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The Symptom Experience of Black Women with Heart Failure Preserved Ejection Fraction

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by

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A dissertation submitted to the faculty of the Medical University of South Carolina in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the College of Nursing.

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Abstract

Background: Heart failure (HF) is a prevalent disease with a complex symptom experience. Black women with Heart Failure preserved Ejection Fraction (HFpEF) are especially burdened by symptoms, and their symptom experience is poorly understood. Clustering HF symptoms to understand which symptoms are experienced together is a potential option for helping patients recognize impending exacerbations.

Methods: The dissertation's first manuscript is an integrative review to examine the current state of HF symptom cluster literature. The second manuscript explores the feasibility and acceptability of a mixed methods HF symptom cluster study of Black women with HFpEF (N=44) and presents preliminary symptom cluster results. The third manuscript presents symptom experience themes from qualitative interviews (N=15) and integrates those findings with quantitative questionnaire data.

Findings: An integrative review of HF symptom cluster literature revealed a need for exploring the symptom experience of Black women with HFpEF using mixed methods. A convergent-parallel mixed methods study protocol met feasibility benchmarks and was deemed acceptable by Black women with HFpEF. Preliminary symptom clusters were identified using quantitative symptom data from symptom questionnaires. Qualitative themes emerged relating to the symptom experience and person, and mixed methods integration provided additional key findings of concordance, discordance, and expansion.

Conclusion: This dissertation describes the symptom experience of Black women with HFpEF, provides valuable information on the recruitment of an understudied population and their acceptability of a study protocol, and builds the foundation for conducting a mixed methods HF symptom cluster study with a larger sample in the future.

Introduction

Background and Gaps in Knowledge

Heart failure (HF) is a severe cardiovascular disease in which up to 30% of patients die within one year after diagnosis (1, 2). HF is the most common cause of hospitalization in the U.S. for those over the age of 65, and almost 25% of patients with HF will be readmitted within 6 months after discharge (3). Persons with HF experience a complex and multifactorial array of symptoms that make symptom self-monitoring and self-management difficult (1, 4-6).

HF symptoms are especially burdensome for Black patients and women. Black Americans are 1.5 times more likely to develop HF compared to White Americans (7). Black Americans also have a 2.5 times greater risk of dying from HF than White Americans (7). Females with HF report more depression, worse quality of life and symptom severity, and more frequent and longer hospitalization than males (2, 4, 8-10). Females also are more likely to be diagnosed with Heart Failure preserved Ejection Fraction (HFpEF) a type of HF caused by diastolic dysfunction in which relaxation of the left ventricle is impaired from increased stiffness (2, 11, 12). This type of HF is poorly understood, and more research is needed to characterize the symptom experience of patients with HFpEF (2, 12).

Females with HF are diagnosed or referred to cardiologists later than males and disproportionately receive fewer recommended therapies or less self-management education (2, 13, 14). Black Americans with HF have been noted to have difficulty recognizing and interpreting HF symptoms (7). An inadequate understanding of the

symptom experience for Black females with HF may lead to delays in treatment and ultimately result in avoidable hospitalizations from HF exacerbations (7).

So far, Black females have been underrepresented in heart failure symptom cluster research. There is a critical need to examine the symptom experience of Black women with HFpEF and how symptoms cluster in this population. This study aims to examine how the intersection of such factors can impact symptom clusters and the symptom experience of Black women with HFpEF using mixed methods.

Heart Failure Symptom Clusters

A symptom cluster is two or more symptoms that occur simultaneously in disease (5). Knowledge about how symptoms cluster can help patients to recognize impending exacerbations more easily, be used for developing more targeted and effective interventions, and assist in determining risk for adverse health outcomes (5, 8, 15-30). A small body of literature exists for HF symptom clusters that validates these potential uses (5, 8, 15-30).

However, research that has been conducted in this area minimally examines sex differences, does not include qualitative methodologies, and lacks racial and ethnic diversity (5, 8, 15-30). Yet, sex/gender and race/ethnicity have a complex interaction that influences health and should be considered when studying symptoms (31). Sex and gender differences in symptom perception and impact are also prevalent in other chronic diseases. Females with Chronic Obstructive Pulmonary Disorder (COPD) report higher levels of anxiety and depression, worse quality of life, worse perceived control of symptoms, and greater functional impairment (32-35). Women are noted to have

increased pain sensitivity and risk, and women with Chronic Venous Disease (CVD) were found to have worse neuropathic pain (burning, throbbing, and night cramps) compared to males (36). Woman's sex/gender in asthma is associated with more severe symptom intensity, frequency, and limitations from symptoms, and women with asthma report poorer quality of life (37). This evidence supports the need for sex/gender-specific exploration of symptom clusters and the symptom experience.

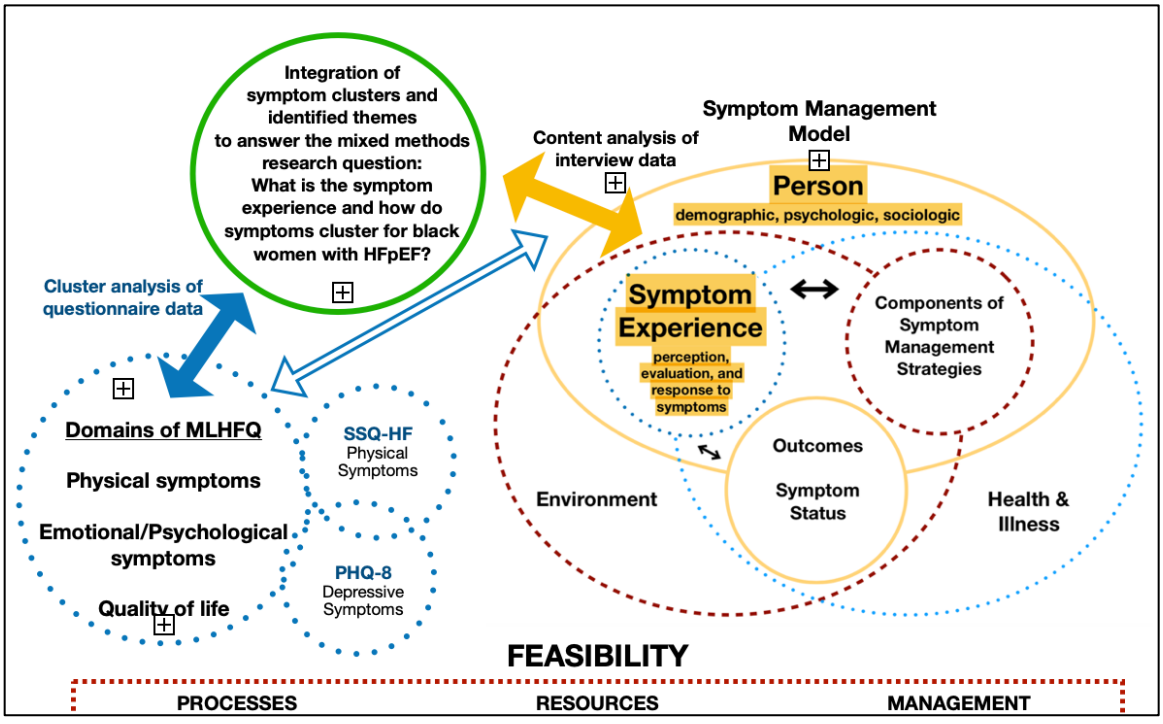
Since few Black females have been included in HF symptom cluster research, it is first necessary to determine if it is feasible to recruit this population, explore if and what barriers and facilitators to adequate recruitment exist, and determine participants' willingness to participate in research studies (38). Qualitative methods are needed to explore the intersection of gender, sex, and race and their impact on the symptom experience, as quantitative instruments alone have limited ability in encompassing such factors. Studying the symptom experience and symptom clusters concerning gender, sex, race, and type of HF is warranted considering the increased burden of HF symptoms, greater risk, and worst outcomes in females, Black Americans, and patients with HFpEF (2, 4, 7, 8, 10).

Theoretical Framework

Many factors contribute to the health disparities and worse outcomes that are evident for multiple conditions, such as societal and cultural stressors (7). The Symptom Management Model (SMM), shown in Figure 1, highlights the multi-faceted nature and complex interactions of symptom components (39). The six components that comprise the SMM are symptom experience, components of symptom management strategies,

outcomes and symptom status, person, environment, and health and illness (39). For this study, symptom experience and person influenced the semi-structured interview guide, as these components are well suited for individual interviews, best answer the overall research question, and allow for exploration of demographic, psychological, and sociological factors that can influence the symptom experience of a Black woman with HFpEF (39). These components also guided content analysis of interview data and the triangulation of questionnaire and interview results (39). The Minnesota Living with Heart Failure Questionnaire (MLHFQ) is a quality-of-life questionnaire that was used to collect quantitative data on physical symptoms, emotional symptoms, and quality of life (40). These three domains of the MLHFQ also influenced interview guide questions, which set the stage for merging of quantitative and qualitative results (40, 41).

Figure 1: Conceptual model of mixed methods feasibility study components within the SMM Framework adapted by the author (38, 39, 40, 46, 48)



Innovation

Current HF practice paradigms diagnose and treat males and females using the same guidelines, despite growing evidence of sex differences in symptom expression, disease burden, and quality of life (1, 2, 4-6). This study is innovative in that it sought to shift this paradigm by emphasizing sex and race, which was consistently lacking in a review of the literature (30). This was done by initially exploring the symptom experience and symptom clusters for Black females with HFpEF using a mixed methods research design.

The convergent mixed methods design is a novel approach to HF symptom cluster research that, to our knowledge, has not been conducted before. Utilizing mixed methods allowed for a more comprehensive exploration of the HF symptom experience and symptom clusters for Black women. Symptom clusters are created based on data from questionnaires, which have a limited ability in assessing personal factors and symptom perceptions, evaluations, and responses. Individual, semi-structured interviews guided by qualitative description allowed for a straight description of the symptom experience as described by participants (42-45).

Examining study feasibility was needed for understanding the nuances of recruitment and data collection within a population of Black females with HFpEF (38). Also, the Symptom Status Questionnaire Heart Failure (SSQ-HF) had not been validated in this population (38, 46). The SSQ-HF was used to assess the presence, frequency, severity, and distress of physical HF symptoms (46). A review of HF symptom cluster literature revealed that out of eight studies conducted in the U.S., five had >70% white participants, and SSQ-HF has not been well validated in a Black population (24-26, 28-

31, 36, 46). This study's findings can increase the population's inclusion in future research, thus expanding the generalizability of HF symptom cluster research long-term.

The National Institute of Nursing Research (NINR) has highlighted symptom cluster research as a critical component to advancing symptom science (21). This study provides valuable insights for recruiting a high-risk and understudied population and determining barriers to success for a mixed methods HF symptom cluster study. This study can also improve research efforts for the health of women by considering sex and gender influences, a specific goal of the 2019-2023 Trans-NIH Strategic Plan for Women's Health Research (47).

Specific Aims and Brief Description of Manuscripts

There are three manuscripts included in this dissertation: (1) an integrative review of heart failure symptom cluster studies; (2) an analysis of the feasibility and acceptability of a mixed methods approach to ascertain symptom clusters in Black women with HFpEF, with reporting of preliminary symptom cluster analysis findings; and (3) a qualitative study examining the symptom experience of Black women with HFpEF and integration of qualitative themes with quantitative symptom data. The aims and a brief description of each manuscript are listed below.

Aim 1: To synthesize the current state of literature related to symptom clusters in heart failure (HF) utilizing the Symptom Management Model (SMM) by Dodd et al., 2001

The first dissertation manuscript is a comprehensive review of HF symptom cluster literature with the following stated purpose: *to determine the current state of*

literature related to symptom clusters in HF using the SMM in order to discover themes within each component of the model (39). The HF symptom experience is complex and should be examined within multiple components to ensure a more comprehensive and holistic understanding. The integrative review revealed that symptom clusters can be useful in clinical practice for monitoring patients remotely; educating patients on self-management and symptom surveillance; determining the risk of cardiac events, hospitalization, morbidity, and mortality; and incorporating psychological symptoms (5, 8, 15-30).

The review also highlights how future research should further examine the effect that social and physical environments have on HF symptoms, as the environment component of the SMM was the least studied. Research on cultural and sex differences related to symptom responses or impact should be conducted rather than only examining if clusters are similar. The included study designs lacked any qualitative component. A mixed methods or qualitative approach to symptom cluster research will result in a richer description of the symptom experience and how each component impacts this experience.

Aim 2: To (1) explore the feasibility and acceptability of a convergent mixed methods symptom cluster study with a population of Black females with HFpEF and (2) explore preliminary HF symptom clusters of physical and psychological/emotional symptoms by cluster analysis of data collected symptom questionnaire data

The second manuscript reports the feasibility and acceptability of the convergent parallel mixed methods dissertation study that examined the symptom experience and how symptoms cluster in Black females with HFpEF. The qualitative and quantitative

data were collected in the same time frame with equal priority. This manuscript also presents preliminary findings from a symptom cluster analysis for this population to describe the symptom clustering technique and identify findings that could later be explored with a larger sample size.

The PI obtained IRB approval (Pro00101261) and recruited participants (N=44) from social media to complete screening and demographics questionnaires, the Single Item Literacy Screener, the Minnesota Living with HF Questionnaire, Symptom Status Questionnaire – HF, and Personal Health Questionnaire – 8 (40, 46, 48, 49). Participants who were interested and consented (N=15) were interviewed about their symptom experience using a semi-structured interview guide. Feasibility outcomes were tracked and measured throughout the study and were analyzed using descriptive statistics (38). An exploratory hierarchical cluster analysis of questionnaire data was conducted in SPSS version 25 (SPSS Inc, Chicago, Illinois) to form preliminary clusters.

All feasibility benchmarks of consent rate, recruitment rate, interview interest rate, survey completion rate, and feasibility and acceptability question scores were met for the study, and participants positively rated acceptability of the study protocol. Three symptom clusters were formed, which included a highly symptomatic cluster (which reported a high proportion of physical and psychological symptoms), a mildly symptomatic cluster (which reported a lower proportion of symptoms, especially less psychological symptoms), and a psychologically symptomatic cluster (which reported fewer physical symptoms but more psychological symptoms than the mildly symptomatic cluster).

Aim 3: To (1) describe the symptom experience of Black women with HFpEF using qualitative descriptive methods and (2) to integrate qualitative themes and quantitative symptom data to examine confirmation, expansion, and discordance of results

The third manuscript presents qualitative results and integrates quantitative findings with identified qualitative themes from the convergent parallel mixed methods study. Qualitative data were collected using individual, semi-structured interviews (N=15) and were analyzed using NVivo 20.3 software (QSR International, Pty, Doncaster, Australia). Analysis was guided by qualitative descriptive methods, and a directed approach to content analysis was used with SMM components and MLHFQ domains as broad code types to guide the development of sub-codes (39, 40, 42-45). Interviews were transcribed and analyzed as they were collected using a constant comparative method (42-45). For mixed methods analysis, quantitative and qualitative data were each analyzed separately, and results were integrated into a joint display and compared and contrasted to highlight confirmation, expansion, and discordance (41-45). Qualitative themes emerged relating to the person and symptom experience. Black women with HFpEF discussed interactions of physical and emotional symptoms, and positive correlations between symptom scales supported this theme. Women reported shortness of breath and chest pain causing worry and fears of death. Participants reported feeling like a burden to others and hid or downplayed their symptoms. Reduced physical functioning impacted family life, household chores, and the ability to work.

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Manuscript 1: Integrative Review

Title: Heart Failure Symptom Clusters: An Integrative Review

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Keywords: Chronic disease, Cognitive symptoms, Disease management, Emotional symptoms, Heart failure, Physical symptoms, Review, Signs and symptoms, Symptom assessment, Symptom clusters

Heart Failure Symptom Clusters: An Integrative Review

Abstract

Background: Patients with heart failure have difficulty recognizing and understanding their symptoms, contributing to 4 out of 5 people with heart failure requiring hospitalization each year in the U.S. Clustering symptoms have been proposed to help patients and clinicians identify and manage heart failure symptoms.

Objectives: The purpose of this integrative review was to determine the current state of literature related to symptom clusters in patients with heart failure using the Symptom Management Model to discover themes within each component of the framework.

Methods: We systematically searched Scopus, ProQuest, and PubMed databases to identify peer-reviewed, original research published in English between 2009 - August 2020. Search terms included "heart failure" AND "symptom cluster" OR "symptom relationships." The Whittemore and Knafl (2005) methodological framework was used to guide this integrative review.

Results: Twenty-nine manuscripts underwent full-text review, and 18 were deemed eligible. Physical and emotional/psychological symptoms clustered together and separately. Younger age, lower education level, and female sex corresponded with more distress from symptom clusters. Clinicians can use symptom clusters for risk assessment.

Conclusions: Symptom cluster data lacked racial diversity and minimally examined sex differences. No studies were identified that used qualitative methods. Current evidence supports the use of heart failure symptom clusters for patient education, self-management, symptom surveillance, and risk assessment. Clinicians should especially

consider emotional/psychological heart failure symptoms, which can be distressing and associated with worse outcomes.

Tweetable abstract: Clinicians can use heart failure symptom clusters for risk assessment, especially psychological symptoms associated with worse outcomes.

What is already known about the topic?

- Heart failure is associated with a substantial symptom burden, affecting patients' quality of life, functional status, and disease outcomes.
- Patient misinterpretation or lack of knowledge related to symptoms contribute to frequent hospitalizations from heart failure.
- Clinicians typically assess for disease-specific individual symptoms rather than clusters of symptoms.

What this paper adds

- Heart failure symptom clusters exist, and physical and emotional/psychological symptoms clustered together and separately.
- Current evidence supports the use of heart failure symptom clusters for patient education, self-management, symptom surveillance, and risk assessment, and clinicians should especially consider emotional/psychological symptoms, which can be distressing and associated with worse outcomes.
- Symptom cluster studies lacked racial diversity, minimally examined sex differences, and did not utilize qualitative methods.

Background

Heart Failure (HF) is a prevalent issue in the United States (U.S.), with an estimated 6.2 million Americans living with this disease (Benjamin et al., 2019). HF is a complex disease in which ventricular filling or ejection of blood is impaired due to structural changes or decreased cardiac functioning (Yancy 2013). HF is the most common cause of hospitalization for those over the age of 65, and 4 out of 5 people with HF require hospitalization each year (Pedrotty & Jessup, 2015; Riegel et al., 2018). Frequent HF hospitalizations are attributed to patient misinterpretation of, or lack of knowledge related to, symptoms, due to the complexity of symptom interactions and inadequate patient education tools, resulting in delays in seeking care and inadequate self-management (Pedrotty & Jessup, 2015; Riegel et al., 2018).

HF is associated with a substantial symptom burden, affecting patients' quality of life, functional status, and disease outcomes (Dodd, Miaskowski, & Lee, 2004; Moser et al., 2014; Pedrotty & Jessup, 2015). Clinicians typically assess for disease-specific individual symptoms; however, they could examine symptoms in clusters (Dodd et al., 2004; Moser et al., 2014). A symptom cluster is when two or more symptoms co-occur in a disease process (Denfeld, 2020). Symptoms can be a derivative of procedures, medications, or the disease process itself (Dodd et al., 2004). Effectively utilizing symptom clusters in clinical practice could result in targeted patient education, enhanced surveillance of exacerbations, and improved health outcomes (Dodd et al., 2004; Moser et al., 2014).

The existence of symptom clusters has been explored in other chronic diseases such as cancer, yet the concept is still relatively new and unrefined (Aktas, 2013). Based upon preliminary database searching, it does not appear there is a large body of evidence for

symptom clusters in HF. Therefore, the purpose of this integrative review is to determine the current state of literature related to symptom clusters in HF using the Symptom Management Model (SMM) to discover themes within each component of the model (Dodd et al., 2001).

Theoretical Framework

Existing evidence about symptom clusters in people with HF will be synthesized using the SMM, depicted in Figure 1 (Dodd et al., 2001). The SMM considers the complex and multi-faceted nature of symptoms and can help identify which areas of symptom management have been well described within the literature and which areas need further exploration (Dodd et al., 2001). The SMM focuses on the three components of symptom experience, management strategies, and outcomes. The three components of the symptom experience include perception, evaluation, and response to symptoms. Management strategies incorporate aspects of treatment decisions, such as when to begin treatment and dosing. Outcomes incorporate various components of symptom status, such as quality of life, morbidity, and mortality. Together, these three components encompass the symptom experience and management as a whole (Dodd et al., 2001).

The SMM was revised in 2001 to include three nursing science domains: person, health and illness, and environment (Dodd et al., 2001). The person domain allows for examining demographic, psychosocial, sociological, physiological, and developmental factors. The health and illness domain includes risk factors, health status, and disease and injury. The environment domain considers the impact of physical, social, and cultural environments, which affect symptom interpretation and treatment decisions.

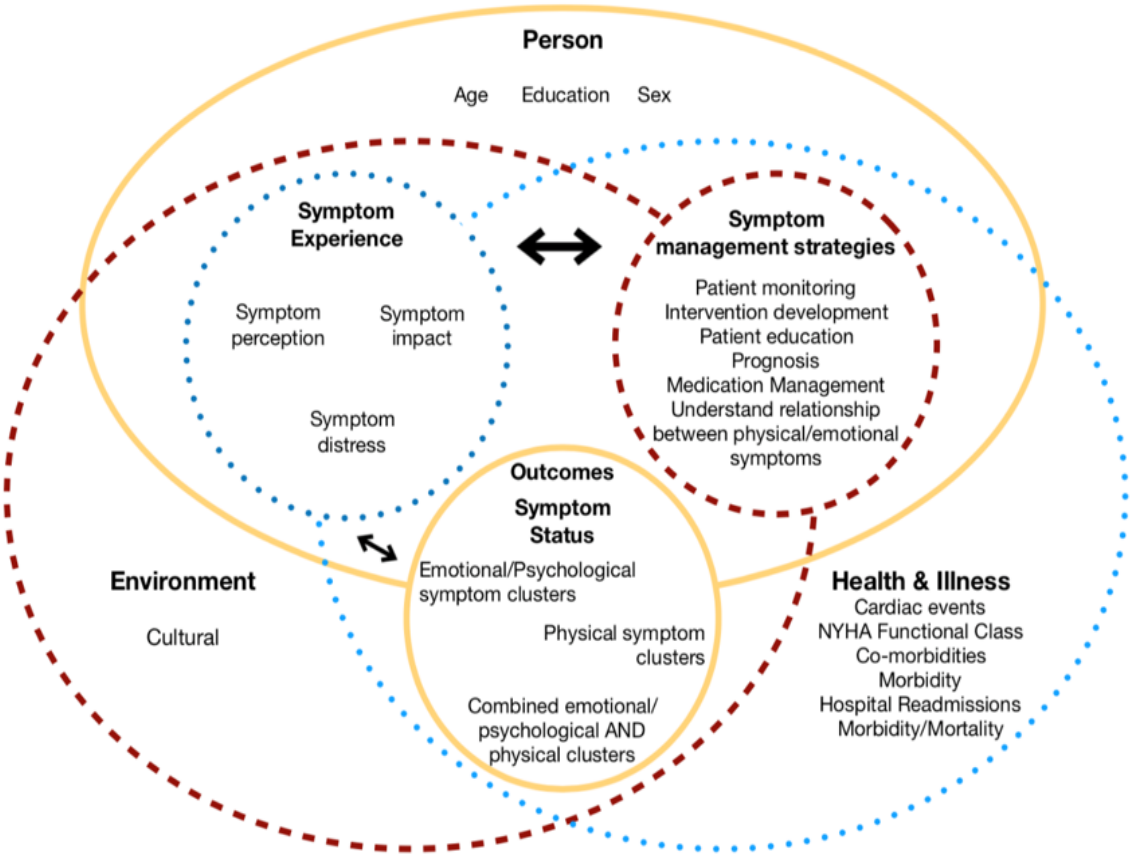

Figure 1

Modified SMM (Dodd et al., 2001)

Methods

The Whittemore and Knafl (2005) methodological framework was used to guide this integrative review. A well-defined literature search was undertaken within Scopus, ProQuest, and PubMed with the assistance of a medical reference librarian using the search terms "heart failure" AND "symptom cluster" OR "symptom relationships." Peer-reviewed, original research articles published in English between 2009 and August 2020

were reviewed to exclude very outdated references while including the essential early HF symptom cluster studies. The search yielded 88 results, as shown in the Prisma flow diagram in figure 2 (Moher et al., 2009). Twenty-three manuscripts remained after duplicates were removed, and titles and abstracts were screened to exclude manuscripts that were not about HF symptom clusters or did not meet the inclusion criteria specified previously. An additional six studies were identified through a review of references for a total of 29 manuscripts. Ten of the 29 manuscripts were excluded for examining symptom patterns or relationships rather than clustering, and one manuscript was excluded for not being specific to people with HF. After exclusions, 18 manuscripts remained for data analysis.

For data evaluation, study quality was assessed using the quantitative non-randomized category of the Mixed Methods Appraisal Tool (MMAT) (Hong et al., 2018). The quality criteria consisted of 7 items, and a "yes," "no," or "can't tell" was assigned to each criterion and displayed in Table 1 (Hong et al., 2018). Manuscripts were analyzed chronologically by year published, beginning with the oldest. Chronologically analyzing the manuscripts allowed for an illustration of research progression over the previous ten years and built a chain of evidence (Whittemore & Knafl, 2005). Data were extracted by hand from manuscripts and organized in a literature table under the SMM components (supplementary material table 1), allowing for systematic comparison. Similar findings were clustered, and themes were identified to summarize and synthesize the evidence.

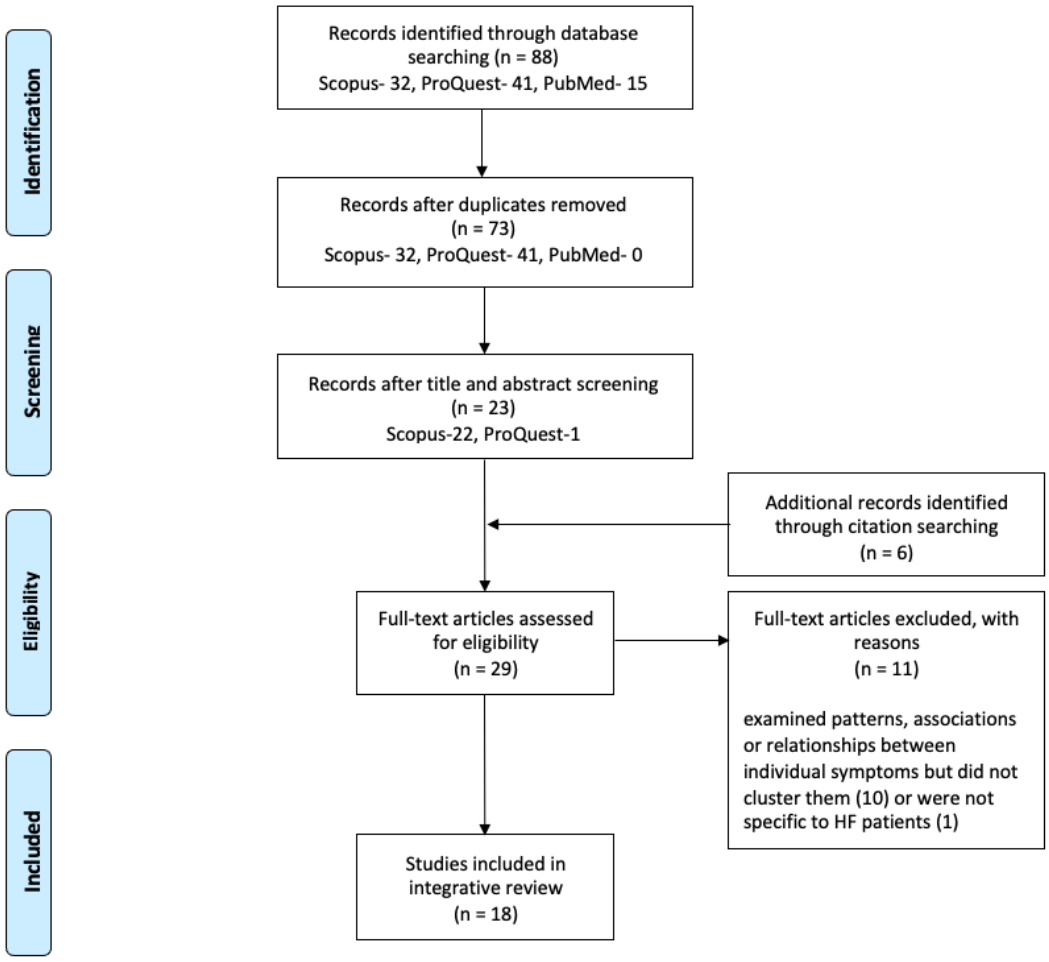

Figure 2

Prisma Flow Diagram (Moher et al., 2009)

Results

Of the 18 included studies, nine were conducted in the U.S., two in the Netherlands, two in Korea, one in Hong Kong, one in the United Kingdom, and one in Taiwan. Two studies were conducted cross-culturally in the U.S. and Asia, and one of those studies included European centers in the Netherlands and Sweden (Moser et al., 2014; Park & Johantgen, 2017). There was a relatively even split of study designs with five cross-

sectional studies, five prospective cohort studies, seven secondary data analyses, and one cluster analysis pilot study, as shown in Table 1. Components of symptom management and outcomes and symptom status were present in all the included studies, and two studies addressed every component of the SMM (Huang et al., 2018; Son & Won, 2018). Prominent results were categorized according to SMM components, beginning with outcomes and symptom status to familiarize the reader with identified symptom clusters, and then person, health and illness, symptom experience, and components of symptom management strategies.

Table 1: *Included studies, study info, Symptom Management Model components present in each study, and Mixed Methods Appraisal Tool Methodological Quality Scoring*

		Symptom Management Model Component (X=present)						
Year, Author	**Study info**	**Person**	**Environ-ment**	**Health & illness**	**Symptom experience**	**Com-ponents of symptom manage-ment**	**Out-comes & symp-tom status**	**MMAT scoring (CT= can't tell)**
2009, Jurgens	-Second-ary data analysis -N=687 -6 sites in the U.S.	X		X	X	X	X	S1: YES S2: YES 3.1: YES 3.2: YES 3.3: CT 3.4: YES 3.5: CT
2009, Jurgens	-Second-ary data analysis -N=687 -6 sites in the U.S.	X		X	X	X	X	S1: YES S2: YES 3.1: YES 3.2: YES 3.3: CT 3.4: YES

								3.5: CT
2009, Schiffer	-Pro-spective cohort -N=285 -The Nether-lands			X		X	X	S1: YES S2: YES 3.1: CT 3.2: YES 3.3: NO 3.4: YES 3.5: YES
2009, Smith	-Pro-spective cohort -N=381 -The Nether-lands	X		X	X	X	X	S1: YES S2: YES 3.1: CT 3.2: YES 3.3: CT 3.4: YES 3.5: YES
2010, Hertzog	-Cluster analysis pilot study -N=139 -Out-patient HF clinic in the Midwest U.S.	X		X	X	X	X	S1: YES S2: YES 3.1: YES 3.2: CT 3.3: YES 3.4: CT 3.5: YES
2010, Lee	-Pro-spective cohort -N=331 -6 hospitals in Ken-tucky, Georgia, and Indiana	X		X	X	X	X	S1: YES S2: YES 3.1: YES 3.2: CT 3.3: CT 3.4: YES 3.5: YES
2010, Song	-Pro-spective cohort -N=421			X	X	X	X	S1: YES S2: YES 3.1: CT

	-2 tertiary medical centers in Seoul, Korea							3.2: YES 3.3: YES 3.4: YES 3.5: YES
2014, Moser	-Cross-sectional obser-vation study -N=720 -Asia (China, Taiwan), Europe (the Nether-lands, Sweden), and the U.S.		X		X	X	X	S1: YES S2: YES 3.1: CT 3.2: YES 3.3: CT 3.4: YES 3.5: YES
2015, Hawkins	-Pro-spective cohort -N=326 -Summa Health System Ohio, U.S.			X		X	X	S1: YES S2: YES 3.1: YES 3.2: YES 3.3: YES 3.4: YES 3.5: YES
2015, Herr	-Cross-sectional -N=117 -U.S. academic medical center	X				X	X	S1: YES S2: YES 3.1: YES 3.2: CT 3.3: NO 3.4: CT 3.5: YES
2015, Lee	-Second-ary data analysis of 2 pro-spective cohort studies	X		X	X	X	X	S1: YES S2: YES 3.1: YES 3.2: CT

	-N=291 -HF clinic in Pacific North-west							3.3: CT 3.4: YES 3.5: YES
2016, Yu	-Second-ary data analysis of a cross-sectional study -N=119 -Hospital in Hong Kong				X	X	X	S1: YES S2: YES 3.1: CT 3.2: CT 3.3: YES 3.4: YES 3.5: YES
2016, Zhang	-Cross-sectional -N=1031 (626 with con-firmed HF) -United Kingdom			X	X	X	X	S1: YES S2: YES 3.1: CT 3.2: CT 3.3: CT 3.4: YES 3.5: YES
2017, Park	-Second-ary analysis of a cross-sectional study -N=240 each region (480 total) -U.S. and Eastern Asia (Taiwan and China)		X		X	X	X	S1: YES S2: YES 3.1: YES 3.2: YES 3.3: YES 3.4: YES 3.5: YES
2018, Huang	-Second-ary data cluster analysis of pro-spective long-itudinal study		X	X	X	X	X	S1: YES S2: YES 3.1: YES 3.2: YES 3.3: CT

	-N=258 -4 HF clinics in Taiwan							3.4: YES 3.5: YES
2018, Son	-Cross-sectional -N=306 -Korea	X	X	X	X	X	X	S1: YES S2: YES 3.1: YES 3.2: NO 3.3: YES 3.4: YES 3.5: YES
2019, Park	-Second-ary data analysis of HF re-pository data (inter-vention and cross-sectional studies) -N=4,011 -U.S.	X		X	X	X	X	S1: YES S2: YES 3.1: YES 3.2: CT 3.3: YES 3.4: YES 3.5: YES
2019, Salyer	-Cross-sectional -N=117 -U.S.					X	X	S1: YES S2: YES 3.1: CT 3.2: YES 3.3: YES 3.4: YES 3.5: YES
2020, Denfeld	-Second-ary data analysis of 2 cohort studies -N= 274 -U.S.			X		X	X	S1: YES S2: YES 3.1: CT 3.2: YES 3.3: YES 3.4: YES

								3.5: YES

*Mixed Methods Appraisal Tool (MMAT) Methodological Quality Criteria (Quantitative nonrandomized) (Hong et al., 2018) S1. Are there clear research questions? S2. Do the collected data allow you to address the research questions? 3.1. Are the participants representative of the target population? 3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)? 3.3. Are there complete outcome data? 3.4. Are the confounders accounted for in the design and analysis? 3.5. During the study period, is the intervention administered (or exposure occurred) as intended?

Outcomes and Symptom Status

Outcomes and symptom status include functional status, emotions, costs, self-care activities, quality of life, morbidity, co-morbidities, and mortality (Dodd et al., 2001). Emotional, depressive, or psychological symptoms formed a cluster in 7 studies, consisting of symptoms such as depression, worrying, anxiety, difficulty concentrating, and poor self-esteem (Jurgens et al., 2009; Lee, 2010; Hawkins et al., 2015; Moser et al., 2014; Schiffer et al., 2009; Smith et al., 2009; Zhang, Hobkirk, Carroll, Pellicori, Clark, & Cleland, 2016). Three studies created somatic/affective and cognitive/affective depression symptom clusters (Hawkins et al., 2015; Schiffer et al., 2009; Smith et al., 2009). Psychological clusters were associated with memory and cognitive problems (Hawkins et al., 2015; Jurgens et al., 2009; Lee, 2010). Psychological symptoms also clustered with physical symptoms, including shortness of breath, daytime sleepiness, and fatigue (Salyer et al., 2019; Yu, Chan, Leung, Hui, & Sit, 2016). A sickness behavior cluster was found to significantly influence quality of life ($b = - 0.603$, $p = 0.0001$) and accounted for 40% of its variance ($F = 75.12$, $R2 = 0.404$, $p = 0.0001$) (Salyer et al., 2019).

For physical symptom clusters, shortness of breath clustered with fatigue with low energy and increased need to rest, trouble sleeping, and difficulty walking or climbing in three studies (Jurgens et al., 2009; Lee, 2010; Moser et al., 2014). Four studies found

lower extremity edema or swelling did not fall within a symptom cluster (Lee, 2010; Moser et al., 2014; Song, Moser, Rayens, & Lennie, 2010; Yu et al., 2016). A gastrointestinal stress cluster was unique to three studies and included loss of appetite, nausea, and decreased hunger (Herr et al., 2015; Salyer et al., 2019; Son & Won, 2018).

Six studies clustered participants by the symptom frequency, severity, and distress they reported (Denfeld et al., 2020; Hertzog, Pozehl, & Duncan, 2010; Huang et al., 2018; Lee, 2015; Park & Johantgen, 2017; Park et al., 2019). Creating clusters of participants based on how they experienced symptoms rather than the symptoms themselves allowed the authors to examine how symptoms may impact participants on an individual level. For instance, Hertzog et al. (2010) found that clusters of participants who reported fewer symptoms or less symptom impact were associated with fewer physical and social limitations and better quality of life (all $p < 0.001$). Denfeld et al. (2020) found that severe physical cluster participants were more likely to be in a severe affective cluster.

Person

The person domain consists of demographics, psychosocial, sociological, physiological, and developmental factors (Dodd et al., 2001). The studies in this review predominately explored age, education level, and sex. Younger age was associated with more psychological or emotional distress than older age, regardless of physical symptom severity (Lee, 2010, Park et al., 2019). Park et al. (2019) found that for every 5-year age increase, a patient with HF was 4.85 times less likely to be in the psychological distress cluster (95% CI = [4.76, 4.95]) and 4.89 times less likely to be in the high physical and

psychological distress cluster (95% CI= [4.82, 4.96]) (Park et al., 2019). Older participants were also more likely to rate symptom severity that matched their hemodynamic profile than younger participants (p= 0.003) (Lee et al., 2015).

Higher educational attainment was associated with inclusion in less severe symptom clusters (Hertzog et al., 2010; Park et al., 2019; Smith et al., 2009; Son & Won, 2018). Participants with less than a high school degree were more likely to be in a physical distress cluster (OR = 0.27; 95% CI = [0.16, 0.48]) and a high distress cluster (OR = 0.16; 95% CI = [0.08, 0.33]) than those with at least some college (Park et al., 2019). One study designed to study sex differences found that men and women had the same symptom clusters, but women had significantly higher distress from their fatigue symptoms and the increased need to rest, sleep disturbances, and feeling depressed than men (Lee et al., 2010). Women also had significantly higher symptom distress scores for a circulatory and GI symptom cluster ($p< 0.001$) and physical symptom cluster ($p< 0.05$) than males in two other studies (Lee, 2010; Son & Won, 2018).

Health & Illness

The health and illness component addresses risk factors, health status, disease, and illness (Dodd et al., 2001). Co-morbid conditions were the most prominent theme found within the health and illness component. Jurgens et al. (2009) found diabetes to be a predictor of inclusion in an emotional symptom cluster (Jurgens et al., 2009). Park et al. (2019) found that participants with diabetes were also 1.91 times more likely to be in a physical distress class (95% CI = [1.32, 2.75]) and 1.66 times more likely to be in a high distress class (95% CI = [1.12, 2.46]) (Park et al., 2019). Participants with atrial

fibrillation were 2.71 times more likely to be in a high distress class (95% CI = [1.85, 3.96]) and had significantly higher symptom scores for bodily pain and energy insufficiency clusters (p=0.015) (Park et al., 2019; Son & Won, 2018). Participants with hypertension were twice as likely to be in a high distress cluster than in a low distress cluster (OR = 2.04; 95% CI = [1.38, 3.02]) (Park et al., 2019).

Multiple studies assessed the relationship between symptom distress and risk. Findings from Jurgens et al. (2009) suggested distress from HF symptoms had little association with degree or type of cardiac dysfunction (Jurgens et al., 2009. However, Schiffer et al. (2009) found that distress from a cognitive/affective depressive symptom cluster was a significant predictor of disease-specific health status (HR=2.3, 95% CI = 1.21-4.44, p=0.01) (Schiffer et al., 2009). Lee et al. (2015) discovered that total symptom distress scores from an emotional/cognitive symptom cluster were an independent predictor of cardiac event-free survival (HR=1.18; 95% CI, 1.03-1.37) (Lee et al., 2015). Participants with severe symptom profiles were 3.3 times more likely to have a clinical HF event, and those with high-severity dyspnea and fatigue had a significantly higher risk for a cardiac event (p=0.016) (Huang et al., 2018; Lee, 2010). Inclusion in a somatic/affective depressive symptom cluster predicted risk of mortality (HR=1.8, 95% CI, 1.03-3.07, p=0.04).

Symptom Experience

Symptom experience incorporates how a person perceives, evaluates, and responds to their symptoms. Manuscripts included in this review focused on symptom distress, impact, and perceptions (Dodd et al., 2001).

For symptom impact, an acute volume overload cluster high in shortness of breath severity accounted for 45.7% of the variance in impact of symptoms on living as desired (Jurgens et al., 2009). This finding coincides with results from a respiratory distress cluster that accounted for 21.3% of the variance (21.3%) of symptom impact (Son & Won, 2018). For symptom distress, lack of energy was the most distressful physical symptom in one study, and orthopnea the least (Song et al., 2010). Although edema is a common HF symptom, it was not particularly distressing to participants or sometimes even noticed unless severe (Lee, 2010; Moser et al., 2014). Those with higher distress from symptoms had a more significant co-morbidity burden (Lee et al., 2010). Distress symptom clusters and functional limitation secondary to breathlessness were independent predictors of quality of life (Yu et al., 2016; Zhang et al., 2016).

Components of symptom management strategies

Creating a symptom management plan includes encompassing the other SMM components and considering them when making symptom management recommendations (Dodd et al., 2001). Authors of the included studies suggested using symptom clusters for patient monitoring, intervention development, patient education on when to seek care, prognosis, proper medication management, and a better understanding of the interplay between physical and psychological symptoms. Multiple studies recommend using symptom clusters for monitoring patients with HF for exacerbations (Huang et al., 2018; Jurgens et al., 2009; Moser et al., 2015; Park & Johantgen, 2017). It has been noted that examining symptoms in clusters could improve surveillance of symptoms and promote early detection of worsening symptoms, which is especially

important considering the increasing utilization of telehealth monitoring without physical assessment (Huang et al., 2018; Jurgens et al., 2009).

Clinicians and researchers can also use symptom clusters to develop interventions that manage an entire cluster of symptoms (Herr et al., 2015; Lee, 2010; Park et al., 2019, Yu et al., 2016). Yu et al. (2016) discussed how these targeted interventions could be more beneficial than addressing symptoms individually due to the synergistic effect clustered symptoms have of causing more distress when they are co-occurring (Yu et al., 2016).

Symptom clusters can also be used as an educational tool to empower people with HF to understand when to seek care and promote awareness of symptoms (Herr et al., 2015; Jurgens et al., 2009; Lee et al., 2010; Moser et al., 2014; Son & Won, 2018; Song et al., 2010). Only 9% of hospitalized patients with HF reported regular monitoring of symptoms before hospitalization, and patients were less efficient at recognizing symptoms when they gradually worsened over time (Song et al., 2010). Clinicians can use symptom clusters to educate patients on alleviating symptoms and discussing symptom management at discharge to reduce hospital re-admissions and decreased functional status (Herr et al., 2015; Moser et al., 2014; Son & Won, 2018).

Discussion

The SMM highlights how symptoms have multi-faceted and complex interactions with various components (Dodd et al., 2001). The results of the included symptom cluster studies coincide with this theory. For instance, lower extremity edema was not clustered with other symptoms in 4 studies and was often not noticed or distressing unless severe

(Lee et al., 2010; Moser et al., 2014; Song & Won, 2010; Yu et al., 2016). Suppose patients are not feeling impacted by symptoms, such as lower extremity edema. In that case, they may delay seeking treatment, as evidence suggests patients with HF are prone to ignore or adapt to symptoms they do not consider significant (Jurgens et al., 2009). Therefore, clinicians need to educate patients on the most concerning symptom clusters that indicate worsening HF disease status.

An example is shortness of breath, a symptom linked to anxiety and depression in a distress symptom cluster, which accounted for 21.3% of the variance in symptom impact when included in a respiratory distress cluster (Son & Won, 2018; Yu et al., 2016). Clinicians can educate patients on the most effective ways to monitor for shortness of breath and the symptoms that cluster alongside it. This education could help patients better recognize signs of impending HF exacerbation rather than attributing shortness of breath to aging or other co-morbidities and not seeking help. Future research should evaluate whether an educational tool for monitoring symptom clusters would be feasible and beneficial (Song et al., 2010).

It is also important to note that none of the studies included in the review contained a qualitative component, showing a significant gap in HF symptom cluster research that future research should address. A qualitative component is needed to begin a more in-depth, robust understanding of how people with HF perceive, interpret, and respond to symptom clusters. Qualitative interviewing is especially warranted for exploring psychological, emotional, and cognitive symptom clusters. The need for clinicians to recognize such symptom clusters and expand assessments beyond physical symptoms was the most prominent theme found within symptom management strategies.

People with higher distress from emotional/cognitive symptoms may be at the highest risk for adverse outcomes, especially younger people who report more distress (Herr et al., 2015; Lee et al., 2010). At this time, the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) guidelines for the management of HF do not propose strategies for addressing psychological symptoms (Lee et al., 2010; Park et al., 2019; Yancy et al., 2013). The ACCF/AHA HF guidelines recognize depression as a common co-morbidity in people with HF that can lead to poor self-care behaviors, worse quality of life and disease outcomes, and the need for more frequent medical services (Yancy et al., 2013). However, the guidelines state that an effective intervention strategy for depressive symptoms is unknown (Yancy et al., 2013; Yancy et al., 2017; Hollenberg et al., 2019). Clustering symptoms may help connect physical and psychological symptoms for improved understanding and management of the disease (Lee et al., 2015). Providers need to listen to how patients feel to assess the risk of adverse events, as clinical data may not accurately reflect their risk alone (Lee et al., 2015).

Of the 18 included studies, 14 had over 30% females in their sample. However, sex differences were not addressed in depth. One study examined sex differences in symptom clusters and found identical clusters, but women reported significantly higher symptom distress from a physical symptom cluster ($p< 0.05$) than males (Lee et al., 2015). This finding indicates that there can be variation in symptom response and the impact the cluster has on quality of life. To further examine sex differences and enhance data's robustness, future research should use qualitative methods to explore the higher levels of symptom distress women experience.

The environment domain was the most understudied. Three manuscripts addressed culture, and none addressed social and physical environment. Son and Won (2018) suggest using the ecological approach to explore differences in symptom clusters across cultures, races, and locations. Park and Johantgen (2017) state that a mixed-methods study design could provide a more holistic depiction of cultural differences in HF symptom clusters.

The MMAT was used to evaluate the included studies' methodological quality (Hong et al., 2018). All of the studies met at least four of the seven criteria, and two studies met all seven (Hawkins, 2015; Park, 2017). A lack of racial diversity for U.S. studies was noted, with 6 out of 9 studies conducted within the U.S. having over 70% White participants (Denfeld et al., 2020; Hawkins et al., 2015; Hertzog et al., 2010; Lee et al., 2010; Lee et al., 2015; Park et al., 2019). Considering that Black Americans are 1.5 times more likely to develop HF than White Americans, diversity and inclusion in HF symptom cluster research is imperative for generalizability to the U.S. population (Parashar et al., 2009). Also, the studies used questionnaires such as the MLHFQ, limiting the number of symptoms that participants can report to only symptoms that appear on the questionnaire. Researchers can explore more symptoms with a qualitative approach, which current HF symptom cluster studies currently lack.

This integrative review has some limitations. Only Scopus, ProQuest, and PubMed were searched, and after exclusions, all included manuscripts were from Scopus. Furthermore, alternate search terms could be added to find additional relevant manuscripts.

Conclusion

The HF symptom experience is complex and should be examined within multiple components to ensure a more comprehensive and holistic understanding. This integrative review synthesized the most prominent themes from current HF symptom cluster research. HF symptom clusters can be useful in clinical practice for determining the risk of cardiac events, hospitalization, morbidity, and mortality. HF symptom clusters that incorporate psychological symptoms are instrumental, as psychological symptoms were often associated with increased risk. Clinicians should examine factors related to the person alongside symptom clusters, especially regarding younger age. Future research should further investigate the effect that social and physical environments have on HF symptoms, as the environment was the least studied SMM component. Future research should explore cultural and sex differences related to symptom responses or impact. The included study designs lacked any qualitative component. A mixed methods or qualitative approach to symptom cluster research will result in a richer description of the symptom experience and how each component impacts this experience.

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Supplementary Material Table 1: *Integrative Review Literature Table with Data Organized within Each Symptom Management Model Component*

Year, Author	Person	Environment	Health & illness	Symptom experience	Components of symptom management	Outcomes & symptom status
2009, Jurgens	-Older age predictor for all 3 clusters -Individuals may have specific symptom clusters that can be identified to improve self-care	NONE	-Diabetes predictor for emotional cluster -Degree of symptom distress has little relationship with cardiac disfunction	- ≥75 reported less symptom *impact* for all 3 clusters -Patients not feeling *impacted* by symptom cluster may delay seeking treatment	-guide patients to monitor for specific symptoms in clusters -understanding clusters = tool for when to seek care -remote monitoring means need for symptom self-identification	3 clusters -acute volume overload cluster: shortness of breath, tired/fatigue/low energy, trouble sleeping at night -emotional cluster: depressed, worried, difficulty concentrating/ remembering -chronic volume overload: lower extremity edema, need to rest, dyspnea on exertion
2009, Jurgens	-Older age predictor for all 3 clusters	NONE	-Diabetes predictor for emotional cluster	- ≥75 reported less symptom *impact* for all 3 clusters	-guide patients to monitor for specific symptoms in clusters	3 clusters -acute volume overload cluster: shortness of breath,

	-Individuals may have specific symptom clusters that can be identified to improve self-care		-Degree of symptom distress has little relationship with cardiac disfunction	-Patients not feeling *impacted* by symptom cluster may delay seeking treatment	-understanding clusters = tool for when to seek care -remote monitoring means need for symptom self-identification	tired/fatigue/low energy, trouble sleeping at night -emotional cluster: depressed, worried, difficulty concentrating/ remembering -chronic volume overload: lower extremity edema, need to rest, dyspnea on exertion
2009, Schiffer	NONE	NONE	-somatic/ affective depressive cluster predictor of all-cause mortality -cognitive/ affective depressive cluster predictor of disease-specific health status	NONE	-depressive clusters can predict mortality and health status; depression should be treated due to prognostic impact	3 clusters -somatic/affective depressive symptoms -cognitive/affective depressive symptoms -total depressive symptoms

2009, Smith	-males, no college education more likely to be in cluster 1 -younger, females, no partner, higher BMI more likely to be in cluster 3	NONE	-cluster 1 less likely to be NYHA class III or IV, have diabetes, or use diuretic -cluster 3 NYHA class III or IV, diuretic use more likely -impaired health at 6-months predicted by cluster 2 (P=.01) and 3 (P=.001) -re-hospitalization more likely in cluster 3 than 1	-vital exhaustion consists of fatigue, cognitive/ affective depressive symptoms, lack of concentration, sleep difficulties	-clinicians should not focus on depressive symptoms in isolation	3 clusters Cluster 1: no VE group (24.1%) Cluster 2: VE symptoms (increased fatigue, decreased concentration) but no cognitive/ affective depression symptoms and sleep difficulties (47.2%) Cluster 3: VE symptoms WITH cognitive/ affective depression symptoms and sleep difficulties (28.6%)
2010, Hertzog	-cluster 1 most educated (p <.05)	NONE	-cluster 1 mostly NYHA class I or II, cluster 2	-symptoms in cluster 2 more bothersome than 3,	-ACE inhibitors prescribed significantly less in cluster 2 than 1	3 clusters -cluster 1: few symptoms reported (n=92)

	-cluster 2 patients less educated (p=.04) and higher BMI than 1 (P = .03)		mostly NYHA class II or III, cluster 3 mostly NYHA class III or IV (p=.03 for all) -Cluster 2 had greater impairment than 1 (P < .001)	regardless of frequency -cluster 2 highest severity and interference with life	(44.4% compared to 74.7%; P = .01)	-cluster 2: very symptomatic (n=18) cluster 3: very symptomatic but different than cluster 2
2010, Lee	-clusters identical by sex -women higher distress from fatigue, sleep disturbances, and feeling depressed	NONE	-total symptom distress score from emotional/ cognitive cluster independent predictor of cardiac event-free survival (hazard ratio, 1.18; 95% confidence	-higher distress from physical cluster for women and NYHA class III/IV ($p < .05$) -higher distress from emotional/ cognitive cluster for young patients ($p < .05$)	- emotional/ cognitive clusters may be highest risk for adverse outcomes -Current guidelines do not include depressive interventions -need education on clusters to increase symptom self-awareness	2 clusters -Physical symptom cluster: dyspnea, increased need to rest, low energy, and sleep disturbances (low energy most distressful, lower extremity edema least) -Emotional/cognitive symptom cluster: worrying, feeling depressed, and cognitive problems (worrying

	-younger in high distress and emo/cog distress groups		interval, 1.03-1.37) -greater comorbidity burden in high distress group than all others		and healthcare-seeking behaviors	most distressful, feeling depressed least) -Lower extremity edema did not cluster
2010, Song	NONE	NONE	-high distress from weary cluster predicted cardiac rehospitalization (HR, 1.45; 95% CI, 1.09-1.93) -high distress from dyspneic symptom cluster predicted cardiac mortality (HR,	-lack of energy most distressful physical symptom, orthopnea least	-weary symptom cluster to assess re-hospitalization risk -better self-monitoring needed (9% reported monitoring, and difficult when symptoms progress slowly)	2 clusters -dyspneic symptom cluster (shortness of breath, difficulty breathing when lying flat, and waking up breathless at night) -weary symptom cluster (lack of energy, lack of appetite, and difficulty sleeping) -Lower extremity edema not included in either cluster

			2.00; 95% CI, 1.16-3.34)			
2014, Moser		-symptoms clustered similarly across cultural groups		-Lower extremity edema often not distressing or noticed by patients unless severe in all 3 regions	-use clusters to assess risk of poor outcomes -similar clusters across cultural groups -better monitoring could improve help seeking and decrease hospitalizations	3 clusters -physical capacity cluster: dyspnea, walking or climbing difficulty, increased need to rest, low energy in all 3 regions (also sleep difficulties in Asia) -emotional/cognitive cluster: worrying, feeling depressed, and cognitive problems in all 3 (also sleep difficulties in U.S.)
2015, Hawkins	NONE	NONE	-HF severity level more highly correlated with somatic symptom cluster (r=0.38) than non-somatic	NONE	-clinicians should aim to treat both depressive symptom clusters due to increased likelihood of cognitive impairment	2 clusters -somatic depressive cluster: sleep disturbance, fatigue, appetite changes -non-somatic cluster: anhedonia, depressed, poor self-esteem, concentration

			(r =0.30)			problems, psychomotor retardation/ agitation, suicidal ideation
2015, Herr	-age did not account for variance in functional limitation or mobility	NONE	NONE	NONE	-cluster specific interventions -sickness behavior and discomforts of illness clusters impact functional limitation and mobility (80% reported limitations with activities of daily living)	3 symptom clusters -sickness behavior cluster: anxiety, depression, daytime sleepiness, cognitive dysfunction, fatigue -discomforts of illness cluster: shortness of breath, lower extremity edema, pain -gastrointestinal stress cluster: loss of appetite and decreased hunger
2015, Lee	-concordant profile older (p=.003), college educated (39.2% vs	NONE	-severe symptom profile patients 3.3 times more likely to have clinical HF event	-most adults with HF do not have concordant symptoms and hemodynamics	-clustering may connect biological with non-biological symptoms for improved understanding of symptoms and management	3 symptom profiles -concordant symptoms: moderate physical and psychological symptoms, good hemodynamics (no mismatch, 18%)

	13.5% severe symptoms and 27.7% poor hemodynamics, p=.008)		-poor hemodynamics profile 3.9% more likely		-symptom perception important in risk-assessment	-severe symptoms: worst symptoms, average hemodynamics (mismatch, 17.9%) -poor hemodynamics: worst hemodynamics, lowest symptom burden (mismatch, 64.2%)
2016, Yu	NONE	NONE	NONE	-63.25% of variance in symptom experience explained by 3 clusters, predict quality of life -anxiety and depression linked to shortness of breath in distress cluster	-managing entire cluster rather than individual symptoms optimal -need for palliative care interventions for symptom distress related to advanced HF	3 symptom clusters -distress cluster (shortness of breath, anxiety, depression) -decondition cluster (fatigue, drowsiness, nausea, reduced appetite) -discomfort cluster (pain, generalized discomfort) -Lower extremity edema and poor sleep quality were not included in any clusters

2016, Zhang	NONE	NONE	-symptom cluster patterns similar between those with and without HF	-Quality of life unlikely to be stable over time -functional limitation secondary to breathlessness is key determinant of quality of life	-clinicians may be able to ask one question regarding quality of life to assess rather than using entire complicated questionnaire	7 clusters -breathlessness -psychological distress -sleep quality -frailty -cognitive/psychomotor function -respiratory system -chest pain -clusters accounted for 65% of variance in quality of life
2017, Park	NONE	-Taiwan/ China lower symptom distress than U.S. in 6/8 symptoms -U.S. had clusters with differing	NONE	-mean sums of Eastern Asia symptom distress scores significantly lower than U.S. (all $p < .05$)	-clinicians may need to consider culture when assessing symptom burden and providing education on symptom self-management	U.S.- 4 clusters -class 1: all mild (25%) -class 2: moderate physical (33%) -class 3: moderate psychological (7%) -class 4: all severe (36%) Eastern Asia- 3 clusters -class 1: all mild (41%)

		psych and physical symptoms, Asia did not				-class 2: all moderate (31%) -class 3: all severe (28%)
2018, Huang	NONE	-14% Taiwan patients lived alone, more in typical cluster (36%) than non-severe (12%) or atypical (13%), p<.05	-Left ventricular dysfunction present in 49% of atypical cluster (p<.05) -more NYHA class III and IV in non-symptom and typical clusters (>70%) than atypical (28%) -higher cardiac event rates for typical cluster (p = .016) and	-higher perceived anxiety = more likely to be in typical cluster (OR = 1.23, p < .05) -higher perceived control = less likely to be in typical cluster (OR = 0.93, p < .05)	-determine how demographics affect clusters for early detection and diagnosis -pay attention to atypical physical symptoms since found to increase risk of 1-year cardiac events (HR 2.11, 95% CI [1.15, 3.88], p=.016)	3 symptom clusters -non-severe cluster (all low severity, n=191) -typical severity cluster (high severity dyspnea/ fatigue, low for lower extremity edema, moderate others, n=28) -atypical severity cluster (low severity dyspnea and fatigue (1.6 and 1.1), high for lower extremity edema, moderate others (1.9-3.7, n=39)

			atypical (p=.001) than non-severe			
2018, Son	-Less educated had higher distress for clusters 2 (p=.026) and 3 (p=.022) -females higher distress (p<.001), married (p=.037) and employed (p=0.12) lower distress for cluster 3	-author proposes that they are filling a gap by examining this relationship within the Korean culture (as opposed to Western culture)	-bodily pain and energy insufficiency cluster = strongest predictor of hospital readmission (OR = 6.59, 95% CI [1.29, 32.79]) -those with atrial fibrillation significantly higher scores for cluster 2 (p=.015) -NYHA class III/IV significantly higher scores for	-respiratory distress cluster accounted for 21.3% variance of symptom *impact* -bodily pain cluster explained 18.86% variance in distress -circulatory/GI cluster explained 17.84% variance in distress	-respiratory distress cluster could be an early sign of worsening HF; clinicians should educate on how to alleviate symptoms at home -highest readmission from bodily pain cluster, patients may think these symptoms don't warrant asking for help and need education	3 symptom clusters identified -respiratory distress cluster: difficulty breathing while lying flat, shortness of breath at rest, waking up breathless at night -bodily pain and energy insufficiency: bodily pain, fatigue, sleep disturbance -circulatory and gastrointestinal distress: feet or ankle swelling, poor appetite, nausea

			all clusters (p<.001)			
2019, Park	-education influenced class 1 or 2 inclusion -older age decreased likelihood of being in psych distress and high distress classes compared to low distress	NONE	- atrial fibrillation 2.81 X likely to be in physical distress class, 2.61 X likely to be in psych distress class, and 2.71 X likely to be in high distress -Patients with diabetes 1.91 X likely to be in physical distress class and 1.66 X likely to be in high distress class	-younger patients with HF show greater distress from psychological symptom cluster than older patients (despite how severe or not severe physical symptoms are)	-tailor interventions to groups of patients and symptoms -focus on psychological health of younger patients with HF -psychological symptoms not addressed in current guidelines for managing HF	4 classes of HF patient symptom clusters -class 1: low distress (mild physical and psychological symptoms) -class 2: physical distress (severe physical, moderate psych) -class 3: psychological distress (severe psych, moderate physical) -class 4: high distress (severe both physical and psychological)

			-Hypertension 2 X as likely to be in high distress			
2019, Salyer	NONE	NONE	NONE	NONE	-manage symptoms of sickness behavior cluster to improve quality of life -hallmark HF symptoms did not negatively affect quality of life (expand assessments to include other symptoms)	3 symptom clusters -sickness behavior cluster: anxiety, depression, daytime sleepiness, cognitive impairment, and fatigue (explains 40% of variance in quality of life) -Discomforts of illness: dyspnea, lower extremity edema, and pain -GI distress cluster: appetite and hunger
2020, Denfeld	NONE	NONE	-incongruent group 98% more likely to have a 180-day event (p = 0.014) than	NONE	-no diuretic was determinant of incongruent group membership	4 symptom clusters -Severe physical (26.3% -Mild physical (73.7%) -Severe affective (21.2%) -Mild affective (78.8%)

			congruent-mild symptom group -congruent-severe group not more likely to have an event within 180 days (p = 0.261) than congruent-mild symptom group		-aldosterone antagonist (0.03) and anti-depressant (0.007) use determinants of congruent-severe group membership	-Those in severe physical cluster more likely to be in severe affective cluster as well Symptom sub-groups -congruent-mild (69.3%) -congruent-severe (16.8%) -incongruent (13.9%)

Manuscript 2: Feasibility Study and Symptom Cluster Analysis

Title: Feasibility of a Mixed Methods Approach to Identifying Symptom Clusters in Black Women with Heart Failure Preserved Ejection Fraction

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Abstract

Background: Clustering symptoms and developing patient profiles could result in more targeted and effective heart failure (HF) interventions down the line. However, Black females remain significantly underrepresented in current HF symptom cluster research, which also minimally examines sex differences and does not include qualitative methodologies.

Objective: This manuscript evaluates the feasibility and acceptability of a study protocol and procedures for a mixed methods approach to ascertain symptom clusters in Black women with HF preserved ejection fraction (HFpEF). It then presents preliminary symptom cluster analysis findings.

Methods: Participants recruited from social media completed screening and demographics questionnaires, the Minnesota Living with HF Questionnaire, Symptom Status Questionnaire – HF, and Personal Health Questionnaire – 8. Feasibility outcomes were measured and analyzed, and a portion of participants were interviewed about their symptoms.

Results: Forty-four Black women were enrolled in the study, with one of the 44 identifying as multiracial. The majority of the participants were married (45.5%) with a mean age of 51.8 years. A hierarchical cluster analysis formed three clusters of participants with statistically significant differences in the proportion of symptoms experienced and co-morbidities. Cluster 1 was highly symptomatic with most participants reporting most symptoms, cluster 2 reported fewer symptoms than cluster 1, especially reporting less depressive symptoms, and cluster 3 reported mostly psychological symptoms.

Conclusions: The results of this study support the feasibility and acceptability of a mixed methods protocol for studying symptom clusters in Black women with HFpEF. Symptom clusters should be further explored with a larger sample.

Feasibility of a Mixed Methods Approach to Identifying Symptom Clusters in Black Women with Heart Failure Preserved Ejection Fraction

Introduction

Heart Failure (HF) is a severe chronic disease that results in 30% of patients dying within one year of diagnosis, and patients often suffering from prominent symptoms that can impact physical functioning and health-related quality of life[1-3-7]. Heart Failure preserved Ejection Fraction (HFpEF) is a specific type of HF caused by diastolic dysfunction in which increased myocardial stiffness impairs relaxation of the left ventricle[8-9]. A symptom cluster consists of two or more symptoms occurring simultaneously in a disease[10]. Current evidence supports the existence and use of HF symptom clusters and patient profiles to characterize which symptoms co-occur and assess risk for adverse health outcomes[4, 10-26].

Existing literature indicates that HF symptoms are especially burdensome to females, who report more depression, worse symptom severity and quality of life, and longer and more frequent hospitalization than males[3-7]. HF with preserved ejection fraction (HFpEF) is more prevalent in females, by a factor of 2 in some studies[2]. Black Americans are 1.5 times more likely to develop HF and have a 2.5 times greater risk of dying from HF than White Americans[27]. Black adults in America are especially adversely

affected by HFpEF, as they tend to be younger, have earlier onset, report worse QoL, and have a greater risk of hospitalization than White Americans with HFpEF[9].

Black women remain significantly underrepresented in current HF symptom cluster research[4, 10-26]. Considering the increased burden of HF symptoms and overall outcomes in women and Black Americans, studying the symptom experience and symptom clusters concerning gender, sex, race, and type of HF is warranted[3-7]. Furthermore, there are limited studies examining sex differences. To our knowledge, there are no current HF symptom cluster studies that include qualitative methodologies[4, 10-26]. Mixed methods and qualitative approaches to symptom cluster research are needed to provide a richer description of the symptom cluster experience and the impact of sex and race/ethnicity on this experience. To achieve this, Black women with HFpEF should be recruited to share their symptom experience through surveys and interviews. However, it is first necessary to determine the feasibility of recruiting Black women with HFpEF, identify potential barriers and facilitators to adequate recruitment, and examine acceptance of a study protocol[28]. Therefore, this manuscript reports the feasibility and acceptability of a study protocol and procedures for a mixed methods approach to ascertain symptom clusters in Black women with HFpEF. We also present preliminary findings from symptom cluster analysis for this population to describe the symptom clustering technique and preliminary findings that can later be explored with a larger sample size.

Methods

Sample

After institutional review board approval, participants were recruited through social media using Facebook ads, posts within Facebook groups, and snowball sampling. Respondents completed a screening survey to determine eligibility online in REDCap or via phone. Participants were eligible if they were 35- to 74 years old, identified as a Black female and woman, and had a self-reported diagnosis of HFpEF (with an ejection fraction greater than or equal to 50%). Exclusion criteria consisted of self-reported cancer or end-stage disease diagnosis (end-stage heart failure, renal disease, respiratory/lung disorder, liver disease, or cancer), stroke or myocardial infarction in the last six months, or a recent hospitalization within the previous four weeks. A sample size of 50 was targeted for this study based on a pragmatic approach to determining the feasibility sample size[29].

Eligible participants gained access to the fully study survey in REDCap or could call the PI to assist in completing the survey if needed. Instructions for completing the survey were presented before the questionnaires, and participants consented to participating in the research study by completing the survey. The symptom cluster survey included a demographics questionnaire with a single item literacy screener (SILS)[30], the Minnesota Living with Heart Failure Questionnaire (MLHFQ)[31], Symptom Status Questionnaire - Heart Failure (SSQ-HF)[32], Personal Health Questionnaire - 8 (PHQ-8)[33], and feasibility and acceptability questions.

Measures

Demographic data were collected using a combination of the screening questionnaire and demographic questionnaire. Symptoms were measured using the

MLHFQ[31], SSQ-HF[32], and PHQ-8[33]. The first questionnaire, the MLHFQ, is a 21-item quality-of-life questionnaire designed for patients with HF, that includes questions related to the impact of physical symptoms, emotional/ psychological symptoms, and HF-related activities on daily life[31]. Participants rate how much an item affected their life in the past month, using a Likert scale of 0-5 ranging from 0 indicating none to 5 very much[31]. The MLHFQ has excellent internal consistency with a Cronbach's α usually ranging from 0.89-0.96 and has been used successfully in forming symptom clusters in multiple other HF symptom cluster studies[4, 10, 11-13, 15, 23, 25, 31]. The MLHFQ is short, easy to administer, validated for its psychometric properties, and has been used to assess quality of life in Black Americans in HF clinical trials[4,10, 11-13, 15, 23, 25, 31,34].

The second questionnaire, the SSQ-HF, measures the presence, frequency, severity, and distress of 7 physical symptoms most commonly reported in HF (shortness of breath during daytime, shortness of breath lying down, fatigue or lack of energy, chest pain, leg or ankle swelling, difficulty sleeping, and dizziness or loss of balance) in the last four weeks[32]. If a symptom is present, the respondent rates frequency, severity, and distress using a Likert scale of 1-4, with 1 being the least and 4 being the most[32]. Cronbach's α for the SSQ-HF is 0.80 and the instrument asks about symptoms in the last four weeks, the same time frame as the MLHFQ[31, 32].

The third questionnaire, the PHQ-8, asks respondents to rate the severity of eight depressive symptoms from 0 (not at all) to 3 (nearly every day) over the past two weeks[33]. This depressive symptom scale is widely used and has a Cronbach's α of 0.83[33].

Finally, the SILS was included to assess health literacy in the study population[30]. The SILS has been validated for assessing the likelihood of low health literacy in a

participant, with a score of >1 indicating a "positive" result for low health literacy[30]. Participants were also asked eleven questions about feasibility and acceptability at the end of the survey related to instructions, study processes, time, compensation, the purpose of the study, and recommendation of the study to others. Feasibility and acceptability questions were adapted from Orsmond & Cohn's guiding questions for feasibility studies[35]. Scores ranged from 1 (completely disagree) to 5 (completely agree) with 5 being the optimal score.

Feasibility Outcomes

The feasibility of study processes, resources, and human and data management were analyzed as the primary aim of this study[28]. Study process feasibility outcomes were assessed by examining consent rate, recruitment rate, interview interest rate, survey completion rate, and feasibility and acceptability question scores. The consent rate was determined by calculating the percentage of eligible participants who consented by completing the next survey after the eligibility survey, with a 90% consent rate as the benchmark. The recruitment rate was assessed by calculating the percentage of participant recruitment goal met for both the survey and interviews. A benchmark goal was >85% of recruitment, with a recruitment goal of 50 survey participants and 15 interview participants. The interview interest rate was determined by calculating the percentage of participants who indicated they were interested in being interviewed at the end of the survey, with the goal interview interest rate of 30%. The percentage of completed surveys without missing data was calculated by dividing the number of fully complete surveys by the total number of surveys and multiplying by 100, with a

benchmark goal of >85%. Feasibility and acceptability question scores were averaged, with a goal average score of 4 or higher.

Resource feasibility outcomes were assessed by examining interview data collection time and recruitment burden. The interview data collection time was assessed by calculating the average interview duration and the range of interview times. The goal interview duration was ≤60 minutes. For recruitment burden, we tracked time spent recruiting for the survey and interviews and calculated an average time per week for each. Recruitment time for the survey included writing and sharing posts in social media groups, responding to potential participants and social media group admins via messages or comments, and management of Facebook ads. Recruitment time for the interviews included emailing and calling participants who indicated interest in being interviewed at the end of the survey. This recruitment time also included time spent scheduling interviews. The recruitment burden benchmark was an average of < 20 hours per week.

The feasibility of management outcomes was examined based on transcription time, software reliability, and adverse patient events. Phone interviews were transcribed using automated software for clear audio and dialects and a transcription service was used when this was not the case. Transcripts were reviewed and edited word-for-word for correctness. The time spent editing transcripts was tracked, with the goal of < 2 hours spent per transcript. Major events related to issues with software and data management platforms or adverse events during data collection were tracked, with a goal of no major events.

Statistical Analysis of Symptom Clusters

A hierarchical cluster analysis was performed in SPSS version 25 (SPSS Inc, Chicago, Illinois) to explore preliminary symptom clusters of physical and emotional/psychological symptoms included in the MLHFQ, SSQ-HF, and PHQ-8[31-33,36,37]. The hierarchical cluster method is used to cluster variables (symptoms) or cases (study participants) and allows the researcher to determine the optimal number of clusters after conducting the analysis rather than a priori[36,37]. Hierarchical clustering creates compact and homogeneous clusters and maximizes differences in clusters[36,37]. The three main steps to hierarchical clustering are calculating distances between variables, linking clusters, and determining the number of clusters based on dendrogram and agglomeration schedule results[37]. Branches of the dendrogram are based on semi-partial r-squared scores, and smaller branches signify more similar clusters[37].

To standardize scoring for symptoms across the three different questionnaires, variables were dichotomized to either yes, the symptom was present for any symptom score other than 0, or no, the symptom was not present. First, a hierarchical cluster analysis was attempted to cluster by symptoms utilizing Euclidean distance and Ward's method of clustering. Ward's method is best for maximizing significant differences between clusters by using the *F* value and forms more homogenous clusters close to equal in size[37]. However, due to the small sample size and the dichotomized variables, this method was not optimal for forming meaningful clusters. Therefore, we employed an alternative strategy to clustering by participant rather than cluster, described by Hertzog et al[14]. We used between-groups linkage method and simple-matching to calculate distance, both of which better suit the small sample size[14]. After conducting the cluster analysis, we reviewed the agglomeration schedule for the point at which coefficients

began significantly decreasing. This drop occurred at stage 41 in the agglomeration schedule. The number of stages, 41, was then subtracted from the total number of cases, 44, suggesting that a 3-cluster solution was optimal.

The clusters were then compared by demographic variables and symptom presence. Comparisons were completed using one-way ANOVA for continuous data, Kruskal-Wallis Test for interval level data, and Fisher's exact test for nominal data, with a significance level of .05 for all tests. Pair-wise comparisons were also completed for Kruskal-Wallis tests using Dunn's (1964) test with a Bonferroni correction within SPSS (SPSS Inc, Chicago, Illinois).

Results

A total of 70 participants were deemed eligible from the screening questionnaire, and of these, 67 participants completed the consent process and the survey. After a review of data to remove participants who did not meet inclusion criteria based on responses to the demographic questionnaire, 44 participants remained for analysis. All 44 participants (Table 1) identified as Black race, with one of the respondents also identifying as White. The average participant age was 51.8 years old, with an age range of 37 to 74. The majority of the participants were married (45.5%) or single (27.3%), with an average of 2 children. Thirty-nine percent of women had a high school diploma or GED, 18.2% reported no high school degree, and 43% of participants had an associate degree or higher. The majority (77.3%) of participants reported "never" or "rarely" needing someone to help them read written materials from their doctor or pharmacist in response to the single item literacy screener[30]. The majority of participants were diagnosed with HF in the last four years (88.6%), with 11.4% of participants diagnosed in

the last five to eight years and no participants reporting a diagnosis for nine years or longer. All participants had some type of insurance, with Medicare and Medicaid being the most common (54.6%). Twenty-six of the 44 participants reported having one or more co-morbidity, with hypertension (34.1%), respiratory diseases (31.8%), and atrial fibrillation (27.3%) being the most commonly reported. Body Mass Index (BMI) was calculated based on self-reported height and weight. The majority of the participants (56.8%) were classified as having a "healthy" BMI within the range of 18.5-24.9, while 6 (13.6%) had an "overweight" BMI of 25-29.9, 11 (25%) were classified as "obese" with a BMI greater than or equal to 30, and 2 were classified as "underweight" with a BMI less than 18.5[38].

Feasibility

Analysis of study processes, resources, and management was conducted to determine this study protocol's feasibility[28], as shown in table 2. Study *process* feasibility results were as follows. The consent rate was 95.7% for the study. A total of 70 participants were recruited using social media over 5 weeks; 67 out of 70 consented to participate in the study. Out of the 67 participants who completed the survey, 38 (56.7%) were interested in being interviewed about their symptom experience. Of those 38, 15 were successfully interviewed, which satisfied 100% of the interview recruitment goal of 15 participants. The other participants who were not interviewed either did not respond to the initial email invitation to be interviewed (N=14), stopped responding during interview scheduling (N=6), or did not answer calls during their scheduled interview time (N=3). Demographic questionnaires of the 67 participants who completed the study were

reviewed to assess eligibility. Twenty-three participants out of 67 were excluded for ages outside criteria (N=19) or not identifying as Black (N=4). Forty-four eligible participants remained for analysis, resulting in 88% of the survey recruitment goal, which was above the 85% benchmark. Out of the 44 included survey respondents, 43 (97.7%) surveys were fully completed without missing data. The average rating across all feasibility and acceptability questions was 4.87 out of 5, and no participants rated feasibility or acceptability lower than a 3 (neither agree nor disagree).

Feasibility outcomes of *resources* were also examined to identify resources needed to conduct the study on a larger scale. Data collection time for phone interviews ranged from 18 to 55 minutes, with an average interview duration of 35 minutes. This time frame only includes the interview, not quantitative survey completion that was completed on REDCap. An average time of 14.4 hours was spent recruiting participants over five weeks for the survey recruitment burden. Recruiting and scheduling participants for interviews took, on average, 5.8 hours per week for 13 weeks. For *management* feasibility outcomes, interview transcripts took less than two hours to edit for accuracy with the assistance of transcription software. No significant events were reported with software reliability or adverse patient events.

Cluster Analysis

A preliminary symptom cluster analysis was conducted with the feasibility study sample to observe the hierarchical clustering technique and identify preliminary findings that could later be explored with a larger sample. Clusters were formed by clustering participants according to the number and types of symptoms reported. The agglomeration

schedule was reviewed to determine the three-cluster solution. We then compared clusters by presence of symptoms (figure 1 and table 3) and demographic variables by cluster (table 4) to validate cluster differences.

Highly Symptomatic Cluster

Cluster 1, the highly symptomatic cluster, reported the most symptoms of the clusters and contained the largest number of participants (26). Over 75% of participants reported experiencing all symptoms except chest pain (65.4%) and dizziness (61.5%). All participants (100%) reported feeling depressed and fatigued (need to rest), and 25 of 26 participants reported shortness of breath, lack of energy, leg swelling, and feeling bad about themselves. The mean age in Cluster 1 was 50.3 years (SD=10.9), and the average BMI was 25 (SD=5.8). Most of the participants in the highly symptomatic cluster reported not having any comorbidities (57.7%). Of the comorbidities that were present, hypertension (23.1%), atrial fibrillation (19.2%), and diabetes (15.4%) were the most commonly reported.

Mildly Symptomatic Cluster

Cluster 2 was mildly symptomatic, as this cluster reported fewer symptoms than cluster 1, especially regarding depressive symptoms. All participants reported a lack of energy, and almost all (93.3%) reported shortness of breath, leg swelling, and fatigue or need to rest. Otherwise, 33.3% of participants or less reported experiencing the rest of the symptoms. Every participant in the study reported experiencing fatigue or need to rest except one participant from this cluster. Cluster 2 was the 2nd largest cluster with 15

participants, who were, on average, 54.1 years old (SD=12.5) with an average BMI of 29.6 (SD=20.9). The most commonly reported comorbidities in cluster 2 were atrial fibrillation (46.7%), hypertension (40%), coronary artery disease (33.3%), and Chronic Obstructive Respiratory Disease (33.3%), while 20% of participants reported not having any comorbidities.

Psychologically Symptomatic Cluster

Cluster 3 reported few physical symptoms, considering the only physical symptom these participants reported was fatigue (need to rest) (3/3, 100%), but this cluster reported more psychological symptoms included in the PHQ-8, such as poor appetite (2/3, 66.6%), feeling bad about themselves (2/3, 66.6%), trouble concentrating (1/3, 33.3%), feeling depressed (1/3, 33.3%), and anhedonia, or inability to feel pleasure (1/3, 33.3%). This psychologically symptomatic cluster was the smallest cluster, with only three participants. The three participants had a mean age of 52.7 years (SD=2.5) and a BMI of 36.6 (SD=11.3). All 3 participants in this cluster reported comorbidities, with 2 (66.7%) reporting diabetes, 2 (66.7%) reporting hyperlipidemia, and all (100%) reporting hypertension.

Comparison of clusters

Clusters were compared according to demographics, comorbidities, and symptoms experienced. No statistically significant differences were observed between clusters for age ($F(2, 41) = 0.574$, $p = .568$)) or BMI ($F(2, 41) = 1.332$, $p = .275$)). For differences in comorbidities, there were statistically significant differences in proportions of those who

reported coronary artery disease (p=.049) and those who reported having no comorbidities (p =.02) between the highly symptomatic and mildly symptomatic clusters. The highly symptomatic cluster reported a statistically significant higher proportion of psychological symptoms than the mildly symptomatic cluster (p <.001). Though not found statistically significant, the highly symptomatic cluster was the most highly educated group, with over 50% of participants having their bachelor's degree or higher.

Discussion

Results from this feasibility study are relevant for a variety of reasons. First, almost all feasibility and acceptability benchmarks were met. Reaching these benchmarks shows that Black females with HFpEF can be successfully recruited via social media for an HF symptom cluster study and, just as importantly, they were satisfied with the study protocol according to their positive responses to acceptability questions. Recruiting via Facebook advertisements and snowball sampling is a viable method, as dynamic Facebook ads can learn overtime who engages with the advertisement the most and shows the ad to users like those individuals, thereby increasing potential reach. Access to the survey link also allows participants to share the study with family members or friends who may also be eligible for the study, further increasing the reach for participant recruitment.

One barrier to reaching 50 participants for the study was having several respondents who were not actually eligible once we analyzed their responses, especially pertaining to age and race/ethnicity. This may have been due to errors while completing the survey, such as a participant not checking Black for the race they identify with or

entering their age incorrectly. In the future, these factors should be analyzed in real-time to allow for discussion with the participant to provide clarity and confirm eligibility. A Facebook ad's benefit is that it enables the recruitment of a large number of participants with minimal time and resources. The largest cost associated with recruiting individuals was compensating them with a $25 Amazon gift card for completing the survey and participating in an interview.

Though a hierarchical cluster analysis requires more than 44 participants for statistically meaningful results, we conducted the cluster analysis to test the process and develop preliminary clusters. The clusters formed in this study were similar to clusters formed in the symptom cluster analysis completed by Hertzog, et al. in 2010, which used similar methods. Comparison between clusters showed statistically significant differences when compared to one another for the presence of almost all symptoms, which validates the number of clusters chosen based on the agglomeration schedule. Interestingly, every participant in the study reported experiencing fatigue (need to rest), except one participant. Though the psychologically symptomatic cluster was small with only three participants, the cluster showed prominent differences in symptoms experienced and comorbidities, especially considering that almost all the symptoms experienced for this cluster were psychological. Though no formal comparison was carried out due to the small cluster size, the observed mean BMI for the psychologically symptomatic cluster was 36.6 (SD=11.3) compared to 29.6 (SD=20.9) for the mildly symptomatic cluster and 25.0 (SD=5.8) for the highly symptomatic cluster. These characteristics should be examined further in future larger studies.

The highly symptomatic cluster had over half of participants reporting every symptom. This group also had the youngest mean age, though not a statistically significant difference. As the youngest and most symptomatic cluster, cluster participants were also statistically significantly more educated than participants in the mildly symptomatic cluster. HF symptom cluster literature has shown a relationship between younger age and more distress from symptoms[15, 17]. This phenomenon should be more closely explored in future larger samples. Qualitative data from interviews will also be integrated with this symptom cluster data in a future manuscript to expand upon these findings and further explain the symptom experience of Black women with HFpEF.

Though this study has a small sample size, the sample was adequate for assessing feasibility and acceptability of the study protocol and allowed for the formation of preliminary clusters of participants as a first step towards developing meaningful symptom clusters for this population. Utilizing social media is a valuable resource for reaching a large number of potential participants[39]. However, participants must be properly screened to ensure accurate eligibility[39]. It is possible that respondents try to gain access to the survey when they are not actually eligible because they did not understand eligibility criteria, wanted to be included in the research, or for monetary gain[39]. Extra measures were added to the survey to deter this from happening, such as adding captchas, a test meant to distinguish humans from bots, screening for surveys completed back-to-back with the same or very similar email addresses and requiring participants to answer an attestation that they were answering questions truthfully[39].

Summary and Implications

The results of this study support the feasibility and acceptability of a mixed methods study protocol for studying symptom clusters in Black women with HFpEF. Preliminary clusters showed statistically significant differences in the proportion of symptoms experienced and comorbidities. Cluster development and differences in clusters should further be explored in a larger sample of participants adequate for hierarchical cluster analysis.

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Tables:

Table 1: Study Sample Demographics

N=44	Frequency (Valid %)	Mean (SD)
DEMOGRAPHICS		
Race/ethnicity		
Black	44 (100%)	
Single item literacy screener		
Never	26 (59.1%)	
Rarely	8 (18.2%)	
Sometimes	5 (11.4%)	
Often	5 (11.4%)	
Always	0 (0%)	
Education		
No High School Diploma	8 (18.2%)	
Diploma or GED	17 (38.6%)	
Associate degree	3 (6.8%)	
Bachelor's Degree	7 (15.9)	
Master's Degree	7 (15.9%)	
Doctoral Degree	2 (4.5%)	
Current marital status		
Single	12 (27.3%)	
Married/ living with partner	20 (45.5%)	

Separated	3 (6.8%)	
Divorced	4 (9.1%)	
Widowed	5 (11.4%)	
Length of HF Diagnosis		
0 – 12 months	11 (25%)	
>1 year – 2 years	15 (34.1%)	
3 years – 4 years	13 (29.5%)	
5 years – 8 years	5 (11.4%)	
Primary Insurance Status		
None	0 (0%)	
Medicare / Medicaid	24 (54.6%)	
Public (marketplace)	7 (15.9%)	
Private (employer)	10 (22.7%)	
Other	3 (6.8%)	
BMI Categories		
Underweight (< 18.5)	2 (4.5%)	
Healthy (18.5 – 24.9)	25 (56.8%)	
Overweight (25 – 29.9)	6 (13.6%)	
Obese (≥ 30)	11 (25%)	
Age (years)		51.75 (11.1)
# of children		2 (range 0-8)
# people in household		3 (range 1-6)

Table 2: Feasibility Outcomes

Feasibility component	Indicator	Criteria	Outcome
Process			
Consent rate	% of eligible participants consented by completing next survey	>90% consent rate	67/70= 95.7 % consented
Recruitment rate	% of participant recruitment goal	>85% of recruitment goal (goal N=50 for survey, goal N=15 for interview)	88% of survey recruitment goal met (N=67 recruited for survey, 44 eligible for analysis) 100% of interview recruitment goal met (N=15 for interview)
Interview interest rate	% of participants interested in an interview	>30% interview interest	38/67= 56.7 % interested in interview

Survey completion rate	% of completed surveys	>85% fully completed surveys	43/44= 97.7 % completed surveys
Feasibility / acceptability scores	Average scores ranging from 1-5	Average score of 4 or higher	4.87 average across all feasibility / acceptability questions
Resources			
Data collection time - Interview	Interview duration average	≤ 60 minutes	Average interview duration = 35 minutes Interview duration range 18 mins - 55 mins
Recruitment burden	Time spent with recruitment / week	< 20 hours	Questionnaire recruitment: 14.4 hours/week average over 5 weeks Interview recruitment: 5.8 hours / week over 13 weeks

Management			
Transcription editing time	Time spent with editing transcripts / checking for accuracy	< 2 hours / interview	100% of interviews transcribed in <2 hours (with assistance of software)
Software reliability	Issues with software / data management platforms	No major events	None reported
Adverse patient events	Adverse events during data collection	No major events	None reported

Table 3: Percent and frequency [% (n)] of symptom presence by cluster

SYMPTOM	**HIGHLY SYMPTO-MATIC CLUSTER n=26**	**MILDLY SYMPTO-MATIC CLUSTER n=15**	**PSYCHO-LOGICALLY SYMPTO-MATIC CLUSTER n=3**	**p-value***
SHORTNESS OF BREATH	96.2 (25)	93.3 (14)	0	.604

SHORTNESS OF BREATH LYING DOWN	76.9 (20)	33.3 (5)	0	**.008**
LACK OF ENERGY	96.2 (25)	100 (15)	0	.634
CHEST PAIN	65.4 (17)	33.3 (5)	0	**.048**
LEG SWELLING	96.2 (25)	93.3 (14)	0	.604
DIFFICULTY SLEEPING	88.5 (23)	13.3 (2)	0	**<.001**
DIZZINESS	61.5 (16)	33.3 (5)	0	.078
FATIGUE NEED TO REST	100 (26)	93.3 (14)	100 (3)	.366
ANHEDONIA	88.5 (23)	13.3 (2)	33.3 (1)	**<.001**
FEELING DEPRESSED	100 (26)	0	33.3	**<.001**
POOR APPETITE	88.5 (23)	33.3 (5)	66.6 (2)	**<.001**
FEELING BAD ABOUT SELF	96.2 (25)	0	66.6	**<.001**
TROUBLE CONCENTRATING	80.8 (21)	13.3 (2)	33.3	**<.001**
SLOW OR RESTLESS	76.9 (20)	0	0	**<.001**

*p-value obtained from Fischer's exact test (only clusters 1 and 2 were compared due to small sample size of cluster 3)

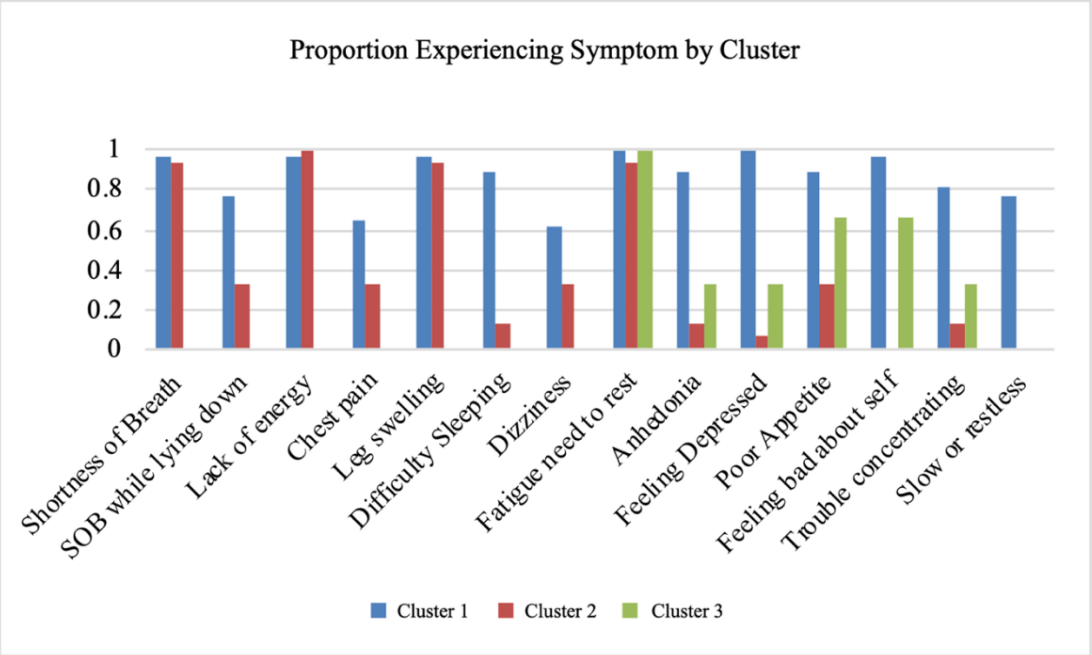
Table 4: Demographic variables by cluster

VARIABLE	% By Cluster: HIGHLY SYMPTO-MATIC CLUSTER n=26	% By Cluster: MILDLY SYMPTO-MATIC CLUSTER n=15	% By Cluster: PSYCHO-LOGICALLY SYMPTO-MATIC CLUSTER n=3	p-value*
HYPERTENSION	23.1	40	100	.21
HYPERLIPIDEMIA	11.5	26.7	66.7	.21
DIABETES	15.4	6.7	66.7	.39
ATRIAL FIBRILLATION	19.2	46.7	0	.07
CORONARY ARTERY DISEASE	7.7	33.3	0	**.049**
ASTHMA	7.7	6.7	0	.70
CHRONIC OBSTRUCTIVE PULMONARY DISEASE	11.5	33.3	0	.10
OBSTRUCTIVE SLEEP APNEA	3.8	3.0	0	.30
NONE	57.7	20	0	**.02**
AGE (Y), MEAN (SD)	50.3 (10.9)	54.1 (12.5)	52.7 (2.5)	.57
BMI, MEAN (SD)	25.0 (5.8)	29.6 (20.9)	36.6 (11.3)	.28

*p-value obtained from Fischer's exact test (only clusters 1 and 2 were compared due to small sample size of cluster 3) or one-way ANOVA

Figures:

Figure 1: Proportion experiencing symptom by cluster



Manuscript 3: Qualitative and Mixed Methods Results

Title: Qualitative and Integrated Results from A Mixed Methods Approach to Symptom Clusters in Black Women with Heart Failure Preserved Ejection Fraction

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Keywords: African American, Chronic disease, Cognitive symptoms, Disease management, Emotional symptoms, Heart failure, Mixed Methods, Physical symptoms, Qualitative Analysis, Review, Signs and symptoms, Symptom assessment, Symptom clusters, Women

Abstract

Background: Black women with Heart Failure preserved Ejection Fraction (HFpEF) have an increased burden of symptoms and worse health outcomes than White patients with HF.

Objective: The purpose of this study was to characterize the symptom experience of Black women with HFpEF and to integrate qualitative themes and quantitative symptom data to examine confirmation, expansion, and discordance of results.

Methods: Using a convergent-parallel mixed methods design, a purposive sample of 44 Black women who were 35 – 74 years old with HFpEF were recruited using social media. Quantitative data including demographics, Single Item Literacy Screener (SILS), Minnesota Living with HF Questionnaire (MLHFQ), Symptom Status Questionnaire – HF (SSQ-HF), and Personal Health Questionnaire – 8 (PHQ-8) were collected through online surveys (N=44). Qualitative interviews were conducted to explore the background and symptom experience of 15 participants. We used a directed approach to content analysis and qualitative descriptive methods to analyze interview data, and descriptive statistics and Pearson correlation to analyze quantitative data. The Symptom Management Model (SMM) guided content analysis of interview data and integration of data, in which findings from both qualitative and quantitative analyses were merged, compared and contrasted.

Results: Ten themes emerged relating to the person and symptom experience. Participants had an average MLHFQ quality of life score of 64.1 out of 105 and 45.5% of participants had scores that indicated major depression on the PHQ-8.

Conclusions: Black women with HFpEF discussed interactions of physical and emotional symptoms. Positive correlations between symptom scales supported this theme. Women reported shortness of breath and chest pain causing worry and fears of death. Participants reported feeling like a burden to others and hid or downplayed their symptoms. Reduced physical functioning impacted family life, household chores, and the ability to work.

Qualitative and Integrated Results from A Mixed Methods Approach to Symptom Clusters in Black Women with Heart Failure Preserved Ejection Fraction

Background

Patients with heart failure (HF) have a complex and multi-factorial symptom experience that makes symptom self-monitoring and self-management challenging[1-5]. Four out of five patients with HF are hospitalized each year with exacerbations that could be avoided with early detection[1]. Females experience worse quality of life (QoL) and functional impairment, and have higher rates of edema, depression, exercise intolerance, and dyspnea on exertion compared to males[3,4]. Little is known about the symptom experience in patients with HF preserved ejection fraction (HFpEF), a type of HF caused by diastolic dysfunction in which relaxation of the left ventricle is impaired from increased stiffness[6,7]. Black patients with HFpEF tend to be younger, report worse QoL, and have a greater risk of hospitalization than White patients[7]. A better understanding of symptoms and symptom experiences in this population may inform approaches to care to improve outcomes.

Qualitative studies are needed to explore how gender, sex, and race interact and impact the symptom experience, as quantitative instruments alone have limited ability in encompassing such factors. Considering the increased burden of HF symptoms, greater risk, and worse outcomes in females, Black Americans, and patients with HFpEF[1,6-8], this study seeks to illuminate the experiences of those who are underdiagnosed, undertreated and have a greater symptom burden[3,4]. A convergent mixed methods approach allows for a more comprehensive examination of the HF symptom experience by integrating qualitative interview data with quantitative symptom data to examine results for confirmation, expansion, and discordance. Thus, the objective of this study was to characterize the symptom experience of Black women with HFpEF and how symptoms affect their life by presenting qualitative themes within the framework of the Symptom Management Model. The integration of qualitative themes with corresponding quantitative symptom scale data will be presented in a joint display and results will be compared and contrasted to examine for convergence, discordance, and expansion.

Methods

A convergent-parallel mixed methods feasibility design was used to collect qualitative and quantitative data in the same time frame with equal priority. Qualitative data were collected using individual, semi-structured interviews with 15 participants. Quantitative data were collected through online surveys using questionnaires and well-validated symptom scales. The study survey consisted of a demographics questionnaire with a single item literacy screener[9], the Minnesota Living with Heart Failure Questionnaire (MLHFQ)[10], Symptom Status Questionnaire - Heart Failure (SSQ-HF)[11],

Personal Health Questionnaire - 8 (PHQ-8)[12], and feasibility and acceptability questions. Each type of data was analyzed separately, results were integrated in a joint display, and common concepts were compared and contrasted. Details of the feasibility study and quantitative symptom cluster results are reported in a previous manuscript[8].

Sample and setting

Following institutional review board approval (Pro00101261), a purposive sample of participants was recruited using Facebook ads and posts within Facebook groups, and snowball sampling by allowing participants to share the link with others who may qualify for the study. Participants responded to a screening survey to determine if they fit the eligibility criteria of a 35- to 74-year-old Black female who identified as a woman and had a self-reported diagnosis of HFpEF (with an ejection fraction greater than or equal to 50%). Participants were not eligible if they reported having cancer or an end-stage disease diagnosis (end-stage heart failure, renal disease, respiratory/lung disorder, liver disease, or cancer), stroke or myocardial infarction in the last six months, or a recent hospitalization within the previous four weeks. At the end of the quantitative survey, participants were asked if they were interested in being interviewed about their symptom experience and their preferred contact method. All participants who were interested in being interviewed (n=38) were contacted via email or phone to schedule individual, semi-structured interviews. We conducted interviews with all participants who responded and consented to an interview, resulting in 15 interview participants.

Theoretical Framework

The Symptom Management Model (SMM) highlights the multi-faceted nature and complex interactions of symptom components[13]. Six components comprise the SMM,[13] symptom experience, components of symptom management strategies, outcomes and symptom status, person, environment, and health and illness. For this study, symptom experience and person influenced the semi-structured interview guide, as these components are well suited for individual interviews, best answered the overall research question, and allowed for exploration of demographic, psychological, and sociological factors that can influence the symptom experience of a Black woman with HFpEF[13]. These components guided content analysis of interview data and the integration of questionnaire and interview results[13,14]. The three domains of the MLHFQ (physical symptoms, emotional symptoms, and QoL)[10] also influenced interview guide questions, which set the stage for the merging of quantitative and qualitative results[14, 15]. Table 1 shows the merging of qualitative and quantitative data collection instruments within the SMM framework.

Qualitative data collection

A semi-structured interview guide was developed to facilitate consistency in data collection while allowing for unanticipated responses and was reviewed by industry experts for completeness and clarity. Our team created open-ended questions about the SMM[13] components of symptom experience (perception, evaluation, and response) and person, and the domains of the MLHFQ[10] (physical symptoms, emotional symptoms, and quality of life) about each participant and their symptom experience. Participants were given the option to conduct interviews either over the phone or via virtual

videoconference. One participant requested a videoconference, and all other participants requested to conduct interviews via telephone, either due to technological capabilities or personal preference.

Participants were asked to discuss their background and to describe their symptoms in the last 4 weeks to correspond with the MLHFQ and SSQ-HF symptom recall time frame[10]. Probes, both questioning and silent, were used to facilitate thoughtful responses from participants[16]. Mirroring was utilized to ensure the PI was capturing the true perspective of each participant by repeating phrases and ideas back to the participant for confirmation of what they meant by their statements[16]. Each interview lasted on average 35 minutes, with times ranging from 18 minutes to 55 minutes.

Qualitative data analysis

Interviews were audio recorded, transcribed verbatim using a professional transcription service, and all transcripts were checked for accuracy. Transcripts were coded with NVivo 13 software (QSR International, Pty, Doncaster, Australia) and qualitative description was used to guide analysis of semi-structured interview data[37-39]. This methodology is data near, meaning it aims to capture the true experience of individuals by keeping analysis close to the given data rather than significantly transforming data[17-19]. Interviews were transcribed and analyzed as they were collected using a constant comparative method[16]. A directed approach to content analysis was used with SMM[13] components and MLHFQ[10] domains as broad code types developed a priori, which guided development of sub-codes[19].

The PI initially performed level 1 coding before coding data within a priori codes[19]. This first step was meant to increase trustworthiness by not allowing broad code structures to result in missing important findings that did not fit within the selected frameworks[19]. Two to three transcripts were analyzed at a time. Codes and emerging themes were then reviewed with the research team qualitative expert and the HF content expert, and codes were revised as needed[16]. Themes emerged from within and across coding categories.

The research team qualitative expert oversaw coding of all interview transcripts and debriefing occurred at each stage of the data analysis process to increase transparency of coding and allow for triangulation of findings to increase credibility[16]. A detailed audit trail was maintained throughout data collection and analysis to support dependability[16]. All codes were developed by the 9th interview, and saturation occurred after the 13th interview was analyzed, in which responses coincided with already developed themes without adding new or differing information[20].

Quantitative Data Collection and Analysis

We collected data on demographics, quality of life, physical symptoms, and emotional / psychological symptoms using well-validated instruments, described in detail in another manuscript[8]. Quantitative data were analyzed for standard descriptive statistics, including medians, ranges, means and standard deviations. We examined the relationship between questionnaire scores using a Pearson correlation analysis after assessing normality using the Shapiro-Wilk's test.

Mixed Methods Integration Analysis

Qualitative and quantitative data were integrated through *methods*, *interpretation*, and *reporting*. In the *methods* stage, we merged qualitative and quantitative data collection instruments within the SMM[13] to better facilitate integration, as shown in Table 1. Qualitative and quantitative data collection were conducted concurrently, and each type of data was analyzed separately in parallel.

Once data analysis was complete and themes were identified from qualitative data, we *interpreted* and *reported* both types of data using a joint display to integrate results (Table 3). The first column of the joint display shows themes that were identified from qualitative data analysis. The themes are organized within the SMM[13] framework, arranged by the headings of perception, evaluation, response, and person. The 2nd column of the joint display contains quotes from interviews that relate to each theme for participant contextualization, and the 3rd column shows quantitative data that corresponds to each qualitative theme. We then integrated these data through the narrative below by discussing data confirmation, expansion, and discordance.

Results

Qualitative Results

We reached out to all participants who indicated they were willing to participate in an interview (N=38), and those who were not interviewed (23/38) either did not respond to initial calls and emails for scheduling or did not answer during their scheduled interview times. If participants did not answer during their scheduled time, the PI attempted to reach out again via email and another phone call until there was no response

from the participant. The demographics for interview participants (n=15) are presented in Table 2. The average age of interviewees was 46.9 years (range 37-60). All participants reported having children, with an average of 3 children, and the average number of household members was four. Most (12/15) of the participants were married or living with a partner, and 3 were single. Five participants did not have a high school degree, 5 had a high school degree or GED, 1 had some college, and 4 had a bachelor's degree. Four of the participants currently worked as a teacher, baker, hairdresser, and receptionist, with 11 reporting not having a job or not working right now.

Ten themes emerged from qualitative interviews related to symptom perception, evaluation, response, and person. Themes were organized according to the SMM[13] framework, as shown in Table 3, and are described below.

Emotional symptoms co-occurring with physical symptoms

Participants often described that their physical and emotional symptoms either co-occurred or interacted with each other. One participant reported that their emotional symptoms impacted their physical symptoms by stating, "Sometimes when… sometimes I become depressed. And the moment I become depressed and start thinking about my condition too much, I find that I start experiencing (physical) symptoms". Feeling worry, sadness, and fear along with physical symptoms was discussed in interviews.

Shortness of breath, fatigue, dizziness, and chest pain occurring together and leg or ankle swelling occurring alone

Participants reported that shortness of breath, fatigue, dizziness, and chest pain co-occurred or caused one another. Participants described this by stating, "The shortness of breath and fatigue and tiredness, that all happens at once", and "Dizziness comes from the shortness of breath". This was especially the case for shortness of breath and fatigue.

Participants also discussed how leg or ankle swelling happened alone or separate from other symptoms. Though a common symptom mentioned in interviews, participants rarely associated feeling swelling with other symptoms.

Shortness of breath and chest pain causing fear, worry, and fears of death

When participants were asked how experiencing their symptoms made them feel, they reported feelings of fear, worry, and fear of death when experiencing shortness of breath and chest pain. One participant described why these two symptoms make her feel this way by stating, "At times with the dizziness, with shortness of breath, fear can kick in because you never know when the day is going to be your day. And by that, I mean that you say goodbye to this Earth or that you may check in to the hospital."

Feeling like a burden to others

Women also reported feeling like a burden to others when they were experiencing symptoms, such as in the quote, "Sometimes that it also makes... it can make me feel like a burden because you're supposed to take care of your children, not your children take care of you." Eight participants explicitly discussed feeling like a burden for needing help with physical tasks and needing emotional support. Feeling like a burden was often

paired with another feeling that others were pitying or judging them when they were suffering from symptoms.

Daily life affected by physical functioning

For symptom evaluation, we identified the theme that daily life was affected by activity level and physical functioning. In interviews, all participants discussed their daily life being affected by decreased physical functioning. They often discussed difficulty leaving the house and completing tasks around the house. One participant stated, "Even with my walker, I'm not going to get there. I mean, I can tell myself. And then, to myself, I'm saying, I'm going to go. And I wouldn't get to the driveway. So, I've got to go back to the house."

Feelings of missing out

The feelings of missing out, either from not being able to do things with friends or family or not being able to eat the types of food they used to enjoy, was a common theme in interviews, in which 11 participants discussed these feelings. One participant described this as "That I'm not experiencing the world at its fullest, you know? And when I do go out, and I get out there, I'm like a kid in a candy store. I want to see everything, but I just can't." Some participants also discussed how it was difficult being around others while they were eating the food they used to be able to enjoy but no longer can.

Reducing activity level

The most prominent symptom response was reduction of activity level, which all interview participants reported. Participants reported that they would "rest," "lay down," or "just relax" if they were experiencing symptoms. Nine participants described how overexerting or overworking themselves caused their symptoms to occur or become more severe.

Not sharing feelings or downplaying symptoms

The theme emerged that participants often downplayed their symptoms or did not share what they were experiencing with others. Ten interview participants discussed hiding or downplaying their symptoms, mostly around their children, extended family, friends, and co-workers. One participant stated, "But that can be real frightening, especially if it happens and if the children sitting around and they're like, 'What's wrong?' And you try to play it off to them like you're okay. But you know you're not, but you still got to try to look okay, at least for them, so you're not instilling fear into them." All participants reported not hiding their symptoms from nurses or doctors. One participant described hiding things from their healthcare team as "self-defeating."

Inability to work or difficulty working due to symptoms

For the person component, we identified the theme that symptoms made working difficult. Most interview participants (11) reported not currently working or having a job. Out of those 11, 1 was retired, 4 were stay-at-home moms or homemakers, and 6 reported not working because of their heart condition. One participant stated, "And I've worked most of my life, but I haven't worked in the last three years because of my heart." The 4

participants with a job reported missing work or not being able to do as much at work due to symptoms, and one even mentioned how she had been thinking of quitting her job due to her symptoms.

Support

We also identified the theme of support. Most participants reported having support from their significant other, family, or religion. Twelve out of fifteen interview participants (80%) were married or living with a partner, with 10 of those participants saying they found support in that person. Seven interview participants said their support system came from their children or other family members. The two participants who discussed not having a support system in family or friends said they leaned on their religion or God for support. Some discussed how difficult it is to share how they feel with their support person. One participant described this as "Yes. And then I have them, but sometimes we build up these walls. So, I would say they can support me for as long as I allow them to support me. Because as soon as I quit expressing how I'm feeling, then they're under the assumption that I'm okay."

Quantitative Results

Quantitative survey respondents (N=44) had mean total quality of life score from the MLHFQ of 64.1 (9.4), and values ranged from 21 to 95, with 105 being the highest possible score, as shown in Table 4. A higher score indicates more of an impact from HF. The average total SSQ-HF score was 39.2 (16.0), and scores ranged from 0 to 68. A score of 84 is the highest possible on the SSQ-HF and indicates more severe physical HF

symptoms. The mean PHQ-8 score was 9.0 (6.2) and ranged from 0 to 24, where 24 is the highest possible score indicating more depressive symptoms. Any score greater than 10 is considered major depression, and any score greater than 20 is considered severe depression. In the sample, 45.5% of participants had a score of 10 or higher, and 2 participants had a score of 20 or higher.

The Shapiro-Wilk's test showed scores were normally distributed for MLHFQ and PHQ-8 scores ($p > .05$), but not for SSQ-HF scores ($p < .05$). Therefore, Spearman correlation was used to assess the relationship between symptom scales. A strong positive correlation was found between MLHFQ scores and SSQ-HF scores (r=.61, $p < .01$), and moderate positive correlations were found between the PHQ-8 and MLHFQ (r=.48, $p < .01$) and the PHQ-8 and SSQ-HF (r=.42, $p < .01$), indicating that as scores for one questionnaire increase, so do scores for the others.

Integrated results

We integrated qualitative themes with quantitative data to gain additional insights on the symptom experience and examine how results converged or diverged. There was concordance between quantitative data and the theme of emotional/psychological and physical symptoms co-occurring. All survey participants, except one, reported experiencing worry and physical symptoms and rated worry as very impactful with an average score of 4 and a median score of 5. Moderate to strong correlations were found between the three scales, which measured different types of symptoms. Forty-six percent of the sample had PHQ-8 scores that indicated major depression.

The theme that shortness of breath, fatigue, dizziness, and chest pain co-occurred aligned with quantitative symptom data. Thirty-nine out of 44 survey participants reported shortness of breath, and 38 of those participants (97%) also reported fatigue. Twenty-two out of 44 participants reported chest pain, with 15 of those participants (68%) also reporting dizziness. Out of the entire study sample, participants (30%) reported experiencing all symptoms of shortness of breath, fatigue, dizziness, and chest pain. Leg and ankle swelling was a common symptom reported by 14 out of 15 interview participants and 89% of survey participants. Interview participants discussed that swelling occurred separately from other symptoms. This phenomenon could not be confirmed with quantitative data, as participants were stating whether they experienced a symptom in a certain time frame, not which symptoms actually showed up together. Participants reported that swelling frequently occurred, with most participants (67%) experiencing it 3 times a week or more. However, most participants did not find swelling to be severe or more than somewhat distressful.

In interviews, shortness of breath and chest pain were described as distressful to participants and were often accompanied by fears of death. However, there was discordance between these feelings and quantitative scores. Average distress scores from chest pain (1.91) were very similar to distress scores from swelling (1.95), where 4 is the highest on the scale. Shortness of breath was slightly more distressful, with an average score of 2.44. Participants reported in both interviews and surveys that overall, symptoms made them feel like a burden to their family and friends. The median score for the MLHFQ item of feeling like a burden was 3.5, with 50% of participants rating feeling like a burden as a 4 or 5.

MLHFQ item scores confirmed the qualitative theme of daily life being affected by physical functioning. Every survey participant reported experiencing difficulty working around the house or yard, with a mean impact score of 3.2 (1.5). All survey participants except one reported experiencing difficulty going places away from home, with a mean impact score of 3.25 (1.5). These scores coincide with interview findings, where all participants discussed their daily life being affected by them having to keep their activity levels low or decreased physical functioning. They often discussed hardships related to leaving the house and difficulty completing tasks around the house. MLHFQ responses also confirmed the theme of feelings of missing out on doing things with friends and family, which all survey participants experienced.

The MLHFQ scores for lying down or resting during the day confirmed interview findings that rest was the most common response to experiencing symptoms, as every interview participant discussed. The MLHFQ item showed how much this impacts participants, considering the average score of 3.5 and median score of 4. Survey participants indicated that their HF made it difficult to work or earn a living according to the MLHFQ item, a prominent interview theme. The majority of survey respondents (52%) rated the MLHFQ item of making your working to earn a living difficult as a 5, very much, making the median score a 5 and the average a 3.5. These high scores coincide with interview findings, as even those who were able to work reported some difficulty with their current jobs.

Discussion

Examining symptom data with a convergent mixed methods design allowed us to identify several prominent findings, including the theme of perceptions that physical and

emotional symptoms interact. Symptom clusters, created using symptom scales, show when participants are experiencing symptoms together or at the same time. With the qualitative interview, we know that some participants believe that their physical symptoms actually trigger their emotional symptoms, or vice versa. This concept should be explored further in future studies, as this could add valuable information about how symptoms cluster. Moderate to strong correlations were found between symptom scale total scores, though the sample was small.

During interviews, participants seemed to create their own symptom clusters of how they believed their symptoms occurred together or interacted. Participants commonly associated shortness of breath, fatigue, dizziness, and chest pain together. Shortness of breath clustering with fatigue has been shown in other HF symptom cluster studies[2,21,22], which is consistent with our findings of 97% of participants reporting shortness of breath along with fatigue. These were two of the most commonly reported symptoms in this study. In the future, the interactions of these symptoms with one another should be more robustly explored.

The participants also noted that leg and ankle swelling often happened alone. This was also information that we exclusively gained from interviews, as the quantitative data simply showed that 89% of participants experienced leg or ankle swelling along with their other reported symptoms. Four other HF symptom cluster studies have found that lower extremity edema did not cluster with other symptoms[2,22-24]. It is possible that patients put swelling in its own category as they considered the symptom more manageable or less distressful. However, distress scores from ankle and leg swelling were similar to those reported for shortness of breath and chest pain. This is contrary to how

participants described these symptoms in interviews, in which fear, worry, and fears of death often coincided with feeling shortness of breath or chest pain, but not swelling. One participant stated, "The feet swelling isn't going to kill you, but when you can't catch the air, that can take you out. And when you get the chest pain, that's stress to your heart. So that again can take you out." Therefore, the perceived threat of a symptom may impact the feelings of fear or worry for participants, which may explain the divergence in results.

Reduced physical functioning was a common theme throughout interviews, as participants stated that low physical functioning impacted their family life, household chores, and ability to work. These interview findings were supported by high MLHFQ scores, especially for making an earning difficult, in which the majority (53%) of participants rated this item as a 5. Most participants discussed not being able to work due to their symptoms or condition, and the four participants who did have jobs discussed the challenge of managing their symptoms while working. Working to provide financial income and a sense of accomplishment in a career both hold meaning, and the impact of not having those should be explored in future interviews.

Participants also reported that experiencing HF symptoms made them feel like a burden to others or that others would judge or pity them if they knew what they were experiencing. These feelings tie into the symptom response of participants hiding or downplaying their symptoms from others. Mothers especially downplayed their symptoms while around their children and working women around their co-workers. Women reported finding support mostly with their significant other or family members, and some mentioned that they found support from God or their religion.

Our study had several limitations. Firstly, participants self-reported their diagnosis of HFpEF based on their ejection fraction being greater than or equal to 50% or the participant reporting their doctor diagnosed them with HFpEF or diastolic heart failure. HFpEF is a complex disease process and asking participants to self-report their diagnosis is inferior to a confirmed diagnosis from a medical chart. Also, data from qualitative interviews of 15 individuals were integrated with quantitative data of 44 individuals as a whole rather than examining quantitative data specific to each interviewed participant. Future studies should aim to link these types of data for further exploration of convergence, divergence, and expansion.

Conclusion

With a mixed-methods design, we were able to examine the symptom experience of Black females with HFpEF. The majority of interview participants discussed that their physical and emotional symptoms interacted with one another beyond simply co-occurrence, and positive correlations between symptom scales supported this theme. Clinicians should include emotional/psychological symptoms and how they interact with physical symptoms in their assessment. Women experienced shortness of breath with fatigue, chest pain, and dizziness, while ankle and leg swelling often occurred alone. Participants may place swelling in its own category as a common symptom that is frequently present but not very distressful, as shown in survey data. Women reported that shortness of breath and chest pain often caused them fear, worry, and fear of death. Though symptom distress scores were not as high as expected for these symptoms, it may be what these symptoms represent to participants that cause fear. Clinicians should pay

close attention to how shortness of breath and chest pain impact their patients. The participants reported their symptoms made them feel like a burden to others, or that others judged or pitied them and often hid or downplayed their symptoms. The prominent qualitative theme confirmed by quantitative data was that reduced physical functioning impacted family life, household chores, and the ability to work.

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What's New and Important?

- Considering the increased burden of HF symptoms, greater risk, and worse outcomes in females, Black Americans, and patients with HFpEF[1,6-8], this study seeks to illuminate the experiences of those who are underdiagnosed, undertreated and have a greater symptom burden[3,4].
- Black women with HFpEF discussed interactions of physical and emotional symptoms and positive correlations between symptom scales supported this theme.
- Participants reported feeling like a burden to others and hid or downplayed their symptoms and reduced physical functioning impacted family life, household chores, and the ability to work.

Tables

Table 1: Merging of SMM components with QUAL and QUANT data collection instruments

SMM Component	QUAL (interview guide)	QUANT (questionnaires)
Perception		
Physical symptoms	What physical / emotional symptoms did you experience in the past 4 weeks?	MLHFQ SSQ-HF
Emotional symptoms	What physical / emotional symptoms did you experience in the past 4 weeks?	MLHFQ PHQ-8
How your symptoms make you feel	How did experiencing those symptoms make you feel?	
Significance- what feeling symptoms means to you	When you experience those symptoms, what does that mean to you?	
Evaluation		
Distress		SSQ-HF
Frequency	How often?	SSQ-HF

		PHQ-8
Severity	How severe?	SSQ-HF
Impact on daily life	How much do they impact your daily life?	MLHFQ
Symptom causes	What do you think causes your symptoms?	
Response		
Management and treatment	How do you think your symptoms can be managed or treated?	
How you respond to experiencing symptoms, or what you do when they become more frequent, severe, impact your life more?	What do you usually do when you are experiencing symptoms? Have you ever hid/downplayed?	
Person		
Demographic	Tell me a little bit about yourself… Living situation Kids Marital status Job Education	Screening questionnaire Demographics questionnaire SILS

Sociologic	Do you have a support system to help?

Table 2: Study Sample Demographics

	Frequency (Valid %) OR Mean (SD)	
	Quantitative sample (n=44)	**Qualitative sample (n=15)**
DEMOGRAPHICS		
Race/ethnicity		
Black	44 (100%)	15 (100%)
Education		
No High School Diploma	8 (18.2%)	5 (33.3%)
Diploma or GED	17 (38.6%)	5 (33.3%)
Associate degree	3 (6.8%)	1 (6.7%)
Bachelor's Degree	7 (15.9)	4 (26.7%)
Master's Degree	7 (15.9%)	0
Doctoral Degree	2 (4.5%)	0
Current marital status		
Single	12 (27.3%)	3 (20%)
Married/ living with partner	20 (45.5%)	12 (80%)
Separated	3 (6.8%)	0
Divorced	4 (9.1%)	0

Widowed	5 (11.4%)	0
Age (years)	51.75 (11.1)	46.9
# of children	2	3
# people in household	3	4
Length of HF Diagnosis		
0 – 12 months	11 (25%)	
>1 year – 2 years	15 (34.1%)	
3 years – 4 years	13 (29.5%)	
5 years – 8 years	5 (11.4%)	
Primary Insurance Status		
None	0 (0%)	
Medicare / Medicaid	24 (54.6%)	
Public (marketplace)	7 (15.9%)	
Private (employer)	10 (22.7%)	
Other	3 (6.8%)	
BMI Categories		
Underweight (< 18.5)	2 (4.5%)	
Healthy (18.5 – 24.9)	25 (56.8%)	
Overweight (25 – 29.9)	6 (13.6%)	
Obese (≥ 30)	11 (25%)	
Single item literacy screener		
Never	26 (59.1%)	
Rarely	8 (18.2%)	

Sometimes	5 (11.4%)
Often	5 (11.4%)
Always	0 (0%)

Table 3: Integration of QUAL and QUANT data organized within the SMM framework

Themes	QUAL - Participant contextualization	QUANT Variables Mean (SD) | Median
Perception		
Emotional symptoms co-occurring with physical symptoms	"Um, I would say the worst my symptoms are, the more, the more that I worry." "If I'm in a lot of pain a lot of times or I have shortness of breath and then it can cause anxiety and worry, you know, it all kind of goes together." "And the moment I become depressed and start thinking about my condition too much, I find that I start experiencing (physical) symptoms."	MLHFQ - making you worry? (N=43) 4.07 (1.3) | 5 MLHFQ by- making you feel depressed? (N=32) 2.34 (2.1) | 1 PHQ-8 - down, depressed, or hopeless? (N=27) 1.16 (1.2) | 1

Shortness of breath, fatigue, dizziness, and chest pain occurring together and leg or ankle swelling occurring alone	"The shortness of breath and fatigue and tiredness, that all happens at once." "I would definitely say the fatigue and shortness of breath. I would say they happen together." "The breathing and the (chest) pain will happen together." "Pain in the chest may come with fatigue and also loss of appetite, but the swollen legs maybe comes alone" "I can also have swollen feet by itself, because swollen feet, I would definitely say, that that's around 24/7."	Shortness of breath AND fatigue- 97% (38/39) Chest pain AND dizziness- 68% (15/22) Shortness of breath, fatigue, dizziness, AND chest pain - 30% (13/44) SSQ-HF Leg or ankle swelling (N=39) -How often? 2.69 (.61) | 3 -How severe? 2.03 (.87) | 2 -How distressful? 1.95 (1.3) | 1
Shortness of breath and chest	"At times with the dizziness, with shortness of breath, fear can kick in because you never	SSQ-HF Chest pain (n=22)

pain causing fear, worry, and fears of death	know when the day is going to be your day. And by that, I mean, that you say goodbye to this Earth or that you may check in to the hospital." "Well, when my heart hurts it's that (that scares me). People get scared of dying when that happens. Or you can't breathe good, you get scared of stuff like that. I mean, I want to live to see my grandkids, you know what I'm saying?" "You get a little scared when you can't catch a breath or when you do get the chest pain, it puts little scares in you."	-How often? 2.50 (.67) | 2.5 -How severe? 1.95 (.49) | 2 How distressful? 1.91 (1.1) | 1.5 SSQ-HF Shortness of breath (N=39) -How often? 2.87 (.89) | 3 -How severe? 2.36 (.81) | 2 How distressful? 2.44 (1.2) | 3
Feeling like a burden to others	"I would definitely say that that feels scary to have to lean on somebody. I would also say if I don't, I don't, I don't want to be a burden on anybody." "Sometimes that it also makes... it can make me feel like a burden because you're supposed	MLHFQ by- making you feel you are a burden to your family or friends? (N=37) 2.93 (1.8) | 3.5

	to take care of your children not your children take care of you."	
Evaluation		
Daily life affected by physical functioning	"Even with my walker, I'm not going to get there. I mean, I can tell myself. And then, to myself, I'm saying, I'm going to go. And I wouldn't get to the driveway. So, I've got to go back to the house." "What normally would take me an hour to clean, takes me well into four or five hours because I had to stop because I just get so out of breath." "It makes me feel uncapable of doing just regular, normal things."	MLHFQ by- making your working around the house or yard difficult? (N=44) 3.20 (1.5) | 3.5 MLHFQ by- making your going places away from home difficult? (N=43) 3.25 (1.5) | 3.5
Feelings of missing out	"That I'm not experiencing the world at its fullest, you know? And when I do go out and I get out there, I'm like a kid in a candy store. I want to see everything, but I just can't." "Um, I feel left out because everybody else, you know, I can't expect them to stop their	MLHFQ by- making you eat less of the foods you like? (N=38) 2.55 (1.5) | 3

	lives and not go just because I can't, I feel left out, but at the same time we do watch movies here at the house." "I guess you can also say sometimes I feel deprived as well, deprived in the sense that I can't have all those seasonings and butters anymore. So, I feel really deprived about that."	MLHFQ by- making your relating to or doing things with your friends or family difficult? (N=44) 3.18 (1.4) | 3
Response		
Reducing activity level as a response to symptoms	"If, if your, if your body's not feeling right, you know, or you're overexerting yourself, check in, and say hey, you got to slow down." "So, first you rest and see if it will go away on its own, and then you decide what to do." "I personally try to keep my activities low."	MLHFQ by- making you sit or lie down to rest during the day? (N=43) 3.50 (1.5) | 4
Not sharing feelings or downplaying symptoms	"Yeah, when I sit down, and my chest is hurting. I sit down, and that's when I'm masking it. They say, well, 'Mom, why are you sitting down?' I say, 'I'm taking a break.'"	n/a

	"You have to act normal. So, you have to pretend that you're okay. I think it's really tiring, really exhausting."	
Person		
Inability to work or difficulty working due to symptoms	"Yeah, it does affect me because I'm a hairdresser. My work includes a lot of moving, standing. So, when I have swollen feet I cannot go to work." "And I've worked most of my life, but I haven't worked in the last three years because of my heart."	MLHFQ by- making your working to earn a living difficult? (N=37) 3.48 (2.0) | 5
Support	"I feel at ease talking about what I feel with my husband and pastor, I really do. […] There ain't nothing I can't go to my husband and talk about." "But I pray. I'm religious. I pray to God. I know He is going to get me through anything. Any trial I go through, I believe He will help me. Even though I'm scared, God don't want me to be scared."	n/a

*N=any score other than 0, MLHFQ Did your HF prevent you from living as you wanted during the past month (4 weeks) by (0-5) PHQ-8 Over the last 2 weeks, how often have you been bothered by any of the following problems (0-3),

Table 4: Questionnaire Total Scores

Questionnaire	Mean (SD)	Median (Minimum-Maximum)
MLHFQ	64.14 (9.42)	63.0 (21 to 95)
SSQ-HF	39.20 (16.03)	41.5 (0 to 68)
PHQ-8	8.98 (6.24)	7.5 (0 to 24)

*MLHFQ=Minnesota Living with Heart Failure Questionnaire, SSQ-HF=Symptom Status Questionnaire – Heart Failure, PHQ-8=Personal Health Questionnaire-8

Summary

Overview of Manuscripts' Contributions

The dissertation compendium consists of 3 manuscripts: (1) an integrative review of heart failure (HF) symptom cluster literature to identify themes within the Symptom Management Model (SMM) and highlight gaps that researchers should pursue in the future; (2) a feasibility study of a convergent mixed methods parallel study protocol for studying the HF symptom experience and how symptoms cluster in Black women with Heart Failure preserved Ejection Fraction (HFpEF); and (3) a qualitative descriptive analysis of individual interviews with Black women with HFpEF about their background and symptom experience, and integration of qualitative themes with quantitative symptom data (1). Together, these manuscripts illuminate the symptom experience of Black women with HFpEF, a population that has been understudied in current HF symptom cluster research (2-19). These manuscripts serve as the first step to inform the design and future implementation of a large-scale mixed methods HF symptom cluster study to form statistically meaningful symptom clusters and integrate qualitative findings to gain new perspectives on this population's symptom experience.

The comprehensive integrative review of HF symptom cluster literature synthesized themes from 18 manuscripts that were eligible for analysis (19). Themes were organized within the SMM (1). The integrative review showed that HF symptom clusters exist and can be used in clinical practice for symptom monitoring and risk assessment. However, current literature minimally examined sex differences in HF symptom clusters and lacked racial diversity, as the majority of participants in American

studies were White (2-19). Additionally, none of the included manuscripts utilized qualitative methods to allow participants to describe their symptom experiences.

The second manuscript reported the results of the feasibility study and preliminary symptom cluster analysis. This study was conducted to determine an innovative symptom cluster study design's feasibility and acceptability in an underrepresented population. This study's results support the study protocol's feasibility and acceptability, as all benchmarks were met. We conducted a hierarchical cluster analysis with the feasibility study sample (N=44) to test processes and form preliminary clusters. Three clusters of individuals were identified, consisting of a highly symptomatic cluster, mildly symptomatic cluster, and a psychologically symptomatic cluster. We compared the preliminary clusters on demographics and questionnaire responses. However, hypothesis testing was not the focus of this study due to the feasibility design and small sample. Further exploration should be conducted in the future with a large sample of participants.

The final manuscript consisted of qualitative and mixed methods integration results. Qualitative themes about the symptom experience of Black women with HFpEF emerged about physical and emotional symptoms co-occurring and interacting, chest pain and shortness of breath causing fear and anxiety, women feeling like a burden to their families, and physical limitations impacting daily life, activities with friends and family, and the ability to work. Quantitative symptom data were integrated with these themes to show how results converged or diverged. Symptom scale results coincided with interview findings. For instance, participants reported high impact scores for feeling like a burden to others, an inability to work, and missing out on activities with friends and families due to their condition, all of which were prominent qualitative themes. Some results diverged.

For instance, interview participants said shortness of breath and chest pain made them feel fear, anxiety, and fear of death, yet survey respondents rated shortness of breath and chest pain symptom distress similar to that of ankle and leg swelling. Ankle and leg swelling often occurred alone and was not noted to be particularly distressful in interviews and was never tied to fears of death. This discordance in results may be due to what the symptom represents. Some participants described their breathing and chest pain as things that could "take you out" or thought of them as dealing directly with the heart. In comparison, they felt the swelling often occurred, and even though it may be bothersome and distressful, they did not feel they would die from it.

Limitations

There were several notable limitations of this dissertation study. First, the integrative review only searched three databases, and all manuscripts that underwent full-text review were from one database. Utilizing more databases and alternative search terms could result in a larger sample of manuscripts. Second, study participants self-reported a diagnosis of HFpEF. We asked participants if their doctor had given them a diagnosis of HFpEF or diastolic HF (with an ejection fraction greater than or equal to 50%). They either responded yes, no or unsure. If participants were unsure, they were encouraged to call the PI to discuss their diagnosis. One participant did call to discuss her eligibility and was deemed eligible for the study. This option was helpful for those who were unsure, but a confirmed diagnosis from a medical chart would be preferable. Third, we did not know which quantitative data belonged to each interview participant due to an attempt to separate patient identifiers from health data for confidentiality purposes. This meant that

mixed methods integration occurred with quantitative data as a whole rather than individual responses. Connecting individual symptom scores to qualitative interview data could have provided us with additional insights.

Importance of Theory, Model, or Framework

The SMM was central to this dissertation. The SMM was used as a framework for an integrative review of HF symptom cluster literature due to its multifaceted nature that encompasses various components that influence the symptom experience as a whole (1). The model was then used to design and plan multiple aspects of the dissertation study, including guiding the research question, informing proposal development, and influencing symptom questionnaire selection. The SMM was also used as a framework for the semi-structured interview guide, qualitative content analysis, triangulation, and merging of qualitative and quantitative results. Utilizing the SMM as a framework from start to finish allowed for the cohesion of findings and concepts across all dissertation studies, ultimately adding strength and rigor to findings.

The dissertation study also further describes how aspects of person and symptom experience, which are components of the SMM, interact to illuminate the symptom experience as a whole. Future research could incorporate more components of the model to further explore interactions. The SMM combined with domains of the MLHFQ provided added information on physical symptoms and emotional symptoms, a distinction that was not present in the model.

Overall Findings

This dissertation's results support the feasibility and acceptability of a mixed methods study protocol for studying symptom clusters in Black women with HFpEF. Recruiting a larger sample to form meaningful clusters should be pursued in future research to describe this population's symptom experience further. The studies also highlight the importance of emotional/psychological symptoms in HF. Current HF treatment guidelines acknowledge emotional/psychological symptoms in HF, but guidelines do not exist to treat or manage these symptoms (20). Other HF symptom cluster studies have shown that emotional and psychological symptoms happen together when they cluster together or happen simultaneously (2-19). However, without the qualitative interviews, we could not explain how these symptoms interact with one another. Many interview participants discussed how they believed their physical symptoms caused their emotional symptoms or vice versa. This finding highlights the value of qualitative methods in symptom cluster research.

Interviews also showed how a woman's background or lifestyle impacts their symptom experience. Minnesota Living with Heart Failure Questionnaire (MLHFQ) scores were high for feeling like a burden to others, and these results were confirmed in qualitative interviews where almost all participants discussed feeling like a burden when they were unable to carry out their normal tasks or needed assistance at work or home (21). The distress women felt when not being able to care for their children, partner, or family members or work, like they used to before diagnosis, was evident and may explain why women have higher rates of depression (23, 24). Exploring whether men also feel like a burden to others and how they characterize their emotional/psychological

symptoms would help find differences and similarities in each sex/gender's symptom experience.

Research Trajectory

This dissertation provides the background knowledge and proof of concept data necessary for conducting a large-scale mixed methods HF symptom cluster study with a population of Black women with HFpEF. Study materials have been developed and tested. Feasibility benchmarks were all met, and participants gave the study high ratings for acceptability. Facebook ad campaigns have also been developed and could be reused for a larger study. To recruit a large enough sample to form statistically significant symptom clusters, additional funding is needed to compensate study participants, run Facebook ad campaigns, and support study staff.

When conducting a larger scale study, it would be ideal to pair quantitative and qualitative data together for each participant rather than only merging quantitative data as a whole with qualitative data. This dissertation aimed to answer the research question of what is the symptom experience and how do symptoms clusters for Black women with HFpEF? Future research could also compare the symptom experience and symptom clusters of Black females with HFpEF to persons of different race/ethnicities, males, and to patients with another type of HF with a reduced ejection fraction. We could also explore how age affects symptom perception and clustering, since younger age has been noted to correspond with more symptom distress and the most symptomatic cluster also had the youngest average age.

Contribution to Health, Nursing and Clinical Care

This dissertation study provides key insights into nursing, research, and clinical care. First, this dissertation illuminates the symptom experience of Black women with HFpEF. While conducting qualitative interviews, many participants discussed their enthusiasm for being included in the research study, helping others by sharing their stories, and wanting their voices to be heard. This enthusiasm for participation shows that underrepresented populations in research may not actually be hard to reach or unwilling to participate, but that recruitment tactics have to be more targeted to achieve diversity and inclusion. When first using Facebook for recruitment, almost all screening questionnaires were completed by White respondents. It took targeted efforts to reach our population of interest, in which we developed Facebook ads geared specifically to our population of interest. When we were only using post within Facebook groups, almost all respondents were White. This feasibility study serves as a steppingstone to recruiting a large population for a full-scale study and provides key information for recruiting Black women in future HF studies.

This dissertation study also highlights the clinical implications of emotional/psychological symptoms. This was a theme in the integrative review, as HF symptom cluster studies found emotional/psychological symptoms tied to worse outcomes and increased cardiac risks. This theme continued in the mixed methods study, as participants discussed interactions between their physical and psychological symptoms, and symptom scales had moderately to strongly correlated. It is imperative that emotional/psychological are recognized, treated, and included in HF treatment guidelines.

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List of Appendices

Appendix A: IRB Approval

Institutional Review Board for Human Research (IRB)
Office of Research
Integrity (ORI)
Medical University of
South Carolina

Palmetto
Place Office Park 1
South Park Circle,
Bldg. 1, Suite 401
Charl
eston, SC. 29407
Federal Wide
Assurance #
1888

APPROVAL:
This is to certify that the research proposal **Pro00101261** entitled:
A Mixed Methods Approach to Symptom Clusters in Black Women with Heart Failure Preserved Ejection Fraction: A Feasibility Study

and submitted by: **Alexandra Ruppe**
Department: **Medical University of South Carolina**
Sponsor: **null, MUSC CON Diversity and Inclusion Dissertation Award**
Sponsor Protocol Version: **1**
Dated: **7/31/2020**

For consideration has been reviewed by **IRB-I - Medical University of South Carolina** and approved with respect to the study of human subjects as adequately protecting the rights and welfare of the individuals involved, employing adequately methods of securing informed consent from these individuals and not involving undue risk in the light of potential benefits to be derived therefrom. Additionally, the Institutional Review Board for Human Research (IRB) recommends approval of the investigator's request for Waiver of Consent pursuant to 45 CFR 46.116(d) because the research involves no more than minimal risk to the subject, the waiver will not adversely affect the rights and welfare of the subjects, and the research could not be practicably carried out without the waiver. No IRB member who has a conflicting interest was involved in the review or approval of this study, except to provide information as requested by the IRB.

Original Approval Date: **8/7/2020**
Required Status Update Report: **8/6/2021**

Type: **Expedited**

Chairman, **IRB-I - Medical**
University of South Carolina Mark Hamner*

Statement of Principal Investigator:

As previously signed and certified, I understand that approval of this research involving human subjects is contingent upon my agreement:

1. To report to the Institutional Review Board for Human Research (IRB) any adverse events or research related injuries which might occur in relation to the human research. I have read and will comply with IRB reporting requirements for adverse events.
2. To submit in writing for prior IRB approval any alterations to the plan of human research.
3. To submit timely status update reports of this research as requested by the IRB.
4. To maintain copies of all pertinent information related to the research activities in this project, including copies of informed consent agreements obtained from all participants.
5. To notify the IRB immediately upon the termination of this project, and/or the departure of the principal investigator from this Institution and the project.

***Electronic Signature**: This document has been electronically signed by the IRB Chairman through the HSSC eIRB Submission System authorizing IRB approval for this study as described in this letter.*

Appendix B: Recruitment Materials

Facebook ad / posts with possible images / text combos

Are you a Black woman with heart failure? Are you 35-74 years old? We want to hear about your experience with symptoms.

Answer questionnaires about your symptoms and how heart failure symptoms affect your life in 20-30 minutes. Additionally, you may participate in an optional interview about your health and symptoms if you are interested.

Receive a $25 Amazon eGift Card as a thank you for your participation.

We need to hear your voice and experiences to help drive heart failure research within the Black female community.

Participants will receive an Amazon eGift Card ($25) by email or text after completing questionnaire and another Amazon eGift Card ($25) if they complete an interview.

Click here to answer screening questions and see if you qualify for the study.

IRB Number: « PRO00101261»
Date Approved «08/07/2020»

Photos:

MUSC
Medical University of South Carolina
Changing What's Possible

Electronic flyer:

Research participants needed

Are you a black woman with heart failure?

We want to hear about your experience with symptoms.

Who: Black women, 35-74 years old, with heart failure

What: Answer questionnaires about your symptoms and how heart failure symptoms affect your life in 20-25 minutes. Additionally, you may participate in an optional interview about your health and symptoms if you are interested.

When/where: At a time easiest for you online, by phone, or through Doximity

Benefits: We need to hear your voice and experiences to help drive heart failure research within the black female community. Participants will receive an Amazon eGift Card by email or text after completing questionnaires and another after interviews.

See if you qualify by answering screening questions at the QR code / link below:

https://is.gd/womenheartfailuresymptoms

or by contacting Alex Ruppe, heart failure nurse, PhD Candidate at Medical University of SC moseleal@musc.edu, (803) 417-6635

Appendix C: Permissions

Permission for Minnesota Living with Heart Failure Questionnaire

MLHFQ - Instructional or Student Use License

The Minnesota Living With Heart Failure® Questionnaire - Educational Use License is the correct license type to choose when the LICENSEE is a student or teacher at an academic institution and will use the Questionnaire exclusively for student project(s) or teaching purposes.

Please read the terms and conditions of this license agreement ("Agreement") carefully.
By clicking "SUBMIT" on the "Accept/acknowledge terms" page during the Checkout process,
you are agreeing to the following terms and conditions on behalf of the Licensee identified below, and you represent and warrant that you are authorized to do so.

Minnesota Living with Heart Failure Questionnaire -
Educational License

License Fee:

License Fee is $0 USD, payable upon checkout.

Licensee: Alexandra Ruppe
Company - Medical University of South Carolina
Contact Email - moseleal@musc.edu
Contact Phone - 8034176635

TERMS AND CONDITIONS - The following terms and conditions govern this Agreement by and between the Regents of the University of Minnesota, a constitutional corporation under the laws of the State of Minnesota, ("University") and the Licensee.

Definitions - For purposes of this agreement, the following terms have the following meanings.

"Accompanying Documentation" means the following:

MLHFQ FDA MDDT Qualification Package (288 KB PDF)

"Approved Copies" means duplicates of the Work that shall include the statement below:

trademark of the Regents of the University of Minnesota.

"Effective Date" means the date when the Licensee clicks the button indicating agreement with all the terms and conditions of the license and has successfully completed payment in the checkout process. The Effective Date is Mar 26, 2020.

"Licensed Mark" means US Trademark Registration No. 2,378,845 for the mark "LIVING WITH HEART FAILURE", registered to the Regents of the University of Minnesota.

"Purpose" Means the use of the Licensed Technology pursuant to the Terms & Conditions of this Agreement, for use by the Licensee, who must be a student or teacher at an academic institution, exclusively for student project(s) or didactic purposes and for no other purpose.

"Licensed Technology" means collectively the Work, the Licensed Mark, Approved Copies and the Accompanying Documentation.

"Term" The Term of this Agreement shall commence on the Effective Date and shall expire, without any further action by the University, on the tenth (10th) anniversary of the Effective Date.

"Work" means the Living with Heart Failure ® Questionnaire and the Instructions for Data Collection and Scoring. This Work is in the English language; and is identified as University **Case #: 94019.**

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Export and Regulatory Restrictions - Copyright - The Licensee shall comply with all then-current applicable export laws and any regulations (e.g. federal, state, local, or provincial) regarding the use of the Licensed Technology in the relevant territory.

Right to Injunctive Relief - Licensee acknowledges and agrees that monetary damages are not sufficient to compensate University in the event of Licensee's material breach or violation of this Agreement, and that University may be irreparably harmed by such breach or violation, and that University will have the right to seek other remedies available to it in law and equity to remedy such breach or violation, including injunctive and equitable relief. If Licensee fails to perform an obligation or otherwise breaches one or more of the terms of this Agreement, Licensee shall pay the University's costs and expenses (including actual attorneys' and investigative fees) to enforce the terms of this Agreement.

Governing Law and Forum - The internal laws of the state of Minnesota shall govern the validity, construction and enforceability of this Agreement, without giving effect to the conflict of laws principles thereof. Any suit, claim, or other action to enforce the terms of this agreement, or any suit, claim or action arising out of or related to this agreement, may be brought only in the state courts of Hennepin County, Minnesota. The Licensee hereby submits to the jurisdiction of that court and waives any objections it may

have to that court asserting jurisdiction over the Licensee or its assets and property. This Agreement is not to be governed by the United Nations Convention on Contracts for the International Sale of Goods, or by the Uniform Computer Information

Transactions Act (UCITA) as may be enacted by the State of Minnesota.

Entire Agreement - This Agreement constitutes the entire understanding of the parties with respect to the subject matter hereof, and supersedes all prior agreements and understandings of the parties on such subject matter. This Agreement may be amended, only in writing, and duly executed by all the parties.

Assignments - The Licensee may not assign or delegate any right or duty under this Agreement, unless the University has consented, in writing, to such assignment or delegation. An assignment or delegation made in violation of this section shall be void and shall not bind the other party.

Compliance With Laws - Licensee represents and warrants that its use of the Licensed Technology will comply with all applicable laws and regulations.

Survival - The following provisions (to the extent they appear in this Agreement) survive termination of the Agreement: "Definitions, University Intellectual Property Rights, Protection of Proprietary Rights, Payment Terms, Termination, Disclaimer, Limitation of Liability, Indemnification, Export Control, Right to Injunctive Relief and Attorney's Fees, Governing Law, and any other provision, which by its nature is intended to survive.

Relationship of the Parties - In entering into, and performing their duties under the Agreement, the parties are acting as independent contractors and independent employers. No provision of the Agreement creates or is to be construed as creating a partnership, joint venture, or agency relationship between the parties. No party has the authority to act for or bind the other party in any respect.

Severability - If a court of competent jurisdiction adjudges a provision of the Agreement to be unenforceable, invalid, or void, such determination is not to be construed as impairing the enforceability of any of the remaining provisions hereof and such provisions will remain in full force and effect.

Notice - In order to be effective, all notices, requests, and other communications that a party is required or elects to deliver must be in writing and must be delivered personally, or by facsimile or electronic mail (provided such delivery is confirmed), or by a recognized overnight courier service or by United States mail, first-class, certified or registered, postage prepaid, return receipt requested, to the other party at its address set forth below or to such other address as such party may designate by notice given under this section:

If to University:

Office for Technology Commercialization,
University of Minnesota Attn: Contracts
Manager
McNama
ra
Alumni
Center
200 Oak
St. SE,
Suite 226
Minneapolis, MN 55455
OTCAgree@umn.edu

If notice alleges breach of the Agreement, a copy must be sent to:

Office of the General Counsel,
University of Minnesota Attention:
Director of Transactional Law
Services.
200 Oak Street, SE Minneapolis, MN, 55455

Contracts@mail.ogc.umn.edu

If to Licensee: As set forth above in the "Licensee" section.

Accept Terms - Clicking "SUBMIT" on the "Accept/acknowledge terms" page during the Checkout process indicates that you agree with the terms and conditions of this license agreement, and agree to receive required notices from the University of Minnesota electronica

Permission for Symptom Status Questionnaire - Heart Failure

From: Seongkum Heo

Sent: Friday, June 19, 2020 3:35 PM

To: Ruppe, Alexandra [moseleal@musc.edu]

Subject: Re: SSQ-HF use for dissertation

Hi Alexandra,

Ok. Great. I attached the instrument.

I hope that everything goes very well for you and your project.

Seongkum Heo, PhD, RN, AHAF, FHFSA

From: Ruppe, Alexandra [moseleal@musc.edu]

Sent: Friday, June 19, 2020 2:07 PM

To: Seongkum Heo [heo_s@mercer.edu]

Subject: Re: SSQ-HF use for dissertation

Exactly! That would be great, Dr. Heo. Thanks so much. I will keep you posted on progress and I can send you manuscripts for approval before submitting any for publication.

From: Seongkum Heo [heo_s@mercer.edu]

Sent: Friday, June 19, 2020 1:32:05 PM

To: Ruppe, Alexandra [moseleal@musc.edu]

Subject: Re: SSQ-HF use for dissertation

Hi Alexandra,

Thank you for your interest.

Yes, I think that it will be good to test in African Americans.

In addition, the items in the MLHFQ does not assess symptoms, but the limitations (or effects) on daily activities, which are different from symptom themselves.

If you want to use SSQ-HF, I will send you the instrument.

Best wishes, Seongkum Heo, PhD, RN, AHAF, FHFSA

Appendix D: Instruments Utilized in Dissertation Study

Section 1: REDCap Survey – Instructions and Screening Questionnaire

Welcome and Instructions:

Thank you for your interest in our study. We are excited to have you!

The purpose of this study is to explore symptoms for Black women with heart failure. Black women have not been included in the majority of heart failure research. It is important that Black women have a voice and the ability to share their symptom experience. The goal of this research is to study clusters of heart failure symptoms in Black women to eventually improve symptom education, monitoring, and treatments.

First, we ask that you complete a short screening questionnaire to see if you are eligible to participate in the study. The screening will take less than 5 minutes. If you are eligible and you would still like to participate, you will be asked to answer questions about your health status, background, and heart failure symptoms. The survey will take about 20-30 minutes to complete. This research study is completely voluntary. Even after you have started the survey, you have the right to refuse to answer any question or stop at any time. Completion of this survey means you consent to participate in the research study. This research study comes with a small risk of loss of confidentiality (meaning someone finding out about your health condition or responses). We have minimized this risk as much as possible by not tying your name or information to any of your responses and keeping all study data on password-protected, encrypted, and secure platforms.

You will receive a $25 Amazon e-gift card as a token of appreciation for your participation in the study. After completing the survey, please fill out the contact

information survey so we know where to send your gift card. You will be asked if you are interested in being contacted for an interview about your symptom experience. These interviews will only be between you and me over the phone or video conference and will take approximately 30 minutes to 1 hour. Interviews will be audio-recorded and transcribed to written word. Audio recordings will be deleted as soon as transcription is complete to protect your identity. If you are asked to participate in an interview, you will receive an additional $25 Amazon e-gift card after it is completed.

Thank you for allowing me the opportunity to share my research study with you. If you have any questions/comments or you would like to answer survey questions over the phone, please call, text, or email me. I would love to hear from you!

Sincerely,

Alex Ruppe, BSN, BSPH, RN Cardiac Nurse

Ph.D. Candidate, Medical University of South Carolina College of Nursing

(803) 417-6635

moseleal@musc.edu

--- PLEASE ANSWER THE FOLLOWING QUESTIONS TO SEE IF YOU ARE ELIGIBLE TO JOIN THE STUDY ---

PLEASE ONLY ANSWER THIS QUESTIONNAIRE ONE TIME PER PERSON

1. Have you ever received a diagnosis of heart failure?

   Yes
   No
   Unsure

2. Did your doctor tell you the type of heart failure you have is called diastolic heart failure (also known as heart failure with preserved ejection fraction)?

   Yes, my ejection fraction is 50% or greater

   No, I have a reduced ejection fraction (<50%)

   Unsure

   (If you are unsure about whether you have diastolic heart failure or heart failure preserved ejection fraction, please contact the primary investigator to determine if you are eligible to participate in this study.

   Alex Ruppe, BSN, BSPH, RN (803) 417-6635

   moseleal@musc.edu)

3. Are you at least 35 years old?

   Yes

   No

4. Are you younger than 75 years?

   Yes

   No

5. Are you female?

   Yes

   No

6. Do you identify as a woman?

   Yes

   No

7. Is the race you primarily identify with Black or African American?

   Yes

   No

8. Have you had a stroke or mini stroke in the past 6 months?

   Yes
   No
   Unsure

9. Have you had a heart attack in the past 6 months?

   Yes
   No
   Unsure

10. Have you been diagnosed with any end-stage disease? (e.g., cancer, renal failure, COPD, liver disease)

    Yes
    No
    Unsure

11. Have you been admitted to the hospital in the last 4 weeks?

    Yes
    No
    Unsure

I agree that I have answered the questions above truthfully and to the best of my knowledge.

☐ X I AGREE

Thank you for participating in this survey! If you were not eligible for this study and the survey ended, we appreciate you taking the time to answer our questions.

If you did qualify to participate in the study, you will see the Heart Failure Survey in your queue below. Please click on "Begin Survey" at the bottom of the page and complete the entire survey to receive your $25 gift card. We are grateful for your time, answers, and feedback and we look forward to furthering research.

If you have any questions, please reach out.

Sincerely,

Alex Ruppe, BSN, BSPH, RN

Cardiac Nurse

Ph.D. Candidate, Medical University of South Carolina College of Nursing

(803) 417-6635

moseleal@musc.edu

If you are having symptoms of depression or sad thoughts and would like to speak with someone or get connected to a treatment center, the Substance Abuse and Mental Health Services Administration (SAMHSA) Treatment Referral Hotline is free, and someone is available to help 24/7. You can call the hotline at 1-800-662-HELP (4357).

If you are currently experiencing severe heart failure symptoms, please contact your doctors about your symptoms. If you do not have a doctor or need help contacting yours, you can reach out to me for assistance.

Section 2: REDCap Survey – Single Item Literacy Screener, Demographics Questionnaire, Feasibility and Acceptability Questions, Contact Information

ABOUT YOU

Single Item Literacy Screener (free for public use)

How often do you need to have someone help you when you read instructions, pamphlets, or other written material from your doctor or pharmacy?

Never
Rarely
Sometimes
Often
Always

How old are you? (Please select your age from the drop-down)

What is your marital status?

Single
Married or living with a partner
Separated
Divorced
Widowed
Other
Prefer not to respond

How long have you been diagnosed with heart failure?

New diagnosis (< 3 months)
3 months - 12 months
1 year - 2 years
3 years - 4 years
5 years - 8 years
9+ years
Unsure
Prefer not to respond

How many children do you have? (please use the drop down to select the number of children)

How many people live in your household (including yourself)? (please use the drop down to select the number of individuals)

What is the HIGHEST level of education you have COMPLETED?

No high school degree
High school degree or GED
Associates degree
Bachelor's degree
Master's degree
Doctoral degree
Prefer not to respond

What is your primary health insurance status?

None
Medicare
Medicaid
Public (from Healthcare Marketplace)
Private (from employer)
Other
Unknown
Prefer not to respond

How tall are you? (please use the drop down to select your height)

How much do you weigh (pounds)? (please use the drop down to select your weight)

Have you been diagnosed with any of the following? (Please check all that apply)

Hypertension (high blood pressure)
High cholesterol
Diabetes
Atrial fibrillation (abnormal heart rhythm)
Coronary Artery Disease (CAD)
Asthma
Chronic Obstructive Pulmonary Disease (COPD)
Obstructive Sleep Apnea (OSA)
None of the above
Unsure

What is your race and ethnicity? Select all that apply.

Black or African American
White
American Indian or Alaska Native

Asian
Hispanic or Latino

How did you hear about this study?

I received an email or phone call.
I saw an ad on Facebook.
I saw a post within a Facebook group.
Someone told me about this study.
Other

How did you complete the survey questions?

I completed the survey questions online and on my own.
I completed the survey questions online with help from someone.
I answered questions over the phone, and the researcher filled out the questionnaires for me.
Other

The way I was contacted about and/or found out about this study seemed like a good match.

Completely disagree
Disagree
Neither agree nor disagree
Agree
Completely agree

I was easily able to access survey questions and follow survey instructions.

Completely disagree
Disagree
Neither agree nor disagree
Agree
Completely agree

The survey questions seemed fitting to me and my condition.

Completely disagree
Disagree
Neither agree nor disagree
Agree
Completely agree

I understood what the survey questions were asking.

Completely disagree
Disagree
Neither agree nor disagree
Agree
Completely agree

The amount of time it took me to complete survey questions was acceptable.

Completely disagree
Disagree
Neither agree nor disagree
Agree
Completely agree

I was easily able to complete all the parts of this study.

Completely disagree
Disagree
Neither agree nor disagree
Agree
Completely agree

The gift card amount ($25) was an acceptable amount of reimbursement.

Completely disagree
Disagree
Neither agree nor disagree
Agree
Completely agree

The purpose of this study was explained to me in a way that I could understand.

Completely disagree
Disagree
Neither agree nor disagree
Agree
Completely agree

I welcomed the opportunity to share my symptom experience.

Completely disagree
Disagree
Neither agree nor disagree
Agree
Completely agree

I would participate in a study such as this one again.

Completely disagree
Disagree
Neither agree nor disagree
Agree
Completely agree

I would recommend participating in a study such as this one to someone I know.

Completely disagree
Disagree
Neither agree nor disagree
Agree
Completely agree

I agree that I have answered the questions above truthfully and to the best of my knowledge.

X I AGREE

Thank you for completing the survey!

Please provide your contact information after submitting your survey so we can send you your $25 Amazon gift card.

Contact Information
Thank you for completing the survey portion of the study! Please provide your contact information below so we can send you your $25 Amazon gift card.

Also, please let us know if you are interested in being contacted about participating in an interview about your symptoms. Participants chosen to participate in interviews will receive an additional $25 Amazon gift card once the interview is completed. Interviews will be done over the phone or through Doxy.me at a time most convenient to you. Please reach out if you have any questions.

What is your name?

What is your phone number?

What is your email address?

How would you like your $25 Amazon gift card to be sent to you?

Email
Text message

Are you interested in being contacted for an interview (for an additional $25 Amazon gift card)?

Yes
No

Section 3: Minnesota Living with Heart Failure Questionnaire

MINNESOTA LIVING WITH HEART FAILURE® QUESTIONNAIRE

The following questions ask how much your heart failure (heart condition) affected your life during the past month (4 weeks). After each question, circle the 0, 1, 2, 3, 4 or 5 to show how much your life was affected. If a question does not apply to you, circle the 0 after that question.

Did your heart failure prevent you from living as you wanted during the past month (4 weeks) by -	**No**	**Very Little**				**Very Much**
1. causing swelling in your ankles or legs?	0	1	2	3	4	5
2. making you sit or lie down to rest during the day?	0	1	2	3	4	5
3. making your walking about or climbing stairs difficult?	0	1	2	3	4	5
4. making your working around the house or yard difficult?	0	1	2	3	4	5
5. making your going places away from home difficult?	0	1	2	3	4	5
6. making your sleeping well at night difficult?	0	1	2	3	4	5
7. making your relating to or doing things with your friends or family difficult?	0	1	2	3	4	5
8. making your working to earn a living difficult?	0	1	2	3	4	5
9. making your recreational pastimes, sports or hobbies difficult?	0	1	2	3	4	5
10. making your sexual activities difficult?	0	1	2	3	4	5
11. making you eat less of the foods you like?	0	1	2	3	4	5
12. making you short of breath?	0	1	2	3	4	5
13. making you tired, fatigued, or low on energy?	0	1	2	3	4	5
14. making you stay in a hospital?	0	1	2	3	4	5
15. costing you money for medical care?	0	1	2	3	4	5
16. giving you side effects from treatments?	0	1	2	3	4	5
17. making you feel you are a burden to your family or friends?	0	1	2	3	4	5
18. making you feel a loss of self-control in your life?	0	1	2	3	4	5
19. making you worry?	0	1	2	3	4	5
20. making it difficult for you to concentrate or remember things?	0	1	2	3	4	5

21. making you feel depressed? 0 1 2 3 4 5

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Instructions for Data Collection and Scoring

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1. Patients should respond to the questionnaire prior to other assessments and interactions that may bias their responses. You might tell the patient that you would like to get his or her opinion before doing your medical assessment.

2. Ample, uninterrupted time should be provided for the patient to complete the questionnaire. We recommend that the patient answer the questions without being influenced by others such as their spouse or family members. Studies show that patient proxies often have different perspectives.

3. We recommend that you use the first question to give the respondent more detailed instructions as follows.

   a. Read the introductory paragraph at the top of the questionnaire.

   b. Read the first question with the respondent – "Did your heart failure prevent you living as you wanted during the last month (4 weeks) by causing swelling in your ankles or legs?" Then tell the respondent -

   - If you did not have any ankle or leg swelling during the past month (4 weeks) you should circle the zero (0) after this question.
   - If you did have swelling that was caused by a sprained ankle or some other cause that you are sure was not related to heart failure, you should circle the zero (0) after this question.
   - If you had swelling that might be related to your heart condition, then rate how much the swelling prevented you from doing things you wanted to do or feeling the way you would like to feel. In other words, how much did the swelling affect your life? Circle either the 0, 1, 2, 3, 4 or 5 to indicate how much the swelling affected your life during the past month – zero (0) means not at all, one (1) means very little and five (5) very much.

4. Ask the patient read and respond to all 21 questions. The entire questionnaire may be read directly to the patient if one is careful not to influence responses by verbal or physical cues.

5. Check to make sure the patient has responded to each question. If a question

does not apply to the patient they should circle the zero (0). Make sure there is only one answer clearly marked for each question.

Instructions for Data Collection and Scoring (cont'd)

1. Score the questionnaire by summating the responses to all 21 questions. In addition, a physical dimension score (items 2, 3, 4, 5, 6, 7, 12, 13 on the version sent with these instructions) and emotional dimension score (items 17, 18, 19, 20, 21) have been identified by factor analysis and may be scored by simple summation to
further characterize the effect of heart failure on a patient's life.

2. Partially complete questionnaires do occur despite best efforts to minimize missing data. However, missing data can greatly bias the data and complicate analysis. To reiterate, you need to make sure the respondents understand to mark zero for any items that do not apply to them, rather than leave a blank. Whenever possible review the questionnaire before the respondent leaves to make sure there are no unanswered questions or questions with more than one answer.

3. Several methods to impute missing data are discussed in the literature.[1, 2] Multiple imputation using completed questions and perhaps other study variables to predict missing responses should be considered.[3] If a missing response is not imputed, the item will be eliminated from that person's score (the sum of responses). Since intermittently missing data can greatly affect within-person changes in scores, you might want to use the same subset of questions to represent a person at all times by omitting questions that have missing data at any point in time. We do not have any recommendations about when missing data become too extensive to render the information being collected useless.

Symptom Status Questionnaire-Heart Failure

Instructions: Please read each of the statements carefully, and then circle the number that best describes your condition or how much you were bothered by these symptoms
during past 4 weeks.

1. Did you have shortness of breath during day time?

0. No **(**If your answer is no—please go to question 2)

1. Yes (If your answer is yes—please fill out 1a, 1b, 1c)

→ **1a. How often?**

1) Less than once per week | 2) 1-2 times per week | 3) 3-5 times per week | 4) Nearly daily

→ **1b. How severe?**

1) Slight | 2) Moderate | 3) Severe | 4) Very severe

→ **1c. How much did it distress or bother you?**

0) Not at all | 1) A little bit | 2) Somewhat | 3) Quite a bit | 4) Very much

2. Did you have shortness of breath when you lay down?

0. No (If your answer is no—please go to question 3)

1. Yes (If your answer is yes—please fill out 2a, 2b, 2c)

→ **2a. How often?**

1) Less than once per week | 2) 1-2 times per week | 3) 3-5 times per week | 4) Nearly daily

→ **2b. How severe?**

1) Slight | 2) Moderate | 3) Severe | 4) Very severe

→ **2c. How much did it distress or bother you?**

0) Not at all | 1) A little bit | 2) Somewhat | 3) Quite a bit | 4) Very much

3. Did you have fatigue or lack of energy?

0. No (If your answer is no—please go to question 4)

1. Yes (If your answer is yes—please fill out 3a, 3b, 3c)

→ **3a. How often?**

1) Less than once per week | 2) 1-2 times per week | 3) 3-5 times per week | 4) Nearly daily

→ **3b. How severe?**

1) Slight | 2) Moderate | 3) Severe | 4) Very severe

→ **3c. How much did it distress or bother you?**

0) Not at all | 1) A little bit | 2) Somewhat | 3) Quite a bit | 4) Very much

4. **Did you have chest pain?**

0. No (If your answer is no—please go to question 5)

1. Yes (If your answer is yes—please fill out 4a, 4b, 4c)

→ **4a. How often?**

1) Less than once per week | 2) 1-2 times per week | 3) 3-5 times per week | 4) Nearly daily

→ **4b. How severe?**

1) Slight | 2) Moderate | 3) Severe | 4) Very severe

→ **4c. How much did it distress or bother you?**

0) Not at all 1) A little bit 2) Somewhat 3) Quite a bit 4) Very much

5. Did you have leg or ankle swelling?

0. No (If your answer is no—please go to question 6)

1. Yes (If your answer is yes—please fill out 5a, 5b, 5c)

5a. How often?

1) Less than once per week 2) 1-2 times per week 3) 3-5 times per week 4) Nearly daily

5b. How severe?

1) Slight 2) Moderate 3) Severe 4) Very severe

5c. How much did it distress or bother you?

0) Not at all 1) A little bit 2) Somewhat 3) Quite a bit 4) Very much

6. Did you have difficulty sleeping at night?

0. No (If your answer is no—please go to question 7)

1. Yes (If your answer is yes—please fill out 6a, 6b, 6c)

6a. How often?

1) Less than once per week 2) 1-2 times per week 3) 3-5 times per week 4) Nearly daily

6b. How severe?

1) Slight 2) Moderate 3) Severe 4) Very severe

6c. How much did it distress or bother you?

0) Not at all 1) A little bit 2) Somewhat 3) Quite a bit 4) Very much

7. **Did you have dizziness or loss of balance?**

0. No (If your answer is no—just check No and stop here)

1. Yes (If your answer is yes—please fill out 7a, 7b, 7c)

→ **7a. How often?**

1) Less than once per week	2) 1-2 times per week	3) 3-5 times per week	4) Nearly daily

→ **7b. How severe?**

1) Slight	2) Moderate	3) Severe	4) Very severe

→ **7c. How much did it distress or bother you?**

0) Not at all	1) A little bit	2) Somewhat	3) Quite a bit	4) Very much

Scoring method and interpretation

1. Sum all scores of a, b, and c for each symptom. For example, dizziness score = 7a+7b+7c.

2. If any person did not experience the symptom give 0 for all the items of the symptom.

3. Thus, possible score range for each symptom will be 0 to 12. These 7 combined scores will be used to get Cronbach's alpha.

4. To get total symptom score, sum all the 7 combined scores. Thus, the total possible score range is 0 to 84 (12*7).

5. Higher scores indicate more severe heart failure symptoms.

Section 5: Personal Health Questionnaire – 8

SMRC
Self-Management
Resource Center

Personal Health Questionnaire
Depression Scale (PHQ-8)

Over the **last 2 weeks**, how often have you been bothered by any of the following problems?
*(circle **one** number on each line)*

How often during the past 2 weeks were you bothered by...	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself, or that you are a failure, or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3

Scoring

If two consecutive numbers are circled, score the higher (more distress) number. If the numbers are not consecutive, do not score the item. Score is the sum of the 8 items. If more than 1 item missing, set the value of the scale to missing. A score of 10 or greater is considered major depression, 20 or more is severe major

depression.

Characteristics

Tested on 1165 subjects with chronic conditions.

No. of items	Observed Range	Mean	Standard Deviation	Internal Consistency Reliability	Test-Retest Reliability
8	0-24	6.63	5.52	.86	NA

Source of Psychometric Data

U.S. National Chronic Disease Self-Management Study. Study described in Ory MG, Ahn S, Jiang L, et al. National study of chronic disease self-management: six month outcome findings. Journal of Aging and Health. 2013 [in press].

Comments

This is an adaptation of the PHQ-9 scale. Since this scale is self-administered in our studies, question #9, "How often during the past 2 weeks were you bothered by thoughts that you would be better off dead, or of hurting yourself in some way?", was deleted. This scale available in Spanish.

References

Kroenke K, Strine TW, Spritzer RL, Williams JB, Berry JT, Mokdad AH. The PHQ-8 as a measure of current depression in the general population. J Affect Disord. 2009; 114(1-3):163-73.

Razykov I, Ziegelstein RC, Whooley MA, Thombs BD. The PHQ-9 versus the PHQ-8--is item 9 useful for assessing suicide risk in coronary artery disease patients? Data from the Heart and Soul Study. J Psychosom Res. 2012; 73(3):163-168.

Self-Management Resource Center
711 Colorado Avenue Palo Alto CA 94303 (650) 242-8040

Section 6: Semi-structured Interview Guide

Symptom Experience Interview guide

Person

To get started, could you tell me a little about yourself so I can get to know you? (probes: living situation, kids, marital status, job, education, etc.)

Great! Thank you for sharing. Now, let's talk about your heart condition and symptoms. I am very interested in how you experience and deal with your symptoms. You have heart failure and having this disease may make you experience physical or emotional discomforts. So, I would like to talk about your symptoms with you if you are comfortable with that.

Perception

1. I would like you to think back to the last 4 weeks. What symptoms did you experience related to your heart condition? (Probes: If you are having trouble thinking of symptoms, I can give you examples: SOB during daytime or lying down, fatigue or lack of energy (need to rest, difficulty with ADLS), chest pain, leg or ankle swelling, difficulty sleeping, dizziness or loss of balance, little interest/pleasure in doing things, feeling down/depressed/hopeless, feeling worried, poor appetite or overeating, trouble concentrating, speaking slowly, feeling restless)

a. Do any of those symptoms happen together or at the same time? Do any of them happen by themselves?

2. How did those symptoms make you feel? (probe: describe physically and emotionally)
3. When you experience symptoms of heart failure, what does that mean to you?

Evaluation

4. Can you explain to me how severe your symptoms are?
5. How often do they occur? (probe: every day, every week, once a month?)
6. How much do they impact your daily life?
7. What do you think causes your symptoms?
8. Do you think your symptoms can be managed or treated?

Response

9. Let's talk about how you respond to your symptoms. What do you usually do when you are experiencing symptoms? (probes: What do you do when you have symptoms that are getting worse? Do you respond to each symptom differently or adjust your daily life? Do you change your behaviors, so you do not experience them as frequently or severely? How do you know when to call the doctor? Do you seek help when your symptoms get worse?)
10. Do you have a support system? (probe: does someone take care of you and make sure you are OK or are you taking care of everyone in your house? Do you share with loved ones how you are feeling? Do you feel you have someone to talk

when you are having a hard time with symptoms? Does talking about your symptoms make you feel better?)

11. My last question for you is- Has there ever been a time when you hid your symptoms from someone else or downplayed how bad they were? I will let you think about it for a minute. It could be a family member, friend, in a social setting, your nurses or doctors, etc. (probe: quiet time to reflect) If yes, could you tell me about it? What was going through your mind and what things made you feel like you needed to hide your symptoms?
12. Is there anything else you want to talk about?

Thank you for your answers. Before we finish, I would like to get some feedback about your experience participating in this study and being interviewed. You can be forthright with me. You will not hurt my feelings. We want to know anything we could have done better.

Follow-up questions

1. What was your overall impression of the study?

2. Did you have any problems accessing links or answering survey questions online?

3. How did you like being interviewed on the phone / virtually?

4. What did you think about the length of time it took you to participate in the study?

5. Did the interview questions seem like they were a good fit?

6. What did you like most about the study?

7. What did you like least about the study?

8. Do you have any recommendations on how we could change the study to make it more appealing to you?

9. Anything else you want to add?

Thank you for participating! I really appreciate you. For your gift card, would you like it to be sent to you by text or email? Okay, let me confirm your information with you.

Appendix E: Qualitative Codes and Code Descriptions

Name	Description
COVID-19	The impact of COVID-19 on their family life, health, interaction with healthcare team, feelings of isolation during quarantine, fears around contracting virus with a chronic condition
Emotional symptoms	Emotional symptoms or feelings in general of how emotional symptoms interact with other symptoms
Fear	Expressing feelings of fear or being scared
Feeling like a burden, others feeling sorry for them	Feeling like a burden, not wanting to be a burden to others, or others watching and feeling sorry for them or treating them in a special way
Feeling mentally weak	Expressing weakness relating to what they feel emotionally rather than physical weakness or fatigue
Frustration	Frustration with limitations or how someone treated them / what they said to them
Hopelessness	Expressing feelings of not having hope, like they are desperate to get better, but it is not working, or that there isn't anything to do to overcome the disease

Name	Description
Sadness and feeling depressed	Feeling down, sad, or depressed
Trouble focusing	Expresses feelings of it being hard to focus or symptoms making it hard to focus
Trouble sleeping	Expresses having trouble sleeping, which may be related to other symptoms experienced as well
Worry	Experiencing feelings of worry or anxiety
Financial stress	Insurance, hospitalizations, medications, not being able to work
Person / Demographic	Person variables ± demographic (Marital status, children, age, and SDOH> education, race/ethnicity, area of the U.S., insurance status, etc.)
Physical symptoms	Experiencing physical symptoms and how those symptoms interact with one another or emotional symptoms
Chest pain	Pain or discomfort in the chest
Cough	Experiencing coughing, whether participant relates it to HF or something else
Dizziness	Experiencing dizziness, loss of balance, or feeling lightheaded
Fatigue	Experiencing fatigue, tiredness, increased need to rest, feeling weak physically

Name	Description
Frequent urination	Need to urinate frequently
Lower extremity edema	Swelling or water retention in the legs, ankles, or feet
Shortness of breath	Feeling short of breath, including dyspnea on exertion, nighttime dyspnea, orthopnea
GI symptoms	Symptoms related to GI and appetite
Quality of life	Health related quality of life
Effect on family activities	Symptoms affecting family activities, being able to do things with their family
Impact on daily life and physical functioning	Having trouble carrying out daily activities due to altered physical functioning from symptoms
Support	Support from family, friends, church, etc. or lack there of
Spirituality	Expressing spirituality or religious beliefs and use of prayer
Symptom experience	The symptom experience includes an individual's perception of a symptom, evaluation of the meaning of a symptom and response to a symptom.
Symptom evaluation	People evaluate their symptoms by making judgements about the severity, cause, treatability and the effect of symptoms on their

Name	Description
	lives (Dodd, 2001).
Severity evaluation	People evaluate how severe a symptom is. This also includes evaluation of the threat posed by a symptom, such as whether or not it is dangerous or has a disabling effect (Dodd, 2001)
Cause evaluation	People evaluate where the symptom is coming from or what is causing the symptom
Symptom perception	Perception of symptoms refers to whether an individual notices a change from the way he or she usually feels or behaves.
Symptom response	Responses to symptoms include physiological, psychological, sociocultural and behavioral components (Dodd, 2001).
Changing diet	Changing what they eat, seasonings and salt intake, fluid and water intake
Fears of death	Mentioning feeling scared of death, not wanting to leave family behind
Hiding or downplaying symptoms	Hiding or not fully telling others how they are feeling or what is occurring with their disease process. This can include downplaying how bad symptoms, or the disease is from others
Reducing activity level	Changing activity level based on what symptoms they are experiencing or trying to avoid feeling symptoms they know occur

Name	Description
	when they overwork themselves
Seeking help, doctor, hospital	Reaching out to their doctor when noticing a change in symptoms or seeking help by visiting the doctor or hospital

Appendix F: IRB Approved Dissertation Proposal

Certification of Successful Dissertation Proposal Defense & Admission to Candidacy

MUSC College of Nursing

Student Information

Name: Alexandra Ruppe, BSN, BSPH, RN

The Advisory Committee for the above-named student certifies that the student has completed the required coursework and has now successfully defended the dissertation proposal.

Title of Dissertation Proposal: A Mixed Methods Approach to Symptom Clusters in Black Women with Heart Failure Preserved Ejection Fraction: A Feasibility Study

Date of Successful Defense: April 29th, 2020

We certify that the above-named student is ready for admission to Candidacy and to proceed with dissertation credits for completion of the research plan as outlined in the approved proposal.

Dissertation Committee

Gayenell S. Magwood
Chair

Sandra B. Dunbar
Committee Membe

Committee Member

Committee Member

Dissertation Proposal: A Mixed Methods Approach to Symptom Clusters in Black Women with Heart Failure Preserved Ejection Fraction: A Feasibility Study

SPECIFIC AIMS

Patients with heart failure (HF) have a complex and multi-factorial symptom experience that makes symptom self-monitoring and self-management difficult (1-4). Four out of five patients with HF are hospitalized each year with exacerbations that could be avoided with early detection (1). Heart failure symptoms can be clustered together into symptom clusters to potentially assess risk of exacerbation and allow symptoms to be identified early, monitored, and managed as a cluster (2, 5-21). However, there are several notable gaps in existing HF symptom cluster studies. In a review of the literature, no studies using qualitative or mixed methods (MM) were identified (5-21). While it is known that females with HF have a greater symptom burden, few HF symptom cluster studies have addressed sex differences (2-21). Females experience worse quality of life (QoL) and functional impairment, and have higher rates of edema, depression, exercise intolerance, and dyspnea on exertion compared to males (3, 4). Females with HF are diagnosed or referred to cardiologists later than males and disproportionately receive fewer recommended therapies or less self-management education (22-24). There is a **critical need** to identify sex specific symptom clusters for females with HF. Additionally, HF symptom cluster research lacks racial/ethnic diversity, with the majority of U.S. studies contain at least 70% White participants, despite Black Americans having a 50% higher incidence of HF (7-9, 11-14, 20). There is especially a need for explaining racial

disparities in patients with HF preserved ejection fraction (HFpEF), a type of HF caused by diastolic dysfunction in which relaxation of the left ventricle is impaired from increased stiffness (25, 26). Black Americans with HFpEF tend to be younger, report worse QoL, and have a greater risk of hospitalization than White patients (26).

The **long-term goal** of this research is to examine the symptom experience of Black women with HFpEF and how symptoms cluster in this population. Achievement of this goal could lead to improved education for HF symptom self-management and self-monitoring. The **purpose** of this MM study is to 1) assess the feasibility and acceptability of this proposed study protocol and procedures for ascertaining symptom clusters in Black women with HFpEF and 2) preliminarily analyze and integrate quantitative and qualitative results (27). This purpose stems from the following **research question**: What is the feasibility and acceptability of study processes, resources, and human and data management of a convergent MM study of symptom clusters in Black women with HFpEF? (27, 28). The **rationale** for this study is that determining feasibility and acceptability for recruitment and implementation in a population that is underrepresented in current HF symptom cluster research is a necessary first step to achieving the long-term research goal. If deemed feasible and acceptable, the proposed study will illuminate the experiences of those who are underrecognized, undertreated and have a greater symptom burden, and an MM approach allows for a more comprehensive examination of the HF symptom experience (3, 4). Black female participants with HFpEF will be recruited from Facebook across the U.S. Participants (n=50) will be administered the Minnesota Living with HF Questionnaire (MLHFQ), a 21-item health related QoL instrument, the Symptom Status Questionnaire-Heart Failure (SSQ-HF), which asks

about the presence, frequency, severity, and distress of 7 physical HF symptoms in the last 4 weeks, and the Personal Health Questionnaire Depression Scale (PHQ-8), which asks about the frequency of 8 depressive symptoms over the last 2 weeks (2, 11, 29, 30). Individual, semi-structured interviews guided by qualitative description will be conducted with at least 15 participants to examine the symptom experience of Black women with HFpEF (31-34). The interview guide follows the Symptom Management Model (SMM)'s *symptom experience* dimension and *person* domain, while also integrating domains of the MLHFQ (35, 36). After results are analyzed, common concepts will be compared through simultaneous integration to create a comparative joint display to represent findings (28, 37). This application addresses the following **specific aims:**

AIM 1: Determine feasibility and acceptability of conducting a convergent mixed methods symptom cluster study with a population of Black females with HFpEF (27).

AIM 2: **Explore preliminary HF symptom clusters** of physical and psychological/emotional symptoms by cluster analysis of data collected from MLHFQ, SSQ-HF, and PHQ-8 respondents(n=50) (29, 30, 36).

AIM 3: Explore the SMM's symptom experience dimension and person domain using 15 individual, semi-structured interviews guided by qualitative description (32, 35).

AIM 4: **Integrate qualitative themes and quantitative symptom data to examine confirmation, expansion, and discordance of results** (28).

IMPACT: The National Institute of Nursing Research (NINR) highlighted symptom cluster research as a critical component to advancing symptom science (11). The proposed study will provide valuable insights for recruiting a high-risk and understudied population and determining barriers to success for an MM HF symptom cluster study.

The proposed study would also improve research efforts for the health of women by considering sex and gender influences, a specific goal of the 2019-2023 Trans-NIH Strategic Plan for Women's Health Research (38).

A. SIGNIFICANCE

Heart failure (HF) is a severe cardiovascular disease in which up to 30% of patients die within 1 year after diagnosis (3, 23). HF is the most common cause of hospitalization in the U.S. for those over the age of 65 and almost 1/4th of patients with HF will be readmitted within 6 months after discharge (39). Inpatient hospitalizations for HF cost over $30 billion a year, accounting for over 60% of total HF related costs in the U.S. (40).

A1. Burden of HF symptoms in females: The lifetime risk for developing HF is 1 in 5 for both males and females, yet on average, less than 25% of females are included in HF clinical trials, and females often do not receive the same recommended therapies as men (23). HF is especially burdensome for females, who report poorer health, more depression, worse quality of life and symptom severity, and more frequent and longer hospitalization than males (1, 17, 23, 41, 42). HF with preserved ejection fraction (HFpEF) is more prevalent in females, by a factor of 2 in some studies (23). This type of HF is poorly understood, and more research is needed to characterize the symptom experience (23, 26).

A2. Greater risk and worse outcomes for Black patients with HF: Black Americans are 1.5 times more likely to develop HF compared to White Americans and at a 2.5 times greater risk of dying from HF compared to White Americans (43). Black females have the highest death rate from HF (80.4 per 100,000) compared to white and Hispanic

females (75.3 and 47.0 per 100,000, respectively) (3). Black Americans also often have difficulty recognizing and interpreting symptoms (43). This can lead to delays in seeking treatment and ultimately result in avoidable hospitalizations from HF exacerbations (43). This cascade of events is why understanding the symptom experience and how symptoms cluster for Black females with HFpEF is necessary.

A3. Symptom clusters in HF: A symptom cluster is two or more symptoms that occur simultaneously in a disease (2, 34). Knowledge about how symptoms cluster can help patients to more easily recognize impending exacerbations, be used for developing more targeted and effective interventions, and assist in determining risk for adverse health outcomes (2, 5-21). A small body of literature exists for HF symptom clusters that validates these potential uses (2, 5-21). However, research that has been conducted in this area minimally examines sex differences, does not include qualitative methodologies, and lacks racial and ethnic diversity (2, 5-21). Since few Black females have been included in HF symptom cluster research, it is first necessary to determine if it is feasible to recruit this population, what barriers and facilitators to adequate recruitment exist, and participants' willingness to participate in research studies (27). Qualitative methods are needed to explore the intersection of gender, sex, and race and impact on the symptom experience, as quantitative instruments alone have limited ability in encompassing such factors. Studying the symptom experience and symptom clusters in relation to gender, sex, race, and type of HF is warranted considering the increased burden of HF symptoms, greater risk, and worst outcomes in females, Black Americans, and patients with HFpEF (1, 17, 23, 42, 43).

A4. The intersection of sex/gender, race/ethnicity, and health: Sex/gender and race/ethnicity have a complex interaction that influences health and should be considered when studying symptoms (44). Many factors contribute to the health disparities and worse outcomes that are evident for multiple conditions, such as societal and cultural stressors. This study aims to examine how the intersection of such factors can impact symptom clusters and the symptom experience of Black women with HFpEF using mixed methods (MM). Sex and gender differences in symptom perception and impact are also prevalent in other chronic diseases. Females with Chronic Obstructive Pulmonary Disorder report higher levels of anxiety and depression, worse quality of life, worse perceived control of symptoms, and greater functional impairment (45-48). Women are noted to have increased pain sensitivity and risk, and women with Chronic Venous Disease were found to have worse neuropathic pain (burning, throbbing, and night cramps) compared to males (49). Woman gender in asthma is associated with more severe symptom intensity, frequency, and limitations from symptoms, and women with asthma report poorer quality of life (50). This evidence supports the need for sex/gender specific exploration of symptom clusters and the
symptom experience.

B. INNOVATION AND CONCEPTUAL FRAMEWORK

B1. Innovation: Current HF practice paradigms diagnose and treat males and females using the same guidelines, despite growing evidence of differences in symptom expression, burden and quality of life by sex (1-4, 23). **This study is innovative in that it seeks to shift this paradigm by placing an emphasis on sex and race that was consistently lacking in a review of the literature** (21). This will be done by initially

exploring the symptom experience and symptom clusters for Black females with HFpEF using MM. The convergent MM design is a novel approach to HF symptom cluster research that, to our knowledge, has not been conducted before. Utilizing MM allows for a more comprehensive exploration of the HF symptom experience and symptom clusters for Black women. Symptom clusters are created based on data from questionnaires, which have a limited ability in assessing personal factors and symptom perceptions, evaluations, and responses. Individual, semi-structured interviews guided by qualitative description allow for a straight description of the symptom experience as described by participants (31-34). Examining study feasibility is needed for understanding the nuances of recruitment and data collection within a population of Black females with HFpEF and validation of the SSQ-HF in this population (27). A review of HF symptom cluster literature revealed that of the eight studies conducted in the U.S., five had >70% white participants, and the SSQ-HF has not been well validated in a Black population (7-9, 11-14, 20, 29). Findings from this study could potentially improve inclusion of the population in future research, thus increasing generalizability of HF symptom cluster research long-term.

B2. Conceptual Framework: The Symptom Management Model (SMM), based on the Symptom Management Theory (SMT), highlights the multi-faceted nature and complex interactions of symptom components (35). Symptom experience, components of symptom management strategies, outcomes and symptom status, person, environment, and health and illness are the six components that comprise the SMM (35). For the present study, symptom experience and person influence the semi-structured interview guide, as these components are well suited for individual interviews, best answer the

overall research question, and were chosen because they allow for exploration of demographic, psychological, and sociological factors that can influence the symptom experience of a Black woman with HFpEF (35). These components will also guide content analysis of interview data and the triangulation of questionnaire and interview results (35). The three domains of the MLHFQ (physical symptoms, emotional symptoms, and QoL) also influenced interview guide questions, which sets the stage for merging of quantitative and qualitative results (28, 36).

C. APPROACH

C1. Design Overview: d

C2. Preliminary studies: In an integrative review of HF symptom cluster science, the PI noted the following prominent findings (21). Current research has validated the existence of HF physical symptom clusters and emotional/psychological symptom clusters and has shown that physical symptoms can cluster with emotional/psychological symptoms (2, 5-7, 9, 10, 20, 13-16, 19). One study found identical symptom clusters for males and females; however, females reported significantly higher distress from symptoms (12). Those who were younger reported more psychological and emotional distress, with no relation to actual severity, and higher education levels were associated with lower symptom severity (5, 8, 9, 11, 19). Symptom clusters can also be used to assess risk of mortality, disease-specific health status, cardiac event-free survival, cardiac event risk, and predicted hospitalization (6-8, 10, 12, 18, 19). The literature also supports the importance of recognizing emotional/psychological symptoms in patients with HF, as they can be the most distressing of HF symptoms and result in the highest risk for adverse outcomes (5, 6, 9, 10, 12-14, 17, 20).

C3. Setting: The study population will be recruited through Facebook using ads and posts within Facebook groups.

C4. Inclusion/exclusion criteria: Inclusion criteria include being a Black female with a self-reported diagnosis of HFpEF (ejection fraction greater than or equal to 50%). Participants must be in the age range of 35 to 74 years old. This age range was determined after a consultation with the dissertation committee HF expert to be representative of most females with HF, while excluding ages that are more likely to result in outliers. Exclusion criteria include having a diagnosis of a severe or end-stage disease, stroke or myocardial infarction in the last 6 months, hospitalization in the last 4 weeks, or if the patient is currently experiencing a HF exacerbation that requires hospitalization.

C5. Recruitment and retention: After receiving IRB approval, participants will be recruited using Facebook posts and ads. Facebook respondents will self-report a diagnosis of HFpEF from a healthcare provider and state their ejection fraction to determine eligibility. Electronic flyers will be distributed via email or Facebook, and will contain study purposes, contact info, a link to the REDCap® screening questionnaire, and will offer an amazon electronic gift card. Participants will also be called to complete screening via phone if interested. If eligible, the PI will provide a link to the REDCap® survey. All survey respondents will be asked about interview participation interest and contact preferences. The PI will reach out to all participants interested in scheduling an interview and will coordinate a time that works best for the subject for informed consent and interviews via phone. Participants will also have the option to meet virtually through a free and HIPAA compliant platform if they have the technological capability.

D. AIM 1: FEASIBILITY Determine feasibility and acceptability of conducting a convergent mixed methods symptom cluster study with a population of Black females with HFpEF (27).

D1. Sample size: This study will utilize purposive sampling to ensure the inclusion of only Black women with HFpEF (52). To determine the sample size for the feasibility study, Leon, Davis, and Kraemer propose a pragmatic approach based on recruitment and needs for establishing feasibility (53). We estimate it will take approximately 2 hours to recruit each potential participant, including calling or emailing the participant, leaving a voicemail, follow-up calls, screening, etc. Further assuming that the PI will be able to spend approximately 25 hours per week (~100 hours a month) actively recruiting, this would result in approximately 50 potential participants a month. If 20% of participants agree to participate, that would result in 10 enrolled participants a month. Since the study is being conducted over 5 months, this would result in a sample size of 50 participants. Therefore, feasibility data will be collected for at least 50 participants.

D2. Variables: Consent rate, recruitment rate, interview interest rate, survey completion rate, feasibility/acceptability scores, data collection time for interviews, recruitment burden, transcription time, software reliability, adverse patient events, inclusion/exclusion criteria, semi-structured interview questions adequate for answering research question, triangulation of quant and qual results

D3. Procedures: Participants fitting the inclusion criteria will be recruited as previously described. To further determine eligibility, the screening form within REDCap® will be accessed and completed by the participant via a link or by the PI in the case of a participant phone call. All screening data will be saved, regardless of whether the patient

is eligible for study participation, for feasibility purposes of assessing inclusion/exclusion criteria. Participants will be asked to provide consent to be contacted for questionnaire and interview portions and to signify their contact preferences. If the patient is deemed eligible for study participation after screening, the PI will provide a link for REDCap® questionnaires or determine a time that works best for the participant to complete aspects of the study via phone. Demographic information will be collected using the REDCap® demographic questionnaire and participants will complete the questionnaires. If the participant is completing study aspects over the phone with the PI, notes will be transcribed to capture the approximate time for completion and any verbalized or observed problems with instrument items or instructions. Following questionnaire completion, participants will be asked if they are interested in participating in an interview. The PI will select participants based on the sampling frame and conduct semi-structured interviews using the interview guide. After the questionnaires are administered and/or the interview is completed, the AIM and FIM questionnaires will be administered to assess participant acceptability and feasibility (51). Feasibility and acceptability measures will be recorded in Excel throughout the entire process. These measures include whether approached subjects agree to participate, number of participants recruited each week and month, completion rate of MLHFQ, amount of time it takes to complete each aspect and the study and total time for all components, functionality and acceptability of data collection platforms.

D4. Data management: All questionnaires will be developed using MUSC's REDCap® application and will be stored on REDCap®'s secure, password-protected server. To minimize risk of missing data, the survey within REDCap® will not allow submission

unless every questionnaire item has an answer. An item can only be skipped if a participant explicitly refuses to answer. In this case, the PI will record a 9 on the questionnaire in REDCap®. Data will remain in REDCap® until analysis, during which it will be exported to SPSS. No patient identifiers will be exported to SPSS and only dissertation committee members will have access to participant data. Exporting of data will be tested before study employment to ensure consistent data formatting. Data on feasibility and acceptability variables will be stored in a secure, password-protected BOX folder on MUSC's server.

Data analysis. The feasibility of study processes, resources, and human and data management will be analyzed as the primary aim of this study (27). The consent rate will be determined by calculating the percentage of eligible participants who consent by completing the next survey, with a goal consent rate of >90%. The recruitment rate will be determined by calculating the percentage of participants successfully recruited out of the recruitment goal. Recruitment of >85% of the 50 participants goal is the benchmark. The interview interest rate will be determined by calculating the percentage of participants who indicate interest in being interviewed, with a goal interview interest rate of >30%. Surveys will be examined for missing data and the percentage of surveys with missing data will be calculated. The survey completion rate goal is >85% fully completed surveys. The feasibility and acceptability question results will be analyzed by calculating a mean score. A mean score of 3 or greater on a scale of 0-5 will support participant acceptability and feasibility. Time to complete interviews will analyzed by calculating the mean and range of interview length. The goal interview length time will be less than 1 hour per interview. Time spent recruiting each week will be tracked and averaged per

week, with a goal of <20 hours spent per week recruiting. Time spent editing transcripts for accuracy will be tracked and averaged, with a goal of <2 hours per interview. Software reliability and adverse patient events will be tracked, with the goal of no major events.

E. AIM 2: QUANTITATIVE Explore preliminary HF symptom clusters of physical and psychological/emotional symptoms by completing cluster analysis of data collected from MLHFQ, SSQ-HF, and PHQ-8 respondents (n=50) (29, 30, 36).

E1. Sample Size Consideration: Sampling method and size for the quantitative portion of the study are the same as previously described for the feasibility aim. A sample size of 50 Black females with HFpEF will allow for *preliminary* clustering of symptoms within this feasibility study.

E2. Variables: MLHFQ physical symptoms (edema, fatigue/increased need to rest, fatigue/low energy, shortness of breath, sleep difficulties), emotional/psychological symptoms (worrying, feeling depressed, cognitive problems), QoL score, SSQ-HF symptoms (presence, frequency, severity and distress of shortness of breath, orthopnea, fatigue, chest pain, lower extremity swelling, difficulty sleeping, dizziness or loss of balance), PHQ-8 responses, age, self-reported ejection fraction, length of time diagnosed with HF, marital status, number of children, household number, highest level of education, height, weight, body mass index, presence of co-morbidities (hypertension (HTN), high cholesterol (HLD), diabetes mellitus (DM), atrial fibrillation (AFIB), coronary artery disease (CAD), asthma, COPD, obstructive sleep apnea (OSA)

E3. Procedures: Demographic and clinical features on each participant will be collected and analyzed using a combination of the screening form and a demographic

questionnaire, which include the variables listed above. Comorbidity diseases were chosen due to commonality in patients with HF and their potential impact on HF symptoms (2, 5-21). The questionnaires will be administered to participants before qualitative interviews to minimize bias (36). The MLHFQ is a quality-of-life questionnaire designed for patient with HF in 1984 by Rector and Cohn (36). The questionnaire includes 21 questions related to the impact of physical symptoms, emotional/ psychological symptoms, and HF related activities on daily life (36). To complete the questionnaire, the participants rate how much an item affected their life in the past month (4 weeks) using a Likert scale of 0-5 with 0 indicating none, 1 very little, and 5 very much (36). The total score ranges from 0 to 105, with a higher scoring indicating worse quality of life and more impact from symptoms and components of HF. The MLHFQ has excellent internal consistency with a Cronbach's α usually ranging from 0.89-0.96 and has shown success in forming symptom clusters in multiple other HF symptom cluster studies (2, 5-7, 9, 17, 18, 20, 36). The questionnaire is short, easy to administer, and has been validated for its psychometric properties (2, 5-7, 9, 17, 18, 20, 36). The domains of the MLHFQ align with study aims and are also implemented in qualitative interviews for data collection consistency. The SSQ-HF is a HF symptom scale established in 2015 that measures the presence, frequency, severity, and distress of 7 physical symptoms mostly commonly reported in HF in the last 4 weeks (29). If a symptom is present, the respondent then rates frequency, severity, and distress using a Likert scale of 1-4, with 1 being less and 4 being most (29). The Cronbach's α for the SSQ-HF is 0.80 and matches the time frame of the MLHFQ (29, 36). The PHQ-8 asks respondents to rate severity of 8 depressive symptoms from 0, not at all, to 3, nearly

every day, over the past 2 weeks (30). This depressive symptom scale is widely used and has a Cronbach's α of 0.83 (30). The participants will read instructions and complete the questionnaires via the REDCap® link, or the PI will read questionnaire items to the participant and record answers in REDCap®.

E4. Data management: Data management practices for the quantitative aim are the same as previously described for the feasibility aim.

Demographic and clinical data analysis. Demographic and clinical variables will be analyzed within SPSS for frequencies and valid percentages and means and standard deviations for descriptive statistics. Results will be displayed in a demographics table.

Cluster analysis. A hierarchical cluster analysis will be used to explore preliminary symptom clusters of physical and emotional/psychological symptoms included in the MLHFQ, SSQ-HF, and PHQ-8 (29, 30, 36, 54, 55). The hierarchical cluster method was chosen because it can be used to cluster variables (symptoms) rather than just cases (study participants) (54, 55). It also allows the researcher to select the best number of clusters after running the analysis rather than having to define the number of clusters at the start, such as in K-means clustering (54, 55). Hierarchical clustering creates compact and homogenous clusters and differences in clusters are maximized (2, 9, 54, 55). The 3 main steps to hierarchical clustering are to calculate distances between variables, link clusters, and then determine the right number of clusters based on dendrogram results (55). For this study, each variable (symptom) will be placed in a separate column and participant data (responses to the questionnaire) will be placed across each row within SPSS and a hierarchical cluster analysis will be run. The analysis will be conducted by clustering variables (symptoms). Therefore, all questionnaire items that represent the

symptoms will be selected as the variables for the analysis. In plots, the dendrogram option will be selected. A dendrogram is a tree like structure that shows a graphic visualization of how clusters are related (55). Branches are based on semi-partial r-squared scores and smaller branches signify more similar clusters (55). All variables will be merged into a single cluster at the start since this is an exploratory analysis and the best number of clusters is unknown. Next, Euclidean distance is the selected method for calculating distance, and it determines which cases are most similar by calculating the square root of the sum of squared distances (55). This method is commonly used for interval level data and places an emphasis on larger distances since it is squared. For clustering method, the ultimate goal is to use Ward's method of clustering, as it is best for maximizing significant differences between clusters by using the *F* value (55). However, single-linkage clustering is best for identifying outliers. Therefore, a single-linkage analysis will be run first to remove outliers and then Ward's method will be used once outliers are removed. The PI will confer with the research team statistician to determine best number of cases by visually examining the dendrogram for dissimilarity between clusters and drawing a cut-off line (55). The analysis will then be repeated, specifying number of cases at the start.

F. AIM 3: QUALITATIVE Explore the SMM's symptom experience dimension and person domain using 15 individual, semi-structured interviews guided by qualitative description (31, 36).

F1. Sample Size: The goal sample size for interviews is 15. We will assess for data saturation during the qualitative data analysis of interviews.

F2. Recruitment and retention: A purposive sampling strategy will be used to recruit at least 15 Black females with HFpEF for the individual, semi-structured interviews. The PI will reach out to all individuals interested in being interviewed to ensure every participant who wants to be interviewed has the opportunity.

F3. Variables: Codes and themes derived from the qualitative analysis will be grouped within SMM's symptom experience dimension and person domain and MLHFQ domains.

F4. Procedures: Individual interviews will be conducted via a free HIPAA compliant videoconference platform, or via telephone if unable to complete through videoconference. The PI will ask participants open-ended questions in a semi-structured interview format about their personal background (e.g., living situation, kids, marital status, job, education) and symptom experience. The interview guide was developed by combining components of the SMM and domains of the MLHFQ (35, 36). An interview guide facilitates consistency in data collection while also allowing for unanticipated responses (31). Participants will be asked to describe their symptoms in the last 4 weeks to correspond with the MLHFQ symptom recall time frame (36). Probes, both questioning and silent, will be used to facilitate thoughtful responses from participants (31). Mirroring during interviews will be utilized to ensure the PI is capturing the true perspective of each participant (31). Individual interviews allow participants to freely share their experience while maintaining confidentiality and allows for higher credibility and validity than focus groups (31).

F5: Data management: Interview audio will be recorded directly on the mobile device being used for the clearest sound quality, and transcribed verbatim. An encrypted, secure,

and HIPAA compliant platform will be used for interview transcription. The PI will confirm the accuracy of transcriptions for all interviews and make edits as needed. The audio recordings and transcripts will be kept in a password protected, electronic folder in MUSC's BOX per IRB requirements. Audio recordings will be destroyed once transcriptions are complete to protect the identity of participants. After transcription, NVivo® will also be used to support thematic coding and analysis by the PI in consultation with dissertation chair (Dr. Magwood, Professor, MUSC) and committee HF expert (Dr. Dunbar, Professor, Emory University).

Data analysis. Qualitative description will guide qualitative analysis of interview data (31-34). The PI will first read through transcripts completely and highlight identified text that may represent aspects of the symptom experience phenomenon (34). This first step is meant to increase trustworthiness by not allowing broad code structures to result in the PI missing important findings that do not fit within the selected frameworks (34). A directed approach to content analysis will then be used with SMM components and MLHFQ domains as broad code types to guide development of sub-codes (34-36). Interviews will be transcribed and analyzed as they are collected using a constant comparative method (31). Two to three transcripts will be analyzed at a time and then codes will be revised as needed (31). The PI will keep a detailed audit trail throughout data collection and analysis to support dependability (31). A detailed audit trail will be valuable in ensuring reproducible methods in a future study (31). The PI has personal experiences from caring for Black females with HF. Therefore, bracketing of those experiences is required before beginning data collection or analysis to increase objectivity (31).

G. AIM 4: INTEGRATION OF RESULTS FROM AIM 2 AND 3 **AIM 4**: **Integrate qualitative themes and quantitative symptom data to examine confirmation, expansion, and discordance of results (28, 37).**

G1. Procedures: Quantitative data and qualitative data will be collected simultaneously and analyzed separately, as previously described (28). Results from will then be merged through triangulation with the components of the SMM and MLHFQ (28, 35, 36).

G2. Data management: Quantitative and qualitative data will continue to be managed as previously described. Data integration files will be stored in a secure, password-protected BOX folder on MUSC's server.

Data analysis. Preliminary symptom clusters and interview themes will undergo simultaneous integration (28). This involves first identifying common concepts. Common concepts will be identified by triangulating results with SMM components and MLHFQ domains (28, 35, 36). Common concepts will then be compared and contrasted to determine how results interact (28). Outcomes from the MM analyses will be used to interpret and explain the convergence or divergence in the results (28). This analysis will provide a richer understanding of the symptom clusters and the symptom experience. Findings will be represented using a comparative joint (28, 37).

H. POTENTIAL PROBLEMS, ALTERNATIVE STRATEGIES, AND BENCHMARKS FOR SUCCESS

H1: Challenges in mixed methods design: MM requires skills and experience with both quantitative and qualitative data collection and analysis, which is challenging for any researcher, especially a novice. However, the dissertation team behind this proposed study has immense experience across a wide spectrum of specialties, and their expertise

will be essential to the success of this study. MM studies also require considerable time and resources. Timeliness is essential, and the PI will continually analyze qualitative data while still conducting other study aspects. Also, integration of results is another skill set and will require considerable time, effort, and collaboration with the dissertation committee.

H2: Recruitment challenges: Due to COVID-19, face-to-face interactions are not currently possible. Recruiting via electronic flyers and calls can be challenging in establishing trust. Recruitment strategies include tailored social media ads using Facebook Ad Manager and collaborating with admins of HF support groups on Facebook. Participants would complete the survey via a REDCap® link and provide their phone number if interested in being contacted for an interview. Snowball sampling could be used to allow participants to share the ad with others that may qualify. Facebook ad manager would allow for detailed tracking of recruitment efforts to support the feasibility aim. The challenge that arises from this recruitment strategy is using self-report of HFpEF diagnosis from participants. HFpEF is a complex disease process that providers themselves find difficult to diagnosis (57). Asking participants to self-report their diagnosis is inferior to a confirmed diagnosis from a medical chart.

H3: Generalizability: This study aims to assess the feasibility of an MM study. A sample size of 50 is adequate for fulfilling feasibility aims; however, the sample size is not adequate to form significant symptom clusters. Future research will be needed to create generalizable symptom cluster evidence.

H4: Future research: If this study shows promise of feasibility, future research will include conducting a full MM research study. With a clear and validated study protocol

and plan, a full study could create new evidence for the symptom experience and symptom clusters for Black women with HFpEF. Findings could be used to create tailored symptom education and self-management strategies for this high-risk population.

H5: Benchmarks for success:

Feasibility Outcomes

Feasibility component	Indicator	Criteria
Process		
Consent rate	% of eligible participants consented by completing next survey	>90% consent rate
Recruitment	% of participant recruitment goal	>85% of recruitment goal (goal N=50 for survey, goal N=15 for interview)
Interview interest rate	% of participants interested in an interview	>30% interview interest
Survey completion rate	% of completed surveys	>85% fully completed surveys
Feasibility / acceptability scores	Average scores ranging from 1-5	Average score of 4 or higher
Resources		

Data collection time - Interview	Interview duration average	≤ 60 minutes
Recruitment burden	Time spent with recruitment / week	< 20 hours
Management		
Transcription time	Time spent with transcription / editing transcripts	< 2 hours / interview
Software reliability	Issues with software / data management platforms	No major events
Adverse patient events	Adverse events during data collection	No major events

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PROTECTION OF HUMAN SUBJECTS

The proposed study qualifies for Institutional Review Board (IRB) exempt review categories 2 and 4. Feasibility, questionnaire and interview data will be collected and analyzed from participants. Medical University of South Carolina (MUSC)'s IRB will serve as the main governing body from which the primary investigator (PI) will seek IRB approval.

Risks to Human Subjects

There is minimal risk to human subjects for the proposed study. Purposive sampling will be used to recruit a minimum of 50 participants from Facebook and word of mouth.

Inclusion criteria: female sex, woman gender, Black race, a confirmed or self-reported diagnosis of heart failure preserved ejection fraction, English speaking, and 35 to 74 years old.

Exclusion criteria: a diagnosis of an end-stage co-morbidity, stroke or myocardial infarction in the last 6 months, and currently experiencing an HF exacerbation that requires immediate hospitalization.

After receiving IRB approval, participants will be recruited using Facebook posts and ads. Facebook respondents will self-report a diagnosis of HFpEF from a healthcare provider and state their ejection fraction to determine eligibility. Electronic flyers will be distributed via email or Facebook, and will contain study purposes, contact info, a link to the REDCap® screening questionnaire, and will offer an amazon electronic gift card ($25 for completing the questionnaire and $25 for completing the interview). Participants will

also be called to complete screening via phone if interested. If eligible, the PI will provide a link to the REDCap® survey. All survey respondents will be asked about interview participation interest and contact preferences. The PI will reach out to all participants interested in scheduling an interview and will coordinate a time that works best for the subject for informed consent and interviews via phone. Participants will also have the option to meet virtually through a free and HIPAA compliant platform if they have the technological capability.

First, demographic information will be collected with a questionnaire in REDCap®, where it will be stored on the secure and password protected server. Next, the PI will administer the Minnesota Living with Heart Failure Questionnaire (MLHFQ). The MLHFQ includes 21 questions related to the impact of physical symptoms, emotional/psychological symptoms, and HF related activities on daily life. To complete the questionnaire, the participants rate how much an item affected their life in the past 4 weeks using a Likert scale of 0-5 with 0 indicating none, 1 very little, and 5 very much. The questionnaire will be administered to a minimum of the 50 participants. Next, the PI will administer the Symptom Status Questionnaire-Heart Failure (SSQ-HF). The SSQ-HF asks about the presence, frequency, severity, and distress of 7 HF symptoms in the last 4 weeks using a Likert scale of 1-4 if a symptom is present with 4 being the most frequent, severe, or distressful. Next, the PI will administer the Personal Health Questionnaire Depression Scale (PHQ-8). The PHQ-8 asks about the frequency of 8 depressive symptoms over the last 2 weeks using a Likert scale of 0-3, with 0 being not at all and 3 being nearly every day. Individual, semi-structured interviews will be conducted with at least 15 participants who agree to be interviewed after responding to the questionnaires.

Interviews will also be conducted by telephone or via a HIPAA compliant platform at a time most convenient to the participant. The PI will ask participants open-ended questions about their sociocultural and demographic background and symptom experience. Participants will be asked to describe their symptoms and their response to symptoms in the last 4 weeks. After the MLHFQ is administered and the interview is complete, participants will be asked questions about feasibility and acceptability of the study protocol. It is predicted that all aspects of the study will take less than 2 hours per encounter if an interview is conducted and less than 1 hour if an interview is not conducted.

The risk to subjects is breach in confidentiality about their disease, background and symptom experiences. There is also a risk that asking about symptoms and how they have affected their life in the last month could bring up negative feelings for the participant. Referral to mental health services may be completed by the PI if deemed necessary. It is also possible that the PI determines the participant may be currently having an acute exacerbation of HF in which they need immediate treatment. In this case, the participant would be referred to the clinic or emergency services, depending on perceived severity, and the PI would follow up to ensure safety of the participant.

Adequacy of Protection Against Risks

Every member of the research team will be required to have human subjects research training (CITI), patient privacy training (HIPAA), and any other training deemed necessary by the IRB. Responses to questionnaires will be recorded within REDCap® and will not be tied to any personal identifiers. No patient identifiers will be exported to SPSS and only the PI and members of the dissertation committee will have

access to REDCap®. Audio from interviews will be recorded on a mobile device and uploaded to MUSC's secure BOX server as soon as possible. An encrypted, secure, and HIPAA compliant platform will be used for interview transcription. The audio recordings and transcripts will be kept in a password protected, electronic folder in MUSC's BOX per IRB requirements. Audio recordings will be destroyed once transcriptions are complete to protect the identity of participants.

Withdrawal of Subjects

Participants will be informed that they are allowed to withdrawal from the study at any time or refuse any aspect of the study. If the participant wishes to be removed from the study, the PI will not require anything in writing from the participants. Any information collected on the participant will be destroyed and the total number of withdrawn participants will be recorded for feasibility purposes.

Potential Benefits of the Proposed Research to Human Subjects and Others

There is no direct benefit to participants. Data from this study will be used to potentially support feasibility of a large, mixed methods study that aims to better understand the symptom experience and how symptoms clusters for Black women with HFpEF. This is a notably high-risk population that could eventually benefit from research focused on describing their symptom experience.

Importance of the Knowledge to be Gained

The proposed study has the potential impact of better understanding symptom clusters and the symptom experience for a high-risk and understudied population. Considering the increased burden of HF symptoms, greater risk, and worst outcomes in females, Black Americans, and patients with HFpEF, it is especially important to study

the symptom experience and symptom clusters in relation to gender, sex, race, and type of HF. Also, examining the feasibility of the proposed mixed methods study would allow others in the field to understand the nuances of recruitment and data collection for a Black, urban population of female participants with HFpEF. Data on recruitment efforts for an understudied population could potentially improve inclusion of the population in future research, thus increasing generalizability of HF symptom cluster research long-term.

Study timeline:

Task	Apr 2020	May 2020	Jun 2020	Jul 2020	Aug 2020	Sept 2020	Oct 2020	Nov 2020	Dec 2020	Jan 2021	Feb 2021	Mar 2021	April 2021
Permission for MLHFQ use													
Enter MLHFQ and surveys into REDcap													
Defend proposal													
Present proposal to Emory research council for approval													
Apply for funding													
Test forms on iPad													
Finalize interview guide													
Develop and refine tracking procedures													
Interviewer training													
Submit to IRB, make revisions for approval													
Study recruitment / enrollment													
Data collection													
Data analysis of QUAL													
Data analysis of feasibility and QUANT													
Integration of QUAL / QUANT													
Write manuscripts, assemble compendium													
Submit for publication													
Final dissertation defense													

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