced it for positively because I felt like it… helped me understand the different stress and emotional aspects of the whole thing" (PT 503, a 63 year old white female). Participant 257, a 64 year old white female who did not complete all of the intervention, described a similar stress impact within the context of family relationships, "Well, I was having some things going on with my family and stuff, and it just helped me to be not so uptight and to learn to deal with the stress and how to take better care of myself."

HF knowledge. All participants described how the intervention positively impacted their HF knowledge. While many described how the intervention gave them specific knowledge on living with HF, "it [the intervention] helps me to understand my heart failure, how to fix me, and what to expect" (PT 176, a 78 year old white female) or "it gave me a lot of information about my condition that I never—I wouldn't have thought of just on my own" (PT 244, a 60 year old black female). Participant 244 who completed the intervention continued to describe how the newly acquired HF knowledge aided with living with HF:

> I felt more comfortable because knowledge is power. The more knowledge you have, I think—I believe, the more knowledge I have of my condition, the better I'm able to make decisions better. I'm able to cope with it on a day-to-day basis, and that's what helped me with the study. The study helped me do that.

Yet one participant, a 59 year old black female who completed the intervention, highlighted how intervention focused on the whole person rather than just HF, in the following statement describing her conversations with the nurse coach, "it was just not a situation of we talked about my heart failure, but it was a situation that we also had an opportunity to talk about other stressors that were involving me that affect my chronic heart condition-stressors that were important to me at the time" (PT 379).

Hope. The ENABLE intervention instilled hope in the face of a serious illness for many participants. While the feeling of hope was more prevalent in participants who completed the intervention, some participants who did not complete all of the intervention also described how the intervention gave them a hopeful outlook, "it changed me, but it helped me. It helped me a lot. Like I said, some of the things may have you down and a lot of stuff. They [the nurse coaches] talk with you about it and make you uplift your confidence in yourself" (PT 251, a 58 year old black female). This quote introduces two elements of the intervention that aided in developing hope, support and confidence in self. The role of support in developing hope is also described by another participant, a 71 year old white female, who completed the intervention:

> For a long time, I had given up. Hey, I know how to live in the real world, too, but I thought it was close. I think this program has helped so much about, "Hey, it gives you some—one word—hope." One word. That's it. Hope, good understanding, support, especially emotional. It helps you see—look out past—down the road. That means a lot. (PT 464)

Another participant, a 77 year old, rural dwelling black female who completed all the intervention, describes how the intervention instilled confidence in being able to live with HF which gave her hope for the future, "it affected me knowin' that—I feel that if I do certain things, I can go on and maybe do somethin' better and hope to get better, you know?" (PT 243).

Provider communication. Many participants experienced improved communication with their healthcare providers. Participants described feeling overwhelmed about their HF care. In particular, participants often described issues with HF-related medication such as the number of medications, unpleasant side effects, or financial burden. For one participant, a 53 year old black male, the intervention helped him overcome his reluctance to talk with his providers about his medication concerns,

> Yeah, [the study was] real helpful. Real helpful. Letting me know, telling my doctor if it ain't working for you- let your doctor know. Tell them. Don't be afraid to talk to them and tell them, let them know 'cause they're the doctor. You got the right, too—that's you. You gotta take the medicine. If you don't think it works, to let them know. Yeah, that was really helpful. Yeah." (PT 434)

Another participant, a 64 year old white female who did not complete all of all of the intervention, described a similar outcome in overcoming her reticence to talk, "it's helped me to ask questions and do things, and just interact with them[the health providers] in a positive way—just not to sit there and, "Okay, okay" (PT 444).

Non-healthcare relationships. In addition to impacting the participants' relationship with their healthcare provider, some participants described how the intervention impacted relationships with their family and friends. Often participants

described how the intervention helped them talk with their family about their illness, "I could explain more things to those people that's involved in my life, like my children, my husband" (PT 244, a 66 year old black female). Another participant described a similar change in talking about her HF with her family, partially aided by her newly acquired HF knowledge:

> I think the most helpful of what I talked about is for me to come to the realization of helping me understand what I have wrong with me, what I need to do to keep myself as healthy as I can, and to be able to talk to my family about it. I am not good at that. I can talk to my husband about it, but it's hard for me to talk to my kids about it. I have a son and a daughter, and one grandchild. (PT 464, a 71 year old white female)

While many of the participants described relationship change related to talking to their families about living with HF, a few participants how the intervention helped them manage family-related stress, ""Well, at the time I think it helped me with my stress and maybe tryin' to cope with my anger and bein' with my husband" (PT 131, a 65 years old white female who did complete the intervention). One participant, a 64 year old white female, described how the intervention encouraged her to seek out new friendships, "since I've been talking to [the nurse coach], I've started to go and went to the nursing home and started going to see my buddy. We talked. It's like I said, every other day, sometimes every day to see him" (PT 444).

Quality of life. When describing the impact of the intervention on QoL, participants tended to focus on how their emotional and mental health changed during the course of the study. One participant, a 63 year old white female who did not complete all of the intervention, described this emotional change concerning acceptance of her HF:

> It affected it [quality of life] real good, ‘cause it taught me the plan that they have in this study for your heart failure, it really helped towards that. You know, you can get depressed sometime thinkin’ about you’ve got this heart failure. It really helped me a lot, ‘cause at the time I was goin’ through it by myself. (PT 488)

This emotional change is echoed by some participants who completed all the intervention, “Being in this program has really helped the quality. It’s helped quantity, too, because I think I’ve forgotten about the five years [prognosis]… This program has helped me so much, emotionally” (PT 464, a 71 year old white female).

Regardless of perceived impact on QoL, all participants seemed to separate physical symptoms from other symptoms. One participant, a 62 year old white male who completed the intervention, highlighted this association of QoL with physical symptoms after describing how the intervention did not change his physical symptoms and therefore his QoL,

> Well, the study, number one, the study did not dictate my quality of life. It does not really have any effect on my quality of life, because my quality of life is dictated to me by the heart failure… You know, it's hard to say that, because some days I don't even feel like getting out of bed, you know? Because I'm just tired. But I'm tired because I'm in heart failure. It's not because I didn't take my medicine, or it's not because I didn't exercise or something, I'm just tired. It's just the way it works, part of it. (PT 446).

For participants who described no QoL outcome change, they often indicated that it was unlikely the intervention would impact their QoL:

> Well, to be honest with you, it really hasn’t influenced my quality of life. Like I say, I’ve just been trying to get back to my normal health and everything, to improve my quality of life. The study really didn’t—I mean, it helped me identify issues that might be happen, but as far as influence my quality of life, I mean- no not really. (PT 487, 55 year old black male)

Healthcare resource use. Many participants described decreased healthcare resource use after completing the intervention. One common description was the use

primary care providers rather than going to the Emergency Department, “So far, I have not been to the hospital, and I have not been to the ER, but I think it helped me because well, talkin’ with her [the nurse coach] and talkin’ to the doctors, they will tell me [how to handle the health issue]” (PT 414, a 74 year old black female who did not complete all of the intervention). Other participants described how intervention-acquired HF knowledge helped them manage their HF before a healthcare visit was needed, “I haven’t had to go to the hospital for the heart, because I’m trying to do the right thing and eat the right thing and just take care of myself. I can’t recall any time that I had to actually go to the hospital for heart failure after that” (PT 241, a 56 year old black male who completed the intervention). Some participants described how stress management learned from the intervention helped keep them from going to the hospital, “I’ve learned to adjust to those little quirks that come along and you relax and they go away. Before then I would call them immediately. It has helped me to understand my situation” (PT 176, a 78 year old white female who completed the intervention).

Many participants indicated that their relationship with the nurse coach also contributed to their decrease use of health services. For example, participant 503, a 63 year old white female who completed the intervention, highlighted this nurse coach contribution, “the interaction with the nurse coach would be probably the biggest factor.” Others, such as participant 464, a 71 year old white female, described how the contribution from nurse coach was multifaceted:

> It helped me, because I talked to her about my medication. She didn’t tell me, “You should take this or you shouldn’t take that or you should do this or you should do that.” She never did that. The nurse coach always was, “Well, if this bothers you, then you should—if this is wrong, well, what is it now?” as far as my heart rate going. “Well, I would go ahead and call the doctor. I would go. She was always that, the hand that led you in the right direction. That way, hey, many

> times if I had a problem and I knew it, well, I'd call and talk to her. I'm talking about the doctor, but that would save a visit.

A few participants also described the intervention as having little impact on their healthcare resource use. Most of these participants responded with short answers, such as "not any" (PT 487, a 55 year old black male who completed the intervention), "none" (PT 453, a 63 year old black female who completed the intervention), or "yeah. I can't see it made any difference [on hospital visits]" (PT 139, a 58 year white male who did not complete all of the intervention) when asked about changes in hospital visits or visits to the emergency room.

Impressions of dose effects. Perspectives on the impact of the intervention dose on changes in QoL or healthcare resource use were split. However, the difference in perspectives were grouped by intervention completion. The majority of participants did not provide detailed descriptions of how the amount or length of calls, the frequency of care, or the duration of the intervention impacted their QoL or resource use. Most tended to respond in few words but when asked to elaborate often discussed overall impact.

Most participants who described a positive outcome change were asked two follow up questions about the role of dose attributes on that outcome change and if the 'dose' of the intervention was modified if they believed they would experience the same change. Other participants who did not describe an intervention effect were asked if changes in dose attributes would likely contribute to future outcome change. Many of the participants did not believe a single element of dose influenced their outcome change. For example, participant 241, a 56 year old black male, described how the frequency did not

impact the "helpfulness" of the intervention, "well, it [frequency] wouldn't have mattered. I mean I'm always able to talk, but I'm glad they—whenever we talked. I don't remember if it was once a month or once a week, but it was a good thing. I mean it helps, I think." He continued to describe how the length of the telephone sessions did not influence outcome change, "no. No. No. No, they didn't. It could have been 15 minutes. It could have been 30 minutes. I think I would have got just as much out of it either way" (PT 241).

However, other participants talked about how the frequency did impact their outcomes, "The calls with the nurse coach, while the intensive calls ended, she still called me about once a month after that just as a follow up. I feel like by the time we got through the six weeks, I was better" (PT 503, a 63 year old white female). Another participant described how it was the context not the length of the calls that influenced outcome change, "I don't think the time [length] of the phone call makes a difference. It's what's discussed in the timeframe" (PT 453, a 63 year old black female).

Summary of Qualitative Results (Specific Aim #3)

Overall the qualitative interview participants described diverse experiences with the ENABLE CHF-PC intervention in three main areas: impressions of ENABLE intervention dose and dose attributes, individual context, and study outcomes. Dose attributes of duration, frequency, amount, intensity, timing, and delivery were frequently described, including the relationship of these attributes on outcome change. While the intervention was well-received by participants, participants varied on how much or how little the intervention dose should be modified to influence outcome change. Participants

also commonly described their study experience within a specific context. Often participants responded to questions about their involvement with the intervention in terms of what were the factors that influenced their uptake such as adequate social support or transportation. One of the most prevalent amplifying factors of the study dose described by the participants was the relationship between the study participant and the nurse coach. Participants also suggested that these factors modified how much of the intervention they needed as well as how they interacted with the intervention activities. Participants also described overall study impact on their health-seeking behaviors, HF knowledge, provider communication, and non-healthcare relationships. However, many participants also described the intervention as having little influence in their lives. The diversity in experience highlights an overarching theme of palliative care behavioral intervention dose as a high individualized process (Figure 15). Dose attributes are filtered through individual participant context prior to intervention initiation and during intervention delivery impacting individual outcome change related to the intervention experience.

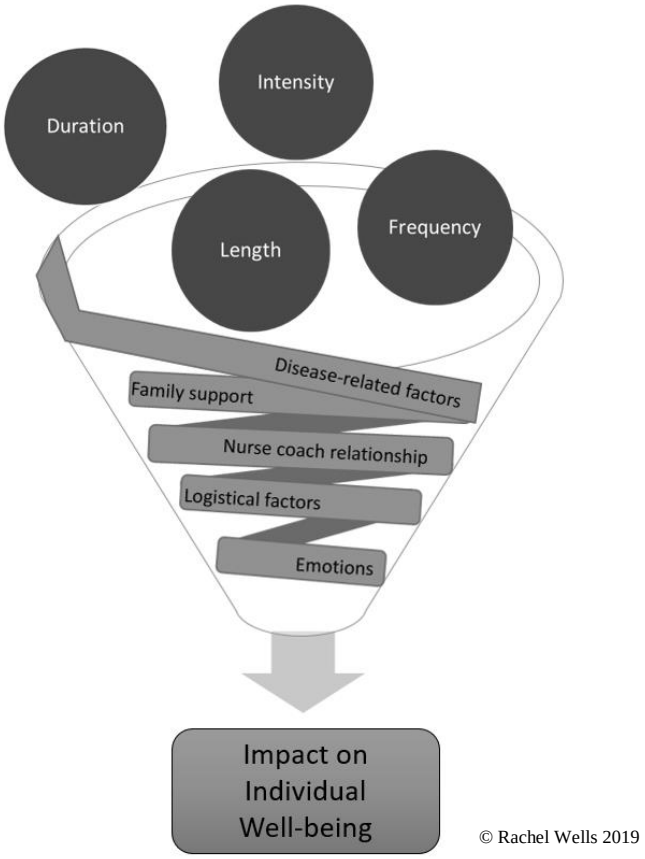


Figure 15. Intervention Funnel of Context. The relationship between dose attributes of the ENABLE CHF-PC intervention and outcome change is subject to amplifying and dampening contextual factors.

Specific Aim #4: Integration of Quantitative and Qualitative Results

The aim of the quantitative and qualitative integration in this study was to determine the intersection of participant intervention dose experiences with key sociodemographic, clinical, and intervention dose variables and how this intersection jointly explain the overall uptake of the ENABLE CHF-PC intervention in Deep South advanced HF patients. As described in Chapter 3, the rationale behind the mixed method design was triangulation and complementarity. To assist with triangulation and complementarity between strands, we created a matrix diagrams to compare, contrast,

and integrate findings. Tables 28-30 presents the main findings by aim for QoL, healthcare resource use, and factors associated with dose, intervention completion, or experience. Quantitative data include the model-estimate mean change between dose groups at 16- and 32-weeks and correlations between dose attributes and QoL and healthcare resource use outcomes. Qualitative data include main themes and exemplar quotes of these themes. The findings were compared across rows for convergence and divergence. When findings diverged, we reviewed the specific aims and research questions associated with the findings to ensure the intent was the same. We also considered if the findings were describing different aspects of the same outcome or experience. The final column includes the integrated findings of the two strands.

Patient-Reported Quality of Life

Findings from both the qualitative and quantitative strands describe the relationship between the ENABLE CHF-PC intervention and patient-reported QoL (Table 28). From the quantitative findings, there is an intervention dose effect for QoL at 16-weeks that is not sustained through 32-weeks. From the qualitative strand, we identified two main findings related to QoL. First, QoL changed for some participants but not all participants. This split in perceived QoL change was not specific to the dose group and was common in the complete and noncomplete group. Merging this split QoL change with the results of the linear mixed models from the quantitative strand, there is some divergence despite the similar research aim. However, the timing of the semi-structure interview in relation to data collection might contribute to some divergence. Intervention dose-related differences was significant at 16-weeks but was not sustained

through 32-weeks. Although these strands occurred concurrently, interviews occurred during 32-week data collection or later. There is convergence in baseline QoL descriptive statistics and experience. Overall, the baseline mean QoL is high and many participants reported they did not experience QoL change due to their 'good' health status.

Second, while dose group did not appear to play a role in perceived QoL change per the semi-structured interviews, participants commonly described QoL in conjunction with either emotional or physical symptoms. Comparing this finding to the quantitative findings, we found convergence. The KCCQ clinical summary score, the measure we used for QoL, is composed of physical function and symptom subscales (Green et al., 2000). The KCCQ clinical summary score change was primarily composed of changes in symptom subscales.

During integration, we identified three mixed methods findings for QoL: (1) QoL change is context-specific and often symptom-driven; (2) Baseline perceived QoL may influence intervention receipt and perception of QoL change; and (3) Intervention dose may impact QoL change however individual dose attributes were not related to QoL change.

Table 28. Integration of Quantitative and Qualitative Quality of Life Results

Result of Interest	Quantitative Results (Specific Aim #1-#2)	Qualitative Results (Specific Aim #3)	Concordance	Integration
Quality of Life	**1) *Intervention dose effect apparent @ 16-weeks*** Between group difference: M (SE): -9.71 (3.18); d=0.47; p=0.002 **2) *Intervention dose effect not sustained @ 32-weeks*** M (SE): 6.23 (2.72); d=0.01; p=0.97 **3) *Dose attributes (amount/frequency) not associated with 16-week change in QoL*** Correlation with amount r_s=0.07, p>0.05 Correlation with frequency r_s=0.03, p>0.05 ***4) Baseline average KCCQ scores high (M(SD)=54.2 (20.5))***	**1) *Quality of life changed for some participants but not all*** *Exemplar quote for positive QoL change (41.7% of Complete dose group responded positively, n=10)* "Very positive affect [on quality of life]…I think the length definitely helped-longer calls." (PT 503) *Exemplar quote for no QoL change (33.3% of Complete dose group responded with no change, n=8)* "I'm gonna say no, but the reason I'm gonna say no is because I already was in a good place with my illness." (PT 453) **2) *Descriptions of relationships between QoL and symptoms versus physical health*** *Exemplar quote for relationship between HF and QoL* "I don't think anything can change my quality of life except my illness and how it's treated. No, answerin' the phone calls and the questions didn't affect my quality of life." (PT 130)	+/-	QoL change is context-specific and often symptom-driven. Perceived/baseline QoL may influence intervention receipt and perception of QoL change. Intervention dose may impact QoL change. Individual dose attributes were not related to QoL change.

Note. + indicates concordance or agreement between quantitative and qualitative results; - indicates discordance or lack of agreement between quantitative and qualitative results; +/- indicates that concordance between some of the quantitative and qualitative results but also discordance; M=mean; SE=standard error; SD= standard deviation; r_s= Spearman's Rho correlation; QoL=quality of life; KCCQ=Kansas City Cardiomyopathy Questionnaire, higher scores indicated higher perceived QoL; PT=patient participant

Patient-Reported Resource Use

Findings from both the qualitative and quantitative strands describe the relationship between the ENABLE CHF-PC intervention and healthcare resource use (Table 29). We found no statistically significant intervention dose effect difference,

indicating that healthcare resource use may not experience dose-related change. Participants reported mixed perceived healthcare resource use effects, similar the QoL split described by participants. Perceived change in healthcare resource use was not aligned with intervention dose group. In this nonaligment, the quantitative and qualitative findings were convergent. However, some participants did report healthcare resource use change which does not converge with the linear mixed model nor correlations. When we reviewed the research aim, questions, and data more closely, some of this divergence occurred when participants were describing different aspects of healthcare resource use. Merging the quantitative and qualitative findings concerning perceived healthcare resource use change, we did find some convergence. Participants described healthcare resource use change as increased self-management and transition of care to primary care providers. These qualitative descriptions did not have an equivalent quantitative outcome measure as the data collection questions focused on hospital and ED visits.

During integration, we identified three mixed methods findings. First, baseline healthcare resource use is low which limits modifiability. Second, healthcare resource use may be context-specific. Third, some participants experienced change that was not measured quantitatively, such as transitions in type of care sought and increased self-management.

Table 29. Integration of Quantitative and Qualitative Healthcare Resource Use Results

Result of Interest	Quantitative Results (Specific Aim #1-#2)	Qualitative Results (Specific Aim #3)	Concordance	Integration
Healthcare Resource Use (hospital days)	**1) *No intervention dose effect apparent @ 16-weeks*** Between group difference: M (SE): -0.41 (0.63); d=0.09; p=0.54 **2) *No Intervention dose effect apparent @ 32-weeks*** M (SE): -0.81 (0.53); d=0.12; p=0.47 **3) *Dose attributes (amount/frequency) not associated with 16-week change in resource use*** Correlation with amount r_s= 0.03, p>0.05 Correlation with frequency r_s=0.01, p>0.05 ***4) Baseline healthcare resource use low*** Hospital days (M(SD)): 2.6 (5.23) ICU days (M(SD)): 0.5 (1.8) ED visits (M(SD)): 0.43 (0.85)	**1) *Healthcare resource use changed for some participants but not all*** *Exemplar quote for positive healthcare resource use change (50% (n=12) of Complete dose group and 33.3% (n=7) of Noncomplete dose group)* "Well, it had it where I didn't have to go to the hospital. I might have went to the hospital couple times since I had the heart failure, but it hadn't been no big deal." (PT 241) *Exemplar quote for no healthcare resource use change (33.3% (n=8) and 42.8% (n=9) of noncomplete dose group)* "No [intervention did not help], I try to stay outta the hospital as often as I can…No, but once I was in there six days, it hit me that I really needed to go to the hospital." (PT 243) "Yeah. I can't see it made any difference." (PT 139) **2) *Healthcare resource use change often included increased self-management and transition of care to primary care providers*** *Exemplar quote for transitions of care* "Just talking to her [the nurse coach] stopped me from going to the emergency room all the time. Yeah, just talking to her, that I just—that's point blank." (PT 434)	+/-	Baseline healthcare resource use is low which limits modifiability. Healthcare resource use is context-specific. Some participants experienced change that was not measured quantitatively, such as transitions in type of care sought and increased self-management.

Note. + indicates concordance or agreement between quantitative and qualitative results; - indicates discordance or lack of agreement between quantitative and qualitative results; +/- indicates that concordance between some of the quantitative and qualitative results but also discordance; M=mean; SE=standard error; SD= standard deviation; r_s= Spearman's Rho correlation; ICU=intensive care unit; ED=emergency department; PT=patient participant

Influence of Context

Results from the qualitative strand and quantitative strands describe the role of

individual context on intervention adherence, intervention dose, and intervention effect (Table 30). Correlations between frequency as operationalized as the number of days between nurse-coach led telephone sessions and baseline outcome measures of anxiety, depression, QoL, functional status, and mental health were statistically significant. Anxiety and depression had a positive association with frequency indicating that as participants endorsed higher anxiety and depression, the number of days between calls increased. Comparing these quantitative findings and qualitative findings, there is convergence. The qualitative findings add descriptions of participants' experiences with the intervention. Participants described how their context of disease-related factors, family support, provider relationship, logistical factors, and emotions influenced how they experienced the ENABLE CHF-PC intervention. For example, HF severity is associated with more days between calls (frequency) which converges with participants' descriptions of instances where their disease impacted their ability to answer a call (Table 30). Some instances of convergence included explanations of different aspects of the same construct. The qualitative theme of logistical factors influence intervention dose and participation may be seen quantitatively in the higher likelihood of intervention completion in retired participants. Some participants described the logistical factor of free time and provided descriptions of how "I wasn't doin' anything at the time that she would call" (PT 480) partially due to their retirement.

During integration, we identified a primary mixed methods finding. Intervention dose and intervention completion is influenced by individual contexts. These contexts described by participants in semi-structured interviews were reflected in correlation/odds

ratios. While comorbidity score was not related to dose attributes, participants described how severity of non-HF disease may have impacted intervention participation.

Table 30. Integration of Quantitative and Qualitative Intervention Dose Results

Result of Interest	Quantitative Results (Specific Aim #1-#2)	Qualitative Results (Specific Aim #3)	Concordance	Integration
Influence of Context	**1) *Age is associated with session count*** r_s=0.13, p<0.05 **2) *HF severity is associated with frequency*** r_s=0.40, p<0.05 **3) *Urban residents are less likely to complete the intervention (only after adjusting for covariates)*** OR=0.8, 95% CI [0.4, 1.8] **4) *Comorbidities are not associated with dose attributes (amount, frequency)*** r_s= -0.03, p>0.05 **5) *Baseline anxiety and depression are associated with frequency*** r_s=0.30, r_s=0.21 , p<0.05 **6) *Retired participants are more likely to complete the intervention*** OR=1.9, 95% CI [0.9, 4.1] ***7) Participants with a caregiver enrolled in study are more likely to complete the intervention*** OR=2.5, 95% CI [1.2, 5.3]	**1) *Disease-related factors*** *Exemplar quote for disease-related factors* "A lot of the time when I do a call, sometime I will be in a lot of pain, so I still would try to go ahead and accept her call and go through it." (PT 265) **2) *Family support*** *Exemplar quote for family support* "I knew a lotta the answers because, like I said, as a caregiver I had because she was on top of it." (PT 375) **3) *Provider relationships*** *Exemplar quote for provider relationships* "… if it hadn't of been somebody that really seemed like they were tryin' to help, you, might not of been so great that long" (PT 131) ***4) Logistical factors*** *Exemplar quote for logistical factors* "I guess, I wasn't doin' anything at the time that she would call" (PT 480) ***5) Emotions*** *Exemplar quote for emotions* "It [the intervention] did occur at the right time because I was worried about it in the beginning, but after the conversations and everything, it calmed me down... I could be relieved from that fear" (PT 356)	+	Contexts described by participants in semi-structured interviews were reflected in correlation/odds ratios. While comorbidity score was not related to dose attributes, participants described how severity of non-HF disease may have impacted intervention participation.

Note. + indicates concordance or agreement between quantitative and qualitative results; - indicates discordance or lack of agreement between quantitative and qualitative results; +/- indicates that concordance between some of the quantitative and qualitative results but also discordance; r_s= Spearman's Rho correlation; OR=odds ratio; CI= 5% confidence interval; PT=patient participant

Summary of Integrated Findings

In summary, the integration of the findings identified that individual context plays a critical role in early palliative care intervention completion and intervention effect in advanced heart failure patients in the Deep South. Additionally, integrated findings for primary outcomes include that QoL may experience a potential dose-related response and healthcare resource use change may not be captured with the current data collection questions.

CHAPTER FIVE

Intervention development guidelines highlight the importance of describing behavioral intervention dose and its potential impact on study outcomes (Bellg et al., 2004; Craig et al., 2008; Currow, Plummer, Kutner, Samsa, & Abernethy, 2012; Hoffmann et al., 2014). Examining dose provides insight into how varying intervention levels impact patients' outcomes and provides direction for future intervention development. However, few report palliative care intervention dose and none have examined palliative care intervention dose effect in advance heart failure to date. To address this gap, the aims of this embedded, concurrent mixed methods study were to examine the dose effects of an early palliative care, multicomponent psychoeducational intervention on the QoL and healthcare resource use of advanced heart failure patients (Specific Aim #1), to examine relationships between sociodemographic/clinical characteristics and dose attributes/intervention completion (Specific Aim #2), and to explore patients' experiences and perspectives on intervention dose, study participation, and study outcomes (Specific Aim #3). To understand dose more fully, the results of the analyses addressing Specific Aims #1-3 were then integrated to jointly explain intervention dose effect on study outcomes (Specific Aim #4). Intervention participation and outcome data from 208 advanced HF patients allocated to receive the ENABLE CHF-PC intervention in the parent study were included in quantitative analyses. A purposive sample of 45 ENABLE CHF-PC intervention patient participants completed

semi-structured interviews and provided descriptions and perspectives on intervention dose and outcomes.

Addressing the questions from Specific Aim #1, our findings suggest that dose may influence QoL outcomes at 16-weeks but not healthcare resource use. We found no significant differences in healthcare resource use between complete versus noncomplete dose groups at 16- and 32-weeks, however, baseline healthcare resource use was low. Addressing the questions from Specific Aim #2, examining relationships between the characteristics of age, residence, comorbidities, and HF severity of ENABLE CHF-PC intervention patient participants and dose attributes and intervention completion, we found several characteristics associated with dose. Those with rural residence, higher educational levels, higher health literacy, and living alone, with a caregiver enrolled in study were all more likely to complete the intervention. We found a positive mild association between age and session count (r_s=0.13, $p<0.05$) and a positive moderate association between NYHA HF class (HF severity) and frequency (r_s=0.40, $p<0.05$). We did not find a significant relationship between dose attributes and comorbidity. Analyses of the quantitative and qualitative data resulted in three integrated findings: 1) intervention dose impacts QoL that may be influenced by individual context, 2) intervention dose does not impact healthcare resource use, however non-measured healthcare resource use change may include changes not measured such as transitions from specialty to primary care, and 3) intervention dose, study participation, and outcomes are filtered through individual disease-related, family support, provider relationships, logistical, and emotional contexts.

Chapter 5 begins with the discussion of these findings in the context of existing literature. Following this discussion, the limitations of this concurrent mixed methods study are presented. Next, future research directions and clinical implications are discussed. The chapter concludes with a brief summary of the findings and discussion.

Discussion

Specific Aim #1: Intervention Dose Effect on Quality of Life and Healthcare Resource Use

Quality of life. Patients living with advanced heart failure often experience poor quality life (Bekelman et al., 2009; Jaarsma, Johansson, Agren, & Stromberg, 2010) and frequent hospitalizations (Benjamin et al., 2019). Participants who completed the intervention experienced higher QoL at 16-weeks than those who did not complete all of the intervention. A possible explanation of the dose-related intervention effect is that the ENABLE CHF-PC intervention led to higher activation which leads to improved QoL (Hibbard, Green, & Tusler, 2009; Hibbard, Mahoney, Stock, & Tusler, 2007; Magnezi, Glasser, Shalev, Sheiber, & Reuveni, 2014; Mosen, et al., 2007) as hypothesized in the parent study (Wells et al., 2018). However, these positive dose-related effects were not sustained through 32 weeks.

Findings from the qualitative strand (Specific Aim #3) contribute to a more comprehensive understanding of these results. A possible explanation for the non-sustained completed intervention effect is high baseline QoL. Many participants reported they did not experience QoL change due to their ‘good’ health status. ENABLE CHF-PC intervention participants reported higher baseline QoL on the KCCQ in comparison to

other similar trials (Bekelman et al., 2018; Rogers et al., 2017). Additionally, participants commonly described QoL in conjunction with either emotional or physical symptoms. Participants who described QoL in terms of emotional symptoms often felt that the intervention impacted their QoL. This split relationship of emotional versus physical symptoms and the influence on QoL has been previously described (Evangelista, Moser, Dracup, Doering, & Kobashigawa, 2004; Heo, Lennie, Chizmuzo, & Moser, 2009; Nieminen et al., 2015; Seongkum et al., 2014) and noted in other palliative care intervention studies for heart failure (Bekelman et al., 2018; Sidebottom et al., 2015; Wong et al., 2016). Additionally, lower-intensity monthly calls may have contributed to the change in intervention effect found at 24- and 32- weeks. On average, participants completed their last ENABLE CHF-PC weekly telephone call and OPCC between 8- and 16- weeks. This intervention effect drop at 24- and 32- weeks during the transition from higher intensity, weekly telephone sessions along with the OPCC to a lower intensity, monthly check-in telephone calls suggests a dose response. However, our dose groups for analyses did not include the amount, frequency, or duration of monthly calls.

While this study was one of the first to examine the dose-related intervention effects, other studies, including three palliative care heart failure RCTs (Rogers et al., 2017, Sidebottom et al., 2015; Wong et al., 2016) found QoL improvements with palliative care interventions at 12- or 24- weeks. Another RCT reported non-significant, but clinically relevant change in the KCCQ (Bekelman et al., 2018). The intervention effect difference of the ‘complete’ dose was not sustained through 32-weeks, a later time point that we could not find a comparison for in the literature. However, at 32-weeks, both dose groups improved >5 points on the KCCQ from baseline, a clinically significant

change (Green et al., 2000). While these studies found positive palliative care intervention effects on QoL (Bakitas, et al., 2017; Bekelman et al., 2018; Brannstromm & Boman, 2014; Evangelista et al., 2012; Kane et al., 2017; Rogers et al., 2017; Sidebottom, Jorgenson, Richards, Kirven, & Sillah, 2015; Wong et al., 2016), no study examined the influence of intervention dose on these outcomes. Additionally, limited information is provided about patient participation in the intervention. Two studies, PAL-HF (Rogers et al., 2017) and CASA (Bekelman et al., 2018) included details about intervention participation. Rogers et al. (2017) report the mean number of healthcare encounters intervention participants received over the 6-month study period (12.6 telephone calls; 21.9 clinic encounters) and highlighted the difficulty in capturing distinct elements of an intervention from clinical encounters. Bekelman et al. (2018) reported the mean number of nurse and social worker visits and intervention amount (13.1 nurse visits averaging 25.3 minutes; 10.1 social worker visits averaging 33.6 minutes). However, comparison between those studies and the current study is limited as they did not report all dose attributes (i.e., frequency, duration, intensity) and there were no additional analyses were completed to examine whether a differential intervention dose effected patient outcomes.

While we found QoL dose group differences in the linear mixed models, mean QoL and healthcare resource use change was not associated with dose attributes of amount and frequency (Tables 18-19). The interaction between dose attributes may have contributed to a larger overall intervention dose impact. This possible explanation is also supported by qualitative findings as patients often described the intervention as “it’s the combination” (PT 198) rather than a single dose attribute.

Healthcare resource use. Participants who completed all of the intervention did not have lower healthcare resource use at 16- or 32-weeks. We found no statistically significant effect differences between dose groups during all data collection time points, indicating that healthcare resource use may not experience dose-related change. Overall, healthcare resource use was low, especially in comparison to larger HF studies (Benjamin et al., 2019; Bergethon et al., 2016; Suter et al., 2014) and trended lower throughout the study. This low healthcare resource use has limited modifiability which is a possible explanation for the lack of healthcare resource use change.

Our findings are consistent with the studies of Bekelman et al. (2018), Rogers et al., (2017), and Sidebottom et al. (2015) in which there were no statistically significant intervention effect on rehospitalization or healthcare utilization use. In contrast, some studies did find decreased hospitalizations or other healthcare resource use (Brannstrom et al., 2014; Pattenden et al., 2013; Wong et al., 2016). There are a number of reasons why healthcare resource use findings might be mixed. First, these mixed findings may be related to the timing of the palliative care interventions as inclusion criteria described by Brannstrom et al. (2017) and Pattenden et al. (2013) included a prognosis of 6 months or less, a hospice eligibility criteria. Second, this embedded concurrent mixed method study occurred at an earlier time in the HF trajectory concurrent to patients seeking aggressive treatment which may contribute to the lack of healthcare resource use change. Rabow et al. (2004) also reported decreased healthcare resource use excluding hospital or ED visits. When considering healthcare resource use, Rabow et al. (2004) also tracked primary care, urgent care, and specialty care clinic visits. By broadening healthcare resource use

change outside of an acute care setting, this finding by Rabow et al. (2004) highlights similar findings from the qualitative strand (Specific Aim #3). Third, when participants described healthcare resource use change, they often described transition of care change from specialty care to self-management or primary care. For example, PT 241, a 56 year old black male, described this transition to self-management as a result of completing the intervention, "I haven't had to go to the hospital for the heart, because I'm trying to do the right thing and eat the right thing and just take care of myself." Another possible explanation for the lack of dose-related intervention effect is that healthcare resource use changed in ways that were not measured quantitatively.

Specific Aim #2: Intervention Dose Attributes and Intervention Completion Associated Characteristics

We found a small, positive association between age and session count, such that older patients tended to complete more sessions. This relationship is consistent with other HF studies, which found increased adherence in older patients (Juarez et al., 2015; Kruger et al., 2015; Rolnick, Pawloski, Hedblom, Asche, & Bruzek, 2013; Ware et al., 2019). However, a HF medication-focused meta-analysis by Oosterom-Calo et al. (2013) was inconclusive about the relationship between age and adherence. The relationship between age and higher completion of telephone sessions may be partially explained by the availability of free time as identified in the qualitative strand (Specific Aim #3). Many of the interviewees identified their available free time as a facilitator for intervention as they did not experience work or childcare time constraints during their study participation. For example, PT 480, a 63 year old black female, described how her

free time contributed to her answering the nurse coach's call, "I guess, I wasn't doin' anything at the time that she would call."

Findings about the relationship between HF severity, as measured by NYHA class or AHA/ACC stage, and participation in HF interventions are mixed (Oosterom-Calo et al., 2013). We found that HF severity was associated with increased number of days between completed telephone sessions. While not statistically significant, HF severity also had a small negative association with telephone sessions completed. Participants with higher NYHA classification (NYHA Class IIIb/IV) were half as likely less likely to complete all of the intervention (Table 20). HF severity as a barrier to intervention completion or adherence, as evidenced by this less frequent session completion, is consistent with other HF studies (Conraads et al., 2012; Riegel et al. 2006; Riegel et al. 2007). Comorbidities are often associated with decreased adherence and intervention completion (Corotto, McCarey, Adams, Khaszanie, & Whellan, 2012; Granger et al., 2009), yet we did not find a significant relationship between dose attributes and comorbidity. This lack of relationship may be related to the prevalence of adaptive coping strategies in the sample (Table 10) as seen in studies with hypertensive (Rueda & Perez-Garcia, 2013) and coronary artery disease patients (Yu, Chen, Zhang, & Liu, 2011). Another possible explanation are sociodemographic and clinical differences in HF samples eligible for palliative care trials. While age, HF severity, and comorbidity had distinct relationships or lack of relationships with intervention completion and dose attributes, the relationship between intervention completion and residence is less clear. The unadjusted odds ratio for residence indicates that urban residents are slightly more likely to complete the intervention (OR=1.1). With the adjusted multivariate logistic

model, this slight likelihood is flipped with urban residents slightly less likely to complete the intervention (OR=0.8) indicating the impact of residence is effected by age, HF severity, and comorbidities. This finding of urban residents being less likely to complete the intervention is not consistent with other literature examining healthcare seeking behavior in HF (Caldwell, Peters, & Dracup, 2005) and palliative care literature (Goodridge et al., 2010). However, this vacillation before and after model adjustment highlights the complexity of examining factors associated with intervention dose and completion as multiple factors may jointly influence participation.

Specific Aim #3: Patients' Experiences with Intervention Dose and Outcomes

We identified three major categories within semi-structured interviews related to impressions of ENABLE intervention dose and dose attributes, individual contexts, and study outcomes (Table 27). First, after assigning participants to groups by dose, gender, race, and residence and comparing responses, we did not identify singular themes within groups. Lack of within group common experiences was surprising given literature reported common HF experiences by gender (Allen, Arslanian-Engoren, & Lynch-Sauer, 2009; Lee et al., 2009), race (Woodard, Hernandez, Lees, & Petersen, 2005), and residence (Weierbach, Glick, & Lyder, 2011). One of the most common findings was the variability in dose experience and study outcomes with participants often describing the ENABLE CHF-PC intervention dose or dose attributes as, "too much", "just right", or "too short." These responses offer a great analogy, the Goldilocks story, to illustrate the experience with intervention dose and dose effects in the ENABLE CHF-PC study. The use of Goldilocks terminology, frequently dubbed the "Goldilocks phenomenon" or

"Goldilocks principle" to describe the "fit" of a study experience, dose, situation or intervention has been referenced previously in cognitive psychology (Kidd, Piantadosi, & Aslin, 2012), heart failure hemodynamics (Headley, 2016), respiratory therapy (Martin & Grocott, 2017), and exercise physiology (Straker, Mathiassen, & Holtermann, 2017) This Goldilocks phenomenon extended beyond dose attributes of amount, duration, and frequency as ENABLE CHF-PC participants frequently described the impact of intervention dose on their QoL and healthcare resource use in similar terms. This Goldilocks phenomenon highlights the complexity of intervention design as, despite shared HF diagnosis, the intervention dose and experience resonated differently with each participant. This differing resonance in early palliative care intervention dose and design may be an argument to consider principles of precision medicine (Kahkoska et al., 2019; National Institute of Health, 2019; Simmons, Wolever, Bechard, & Synderman, 2014), adaptive interventions (Collins, Murphy, & Bierman, 2004), and SMART trial design (Lei, Nahum-Shani, Lynch, Oslin, & Murphy, 2012).

While participants were divided regarding the influence of intervention dose on their study experience and QoL and healthcare resource use outcomes, almost all described the role of individual contexts on how they experienced intervention dose and the ENABLE CHF-PC study. Common contexts described by participants include disease-related factors, social support, nurse coach or provider relationships, logistical factors, and emotions (Table 27). Participants often reported that their emotional state of mind influenced their engagement with the intervention. For example, one participant described a relationship between her anxiety and her willingness to complete the telephone session. This participant described how her anxiety acted as a barrier to

participation, a finding consistent with other behavioral intervention literature outside of palliative care (Leslie, McCowan, & Pell, 2019; McGrady, McGinnis, Badenhop, Bentle, & Rajput, 2009; Sundborn & Bingefors, 2013).

Limitations of the Study

To our knowledge, this concurrent mixed methods study is one of the first studies to explore the role and influence of an early palliative care intervention dose. Given this innovative exploration of psychoeducational intervention dose, we encountered a paucity of frameworks to direct the operationalization of dose and dose attributes of the intervention. The difficulty in defining cumulative dose may have led to misclassification of intervention exposure. To minimize the potential for inaccurately measuring dose of the ENABLE CHF-PC intervention, which may be composed of additive or multiplicative relationships between dose attributes and differential weights of components like the OPCC, we defined dose for analysis as a dichotomous 'complete or noncomplete' variable based on the protocol definition of the intervention. Measurement of the dichotomous dose variable was verified in multiple sources including the ENABLE CHF-PC dataset, nurse coach notes, and the OPCC clinic notes.

This study used the ENABLE CHF-PC RCT as a data source. As the intervention in the ENABLE CHF-PC RCT was designed as a single level of intervention dose, we created post-hoc dose groups. Given this post-hoc creation, self-selection bias is another potential limitation as participants determined how much of the intervention they received. While all patients were offered and encouraged to complete all 6 telephone-based sessions and the one-time, in-person OPCC, patients completed varying amounts of

the intervention components. This selection bias may have contributed to the differences in outcome change, as this type of bias may lead to underestimation or overestimation of the true association between exposure to the intervention and QoL and healthcare resource use change. To address this limitation, we compared the dose groups and controlled for differences between the groups in our mixed models.

One limitation of the qualitative strand is researcher bias in the collection, analysis, and interpretation of the qualitative data. The PI was a former nurse coach and current research assistant for the ENABLE CHF-PC parent study. To minimize bias during the interview, all participants were interviewed by study staff who were not assigned to deliver the intervention to them. Other strategies to address researcher bias was the use of field notes, journaling, and member checking (Cooney, 2011; Miles, Huberman, Saldana, 2019). The delay from the completion of the intervention and the semi-structured interview contributed (3 weeks to 2 years 7 months) to the possible limitation of limited recall. We attempted to mitigate this recall bias by noting recall difficulties on the field notes and referring frequently to the notes during analysis and interpretation. Additionally, several interviews were truncated due to significant recall difficulties per the request of the interviewees. While some participants may have had difficulty recalling certain details of the intervention, the overall themes were found throughout multiple interviews.

Another possible limitation of the qualitative strand is social desirability bias (Polit & Beck, 2017). To minimize the possibility of participants responding to interview questions in a ‘favorable’ or socially desirable fashion, interviewers frequently assured

participants that there were ‘no right or wrong answers’ and were interviewed by unfamiliar study staff, a strategy highlighted by Nederhof (1985).

While both complete and noncomplete groups were well represented in the interview sample, interviewees who did not complete all the intervention completed more of the telephone sessions than the noncomplete subsample in the quantitative strand. Additionally, the interview sample also included less males. To address this limitation, we assigned dose group, gender, race, and residence attributes during the analysis to aid with comparison and found few differences between male and female interview participants’ responses.

Implications

This study highlighted the need for additional research in the influence of palliative care intervention dose on outcomes of patients with advanced heart failure. Future research may examine the palliative care intervention dose relationships in greater detail. As the parent study is guided by an intention-to-treat principle and intervention participants self-selected the ‘dose’ they received, future analyses of this dataset should include comparison with usual care participants as a counterfactual to the ‘complete’ and ‘noncomplete’ dose groups. Caregivers of patients also participated in the parent ENABLE CHF-PC study and future analyses should examine the influence of dyadic relationships on intervention completion and dose-related intervention effect. Prior research suggests that dyadic relationships impact HF self-management, though findings are mixed (Buck et al., 2018). Additionally, heterogeneity in perceived outcome change described by participants in the qualitative strand suggests that effect modification might

be present. Given the potential of heterogeneity of treatment effects, a responder analysis, a type of sensitivity analysis that dichotomizes the sample into two groups based on a cut point change in a specific outcome (Kieser, Friede, & Gondan, 2013), might provide more insight into subgroups who may optimally benefit from this type of intervention. Examining heterogeneity of treatment effects may also inform intervention development particularly if a responder 'phenotype' emerges.

Context is an important consideration for future palliative care interventions for advanced heart failure patients. Findings from both the quantitative and qualitative strand highlighted the importance of individual context in engagement, adherence, and perception of study-related change in early palliative care psychoeducational interventions. In particular, participants described how disease-related factors and their relationship with the nurse coach greatly impacted their study experience and outcomes. Future research may consider exploring more fully the role of these individual contextual factors. One approach for palliative care intervention studies may be designing adaptive interventions, including assessment points that tailor the intervention to the individual needs and context that the participant is experiencing. While patients described a highly individualized approach to participating in the intervention, one common context that influenced intervention participation and outcomes was mood. This impact of mood on intervention participation and effects is consistent with other literature (Navidian, Yaghoubinia, Ganjali, Khoshimaee, 2015). Additionally, previous studies have examined mood as a predictor of mortality and QoL in heart failure (Chen,Kao, Cheng, & Chang, 2018; Hallas, Wray, Andreou, & Banner, 2011). Given the association of anxiety and depression on frequency and amount and QoL, assessment of mood would be an ideal

decision point for providing different intervention intensity. This adaptive intervention design has been tested in HF with positive outcomes. For example, a previous study of an adaptive telephone-based intervention focused on HF patient education reported improved self-care behaviors and reduced hospitalizations (Unverzagt,et al., 2016).

Findings from the quantitative strand suggest that dose of an intervention may influence QoL outcomes. A larger study with a priori dose categories may provide a more comprehensive understanding of this relationship. Future work may investigate the timing of effect as our study found significant changes in QoL were not sustained during the study period. In addition to a priori doses of a palliative care intervention, future work may explore the relationships between dose attributes, cumulative dose, and outcome change. As this study focused on describing dose of the ENABLE CHF-PC intervention based on literature-derived definitions, we did not propose a model for how these attributes interact to comprise a cumulative dose. Further investigation of a dose model may address some of the mixed findings of this study as correlations of individual dose attributes were not related to outcome change but greater dose exposure resulted in higher change on QoL measures. Palliative care behavioral intervention dose may need to be conceptualized differently from dose in psychology, exercise physiology, nutrition, education, or pharmacology. Additionally, developing and testing an outcome or behavior change dose framework within palliative care is a necessary next step for comparison of multiple studies.

The findings of this study suggest that increased exposure to early palliative care services may be beneficial to certain subgroups of advanced HF patients in the Deep South. Our findings reinforce the need for early palliative care for advanced HF patients

as many patients endorsed the timing or requested earlier timing of the intervention. Consideration should be given to the types of measureable contexts and assessments that might act as clinical triggers to help identify HF patients who may benefit from more intense early exposure.

HF education needs remain high as HF progresses and patients identified a common impact of increased knowledge related to study participation. Information about management of heart failure and self-care are needed throughout the HF trajectory. Nurses can play a vital role in continuing HF education as members of a palliative care team. Patients also highlighted the importance of health care professionals 'taking time' to listen to their experiences about living with HF. These findings highlight the role of perception of healthcare providers' listening and its relationship to perceived support. While future research is needed to more fully understand this relationship, these findings may provide insight into provider-patient relationship and communication.

Conclusion

To address the overall research question that guided this study, "does dose impact an early palliative care intervention effect for advanced heart failure patients?," both qualitative and quantitative findings indicate that dose effects depend on which outcome is examined and the individual, community, and health services context. While the results of this study suggest that QoL may be influenced by the dose of the intervention, little effect was seen on healthcare resource use. A possible explanation for the lack of intervention dose effect in healthcare resource use is the focus on hospital associated resource use only. Findings from the qualitative strand indicate that some healthcare

resource use changes were actions not measured, such as seeking out primary care or self-management. Additionally, healthcare resource use in the study sample was low in comparison to other HF studies (Akintoye et al., 2017; Blecker, Paul, Taksler, Ogedegbe, & Katz, 2013; Dharmarajan et al., 2013). This study also contributes to the body of knowledge around intervention completion and adherence in palliative care and heart failure intervention studies. While some of our sociodemographic and clinical characteristics associated with intervention completion are consistent with the literature such as age and HF severity, others such as rural residence and comorbidity were not. Additionally, to our knowledge, this is one of the first studies to examine the relationships of palliative care intervention dose attributes with QoL and healthcare resource use outcome change. Future work should address development of a behavioral intervention dose model and application of individual context of advanced heart failure patients through adaptive intervention design, SMART designs, or targeted assessment for specialized palliative care services. Our study provides support to current palliative care models for advanced heart failure, such as the one proposed by Allen et al. (2012), where palliative care is introduced at the onset of disease and dynamically adapts to palliative care needs as the disease progresses.

References

Abebe, T. B., Gebreyohannes, E. A., Tefera, Y. G., & Abegaz, T. M. (2016). Patients with HFpEF and HFrEF have different clinical characteristics but similar prognosis: a retrospective cohort study. *BMC Cardiovascular Disorders, 16*, 232. doi:10.1186/s12872-016-0418-9

Adler, E. D., Goldfinger, J. Z., Kalman, J., Park, M. E., & Meier, D. E. (2009). Palliative care in the treatment of advanced heart failure. *Circulation, 120*, 2597-2606. doi:10.1161/CIRCULATIONAHA.109.869123

Agar, M., Ko, D. N., Sheehan, C., Chapman, M., & Currow, D. C. (2013). Informed consent in palliative care clinical trials: challenging but possible. *Journal of Palliative Medicine, 16*, 485-491. doi:10.1089/jpm.2012.0422

Agency for Healthcare Research and Quality. (2014). Transforming the organization and delivery of primary care. Retrieved from https://pcmh.ahrq.gov/

Ahia, C. L., & Blais, C. M. (2014). Primary palliative care for the general internist: Integrating goals of care discussions into the outpatient setting. *Ochsner Journal, 14*, 704-711.

Aiken, L. S., Butner, J., Lockhart, C. A., Volk-Craft, B. E., Hamilton, G., & Williams, F. G. (2006). Outcome evaluation of a randomized trial of the PhoenixCare intervention: Program of case management and coordinated care for the seriously chronically ill. *Journal of Palliative Medicine, 9*, 111-126. doi:10.1089/jpm.2006.9.111

Akintoye, E., Briasoulis, A., Egbe, A., Adegbala, O., Alliu, S., Sheikh, M., . . . Levine, D. (2017). Seasonal variation in hospitalization outcomes in patients admitted for heart failure in the United States. *Clinical Cardiology, 40*, 1105-1111. doi:10.1002/clc.22784

Allen, J. W., Arslanian-Engoren, C., & Lynch-Sauer, J. (2009). The lived experience of middle-aged women with New York Heart Association Class III heart failure: A pilot study. *Progress in Cardiovascular Nursing, 24*, 96-101.

Allen, K. R., Hazelett, S. E., Radwany, S., Ertle, D., Fosnight, S. M., & Moore, P. S. (2012). The promoting effective advance care for elders (PEACE) randomized pilot study: Theoretical framework and study design. *Population Health Management, 15*, 71-77. doi:10.1089/pop.2011.0004

Allen, L. A., Stevenson, L. W., Grady, K. L., Goldstein, N. E., Matlock, D. D., Arnold, R. M., . . . Spertus, J. A. (2012). Decision making in advanced heart failure. *Circulation, 125*. doi:10.1161/CIR.0b013e31824f2173

Alpert, C. M., Smith, M. A., Hummel, S. L., & Hummel, E. K. (2017). Symptom burden in heart failure: assessment, impact on outcomes, and management. *Heart Failure Reviews, 22,* 25-39. doi:10.1007/s10741-016-9581-4

Alvarez, J. S., Goldraich, L. A., Nunes, A. H., Zandavalli, M. C., Zandavalli, R. B., Belli, K. C., . . . Clausell, N. (2016). Association between spirituality and adherence to management in outpatients with heart failure. *Arquivos Brasileiros de Cardiologia, 106,* 491-501. doi:10.5935/abc.20160076

American Heart Association. (2018). Classes of heart failure. Retrieved from http://www.heart.org/HEARTORG/Conditions/HeartFailure/AboutHeartFailure/Classes-of-Heart-Failure_UCM_306328_Article.jsp#.WxYk-0xFzVI

American Heart Association. (2017). Heart and stroke statistics. Retrieved from https://www.heart.org/en/about-us/heart-and-stroke-association-statistics

Ammari, A. B., Hendriksen, C., & Rydahl-Hansen, S. (2015). Fecruitment and reasons for non-participation in a family-coping-orientated palliative home care trial (FAMCOPE). *Journal of Psychosocial Oncology, 33,* 655-674. doi:10.1080/07347332.2015.1082168

Ariel, A. H., & Perri, M. G. (2016). Effect of dose of behavioral treatment for obesity on binge eating severity. *Eating Behaviors, 22,* 55-61. doi:10.1016/j.eatbeh.2016.03.032

Arozullah, A.M., Yarnold, P.B., Bennett, C.L., et al. (2007). Development and validation of a short-form, rapid estimate of adult literacy in medicine. *Medical Care, 45,* 1026–33. doi: 10.1097/MLR.0b013e3180616c1b

Audrey, S. (2011). Qualitative research in evidence-based medicine: improving decision-making and participation in randomized controlled trials of cancer treatments. *Palliative Medicine, 25,* 758-765. doi:10.1177/0269216311419548

Bahrami, H., Kronmal, R., Bluemke, D. A., & et al. (2008). Differences in the incidence of congestive heart failure by ethnicity: The multi-ethnic study of atherosclerosis. *Archives of Internal Medicine, 168,* 2138-2145. doi:10.1001/archinte.168.19.2138

Bakitas, M., Dionne-Odom, J. N., Pamboukian, S. V., Tallaj, J., Kvale, E., Swetz, K. M., . . . Kono, A. T. (2017). Engaging patients and families to create a feasible clinical trial integrating palliative and heart failure care: results of the ENABLE CHF-PC pilot clinical trial. *BMC Palliative Care, 16,* 45. doi:10.1186/s12904-017-0226-8

Bakitas, M., Lyons, K. D., Hegel, M. T., Balan, S., Brokaw, F. C., Seville, J., . . . Ahles, T. A. (2009). Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer: The project ENABLE II randomized controlled

trial. *Journal of the American Medical Association, 302*, 741-749. doi:10.1001/jama.2009.1198

Bakitas, M., Macmartin, M., Trzepkowski, K., Robert, A., Jackson, L., Brown, J. R., . . . Kono, A. (2013). Palliative care consultations for heart failure patients: How many, when, and why? *Journal of Cardiac Failure, 19*, 193-201. doi:10.1016/j.cardfail.2013.01.011

Barry, D., Frew, A. H., Mohammed, H., Desta, B. F., Tadesse, L., Aklilu, Y., . . . Sibley, L. M. (2014). The effect of community maternal and newborn health family meetings on type of birth attendant and completeness of maternal and newborn care received during birth and the early postnatal period in rural Ethiopia. *Journal of Midwifery & Womens Health, 59*-Suppl 1, S44-54. doi:10.1111/jmwh.12171

Bauer, L. K., Caro, M. A., Beach, S. R., Mastromauro, C. A., Lenihan, E., Januzzi, J. L., & Huffman, J. C. (2012). Effects of depression and anxiety improvement on adherence to medication and health behaviors in recently hospitalized cardiac patients. *American Journal of Cardiology, 109*, 1266-1271. doi:10.1016/j.amjcard.2011.12.017

Beatty, L., & Binnion, C. (2016). A systematic review of predictors of, and reasons for, adherence to online psychological interventions. *International Journal of Behavioral Medicine, 23*, 776-794. doi:10.1007/s12529-016-9556-9

Bekelman, D. B., Allen, L. A., McBryde, C. F., Hattler, B., Fairclough, D. L., Havranek, E. P., . . . Meek, P. M. (2018). Effect of a collaborative care intervention vs usual care on health status of patients with chronic heart failure: The CASA randomized clinical trial. *JAMA Internal Medicine, 178*, 511-519. doi:10.1001/jamainternmed.2017.8667

Bekelman, D. B., Havranek, E. P., Becker, D. M., Kutner, J. S., Peterson, P. N., Wittstein, I. S., . . . Dy, S. M. (2007). Symptoms, depression, and quality of life in patients with heart failure. *Journal of Cardiac Failure, 13*, 643-648. doi:10.1016/j.cardfail.2007.05.005

Bekelman, D. B., Hooker, S., Nowels, C. T., Main, D. S., Meek, P., McBryde, C., . . . Heidenreich, P. A. (2014). Feasibility and acceptability of a collaborative care intervention to improve symptoms and quality of life in chronic heart failure: Mixed methods pilot trial. *Journal of Palliative Medicine, 17*, 145-151. doi:10.1089/jpm.2013.0143

Bekelman, D. B., Rumsfeld, J. S., Havranek, E. P., Yamashita, T. E., Hutt, E., Gottlieb, S. H., . . . Kutner, J. S. (2009). Symptom burden, depression, and spiritual well-being: a comparison of heart failure and advanced cancer patients. *Journal of Geriatrics Internal Medicine, 24*, 592-598. doi:10.1007/s11606-009-0931-y

Bellg, A. J., Borrelli, B., Resnick, B., Hecht, J., Minicucci, D. S., Ory, M., . . . Czajkowski, S. (2004). Enhancing treatment fidelity in health behavior change studies: best practices and recommendations from the NIH behavior change consortium. *Health Psychology, 23*. doi:10.1037/0278-6133.23.5.443

Benjamin Emelia, J., Muntner, P., Alonso, A., Bittencourt Marcio, S., Callaway Clifton, W., Carson, A.P.… Virani, S. S. (2019). Heart disease and stroke statistics—2019 update: A report from the American Heart Association. *Circulation, 139,* e56-e528. Retrieved from https://doi.org/10.1161/CIR.0000000000000659. doi:10.1161/CIR.0000000000000659

Bibbins-Domingo, K., Pletcher, M. J., Lin, F., Vittinghoff, E., Gardin, J. M., Arynchyn, A., . . . Hulley, S. B. (2009). Racial differences in incident heart failure among young adults. *New England Journal of Medicine, 360,* 1179-1190. doi:10.1056/NEJMoa0807265

Bjelland, I., Dahl, A. A., Haug, T. T., & Neckelmann, D. (2002). The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *Journal of Psychosomatic Research, 52,* 69-77.

Blecker, S., Paul, M., Taksler, G., Ogedegbe, G., & Katz, S. (2013). Heart failure–associated hospitalizations in the United States. *Journal of the American College of Cardiology, 61,* 1259-1267. doi:https://doi.org/10.1016/j.jacc.2012.12.038

Bleehen, N. M., Girling, D. J., Machin, D., & Stephens, R. J. (1993). A randomised trial of three or six courses of etoposide cyclophosphamide methotrexate and vincristine or six courses of etoposide and ifosfamide in small cell lung cancer (SCLC). II: Quality of life. Medical Research Council Lung Cancer Working Party. *British Journal of Cancer, 68,* 1157-1166.

Blinderman, C. D., Homel, P., Billings, J. A., Portenoy, R. K., & Tennstedt, S. L. (2008). Symptom distress and quality of life in patients with advanced congestive heart failure. *Journal of Pain & Symptom Management, 35,* 594-603. doi:10.1016/j.jpainsymman.2007.06.007

Borlaug, B. A., & Paulus, W. J. (2011). Heart failure with preserved ejection fraction: pathophysiology, diagnosis, and treatment. *European Heart Journal, 32,* 670-679. doi:10.1093/eurheartj/ehq426

Bouça-Machado, R., Rosário, M., Alarcão, J., Correia-Guedes, L., Abreu, D., & Ferreira, J. J. (2017). Clinical trials in palliative care: A systematic review of their methodological characteristics and of the quality of their reporting. *BMC Palliative Care, 16,* 10. doi:10.1186/s12904-016-0181-9

Brannstrom, M., & Boman, K. (2014). Effects of person-centred and integrated chronic heart failure and palliative home care. PREFER: a randomized controlled study. *European Journal of Heart Failure, 16*, 1142-1151. doi:10.1002/ejhf.151

Brumley, R., Enguidanos, S., Jamison, P., Seitz, R., Morgenstern, N., Saito, S., . . . Gonzalez, J. (2007). Increased satisfaction with care and lower costs: results of a randomized trial of in-home palliative care. *Journal of American Geriatric Society, 55*, 993-1000. doi:10.1111/j.1532-5415.2007.01234.x

Buck, H. G., Hupcey, J., Wang, H.-L., Fradley, M., Donovan, K. A., & Watach, A. (2018). Heart failure self-care within the context of patient and informal caregiver dyadic engagement: A mixed methods study. *Journal of Cardiovascular Nursing, 33*, 384-391. doi:10.1097/jcn.0000000000000465

Buttorff, C., Ruder, T., & Bauman, M. (2017). Multiple chronic conditions in the United States. [pdf] Santa Monica, CA: RAND Corp. Retrieved from https://www.rand.org/content/dam/rand/pubs/tools/TL200/TL221/RAND_TL221.pdf

Cagle, J. G., Bunting, M., Kelemen, A., Lee, J., Terry, D., & Harris, R. (2017). Psychosocial needs and interventions for heart failure patients and families receiving palliative care support: a systematic review. *Heart Failure Reviews, 22*, 565-580. Retrieved from https://doi.org/10.1007/s10741-017-9596-5. doi:10.1007/s10741-017-9596-5

Caldwell, M. A., Peters, K. J., & Dracup, K. A. (2005). A simplified education program improves knowledge, self-care behavior, and disease severity in heart failure patients in rural settings. *American Heart Journal, 150*, 983. doi:10.1016/j.ahj.2005.08.005

Callahan, C. M., Unverzagt, F. W., Hui, S. L., Perkins, A. J., & Hendrie, H. C. (2002). Six-item screener to identify cognitive impairment among potential subjects for clinical research. *Medical Care, 40*, 771-781. doi:10.1097/00005650-200209000-00007

Campbell, D. J. T., Tam-Tham, H., Dhaliwal, K. K., Manns, B. J., Hemmelgarn, B. R., Sanmartin, C., & King-Shier, K. (2017). Use of mixed methods research in research on coronary artery disease, diabetes mellitus, and hypertension. *Circulation: Cardiovascular Quality and Outcomes, 10*. e003310. Retrieved from https://www.ahajournals.org/doi/abs/10.1161/CIRCOUTCOMES.116.003310. doi:doi:10.1161/CIRCOUTCOMES.116.003310

Candy, B., Vickerstaff, V., Jones, L., & King, M. (2018). Description of complex interventions: analysis of changes in reporting in randomised trials since 2002. *Trials, 19*, 110. doi:10.1186/s13063-018-2503-0

Carroll, C., Patterson, M., Wood, S., Booth, A., Rick, J., & Balain, S. (2007). A conceptual framework for implementation fidelity. *Implementation science, 2*, 40-40.

Center to Advance Palliative Care (n.d.). About palliative care. Retrieved from https://www.capc.org/about/palliative-care/

Centers for Disease Control and Prevention, National Center for Health Statistics. (2018). Chronic illness. Retrieved from https://www.cdc.gov/chronicdisease/about/multiple-chronic.htm

Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion. (2019). About chronic diseases. Retrieved from https://www.cdc.gov/chronicdisease/about/index.htm

Chan, A.-W., Tetzlaff, J. M., Gøtzsche, P. C., Altman, D. G., Mann, H., Berlin, J. A., . . . Moher, D. (2013). SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ : British Medical Journal, 346*, e7586.

Charlson, M. E., Pompei, P., Ales, K. L., & MacKenzie, C. R. (1987). A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *Journal of Chronic Disease, 40*, 373-383.

Collins, L. M., Murphy, S. A., & Strecher, V. (2007). The multiphase optimization strategy (most) and the sequential multiple assignment randomized trial (smart). new methods for more potent ehealth interventions. *American Journal of Preventive Medicine, 32*. doi:10.1016/j.amepre.2007.01.022

Collins, L. M., Murphy, S. A., & Bierman, K. L. (2004). A conceptual framework for adaptive preventive interventions. *Prevention Science, 5*, 185-96.

Cooney, A. (2011). Rigour and grounded theory. *Nurse Researcher, 18*, 17-22.

Conraads, V. M., Deaton, C., Piotrowicz, E., Santaularia, N., Tierney, S., Piepoli, M. F. . . . . Jaarsma, T. (2012). Adherence of heart failure patients to exercise: barriers and possible solutions. *European Journal of Heart Failure, 14*, 451-458.

Corotto, P. S., McCarey, M. M., Adams, S., Khazanie, P., & Whellan, D. J. (2013). Heart failure patient adherence: Epidemiology, cause, and treatment. *Heart Failure Clinics, 9*, 49-58. Retrieved from https://doi.org/10.1016/j.hfc.2012.09.004. doi:10.1016/j.hfc.2012.09.004

Craig, P., Dieppe, P., Macintyre, S., Michie, S., Nazareth, I., & Petticrew, M. (2008). Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ: British Medical Journal*, 337.

Creswell, J.W. & Poth, C.N. (2018). Qualitative inquiry and research design: Choosing among five approaches. Thousand Oaks, California: SAGE Publications.

Cummings, G. G., Olivo, S. A., Biondo, P. D., Stiles, C. R., Yurtseven, O., Fainsinger, R. L., & Hagen, N. A. (2011). Effectiveness of knowledge translation interventions to improve cancer pain management. *Journal of Pain & Symptom Management, 41*, 915-939. doi:10.1016/j.jpainsymman.2010.07.017

Currow, D. C., Plummer, J. L., Kutner, J. S., Samsa, G. P., & Abernethy, A. P. (2012). Analyzing phase III studies in hospice/palliative care. a solution that sits between intention-to-treat and per protocol analyses: the palliative-modified ITT analysis. *Journal of Pain and Symptom Management, 44*, 595-603. doi:10.1016/j.jpainsymman.2011.10.028

Curry, L. A., Nembhard, I. M., & Bradley, E. H. (2009). Qualitative and mixed methods provide unique contributions to outcomes research. *Circulation, 119*, 1442-1452. doi:10.1161/circulationaha.107.742775

Davis, M. P., Temel, J. S., Balboni, T., & Glare, P. (2015). A review of the trials which examine early integration of outpatient and home palliative care for patients with serious illnesses. *Annual of Palliative Medicine, 4*, 99-121.

Desai, A. S., & Stevenson, L. W. (2012). Rehospitalization for heart failure. *Circulation, 126*, 501, 501-506.

Dharmarajan, K., & Rich, M. W. (2017). Epidemiology, pathophysiology, and prognosis of heart failure in older adults. *Heart Failure Clinics, 13*, 417-426. doi:10.1016/j.hfc.2017.02.001

Dharmarajan, K., Wang, Y., Lin, Z., Normand, S.-L. T., Ross, J. S., Horwitz, L. I., . . . Krumholz, H. M. (2017). Association of changing hospital readmission rates with mortality rates after hospital dischargeassociation of reduced hospital readmission rates with mortality rates after dischargeassociation of reduced hospital readmission rates with mortality rates after discharge. *JAMA, 318*, 270-278. Retrieved from https://doi.org/10.1001/jama.2017.8444. doi:10.1001/jama.2017.8444

Dicko, A., Brown, J. M., Diawara, H., Baber, I., Mahamar, A., Soumare, H. M., . . . Gosling, R. (2016). Primaquine to reduce transmission of Plasmodium falciparum malaria in Mali: a single-blind, dose-ranging, adaptive randomised phase 2 trial. *Lancet Infectious Diseases, 16*, 674-684. doi:10.1016/S1473-3099(15)00479-X

Dickson, V. V., Buck, H., & Riegel, B. (2013). Multiple comorbid conditions challenge heart failure self-care by decreasing self-efficacy. *Nursing Research, 62*, 2-9. doi:10.1097/NNR.0b013e31827337b3

Dionne-Odom, J., Hooker, S. A., Bekelman, D., Ejem, D., McGhan, G., Kitko, L., . . . Bakitas, M. A. (2017). Family caregiving for persons with heart failure at the intersection of heart failure and palliative care: A state-of-the-science review. *Heart Failure Reviews*. *22*, 543-557. doi:10.1007/s10741-017-9597-4

Diop, M. S., Rudolph, J. L., Zimmerman, K. M., Richter, M. A., & Skarf, L. M. (2017). Palliative care interventions for patients with heart failure: A systematic review and meta-analysis. *Journal of Palliative Medicine, 20*, 84-92. doi:10.1089/jpm.2016.0330

Dishman, R. K., Vandenberg, R. J., Motl, R. W., Wilson, M. G., & DeJoy, D. M. (2010). Dose relations between goal setting, theory-based correlates of goal setting and increases in physical activity during a workplace trial. *Health Education Research, 25*, 620-631.

Dodd, S., White, I. R., & Williamson, P. (2012). Nonadherence to treatment protocol in published randomised controlled trials: a review. *Trials, 13*, 84. doi:10.1186/1745-6215-13-84

Duke, S., & Bennett, H. (2009). Review: A narrative review of the published ethical debates in palliative care research and an assessment of their adequacy to inform research governance. *Palliative Medicine, 24*, 111-126. Retrieved from https://doi.org/10.1177/0269216309352714. doi:10.1177/0269216309352714

Dunbar, S. B., Khavjou, O. A., Bakas, T., Hunt, G., Kirch, R. A., Leib, A. R., . . . Whitsel, L. P. (2018). Projected costs of informal caregiving for cardiovascular disease: 2015 to 2035: A policy statement from the American Heart Association. *Circulation. 137,* e558–e577. doi:10.1161/cir.0000000000000570

Dunderdale, K., Thompson, D. R., Beer, S. F., Furze, G., & Miles, J. N. (2008). Development and validation of a patient-centered health-related quality-of-life measure: The chronic heart failure assessment tool. *Journal of Cardiovascular Nursing, 23*, 364-370. doi:10.1097/01.JCN.0000317439.82704.e8

Düngen, H.-D., Musial-Bright, L., Inkrot, S., Apostolovic, S., Edelmann, F., Lainscak, M., . . . Lainščak, M. (2014). Heart rate following short-term beta-blocker titration predicts all-cause mortality in elderly chronic heart failure patients: Insights from the CIBIS-ELD trial. *European Journal of Heart Failure, 16*, 907-914. doi:10.1002/ejhf.121

Durant, R. W., Davis, R. B., St George, D. M., Williams, I. C., Blumenthal, C., & Corbie-Smith, G. M. (2007). Participation in research studies: factors associated with failing to meet minority recruitment goals. *Annuals of Epidemiology, 17*. doi:10.1016/j.annepidem.2007.02.003

Ekman, I., Cleland, J. G., Swedberg, K., Charlesworth, A., Metra, M., & Poole-Wilson, P. A. (2005). Symptoms in patients with heart failure are prognostic predictors: insights from COMET. *Journal of Cardiac Failure, 11*, 288-292.

Ekman, I., Cleland, J. G. F., Andersson, B., & Swedberg, K. (2005). Exploring symptoms in chronic heart failure. *European Journal of Heart Failure, 7*, 699-703. doi:10.1016/j.ejheart.2005.07.003

Elia, N., Von Elm, E., Chatagner, A., Pöpping, D. M., & Tramèr, M. R. (2016). How do authors of systematic reviews deal with research malpractice and misconduct in original studies? A crosssectional analysis of systematic reviews and survey of their authors. *BMJ Open, 6*. doi:10.1136/bmjopen-2015-010442

Emanuel, E. J., Fairclough, D. L., Wolfe, P., & Emanuel, L. L. (2004). Talking with terminally ill patients and their caregivers about death, dying, and bereavement: Is it stressful? is it helpful? *Archives of Internal Medicine, 164*, 1999-2004. doi:10.1001/archinte.164.18.1999

Epiphaniou, E., Hamilton, D., Bridger, S., Robinson, V., Rob, G., Beynon, T., . . . Harding, R. (2012). Adjusting to the caregiving role: the importance of coping and support. *International Journal of Palliative Nursing, 18*(11), 541-545.

Evangelista, L. S., Lombardo, D., Malik, S., Ballard-Hernandez, J., Motie, M., & Liao, S. (2012). Examining the effects of an outpatient palliative care consultation on symptom burden, depression, and quality of life in patients with symptomatic heart failure. *Journal of Cardiac Failure, 18*, 894-899. doi:10.1016/j.cardfail.2012.10.019

Evangelista, L. S., Moser, D., Dracup, K., Doering, L., & Kobashigawa, J. (2004). Functional status and perceived control influence quality of life in female heart transplant recipients. *Journal of Heart and Lung Transplantation, 23,* 360-367. Retrieved from http://www.sciencedirect.com/science/article/pii/S1053249803001967. doi:https://doi.org/10.1016/S1053-2498(03)00196-7

Fang, J. C., Ewald, G. A., Allen, L. A., Butler, J., Westlake Canary, C. A., Colvin-Adams, M., . . . Givertz, M. M. (2015). Advanced (stage D) heart failure: A statement from the Heart Failure Society of America guidelines committee. *Journal of Cardiac Failure, 21*, 519-534. doi:10.1016/j.cardfail.2015.04.013

Feldman, D., Pamboukian, S. V., Teuteberg, J. J., Birks, E., Lietz, K., Moore, S. A., . . . Rogers, J. (2013). The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: Executive summary. *Journal of Heart Lung Transplantation, 32*, 157-187. doi:10.1016/j.healun.2012.09.013

Ferdinand, K. C. (2013). Obesity and hypertension: It's about more than the numbers. *Obesity, 21*, 657-658. doi:10.1002/oby.20372

Fetters, M. D., Curry, L. A., & Creswell, J. W. (2013). Achieving integration in mixed methods designs-principles and practices. *Health Services Research, 48*, 2134-2156. doi:10.1111/1475-6773.12117

Fitzpatrick, J., Mavissakalian, M., Luciani, T., Xu, Y., & Mazurek, A. (2018). Economic impact of early inpatient palliative care intervention in a community hospital setting. *Journal of Palliative Medicine, 21*, 933-939. doi:10.1089/jpm.2017.0416

Flemming, K., Adamson, J., & Atkin, K. (2008). Improving the effectiveness of interventions in palliative care: the potential role of qualitative research in enhancing evidence from randomized controlled trials. *Palliative Medicine, 22*, 123-131.

Friedmann, E., Thomas, S. A., Liu, F., Morton, P. G., Chapa, D., & Gottlieb, S. S. (2006). Relationship of depression, anxiety, and social isolation to chronic heart failure outpatient mortality. *American Heart Journal, 152*, 940.e941-948. doi:10.1016/j.ahj.2006.05.009

Fryer, D.R. (n.d.). Origins of the deep south. Retrieved from https://www.lehigh.edu/~ejg1/sylx/fryer.htm

Gadoud, A., Jenkins, S. M., & Hogg, K. J. (2013). Palliative care for people with heart failure: Summary of current evidence and future direction. *Palliative Medicine, 27*, 822-828. doi:10.1177/0269216313494960

Gaertner, J., Siemens, W., Antes, G., Meerpohl, J. J., Xander, C., Schwarzer, G., ... Becker, G. (2015). Specialist palliative care services for adults with advanced, incurable illness in hospital, hospice, or community settings-protocol for a systematic review. *Systematic Reviews, 4*, 124.

Gapstur, R. (2007). Symptom burden: A concept analysis and implications for oncology nurses. *Oncology Nursing Forum, 34*, 673

Gelfman, L. P., Du, Q., & Morrison, R. S. (2013). An update: NIH research funding for palliative medicine 2006 to 2010. *Journal of Palliative Medicine, 16*, 125-129. doi:10.1089/jpm.2012.0427

Gerber, Y., Weston, S. A., Redfield, M. M., & et al. (2015). A contemporary appraisal of the heart failure epidemic in olmsted county, minnesota, 2000 to 2010. *JAMA Internal Medicine, 175*, 996-1004. doi:10.1001/jamainternmed.2015.0924

GetPalliativeCare.org. (2012). Quality of life. Retrieved from https://getpalliativecare.org/quality-of-life/

Gill, A., Chakraborty, A., & Selby, D. (2012). What is symptom burden: A qualitative exploration of patient definitions. *Journal of Palliative Care, 28*, 83-89.

Glaser, B. G., & Strauss, A. L. (1967). The discovery of grounded theory: Strategies for qualitative research. New York, NY: Aldine De Gruyter.

Glasziou, P., Meats, E., Heneghan, C., & Shepperd, S. (2008). What is missing from descriptions of treatment in trials and reviews? *BMJ : British Medical Journal, 336*, 1472-1474. doi:10.1136/bmj.39590.732037.47

Goetz, J. P., & LeCompte, M. D. (1981). Ethnographic research and the problem of data reduction. *Anthropology and Education Quarterly, 12*, 51-70. doi:10.1525/aeq.1981.12.1.05x1283i

Goode, A. D., Winkler, E. A., Lawler, S. P., Reeves, M. M., Owen, N., & Eakin, E. G. (2011). A telephone-delivered physical activity and dietary intervention for type 2 diabetes and hypertension: Does intervention dose influence outcomes? *American Journal of Health Promotion, 25*, 257-263. doi:10.4278/ajhp.090223-QUAN-75

Goode, A. D., Winkler, E. A. H., Reeves, M. M., & Eakin, E. G. (2015). Relationship between intervention dose and outcomes in living well with diabetes-A randomized trial of a telephone-delivered lifestyle-based weight loss intervention. *American Journal of Health Promotion, 30*, 120-129.

Goodlin, S. J. (2009). Palliative care in congestive heart failure. *Journal of the American College of Cardiology, 54*, 386-396. doi:https://doi.org/10.1016/j.jacc.2009.02.078

Goodridge, D., & Duggleby, W. (2010). Using a quality framework to assess rural palliative care. *Journal of Palliative Care, 26*, 141-150. Retrieved from https://doi.org/10.1177/082585971002600302. doi:10.1177/082585971002600302

Granger, B. B., Ekman, I., Granger, C. B., Ostergren, J., Olofsson, B., Michelson, E., . . . Swedberg, K. (2009). Adherence to medication according to sex and age in the CHARM programme. *European Journal of Heart Failure, 11*, 1092-1098. Retrieved from https://doi.org/10.1093/eurjhf/hfp142. doi:10.1093/eurjhf/hfp142

Green, C. P., Porter, C. B., Bresnahan, D. R., & Spertus, J. A. (2000). Development and evaluation of the Kansas City Cardiomyopathy Questionnaire: A new health status measure for heart failure. *Journal of the American College of Cardiology, 35*, 1245.

Guetterman, T. C., Fetters, M. D., & Creswell, J. W. (2015). Integrating quantitative and qualitative results in health science mixed methods research through joint displays. *Annuals of Family Medicine, 13*, 554-561. doi:10.1370/afm.1865

Guzman-Clark, J. R., van Servellen, G., Chang, B., Mentes, J., & Hahn, T. J. (2013). Predictors and outcomes of early adherence to the use of a home telehealth device by older veterans with heart failure. *Telemedicine and e-Health, 19*, 217-223. doi:10.1089/tmj.2012.0096

Hallas, C. N., Wray, J., Andreou, P., & Banner, N. R. (2011). Depression and perceptions about heart failure predict quality of life in patients with advanced heart failure. *Heart & Lung, 40*, 111-121. doi:10.1016/j.hrtlng.2009.12.008

Handley, M. A., Schillinger, D., & Shiboski, S. (2011). Quasi-experimental designs in practice-based research settings: design and implementation considerations. *Journal of American Board of Family Medicine, 24*, 589-596. doi:10.3122/jabfm.2011.05.110067

Happ, M. B., Dabbs, A. D., Tate, J., Hricik, A., & Erlen, J. (2006). Exemplars of mixed methods data combination and analysis. *Nursing Research, 55*, S43-49.

Harrell, F. (2015). Regression modeling strategies with applications to linear models, logistic and ordinal regression, and survival analysis. 2nd Ed. Switzerland: Springer

Hasson, H. (2010). Systematic evaluation of implementation fidelity of complex interventions in health and social care. *Implementation Science, 5*, 67. Retrieved from https://doi.org/10.1186/1748-5908-5-67. doi:10.1186/1748-5908-5-67

Hasson, H., Blomberg, S., & Dunér, A. (2012). Fidelity and moderating factors in complex interventions: a case study of a continuum of care program for frail elderly people in health and social care. *Implementation Science, 7*, 23. Retrieved from https://doi.org/10.1186/1748-5908-7-23. doi:10.1186/1748-5908-7-23

Headley, J. N. (2002). Invasive hemodynamic monitoring: physiological principles and clinical applications. Irvine: Edwards Lifesciences. Available at http://ht.edwards.com/resourcegallery/products/swanganz/pdfs/invasivehdmphysprincbook.pdf.

Heidenreich, P. A., Albert, N. M., Allen, L. A., Bluemke, D. A., Butler, J., Fonarow, G. C., . . . Trogdon, J. G. (2013). Forecasting the impact of heart failure in the united states a policy statement from the american heart association. *Circulation: Heart Failure, 6*, 606-619. doi:10.1161/HHF.0b013e318291329a

Heller, C., Balls-Berry, J. E., Nery, J. D., Erwin, P. J., Littleton, D., Kim, M., & Kuo, W. P. (2014). Strategies addressing barriers to clinical trial enrollment of

underrepresented populations: A systematic review. *Contemporary Clinical Trials, 39*, 169-182. doi:10.1016/j.cct.2014.08.004

Heo, S., Lennie, T. A., Okoli, C., & Moser, D. K. (2009). Quality of life in patients with heart failure: ask the patients. *Heart & Lung, 38*, 100-108. doi:10.1016/j.hrtlng.2008.04.002

Heo, S., Moser, D. K., Riegel, B., Hall, L. A., & Christman, N. (2005). Testing a published model of health-related quality of life in heart failure. *Journal of Cardiac Failure, 11*, 372-379. doi:https://doi.org/10.1016/j.cardfail.2004.12.001

Heo, S., Moser, D. K., & Widener, J. (2007). Gender differences in the effects of physical and emotional symptoms on health-related quality of life in patients with heart failure. *European Journal of Cardiovascular Nurssing, 6*, 146-152. doi:10.1016/j.ejcnurse.2006.06.008

Hibbard, J. H., Greene, J., & Tusler, M. (2009). Improving the outcomes of disease management by tailoring care to the patient's level of activation. *American Journal of Managed Care, 15*, 353-360.

Hibbard, J. H., Mahoney, E. R., Stock, R., & Tusler, M. (2007). Do increases in patient activation result in improved self-management behaviors? *Health Services Research, 42*, 1443-1463.

Higginson, I. J., Evans, C. J., Grande, G., Preston, N., Morgan, M., McCrone, P., . . . Todd, C. (2013). Evaluating complex interventions in End of Life Care: the MORECare Statement on good practice generated by a synthesis of transparent expert consultations and systematic reviews. *BMC Medicine, 11*, 111-111.

Hobfoll, S. E., Walter, K. H., & Horsey, K. J. (2008). Dose and fit are vital to intervention success. *Psychiatry, 71*, 308-318. doi:10.1521/psyc.2008.71.4.308

Hoekstra, T., Jaarsma, T., Van Veldhuisen, D. J., Hillege, H. L., Sanderman, R., & Lesman-Leegte, I. (2013). Quality of life and survival in patients with heart failure. *European Journal of Heart Failure, 15*, 94-102. doi:10.1093/eurjhf/hfs148

Hoffmann, T. C., Glasziou, P. P., Boutron, I., Milne, R., Perera, R., Moher, D., . . . Michie, S. (2014). Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ, 348*, g1687. doi:10.1136/bmj.g1687

Holmes, E. A. F., Hughes, D. A., & Morrison, V. L. (2014). Predicting adherence to medications using health psychology theories: A systematic review of 20 years of empirical research. *Value in Health, 17*, 863-876. doi:https://doi.org/10.1016/j.jval.2014.08.2671

Holm, M., Carlander, I., Fürst, C. J., Wengström, Y., Årestedt, K., Öhlen, J., & Henriksson, A. (2015). Delivering and participating in a psycho-educational intervention for family caregivers during palliative home care: A qualitative study from the perspectives of health professionals and family caregivers. *BMC Palliative Care, 14*, 16. doi:10.1186/s12904-015-0015-1

Hopp, F. P., Zalenski, R. J., Waselewsky, D., Burn, J., Camp, J., Welch, R. D., & Levy, P. (2016). Results of a hospital-based palliative care intervention for patients with an acute exacerbation of chronic heart failure. *Journal of Cardiac Failure, 22,* 1033-1036. doi:10.1016/j.cardfail.2016.04.004

Howard, K. I., Kopta, S. M., Krause, M. S., & Orlinsky, D. E. (1986). The dose-effect relationship in psychotherapy. *American Psychologist, 41*, 159-164. doi:10.1037/0003-066X.41.2.159

Howie, L., & Peppercorn, J. (2013). Early palliative care in cancer treatment: rationale, evidence and clinical implications. *Therapeutic Advances in Medical Oncology, 5*, 318–323. http://doi.org/10.1177/1758834013500375

Hroscikoski, M. C., Solberg, L. I., Sperl-Hillen, J. M., Harper, P. G., McGrail, M. P., & Crabtree, B. F. (2006). Challenges of change: A qualitative study of chronic care model implementation. *Annals of Family Medicine, 4,* 317-326. doi:10.1370/afm.570

Huberman, A. & Miles, M. (1994). Data management and analysis methods. In N.K. Denzin & Y.S. Lincoln (Eds.), *Handbook of qualitative research.* Thousand Oaks, CA: Sage

Hudson, P., Aranda, S., & McMurray, N. (2001). Randomized controlled trials in palliative care: overcoming the obstacles. *International Journal of Palliative Nursing, 7*, 427-434. doi:10.12968/ijpn.2001.7.9.9301

Hudson, P. (2004). A critical review of supportive interventions for family caregivers of patients with palliative-stage cancer. *Journal of Psychosocial Oncology, 22*, 77-92.

Huffman, M. D., Berry, J. D., Ning, H., Dyer, A. R., Garside, D. B., Cai, X., . . . Lloyd-Jones, D. M. (2013). Lifetime risk for heart failure among white and black americans: cardiovascular lifetime risk pooling project. *Journal of the American College of Cardiology, 61,* 1510-1517. doi:https://doi.org/10.1016/j.jacc.2013.01.022

Hui, D., Glitza, I., Chisholm, G., Yennu, S., & Bruera, E. (2013). Attrition rates, reasons, and predictive factors in supportive care and palliative oncology clinical trials. *Cancer, 119*, 1098-1105. Retrieved from https://doi.org/10.1002/cncr.27854. doi:10.1002/cncr.27854

Hunt, S. A., Baker, D. W., Chin, M. H., Cinquegrani, M. P., Feldmanmd, A. M., Francis, G. S., . . . Smith, S. C. (2001). ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult: Executive summary a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1995 Guidelines for the Evaluation and Management of Heart Failure). *Circulation, 104*, 2996.

Hunt, S. A. (2005). ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: A report of the American College of Cardiology/American Heart Association task force on practice guidelines (Writing committee to update the 2001 guidelines for the evaluation and management of heart failure). *Journal of the American College of Cardiology, 46*, e1-82. doi:10.1016/j.jacc.2005.08.022

Hussain, J. A., Bland, M., Langan, D., Johnson, M. J., Currow, D. C., & White, I. R. (2017). Quality of missing data reporting and handling in palliative care trials demonstrates that further development of the CONSORT statement is required: a systematic review. *Journal of Clinical Epidemiology, 88*, 81-91. doi:10.1016/j.jclinepi.2017.05.009

Institute of Healthcare Improvement. (2017). Changes to improve chronic care. Retrieved from http://www.ihi.org/resources/Pages/Changes/ChangestoImproveChronicCare.aspx

Institute of Medicine. (2015). Dying in America: Improving quality and honoring indivdual preferences near the end of life. Retrieved from https://www.nap.edu/catalog/18748/dying-in-america-improving-quality-and-honoring-individual-preferences-near

Iyer, S., Reeves, S., Varadarajan, K., & Alessandrini, E. (2011). The acute care model: A new framework for quality care in emergency medicine. *Clinical Pediatric Emergency Medicine, 12*, 91-101.

Jaarsma, T., Johansson, P., Ågren, S., & Strömberg, A. (2010). Quality of life and symptoms of depression in advanced heart failure patients and their partners. *Current Opinions in Supportive and Palliative Care, 4*, 233-237.

Jenerette, C. M., Funk, M., Ruff, C., Grey, M., Adderley-Kelly, B., & McCorkle, R. (2008). Models of inter-institutional collaboration to build research capacity for reducing health disparities. *Nursing Outlook, 56,* 16-24. doi:10.1016/j.outlook.2007.11.001

Jessup, M., Abraham, W. T., Casey, D. E., Feldman, A. M., Francis, G. S., Ganiats, T. G., . . . Yancy, C. W. (2009). 2009 focused update: ACCF/AHA guidelines for the diagnosis and Management of Heart Failure in adults: A report of the American

College of Cardiology Foundation/American Heart Association task force on practice guidelines: developed in collaboration with the International Society for Heart and Lung Transplantation. *Circulation, 119.* doi:10.1161/CIRCULATIONAHA.109.192064

Johnson, R. B., & Schoonenboom, J. (2016). Adding qualitative and mixed methods research to health intervention studies: Interacting with differences. *Qualitative Health Research, 26,* 587-602. doi:10.1177/1049732315617479

Johansson, P., Dahlström, U., & Broström, A. (2006). Factors and interventions influencing health-related quality of life in patients with heart failure: A review of the literature. *European Journal of Cardiovascular Nursing, 5,* 5-15. doi:10.1016/j.ejcnurse.2005.04.011

Jones, T. A., Olds, T. S., Currow, D. C., & Williams, M. T. (2017). Feasibility and pilot studies in palliative care research: A systematic review. *Journal of Pain and Symptom Management, 54*, 139-151.e134. doi:10.1016/j.jpainsymman.2017.02.015

Jonkman, N. H., Schuurmans, M. J., Groenwold, R. H. H., Hoes, A. W., & Trappenburg, J. C. A. (2016). Identifying components of self-management interventions that improve health-related quality of life in chronically ill patients: Systematic review and meta-regression analysis. *Patient Education and Counseling, 99*, 1087-1098.

Juenger, J., Schellberg, D., Kraemer, S., Haunstetter, A., Zugck, C., Herzog, W., & Haass, M. (2002). Health related quality of life in patients with congestive heart failure: Comparison with other chronic diseases and relation to functional variables. *Heart, 87,* 235-241.

Kahkoska, A. R., Lawson, M. T., Crandell, J., Driscoll, K. A., Kichler, J. C., Seid, M., Maahs, D. M., Kosorok, M. R., & Mayer-Davis, E. J. (2019). Assessment of a precision medicine analysis of a behavioral counseling strategy to improve adherence to diabetes self-management among youth: A post hoc analysis of the FLEX Trial. *JAMA Network Open, 2,* e195137. doi: 10.1001/jamanetworkopen.

Kane, P. M., Daveson, B. A., Ryan, K., Ellis-Smith, C. I., Mahon, N. G., McAdam, B., . . . Murtagh, F. E. M. (2017). Feasibility and acceptability of a patient-reported outcome intervention in chronic heart failure. *BMJ Supportive and Palliative Care, 7,* 470-479. doi:10.1136/bmjspcare-2017-001355

Kane, P. M., Murtagh, F. E., Ryan, K. R., Brice, M., Mahon, N. G., McAdam, B., . . . Daveson, B. A. (2018). Strategies to address the shortcomings of commonly used advanced chronic heart failure descriptors to improve recruitment in palliative care research: A parallel mixed-methods feasibility study. *Palliative Medicine, 32,* 517-524. doi:10.1177/0269216317706426

Kato, N., Kinugawa, K., Ito, N., Yao, A., Watanabe, M., Imai, Y., . . . Kazuma, K. (2009). Adherence to self-care behavior and factors related to this behavior among patients with heart failure in Japan. *Heart & Lung, 38,* 398-409. doi:10.1016/j.hrtlng.2008.11.002

Kavalieratos, D., Corbelli, J., Zhang, D., & et al. (2016). Association between palliative care and patient and caregiver outcomes: A systematic review and meta-analysis. *Journal of the American Medical Association (JAMA), 316,* 2104-2114. doi:10.1001/jama.2016.16840

Kavalieratos, D., Mitchell, E. M., Carey, T. S., Dev, S., Biddle, A. K., Reeve, B. B., . . . Weinberger, M. (2014). "Not the 'grim reaper service'": An assessment of provider knowledge, attitudes, and perceptions regarding palliative care referral barriers in heart failure. *Journal of American Heart Association, 3*, e000544. doi:10.1161/JAHA.113.000544

Kelkar, A.A., Spertus, J., Pang, P., Pierson, R.F., Cody, R.J., Pina, I.L., Hernandez,A., & Butler, J. (2016). Utility of patient-reported outcome instruments in heart failure. *Journal of the American College of Cardiology: Heart Failure*, *4,* 165-175. doi: 10.1016/j.jchf.2015.10.015

Kidd, C., Piantadosi, S. T., & Aslin, R. N. (2012). The goldilocks effect: Human infants allocate attention to visual sequences that are neither too simple nor too complex. *PLoS One, 7*. https://doi.org/10.1371/journal.pone.0036399

Kim, H.S., Sefcik, S. J., & Bradway, C. (2017). Characteristics of qualitative descriptive studies: A systematic review. *Research in Nursing Health, 40*, 23-42. doi:doi:10.1002/nur.21768

Konstam, V., Salem, D., Pouleur, H., Kostis, J., Gorkin, L., Shumaker, S., . . . Yusuf, S. (1996). Baseline quality of life as a predictor of mortality and hospitalization in 5,025 patients with congestive heart failure. *American Journal of Cardiology, 78*, 890-895.

Kovacs, A., Papp, Z., & Nagy, L. (2014). Causes and pathophysiology of heart failure with preserved ejection fraction. *Heart Failure Clinics, 10*, 389-398. doi:10.1016/j.hfc.2014.04.002

LeBlanc, T. W., Lodato, J. E., Currow, D. C., & Abernethy, A. P. (2013). Overcoming recruitment challenges in palliative care clinical trials. *Journal of Oncology Practice, 9*, 277-282. doi:10.1200/jop.2013.000996

Lee, C. S., Gelow, J. M., Denfeld, Q. E., Mudd, J. O., Burgess, D., Green, J. K., . . . Jurgens, C. Y. (2014). Physical and psychological symptom profiling and event-

free survival in adults with moderate to advanced heart failure. *Journal of Cardiovascular Nursing, 29,* 315-323. doi:10.1097/JCN.0b013e318285968a

Lee, C. S., Riegel, B., Driscoll, A., Suwanno, J., Moser, D. K., Lennie, T. A., . . . Worrall-Carter, L. (2009). Gender differences in heart failure self-care: a multinational cross-sectional study. *International Journal of Nursing Studies, 46,* 1485-1495.

Legrand, K., Bonsergent, E., Latarche, C., Empereur, F., Collin, J. F., Lecomte, E., . . . Briançon, S. (2012). Intervention dose estimation in health promotion programmes: a framework and a tool. Application to the diet and physical activity promotion PRALIMAP trial. *BMC Medical Research Methodology, 12,* 146. doi:10.1186/1471-2288-12-146

Lei, H., Nahum-Shani, I., Lynch, K., Oslin, D., & Murphy, S. A. (2012). A "SMART" design for building individualized treatment sequences. *Annual Review of Clinical Psychology, 8,* . 21-48.

Levy, W.C., Mozaffarian, D., Linker, D.T., Sutradhar, S.C., Anker, S.D, … Packer, M. (2006). The Seattle heart failure model: Prediction of survival in heart failure. *Circulation. 113,* 1424-1433.

Lincoln, Y.S. & Guba, E.G. (1985). Naturalistic inquiry. Thousand Oaks, California: SAGE Publications.

Litman, J.A., (2006). The COPE Inventory: Dimensionality and relationships with approach- and avoidance-motives and positive and negative traits. *Personality and Individual Differences*. *41,* 273-284.

Lokker, M. E., Gwyther, L., Riley, J. P., van Zuylen, L., van der Heide, A., & Harding, R. (2016). The prevalence and associated distress of physical and psychological symptoms in patients with advanced heart failure attending a South African medical center. *Journal of Cardiovascular Nursing, 31,* 313-322. doi:10.1097/jcn.0000000000000256

Lotfizadeh, A. D., Kazemi, E., Pompa-Craven, P., & Eldevik, S. (2018). Moderate effects of low-intensity behavioral intervention. *Behavior Modification,* doi:10.1177/0145445518796204

Lukens, E. P., & McFarlane, W. R. (2004). Psychoeducation as evidence-based practice: considerations for practice, research, and policy. *Brief Treatment And Crisis Intervention, 4,* 205-225. doi.org/10.1093/brief-treatment/mhh019

Lundholm, K., Daneryd, P., Bosaeus, I., Korner, U., & Lindholm, E. (2004). Palliative nutritional intervention in addition to cyclooxygenase and erythropoietin

treatment for patients with malignant disease: Effects on survival, metabolism, and function. *Cancer, 100*, 1967-1977. doi:10.1002/cncr.20160

Luyster, F. S., Hughes, J. W., & Gunstad, J. (2009). Depression and anxiety symptoms are associated with reduced dietary adherence in heart failure patients treated with an implantable cardioverter defibrillator. *Journal of Cardiovascular Nursing, 24*, 10-17. doi:10.1097/01.jcn.0000317469.63886.24

Lyons, K. D., Bakitas, M., Hegel, M. T., Hanscom, B., Hull, J., & Ahles, T. A. (2009). Reliability and validity of the Functional Assessment of Chronic Illness Therapy-Palliative care (FACIT-Pal) scale. *Journal of Pain & Symptom Management, 37*, 23-32. doi:10.1016/j.jpainsymman.2007.12.015

MacDougall, J. (2012). Dose response analysis in clinical trials. *Encyclopedia of Biopharmaceutical Statistics, Third Edition*. CRC Press

Mackin, M. L., Herr, K., Bergen-Jackson, K., Fine, P., Forcucci, C., & Sanders, S. (2009). Research participation by older adults at end of life: barriers and solutions. *Research in Gerontological Nursing, 2*, 162-171.

Magnezi, R., Glasser, S., Shalev, H., Sheiber, A., & Reuveni, H. (2014). Patient activation, depression and quality of life. *Patient Education and Counseling, 94*, 432-437. doi:10.1016/j.pec.2013.10.015

Malagon-Maldonado, G. (2014). Qualitative research in health design. *HERD: Health Environments Research & Design Journal, 7*, 120-134. doi:10.1177/193758671400700411

Manojlovich, M., & Sidani, S. (2008). Nurse dose: what's in a concept? *Research in Nursing Health, 31*, 310-319. doi:10.1002/nur.20265

Marshall, R., & Rossman, G.B. (2016). Designing qualitative research. Thousand Oaks, California: SAGE Publications.

McCormick, E., Chai, E., & Meier, D. E. (2012). Integrating palliative care into primary care. *Mount Sinai Journal of Medicine, 79*, 579-585. doi:10.1002/msj.21338

Miles, M.B., Huberman, A.M, & Saldana, J. (2014). *Qualitative data analysis: A methods sourcebook*. Thousand Oaks, CA: Sage

Miles, M.B., Huberman, A.M., Saldana, J. (2019). Qualitative Data Analysis: A Methods Sourcebook. Newbury Park, CA: SAGE Publications.

Miller, W. R., & Rollnick, S. (2014). The effectiveness and ineffectiveness of complex behavioral interventions: impact of treatment fidelity. *Contemporary Clinical Trials, 37*, 234-241. doi:10.1016/j.cct.2014.01.005

Moffatt, S., White, M., Mackintosh, J., & Howel, D. (2006). Using quantitative and qualitative data in health services research - What happens when mixed method findings conflict? [ISRCTN61522618]. *BMC Health Services Research, 6*, 28. doi:10.1186/1472-6963-6-28

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2010). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *International Journal of Surgery, 8*, 336-341.

Moher, D., Schulz, K.F., Altman, D., for the CONSORT Group. (2001). The CONSORT statement: Revised recommendations for improving the quality of reports of parallel-group randomized trials. *Journal of the American Medical Association. 15*, 1987–1991. doi:10.1001/jama.285.15.1987

Moises, G., Neil, P., & Adam, K. (2011). Cognitive impairment in patients with advanced heart failure and its implications on decision-making capacity. *Congestive Heart Failure, 17*, 175-179. doi:doi:10.1111/j.1751-7133.2011.00242.x

Morse, J. (2015). Critical analysis of strategies for determining rigor in qualitative inquiry. *Qualitative Health Research, 25*, 1212-1222. doi:10.1177/1049732315588501

Mosen, D. M., Schmittdiel, J., Hibbard, J., Sobel, D., Remmers, C., & Bellows, J. (2007). Is patient activation associated with outcomes of care for adults with chronic conditions? *The Journal of Ambulatory Care Management, 30*, 21-29.

Mozaffarian, D., Anker, S.D., Anand, I., Linker, D.T., Sullivan, M.D., Cleland, J.G., … Levy, W.C. (2007). Prediction of mode of death in heart failure: The Seattle heart failure model. *Circulation, 116*, 392-398. doi: 10.1161/CIRCULATIONAHA.106.687103

Munday, D. F., Johnson, S. A., & Griffiths, F. E. (2003). Complexity theory and palliative care. *Palliative Medicine, 17*, 308-309. doi:10.1191/0269216303pm771oa

Munhall, P.L. (2012). Nursing research: A qualitative perspective. Sudbury, Massachusetts: Jones & Bartlett Learning

National Consensus Project. (2018). Clinical practice guidelines for quality palliative care. [Adobe Digital portable document version]. Retrieved from http://www.nationalconsensusproject.org/Guideline.pdf

National Heart, Lung, and Blood Institute. (n.d.). Heart failure. Retrieved from https://www.nhlbi.nih.gov/health-topics/heart-failure

National Institute of Health. (2019). Precision medicine. Retrieved from https://ghr.nlm.nih.gov/primer/precisionmedicine/definition

National Institute of Mental Health. (2018). Depression. https://www.nimh.nih.gov/health/topics/depression/index.shtml

National Institute of Mental Health. (2016). Anxiety. https://www.nimh.nih.gov/health/topics/anxiety/index.shtml

Navidian, A., Yaghoubinia, F., Ganjali, A., & Khoshsimaee, S. (2015). The effect of self-care education on the awareness, attitude, and adherence to self-care behaviors in hospitalized patients due to heart failure with and without depression. *PLoS One, 10*, e0130973. doi:10.1371/journal.pone.0130973

Nederhof, A.J. (1985) Methods of coping with social desirability bias: a review. European Journal of Social Psychology. 15: 263-280.

Neergaard, M. A., Olesen, F., Andersen, R. S., & Sondergaard, J. (2009). Qualitative description – The poor cousin of health research? *BMC Medical Research Methodology, 9*, 52. doi:10.1186/1471-2288-9-52

Newington, L., & Metcalfe, A. (2014). Factors influencing recruitment to research: qualitative study of the experiences and perceptions of research teams. *BMC Medical Research Methodology, 14*, 10. doi:10.1186/1471-2288-14-10

O'Cathain, A., Murphy, E., & Nicholl, J. (2010). Three techniques for integrating data in mixed methods studies. *BMJ, 341*, c4587. Retrieved from http://www.bmj.com/content/341/bmj.c4587.abstract. doi:10.1136/bmj.c4587

O'Connor, M. K., Netting, F. E., & Thomas, M. L. (2008). Grounded theory: Managing the challenge for those facing institutional review board oversight. *Qualitative Inquiry, 14*, 28-45.

Oertle, M., & Bal, R. (2010). Understanding non-adherence in chronic heart failure: a mixed-method case study. *Quality and Safety in Health Care, 19*, e37.

Onwuegbuzie, A. J., & Leech, N. L. (2007). Sampling designs in qualitative research: Making the sampling process more public. *The Qualitative Report, 12*, 238-254. Retrieved from http://nsuworks.nova.edu/tqr/vol12/iss2/7

Oosterom-Calo, R., van Ballegooijen, A. J., Terwee, C. B., te Velde, S. J., Brouwer, I. A., Jaarsma, T., & Brug, J. (2013). Determinants of adherence to heart failure medication: A systematic literature review. *Heart Failure Reviews, 18*, 409-427. doi:10.1007/s10741-012-9321-3

Ownby, R. L., Acevedo, A., Goodman, K., Caballero, J., & Waldrop-Valverde, D. (2015). Health literacy predicts participant understanding of orally-presented

informed consent information. *Clinical Research Trials, 1*, 15-19. doi:10.15761/crt.1000105

Palinkas, L. A., Horwitz, S. M., Green, C. A., Wisdom, J. P., Duan, N., & Hoagwood, K. (2015). Purposeful sampling for qualitative data collection and analysis in mixed method implementation research. *Administration and policy in mental health, 42,* 533-544. doi:10.1007/s10488-013-0528-y

Pantilat, S. Z., O'Riordan, D. L., Dibble, S. L., & Landefeld, C. S. (2010). Hospital-based palliative medicine consultation: a randomized controlled trial. *Archives of Internal Medicine, 170,* 2038-2040. doi:10.1001/archinternmed.2010.460

Patel, H., Shafazand, M., Schaufelberger, M., & Ekman, I. (2007). Reasons for seeking acute care in chronic heart failure. *European Journal of Heart Failure, 9,* 702-708. doi:10.1016/j.ejheart.2006.11.002

Pattenden, J. F., Mason, A. R., & Lewin, R. J. (2013). Collaborative palliative care for advanced heart failure: outcomes and costs from the 'Better Together' pilot study. *BMJ Supportive & Palliative care, 3,* 69-76. doi:10.1136/bmjspcare-2012-000251

Payne, S. A., & Turner, J. M. (2008). Research methodologies in palliative care: A bibliometric analysis. *Palliative Medicine, 22,* 336-342. doi:10.1177/0269216308090072

Perri, M. G., Limacher, M. C., von Castel-Roberts, K., Daniels, M. J., Durning, P. E., Janicke, D. M., . . . Martin, A. D. (2014). Comparative effectiveness of three doses of weight-loss counseling: two-year findings from the rural LITE trial. *Obesity, 22*, 2293-2300. doi:10.1002/oby.20832

Plano Clark, V.L, & Ivankova, N.V. (2016). Mixed methods research: A guide to the field. Thousand Oaks, CA: SAGE Publications.

Polit, D.E. & Beck, C.T. (2017). *Nursing research: Generating and assessing evidence for nursing practice.* Philadelphia, PA: Wolters Kluwer Health.

Preston, N. J., Fayers, P., Walters, S. J., Pilling, M., Grande, G. E., Short, V., . . . Todd, C. J. (2013). Recommendations for managing missing data, attrition and response shift in palliative and end-of-life care research: Part of the MORECare research method guidance on statistical issues. *Palliative Medicine, 27*, 899-907. doi:10.1177/0269216313486952

Quill, T. E., & Abernethy, A. P. (2013). Generalist plus specialist palliative care — Creating a more sustainable model. *New England Journal of Medicine, 368*, 1173-1175. doi:10.1056/NEJMp1215620

Rabow, M. W., Dibble, S. L., Pantilat, S. Z., & McPhee, S. J. (2004). The comprehensive care team: a controlled trial of outpatient palliative medicine consultation. *Archives of Internal Medicine, 164,* 83-91. doi:10.1001/archinte.164.1.83

Ramos, S., Prata, J., Bettencourt, P., Goncalves, F. R., & Coelho, R. (2016). Depression predicts mortality and hospitalization in heart failure: A six-years follow-up study. *Journal of Affective Disorder, 201*, 162-170. doi:10.1016/j.jad.2016.05.024

Reed, D., Titler, M. G., Dochterman, J. M., Shever, L. L., Kanak, M., & Picone, D. M. (2007). Measuring the dose of nursing intervention. International Journal of *Nursing Terminology and Classification, 18*, 121-130. doi:10.1111/j.1744-618X.2007.00067.x

Revicki, D. A., Chen, W. H., Harnam, N., Cook, K. F., Amtmann, D., Callahan, L. F., . . . Keefe, F. J. (2009). Development and psychometric analysis of the PROMIS pain behavior item bank. *Pain, 146*, 158-169. doi:10.1016/j.pain.2009.07.029

Riegel, B., & Dickson, V. V. (2016). A qualitative secondary data analysis of intentional and unintentional medication nonadherence in adults with chronic heart failure. *Heart and Lung: Journal of Acute and Critical Care, 45*, 468-474.

Riegel, B., Dickson, V., Goldberg, L. R., & Deatrick, J. A. (2007). Factors associated with the development of expertise in heart failure self-care. *Nursing Research, 56*, 235-243. doi:10.1097/01.NNR.0000280615.75447.f7

Riegel, B., Dickson, V. V., Hoke, L., McMahon, J. P., Reis, B. F., & Sayers, S. (2006). A motivational counseling approach to improving heart failure self-care: mechanisms of effectiveness. *Journal of Cardiovascular Nursing, 21*, 232-241.

Roffman, C. E., Buchanan, J., & Allison, G. T. (2016). Charlson Comorbidities Index. *Journal of Physiotherapy, 62*, 171. doi:10.1016/j.jphys.2016.05.008

Rogers, J. G., Patel, C. B., Mentz, R. J., Granger, B. B., Steinhauser, K. E., Fiuzat, M., . . . Tulsky, J. A. (2017). Palliative care in heart failure: The PAL-HF randomized, controlled clinical trial. *Journal of the American College of Cardiology, 70*, 331-341. doi:10.1016/j.jacc.2017.05.030

Roobottom, C. A., & Loader, R. (2016). Virtual special issue radiation dose reduction in CT: Dose optimisation gains both increasing importance and complexity! *Clinical Radiology, 71*, 438-441. doi:10.1016/j.crad.2016.02.004

Rueda, B., & Pérez-García, A. M. (2013). Coping strategies, depressive symptoms and quality of life in hypertensive patients: Mediational and prospective relations. *Psychology & Health, 28*, 1152-1170. Retrieved from https://doi.org/10.1080/08870446.2013.795223. doi:10.1080/08870446.2013.795223

Ruppar, T. M., Delgado, J. M., & Temple, J. (2015). Medication adherence interventions for heart failure patients: A meta-analysis. *European Journal of Cardiovascular Nursing, 14,* 395-404. Retrieved from https://doi.org/10.1177/1474515115571213. doi:10.1177/1474515115571213

Rustoen, T., Valeberg, B. T., Kolstad, E., Wist, E., Paul, S., & Miaskowski, C. (2014). A randomized clinical trial of the efficacy of a self-care intervention to improve cancer pain management. *Cancer Nursing, 37,* 34-43. doi:10.1097/NCC.0b013e3182948418

Sahlen, K. G., Boman, K., & Brannstrom, M. (2016). A cost-effectiveness study of person-centered integrated heart failure and palliative home care: Based on a randomized controlled trial. *Palliative Medicine, 30,* 296-302. doi:10.1177/0269216315618544

Saldana, J. (2013). The coding manual for qualitative researchers. London, England: Sage

Sandelowski, M. (1995). Sample size in qualitative research. *Research in Nursing and Health, 18,* 179-183. doi:10.1002/nur.4770180211

Sandelowski, M. (2000). Whatever happened to qualitative description? *Research in Nursing and Health, 23,* 334-340.

Sandelowski, M. (2010). What's in a name? Qualitative description revisited. *Research in Nursing and Health, 33,* 77-84. doi:10.1002/nur.20362

Schildmann, E. K., & Higginson, I. J. (2011). Evaluating psycho-educational interventions for informal carers of patients receiving cancer care or palliative care: Strengths and limitations of different study designs. *Palliative Medicine, 25,* 345-356. doi:10.1177/0269216310389223

Schofield, P., Ugalde, A., Carey, M., Mileshkin, L., Duffy, M., Ball, D., & Aranda, S. (2008). Lung cancer: challenges and solutions for supportive care intervention research. *Palliative and Supportive Care, 6,* 281-287. doi:10.1017/s1478951508000424

Schwarz, E. R., Baraghoush, A., Morrissey, R. P., Shah, A. B., Shinde, A. M., Phan, A., & Bharadwaj, P. (2012). Pilot study of palliative care consultation in patients with advanced heart failure referred for cardiac transplantation. *Journal of Palliative Medicine, 15,* 12-15. doi:10.1089/jpm.2011.0256

Sendall, M., McCosker, L., Crossley, K., & Bonner, A. (2017). A structured review of chronic care model components supporting transition between healthcare service delivery types for older people with multiple chronic diseases. *Health Information Management Journal, 46,* 58-68. doi:10.1177/1833358316681687

Seongkum, H., Moser, D. K., Lennie, T. A., Fischer, M., Smith, E., & Walsh, M. N. (2014). Modifiable correlates of physical symptoms and health-related quality of life in patients with heart failure: A cross-sectional study. *International Journal of Nursing Studies, 51*, 1482-1490.

Shafazand, M., Patel, H., Ekman, I., Swedberg, K., & Schaufelberger, M. (2012). Patients with worsening chronic heart failure who present to a hospital emergency department require hospital care. *BMC Respiratory, 5*, 132. doi:10.1186/1756-0500-5-132

Shen, B. J., Eisenberg, S. A., Maeda, U., Farrell, K. A., Schwarz, E. R., Penedo, F. J., . . . Mallon, S. (2011). Depression and anxiety predict decline in physical health functioning in patients with heart failure. *Annuals of Behavior Medicine, 41*, 373-382. doi:10.1007/s12160-010-9251-z

Shinall, M. C., Ely, E. W., Karlekar, M., Robbins, S. G., Chandrasekhar, R., & Martin, S. F. (2018). Psychometric Properties of the FACIT-Pal 14 Administered in an Outpatient Palliative Care Clinic. *American Journal of Hospice and Palliative Care, 35*, 1292-1294. doi:10.1177/1049909118763793

Sidani, S., Manojlovich, M., & Covell, C. (2010). Nurse dose: Validation and refinement of a concept. *Research and Theory for Nursing Practice, 24*, 159-171.

Sidebottom, A. C., Jorgenson, A., Richards, H., Kirven, J., & Sillah, A. (2015). Inpatient palliative care for patients with acute heart failure: Outcomes from a randomized trial. *Journal of Palliative Medicine, 18*, 134-142. doi:10.1089/jpm.2014.0192

Sikorskii, A., Given, C., Given, B., Jeon, S., & McCorkle, R. (2006). Testing the effects of treatment complications on a cognitive-behavioral intervention for reducing symptom severity. *Journal of Pain and Symptom Management, 32*, 129-139. doi:10.1016/j.jpainsymman.2006.02.013

Simmons, L. A., Wolever, R. Q., Bechard, E. M., & Snyderman, R. (2014). Patient engagement as a risk factor in personalized health care: A systematic review of the literature on chronic disease. *Genome Medicine, 6*, 16

Solano, J. P., Gomes, B., & Higginson, I. J. (2006). A Comparison of Symptom Prevalence in Far Advanced Cancer, AIDS, Heart Disease, Chronic Obstructive Pulmonary Disease and Renal Disease. *Journal of Pain and Symptom Management, 31*, 58-69. doi:https://doi.org/10.1016/j.jpainsymman.2005.06.007

Stanek, E. J., Oates, M. B., McGhan, W. F., Denofrio, D., & Loh, E. (2000). Preferences for treatment outcomes in patients with heart failure: Symptoms versus survival. *Journal of Cardiac Failure, 6*, 225-232. doi:10.1054/jcaf.2000.9503

Steinke, E. E. (2004). Research ethics, informed consent, and participant recruitment. *Clinical Nurse Specialist, 18*, 88-95; quiz 96-87.

Stirman, S. W., Miller, C. J., Toder, K., & Calloway, A. (2013). Development of a framework and coding system for modifications and adaptations of evidence-based interventions. *Implementation Science, 8*, 65. Retrieved from https://doi.org/10.1186/1748-5908-8-65. doi:10.1186/1748-5908-8-65

Strachan, P. H., Joy, C., Costigan, J., & Carter, N. (2014). Development of a practice tool for community-based nurses: the Heart Failure Palliative Approach to Care (HeFPAC). *European Journal of Cardiovascular Nursing, 13*, 134-141. doi:10.1177/1474515113519522

Straker, L., Mathiassen, S. E., & Holtermann, A. (2018). The 'goldilocks principle': Designing physical activity at work to be 'just right' for promoting health. *British Journal of Sports Medicine, 52*, 818-819. doi: 10.1136/bjsports-2017-097765.

Stygles, N., Klein-Fedyshin, M., & Kavalieratos, D. (2017). Response to the article "Palliative Care Interventions for Patients with Heart Failure: A systematic review and meta-analysis". J*ournal of Palliative Medicine*, *20*, 582-583. Retrieved from https://doi.org/10.1089/jpm.2017.0060. doi:10.1089/jpm.2017.0060

Suter, L. G., Li, S.-X., Grady, J. N., Lin, Z., Wang, Y., Bhat, K. R., . . . Bernheim, S. M. (2014). National patterns of risk-standardized mortality and readmission after hospitalization for acute myocardial infarction, heart failure, and pneumonia: Update on publicly reported outcomes measures based on the 2013 release. *Journal of General Internal Medicine, 29*, 1333-1340.

Svetkey, L. P., Batch, B. C., Lin, P. H., Intille, S. S., Corsino, L., Tyson, C. C., . . . Bennett, G. B. (2015). Cell phone intervention for you (CITY): A randomized, controlled trial of behavioral weight loss intervention for young adults using mobile technology. *Obesity, 23*, 2133-2141. doi:10.1002/oby.21226

Tabachnick B.G. & Fidell L.S. (2013). Using multivariate statistics, 6th Ed. Upper Saddle River, NJ: Pearson

Tassé, A. M. (2016). A comparative analysis of the legal and bioethical frameworks governing the secondary use of data for research purposes. *Biopreservation and Biobanking, 14*, 207-216. doi:10.1089/bio.2015.0121

Teresi, J. A., Ocepek-Welikson, K., Cook, K. F., Kleinman, M., Ramirez, M., Reid, M. C., & Siu, A. (2016). Measurement equivalence of the Patient Reported Outcomes Measurement Information System((R)) (PROMIS((R))) Pain Interference Short Form Items: Application to ethnically diverse cancer and palliative care populations. *Psychological Testing and Assesment Modeling, 58*, 309-352.

The R Project. The R Project for Statistical Computing. (26, April 19). Retrieved June 4, 2019, from https://www.r-project.org/

The Stack Exchange. Negative Binomial Distribution. (14 October 17) Retrieved June 4 2019 from https://stats.stackexchange.com/questions/307814/negative-binomial-distribution(Conraads et al., 2012)

Thomson, J. L., Zoellner, J. M., Tussing-Humphreys, L. M., & Goodman, M. H. (2016). Moderators of intervention dose effects on diet quality and physical activity changes in a church-based, multicomponent, lifestyle study: Delta Body and Soul III. *Health Education Research, 31*, 339-349. doi:10.1093/her/cyw008

Tran, T. T., Palmer, H. R., Weston, J., Hirsch, E. B., Shah, D. N., Cottreau, J., . . . Garey, K. W. (2012). Evaluation of a daptomycin dose-optimization protocol. *American Journal of Health-System Pharmacy, 69*, 979-984. doi:10.2146/ajhp110279

Tsertsvadze, A., Yazdi, F., Fink, H. A., MacDonald, R., Wilt, T. J., Bella, A. J., . . . Moher, D. (2009). Oral sildenafil citrate (viagra) for erectile dysfunction: a systematic review and meta-analysis of harms. *Urology, 74*, 831-836.e838. doi:10.1016/j.urology.2009.04.026

Ulrich, C. M., Wallen, G. R., Fiester, A., & Grady, C. (2005). Respondent burden in clinical research: when are we asking too much of subjects?. Retrieved fromhttp://repository.upenn.edu/bioethics_papers/31.

University of Alabama at Birmingham. (n.d.) Division of preventive medicine: Recruitment and retention shared facility. Retrieved from https://www.uab.edu/medicine/dopm/affiliated-centers/shared-facilities/rrsf

Unverzagt, S., Meyer, G., Mittmann, S., Samos, F.-A., Unverzagt, M., & Prondzinsky, R. (2016). Improving treatment adherence in heart failure. *Deutsches Arzteblatt international, 113*, 423-430.

U.S. Department of Health and Human Services. (2017). Mood disorders. Retrieved from https://www.mentalhealth.gov/

Voils, C. I., Chang, Y., Crandell, J., Leeman, J., Sandelowski, M., & Maciejewski, M. L. (2012). Informing the dosing of interventions in randomized trials. *Contemporary Clinical Trials, 33*, 1225-1230. doi:10.1016/j.cct.2012.07.011

Voils, C. I., King, H. A., Maciejewski, M. L., Allen, K. D., Yancy, W. S., & Shaffer, J. A. (2014). Approaches for informing optimal dose of behavioral interventions. *Annals of Behavioral Medicine, 48*, 392-401. doi:10.1007/s12160-014-9618-7

Wagner, E. H., Austin, B. T., Davis, C., Hindmarsh, M., Schaefer, J., & Bonomi, A. (2001). Improving chronic illness care: translating evidence into action. *Health Affairs, 20,* 64-78.

Wagner, E. H., Austin, B. T., & Von Korff, M. (1996). Improving outcomes in chronic illness. *Management and Care Quality, 4,* 12-25.

Wallen, G. R., & Berger, A. (2004). Mixed methods: In search of truth in palliative care medicine. *Journal of Palliative Medicine, 7,* 403-404. doi:10.1089/1096621041349509

Walshe, C. (2017). Palliative care research: State of play and journal direction. *Palliative Medicine, 31,* 3-4. doi:10.1177/0269216316680139

Washington, T., Zimmerman, S., Cagle, J., Reed, D., Cohen, L., Beeber, A. S., & Gwyther, L. P. (2014). Fidelity decision making in social and behavioral research: alternative measures of dose and other considerations. *Social Work Research, 38,* 154-162. doi:10.1093/swr/svu021

Webster, R., Patel, A., Selak, V., Billot, L., Bots, M. L., Brown, A., . . . Rodgers, A. (2016). Effectiveness of fixed dose combination medication ('polypills') compared with usual care in patients with cardiovascular disease or at high risk: A prospective, individual patient data meta-analysis of 3140 patients in six countries. *International Journal of Cardiology, 205,* 147-156. doi:10.1016/j.ijcard.2015.12.015

Weierbach, F. M., Glick, D. F., & Lyder, C. H. (2011). Family and friends to the rescue: experiences of rural older adults with heart failure. *Research in Gerontological Nursing, 4,* 261-270. doi:10.3928/19404921-20110106-01

Wells, R., Stockdill, M. L., Dionne-Odom, J. N., Ejem, D., Burgio, K. L., Durant, R. W., . . . Bakitas, M. (2018). Educate, Nurture, Advise, Before Life Ends Comprehensive Heartcare for Patients and Caregivers (ENABLE CHF-PC): study protocol for a randomized controlled trial. *Trials, 19,* 422. doi:10.1186/s13063-018-2770-9

White, C. D., Hardy, J. R., Gilshenan, K. S., Charles, M. A., & Pinkerton, C. R. (2008). Randomised controlled trials of palliative care - A survey of the views of advanced cancer patients and their relatives. *European Journal of Cancer, 44,* 1820-1828. doi:10.1016/j.ejca.2008.05.003

Woodard, L. D., Hernandez, M. T., Lees, E., & Petersen, L. A. (2005). Racial differences in attitudes regarding cardiovascular disease prevention and treatment: A qualitative study. Patient Education and Counseling, 57(2), 225-231.

Wong, F. K. Y., Ng, A. Y. M., Lee, P. H., Lam, P. T., Ng, J. S. C., Ng, N. H. Y., & Sham, M. M. K. (2016). Effects of a transitional palliative care model on patients with end-stage heart failure: A randomised controlled trial. *Heart, 102*, 1100-1108. doi:10.1136/heartjnl-2015-308638

World Helath Organization. (n.d.). Definition of palliative care. Retrieved from http://www.who.int/cancer/palliative/definition/en/

Xia, Y., Tong, G., Feng, R., Chai, J., Cheng, J., & Wang, D. (2014). Psychosocial and behavioral interventions and cancer patient survival again: Hints of an adjusted meta-analysis. *Integrative Cancer Therapy, 13*, 301-309. doi:10.1177/1534735414523314

Xie, K., Gelfman, L., Horton, J. R., & Goldstein, N. E. (2017). State of research on palliative care in heart failure as evidenced by published literature, conference proceedings, and NIH Funding. *Journal of Cardiac Failure, 23*, 197-200. doi:10.1016/j.cardfail.2016.10.013

Xu, Z., Chen, L., Jin, S., Yang, B., Chen, X., & Wu, Z. (2018). Effect of palliative care for patients with heart failure. *International Heart Journal, 59*, 503-509. doi:10.1536/ihj.17-289

Yancy, C. W., Jessup, M., Bozkurt, B., Butler, J., Casey, D. E., Jr., Colvin, M. M., . . . Westlake, C. (2016). 2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An update of the 2013 accf/aha guideline for the management of heart failure: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *Journal of the American College of Cardiology, 68*, 1476-1488. doi:10.1016/j.jacc.2016.05.011

Yancy, C. W., Jessup, M., Bozkurt, B., Butler, J., Casey, D. E., Jr., Colvin, M. M., . . . Westlake, C. (2017). 2017 ACC/AHA/HFSA focused update of the 2013 accf/aha guideline for the management of heart failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *Journal of the American College of Cardiology, 70*, 776-803. doi:10.1016/j.jacc.2017.04.025

Yancy, C. W., Jessup, M., Bozkurt, B., Butler, J., Casey Jr, D. E., Drazner, M. H., . . . Wilkoff, B. L. (2013). 2013 ACCF/AHA guideline for the management of heart failure: A report of the American college of cardiology foundation/american heart association task force on practice guidelines. *Journal of the American College of Cardiology, 62*, e147-e239. doi:10.1016/j.jacc.2013.05.019

Yoong, J., Park, E. R., Greer, J. A., & et al. (2013). Early palliative care in advanced lung cancer: A qualitative study. *JAMA Internal Medicine, 173*, 283-290. doi:10.1001/jamainternmed.2013.1874

Young, R., & Johnson, D. R. (2015). Handling missing values in longitudinal panel data with multiple imputation. *Journal of Marriage and the Family, 77*, 277-294. doi:10.1111/jomf.12144

Young, L., Montgomery, M., Barnason, S., Schmidt, C., & Do, V. (2015). A conceptual framework for barriers to the recruitment and retention of rural CVD participants in behavior intervention trials. *GSTF Journal of Nursing and Health Care (JNHC),2,* 16. doi:10.7603/s40743-015-0016-4

Yu, X. N., Chen, Z., Zhang, J., & Liu, X. (2011). Coping mediates the association between Type D personality and perceived health in Chinese patients with coronary heart disease. *International Journal of Behavior Medicine, 18,* 277-284. doi:10.1007/s12529-010-9120-y

Zambroski, C. H., Buck, H., Garrison, C. M., & McMillan, S. C. (2014). Lessons from the field: challenges in accruing hospice heart failure patients to intervention research. *Journal of Cardiovascular Nursing, 29*, 91-97. doi:10.1097/JCN.0b013e3182784cc0

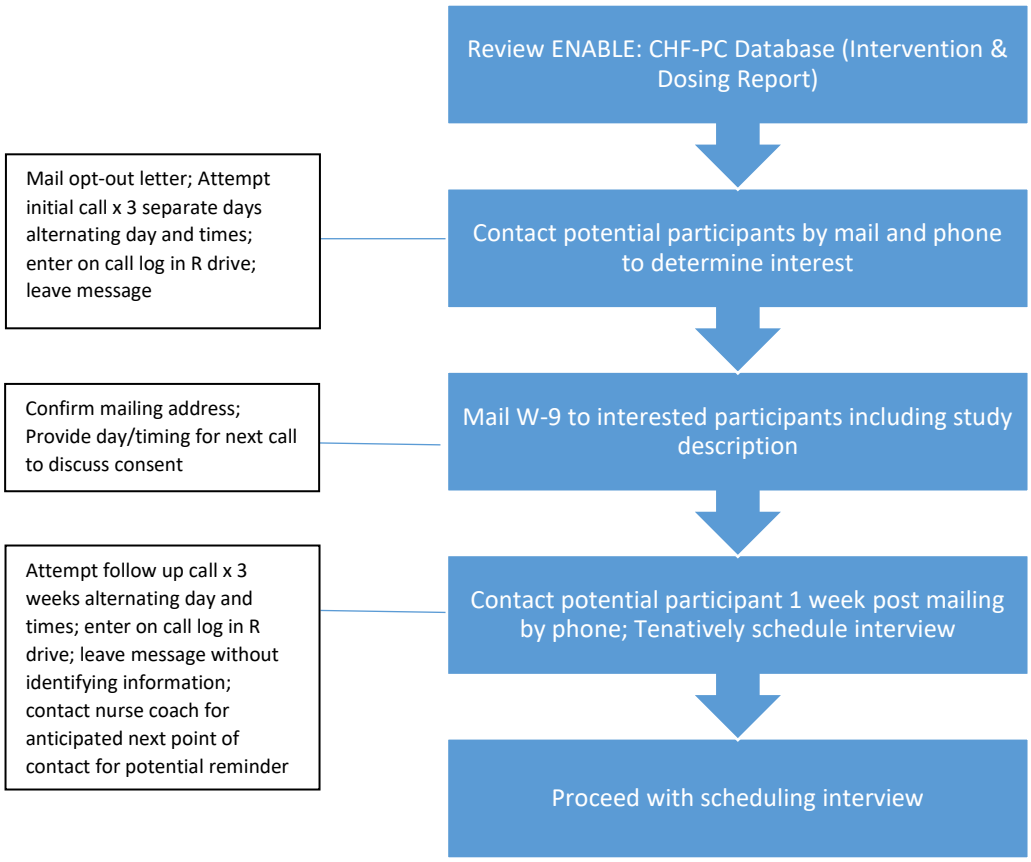
Zambroski, C. H., Moser, D. K., Bhat, G., & Ziegler, C. (2005). Impact of symptom prevalence and symptom burden on quality of life in patients with heart failure. *European Journal of Cardiovascular Nursing, 4*, 198-206. doi:10.1016/j.ejcnurse.2005.03.010

Zhang, K. M., Dindoff, K., Arnold, J. M., Lane, J., & Swartzman, L. C. (2015). What matters to patients with heart failure? The influence of non-health-related goals on patient adherence to self-care management. *Patient Education and Counseling, 98*, 927-934. doi:10.1016/j.pec.2015.04.011

APPENDIX A

QUALITATIVE STRAND PARTICIPANT RECRUITMENT AND WORKFLOW

Participant Recruitment Flow Diagram



DOSE$_{\text{ENABLE CHF-PC}}$ **Workflow** [vDecember 13 2018 w/ UAB only]

Pre-Interview/Interview/Post Interview Steps

Action	UAB
STEPS	
1. Patient Identification [Email]	• On Friday afternoon, Rachel Wells [PI] will email nurse coaches/study staff **3** study participants' study IDs for interview scheduling for the following week.
2. Contact Attempt	• Rachel Wells/Nurse Coach will attempt to contact the intervention study participants **3** times-alternating morning/afternoon call attempt times. • Create a new interview field note for each study participant who is contacted/or has been attempted to be contacted. Copy the Interview Field Note_MASTER file in the Interview Field Note folder in the R01 folder on the R drive. *R:\Bakitas\R0-1 ENABLE CHF PC\DOSE\Interview Field Notes* • Every call attempt will be recorded on the interview field note with any action taken (for example, 12/13/18 @ 1459: Attempted to reach participant. No answer. Left voicemail requesting a call back at 934-0962.) • When participant is reached, please perform the following tasks: (1) Review the study information sheet (2) Schedule an interview time within the next 2 weeks if possible (interview will take 30-35 minutes for study participant; 45-50 minutes for interviewer) (3) Confirm the study participant's contact address in REDCap

- If during the course of call attempts, the interview staff are notified that the participant has died or withdrawn from study, the staff should confirm the death/withdraw in REDCap

  IF REDCap does NOT reflect the correct status, email Sally Engler and Rachel Wells with status change and data of status change if known (for example, PT 3330000 died on 11/20/2018)

- If after 3 call attempts the nurse coach/ interview staff is still unable to reach the study participant, please use the Unable to Reach email template to notify Rachel Wells [PI] of failed attempts.
  - Save/Move the field note with the call attempts in the Unable to Contact folder in the Interview Field Notes folder in Dose folder in the R01 folder on the R drive. *R:\Bakitas\R0-1 ENABLE CHF PC\DOSE\Interview Field Notes\Unable to Contact*
  - Create a new folder and rename the folder the study participant's ID and save the Word document in the folder.

Unable to reach

3. Interview

LIST of all items needed for interviews:
UAB Patient: 3-page interview guide, open interview field note, REDCap field notes open, recorder, headset-quick tap setup

- Prior to interview:
  - Confirm study ID in REDCap (cannot perform study ID if patient participant was assigned to you)
  - Review and note the number of completed sessions/palliative care clinic visit completed on the field notes.
  - Note date of randomization, date of last completed nurse coach session (NOT monthly calls), and date of completed palliative care clinic visit on field note.
  - Set up recording equipment and confirm battery life on recorder

Unable to complete as scheduled

- Call patient participant: If unable to complete interview as scheduled, reschedule for another day. If unable to reach participant, the 3 call

attempts begin again (with this scheduled attempt counting as CALL #1).

Interview

- When participant is reached, please perform the following tasks:

(1) Review study/interview purpose as scripted
(2) Please SAY at the beginning of each recorded session:
    (a) The study ID number
    (b) Your name
    (c) The date of the session
(3) Follow interview guide: Please note this is a semi-structured interview guide. If questions need to be reworded, asked out of order, or you need additional inquiry to understand the patient's reply- it is okay to 'drift' slightly from the script. Please note each deviation with reasoning on field notes.
(4) After the completion of the last question on the interview guide, stop recorder.

Note for field note

(5) Review 2-week processing time to receive the $25 compensation check.
(6) Inform the participant if they need an updated W-9, we will send them a stamped, addressed envelope with a new W-9 to sign and return. It will add 1-2 weeks to the processing time. If their address has changed since they filled out their previous W-9, they will need to fill out a new W-9. If their address has changed, please note new address on field notes.

Note for field note

(7) Inform patient that at the conclusion of all the interviews (approximately end of January/February), they will receive a summary document in the mail briefly summarizing the themes found in the interviews.

Post-Interview Steps

(8) Ask patient if they will be willing to participate in a 5 minute call to check in to see if 'we are on the right direction' with the identified themes. Note response on field notes.
(9) Provide them Rachel Wells contact information (934-0962) should they later think of information they would want to share about

their study experience/follow up on questions asked today

- Complete field note: noting your impression of how the interview went; prevailing 'themes' or common impressions (i.e. role of nurse coach/therapeutic alliance; 'activation as predictor', or 'empowerment')
- Save field note in Interview Field Note folder in the Dose folder in the R01 folder on the R drive → *R:\Bakitas\R0-1 ENABLE CHF PC\DOSE\Interview Field Notes*
- Name the field note the study participant ID. (for example, Study Patient Participant 333000 would be named "PT_333000_Field Note.doc")
- Save the recording.
  (1) Download the file into appropriate drive and folder. The folder in on the R drive → *R:\Bakitas\R0-1 ENABLE CHF PC\DOSE\Recordings\NEED TO SEND TO LANDMARK* Each study id will need its own folder. If it has not already been created, right click and create a new folder with the study id as the name "333xxxx". Within each study ID folder, if a patient AND caregiver are enrolled, create 2 new folders with the names "patient" and "caregiver."
  (2) Connect the recorder to computer either via USB port or recorder-specific adapter cable
  (3) Hard drive folder/files on the recorder should appear within a box up box on the desktop screen. If not, go to the "Computer" drive location to find the connected device. It is found through the start menu.
  (4) Select the first file to be copied. Right click on file name and copy.
  (5) Go to the *R:\Bakitas\R0-1 ENABLE CHF PC\DOSE\Recordings\NEED TO SEND TO LANDMARK* folder. Click on the folder named subject ID number (e.g. 3330001 is an example).
  (6) Right click and paste the copy of the audio recording into the folder. Click on the recording and ensure the copy works.

Notification of Completion

(7) After checking the copy, right click on the file and select Rename. Name the file in the following convention: STUDY ID. For example, the file would be named: 3330000
(8) Repeat steps 1-7 for any additional files.
(9) After checking all audio recordings on the R drive, select all the audio files on the recorder drive and delete. Nurse Coaches may also manually delete files form the recorder if needed.

- Notify Rachel Wells of completed interview using Completed Interview Email Template_Master found in the Interview Field Note folder in the Dosefolder of the R01 folder in the R drive → *R:\Bakitas\R0-1 ENABLE CHF PC\DOSE\Interview Field Notes.* Insert template or copy template from word document into body of email. Complete address change areas *if address has changed since patient enrolled in study.* Note date of completion.

APPENDIX B

LETTER AND STUDY INFORMATION SHEET FOR QUALITATIVE STRAND

ENABLE: Comprehensive Heartcare for Patients and Caregivers

NB 352 | School of Nursing

UAB | The University of Alabama at Birmingham

NB 352 | 1720 2nd Avenue S |

Birmingham, Alabama 35294-1210

<Month, day, year>

Dear Mr./ Mrs.

Thank you for participation in the ENABLE CHF-PC (Comprehensive Heartcare for Patients and Caregivers) study. I write to you today to invite you to participate in a one-time call to ask about your experience with the ENABLE CHF-PC study. As a reminder, in the ENABLE study you spoke by phone with a Nurse Coach about several topics related to heart failure, supportive care and self-care techniques and attended a palliative care clinic appointment.

The goal of this call is to get feedback about your experiences with the ENABLE CHF-PC program and your thoughts on factors that affected your experience. An additional information sheet concerning this call is included with this letter. Your study experiences are unique and may provide valuable insight for future studies for those living with advanced heart failure and their caregivers. With your insights, we can help improve supportive care services in the future.

If you participate in this one-time call, this is what will happen:

1. An ENABLE study representative will call you and interview you over the phone. The phone call will last around 25 minutes. The interviewer will ask you open-ended questions about:

a. Your experiences with your nurse coach

b. Your opinion about the ENABLE CHF-PC telephone sessions including questions about the guidebook, topics, and length and timing of the phone calls

c. Factors that helped or hindered your participation with the ENABLE CHF-PC study

2. You will receive a $25.00 check by mail as a token of our immense appreciation.

Taking part in this one-time call is voluntary. The decision to participate is yours.

If you do not wish to be contacted, please call (205) 934-0962 and request that no further contact be made. Agreement to be contacted or a request for more information does not require you to participate.

If you have questions about the study, please contact the Rachel Wells, PhD Student/Research Assistant at (205) 934-0962 or Dr. Marie Bakitas, Principal Investigator at (205) 934-5277. Thank you for considering participating in this important ENABLE CHF-PC follow up call,

Sincerely,

Marie Bakitas, DNSc, CRNP CNL	Rachel Wells, MSN, RN,
Associate Director, UAB Center for Palliative & Supportive Care	ENABLE CHF-PC Research Assistant
Principal Investigator	UAB SON PhD student
(205) 934-5277	(205) 934-0962

PATIENT INFORMATION SHEET

TITLE OF RESEARCH: Randomized Trial of ENABLE CHF-PC for Heart Failure Patients and Caregivers

IRB PROTOCOL NO.: X140813007

INVESTIGATOR: Marie Bakitas, DNSc, CRNP

SPONSOR: National Institutes of Health/ National Institute of Nursing Research

We are asking you to take part in a one-time phone interview for the Randomized Trial of ENABLE CHF-PC for Heart Failure Patients and Caregivers, a study in which you are already enrolled as a participant. The ENABLE CHF-PC study is funded by the National Institutes of Health/ National Institute of Nursing Research. The Principal Investigator is Dr. Marie Bakitas, DSNc, CRNP from the UAB School of Nursing. This phone interview seeks to address two things: First, we would like you to describe your experiences with the ENABLE intervention. Second, we want to hear your thoughts on factors that affected your experience with the ENABLE intervention. For this additional phone interview, we expect to interview 80 enrolled persons with heart failure and 40 enrolled family caregivers.

If you enter the study, you will be asked to participate in a one-on-one telephone interview. You will be asked about your experience as an ENABLE study participant, including your interactions with the nurse coaches. (You will also be asked about the ENABLE intervention-related interactions between you and your family member who helps you with your medical care.) The interview will be audio recorded and will last about 30 minutes. The interview will be scheduled on a day and time that is convenient for you.

There is minimal risk from participating in this study. You may find some interview questions emotionally discomforting. You are free to pause or stop the interview at any time for any reason. At the end of the interview, the interviewer will discuss a 1-page handout of Resources and Support Services for Patients and Families living with heart failure that will be mailed to your home upon completion of the call.

There is a possibility of loss of confidentiality. However, precautions will be employed to minimize this risk: each digitally-recorded interview will be de-identified and assigned a unique code. A codebook linking your name with your designated code will be available exclusively to the study coordinator and kept in a locked file cabinet in her research office and will be deleted at the end of data analysis.

You will be mailed a $25 check when you complete the phone interview. This check generally comes 2 weeks after completing the interview.

There is no direct benefit to participating in this interview. However, participants may benefit from knowing that their participation in the study may help other patients with heart failure and their family caregivers.

Information obtained about you for this study will be kept confidential to the extent allowed by law. However, research information that identifies you may be shared with the UAB Institutional Review Board (IRB) and others who are responsible for ensuring compliance with laws and regulations related to research, including people on behalf of the NIH/ National Institute of Nursing Research and the Office for Human Research Protections (OHRP). The information from the research may be published for scientific purposes; however, your identity will not be given out.

Whether or not you take part in this phone interview is your choice. There will be no penalty if you decide not to complete the phone interview. If you decide not to participate in this phone interview, you will not lose any benefits you are otherwise owed. You are free to pause or stop the phone interview at any time for any reason. Your choice to pause or stop the phone interview will not affect your relationship with this institution.

There will be no cost to you for taking part in this study. If you choose to participate in an interview over the telephone or using a cellphone, you may incur charges from your telephone or cellphone service provider.

If you would like to participate or if you have any questions, concerns, or complaints about the research, you may contact the study Research Assistant, Rachel Wells, MSN, RN, CNL at (205) 934-0962. You may also contact the study Principal Investigator, Dr. Marie Bakitas at (205) 934-5277 or after hours at (603) 398-7766.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll-free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday. You may also call this number in the event the research staff cannot be reached or you wish to talk to someone else.

The Research Assistant for this phone interview, Rachel Wells, will be contacting you in the near future regarding your participation. If you do not wish to be contacted, please call Rachel Wells at (205) 934-0962.

APPENDIX C

REVISED SEMI STRUCTURED INTERVIEW GUIDE

INTERVIEW GUIDE

Hi [PARTICIPANT'S NAME]. Thank you so much for talking with me today. My name is Rachel Wells and I am with the ENABLE Heart failure study. I expect that this interview will take about ~30 minutes or so of your time. Is this still a good time?

As a reminder, the ENABLE CHF PC study included 6 weekly calls with a nurse coach who went over topics like problem solving, self-care, symptom management, core values, advance care planning, and life review. The nurse coach during calls with you often referred to a guidebook- the CYC or Charting Your Course manual. This study also included a one-time in person palliative care clinic visit that would have occurred at Kirklin Clinic, the Acton Road Clinic, or at the VA.

We are interested in learning about how to improve the experience of persons living with heart failure. Today I want to get your views on four topics:

First, we want to learn about your experience with the ENABLE intervention- your calls with your nurse coach and the palliative care clinic visit. Second, what you found helpful about the intervention. Third, what you found least helpful about the intervention.

Specifically we are interested in your perspective in the 'dosing' aspects of the study- that is the impact of the amount of time spend, the number of times we contacted you, and your interactions with your nurse coach and palliative care clinic clinician- on you and how you live with heart failure. We are interested in your thoughts about how these elements of time, contact, and interactions may or may not have influenced things like your quality of life, your symptoms, or even things like your visits to the hospital. While everyone was offered the same study activities, not everyone took part in all the activities and we are interested in learn more about why that might be.

We will share what we learn from these interviews with others in health care in an effort to improve heart failure care. With everything I ask about today, there are no right or wrong answers, I am simply interested in your experience and perspective.

This interview is confidential. Nothing you say will be linked to you specifically. When we report the results of this study, it will only be a group of themes. We will not use any specific names or situations. Also, your responses will not be linked with your UAB clinicians.

I will be recording the interview; only members of our research team at the University of Alabama at Birmingham will hear or read transcripts of these recordings. Your name will not be connected to these recordings or transcripts. I also want to emphasize that you may pause or stop at any time and for any reason during the interview.

Do you have any questions for me before we start the interview and I begin the

recording? OK, let's get started…[TURN RECORDER ON]

STATE STUDY ID, INTERVIEWER, DATE…

I'd like to start by asking you a few questions about your ENABLE study experience.

1. **Tell me in your own words about your experience with the ENABLE CHF-PC study. [Rapport building/Recall]**
   Prompts- Why did you say yes?; What would you tell a friend about being in this study/program

2. **How has participating in this study been for you in general? [Main effect of study]**
   Prompt- How has it affected your overall heart failure care?

3. **Thinking back over your experience with the ENABLE study, how involved or engaged with the study would you say you were? [Intensity]**
   a. If you had to say on a scale from 1 to 5 with 1 being not involved or attuned at all (i.e. watching TV, doing another activity at the same time) to 5 being the most involved possible (i.e. setting time aside, reviewed guidebook prior to call, going to a location to not be disturbed during the call), where would you rate your involvement with the study?
   b. Tell me more about choosing "x"

4. **Tell me in your own words how much time you devote[d] each week to the study activities. [Amount/Intensity]**
   Prompts –Such as reviewing the guidebook, reviewing with your nurse coach during the phone sessions or thinking about the study content.

Your nurse coach was [Nurse Coach name]….

5. **Tell me about talking with your nurse coach.[Intensity]**
   Prompt - How would you describe your interaction with your nurse coach to someone who is not in the study? Some people have said their relationship with their NC helped them understand the material, whereas others felt like their interactions with the NC were not as useful
   Hypothetical situation: Different nurse coach

6. **In your own words, tell me what you thought about the time spent on the telephone calls [Amount]**
   Prompt: Helpful? Length? Too short or long?

7. **You received [more/less] than the sessions/visits offered. If you did not complete all the phone sessions, what were some of the reasons? OR If you completed all the phone sessions, what were some of the reasons/facilitators?**

[Predictors of Completion]
Prompt- If you were a stakeholder helping us develop a new version of this study, what would be some of the reasons why you think people would not be able to participate in all the phone calls? OR would be able to participate in all the phone calls?

and you saw a healthcare provider at the UAB palliative care clinic

8. **Have you had your appointment? Tell me about your appointment.**
Prompt - How would you describe your interactions with the clinician at the visit? (*Intensity Scale 1 to 5*) How did it go? What part did you like? What parts didn't you like?

9. **If you did not go to the in person palliative care clinic visit, what were some of the reasons? [Predictors of Completion]**
OR
If you went to the in person palliative care clinic visit, what were some of the reasons/facilitators?
Prompt- If you were a stakeholder helping us develop a new version of this study, what would be some of the reasons why you think people would not attend this one time in person clinic visit?

Some studies examine medication and provide different 'doses' or amounts to participants to determine the best fit for a condition. In our study, instead of using medication, we have nurse coaches using the telephone and a guidebook to talk about palliative care and an in-person palliative care clinic visit. These parts make up our 'dose.' While everyone was offered the same study activities, not everyone took part in all the activities and we are interested in learning more about why that might be.

10. **In your own words, how would you describe the 'dose' or amount of study activities you received?**
Prompt- Did you receive the 'right amount'? Too much? Too little?

11. **We talked about different topics - What, if any, parts of the intervention were helpful to you**? **Tell me what about those parts were helpful**
Prompt- problem solving, self-care, symptom management, advance care planning, legacy building, life review, the palliative care clinic visit.

12. **What, if any, parts of the intervention were least helpful to you**? **Tell me what about those parts were least helpful**
Prompt- problem solving, self-care, symptom management, advance care planning, legacy building, life review, the palliative care clinic visit.

For this next part, I'm going to ask you to reflect or think back on your quality of

life, symptoms, and visits to the hospital you may have had during the time you were in the study

13. **What influence or impact, if any, has this study had on your quality of life?**
    - **a.** Did certain aspects or elements like the length of the phone calls play a bigger role in this change?
    - **b.** Did the length of the study (48 weeks) play a bigger role in this change?
    - **c.** Did how frequently the nurse coach called play a bigger role in this change?
    - **d.** Did the type of interactions you had with your nurse coach play a bigger role in this change?
    - **e.** In your opinion, would you experience the same change if you had phone calls than lasted shorter or longer? If we called you once a month versus once a week?

    ** Tell me more…

14. **What influence, if any, did this study have on your number of visits to the hospital or emergency room (sought care)?**
    Prompt:
    a. Did certain aspects or elements like the length of the phone calls, the length of the study (48 weeks), how frequently the nurse coach called, or the type of interactions you had with your nurse coach play a bigger role in this change?

    b. In your opinion, would you experience the same change if you had phone calls than lasted shorter or longer? If we called you once a month versus once a week?

       ** Tell me more…

15. **How was this interview for you? Is there anything else about your experience with the ENABLE: CHF-PC study that you would like us to know?**

Okay, thank you so much for your time. I am going to stop the recorder now.

APPENDIX D

INSTRUMENTS USED IN PARENT STUDY

Description of Outcome Measures and Data Collection Schedule

Construct	Instrument	Description of Measure	Reliability	Schedule
Primary Outcomes				
Quality of Life	Kansas City Cardiomyopathy Questionnaire (KCCQ)	5 domains: physical limitations, symptoms, self-efficacy, social interference, and QOL; 23 items	Subscales α =0.62 to 0.90	Every 8 weeks for 32 weeks
Healthcare Resource Use	Patient Resource Use	Hospital visits, Inpatient days, ICU days, ED visits, hospice use, palliative care provider visits, AD completion, DNR orders.	NA	
Anxiety /Depressive Symptoms	Hospital Anxiety and Depression Scale (HADS)	2 domains measuring depression and anxiety; 14 items	Subscales α=0.82 to 0.83	
Symptom Burden	FACIT-Pal (14-item)	The 14-item scale includes 4 domains: physical, social/family, emotional, and functional well-being.	Subscales α=0.75 to 0.93	
Activation	Patient Assessment of Chronic Illness Care (PACIC)	5 dimensions: activation, delivery system/decision support, goal setting, problem solving, and coordination; 20 items.	Subscales α=0.62 to 0.90	
Self-reported health	PROMIS SF Global Health10	2-domains: physical and mental health, 10 items	Subscales α=0.81 to 0.86	
Spiritual/ Religious Coping	Brief Multidimensional Measure of Religiousness / Spirituality	Assesses two patterns of religious/ spiritual coping with stressful life events: positive religious/spiritual coping reflective of benevolent religious methods of understanding and dealing with life stressors; and negative religious/spiritual coping reflective of religious struggle in coping.	Subscale α=0.83	Baseline
Reciprocal relationships	Dyadic Adjustment Scale 7-item-SF (DAS7-SF)	Measures the degree of agreement on relational factors such as shared philosophy, goals and time spent together.	Subscales For PTs: α=0.70; For CGs: α=0.79	
Coping style	Brief Cope	2 subscales: active and avoidant coping; 28 items.	α=0.68 to 0.79	
Social Support	Multidimensional Scale of Perceived Social Support (MSPSS)	Perceived adequacy of support from family and friends, 12 items.	α=0.81	
Health literacy	Rapid Estimate of Adult Literacy in Medicine (REALM-SF/RLM)	Measure of health literacy and numeracy based on ability to recognize common health-related terms, 7 items.	α>0.80	
Demographics	Demographic Questionnaire	Age, gender, race, marital status, religion, education, occupation, health insurance, smoking, comorbidities, year of diagnosis, heart failure related medications, blood pressure, ejection fraction	NA	

APPENDIX E

STUDY OUTCOME VARIABLES OF INTEREST

Description of Dose Variables of Interest and Collected Outcome Measure

Variable	**Definition**	**ENABLE CHF-PC Outcome Measure**
Quality of life	Sum of patient-determined multi-factored daily living experience (Getpalliativecare.org, 2012)	Kansas City Cardiomyopathy Questionnaire
Symptom burden	Patient-determined physiologic burden related to a disease process (Gapstur, 2007)	Memorial Symptom Assessment Scale- HF
Depression	State of distress related to loss of pleasure response (Snaith, 2003)	Hospital Anxiety and Depression Scale
Healthcare Resource Use	Amount or cost of services related to a disease process (Agency for Healthcare Research and Quality, 2014)	3 questions with numerical response: 1) Number of ED visits, 2) Number of non-ICU hospital days; 3) Number of ICU hospital days
Heart Failure Stage	Severity classification based on physical activity limitations (AHA, 2018)	New York Heart Association classes I-IV
Residence	RUCA-determined rural or urban residence by zipcode	Self-reported demographic form;
Comorbidity	Co-occurrence of disease in one person (Centers for Disease Control and Prevention, 2018)	Charlson Comorbidity Index
Age	Current year – birth year	Years

Note. ENABLE: CHF-PC = Educate, Nurture, Advise Before Life Ends: Comprehensive Heartcare for Patients and Caregivers study (ENABLE: CHF-PC, ClinicalTrials.gov ID: NCT02505425); HF= heart failure; ED = Emergency Department; ICU = Intensive Care Unit

APPENDIX F

DATA COLLECTION INSTRUMENTS

Patient Demographics Self Reported

Interviewer ID

- ◯ Sally Engler
- ◯ C D Johnson
- ◯ C Y Johnson
- ◯ James Mapson
- ◯ Julie Schach
- ◯ Libby Bibb

MRN: [screening_or_preba_arm_1][patient_mrn]

Hello, my name is _____, I am calling from the Recruitment and Retention Shared Facility at the University of Alabama at Birmingham on behalf of the ENABLE Heart Failure study. May I speak with _____?

Today, the purpose of my call is to ask you questions. Is now a good time?

First, I would like to ask you a few questions about yourself. Remember all answers given during this interview are confidential and there are no right or wrong answers.

The following questions that I am going to ask you relate to characteristics or demographics about you that best describe you as an individual.

What is your current age? _____

What is your gender?

- ◯ Male
- ◯ Female

Are you Hispanic?

- ◯ Not Hispanic or Latino
- ◯ Hispanic or Latino
- ◯ No Response/Skip

What is your race?

- ◯ White or Caucasian
- ◯ American Indian/Alaska Native
- ◯ Asian
- ◯ Native Hawaiian or other Pacific Islander
- ◯ Black or African American
- ◯ Other
- ◯ No response/Skip

If Other Race please specify: _____

What is your religious preference?□□Protestant can include: Pentecostal, Adventist, Baptist, Presbyterian, Congregational, Methodist, Anglican, Lutheran, Pietism, Puritan, Anglican, Evangelical, Unitarian, Quaker, Christian Science

- ◯ Protestant
- ◯ Catholic
- ◯ Jewish
- ◯ Other
- ◯ None
- ◯ No response/Skip

If Other Religion, Please specify: _____

How frequently do you attend religious services?

- ◯ Never
- ◯ Occasionally
- ◯ Regularly
- ◯ Not Applicable
- ◯ No Response/Skip

- ☐ Military program
- ☐ Medicare + Private
- ☐ Don't know
- ☐ No response/Skip

The next set of questions relates to your experience with smoking and other tobacco use.

Have you ever smoked cigarettes?

- ◯ Yes
- ◯ No
- ◯ No response/Skip

How would you describe your cigarette smoking habits?

- ◯ Currently smoke
- ◯ Used to smoke
- ◯ No response/Skip

How many packs do you smoke a day?

- ◯ Less than 1/2 pack
- ◯ 1/2 pack
- ◯ 1 pack
- ◯ 1 1/2 packs
- ◯ 2 packs
- ◯ 2 1/2 packs
- ◯ 3 packs
- ◯ No response/Skip

How many years have you been smoking?

_____
(Enter NA for non-applicable or participant wants to skip)

How long has it been since you smoked?

- ◯ Less than 1 month
- ◯ 1-6 months
- ◯ 6-12 months
- ◯ More than 12 months
- ◯ No response/Skip

When you did smoke, how many packs, on average did you smoke a day?

- ◯ Less than 1/2 pack
- ◯ 1/2 pack
- ◯ 1 pack
- ◯ 1 1/2 packs
- ◯ 2 packs
- ◯ 2 1/2 packs
- ◯ 3 packs
- ◯ No response/Skip

Have you ever used other tobacco products, like cigars or chewing tobacco?

- ◯ No
- ◯ Yes

Finally we would like to ask you a few questions about your use of alcohol...

How many drinks of alcoholic beverages do you have in a typical week?

_____
(If greater than or equal to 5, please have the participant answer the following questions)

Have you ever thought you should cut back?

- ◯ Yes
- ◯ No
- ◯ No response/Skip

Have you ever felt annoyed by people criticizing your drinking?

- ◯ Yes
- ◯ No
- ◯ No response/Skip

Have you ever felt guilty about your drinking?

- ◯ Yes
- ◯ No
- ◯ No response/Skip

Have you ever had a morning eye-opener to relieve hangover or nerves?

- ◯ Yes
- ◯ No
- ◯ No response/Skip

CAGE Score (Score of >= 2 is clinically significant) _____

On what date was this form completed? _____

Patient Resource Use Self Reported

MRN: [screening_or_preba_arm_1][patient_mrn]

Interviewer ID

- ◯ Sally Engler
- ◯ C D Johnson
- ◯ C Y Johnson
- ◯ James Mapson
- ◯ Julie Schach
- ◯ Libby Bibb

Which measurement occasion is this?

- ◯ Baseline
- ◯ 8 Weeks
- ◯ 16 Weeks
- ◯ 24 Weeks
- ◯ 32 Weeks
- ◯ 40 Weeks
- ◯ 48 Weeks

Next, I would like to know about your use of various healthcare services in the past 2 months. Some of these items will ask you to tell me how many times you might have been to one of these places. Whereas other questions will have responses that you will find on Page 1 of your Response Sheets. "No", "Yes" or "Don't Know"

What is today's date?

_____

In the last 2 months (8 weeks), how many times have you been admitted to the hospital?

_____

Considering the number of times that you have been admitted to the hospital in the last 2 months, how many days total have you been in the hospital as an inpatient?

_____
(Enter '0' if none; Enter 999 if missing; Based on how many times hospitalized they stated in the previous question...Prompt by saying 'you were admitted to the hospital times, how many days did you spend during each of those admissions?' then add up the stated days each time.)

Did any of these hospitalizations happen at someplace other than UAB?

- ◯ No
- ◯ Yes
- ◯ Don't know
- ◯ No response/skip

Which hospitals other than UAB were you admitted as an inpatient?

_____

In the last 2 months (8 weeks), how many days were you in the intensive care unit (ICU)?

_____
(Enter '0' if none; Enter 999 if missing)

Did you spend any of these days in the ICU at someplace other than DHMC/UAB?

- ◯ No
- ◯ Yes
- ◯ Don't know
- ◯ No response/Skip

At which hospital(s) other than UAB did you spend these days in the ICU?

_____

In the last 2 months (8 weeks), how many times have you gone to the emergency department/room of any hospital?

_____
(Enter '0' if none; Enter 999 if missing)

Which hospital emergency departments/rooms did you go to?

_____

In the last 2 months (8 weeks), have you been involved with a hospice program?

◯ No
◯ Yes
◯ Don't know
◯ No response/Skip

Which one(s)?

_____

In the last 2 months (8 weeks), have you been seen by a palliative care provider?

◯ No
◯ Yes
◯ Don't know
◯ No response/Skip

What was the date of your most recent visit?

_____
(If person doesn't remember exact day, ask them for their best guess)

Have you completed an advance directive (a document like a living will or a durable power of attorney for health care)?

◯ No
◯ Yes
◯ Don't know
◯ No response/Skip

On what date did you complete the advance directive?

_____
(If person doesn't remember exact day, ask them for their best guess)

Do you have a do-not-resuscitate order?

◯ No
◯ Yes
◯ Don't know
◯ No response/Skip

What was the date you completed the DNR?

_____
(If person doesn't remember exact day, ask them for their best guess)

Patient KCCQ Kansas City Cardiomyopathy Questionnaire

MRN: [screening_or_preba_arm_1][patient_mrn]

Interviewer ID

- ◯ Sally Engler
- ◯ C D Johnson
- ◯ C Y Johnson
- ◯ James Mapson
- ◯ Julie Schach
- ◯ Libby Bibb

Which measurement occasion is this?

- ◯ Baseline
- ◯ 8 Weeks
- ◯ 16 Weeks
- ◯ 24 Weeks
- ◯ 32 Weeks
- ◯ 40 Weeks
- ◯ 48 Weeks

The following questions refer to your heart failure and how it may affect your life.

Turn to Page 3 of your Patient Survey Answer Choices. Please listen to the following questions and choose the answer that best applies to you. There are no right or wrong answers.

1. Heart failure affects different people in different ways. Some feel shortness of breath while others feel fatigue.

Please indicate how much you are limited by heart failure (shortness of breath or fatigue) in your ability to do the following activities over the past 2 weeks.

1a. Dressing yourself

- ◯ Extremely limited
- ◯ Quite a bit limited
- ◯ Moderately limited
- ◯ Slightly limited
- ◯ Not at all limited
- ◯ Limited for other reasons or did not do the activity

1b. Showering/Bathing

- ◯ Extremely limited
- ◯ Quite a bit limited
- ◯ Moderately limited
- ◯ Slightly limited
- ◯ Not at all limited
- ◯ Limited for other reasons or did not do the activity

1c. Walking 1 block on level ground

- ◯ Extremely limited
- ◯ Quite a bit limited
- ◯ Moderately limited
- ◯ Slightly limited
- ◯ Not at all limited
- ◯ Limited for other reasons or did not do the activity

1d. Doing yardwork, housework, or carrying groceries

- ◯ Extremely limited
- ◯ Quite a bit limited
- ◯ Moderately limited
- ◯ Slightly limited
- ◯ Not at all limited
- ◯ Limited for other reasons or did not do the activity

1e. Climbing a flight of stairs without stopping

- ◯ Extremely limited
- ◯ Quite a bit limited
- ◯ Moderately limited
- ◯ Slightly limited
- ◯ Not at all limited
- ◯ Limited for other reasons or did not do the activity

1f. Hurrying or jogging (as if to catch a bus)

- ◯ Extremely limited
- ◯ Quite a bit limited
- ◯ Moderately limited
- ◯ Slightly limited
- ◯ Not at all limited
- ◯ Limited for other reasons or did not do the activity

For the next series of questions, I'd like to ask about your heart failure symptoms. We are now moving to Question 2. The response choices will change from question to question and I will tell you which Question we are on.

2. Compared with 2 weeks ago, have your symptoms of heart failure (shortness of breath, fatigue, or ankle swelling) changed? My symptoms of heart failure have become...

- ◯ Much worse
- ◯ Slightly worse
- ◯ Not changed
- ◯ Slightly better
- ◯ Much better
- ◯ I've had no symptoms over the last 2 weeks
- ◯ No response/Skip

3. Over the past 2 weeks, how many times did you have swelling in your feet, ankles, or legs when you woke up in the morning?

- ◯ Every morning
- ◯ 3 or more times per week but not every day
- ◯ 1-2 times per week
- ◯ Less than once a week
- ◯ Never over the past 2 weeks
- ◯ No response/Skip

4. Over the past 2 weeks, how much has swelling in your feet, ankles, or legs bothered you? It has been...

- ◯ Extremely bothersome
- ◯ Quite a bit bothersome
- ◯ Moderately bothersome
- ◯ Slightly bothersome
- ◯ Not at all bothersome
- ◯ I've had no swelling
- ◯ No response/Skip

5. Over the past 2 weeks, on average, how many times has fatigue limited your ability to do what you want?

- ◯ All of the time
- ◯ Several times per day
- ◯ At least once a day
- ◯ 3 or more times per week but not every day
- ◯ 1-2 times per week
- ◯ Less than once a week
- ◯ Never over the past 2 weeks
- ◯ No response/Skip

6. Over the past 2 weeks, how much has your fatigue bothered you? It has been ...

- ◯ Extremely bothersome
- ◯ Quite a bit bothersome
- ◯ Moderately bothersome
- ◯ Slightly bothersome
- ◯ Not at all bothersome
- ◯ I've had no fatigue
- ◯ No response/Skip

Please turn to page 4 of your Answer Sheets

7. Over the past 2 weeks, on average, how many times has shortness of breath limited your ability to do what you wanted?

- ◯ All of the time
- ◯ Several times per day
- ◯ At least once a day
- ◯ 3 or more times per week but not every day
- ◯ 1-2 times per week
- ◯ Less than once a week
- ◯ Never over the past 2 weeks
- ◯ No response/Skip

8. Over the past 2 weeks, how much has your shortness of breath bothered you? It has been ...

- ◯ Extremely bothersome
- ◯ Quite a bit bothersome
- ◯ Moderately bothersome
- ◯ Slightly bothersome
- ◯ Not at all bothersome
- ◯ I've had no shortness of breath
- ◯ No response/Skip

9. Over the past 2 weeks, on average, how many times have you been forced to sleep sitting up in a chair or with at least 3 pillows to prop you up because of shortness of breath?

- ◯ Every night
- ◯ 3 or more times a week, but not every day
- ◯ 1-2 times a week
- ◯ Less than once a week
- ◯ Never over the past 2 weeks
- ◯ No response/Skip

10. Heart failure symptoms can worsen for a number of reasons. How sure are you that you know what to do, or whom to call, if your heart failure gets worse?

- ◯ Not at all sure
- ◯ Not very sure
- ◯ Somewhat sure
- ◯ Mostly sure
- ◯ Completely sure
- ◯ No response/Skip

11. How well do you understand what things you are able to do to keep your heart failure symptoms from getting worse? (for example, weighing yourself, eating a low salt diet etc.)

- ◯ Do not understand at all
- ◯ Do not understand very well
- ◯ Somewhat understand
- ◯ Mostly understand
- ◯ Completely understand
- ◯ No response/Skip

12. Over the past 2 weeks, how much has your heart failure limited your enjoyment of life?

- ◯ It has extremely limited my enjoyment of life
- ◯ It has limited my enjoyment of life quite a bit
- ◯ It has moderately limited my enjoyment of life
- ◯ It has slightly limited my enjoyment of life
- ◯ It has not limited my enjoyment of life at all
- ◯ No response/Skip

Please turn to page 5 of your Answer Sheets

13. If you had to spend the rest of your life with your heart failure the way it is right now, how would you feel about this?

- ◯ Not at all satisfied
- ◯ Mostly dissatisfied
- ◯ Somewhat satisfied
- ◯ Mostly satisfied
- ◯ Completely satisfied
- ◯ No response/Skip

14. Over the past 2 weeks, how often have you felt discouraged or down in the dumps because of your heart failure?

- ◯ I felt that way all of the time
- ◯ I felt that way most of the time
- ◯ I occasionally felt that way
- ◯ I rarely felt that way
- ◯ I never felt that way
- ◯ No response/Skip

Question 15 has four items about *How much your heart failure may affect your lifestyle?*
Please indicate how your heart failure may have limited your participation in the following activities over the past 2 weeks.

15a. Hobbies, recreational activities

- ◯ Severely limited
- ◯ Limited quite a bit
- ◯ Moderately limited
- ◯ Slightly limited
- ◯ Did not limit at all
- ◯ Does not apply or did not do for other reasons

15b. Working or doing household chores

- ◯ Severely limited
- ◯ Limited quite a bit
- ◯ Moderately limited
- ◯ Slightly limited
- ◯ Did not limit at all
- ◯ Does not apply or did not do for other reasons

15c. Visiting family or friends outside of your home

- ◯ Severely limited
- ◯ Limited quite a bit
- ◯ Moderately limited
- ◯ Slightly limited
- ◯ Did not limit at all
- ◯ Does not apply or did not do for other reasons

15d. Intimate relationships with loved ones

- ◯ Severely limited
- ◯ Limited quite a bit
- ◯ Moderately limited
- ◯ Slightly limited
- ◯ Did not limit at all
- ◯ Does not apply or did not do for other reasons

On what date was this form completed? _____

(INTERVIEWER: Ask participant how they are doing?and if they need to take a break?)

Patient FACIT-PAL -14 (Version 4)

MRN: [screening_or_preba_arm_1][patient_mrn]

Interviewer ID

- ◯ Sally Engler
- ◯ C D Johnson
- ◯ C Y Johnson
- ◯ James Mapson
- ◯ Julie Schach
- ◯ Libby Bibb

Which measurement occasion is this?

- ◯ Baseline
- ◯ 8 Weeks
- ◯ 16 Weeks
- ◯ 24 Weeks
- ◯ 32 Weeks
- ◯ 40 Weeks
- ◯ 48 Weeks

Now, I'm going to read statements that other people with your heart failure condition have said are important.

On page 5 of Your Response Sheets look at the table for the Facit-Pal 14.

Please rate each statement as it applies to the past 7 days with 'Not at all', 'A little bit', 'Somewhat', 'Quite a bit', or 'Very much'.

	Not at all	A little bit	Somewhat	Quite a bit	Very much	Skip/No response
I have a lack of energy	◯	◯	◯	◯	◯	◯
I have nausea	◯	◯	◯	◯	◯	◯
I have pain	◯	◯	◯	◯	◯	◯
I worry that my condition will get worse	◯	◯	◯	◯	◯	◯
I am able to enjoy life	◯	◯	◯	◯	◯	◯
I am sleeping well	◯	◯	◯	◯	◯	◯
I am content with the quality of my life right now	◯	◯	◯	◯	◯	◯
I get emotional support from my family	◯	◯	◯	◯	◯	◯
I feel hopeful	◯	◯	◯	◯	◯	◯
I feel sad	◯	◯	◯	◯	◯	◯
I feel like a burden to my family	◯	◯	◯	◯	◯	◯
I am constipated	◯	◯	◯	◯	◯	◯

I am able to openly discuss my concerns with the people closest to me	○	○	○	○	○	○
I have been short of breath	○	○	○	○	○	○

BMMRS - Religious/ Spiritual Coping

The next set of questions relate to Religious and Spiritual Coping and the Answer Choices are in the table at the bottom of page 5.

Think about how you try to understand and deal with major problems in your life. To what extent is each of the following involved in the way you cope?

	Not at all	Somewhat	Quite a bit	A great deal)
a) I think about how my life is part of a larger spiritual force.	○	○	○	○
b) I work together with God as partners to get through hard times.	○	○	○	○
c) I look to God for strength, support, and guidance in crisis	○	○	○	○
d) I feel God is punishing me for my sins or lack of spirituality.	○	○	○	○
e) I wonder whether God has abandoned me.	○	○	○	○
f) I try to make sense of the situation and decide what to do without relying on God.	○	○	○	○
g) To what extent is your religion involved in understanding or dealing with stressful situations in any way?	○	○	○	○

On what date was this form completed? _____

Patient HADS: Hospital And Anxiety Depression Scale

MRN: [screening_or_preba_arm_1][patient_mrn]

Interviewer ID
- ◯ Sally Engler
- ◯ C D Johnson
- ◯ C Y Johnson
- ◯ James Mapson
- ◯ Julie Schach
- ◯ Libby Bibb

Which measurement occasion is this?
- ◯ Baseline
- ◯ 8 Weeks
- ◯ 16 Weeks
- ◯ 24 Weeks
- ◯ 32 Weeks
- ◯ 40 Weeks
- ◯ 48 Weeks

This questionnaire is designed to help us know how you feel. I will read each item to you.

The answer choices are listed on pages 6 and 7 for this set of questions.

Tell me which choice comes closest to how you have been feeling in the past week.

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

1. I feel tense or "wound up."
- ◯ Most of the time
- ◯ A lot of the time
- ◯ From time to time, occasionally
- ◯ Not at all
- ◯ Don't know, skip, N/A

2. I still enjoy the things I used to enjoy.
- ◯ Definitely as much
- ◯ Not quite as much
- ◯ Only a little
- ◯ Hardly at all
- ◯ Don't know, skip, N/A

3. I get a sort of frightened feeling as if something awful is about to happen.
- ◯ Very definitely, and quite badly
- ◯ Yes, but not too badly
- ◯ A little, but it doesn't worry me
- ◯ Not at all
- ◯ Don't know, skip, N/A

4. I can laugh and see the funny side of things.
- ◯ As much as I always could
- ◯ Not quite so much now
- ◯ Definitely not so much now
- ◯ Not at all
- ◯ Don't know, skip, N/A

In the Past Week...

5. Worrying thoughts go through my mind.
- ◯ A great deal of the time
- ◯ A lot of the time
- ◯ From time to time but not too often
- ◯ Only occasionally
- ◯ Don't know, skip, N/A

6. I feel cheerful.
- ◯ Not at all
- ◯ Not often
- ◯ Sometimes
- ◯ Most of the time
- ◯ Don't know, skip, N/A

7. I can sit at ease and feel relaxed.
- ◯ Definitely
- ◯ Usually
- ◯ Not often
- ◯ Not at all
- ◯ Don't know, skip, N/A

8. I feel as if I am slowed down.
- ◯ Nearly all the time
- ◯ Very often
- ◯ Sometimes
- ◯ Not at all
- ◯ Don't know, skip, N/A

9. I get a sort of frightened feeling like butterflies in the stomach.
- ◯ Not at all
- ◯ Occasionally
- ◯ Quite often
- ◯ Very often
- ◯ Don't know, skip, N/A

Please turn to Page 7 for the Next group of responses beginning with question 10.

In the Past Week...

10. I have lost interest in my appearance.
- ◯ Definitely
- ◯ I don't take so much care as I should
- ◯ I may not take quite as much care
- ◯ I take just as much care as ever
- ◯ Don't know, skip, N/A

11. I feel restless as if I have to be on the move.
- ◯ Very much indeed
- ◯ Quite a lot
- ◯ Not very much
- ◯ Not at all
- ◯ Don't know, skip, N/A

12. I look forward with enjoyment to things.
- ◯ As much as I ever did
- ◯ Rather less than I used to
- ◯ Definitely less than I used to
- ◯ Hardly at all
- ◯ Don't know, skip, N/A

13. I get sudden feelings of panic.
- ◯ Very often indeed
- ◯ Quite often
- ◯ Not very often
- ◯ Not at all
- ◯ Don't know, skip, N/A

14. I can enjoy a good book or radio or TV program.

- ◯ Often
- ◯ Sometimes
- ◯ Not often
- ◯ Very seldom
- ◯ Don't know, skip, N/A

On what date was this form completed? _____

Thank you for answering our questions today, this concludes our interview.

Thanks for participating in the ENABLE CHF-PC study. Remember, we will be processing a $10 check that will be mailed to you within the next two weeks.

Also, we will give you a call in about 8 weeks for your next set of questionnaires to see how you are doing at that time. Have a good day. Goodbye.

On what date was this form completed? _____

APPENDIX G

IRB AMENDMENT APPROVALS

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM
Office of the Institutional Review Board for Human Use

470 Administration Building
701 20th Street South
Birmingham, AL 35294-0104
205.934.3789 | Fax 205.934.1301 | irb@uab.edu

APPROVAL LETTER

TO: Bakitas, Marie A

FROM: University of Alabama at Birmingham Institutional Review Board
Federalwide Assurance # FWA00005960
IORG Registration # IRB00000196 (IRB 01)
IORG Registration # IRB00000726 (IRB 02)

DATE: 20-Jun-2018

RE: IRB-140813007
Randomized Trial of ENABLE CHF-PC for Heart Failure Patients and Caregivers

---

The IRB reviewed and approved the Revision/Amendment submitted on 24-May-2018 for the above referenced project. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services.

Type of Review: Expedited
Expedited Categories: 7
Determination: Approved
Approval Date: 20-Jun-2018
Expiration Date: 08-Aug-2018

The following apply to this project related to informed consent and/or assent:

- Waiver (Partial) of HIPAA

Documents Included in Review:

- Patient information sheet
- Amendment adding a data collection point
- Interview Guide
- Caregiver information sheet

Project Revision/Amendment Form

Form version: June 26, 2012

In MS Word, click in the white boxes and type your text; double-click checkboxes to check/uncheck.

- **Federal regulations require IRB approval before implementing proposed changes. See Section 14 of the IRB Guidebook for Investigators for additional information.**
- **Change means any change, in content or form, to the protocol, consent form, or any supportive materials (such as the Investigator's Brochure, questionnaires, surveys, advertisements, etc.). See Item 4 for more examples.**

1. Today's Date	February 5, 2019

2. Principal Investigator (PI)

Name (with degree)	Marie Bakitas, DNSc, CRNP	**Blazer ID**	mbakitas
Department	Nursing	**Division (if applicable)**	Adult/Acute Health
Office Address	MT412-C	**Office Phone**	205.934.5277
E-mail	mbakitas@uab.edu	**Fax Number**	205.996.1297

Contact person who should receive copies of IRB correspondence (Optional)

Name	Sara "Sally" E. Engler	**E-Mail**	sengler@uab.edu
Phone	205.996.7564	**Fax Number**	
Office Address (if different from PI)	**MT412-C**		

3. UAB IRB Protocol Identification

3.a. Protocol Number	X140813007
3.b. Protocol Title	Randomized Trial of ENABLE CHF-PC for Heart Failure Patients and Caregivers

3.c. Current Status of Protocol—Check ONE box at left; provide numbers and dates where applicable

☐	**Study has not yet begun**	**No participants, data, or specimens have been entered.**	
☐	**In progress, open to accrual**	**Number of participants, data, or specimens entered:**	361 patients and 127 caregivers
☐	**Enrollment temporarily suspended by sponsor**		
☒	**Closed to accrual, but procedures continue as defined in the protocol (therapy, intervention, follow-up visits, etc.)**		
	Date closed:	**Number of participants receiving interventions:**	26 Patients and 10 Caregivers
		Number of participants in long-term follow-up only:	54 patients; 28 caregivers
☐	**Closed to accrual, and only data analysis continues**		
	Date closed:	**Total number of participants entered:**	

4. Types of Change

Check all types of change that apply, and describe the changes in Item 5.c. or 5.d. as applicable. To help avoid delay in IRB review, please ensure that you provide the required materials and/or information for each type of change checked.

☐ **Protocol revision (change in the IRB-approved protocol)**
In Item 5.c., if applicable, provide sponsor's protocol version number, amendment number, update number, etc.

☐ **Protocol amendment (addition to the IRB-approved protocol)**
In Item 5.c., if applicable, provide funding application document from sponsor, as well as sponsor's protocol version number, amendment number, update number, etc.

☒ **Add or remove personnel**
In Item 5.c., include name, title/degree, department/division, institutional affiliation, and role(s) in research, and address whether new personnel have any conflict of interest. See "Change in Principal Investigator" in the IRB Guidebook if the principal investigator is being changed.

☐ **Add graduate student(s) or postdoctoral fellow(s) working toward thesis, dissertation, or publication**
In Item 5.c., (a) identify these individuals by name; (b) provide the working title of the thesis, dissertation, or publication; and (c) indicate whether or not the student's analysis differs in any way from the purpose of the research described in the IRB-approved HSP (e.g., a secondary analysis of data obtained under this HSP).

☐ **Change in source of funding; change or add funding**
In Item 5.c., describe the change or addition in detail, include the applicable OSP proposal number(s), and provide a copy of the application as funded (or as submitted to the sponsor if pending). Note that some changes in funding may require a new IRB application.

☐ **Add or remove performance sites**
In Item 5.c., identify the site and location, and describe the research-related procedures performed there. If adding site(s), attach notification of permission or IRB approval to perform research there. Also include copy of subcontract, if applicable. If this protocol includes acting as the Coordinating Center for a study, attach IRB approval from any non-UAB site added.

☐ **Add or change a genetic component or storage of samples and/or data component—this could include data submissions for Genome-Wide Association Studies (GWAS)**
To assist you in revising or preparing your submission, please see the IRB Guidebook for Investigators or call the IRB office at 934-3789.

☐ **Suspend, re-open, or permanently close protocol to accrual of individuals, data, or samples (IRB approval to remain active)**
In Item 5.c., indicate the action, provide applicable dates and reasons for action; attach supporting documentation.

☐ **Report being forwarded to IRB (e.g., DSMB, sponsor or other monitor)**
In Item 5.c., include date and source of report, summarize findings, and indicate any recommendations.

☐ **Revise or amend consent, assent form(s)**
Complete Item 5.d.

☐ **Addendum (new) consent form**
Complete Item 5.d.

☐ **Add or revise recruitment materials**
Complete Item 5.d.

☒ **Other (e.g., investigator brochure)**
Indicate the type of change in the space below, and provide details in Item 5.c. or 5.d. as applicable.
Include a copy of all affected documents, with revisions highlighted as applicable.

▶ Add a Data Collection Point among enrolled Usual Care Participants

5. Description and Rationale

In Item 5.a. and 5.b, check Yes **or** No **and see instructions for** Yes **responses.**
In Item 5.c. and 5.d, describe—and explain the reason for—the change(s) noted in Item 4.

☐Yes ☒ No	**5.a. Are any of the participants enrolled as normal, healthy controls?** If yes, describe in detail in Item 5.c. how this change will affect those participants.
☐Yes ☒ No	**5.b. Does the change affect subject participation, such as procedures, risks, costs, location of services, etc.?** If yes, FAP-designated units complete a FAP submission and send to fap@uab.edu. Identify the FAP-designated unit in Item 5.c. For more details on the UAB FAP, see www.uab.edu/cto.

5.c. Protocol Changes: In the space below, briefly describe—and explain the reason for—all change(s) to the protocol.

- **Add a Data Collection Point among Enrolled Usual Care Participants:**

  Since the ENABLE CHF-PC randomized trial's recruitment began in December of 2015, 207 UAB patients and 77 family caregivers were randomly assigned to the ENABLE CHF-PC usual care group. As part of the usual care group, these participants answer data questionnaires every 8 weeks for 48 weeks. The questionnaires include questions about quality of life, symptom burden, caregiver burden, mood, and healthcare-related resource use.

  While interviewing ENABLE CHF-PC intervention patients and caregivers about their study experience and participation, some indicated that they found the data questionnaires to be beneficial. Both ENABLE CHF-PC intervention and usual care participants completed data questionnaires and may have experienced beneficial or therapeutic effects both from the type of questions asked during the data collection calls and the data collector completing the call.

  Given that the ENABLE CHF-PC study examines patient-reported outcomes of participants receiving an early palliative care intervention versus outcomes of those receiving standard, usual care, it is of great importance to gain insights from the current sample of usual care participants about their experiences with and perspectives on the data collection questionnaires and process of the ENABLE CHF-PC study. Therefore, it will be beneficial to conduct a one-time semi-structured phone interview among the UAB usual care participants – patients and their family caregivers - to describe their experiences with the data collection questionnaires and to understand participants' thoughts on what impact, if any, did these data collection questionnaires have on their quality of life, symptom burden, caregiver burden, mood, or resource use. The goal for completions is 20 patients and 10 family caregivers with this proposed additional data collection point.

  All enrolled UAB usual care participants will be contacted by a study Research Assistant (PhD Student: Rachel Wells) or other study staff. During the call, an Information Sheet will be read to the participant over the phone. (See the PT and CG versions attached with this submission) If the participant agrees to the phone interview, the interview will be scheduled at a time that is convenient for the

participant. Following this initial contact, the information sheet will be mailed to the participants' homes who have expressed an interest in completing the one-on-one phone interview. This one-time phone interview will last about 30 minutes and consists of 13 open-ended questions developed to capture the experiences and thoughts of participants about data collection in the ENABLE CHF-PC study. (See the Interview Guide attached with this submission) ENABLE participants completing this additional data collection point, the semi-structured interview, will receive a $25 payment via mail.

Each one-on-one phone interview will be digitally recorded and transcribed for analysis using NVIVO® qualitative analysis software. Ultimately, the responses to the open-ended questions about participants' experiences with and perspectives on the questionnaires collected during the ENABLE CHF-PC study will be categorized and coded according to themes, patterns and relationships revealed from the multiple patient and caregiver interview transcripts.

- **Remove Inactive Personnel from the Study Protocol:**
  Libby Bibb
  Linda W. Jones
  James A. Mapson
  Kiana Minor
  Shunté Fisher
  Oladele Osisami
  Elizabeth Sockwell
  Richard A. Taylor
  Jennifer Parker Frost
- **Update interview guide for ENABLE CHF-PC Intervention Dose data point:**
  As part ongoing additional data collection concerning variation in fulfilling or completing study activities including 6 phone-based, nurse-led psychoeducational palliative care sessions and 1 in-person comprehensive palliative care clinic visit, we are conducting one-time semi-structured phone interviews with participants randomized to receive the ENABLE intervention. All enrolled UAB intervention participants are contacted by either a study Research Assistant (PhD Student: Rachel Wells) or other study staff. During the call, the approved Information Sheet is read to the participant over the phone. If the participant agrees to the phone interview, the interview is scheduled at a time that is convenient for the participant. This one-time phone interview last about 30 minutes and consists of open-ended questions developed to capture the experiences and thoughts of participants about the ENABLE CHF-PC intervention program. (See the updated Interview Guide attached with this submission) ENABLE participants completing this additional data collection point, the semi-structured interview, receive a $25 payment via mail. These interviews are transcribed and analyzed using a constant comparison approach. Consistent with this approach, interview questions that perform poorly or are confusing for participants are modified to more closely align with the data collection purpose of examining study experience. The updated interview guide

consists of 15 questions with different phrasing and order as compared to the prior interview guide. All changes are highlighted in yellow.

5.d. Consent and Recruitment Changes: In the space below,
(a) describe all changes to IRB-approved forms or recruitment materials and the reasons for them;
(b) describe the reasons for the addition of any materials (e.g., addendum consent, recruitment); and
(c) indicate either how and when you will reconsent enrolled participants or why reconsenting is not necessary (not applicable for recruitment materials).

Also, indicate the number of forms changed or added. For new forms, provide 1 copy. For revised documents, provide 3 copies:
• a copy of the currently approved document (showing the IRB approval stamp, if applicable)
• a revised copy highlighting all proposed changes with "tracked" changes
• a revised copy for the IRB approval stamp.

- Changes are not needed for the current approved study consent forms; however, an additional patient and caregiver information sheet for the Usual Care semi-structured interview data collection (See PT & CG Information Sheets attached with this submission) will be read by phone to existing participants who are already consented into the parent study. A copy of the information sheet will be mailed to each person prior to scheduling the phone interview.

Signature of Principal Investigator  Date 2/5/2019

FOR IRB USE ONLY

☐ Received & Noted ☐ Approved Expedited* ☐ To Convened IRB

_____ _____

Signature (Chair, Vice-Chair, Designee) Date

DOLA _____

Change to Expedited Category **Y / N / NA**

*No change to IRB's previous determination of approval criteria at 45 CFR 46.111 or 21 CFR 56.111

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM
Office of the Institutional Review Board for Human Use

470 Administration Building
701 20th Street South
Birmingham, AL 35294-0104
205.934.3789 | Fax 205.934.1301 |
irb@uab.edu

APPROVAL LETTER

TO: Bakitas, Marie A

FROM: University of Alabama at Birmingham Institutional Review Board
Federalwide Assurance # FWA00005960
IORG Registration # IRB00000196 (IRB 01)
IORG Registration # IRB00000726 (IRB 02)

DATE: 11-Mar-2019

RE: IRB-140813007
Randomized Trial of ENABLE CHF-PC for Heart Failure Patients and Caregivers

---

The IRB reviewed and approved the Revision/Amendment submitted on 11-Mar-2019 for the above referenced project. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services.

Type of Review: Expedited
Expedited Categories: 7
Determination: Approved
Approval Date: 11-Mar-2019
Expiration Date: 26-Jul-2019

The following apply to this project related to informed consent and/or assent:

- Waiver (Partial) of HIPAA

Please note: Libby Bibb, Linda W. Jones, James A. Mapson, Kiana Minor, Shunté Fisher, Oladele Osisami, Elizabeth Sockwell, Richard A. Taylor, and Jennifer Parker Frost have been removed from the protocol as study personnel.

Documents Included in Review:

- prof.190311
- UC CG info sheet
- UC PT info sheet
- waiverdocumentation.190311.pdf
- Interv Guide IV Revised Tracked 02-06-19
- Interv Guide IV Revised Clean 02-06-19
- UC Interview Guide

APPENDIX H

INITIAL INTERVIEW GUIDE

INTERVIEW GUIDE

Hi [PARTICIPANT'S NAME]. Thank you so much for talking with me today. My name is Rachel Wells and I am with the ENABLE Heart failure study.

I expect that this interview will take about ~30 minutes or so of your time. Is this still a good time?

[Introductory Script] ***We are interested in learning about how to improve the experience of persons living with heart failure. Today I want to get your views on four topics: First, we want to learn about your experience with the ENABLE intervention- your calls with your nurse coach and the palliative care clinic visit. Second, what you found helpful about the intervention. Third, what you found least helpful about the intervention. Finally, I would like for you to tell me about your experience with data collection calls. We will share what we learn from these interviews with others in health care in an effort to improve heart failure care. With everything I ask about today, there are no right or wrong answers, I am simply interested in your experience and perspective.***

This interview is confidential. Nothing you say will be linked to you specifically. When we report the results of this study, it will only be a group of themes. We will not use any specific names or situations. Also, your responses will not be linked with your UAB clinicians.

I will be recording the interview; only members of our research team at the University of Alabama at Birmingham will hear or read transcripts of these recordings. Your name will not be connected to these recordings or transcripts. I also want to emphasize that you may pause or stop at any time and for any reason during the interview.

Do you have any questions for me before we start the interview and I begin the recording?

OK, let's get started…[TURN RECORDER ON]

I'd like to start by asking you a few questions about your ENABLE study experience.

2. You should have received materials in the mail. A book called Charting Your Course (CYC). **What you do you think about the book?**
Prompts – length of the book, the content of the book and the visual aids presented including the handouts or worksheets.

3. **Tell me in your own words how much time you devote[d] to the study activities.**
Prompts –Such as reviewing the guidebook, reviewing with your nurse coach during the phone sessions or thinking about the study content.

Your nurse coach was [Nurse Coach name]….

4. **Tell me about talking with your nurse coach.**
Prompt - How would you describe the experience to someone who is not in the study? How have the calls been? Helpful? Length? Too short or long?

and you saw a healthcare provider at the UAB palliative care clinic

5. **Have you had your appointment? Tell me about your appointment.**
Prompt - How did it go? What part did you like? What parts didn't you like?

6. **How has participating in this study been for you in general?**
Prompt- How has it affected your overall heart failure care? How do you think it has affected your (relationship with patient)/caregiver who is enrolled in the study with you?

Okay thank you. When we hear the words palliative care and intervention, different people have different things come to mind. For this next part, I'd like to learn about your views on what parts of the study were helpful to you and what role, if any, the study activities play in how you deal with having heart failure.

7. **Tell me what you think about when you hear the words 'palliative care' or 'dose.'**

Some studies examine medication and provide different 'doses' or amounts to participants to determine the best fit for a condition. In our study, instead of using medication, we have nurse coaches using the telephone and a guidebook to talk about palliative care and an in-person palliative care clinic visit. These parts make up our 'dose.' While everyone was offered the same study activities, not everyone took part in all the activities and we are interested in learn more about why that might be.

8. **In your own words, how would you describe the 'dose' or amount of study activities you received?**
   Prompt- Did you receive the 'right amount'? Too much? Too little?

9. **What, if any, parts of the intervention were helpful to you**? **Tell me what about those parts were helpful**
   Prompt- problem solving, self-care, symptom management, advance care planning, legacy building, life review, the palliative care clinic visit

10. Some people have had positive and negative experiences related to their research study experience. **Can you tell me about some of the positive experiences? How about the negative experiences?**

11. **What, if any, parts of the intervention were least helpful to you**? **Tell me what about those parts were least helpful**
    Prompt- problem solving, self-care, symptom management, advance care planning, legacy building, life review, the palliative care clinic visit

12. **What role, if any, has this intervention played in how you live with illness?**
    Prompts- How would you say being part of this study has influenced your heart

    failure care? How would you say being part of this study has influenced any decisions you make about your healthcare, treatments, your interactions with your physicians and nurses? Positive/negative roles?

The next few questions are about the data collection calls you receive separately from the nurse coach calls… this is the part of the study where you are asked multiple survey questions about your symptoms and quality of life along with health questions….

13. **What role, if any, did the questionnaires play in your overall experience in your participation in the study?**
Prompts- Number of questionnaires or the order that they were asked? Tell me what about those questionnaires did not 'fit' with your experience, *Review questionnaires if needed*

14. **How was this interview for you? Is there anything else about your experience with the ENABLE: CHF-PC study that you would like us to know?**

Okay, thank you so for your time. I am going to stop the recorder now.

APPENDIX I

FIELD NOTE TEMPLATE

Interview Field Notes

Call attempt #1:	Address Change:
Call attempt #2:	*Address change in REDCap?*
Call attempt #3:	Status Change:
IF INTERVIEW SCHEDULED:	*Status change in REDCap?*
Call attempt #4:	NC Sessions Completed:
Call attempt #5:	*How far out from randomized was last session?*
Call attempt #6:	PCT Completed:

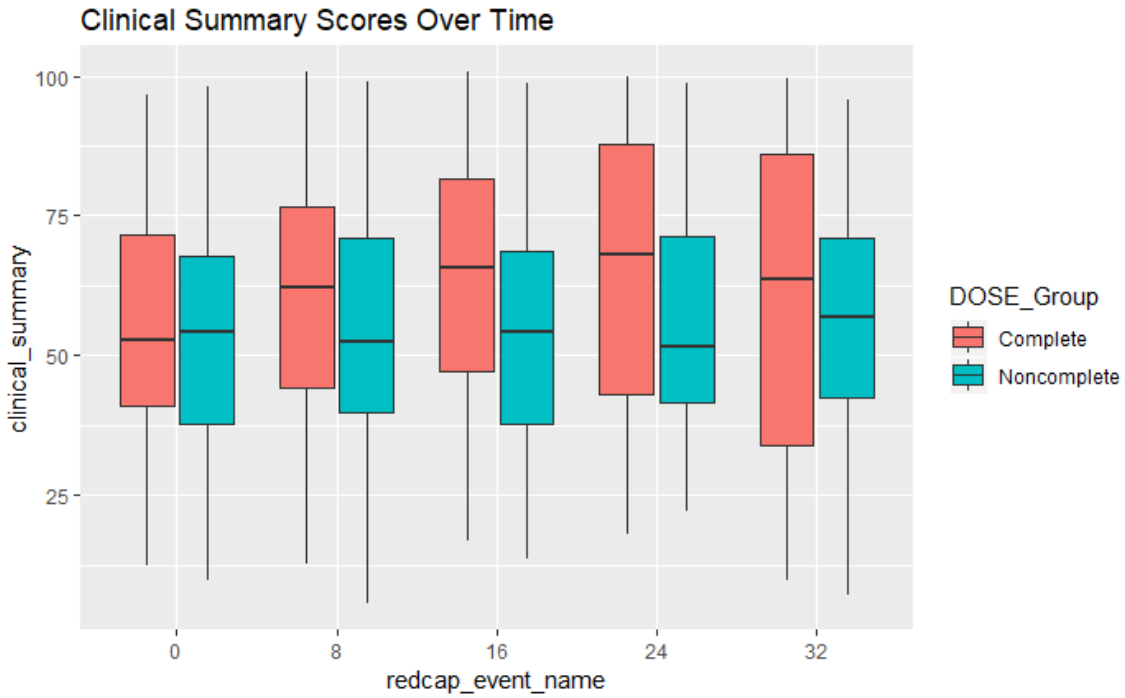
Note categories:

- OVERVIEW OF INTERVIEW- A 1-2 sentence take-away from the interview; a brief summary; including assessment of participant recall and interview quality
- PERSONAL - How I related personally to the participants and/or their experience; how I performed during the interview including notes to improve interview performance in the future
- STUDY DESIGN – Interview technique; including question performance and problems with the study design, personal or ethical dilemmas
    - FUTURE DIRECTIONS – future directions for the interview guide, study, or study design
- THEMES AND DEFINITIONS – Thoughts on prevailing themes and how defined in interview
- EMERGING THEMES – new themes not previously heard in other interviews
- COMMON CODES & THEMES – comment on any current list of codes and data's relationship to it

Date (MM/DD/YYYY) @ xx:xx am/pm	Dose Study, #3330xxx

APPENDIX J

BOXPLOTS OF PRIMARY OUTCOMES BY DOSE GROUP AND DATA COLLECTION TIME POINTS


Clinical Summary Scores Over Time
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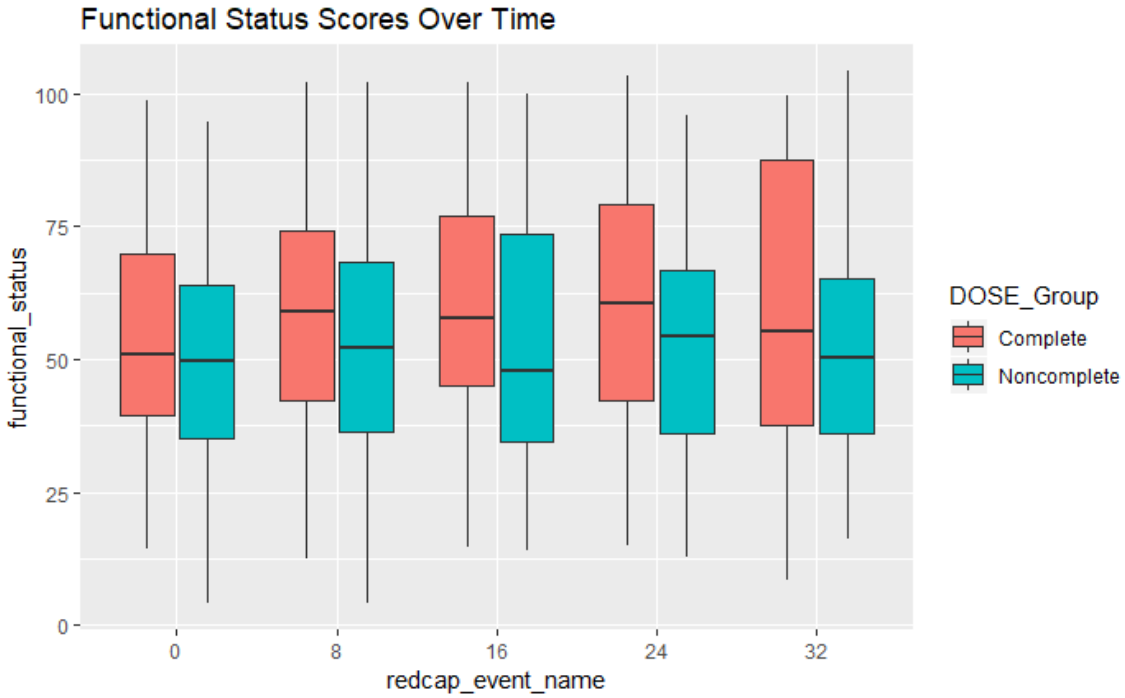
75
50
25
0
8
16
24
32
redcap_event_name
DOSE_Group
Complete
Noncomplete


Functional Status Scores Over Time
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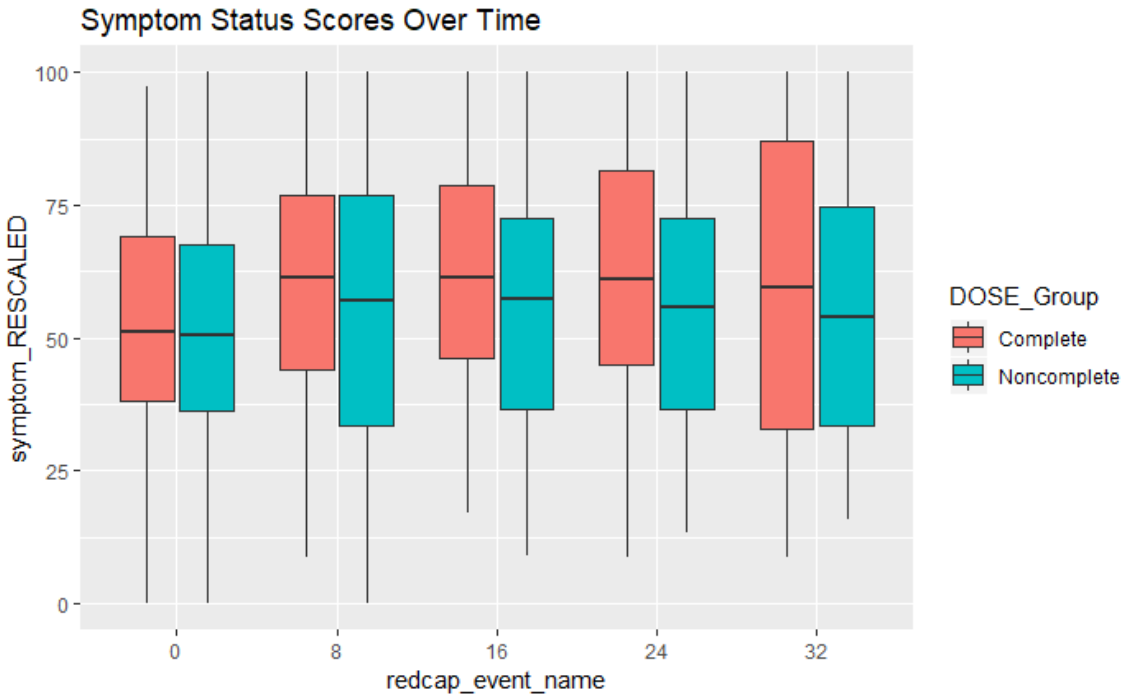
0
8
16
24
32
redcap_event_name
DOSE_Group
Complete
Noncomplete


Symptom Status Scores Over Time
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50
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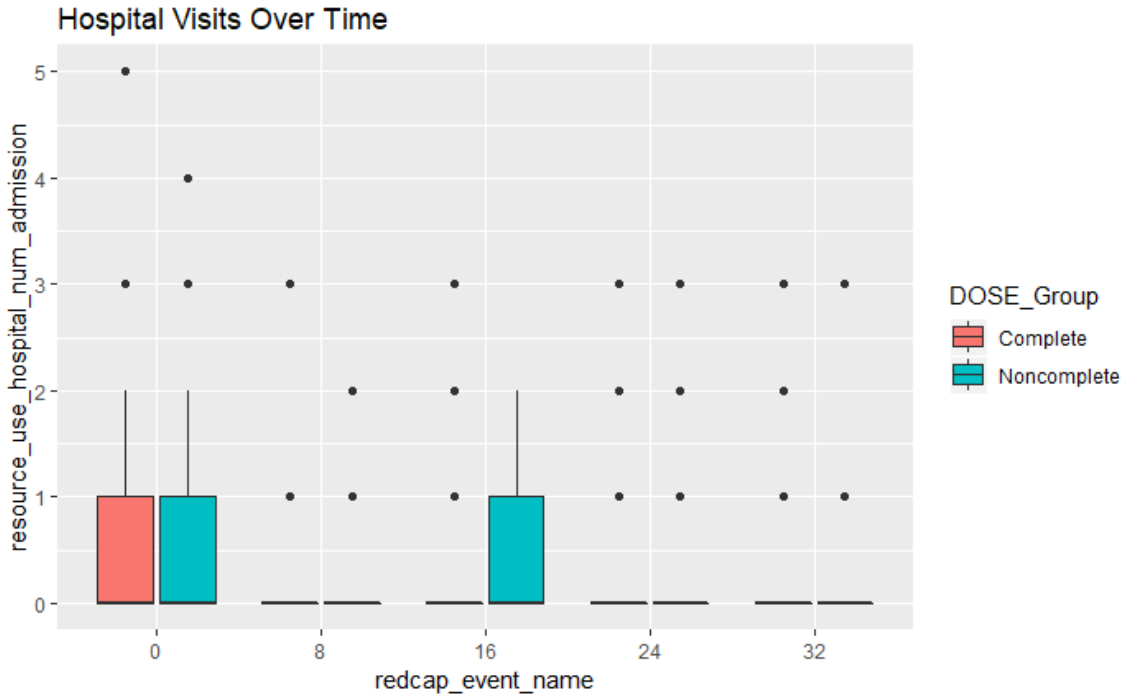
0
0
8
16
24
32
redcap_event_name
DOSE_Group
Complete
Noncomplete


Hospital Visits Over Time
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4
3
2
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16
24
32
redcap_event_name
DOSE_Group
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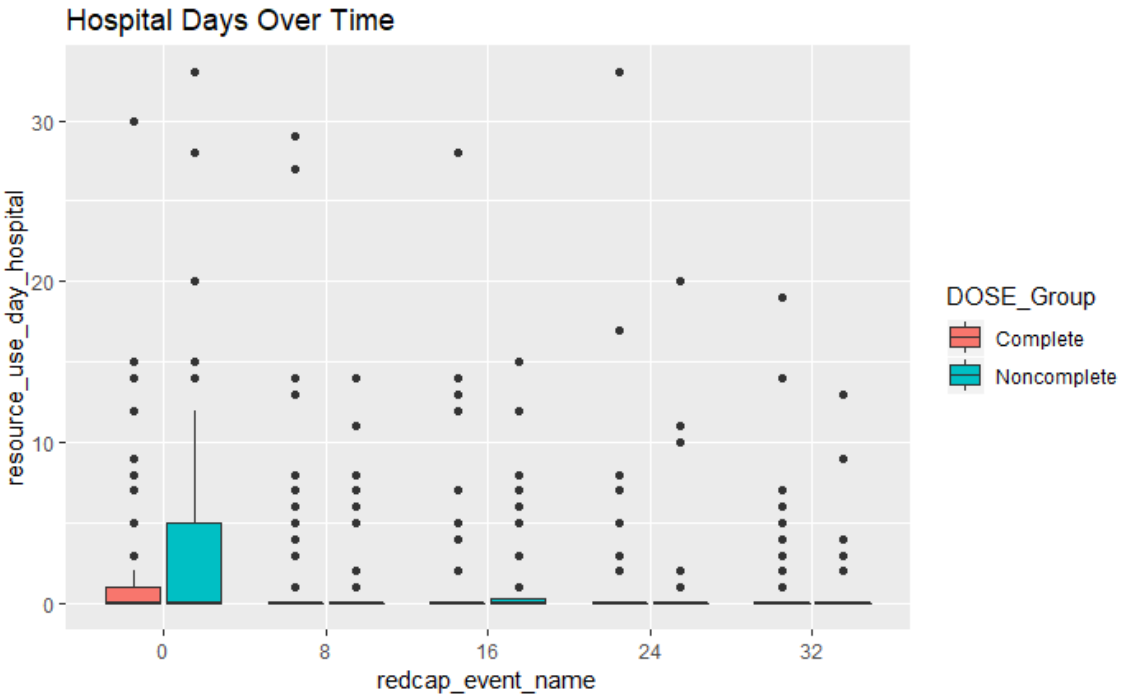
Hospital Days Over Time
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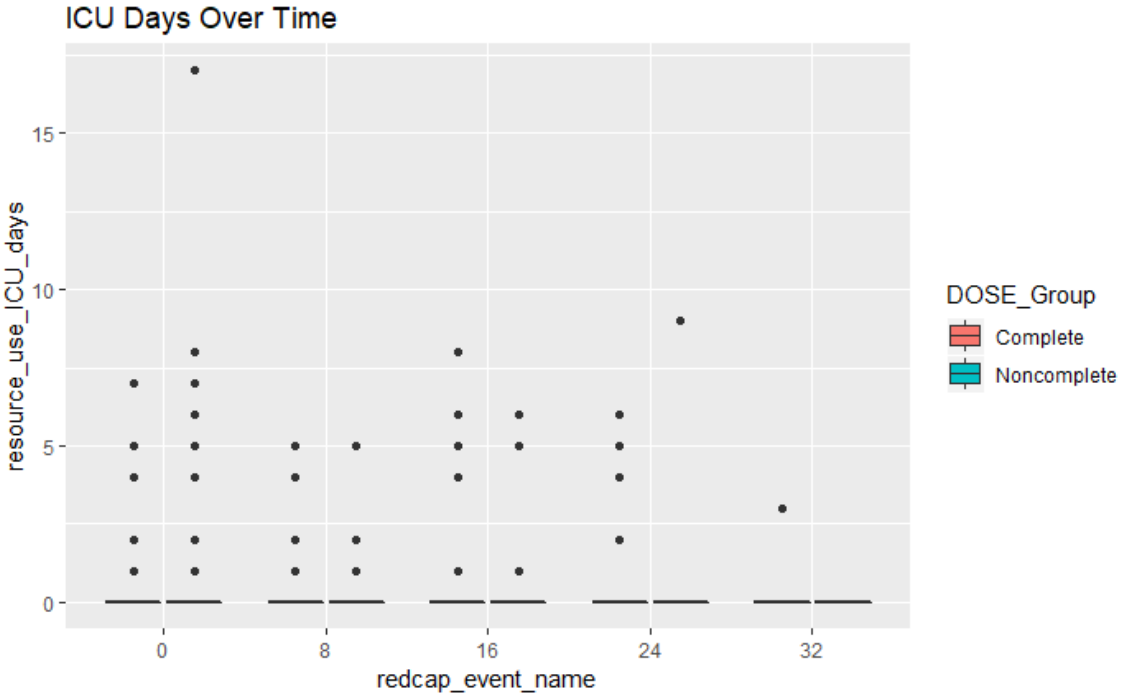
8
16
24
32
redcap_event_name
DOSE_Group
Complete
Noncomplete


ICU Days Over Time
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Complete
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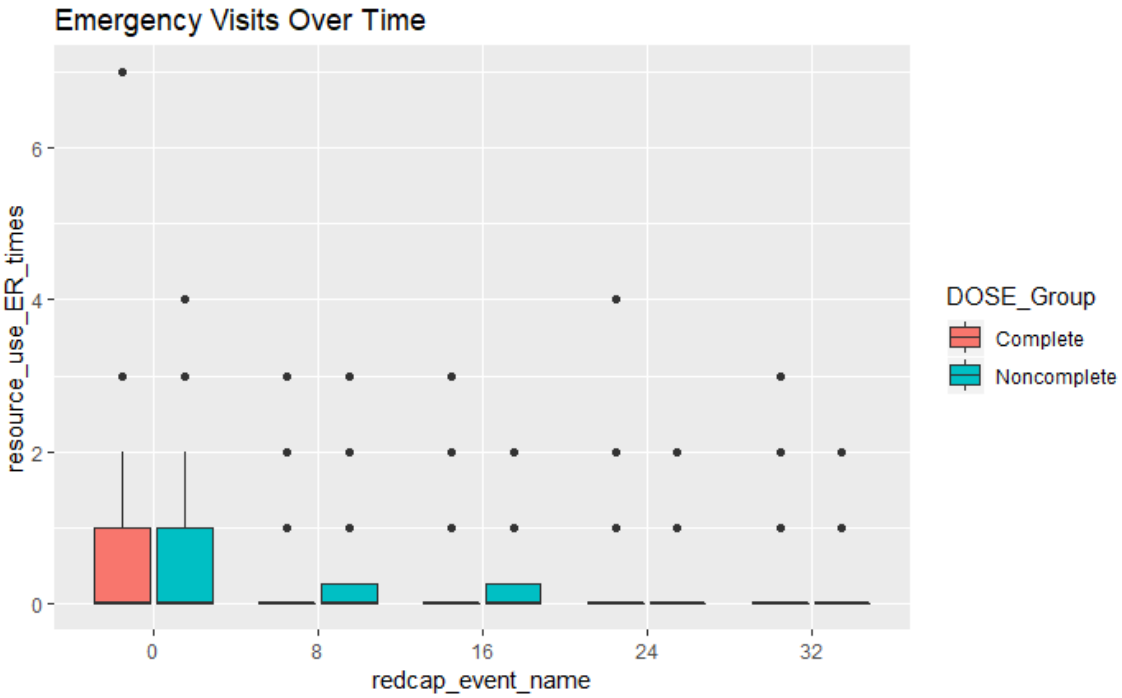
Emergency Visits Over Time
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0
8
16
24
32
redcap_event_name
DOSE_Group
Complete
Noncomplete

APPENDIX K

LINEAR MIXED MODELS WITH DATA-SELECTED COVARIATES

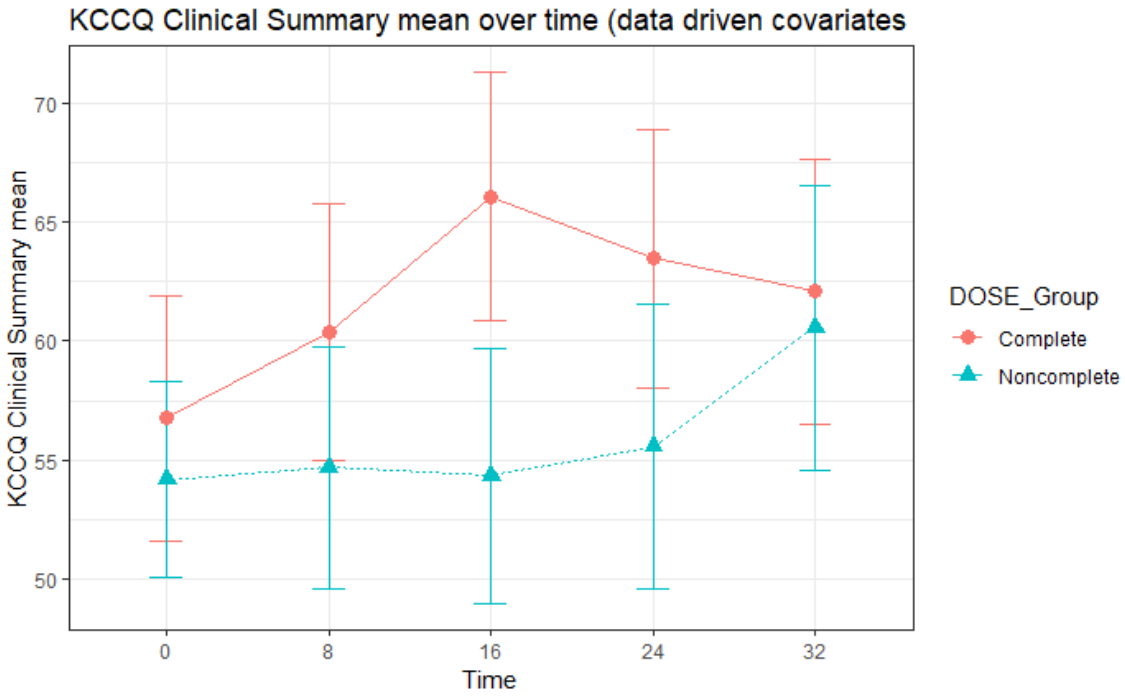


Figure 1. KCCQ Clinical summary over time by dose group

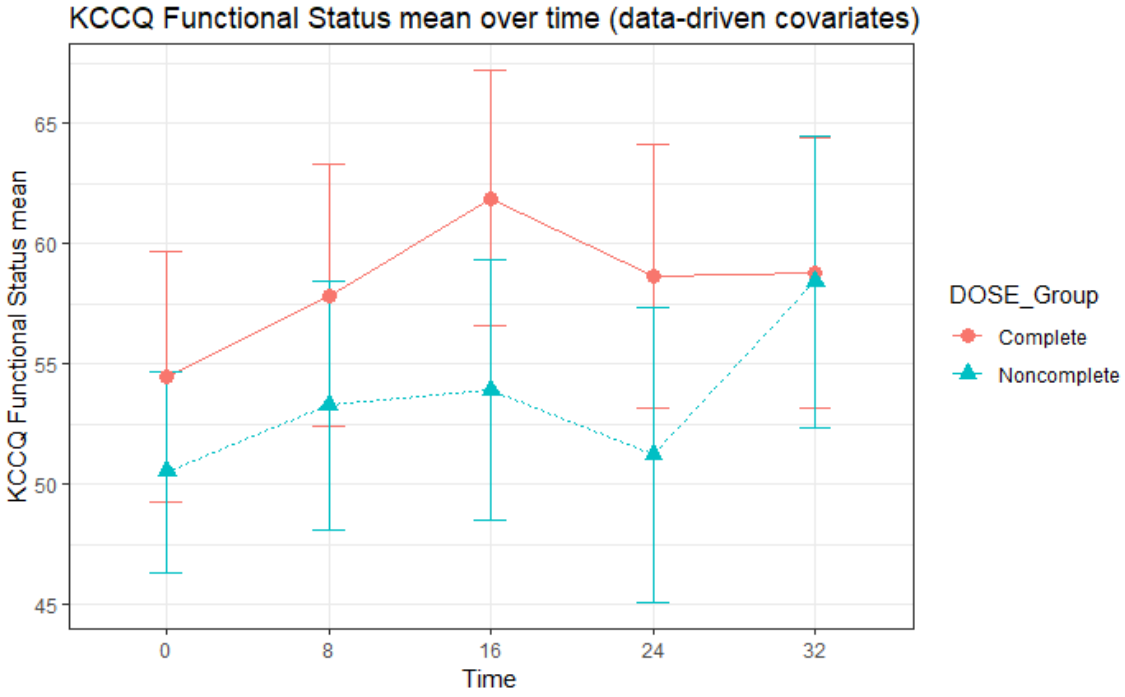


Figure 2. KCCQ Functional status over time by dose group

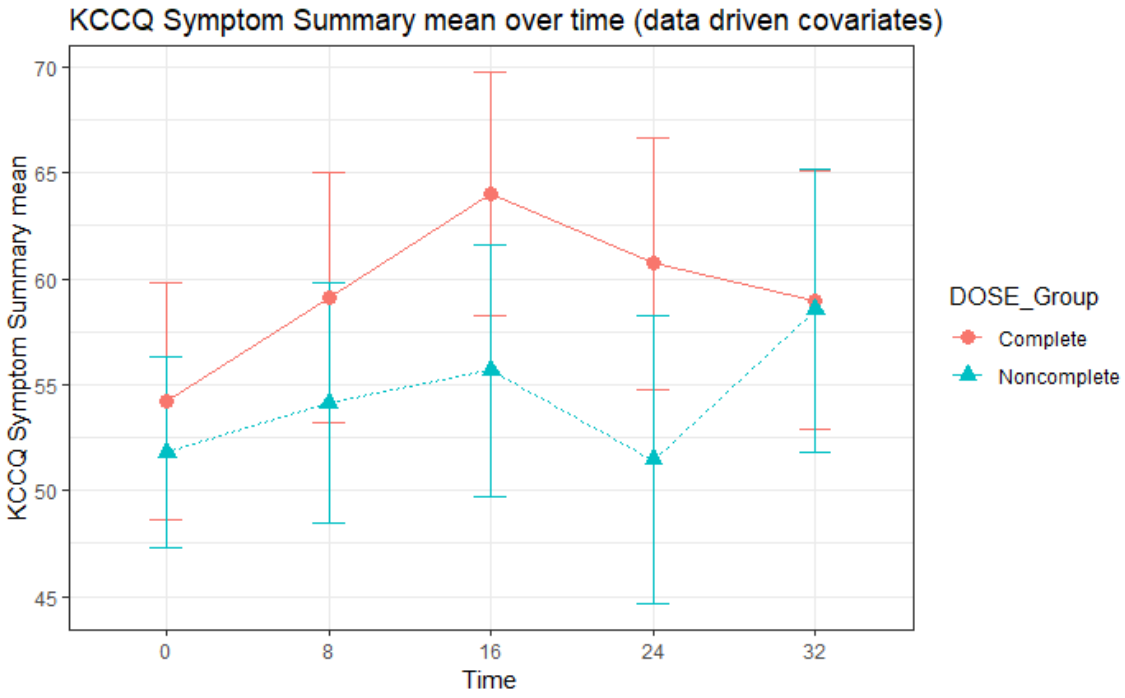


Figure 3. KCCQ Symptom summary over time by dose group

APPENDIX L

SPAGHETTI PLOTS

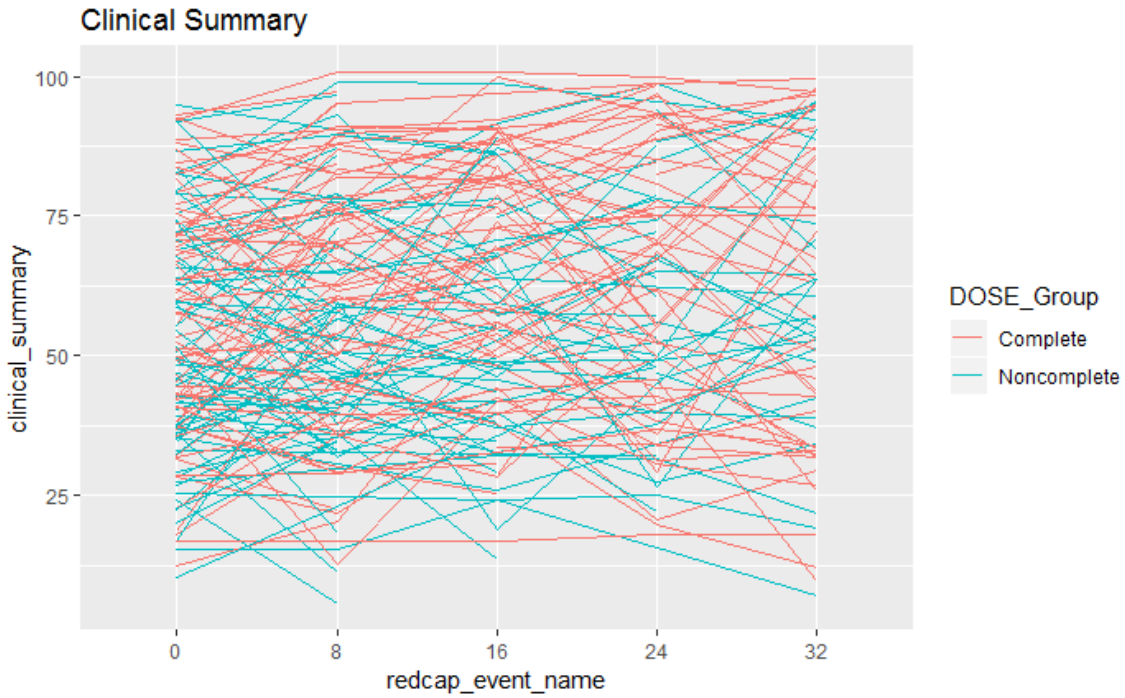


Figure 1. Kansas City Cardiomyopathy Questionnaire clinical summary over data collection time points by intervention completion groups.

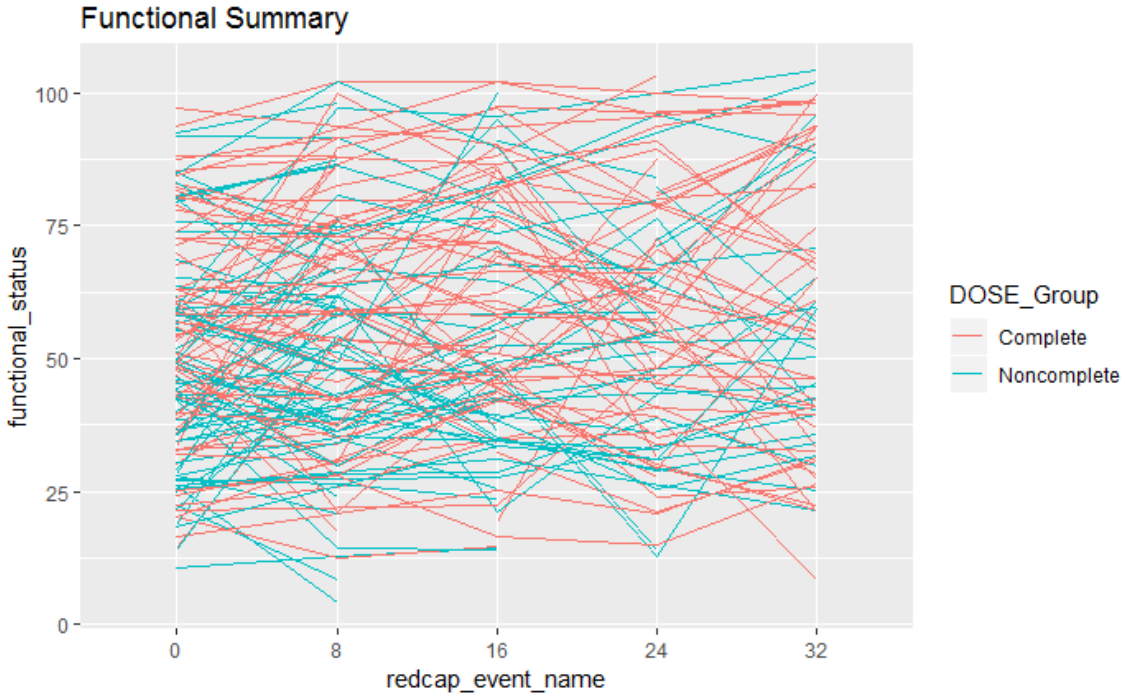


Figure 2. Kansas City Cardiomyopathy Questionnaire functional status scores over data collection time points by intervention completion groups.

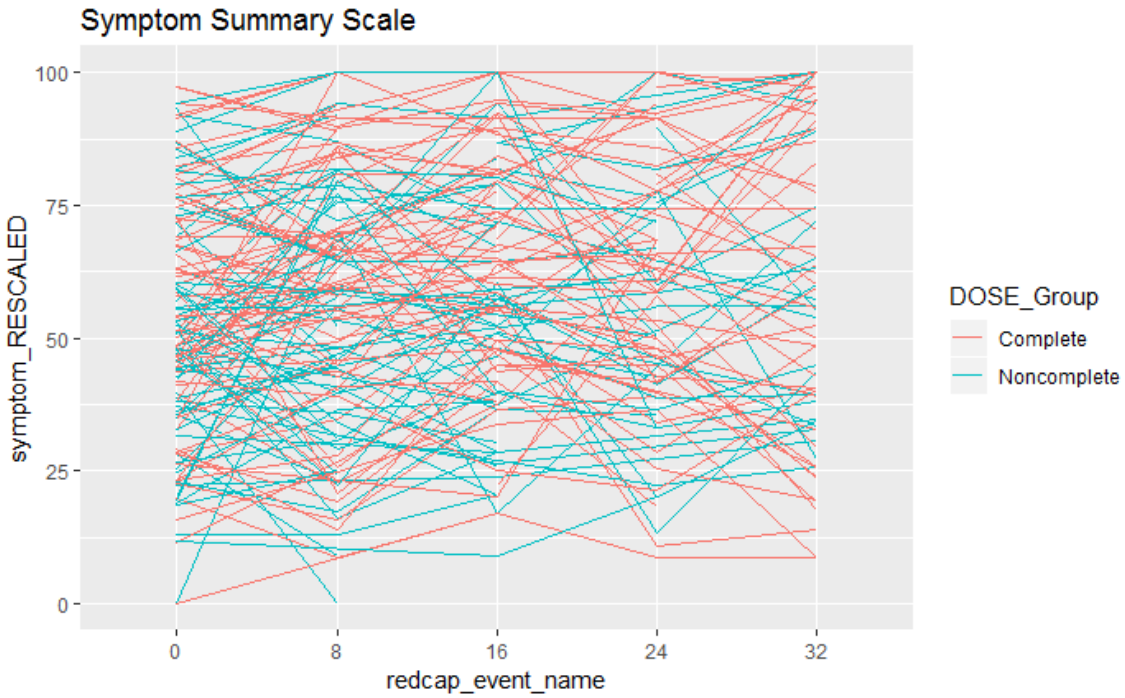


Figure 3. Kansas City Cardiomyopathy Questionnaire symptom summary over data collection time points by intervention completion groups.

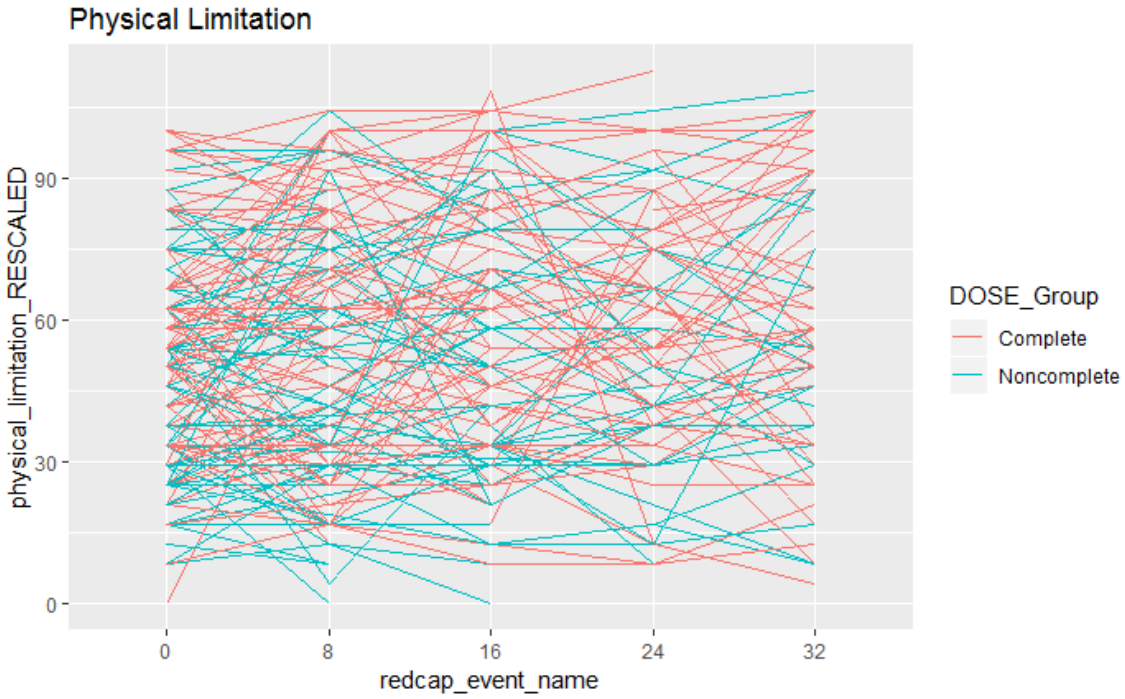


Figure 4. Kansas City Cardiomyopathy Questionnaire physical limitation scores over data collection time points by intervention completion groups.

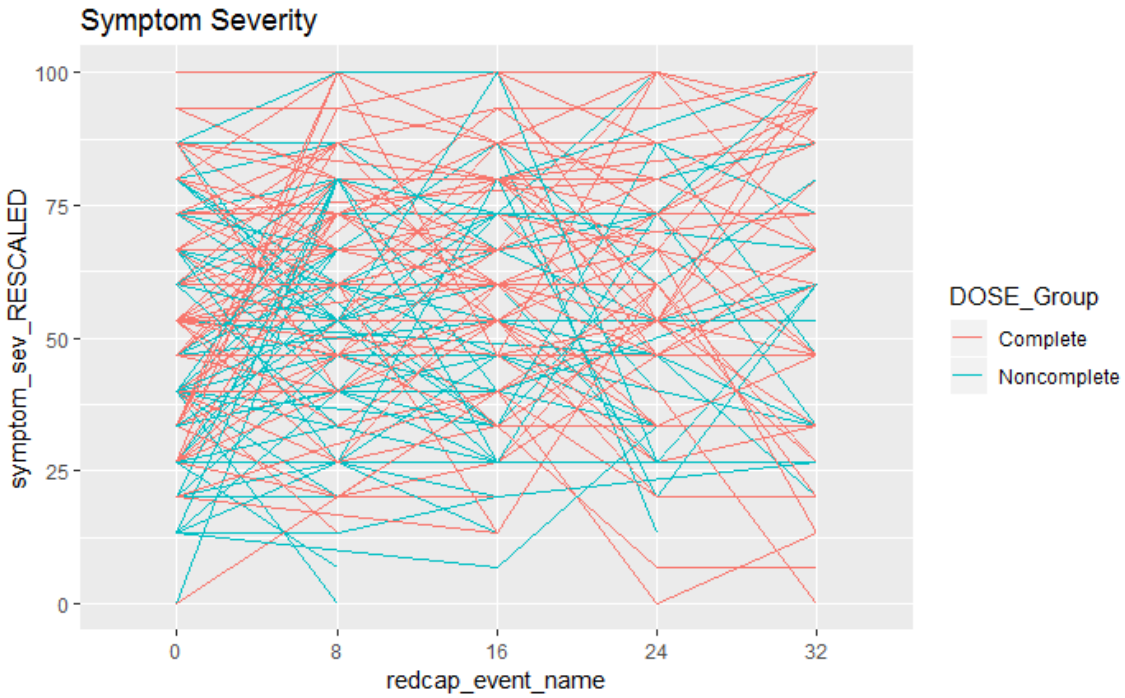


Figure 5. Kansas City Cardiomyopathy Questionnaire symptom severity scores over data collection time points by intervention completion groups.

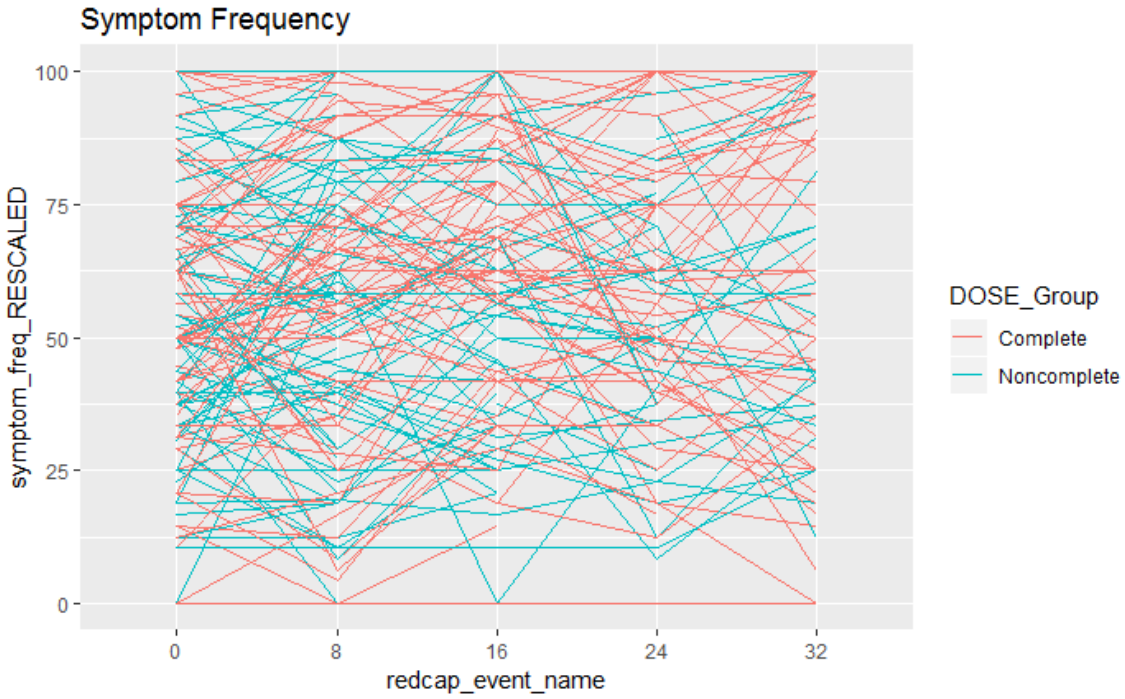


Figure 6. Kansas City Cardiomyopathy Questionnaire symptom frequency scores over data collection time points by intervention completion groups.

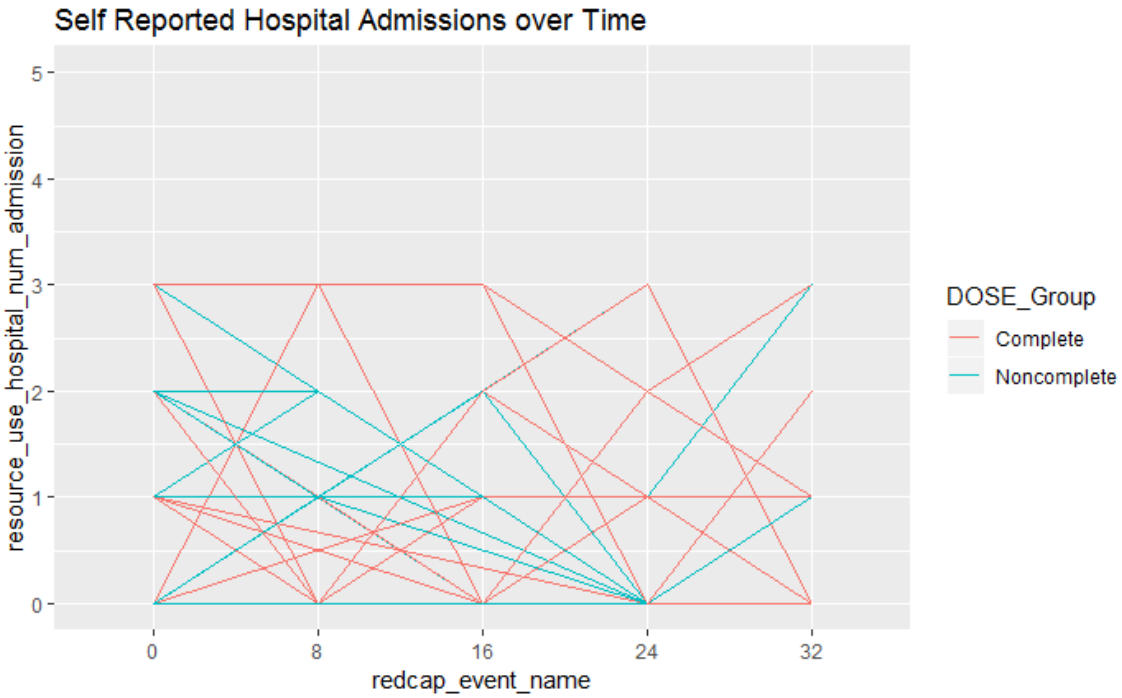


Figure 7. Self-reported hospital admissions during the past 8 weeks over data collection time points by intervention completion groups.

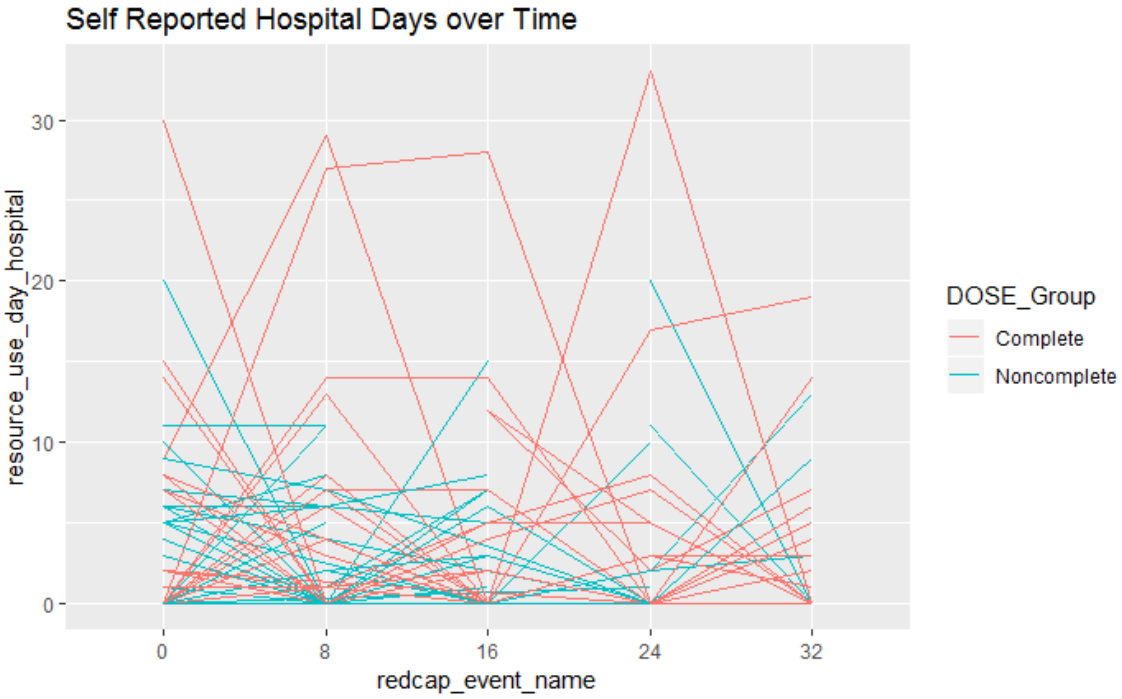


Figure 8. Self-reported hospital days during the past 8 weeks over data collection time points by intervention completion groups.

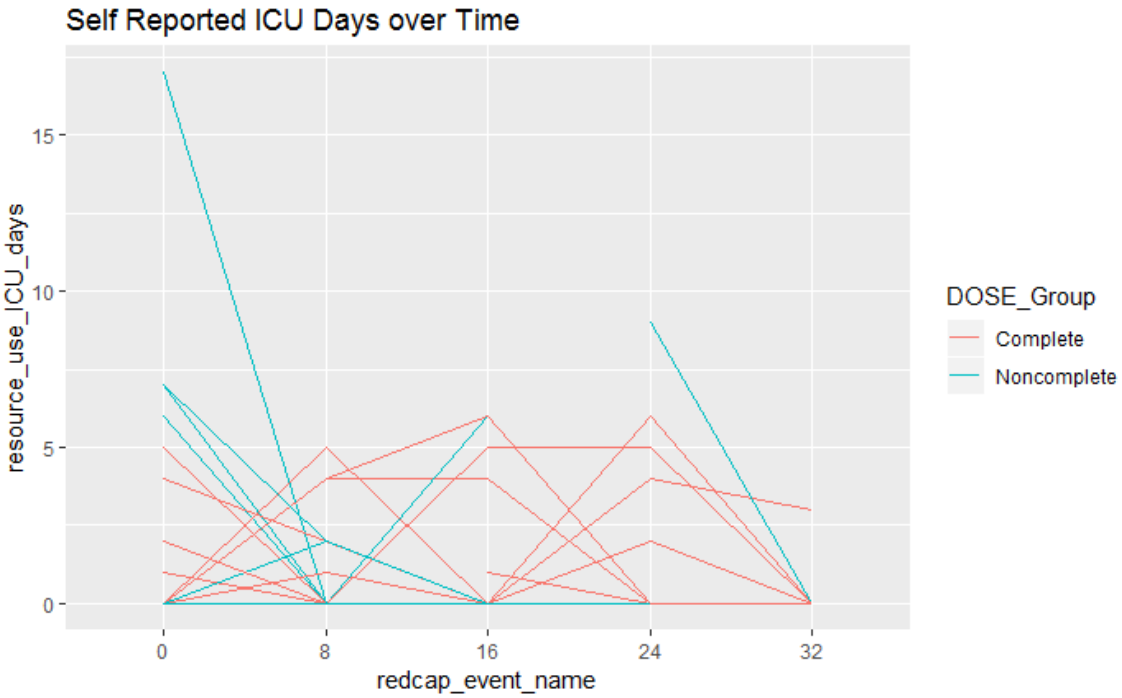


Figure 9. Self-reported intensive care (ICU) days during the past 8 weeks over data collection time points by intervention completion groups.

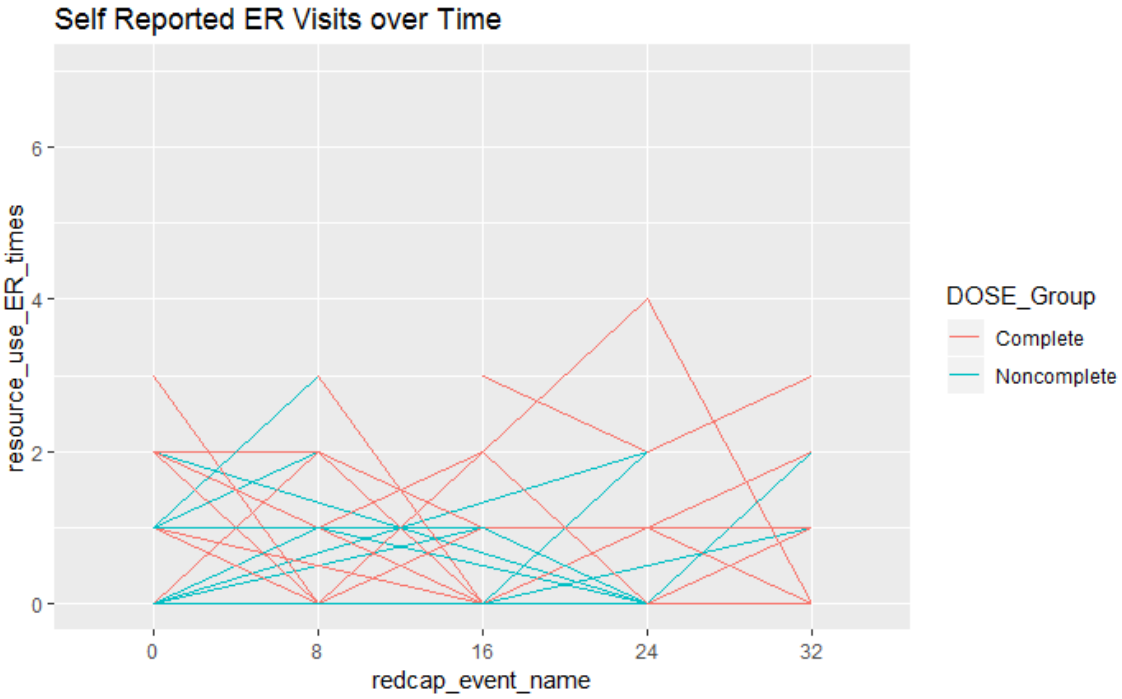
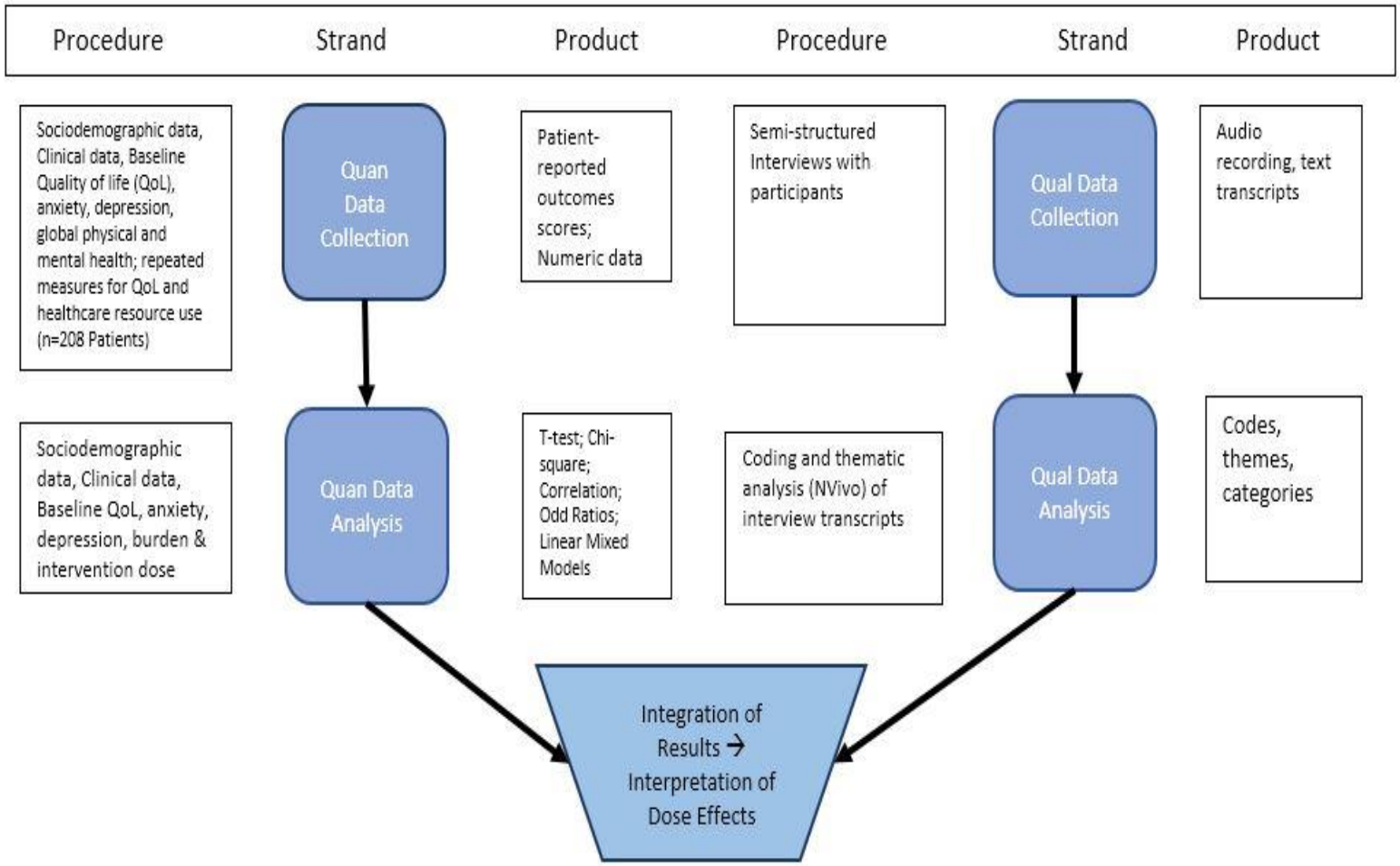


Figure 10. Self-reported emergency department visits during the past 8 weeks over data collection time points by intervention completion groups.

APPENDIX M

PROCEDURAL DIAGRAM


Procedure
Strand
Product
Procedure
Strand
Product
Sociodemographic data, Clinical data, Baseline Quality of life (QoL), anxiety, depression, global physical and mental health; repeated measures for QoL and healthcare resource use (n=208 Patients)
Quan Data Collection
Patient-reported outcomes scores; Numeric data
Semi-structured Interviews with participants
Qual Data Collection
Audio recording, text transcripts
Sociodemographic data, Clinical data, Baseline QoL, anxiety, depression, burden & intervention dose
Quan Data Analysis
T-test; Chi-square; Correlation; Odd Ratios; Linear Mixed Models
Coding and thematic analysis (NVivo) of interview transcripts
Qual Data Analysis
Codes, themes, categories
Integration of Results → Interpretation of Dose Effects

APPENDIX N

GUIDE FOR MEMBER CHECKING WITH SUMMARY OF QUALITATIVE FINDINGS

Participant Feedback Form

Instructions: Read this form to participants during member checking calls. Summarize major points in the feedback column. Please note participant study ID along with dose category. The study findings are on the left column. The feedback from participants goes on the right column- while each major finding (I-III) category is highlighted- the themes/codes are not part of the guide script- though you may choose to highlight them as needed during the conversation.

Feedback Guide

Interviewer: Hello. As you might remember, you participated in a one-time telephone interview about your experience with the ENABLE CHF-PC study. During this interview, we asked if we could check back in with you after all interviews were complete to talk about the findings of these calls. Is this still a good time for us to briefly talk about these findings? This call should take about 5 minutes.

IF NOT: Okay. Are you still willing to take about our findings at a later day? What day would be best in the next week for me to give you a call back? Is there a certain time of day you prefer? Again, this call should take about 5 minutes.

IF YES: This call today gives you a chance to comment on the findings from this interview study. The findings I will talk about today summarize the major points talked about by all participants *as a whole*. We did look at responses from participants who did and did not complete all of the study parts – overall, there were not many differences between these two groups. *Not all findings will relate to your experience and that is okay*. If the findings do not relate to your experience, just let me know and we will make a note that it was not true in your case. We appreciate you talking to us today and if it is okay with you, I'd like to begin. These calls are not recorded but I will take notes as we talk.

Overall, people found the ENABLE intervention to be helpful and beneficial. Many people felt the dose of intervention was "just right"- a few found the calls too long, too frequent, whereas a few others found the calls too short and did not like the change from weekly to monthly calls. Almost all found the session on problem solving to be the most impactful and a few did not like the advance care planning session. Do you have thoughts/feedback on this finding? [pause]

One of the main findings is the importance of your individual context on your intervention experience- so how bad you felt your HF is, your day to day living with HF, your needs related to your heart failure, the support of your family and friends, issues with day to day living such as having free time or access to transportation, your state of mind/emotional state at the start of the intervention, or one of the most influential, the relationship you had with your nurse coach. Many people described how these things- the background of your everyday life- influenced how much of the intervention they received

and played a role in what changes they experienced from participating in the intervention. Do you have thoughts/feedback on this finding? [pause]

We asked you all about how participating in this study impacted you- and we got many responses whether it helped with changing health habits (like diet), it gave you knowledge about HF, it help spark "hope" about living with HF, or improved how you talked with your doctors about your HF. Other people also said the intervention helped them talk to their family/friends about living with HF. Overall, most felt like their quality of life improved and less felt like they used less medical services related to the study but not everybody felt that way. When we asked if there was a relationship between how much of the intervention you received- how long the calls were or how often we called- most people did not feel like there was a relationship. Do you have thoughts/feedback on these findings? [pause]

One of the biggest take-aways we got from these interviews with you all is that understanding where you are and who you influences how you interact with a study and a study intervention. One thing this might tell us is rather than thinking in terms of a single dose for everyone of this type of intervention with the phone calls and the clinic visit- we might consider how similar 'contexts'- how bad you felt your HF is or how you are coping with your HF- might need different 'doses' or exposures to the intervention. As one of your fellow participants summarized, 'I think that depends upon the individual.' Do you have thoughts/feedback on these findings? [pause]

Study Findings		Participant Feedback
I. Impressions of ENABLE intervention dose and dose attributes		
a. Duration	1) 'You could've shortened it' 2) Disbelief of duration	
b. Frequency	1) "Seemed more" 2) Request for more	
c. Intensity	1) Descriptions of participant-rated > 5 intensity 2) Descriptions of participant-rated < 5 intensity 3) Guidebook-related preparation 4) Mental preparation	
d. Length of calls	1) "Worth the length" 2) "Just right" 3) "A little bit too long for my patience"	
e. Sum of parts	1) "It's the combination"	
f. Delivery	1) Telephone 2) In-person	

g. Timing	1) “Could be earlier” 2) “Others could use it more”	
II.Dose-modifying factors- The influence of context on intervention experience-		
a. Disease-related factors	1) Perceived disease severity 2) Perceived HF related knowledge deficit 3) HF impact in daily life	
b. State of mind	1) Anxiety 2) Depression 3) Optimistic disposition	
c. Social support/non-healthcare resources	1) Family/friend support 2) Free time 3) Transportation	
d. Interactions with providers	1) Nurse coach 2) Palliative care clinician	
III.Study outcomes		
a.Overall study effect	1) Health promoting habits 2) HF knowledge 3) “Hope” 4) Provider communication 5) Non-healthcare relationships 6) Quality of life 7) Healthcare resource use	
b. Dose-dependent effect	1) Experiences with dose-dependent change 2) No impact	