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Understanding the importance of symptom recognition in self-management of heart failure

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Thesis submitted in fulfilment of the requirements for the Degree of Doctor of Philosophy

School of Medicine, Dentistry and Nursing

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Abstract

Background: Heart failure is a clinical syndrome characterised by key symptoms that can be distressing to the affected individual and those caring them. These symptoms are associated with poor quality of life and a high rate of repeated hospital admission in people with heart failure. Thus, the rapid detection and management of symptoms linked to heart failure is important for people and their families. Current evidence related to heart failure is dominated by those of young age, a reduced ejection fraction, and male sex. To support more inclusive and equal symptom assessment and management in heart failure for the entire population, studies that include individuals with all forms of heart failure are essential.

Aim: This thesis investigated the full spectrum of symptoms and associated factors in people living with and dying from all forms of heart failure.

Methods: A sequential, multiple studies design including three studies was adopted, underpinned by critical realism and the Situation-Specific Theory of Heart Failure Self-care. ***Study 1*** was a mixed-methods systematic review and narrative synthesis of existing literature to explore the full spectrum of symptoms experienced by people living with heart failure, and to compare these to those outlined within the European Society of Cardiology (ESC) Guidelines for the management of the syndrome. ***Study 2*** was a secondary analysis of data derived from a randomised control trial of disease management conducted in Australia that included people of varying ages. The analysis investigated sex-stratified differences in symptoms and symptoms change over one year across the full range of heart failure subtypes. ***Study 3*** was a descriptive qualitative study exploring the full spectrum of symptoms, and heart failure-associated breathlessness in the Turkish socio-cultural-behavioural context.

Results: ***Study 1*** indicated that people with heart failure experienced many symptoms, and these symptoms can be very diverse and affected by multiple factors. As well as typical and less typical symptoms identified from the current European Society of Cardiology Guidelines, 37 other symptoms were identified. This includes a dry mouth, numbness in hands/feed, feeling drowsy, difficulty sleeping, and feeling anxious/nervous. Age (younger versus older) and setting (hospital versus community) were associated with various European Society of Cardiology Guidelines' symptoms. There was a paucity of data on women's symptoms in the current literature. ***Study 2:*** Sex-stratified differences were detected in the secondary analysis of the symptomatic status of the trial cohort at baseline and at one-year follow-up. Different factors were associated with worsening symptom trajectory on a sex-specific basis; for men, this included a history of hypertension and non-

English-speaking background; and for women, a history of coronary artery disease and presenting with acute pulmonary oedema. Women with heart failure with preserved ejection fraction had worse symptomatic profiles over one year than women with reduced or mildly reduced ejection fraction. ***Study 3:*** Among 20 Turkish individuals with self-reported heart failure, 31 physical and 7 psycho-socio-behavioural symptoms were reported. Based on a reflexive thematic analysis of semi-structured interviews, knowledge and awareness of heart failure and breathlessness were poor among Turkish individuals. The socio-cultural-behavioural context affected their breathlessness and self-management strategies. They expressed a need for adequate education, psychological support, and long-term management strategies.

Conclusion and Implications: This PhD found a more diverse range of symptoms among the heart failure population than have previously been described. Symptoms such as difficulty sleeping, drowsiness, dry mouth, and feelings of anxiety and nervousness—though less typical—require attention to improve their management in heart failure. Additionally, socio-demographic and clinical profiles affect individual experiences of different symptoms. In routine clinical practice, identification of this more diverse range of symptoms can be achieved by applying a more individualised person-centred symptom assessment protocol. Consequently, health care providers can then support self-management strategies to enable appropriate person-centred symptom assessment.

Lay summary

Heart failure is a health problem that affects 1%–2% of adults. Heart failure occurs when the heart is not pumping blood as well as it should. This affects every part of the body, including the lungs. Symptoms of heart failure include shortness of breath (sometimes, even at rest), feelings of increasing tiredness and weakness, plus swelling of the ankles. Sometimes these symptoms can be so bad that people need to go to the hospital. These symptoms affect both the person with heart failure and their families. Naturally, when people experience symptoms, they try to manage them as best they can without knowing why they are happening. Previous studies of symptoms and heart failure have typically included more males, younger people, and those who develop heart failure following a heart attack. This means that we have limited knowledge of symptoms in many people affected by heart failure, including females, older people, and those who develop heart failure without heart attack. This lack of knowledge also includes people from different cultures and backgrounds who can have different symptoms due to heart failure as well. So, this PhD focused on studying all the symptoms that any person with heart failure might experience, regardless of their sex, age, medical history and where they come from.

The first thing I did was look at the information that was already available from previously published research studies. I wanted to know how many symptoms were reported and how common they were. I found there were more symptoms than we originally thought, and that younger and older people had different symptoms. People in hospitals also had different symptoms than those who were living in their homes. Overall, I concluded that there was not enough information about the symptoms that women with heart failure experience. Nor was there enough information on the symptoms people (men and women) with all types of heart failure have.

I then analysed the data collected from a trial that tested two different types of heart failure care in a typical group of older men and women with all forms of the condition. I found that there were key differences in symptoms reported by men and women, and these symptoms depended on what type of heart failure they had. Follow-up after a year showed that these symptoms got worse, and were different for men and women according to their background and medical history.

Finally, I spoke with people in Türkiye who said that they had heart failure, discussing their breathing problems and other symptoms. They told me that they had a range of physical symptoms, as well as some emotional symptoms. They indicated that they did not clearly understand how their heart failure would cause the significant and common breathing problem they reported, and that it had affected their religious practices and beliefs. In response, they tried using cultural methods to manage their breathing problems without success. They expressed a need for education, emotional support, and long-term assistance.

This research discovered that the symptoms associated with heart failure are very different in different people. Sometimes, people with heart failure might have trouble sleeping, feel very sleepy, have a dry mouth, or feel worried. These things are not very common, but it is important to take care of them. Also, how someone feels can be different based on their age or other health issues. All symptoms greatly affect the affected person’s quality of life. All can be better managed if those caring for people with heart failure listen more closely to what that person has to say about their symptoms.

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List of publications/dissemination of the research

All papers and conference presentations arising from this thesis are listed below:

Publication:

- **Paper (Chapter 6):** Seckin, M., Johnston, B., Petrie, M. C., Stewart, S., & Chan, Y.-K., "Characteristics of symptoms and symptom change across different heart failure subtypes: A sex-stratified analysis", *European Journal of Cardiovascular Nursing*, 2022, zvac099, https://doi.org/10.1093/eurjcn/zvac099

Conference presentations:

Oral presentations:

- ***Oral presentation at RCN International Nursing Research Conference 2023 in Manchester***

  Title: "Symptoms and associated (biological, psychological, and cultural) factors in people with heart failure."

- ***Oral Abstract Presentation at ACNAP 2023 in Edinburg***

  Seckin, M., Johnston, B., Stewart, S., & Petrie, M. C. (2023). "Full spectrum of symptoms associated with heart failure: a mixed-method systematic review and narrative synthesis." *European Journal of Cardiovascular Nursing*, Volume 22, Issue Supplement_1, August 2023, zvad064.152. https://doi.org/10.1093/eurjcn/zvad064.152

- ***Oral Presentation at STIR-UP Research Event 2023 in Stirling***

  Title: "Understanding symptoms and associated (biological, psychological, and cultural) factors in people at different stages of the heart failure journey (including palliative and end-of-life care)."

- ***Free paper presentation at Palliative Care Congress in Edinburgh*** (2023)

  Seckin, M., Johnston, B., Petrie, M. C., & Stewart, S. (2023). "19 Typical and less typical symptoms associated with heart failure: a mixed-method systematic review and narrative synthesis." http://dx.doi.org/10.1136/spcare-2023-PCC.19

- Presented the second study of my PhD thesis in the Induction Day for Singaporean students in Nursing at the **University of Glasgow** (2022)

Title: "Sex-stratified differences in symptom profile and trajectory according to underlying heart failure subtypes."

- Presented the second study of my PhD thesis at the ***School of Medicine, Dentistry and Nursing Postgraduate Research Day***, University of Glasgow (2022)

  Title: "Heterogeneity in men and women with different heart failure subtypes."

- Presented my PhD thesis in the ***University of Glasgow 3MT competition*** (2022)

  3MT 2022 – Muzeyyen Seckin – MVLS – Individual symptoms and person-led care intervention in heart failure. https://www.youtube.com/watch?v=fC0Uarx4wMc

- Presented my PhD thesis in the ***University of Glasgow 3MT competition*** (2021)

  3MT 2021 – Muzeyyen Seckin – MVLS – Symptoms and person-led care in heart failure. https://www.youtube.com/watch?v=c80qCAzMkKY

- Presented the first study of my PhD thesis in the ***School of Medicine, Dentistry and Nursing Postgraduate Annual Review Presentation Day***, University of Glasgow (2021)

  Title: "Typical and atypical symptoms and person-led care interventions in heart failure."

- Presented my PhD thesis in the ***University of Glasgow 3MT competition*** (2020)

  3MT 2020 MVLS – Muzeyyen Seckin – Symptoms and Person-led Care in Advanced Heart Failure. https://www.youtube.com/watch?v=ud1wGkIVBn0

Poster presentations:

- At **13th EAPC World Research Congress 2024** (Barcelona, Spain) (accepted)

  Title: "Understanding the full spectrum of symptoms experienced by individuals with heart failure."

- At **EANS 2023 Summer Conference** (Oslo, Norway)

  Title: "Breathlessness experience of Turkish individuals with self-reported heart failure: A qualitative study."

- At ***ACNAP 2023 in Edinburgh***

  Seckin, M., Johnston, B., Stewart, S., & Petrie, M. C. (2023). "'Not being able to breathe is the end of the world': a descriptive qualitative study of breathlessness experiences of individuals with heart failure in Turkey." *European Journal of Cardiovascular Nursing*, Volume 22, Issue Supplement_1, August 2023, zvad064.15. https://doi.org/10.1093/eurjcn/zvad064.153

- At ***Palliative Care Congress in Edinburgh*** (2023)

  Seckin, M., Johnston, B., Petrie, M. C., & Stewart, S. (2023). "169 Breathlessness experiences of individuals with heart failure in Turkey: a descriptive qualitative study." http://dx.doi.org/10.1136/spcare-2023-PCC.189

- At the ***School of Medicine, Dentistry and Nursing Postgraduate Research Day***, University of Glasgow (2021)

  Title: "Understanding individual symptom experiences and influencing factors in heart failure: A mixed-methods systematic review."

- At the ***Palliative Care and Heart Failure Virtual Conferences in Birmingham*** (2021)

  Title: "Understanding individual symptom experiences and influencing factors in heart failure: A mixed-methods systematic review."

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Finally, I want to express my gratitude to everyone who kindly gave me their time when I was pursuing my PhD. It was an expensive, meaningful gift that will be etched in my memory. I wish you health and happiness forever.

Thesis dedication

To individuals living with heart failure and their informal caregivers:

This thesis and its experiences are dedicated to your well-being and care. It is my sincere hope that this endeavour will assist you in enhancing your quality of life by fostering a deeper understanding of multiple symptoms associated with heart failure.

Throughout this journey, two vital lessons have emerged. First, it is essential to recognise that experiencing some symptoms is an aspect of living with heart failure. Awareness of this fact empowers you to deal effectively with these symptoms and manage their impact on your daily life. Second, life is replete with unpredictable events, necessitating a focus on cultivating personal happiness and establishing life goals that bring you joy and fulfilment, regardless of the challenges encountered.

May you always strive to attain happiness and optimal health to the best of your ability.

Sincerely.

Author’s declaration

I hereby declare that, except where explicit reference is made to the contribution of others, this PhD thesis is the result of my own work and has not been submitted for any other degree at the University of Glasgow or any other institution.

Printed name: Muzeyyen Seckin

Abbreviations

Abbreviation	Description
ACEi	Angiotensin-converting Enzyme Inhibitor
AF	Atrial Fibrillation
AHF	Acute Heart Failure
AI	Artificial Intelligence
ARBs	Angiotensin Receptor Blockers
BNP	B-type Natriuretic Peptide
CAD	Coronary Artery Disease
CHF	Chronic Heart Failure
CI	Confidence Interval
CINAHL	Nursing and Allied Health Literature database
COPD	Chronic Obstructive Pulmonary Disease
COREQ	The Consolidated Criteria for Reporting Qualitative Research
CR	Critical Realism
CRF	Chronic Renal Failure
CRT	Cardiac Resynchronization Therapy
DM	Diabetes Mellitus
Embase	Excerpta Medical Database
ECG	Electrocardiogram
EF	Ejection Fraction
EoL	End of life
ESC	European Society of Cardiology
GBD	Global Burden of Disease
GDPR	General Data Protection Regulation
HF	Heart Failure
HFmrEF	Heart Failure with Mildly Reduced Ejection Fraction
HFpEF	Heart Failure with Preserved Ejection Fraction
HFrEF	Heart Failure with Reduced Ejection Fraction
HRQoL	Health-related Quality of Life
ICD	Implantable Cardioverter Defibrillators
IHD	Ischemic Heart Disease
IPOS	Integrated Palliative Care Outcome Scale
JBI	Joanna Briggs Institute
JVP	Jugular Venous Pressure
KCCQ	Kansas City Cardiomyopathy Questionnaire
LVAD	Left Ventricular Assist Device
LVEF	Left Ventricular Ejection Fraction
Medline	Medical and Biomedicine database
MeHS	Medical Subject Headings
MRAs	Mineralocorticoid Receptor Antagonists
MMSR	Mixed-methods Systematic Review
MRC	Medical Research Council
NHIR	National Institute for Health Research

NICE	National Institute for Health and Care Excellence
NT-proBNP	N-terminal Pro-B-type Natriuretic Peptide
NYHA	New York Heart Association
PPI	Patient and Public Involvement
PROs	Patient-reported Outcomes
PROMs	Patient-reported Outcome Measures
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International Prospective Register of Systematic Reviews
PsycINFO	Psychological Literature database
QoL	Quality of Life
RCTs	Randomised Control Trials
SGLT2i	Sodium Glucose Cotransporter-2 Inhibitor
SIGN	Scottish Intercollegiate Guide Network
SMM	Symptom Management Model
TJCN	Turkish Journal of Cardiovascular Nursing
TSC	Turkish Society of Cardiology
TSM	Theory of Symptom Management
UK	United Kingdom
USA	United States of America
WHICH? Trial	Which Heart Failure Intervention is Most Cost-effective in Reducing Hospital Stays?
WHO	World Health Organisation

Chapter One - Introduction

1.1. Introduction

This chapter is the introductory section to this PhD thesis. It identifies an under-investigated research problem, and the study aims/questions that address this deficit with the thesis structure. Additionally, the impact of COVID-19 on the PhD research programme is presented in this chapter. More details will be provided in the following chapters.

To provide clarification, the term "Türkiye" (Turkey) is used to refer to the country of focus in this thesis, as it aligns with the formal request made by Ankara to the United Nations, designating Turkey as "Türkiye".

1.2. Personal motivation for conducting the study

The first ideas for this thesis emerged when I was in postgraduate school. During my nursing education in Türkiye, I realised that most nurse researchers prefer to specialise in diabetes, haemodialysis, paediatrics, and nurse education rather than heart failure. As a matter of fact, the General Directorate of Health Services in Türkiye (Directorate of Education and Certification) runs a total of 55 different training certificate programmes for nurses, and none of these programmes is specifically related to heart failure or even cardiovascular nursing (Sağlik Hizmetleri Genel Müdürlüğü, 2023). This inspired me to pursue my study of cardiovascular diseases, specifically heart failure. During my master's degree, I studied heart failure and took additional courses to further develop my knowledge. Following this, I chose to explore the effects of telephone coaching, one of the nurse-based interventions, on quality of life, depression, and anxiety in heart failure with a systematic review for my master's thesis. With this systematic review, I realised it would not be possible to provide effective nursing care in heart failure without understanding the symptom profile and influencing factors. People with heart failure experience symptoms differently depending on their individual characteristics within their socio-cultural-behavioural context. I was concerned about the individuals living with heart failure and the totality of what the symptoms they experience.

The idea of this thesis further developed when I was looking for a supervisor for my PhD study. After meeting with Professor Bridget Johnston, I realised the importance of understanding the full spectrum of symptoms from patients' perspectives, which is really important to develop a more effective and systematic symptom assessment intervention for them and their informal caregivers (family members, friends, and neighbours). During our supervision meetings (with my three supervisors), we discussed the importance of understanding individual symptom profiles (related to heart failure or not) from individuals' perspectives to provide the optimum management goals for them. We discussed that the clinical assessment did not account for women, the elderly, and different heart failure subtypes, thereby leading to inadequate symptom assessment in these specific groups. This served as the impetus for the emergence of the topics addressed in this doctoral project.

In addition to these two ideas, the process of "Patient and Public Involvement (PPI)", particularly during my meeting with Robbie, helped me to understand the uniqueness of the symptom experiences of each individual with heart failure. I realised the importance of their guidance for symptom assessments and management after listening to their real-life stories and concerns. Each individual attributes their own specific meaning or importance to a symptom they nevertheless have in common with many others, because many factors influence the symptom occurrence or meaning. For example, one of my public advisors stated that he has siblings diagnosed with heart failure, but their perspectives on treatment and symptoms are completely different. This indicates the importance of understanding the self-reported symptoms from the patient's perspective, suggesting that it is the core element for evaluating the potential of management strategies and care plans in heart failure.

These experiences have led me to think about identifying the full spectrum of symptoms and influencing factors of individuals living with heart failure, considered from their own perspectives.

1.3. Research problem

Multiple symptoms, such as breathlessness, pain, fatigue, and sleep difficulties, are common in individuals with heart failure (HF) (Wang et al., 2023). These symptoms have a negative effect on patient-reported outcomes such as functional capacity and quality of life when they remain underdiagnosed and undertreated (Wang et al., 2023, Zhang et al., 2016, Alpert et al., 2017). These symptoms are also associated with repeated hospital admissions and a lower survival rate (Stanek et al., 2000, Vongmany et al., 2016, Ali et al., 1996, Rahimi et al., 2014).

Corrine Jurgens (2016) suggested that assessment of both typical and atypical symptoms was deemed valuable from the patients' perspective, particularly in relation to subgroups among individuals with heart failure, including age, biological sex, and type of heart failure.

Researchers have inadvertently missed two important issues when implementing heart failure research to support inclusive and equal heart failure management for all. Firstly, researchers mostly consider the typical and less typical single or multiple symptoms occurring in heart failure (Heo et al., 2019b, Heo et al., 2020, Graven et al., 2020). These symptoms are generally selected from current heart failure guidelines, such as the European Society of Cardiology (ESC) Guidelines for Heart Failure (McDonagh et al., 2021). There are six typical and ten less typical symptoms identified within the ESC Guidelines (**Table 2-1: Background)**. This prompted us to consider the plausibility of effectively treating or managing symptoms by concentrating solely on a restricted set of typical and less typical symptoms outlined in the current clinical management guidelines, with the aim of enhancing overall care and quality of life. This raised the first question of this PhD research: "*What is the full spectrum of symptoms experienced by people with heart failure?*" Secondly, symptoms vary between patients according to individual differences (Riegel et al., 2022). Until now, little attention has been devoted to comprehensively exploring the experiences of culturally diverse individuals who are female, elderly, and with those with heart failure with a preserved ejection fraction. This raised another question for this PhD research: "*Does an individual with heart failure experience the same symptoms regardless of any differences in their socio-demographic and clinical profile (including biological sex, age, heart failure subtypes, and Turkish culture)?*"

A challenge in the successful symptom assessment of heart failure is the lack of a comprehensive understanding and awareness of the full spectrum of symptoms. Symptoms of understudied populations such as women, those with heart failure with preserved ejection fraction (HFpEF), the elderly, and Turkish individuals are often not represented in previous symptom lists. This present PhD research focused on self-reported symptoms from patients' perspectives with respect to settings, age, biological sex, heart failure phenotypes and Turkish cultural/social context.

1.4. Thesis overview

This PhD thesis included three sequential research studies to explore self-reported symptoms in heart failure. It starts from a broad overall symptom perspective with a mixed-method systematic review (*study 1*) of the literature. It narrows down to an exploration of real-life clinical cohort symptoms with a secondary data analysis of the dataset from an existing trial from Australia (*study 2*), the WHICH?II Trial, with a focus on biological sex and heart failure subtypes; and then a personal symptom profile perspective with a descriptive qualitative study from Türkiye (*study 3*) (**Figure 1-1**).

1.4.1. Overall aim

The primary aim of this PhD thesis is to explore the full spectrum of self-reported symptoms in people with heart failure from their (individual) perspectives. The main objectives are as follows:

- To fully explore self-reported symptoms of individuals with heart failure.
- To identify typical and less typical symptoms listed in ESC Guidelines for heart failure, as well as those not listed by these guidelines in people with heart failure.
- To explore the association between symptoms and individual characteristics (hospital versus out-patients, younger versus older, men versus women) in heart failure.
- To assess potential differences in the range of symptoms reported by men and women with respect to the most common heart failure subtypes they (men and women) typically develop.
- To explore the risk factors for worsening heart failure symptoms among women and men during structured one-year follow-up.
- To explore the full spectrum of self-reported symptoms reported by Turkish individuals with self-reported heart failure.
- To explore the differences in breathlessness experience according to socio-cultural perspective in Türkiye.

1.4.2. Research questions

The main research questions of the PhD project:

- What is the full spectrum of symptoms experienced by people with heart failure?
- Does an individual with heart failure experience the same symptoms regardless of any differences in their socio-demographic and clinical profile (including biological sex, age, heart failure subtypes, and Turkish culture)?

Sub-questions of each independent study of the project:

Study 1: A mixed-methods systematic review main questions:

What is the full spectrum of symptoms experienced by people with heart failure?

- How common were typical and less typical symptoms listed in the ESC Guidelines for heart failure?
- Were there symptoms of heart failure that were not listed in the ESC Guidelines? How common were these?
- Did ESC-defined typical and less typical symptoms vary from community to hospital?
- How does age affect ESC typical and less typical symptoms?
- How does sex affect ESC typical and less typical symptoms?

Study 2: Secondary data analysis main research questions:

How do symptoms of heart failure differ between men and women, with respect to biological sex and heart failure types?

How do these symptoms change in the 12 months following a hospital admission in men and women, with respect to heart failure subtypes?

- What are sex-stratified differences in symptom changes over one year associated with heart failure with respect to LVEF-based heart failure subtypes?
- What are the baseline predictors of worsening heart failure symptoms in men and women separately?

Study 3: Qualitative study main research questions:

How is breathlessness described from a patient perspective in Türkiye?
What symptoms are experienced by Turkish individuals with heart failure?

- What are the impacts/consequences of breathlessness on daily life and health for people with heart failure in Türkiye?
- How do they manage their breathlessness?
- What are the health needs of individuals with heart failure in Türkiye?

1.4.3. Thesis structure

The primary aim of this PhD project was achieved in three consecutive studies, which supports the interpretation stage (**Figure 1-1**).

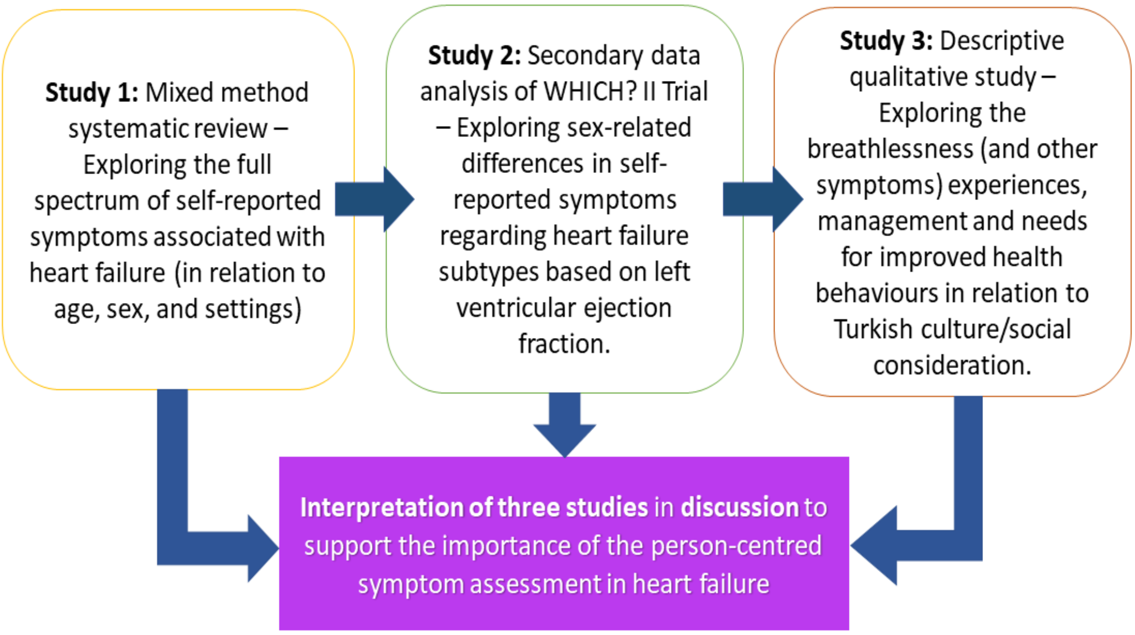


Figure 1-1: Outline of this PhD research

The **first two chapters** are the introductory chapters for this thesis and the topic. **Chapter 1** presents the research problem and the aims and questions of the thesis, along with the structure of the thesis. In **Chapter 2**, a review of literature on heart failure and symptoms is presented.

Chapter 3 provides detail about the literature pertaining to the selected methods. The critical realist perspective and the sequential design of the PhD programme are justified in this chapter.

Chapter 4 presents the methods for Studies I, II and III. The methods of each study are presented with explanations and steps. Patient and public involvement (PPI) is explained in this chapter.

Chapter 5 presents the findings of study one, a mixed-methods systematic review (MMSR). This review investigated a wide range of heart failure symptoms and examined how, in previously published research, the ESC typical and less typical symptoms change according to age, setting, and biological sex. The systematic review's findings were used as supplementary data for the overarching findings in this project.

In **Chapter 6**, the finding of the second study (secondary data analysis of the WHICH? II Trial data) is presented to explore self-reported symptom profiles and influencing demographic factors in (sub-populations of) people living with chronic heart failure. The third study (descriptive qualitative study) is presented in **Chapter 7** to identify the cultural consideration in breathlessness in heart failure among Turkish individuals.

The findings of all three individual studies (the mixed-methods systematic review, secondary data analysis, and qualitative study) are discussed in **Chapter 8** based on the overarching key findings, and provide a comprehensive and systematic symptom assessment strategy.

Finally, the conclusion of the project, and recommendations for research, policy and practice, are presented in **Chapter 9**.

1.5. Covid-19 impact

The global pandemic of Covid-19 reached the UK in March 2020. The pandemic caused an increased risk of sudden and unexpected deaths, as well as numerous hospital admissions, especially among people with comorbidities such as diabetes, hypertension, and cardiovascular diseases (Wang et al., 2020a, Nishiga et al., 2020). Social restrictions and isolation prevented people from being physically together. Additionally, Covid-19 affected academic studies by increasing the need for Covid-19 research while reducing the risk for vulnerable participants living with chronic conditions and for researchers. I started my PhD and moved to Glasgow from Türkiye just a few months before the Covid-19 pandemic began. This PhD research was one of the projects affected by the Covid-19 pandemic. I had to self isolate, and most university buildings including the library shut. I was unable to meet face-to-face with my supervisors for several months. The study population were people living with heart failure, which includes the risk group for the higher risk of Covid-19 disease (Nishiga et al., 2020). During this period, my supervisory team and I decided to make some changes in the first research proposal due to unforeseen issues such as not being able to use the university facilities, to recruit the participants for studies, and to obtain ethical approval from the university or NHS institutions. Therefore, it was decided to perform a secondary data analysis of the WHICH?II Trial data, rather than a survey study. This secondary data analysis was performed to understand symptom differences and worsening symptom trajectories due to the limited number of symptoms (10 symptoms) included in the original study. This will be explained later in the secondary data analysis method and findings sections. After these changes, the third study was redesigned, taking into account the first two studies.

1.6. Chapter summary

This chapter provided details about what the research problem is in healthcare. Finally, very brief information about overall thesis aims and structure were addressed in this chapter. In the next chapter, the existing evidence-based information regarding heart failure and symptoms in heart failure, socio-political situation and healthcare system in Turkiye and the rational for this PhD research are presented.

Chapter Two - Background

2.1. Introduction

This chapter begins by presenting the contextual background issue that provides a strong rationale for conducting this academic research. It commences with a broad background to the syndrome of heart failure, including its accepted definition, epidemiology and current care, and treatments. This chapter then provides details on the current knowledge-base in respect to understanding heart failure-related symptoms and the self-management strategies to address these symptoms. Following this, current heart failure research from a nursing perspective is highlighted. Next, the socio-political situation and healthcare system in Türkiye are explained, to provide background for the qualitative study. Before the summary of the chapter, evidence of the importance and rationale of this PhD study is covered again.

2.2. Heart failure

2.2.1. Current definition and natural history of heart failure

Heart failure is a symptom-driven, complex clinical syndrome resulting from a functional or structural abnormality of the heart that results in elevated intracardiac pressure and/or inadequate cardiac output at rest and/or during exercise (McDonagh et al., 2021, Yancy et al., 2013, Tsutsui et al., 2021). As currently reported (prior to the research reported in this thesis), individuals with heart failure experience single or multiple distressing (typical or less typical) physical and psychological symptoms, mainly breathlessness, fatigue, ankle swelling and depression (see **Table 2-1** for typical and less typical symptoms of heart failure from ESC Guidelines) (McDonagh et al., 2021). These symptoms are strongly associated with reduced exercise capacity, quality of life and self-efficacy (Wang et al., 2023, Zhang et al., 2016, Alpert et al., 2017). Individuals with advanced heart failure nearing end-of-life experience more severe symptoms, and depend on their informal caregivers and the healthcare treatments (including heart transplantation or long-term mechanical circulatory support) (Crespo-Leiro et al., 2018).

Heart failure can be caused by numerous mechanisms, with mainly ischemic heart disease (IHD) (26.5%) as the most common (McDonagh et al., 2021, Tsutsui et al., 2019, Bragazzi et al., 2021). This aetiology may vary by geography (Savarese et al., 2022, MacDonald et al., 2020). For example, IHD affects mostly higher income countries (Bragazzi et al., 2021, Johansson et al., 2021), whereas hypertension and rheumatic heart disease are more common in low-income counties (Savarese et al., 2022).

Table 2-1: Symptoms and signs typical of heart failure (from ESC (2021) Guidelines)

Symptoms
Typical
Breathlessness
Orthopnoea
Paroxysmal nocturnal dyspnoea
Reduced exercise tolerance
Fatigue, tiredness, increased time to recover after exercise
Ankle swelling
Less typical
Nocturnal cough
Wheezing
Bloated feeling
Loss of appetite
Confusion (especially in the elderly)
Depression
Palpitations
Dizziness
Syncope
Bendopnea

Despite the expanding range of medical treatments available for heart failure, the progression of the disease, accompanied by its symptoms and other related issues, leads to a decline in the overall quality of life. This decline affects various domains, including physical, psychological, social, financial and spiritual aspects. Despite treatment, ongoing symptoms and symptom burden in heart failure remains high and often under-addressed. These ongoing symptoms lead to hospitalisations (Butler et al., 2014, Ambrosy et al., 2014, Brush et al., 2006).

Hospitalisations in individuals with heart failure are frequent (1.34 per person-year) (Gerber et al., 2015). Among people over 65, heart failure is the most common cause of hospitalisation (Blecker et al., 2013). A third of people with heart failure have previously been hospitalised for their condition (Greene et al., 2018a, Crespo-Leiro et al., 2016), and 50% are readmitted within a year of receiving their initial diagnosis (Nichols et al., 2015, Lawson et al., 2019). Annualised cardiovascular mortality rates increased from 29–53 deaths per 100 person-years at risk in heart failure patients who had experienced one prior repeated heart failure hospitalisation (Lindmark et al., 2021). In a systematic review of 19 studies, cardiovascular diseases accounted for more than 50% of overall deaths, and heart failure was generally the most common cause of death, but varied between 8% and 64% (Jones et al., 2019). According to age, comorbidity burden, as well as heart failure phenotypes, the many causes of death may reflect the heterogeneity of the population of those with heart failure (Savarese et al., 2022, Hobbs et al., 2007, Mastenbroek et al., 2014).

In the West, the annual cost of healthcare for an individual with heart failure might reach €25,000, with the majority of expenses connected to direct expenses (hospitalisations and in-patient treatment) and non-cardiovascular comorbidities (Savarese et al., 2022). On a more global scale, a comprehensive examination of the direct and indirect expenses of heart failure across 197 countries in 2012 projected the cumulative costs to be $108 billion (Cook et al., 2014).

2.2.2. Epidemiology of heart failure: worldwide

Heart failure has been defined as a global pandemic, with 64.3 million people estimated to suffer from heart failure worldwide in 2017 (GBD, 2018). Of these, 34.8 million are women and 29.5 million are men (Bragazzi et al., 2021). The prevalence of heart failure ranges between 1%–3% in the general population worldwide (Savarese et al., 2022). This is expected to rise due to the improved survival following a heart failure diagnosis associated with the availability of life-saving evidence-based treatments and the overall longer life expectancy of the general population (Savarese et al., 2022).

With its decline in high-income developed countries, heart failure may become less common globally, but it is becoming more common in low- and middle-income countries (Groenewegen et al., 2020, Bragazzi et al., 2021). For example, the prevalence of heart failure in Türkiye was 2.9% in 2012, affecting 1.5 million people and putting another 3 million at risk (Değertekin et al., 2012). This rate is higher than in the UK, where the prevalence was 1.6% in 2014, age and sex-standardised (Conrad et al., 2018); Australia, where it ranged from 1.0% to 2.0% (Sahle et al., 2016); and the USA (2.4% in 2012) (Heidenreich et al., 2013).

The reported incidence of heart failure is 1 to 20 cases per 1000 person-years with variations depending on populations and geographic regions. The majority of data come from Europe and North America, where the average incidence appears to be 2–3 cases per 1000 people, according to relevant data available after 2000 (Savarese et al., 2022). The incidence rate of heart failure ranges between 0.7 (Hong Kong in 1997) (Hung et al., 2000) and 5.3 (Canada 2010–2013, age- and sex-standardised) (Public Health Agency of Canada, 2018) cases per 1000 people among countries. Among 12 European countries from the HFA ATLAS study, the median yearly incidence rate of heart failure in 2018–2019 was 3.2 per 1000 person-years (Seferović et al., 2021). Incidence rates of heart failure per 1000 person-years is 3.3 in the UK in 2014 (Conrad et al., 2018), whereas it was 1.3 in Scotland in 2020–2021 (Public Health Scotland, 2023).

Patient age and sex are one of the risk factors for heart failure incidence (Bleumink et al., 2004, Ødegaard et al., 2020, Savarese et al., 2022). Regardless of sex, the incidence rate increased with age, rising from 1.4 per 1000 person-years among individuals aged 55–59 to 47.4 per 1000 person-years in individuals aged 90 years or older (Bleumink et al., 2004). After adjusting for age and sex, low socio-economic status is another risk factor for developing heart failure, increasing likelihood by 43%–87% (Conrad et al., 2018, Potter et al., 2019).

2.2.3. Types of heart failure

There are variety of terminology frameworks to define or classify the subsets or subtypes of heart failure. Ejection fraction (EF) categories are predominantly described/applied by clinical guidelines (Tsutsui et al., 2021, McDonagh et al., 2021, Yancy et al., 2013) and clinical trials (Solomon et al., 2019, Williams and Evans, 2020). According to the recently updated ESC Guidelines criteria (McDonagh et al., 2021), heart failure can be categorised into three distinct phenotypes based on the measurement of left ventricular ejection fraction (LVEF):

- heart failure with reduced ejection fraction (HFrEF-LVEF ≤40%);
- heart failure with mildly-reduced ejection fraction (HFmrEF-LVEF 41%–49%);
- heart failure with preserved ejection fraction (HFpEF-LVEF ≥50%).

Among 23047 individuals with heart failure (in both in-patient and out-patient settings) from 40 countries (Joseph et al., 2020), the prevalence of HFrEF, HFmrEF, and HFpEF were 54%, 21% and 24%, respectively. Although HFrEF appears to predominate in heart failure, ranging between 60% (Chioncel et al., 2017) and 81% (MacDonald et al., 2020), studies have shown differences in the prevalence of LVEF-based heart failure subtypes according to study population and country. For example, individuals with acute heart failure had higher HFpEF in Japan (43%, n=1245) (Shiga et al., 2019) and Spain (52%, n=2803) (Santas et al., 2020), while they had higher HFrEF in Italy (77%, n=1669) (Senni et al., 2014). Likewise, the Swedish Heart Failure Registry study indicated that 56% of 42.061 individuals had HFrEF (Koh et al., 2017) whereas in the USA, 47% of 40.239 individuals had HFpEF (Cheng et al., 2014).

The prevalence of HFpEF appears to have increased over time. In contrast, the prevalence of cases of HFrEF has remained stable (Savarese et al., 2022, Owan et al., 2006). This difference is increased among those of advancing age and female gender. Previous studies indicated that there are sex-related differences in heart failure subtypes (Stolfo et al., 2019, Lam et al., 2019). For example, while the total prevalence of HFrEF is 51.4% in Türkiye, HFpEF is more common among women (57.5%) and those over 70 years of age (36.7%) (Cavusoglu et al., 2022). Compared to European countries, Türkiye exhibits a significantly younger cohort of individuals affected by heart failure, indicating a potentially high prevalence of HFrEF among men.

Heart failure subtypes are associated with potentially different rates of hospitalisation and mortality. In cause-of-death data categorised by LVEF, heart failure-related mortality was higher in individuals with HFrEF than in those with HFpEF (Jones et al., 2019). In contrast, non-cardiovascular mortality was higher in HFpEF (30.7%) than in HFmrEF (27.8%) and HFrEF (20.1%) at 1 year (Chioncel et al., 2017). In Türkiye, individuals with HFrEF are admitted to hospital at higher rates than those with HFpEF and HFmrEF (Cavusoglu et al., 2022), and the mortality risk was higher for individuals with HFrEF compared to other subtypes (Yılmaz et al., 2020).

Also, heart failure classification can be based on acute or chronic presentation (McDonagh et al., 2021), disease progression (Yancy et al., 2013) and right ventricular dysfunction (McDonagh et al., 2021). Acute heart failure (AHF) and chronic heart failure (CHF) are the two main types of heart failure presentations (McDonagh et al., 2021). Heart failure syndrome can occur in two ways: as an emergency hospitalisation (known as “acute heart failure”) or in a more subtle form known as “chronic heart failure”. In the out-patient setting, acute heart failure may lead to hospital admission or treatment with intravenous diuretic therapy (McDonagh et al., 2021). The severity of heart failure is described using simple terminology and the New York Heart Association (NYHA) classification (McDonagh et al., 2021). This exclusively relies on heart failure symptoms such as palpitations, fatigue, and shortness of breath. There are four distinct classes (I, II, III, and IV) of symptom severity (ranging from no symptoms to severe limitations) in the NYHA classification.

2.2.4. Current treatments and care for heart failure

Evidence-based interventions are critical to the successful management of heart failure. The main goals of treatment and management for individuals with heart failure are to reduce mortality; prevent readmissions for worsening heart failure; and improve quality of life, functional capacity and clinical status (McDonagh et al., 2021). Guideline-directed pharmacological and non-pharmacological heart failure management strategies and approaches have proved to be effective (McDonagh et al., 2021, Maddox et al., 2021, Sabouret et al., 2022, NICE, 2018). These management strategies are selected on the basis of heart failure phenotypes, underlying causes, comorbidities and symptoms.

Historically, the most well-proven therapeutic prospects in the literature have been for HFrEF. Disease-specific, evidence-based treatments for HFrEF mainly focus on guidelines for beta-blockers, angiotensin-converting enzyme (ACE) inhibitor, angiotensin receptor blockers (ARBs), and mineralocorticoid receptor antagonists (MRAs) (McDonagh et al., 2021, SIGN, 2016, Malgie et al., 2023). A 2022 systematic review of 75 clinical trials involving 95,444 people with HFrEF found that combining the four essential medications (MRAs, beta-blockers, ACEi, and sodium glucose cotransporter-2 inhibitors (SGLT2i)) prescribed for heart failure was the most successful strategy for reducing symptoms and avoiding hospitalisations (Tromp et al., 2022). In addition to these pharmacotherapies in HFrEF, additional device therapies have been proved to be effective. One of them is implantable cardioverter defibrillators (ICDs), which significantly reduce the rate of sudden cardiac death risk (Dinatolo et al., 2018). According to a systematic review of ten clinical trials, the clinical benefit of ICD implanted according to current guidelines has decreased dramatically over time due to a reduction in the incidence of unexpected cardiac death and a rise in ICD unresponsive patients (Disertori et al., 2020). Cardiac resynchronization therapy (CRT) is another treatment option to improve survival rate (Dinatolo et al., 2018). Left ventricular assist devices (LVADs) are also beneficial to improve survival, but the survival was only two years. Also, individuals with advanced heart failure experience more severe symptoms upon optimal medical therapy and should be considered for heart transplantation (McDonagh et al., 2021).

In contrast to HFrEF, evidence-based treatment and clinical trials for HFpEF and HFmrEF have gained importance in recent years. The fact that the clinical profiles of individuals with HFpEF are different from those with HFrEF has increased the importance of this matter in evidence-based treatment. The most notable difference between HFrEF and HFpEF are the following sex-specific variations (Pandey et al., 2018, Lam et al., 2019, Stolfo et al., 2019). More studies of HFrEF with a higher male population have been included in treatment guidelines, so evidence-based treatment does not stratify heart failure treatment for HFpEF and the female population (Lam et al., 2019, Regitz-Zagrosek, 2020). In addition, the increasing number of elderly individuals with HFpEF, and higher levels of multimorbidity among this cohort, require different management pathways (Stewart et al., 2022, Stewart et al., 2016a). Recently, this issue has been addressed as a future challenge in heart failure management in many national and international governmental or non-profit organisations, conferences, and publications (Lourenco et al., 2018, SHFNF, 2018, Packer, 2018).

In addition to these pharmacological treatments, heart failure-specific cardiac rehabilitation and other disease management approaches such as self-care, exercise, disease-specific education, dietary advice, social support, and nurse follow-up are the other heart failure management strategies to reduce the intensity of symptoms by optimising functional status, increasing control, and improving health-related quality of life (Dinatolo et al., 2018, McDonagh et al., 2021, Anderson and Taylor, 2014). Mainly, controlling symptoms of heart failure is the key goal of treatment methods. In recent decades, these evidence-based treatment developments in heart failure have been impressive and proved to be effective to improve patients' health and well-being. Nevertheless, some individuals may still experience distressful and burdensome symptoms, especially those at the end-of-life phase (Truby and Rogers, 2020). Assessing ongoing symptoms is a part of the assessment of palliative care needs in individuals with heart failure. Palliative care for optimal management of symptoms and improvement of quality of life is a strategy for heart failure (Hill et al., 2020, Kyriakou et al., 2020, Årestedt et al., 2014). Recently, this matter has been addressed in many national and international conferences, workshops, and publications. One of these, the Heart Failure Association of the ESC, has published a position paper about integrating palliative care approaches into heart failure care (Hill et al., 2020). Recently, countries have been working to develop their specialist palliative care for people with heart failure and their caregivers. For example, this service is provided by the Marrie Curie Hospice project in Glasgow, supported by the British Heart Foundation (BHF) and Marie Curie Cancer Care.

2.3. Symptomatology of heart failure

Symptoms are an important indicator and aspect of heart failure, which are frequently evaluated by clinicians and researchers. Understanding individuals with heart failure depends extensively on their symptoms, as these manifestations can reveal both the nature of the disease and the individual's personal experience and perspective of their condition. This section presents terminologies of symptoms; their assessment and implications in heart failure; and the importance of the symptoms and associated factors in this PhD research.

2.3.1. Conceptual definition of a symptom

> *"The appearance of the symptom usually involves the verbal articulation of the patient's subjective experience of the symptom(s) and the possible bodily manifestation that accompanies it."* – (Eriksen and Risør, 2014, p.89)

Symptoms are subjective events that an individual perceives as a sign or attribute of a condition that deviates from normal function, sensation, or appearance (Rhodes and Watson, 1987). They only become known when someone reports feeling a symptom, because it is subjective experience reflecting the changes (Dodd et al., 2001a). The common features of symptoms include the subjective nature of the symptoms, the perceived event as a deviation from normal function, the multi-layered nature of the symptom, and the presentation of a mental response to the symptoms (Armstrong, 2003). This means symptoms reflect the reality of the person in the context of their cultural and personal situation (Lenz et al., 1997, Armstrong, 2003).

The following conceptual definitions of symptoms are also used in the literature. One of these is the **Sign(s)** most often confused with symptoms. Signs, or objective clinical manifestations, are frequently included in the definition of symptoms, which are described as distinguishing characteristics indicative of a disease category used to identify a patient's condition (Rhodes and Watson, 1987). Some complementary symptom terms are generally used to describe the symptoms as a reflection of the reality of the individuals, such as symptom perception (Posey, 2006), attribution (Robbins and Kirmayer, 1991), and status (Landrum, 2009, Heo et al., 2005). The symptom perception includes symptom meaning (what individuals attribute to their experience of symptoms – could be negative or positive) and existential meaning (individuals' feelings of vulnerability and mortality as a result of symptoms that remind them of their diagnosis) (Armstrong, 2003). In cancer, for example, individuals' situational meaning (their perception of a new event and their ability to manage it) or existential meaning (universal representations of their placement in the universe – related to culture) can be influenced by each individual symptom as well as by the interaction of various symptoms (Richer and Ezer, 2000). These multiple symptoms are described as the "symptoms experience" (Armstrong, 2003, Posey, 2006) and "symptoms cluster" (Dodd et al., 2001b, Miaskowski et al., 2004). Frequency, severity, and impact on normal activity and enjoyment of life are used to describe symptom characteristics (Todero et al., 2002). Symptom burden in heart failure can be defined as the total subjective experience of heart failure symptoms (including symptom prevalence, frequency, and severity) that have a negative effect on the patient or the patient's family, and are a fluid phenomenon that can be measured over the course of the patient's disease (Stockdill et al., 2019).

Other terms used in this project are "**stratified realities in symptoms**" and "**typical, less typical, or atypical symptoms**". *Stratified realities in symptoms* refers to the observation that symptoms can vary in intensity, perception, and impact from person to person, influenced by factors such as their socio-cultural background, personal beliefs, and behavioural context. The terms *typical, less typical, or atypical symptoms* of heart failure are used in this current project. However, there was no specific conceptual description of these terms in heart failure. Additionally, from a critical realist perspective, the researcher believes the these (typical, less typical and atypical) symptoms will vary according to a range of individual characteristics.

2.3.2. Assessing symptoms in heart failure

Current clinical management guidelines and reports provide a list of possible typical and less typical symptoms associated with heart failure diagnosis or worsening trajectory (Bozkurt et al., 2021). Breathlessness, fatigue, and ankle swelling are the typical symptoms of heart failure. Over four decades, the NYHA classification has been used and recommended to identify the heart failure symptom severity in clinical trials (Solomon et al., 2019, Teerlink et al., 2021, Williams and Evans, 2020) and current clinical management guidelines (McDonagh et al., 2021, Yancy et al., 2013). Other symptoms are mostly under-reported or -investigated. However, as many as 32 different symptoms have assessed among the heart failure cohort.

A critical review of heart failure measures shows that five instruments are used for symptom assessment in heart failure, and between 13 and 32 different symptoms and signs are assessed in the research via these symptom evaluating tools (Lee and Moser, 2013). **Table 2-2** indicates the most commonly used instruments or measurements, including the Kansas City

Cardiomyopathy Questionnaire (KCCQ) (Green et al., 2000), the Minnesota Living with Heart Failure Questionnaire (MLHFQ) (Rector and Cohn, 1992), and the Heart Failure Somatic Perception Scale (HFSPS) (Jurgens et al., 2017, Pucciarelli et al., 2019) for symptoms assessment. Although some of these tools, such as the Edmonton Symptom Assessment Scale (ESAS) and Patient Health Questionnaire (PHQ), are not HF-specific, they were included in the table due to their common usage in heart failure research. There are between 3 and 32 overall symptoms in these tools, both physical (ranging from 3–27) and psychological (ranging from 2–5). Many of these tools do not include the psychological symptoms. The main limitation of the updated or adapted versions of the current scales/instrument such as HFSPS is an inclusion of a narrow set of symptoms from previous instruments/scales rather than the full spectrum of symptoms. These instruments are mostly used to assess symptom severity.

Recently, clinical status has been assessed with symptoms and other patient outcomes such as quality of life, overall well-being, and functional status by using standardised tools and measurements from the patients’ perspective in heart failure (Mendes et al., 2024). These patient-reported outcome measures may support their therapeutic and non-therapeutic choices and management of heart failure. KCCQ and MLHF are the most commonly used heart failure-specific patient-reported outcome measures (Mendes et al., 2024). All these tools are valid, reliable, and show good responsiveness in the heart failure population.

Table 2-2: Common symptom measurements/instruments and purpose

Tool	**Number of symptoms**			**Measurement purpose**
	Total	Physical	Psychological	
New York Heart Association (NYHA) classification (Bennett et al., 2002)	4	4		Symptom severity Functional limitations, status, and classification
Heart Failure Symptom Survey (HFSS) (Pozehl et al., 2006)	14	12	2	Symptom severity and frequency
Memorial Symptom Assessment Scale – Heart Failure (MSAS-HF) (Hu et al., 2021, Portenoy et al., 1994, Lin et al., 2020)	32	27	5	Symptom severity, burden, distress, and occurrence
Kansas City Cardiomyopathy Questionnaire (KCCQ) (Green et al., 2000)	3	3		Total symptoms Symptom frequency, burden, severity, and stability
M.D. Anderson Symptom Inventory-Heart Failure (MDASI-HF) (Fadol et al., 2008, Fadol et al., 2019)	12	8	3	Symptom severity Overall symptom interference
Cardiac Symptom Survey (CSS) (Krethong et al., 2008, Nieveen et al., 2008, Barnason et al., 2006)	10	8	2	Symptom severity, characteristics, occurrence, and frequency
Minnesota Living with Heart Failure Questionnaire (MLHFQ) (Moser et al., 2014, Rector and Cohn, 1992)	9	6	3	Symptom occurrence and severity
Edmonton Symptom Assessment Scale (ESAS) (Hui and Bruera, 2017)	10	7	3	Symptom distress
Heart Failure Somatic Perception Scale (HFSPS) (Lee et al., 2015, Pucciarelli et al., 2019, Jurgens et al., 2017)	18	18		Symptom occurrence and severity
Heart Failure Somatic Awareness Scale (Jurgens et al., 2006)	12	12		Symptom severity
Patient Health Questionnaire (PHQ) (Kroenke et al., 2001, Lee et al., 2015)	9	4	5	Symptom frequency and severity (mostly for depression)

2.3.3. Implication of symptoms in heart failure

A comprehensive and extensive symptom assessment of individuals may lead to better outcomes in terms of well-being and self-management (McDonagh et al., 2021, Jonkman et al., 2016, Kalogirou et al., 2020). The science of symptoms in heart failure has been instrumental in facilitating clinical assessments, managing symptoms, and devising targeted interventions and outcome measures.

Worsening symptom trajectory is strongly associated with repeated hospital admission and reduced quality of life in heart failure (Greene et al., 2018b). Early recognition of this clinical symptom deterioration is important (Hollenberg et al., 2019). The reasons and risk factors for deterioration are mostly assessed and investigated by healthcare professional and researchers (Lin et al., 2021, Butler et al., 2014). Although identification of the full spectrum of symptoms is required, healthcare providers mostly consider only typical symptoms of heart failure. A study of patients with heart failure and cardiologists from ten different countries showed that cardiologists tend to underreport less typical symptoms (such as nocturia, bloated feeling, and shortness of breath when lying flat) while they are aware of the most typical symptoms listed in the guidelines that patients experience (such as shortness of breath on exertion and fatigue) (Wirta et al., 2018). Furthermore, heart failure is mostly based on the presence of symptoms (including fatigue and dyspnoea) which is not specific only to this syndrome or a single disease (Bozkurt et al., 2021) (see **Table 2-3**). These symptoms can include one to a wide variety of symptoms, due to the presence of a complex aetiology (Wang et al., 2023, Lee and Oh, 2022, Lee and Riegel, 2018, Dickson et al., 2013). Individuals are satisfied with care if they receive care for symptoms of both heart failure and comorbidity (Talabani et al., 2020). If only these listed symptoms are evaluated to treat or manage heart failure, it will not be possible to develop any effective interventions or strategies to improve general health and well-being and reduce the adverse outcomes of heart failure.

Symptom management is important because it is strongly associated with better outcomes in heart failure (McDonagh et al., 2021). Reducing symptom burden is the one of the main goals of heart failure management. From a conceptual perspective, symptom management strategies (Dodd et al., 2001a) are interconnected with the concept of symptom experiences (including perception, evaluation, and response of symptoms), which is affected by individual characteristics within the social-cultural-behavioural context. An effective symptom assessment is essential to provide effective symptom management in the heart failure population. This will be discussed in detail in the section on self-management strategies.

Table 2-3: Common symptoms in heart failure and comorbidities

Symptoms	HF	COPD	CRF	AF	DM
Breathlessness	X	X	X	X	
Fatigue	X	X	X	X	X
Exercise intolerance	X	X	X	X	X
Chest pain, tightness	X	X		X	
Orthopnoea	X	X			
Paroxysmal nocturnal dyspnoea	X			X	
Dizziness/light-headedness	X			X	
Palpitations	X			X	
Lower-extremity oedema	X		X		
Sleep problems	X				X
Depression	X				X

(Jowsey et al., 2009, Janssen et al., 2011, Dickson et al., 2011, Lawson et al., 2018, Vuckovic et al., 2020)

HF: Heart Failure; COPD: Chronic Obstructive Pulmonary Disease; CRF: Chronic Renal Failure; AF: Atrial Fibrillation; DM: Diabetes Mellitus.

As mentioned previously, symptom control is the key goal of heart failure management. Patient-reported outcomes, including symptoms and health-related quality of life (HRQoL), have been used mostly as a secondary outcome in previous clinical trials (Jensen et al., 2019, McMurray et al., 2014, Solomon et al., 2019). These heart failure studies tend to focus on the typical symptoms of heart failure, such as dyspnoea, ankle swelling, and fatigue. However, recent studies have shown that individuals with heart failure experience various and multiple symptoms including sleep problems, constipation, dry mouth, and anxiety (Abshire et al., 2015, Alkan and Nural, 2017). Common typical symptoms of heart failure are not always the best predictors of deterioration (Lawson et al., 2022). Without recognition of the full spectrum of symptoms, individuals may not be able to manage them properly. In comparison to standard treatment, individualised care planning improves some measures of people's physical and mental health status, as well as their ability to self-manage their conditions (Coulter et al., 2015). Unique individual symptoms should be considered.

2.3.4. Factors affecting symptoms

Symptoms of heart failure can differ based on individual characteristics among any heart failure cohort (Jurgens, 2016, Vuckovic et al., 2020, Jurgens et al., 2009). According to Jurgens (2016), symptoms of heart failure are heterogenous, with daily fluctuations that can vary between individuals. Multiple factors influence individuals' ability to recognise symptoms earlier, which are potential barriers to heart failure intervention or strategies (Holden et al., 2015, Siabani et al., 2013, Vuckovic et al., 2020, Riegel et al., 2022). Researchers have investigated factors associated with symptoms, including socio-demographic factors (such as age, biological sex, and ethnicity), clinical factors (such as heart failure subtypes, comorbidity, and depression), and biological factors (Whitaker et al., 2015).

Symptoms are subjective and meaningful. From a critical realist perspective, this subjective symptom knowledge production is relative, and associated with the particular context in which the individual lives and functions. These contexts are strongly related to our beliefs and theories about the world. This conceptualisation of symptoms sees their mechanisms and structures as interrelated to one's biological, socio-cultural, economic, and behavioural contexts. For example, typical heart failure symptoms such as ankle swelling, breathlessness and fatigue differ between men and women (Caruana et al., 2000, Heo et al., 2019b), due to various factors such as hormonal differences, variations in body fat distribution and vascular function influenced by mechanisms of knowledge production. The context of the world we live in and the way we perceive manifestations will influence how we view our symptoms and express them as symptoms. Symptom assessment needs to be comprehensive and focused on the individual's symptoms experience. Therefore, such a heterogenous view of the symptom reality of individuals can provide true scientific understanding in this context.

2.4. Nursing research in heart failure

Given the individual and complex needs of those affected, nursing is at the forefront of heart failure care and exploring better ways (through research) on how to deliver better health outcomes – especially via coordinated team care (Packer, 2018). Nurses can help to assess, address, monitor, and manage symptoms with the goal of improving the quality of life and care for patients and their informal caregivers. Nurse professionals are increasingly using data-driven care based on data analysis and interpretation to personalise treatment plans and predict heart failure exacerbations. Over the past decades, nurse researchers have contributed to improving the understanding of the importance of patients' experiences, and incorporating these insights into heart failure care. Their research has focused on early symptom recognition (Pereira Sousa et al., 2021), optimisation of medication (Driscoll et al., 2015), remote-monitoring/telehealth interventions, patient and caregiver education (Ågren et al., 2013), self-management (Cui et al., 2019), transitional care programmes (You et al., 2020), symptom management and palliative care (Dionne-Odom et al., 2020, Bakitas et al., 2020), psycho-social support (Mo et al., 2020), quality of life (Jiang et al., 2021), self-care (Creber et al., 2015), community outreach and prevention (Stewart et al., 2015, Chan et al., 2023), and addressing health disparities (Stockdill et al., 2023).

Nurse-led managements including telephone, clinic, and home follow-up interventions improve outcomes for patients and their families in many countries (Driscoll et al., 2015, Lambrinou et al., 2012, Inglis et al., 2015, Allida et al., 2020). They encourage patient-centred research, including patient-reported outcomes throughout the patient journey. In recent years, internationally recognised research has been conducted in countries such as Scotland (Blue et al., 2001, Raftery et al., 2005) and Australia (Stewart et al., 2012, Scuffham et al., 2017, Stewart et al., 2016b), considering the positive effects of nursing care and follow-up given by heart failure specialist nurses. Nurse researchers have helped to answer questions on the most effective and best care delivery strategies in heart failure. With their expertise and high leadership in heart failure, during the covid-19 pandemic, they were instrumental in the rapid developments in evidence-based care towards implementing remote care to prevent adverse outcomes (Ferguson et al., 2020, Inglis et al., 2020). They have contributed strongly to national and international guidelines and policies for the care and management of heart failure.

2.4.1. Current research into heart failure-related symptoms

In this section, the state of science of nurse-led symptom research into heart failure is explored in brief. Over the last decade, nurse-led studies of heart failure symptoms have significantly improved our understanding and management of this condition. Their published studies have explored numerous aspects of the role of symptom assessment and management in the care decisions process of patients and caregivers (Lee and Oh, 2022, Santos et al., 2020, Vuckovic et al., 2020, Lin et al., 2020). For example, self-reported individual symptoms and their interactions (as a cluster) have been highlighted by nurse researchers as a crucial element in care for people with heart failure (Austin et al., 2021, Herr et al., 2014, Qiu et al., 2022, Wang et al., 2023). Many nurse researchers have contributed a clearer understanding of individual differences in symptom perception (Lee and Riegel, 2018, Santos et al., 2021, Santos et al., 2020, Lee and Oh, 2022, Reeder et al., 2022, Skotzko, 2009) and self-care and management strategies (Siabani et al., 2013, Harkness et al., 2015, Reeder et al., 2015, Riegel et al., 2021). Nurse researchers highlight the importance of symptom-based care in heart failure. Nurse home visits or telehealth supports improve symptom recognition and management, and health-related quality of life in heart failure (Taniguchi et al., 2020, Bakitas et al., 2020, Jiang et al., 2021).

2.5.2. Current research in self-management of heart failure

In this section, the state of science regarding self-management in heart failure is explored in brief. Self-care can be conceptualised as “a naturalistic decision-making process that influences actions that maintain physiologic stability (self-care maintenance), facilitate the perception of symptoms (symptom perception), and direct the management of those symptoms (self-care management)” (Riegel et al., 2016, p.226). Self-management is the process of patients recognising needs, utilising resources, solving problems, and participating actively in their care (Jones et al., 2011, Johnston et al., 2014). The concept of self-management focuses on symptom control and additionally preparing for death and maintaining normality in any diseases (Johnston et al., 2012, Johnston et al., 2009).

For optimal symptom control in heart failure, self-management strategies are important. Symptom management models/theories use a framework to organise the concepts of symptom management strategies, which aligns with the concept of self-management (Henly et al., 2003, Larson et al., 1999, Dodd et al., 2001a). These symptom management models include the identification of symptoms experience as a core component of effective symptom management strategies. One such example is Symptom Management Theory, derived from the Symptom Management Model (SMM) (Larson et al., 1994, Dodd et al., 2001a), subsequently updated to the Theory of Symptom Management (TSM) (Bender et al., 2018, Humphreys et al., 2014). It included symptoms experiences and symptom management strategies in its theoretical lens. Symptom experience includes perception and evaluation (as the individual’s perception of their needs) and response as active participation. Then, active problem solving and resource utilisation processes are located under symptom management strategies. Antecedents, in the form of factors such as person, environment, and health/illness associated with the concepts of symptom experience and management, occur before the consequences of the event. Likewise, the Situation-Specific Theory of Heart Failure Self-care (Riegel et al., 2016) indicated that symptom perception affecting person, illness, and environmental factors is one of the key elements of self-care in heart failure.

As mentioned above, self-care management is important for symptom control in heart failure, a symptom-driven condition. Self-care or management in heart failure reduces hospital admissions, mortality risk, and costs of care, and increases quality of life by supporting symptom control (Ditewig et al., 2010, Riegel et al., 2011, Vuckovic et al., 2020, Wang et al., 2011, Jonkman et al., 2016). A meta-analysis of eight randomised controlled trials (RCTs) from five different countries (the USA, UK, Australia, Brazil, and Spain) found that nurse-led heart failure self-care education significantly reduced mortality and readmission risk (Son et al., 2020). Promoting self-management strategies for each individual with heart failure is important for effective and holistic care management.

Symptoms affect self-care strategies (Riegel et al., 2019, Cameron et al., 2010, Reeder et al., 2015). Understanding of self-monitoring and self-management of symptoms is the key for effective heart failure management (Riegel et al., 2002, Jaarsma et al., 2021, Riegel et al., 2022, Vuckovic et al., 2020). According to the Situation-Specific Theory of Heart Failure Self-care (Riegel et al., 2016), this requires that individuals recognise their symptom changes; evaluate the changes; decide on possible actions; implement treatment or care; and evaluate the outcomes. Self-care behaviours can be influenced by many factors, such as culture, age, and sex (Alassoud et al., 2020, Riegel and Carlson, 2002, Dickson et al., 2012). These factors can sometimes be a barrier as well as a facilitator. These barriers and facilitators are explored by nurse researchers to understand self-care strategy behaviours and practices (Siabani et al., 2013, Son et al., 2020).

Recently, many researchers have highlighted the importance of caregivers' support in symptom assessment and self-care management in heart failure (Vellone et al., 2021, Buck et al., 2015, Harkness et al., 2016). In a qualitative systematic review, caregivers were determined to be a good reporters of heart failure symptoms because they observed and monitored patients' symptoms that might go unnoticed by both patients and healthcare providers (Strachan et al., 2014). In particular, the caregiver can support timely symptom detection, recognition, and action (Clark et al., 2014). Several studies have provided details on patient–caregiver concordance in patients' most observed heart failure symptoms (Quinn et al., 2010, Sharifi et al., 2018, Lee et al., 2017). For example, the three most distressing symptoms (fatigue, shortness of breath with activity, and oedema) were reported by both people with heart failure and their informal caregivers (Quinn et al., 2010). Therefore, informal caregivers (often family members or friends of individuals) can assist in the assessment and management of heart failure symptoms, especially in those with cognitive impairment or advanced age.

2.6. Heart failure in Türkiye

The total prevalence of HFrEF is 51.4% in Türkiye and HFpEF is more common among women (57.5%) and those over 70 years of age (36.7%) (Cavusoglu et al., 2022). Compared to European countries, Türkiye exhibits a significantly younger cohort of individuals affected by heart failure, indicating a potentially high prevalence of HFrEF among men. Individuals with HFrEF are admitted to hospital at higher rates than those with HFpEF and HFmrEF (Cavusoglu et al., 2022), and the mortality risk was higher for individuals with HFrEF compared to other subtypes (Yılmaz et al., 2020). The estimated total annual national economic burden of heart failure in Türkiye in 2021 was one billion dollars (Cavusoglu et al., 2022).

Although recommendations for heart failure management in Türkiye come from the international clinical guidelines, it would be a mistake to use them in the Turkish context without careful consideration. The context of heart failure in Türkiye is different to that of these countries. According to the Turkish Society of Cardiology (TSC, 2022), hypertension and coronary heart disease are the two main causes of heart failure in the country. In Türkiye, non-ischemic aetiology (64%) predominates in HFpEF, but ischemic aetiology in HFrEF (65%) and HFmrEF (61%) (Cavusoglu et al., 2022). Contrary to the clinical studies published so far, the female population in Türkiye also comprises a significant proportion of the heart failure population (37% in HFrEF, 45% in HFmrEF, and 58% in HFpEF). There is also a significant disparity in age of onset, with heart failure diagnosed ten years earlier in Türkiye than in Western countries (TSC, 2022). Therefore, different risk patterns, younger patients, and a higher proportion of women in the population may require different pathways in heart failure care in the Turkish context.

In the acute phase, patients freely benefit from emergency services and cardiac facilities. For ongoing monitoring and management, community-based care services include family physicians providing regular follow-up, medication management, and lifestyle modification counselling. Additionally, other support services, such as home visits and cardiac rehabilitation, are provided for patients with heart failure. Recently, the Turkish Society of Cardiology has been offering patient education information and support groups to increase awareness and promote the effective management of heart failure in Türkiye (Tokgözoğlu et al., 2015). Their recent survey indicated that 30% of 2,307 heart failure outpatients were not aware of their diagnosis, and 70% of the participants lacked adequate knowledge related to heart failure (Karabulut et al., 2024). When it comes to patient education, nurses are essential. They ensure that people with heart failure receive all the knowledge and assistance they need to effectively manage their illness and enhance their overall quality of life.

The first and basic nursing care guide for heart failure was published in 2003 and updated in 2007 (Enç et al., 2007). In 2013, a study indicated that 60% of nurses were not familiar with this care guideline (Enç and Öz Alkan, 2013). In 2010, *Turkish Journal of Cardiovascular Nursing* (TJCN) was launched by the Cardiovascular Nursing Technicians Working Group of the Turkish Society of Cardiology (TSC – foundation year: 1963 and ESC member since 1966) (ESC, 2022). This journal has begun to publish many studies on the life experiences of individuals with heart failure. Recently, heart failure nurse-led studies has been conducted to identify quality of life, self-care strategies, health status, psycho-social-behavioural symptoms (mostly hopelessness, anxiety, and depression), medical adherence, and cardiac rehabilitation among the heart failure population since 2008 (Sezgin and Mert, 2017, Türker and Tanrıkulu, 2022). However, there is no specific nurse-led heart failure intervention related to the Turkish context or any specific policy for heart failure specialist nurse education/training.

2.7. Gaps in evidence

The following are the gaps identified in the current evidence base. Firstly, no studies investigate the full spectrum of symptoms associated with heart failure in the literature. Secondly, symptoms were not fully represented for women, elderly people, those with HFpEF, and Turkish culture in heart failure. The following are therefore key common issues to be addressed in future research for understanding the importance of the full spectrum of symptoms to improve detection and management of them:

- Increase awareness and recognition of the full spectrum of symptoms (related to heart failure or not) from patients' perspectives.
- Evaluate associated factors related to individual symptoms or worsening trajectory of symptoms based on sex-related differences.
- Improve individualised symptom assessment strategies inside and outside of hospitals.

2.8. Socio-political situation and healthcare system in Türkiye

Türkiye, with a population of 83.4 million, is located between the Black and Mediterranean Seas (WorldAtlas, 2023b). About 90% of this population adheres to Islam (with diverse sects, but mainly Sunni) (WorldAtlas, 2023a), and there is a high degree of linguistic and cultural heterogeneity, with multiple spoken languages, such as Turkish (the official language), Kurdish, and Arabic (WorldAtlas, 2023b). Türkiye is a presidential republic characterised by a multi-party system encompassing diverse ideological and practical orientations, but "bounded communities", such as ultra-nationalists, religious conservatives, and Kemalists (Öniş, 2015). Thus, people vote based on their identities in the socio-political groups. Sunni-Muslim nationalism had recently represented the strongest trend within the Turkish political system. Türkiye is globally acknowledged as a prominent nation within the Islamic world, primarily related to its Sunni-Muslim identity. This emphasis of the Sunni-Muslim identity has affected both national and international politics and policies for the last 20 years. Concomitantly, Türkiye has been facing many crises, such as a high inflation rate (with the Covid-19 pandemic), currency crises, and refugee burdens (Öniş, 2023, Kutlay and Öniş, 2023). The combination of these crises and the high population cause inequalities, poverty, and unemployment rate in Türkiye.

Despite these socio-economic challenges, the Ministry of Health (MoH) implemented successful health policies. From 2003 to 2013, the Health Transformation Programme (HTP) helped to restructure health system financing, delivery, and regulation (Atun et al., 2013). As a part of this programme, five pre-existing insurance schemes were consolidated into a mandatory General Health Insurance Scheme, adopting a single-payer system. Türkiye successfully reformed its health system, granting citizens the right to universal health coverage, thereby reducing inequities in financing, access to services, and health outcomes (Atun et al., 2013). In 2021, 99% of the population had this compulsory social health insurance (OECD, 2023). This health insurance is comprehensive and finances almost all services in Türkiye, such as primary, preventive, in-patient, and ambulatory care. Other areas covered for free without any eligibility criteria include paediatrics, long-term medical support care, infectious disease treatment, drug abuse and addiction prevention services, childbirth services, and emergency care.

The health service is delivered predominantly through a public system (World Health Organization, 2022). People also use private providers on a basis of their insurance or out-of-pocket payment. Each individual is registered with a family healthcare centre staffed by family physicians and other healthcare professionals who provide primary care and referrals to specialist services. In addition to these family health care centres, multi-purposed health life centres operate to improve healthy lifestyles in community health. The Ministry of Health owns 59% of all (general, secondary, and tertiary care) hospitals, followed by the private sector (with 37%) for secondary care, and universities (with 4%) for highly specialised and complex tertiary care hospitals (World Health Organization, 2022).

While an improvement has been achieved in health indicators with all these reforms (such as increasing life expectancy, reducing unmet health needs, and child and maternal health) (World Health Organization, 2022), unfortunately, the health system has started to face difficulties as a result of national and international political factors. The first challenge in the health system is the high rate of emigration of doctors and nurses from Türkiye to other countries. According to Türk Hemşireler Derneği (THD, 2023), 46% of 7309 nurses surveyed are actively working to fulfil the requirements (language and diploma equivalency) to emigrate to other countries, while all the remainder report having considered the possibility of emigrating. The second problem is the refugee burden. Türkiye hosts the largest number of refugees of any nation worldwide (UNHCR, 2023), due to events such as the Syrian Civil War and prolonged political disturbance in Iraq. Presently, Türkiye accommodates approximately 3.6 million officially registered Syrian refugees, in addition to nearly 320,000 individuals of concern from diverse nationalities (UNHCR, 2023). Recently, Türkiye has had fewer hospital beds and healthcare workers (physicians and nurses) per population than most European countries (World Health Organization, 2022). This gap will only increase, given the combination of a growing population and more refugees from other countries (such as Iraq, Iran, and Afghanistan). Besides the ongoing health workforce shortage, another challenge is persistent geographic inequalities related to distribution of healthcare workers between western and eastern cities of the country, or between rural and urban areas of the cities (World Health Organization, 2022).

2.9. Rationale of this PhD thesis

Evidence from previous studies regarding the symptoms typically experienced by individuals living with heart failure indicates the need to investigate the full spectrum of heart failure and symptoms with respect to LVEF-based heart failure subtypes, older age, biological sex, Turkish culture to support more inclusive and equal heart failure management for an effective and comprehensive symptom assessment. Therefore, this PhD project aimed to investigate the full spectrum of symptoms associated with heart failure, and the stratified realities in symptoms and symptom changes. Understanding the full spectrum of symptoms can provide the most effective symptom assessment. **Box 2-1** provides details about the directions of this project to understand symptoms reflecting the reality of individuals with respect to their socio-cultural-behavioural context.

Box 2-1: Directions for symptom research in heart failure for this research

1. **Understanding the full spectrum of symptoms**
    - Evaluating symptoms not listed in the ESC Guidelines but experienced by people with heart failure. Without understanding individual symptoms profile, identification of the most problematic ones and symptoms cluster would not be possible.
2. **Underlying the mechanism and priority symptoms**
    - Identifying the importance of individual self-reported symptoms for effective symptom assessment in heart failure.
    - Evaluating uniqueness of symptom profiles for each individual with respect to their socio-cultural-behavioural context.
    - Identifying the worsening trajectory of symptoms in different subgroups of individuals identified.
3. **Measurement of symptoms**
    - A multimethod approach is adopted (combining qualitative and quantitative approaches) to identify subjective symptoms (based on one-on-one communication).
    - Comparing/contrasting of individual symptoms and symptom changes.
    - Identifying the correlates of worsening heart failure symptoms.
    - Identifying the best comprehensive and systematic symptom assessment measurement for individuals.
4. **Targeted strategy**
    - Identifying the importance of self-reported symptoms to personalise symptom assessment: the most effective symptom assessment strategy.

2.10. Chapter summary

This chapter has presented some key background details in relation to heart failure. In doing so, it identifies the gap in evidence in respect to understanding the full spectrum of symptoms experienced by people living with heart failure (the focus and starting-point for the research described in this thesis). Although prior research studies reported more symptoms than listed in the current clinical guidelines, there is a lack of investigation of the full spectrum of symptom experiences of people with heart failure with respect to their individual characteristics within their socio-cultural-behavioural context.

The decisions made in developing the research design and the study process relevant to the pre-established literature are discussed in the following chapter.

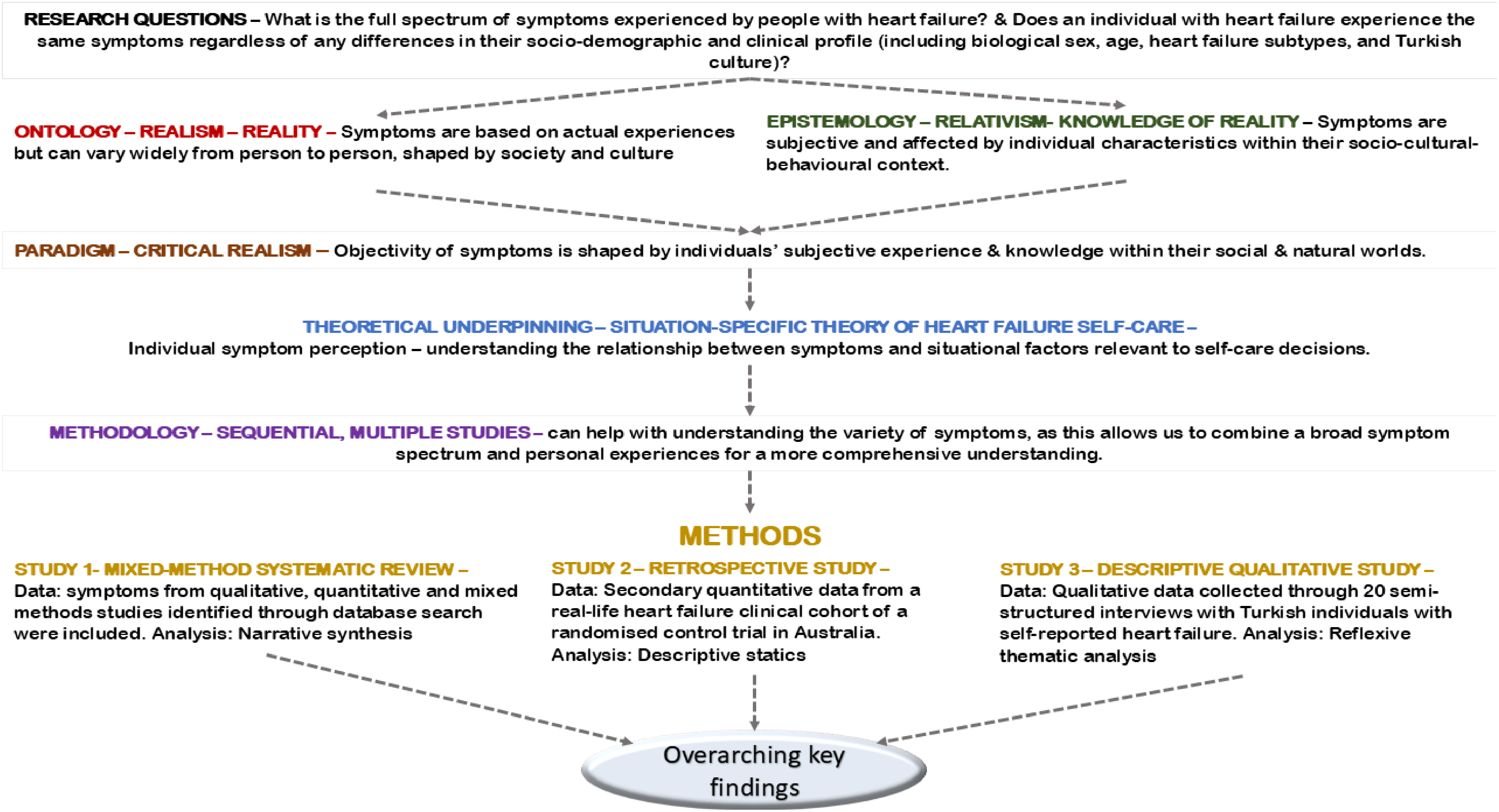
Chapter Three - Literature pertaining to selected methods

3.1. Introduction

This chapter describes the literature pertaining to the selected methods described in this PhD research, which investigated the full spectrum of symptoms through a series of the studies. Firstly, common research paradigms are presented – such as positivism, interpretivism, and pragmatism. Then, critical realism (CR), a philosophical orientation, is introduced to clarify the epistemological and ontological perspective of the researcher. The choice of a multiple studies or methods approach is justified. Details are provided about sequential, multiple studies approach, as well as a discussion of the rationale for employing a mixed-methods systematic review, along with the methods for collecting and analysing quantitative and qualitative data, within reference to the relevant literature. Following this theoretical underpinning, the Situation-Specific Theory of Heart Failure Self-care (revised and updated in 2016) (Riegel et al., 2016) is introduced. **Figure 3-1** presents the overview of the study based on my philosophical position and chosen theoretical underpinning to inform the selection of a sequential, multiple studies approach to data collection and analysis methods.

3.2. Philosophical assumptions and the approach to reality and knowledge

Each research process starts with problem identification and specification of research question/hypothesis, followed by a paradigm choice of theoretical/conceptual framework (Sumner and Tribe, 2004, Polit and Beck, 2017). A paradigm, which offers a broad perspective on the nature of reality and our relationship to it, is essentially a worldview (Creswell, 2015, Guba and Lincoln, 1994, Polit and Beck, 2017). Paradigms can frequently be described in terms of how they address fundamental philosophical issues regarding the ontological or epistemological assumptions (Polit and Beck, 2017). An ontology ("What is the real – reality?") is a set of fundamental presumptions about how things interact in the world under study (Creswell and Plano Clark, 2018). Epistemology ("What can we know?") is focused on "how we know what we know," as well as the nature, history, and scope of knowledge. Both ontology and epistemology help to determine specific methods for research design (Guba and Lincoln, 1994).



RESEARCH QUESTIONS – What is the full spectrum of symptoms experienced by people with heart failure? & Does an individual with heart failure experience the same symptoms regardless of any differences in their socio-demographic and clinical profile (including biological sex, age, heart failure subtypes, and Turkish culture)?

ONTOLOGY – REALISM – REALITY – Symptoms are based on actual experiences but can vary widely from person to person, shaped by society and culture

EPISTEMOLOGY – RELATIVISM- KNOWLEDGE OF REALITY – Symptoms are subjective and affected by individual characteristics within their socio-cultural-behavioural context.

PARADIGM – CRITICAL REALISM – Objectivity of symptoms is shaped by individuals' subjective experience & knowledge within their social & natural worlds.

THEORETICAL UNDERPINNING – SITUATION-SPECIFIC THEORY OF HEART FAILURE SELF-CARE –
Individual symptom perception – understanding the relationship between symptoms and situational factors relevant to self-care decisions.

METHODOLOGY – SEQUENTIAL, MULTIPLE STUDIES – can help with understanding the variety of symptoms, as this allows us to combine a broad symptom spectrum and personal experiences for a more comprehensive understanding.

METHODS

STUDY 1- MIXED-METHOD SYSTEMATIC REVIEW –
Data: symptoms from qualitative, quantitative and mixed methods studies identified through database search were included. Analysis: Narrative synthesis

STUDY 2 – RETROSPECTIVE STUDY –
Data: Secondary quantitative data from a real-life heart failure clinical cohort of a randomised control trial in Australia. Analysis: Descriptive statics

STUDY 3 – DESCRIPTIVE QUALITATIVE STUDY –
Data: Qualitative data collected through 20 semi-structured interviews with Turkish individuals with self-reported heart failure. Analysis: Reflexive thematic analysis

Overarching key findings

Figure 3-1: Overview of the PhD research

3.2.1. Research paradigms in healthcare

The philosophical approach of the researcher influences the research question, studied population, selected subject, research process, and interpretation of the results (Weaver and Olson, 2006). The paradigm is built on the shared beliefs and presuppositions of important concepts (Bahramnezhad et al., 2015). In this study, these concepts would be those such as *person*, *health*, *environment*, and *nursing*. Nursing researchers employ philosophical statements to assess the consistency of individual, collective, organisational, and social beliefs/values (Parker, 2006). The methods and research approaches used are based on and reflect the ontology, epistemology, and methodology of the paradigm (Houghton et al., 2012, Kelly et al., 2018). The following common paradigms are generally used in healthcare research.

Positivism: The positivist philosophy is based on the presumption that phenomena may be studied using logic, measurement, and deductive reasoning to demonstrate absolute truths. Empiricism, the primary assumption of positivism, asserts that what can be observed with the five senses is factual, implying the presence of an objective, universal reality that is the object of universal rules and procedures (Polit et al., 2013, Ryan, 2018). Within this philosophical framework, the researcher's role is that of objectivity and distance, of explorer of universal realities, and verifier of concepts/hypotheses in the pursuit of unbiased universal truths through the use of quantifiable measurements reflecting quantitative methods, including mathematical and statistical analytical procedures to generalise the findings of the phenomenon under study (Kelly et al., 2018).

Post-positivism: Post-positivism as a paradigm highlights the epistemological attitude that research outputs include an estimation of truth as opposed to absolute truth, as is expressed in the positivist stance, and it shows an epistemological and ontological evolutionary process in interpreting the world (Creswell and Creswell, 2018). Some fundamental presumptions of this paradigm reflect an "epistemological scepticism", which holds that knowledge is hypothetical rather than absolute (Weaver and Olson, 2006). The goal of research, in this view, is to establish statements, then innovate, abandon, or refine them to make other, more firmly supported assumptions (Kelly et al., 2018). Ontologically, the post-positivist viewpoint presupposes that our understanding of reality may not be absolute (Welford et al., 2011). Post-positivism can be described by the terms intuitive, comprehensive, inductive, and exploratory (Kelly et al., 2018).

Interpretivism: The interpretivist paradigm adopts a subjectivist and intersubjectivist epistemic attitude (Weaver and Olson, 2006). The ontological position acknowledges the possibility of many realities while reflecting lived experience, cultural influence, and meaning (Welford et al., 2011). This paradigm places a strong focus on the awareness of potential "multiple realities," which are explained from the emic standpoint of "lived experience" (Welford et al., 2011, Weaver and Olson, 2006). The goal of interpretivism is to create objective results from a subjective viewpoint. A subjectivist perspective is reflected in the researcher's role as interpretation. Recognising that one's personal experiences may have influenced one's views is a necessary component of this position for the researcher (Rolfe, 2006). Approaches within this paradigm consequently place a strong emphasis on reflexivity.

Constructivism: The constructivist paradigm, which is sometimes associated with interpretivism, essentially challenges both the positivist and post-positivist perspectives (Creswell and Creswell, 2018). Constructivism focuses on "how we know" and, essentially, "what meanings we give to this knowledge" from an epistemological standpoint and addresses the unique experience of each individual (Kelly et al., 2018, Young and Collin, 2004).

Pragmatism: From an ontological and epistemological standpoint, the pragmatic paradigm demonstrates a pluralistic emphasis on both comprehending the world and how to answer research questions or problems (Polit and Beck, 2017). In order to engage and address the complexity of real-world research addressing a variety of real-life difficulties, emphasis is placed on "methodological openness" (Creswell and Creswell, 2018). To better address the study question, pragmatic researchers may employ a variety of research methodologies in their research (Onwuegbuzie and Leech, 2005).

Critical social theory: A critical theory viewpoint presupposes that truth exists in the form of "accepted realities" shaped by political, social, cultural, gender, and economic elements that have come to be seen as "real" over time (Weaver and Olson, 2006). Critical social theory researchers have concentrated on raising public awareness and knowledge of social issues as well as making sure that the concerns of marginalised groups are represented (Parlour and McCormack, 2012). Since these are the primary ways that power is differentiated in society, factors such as gender, race, and class concerns are of great interest to critical theorists (Weaver and Olson, 2006).

The choice of the critical realism paradigm for this PhD thesis is driven by the need to move beyond individual experiences and gain a more comprehensive understanding of how heart failure symptoms are perceived and interpreted within the context of society and culture. Critical realism permits the researcher to delve deeper into the experiences of heart failure symptoms. It recognises that there are different layers of reality, including the personal experiences of individuals and the wider societal and cultural influences that shape these experiences. This paradigm provides a framework for comprehending how these personal symptom experiences are interconnected with and shaped by the social and cultural context.

3.2.2. Critical realism

In terms of knowledge generation, critical realism emphasises the possibility of recognising both individual and collective meaning generation. A realist ontology and an interpretive epistemology are combined in critical realism (Alderson, 2021). It is a position that maintains a concept of truth and reality while acknowledging that human practises always shape how we experience and know things – practices that can be said to give rise to perspectival and contextual truths (Braun and Clarke, 2022). It combines ontological realism with epistemological relativism. Critical realism was chosen to explain objective symptoms (reality) shaped by individual's subjective knowledge and understanding (relativism) through their characteristics (including age, settings, biological sex, heart failure subtypes and culture).

Roy Bhaskar (1944–2014), a philosopher of science, played a seminal role in the formulation and dissemination of critical realism (Bhaskar, 1978). The orientation describes a transition between the social and natural worlds by integrating general scientific and social science philosophies (Bhaskar, 1978, McEvoy and Richards, 2006). The purpose of research is to promote deeper levels of reasoning and comprehension rather than to identify (for positivists) generalisable laws based on statistical relationships between dependent and independent variables or (for interpretivists) the lived experiences or beliefs of social actors (McEvoy and Richards, 2006). There are three levels of ontology in critical realism (Bhaskar, 1978, Buch-Hansen and Nielsen, 2020): "***the empirical***" (what can be observed or experienced), "***the actual***" (what is going on that may not be observed but which is regulating the empirical), and "***the real***" (what is hidden but a necessary precondition for the actual and empirical). Its guiding concepts recognise that society and people coexist in a social environment; mechanisms and structures impact on existence; and that a human being acting as an individual can sometimes not be aware of the influence that larger social structures have on them (Buch-Hansen and Nielsen, 2020, Alderson, 2021, p.49-51). This essentially indicates that the link between ontology and epistemology is being reoriented, acknowledging the necessity of analysing what is real (ontology) through the lens of what is understood and known (epistemology) (Buch-Hansen and Nielsen, 2020).

According to critical realists, the nature of the research problem should be taken into consideration while choosing a method (McEvoy and Richards, 2006). In fact, considering this angle, it is advised that the best course of action is to combine quantitative and qualitative approaches or techniques triangulation, a strategy that entails employing more than one method or source of data to analyse a social phenomenon. The application of these quantitative and qualitative methodologies is crucial from a critical realist standpoint (Pratschke, 2003). Therefore, the researcher has chosen critical realism as a philosophical position in this PhD thesis, which adopts a multiple studies research approach.

3.2.2.1. Critical realism in this project

Critical Realism paradigm was chosen to investigate heart failure symptoms because it offers a comprehensive perspective that goes beyond mere subjectivity and allows for a more comprehensive examination of how these symptoms are perceived, experienced, and influenced within the broader social and cultural environment. More simply, critical realism has been chosen as the best way to explain objective symptoms regarding the stratified reality of human knowledge and understanding shaped by society and culture. In the following, the PhD researcher explain these in detail in terms of the three domains of critical realism.

Real domain (symptom mechanism and structure): When people evaluate symptoms they experience (feelings of physical or mental change), the inner and external meanings of symptoms are shaped by an individual subjective understanding of themselves and their world (relativism – knowledge). Their subjective knowledge and understanding create different single- or multi-layered symptoms. Thus, symptom experiences may occur in the real domain with respect to the individual differences shaped by their socio-cultural beliefs/values. Understanding the mechanism and structure of individual symptoms is the first step towards managing them. Since symptoms are subjective, the process for the evaluation of symptoms should be based on one-on-one communication.

Actual domain (symptoms that generating by mechanisms and structures): In this domain, symptoms occur spontaneously. However, the reality of symptoms is ordered into various strata such as society, physical, and psychological ones.

Empirical domain (outcomes of observed and experienced symptoms): Objective clinical outcomes (including symptoms or symptom-related issues such as quality of life and symptom management) can be observed and identified in this domain. However, these symptom outputs/outcomes in the empirical domain are a result of the causal mechanism existing in the real domain, and then events in the actual domain.

Pragmatic critical realism combines two approaches to truth testing knowledge claims (Heeks et al., 2019, Imran, 2024). First, from a critical realist perspective, it offers evidence supporting proposed mechanisms in various contexts. Second, from a pragmatic perspective, it focuses on applying this knowledge in different contexts to achieve intended outcomes. This combination allows for a gradual accumulation of triangulated evidence across different contexts, confirming that the proposed mechanisms effectively achieve their intended practical purposes (Heeks et al., 2019, Imran, 2024). Pragmatic critical realist based research helps us understand the nature of proposed mechanisms in specific contexts, thereby guiding practical actions (Imran, 2024). It can offer a holistic and practical approach to address complex issues. In mixed-methods and multimethod studies, pragmatic critical realism is an effective approach to integrate quantitative and qualitative methods in research (Imran, 2024). It aims to provide valid knowledge claims based on practical effectiveness in various contexts (Heeks et al., 2019). With that in mind, the researcher employed the critical realist paradigm as the primary framework to elucidate the impacts of bio-psycho-socio-cultural differences on people's understanding of symptom realities. She then utilised pragmatism to strengthen practical actions and foundations within the PhD research programme. This approach enables the examination of diverse perspectives and layered realities related to symptoms and self-management in heart failure research.

3.3. Methodological decision

A multiple studies design was chosen for this PhD research to comprehensively explore the complex and multifaceted nature of heart failure-related symptoms in order to address the research main aims. The combination of different study approaches (mixed-method systematic review, quantitative (such as questionnaires and clinical measures) and qualitative approaches (such as in-depth interviews) enabled the research to capture both objective, measurable aspects of heart failure symptoms and also patients' subjective experiences and narratives. The investigation of complex or sensitive issues in healthcare can benefit from a more flexible, methodological approach. Therefore, a multiple studies approach was selected in order to develop a more complete picture of what kind of symptoms are experienced by people living with heart failure and their individual characteristics for the differences of symptoms.

Why a multiple studies design was chosen

This PhD research extensively explored the full spectrum of heart failure symptoms and the factors affecting these symptoms. While systematic reviews of RCTs and RCTs traditionally provide robust evidence (Aveyard, 2019), they often prioritise limited typical heart failure symptoms as secondary outcomes, as highlighted in Chapter 2. This approach might overlook the broader range of symptoms experienced by individuals with heart failure, disregarding their unexplained individual perspectives. From a critical realist perspective, this study aims to delve into the personalised assessment of symptoms, acknowledging their varied influences, including psycho-socio-cultural aspects. Using a mixed-method design can provide a more comprehensive picture for understanding issues and problems in healthcare to improve the well-being of patients and society (Farquhar et al., 2011, Richards and Rahm Hallberg, 2015). In mixed-method designs such as exploratory and explanatory, sequential phases are interdependent, with later phases informed by earlier ones to explain or explore earlier findings (Creswell and Plano Clark, 2018, Creswell and Creswell, 2018). In this PhD thesis programme, the main aims are not to explain or explore earlier studies' findings, but rather to identify different mechanisms and structures to highlight the importance of individual symptom assessment from a critical realist perspective. By integrating different methods, this multiple (multimethod) studies approach allows for a comprehensive understanding, enabling a nuanced exploration of individual experiences within the complex context of heart failure.

3.4. Sequential, multiple studies design

The rationale for choosing a multiple studies design was to thoroughly investigate the complex and multifaceted nature of symptoms associated with heart failure to address the main of research aims. This approach seamlessly facilitated the comprehensive exploration of both the objective, quantifiable aspects of heart failure symptoms and the subjective experiences and narratives of patients. Multiple design approach is described as the use of different research designs within a single project to address different aspects of a broader research question (Anguera et al., 2018). It is crucial to keep in mind this design is open to a full variety of possible methodological variations or combinations. This design can be sequential or parallel. The designs or studies might not necessarily feed into each other. They can be independent studies, exploring the same phenomenon (Anguera et al., 2018). However, the studies in this current PhD thesis programme are organised to progress from literature reviews to clinical studies, and finally to individual perspectives on understanding symptoms and the associated personal and clinical factors.

A sequential, multiple studies design was adopted to answer the research questions of this PhD research (**Figure 3-2**). The study comprised three sequential studies: a mixed-method systematic review, a secondary data analysis, and a descriptive study. A mixed-methods systematic review investigated the full spectrum of symptoms from the previously published literature in the heart failure cohort. Secondary data analysis was performed to explore sex-specific and stratified differences in symptoms pertaining to heart failure subtypes. Subsequently, semi-structured interviews were conducted with Turkish people to identify their symptoms, breathlessness experiences and management, and their health needs. Separate findings, as provided in Chapters 5, 6 and 7, were produced by collecting (for only qualitative) and analysing data for each component independently. In Chapter 8, these results are combined and examined.

Despite the challenges posed by the diverse methodologies in multiple studies, the use of triangulation is suggested to provide a more accurate understanding of the phenomenon under study (Brewer and Hunter, 2006). The triangulation approach is employed in primary care research with the aim of bringing together and reconciling numerical (quantitative) and textual (qualitative) data (O’Cathain et al., 2010, Farmer et al., 2006, Foster, 1997, Erzberger and Prein, 1997, Morse, 1991). It may be applied to explain the agreement between two distinct sets of results or to explain the process of researching a subject using several techniques to obtain a clearer picture (O’Cathain et al., 2010). (O’Cathain et al., 2010, Erzberger and Prein, 1997). In multiple method studies such as this one, the latter interpretation is frequently adopted. Particular attention was paid to the areas where the results from each method concur (convergence), provide additional information on the same topic (complementarity), or seem to contradict one another (discrepancy or divergence) (O’Cathain et al., 2010, Morgan, 1998, Erzberger and Prein, 1997). The interaction took place at the triangulation step, when the findings were evaluated jointly to derive an interpretation of the overall findings.

The main rationale for the use of triangulation is to reduce the liabilities of the use of a single strategy and increase the ability to interpret findings (Denzin, 1978, Altricher et al., 1996, Morgan, 1998). Additionally, it bolsters the validity and applicability of findings (Bogdan and Biklen, 1997), instilling greater confidence in the research dataset (Erzberger and Prein,

1997) and the opportunity for a deeper and better understanding of the phenomenon studied (O'Cathain et al., 2010). However, it necessitates more time and effort to finalize findings (Denzin, 1978, Altricher et al., 1996, Morgan, 1998), along with increased data collection, planning, organisation, and resource allocation (O'Donoghue and Punch, 2003). It may also create the possibility of disharmony among the findings due to a lack of understanding of the phenomena studied (Thurmond, 2001).

After the data analyses of these three studies, the overarching key findings of this PhD thesis programme were summarised from the results of these studies. A table display was designed and employed to help decide on the overarching key findings or meta-themes. A table display or matrix can often be useful in summarising key decisions in one column with the supporting evidence in the other columns. Data from different methods can be organised and presented visually in matrices and diagrams. The final synthesis of the results provided a comprehensive understanding of symptom assessment in heart failure.

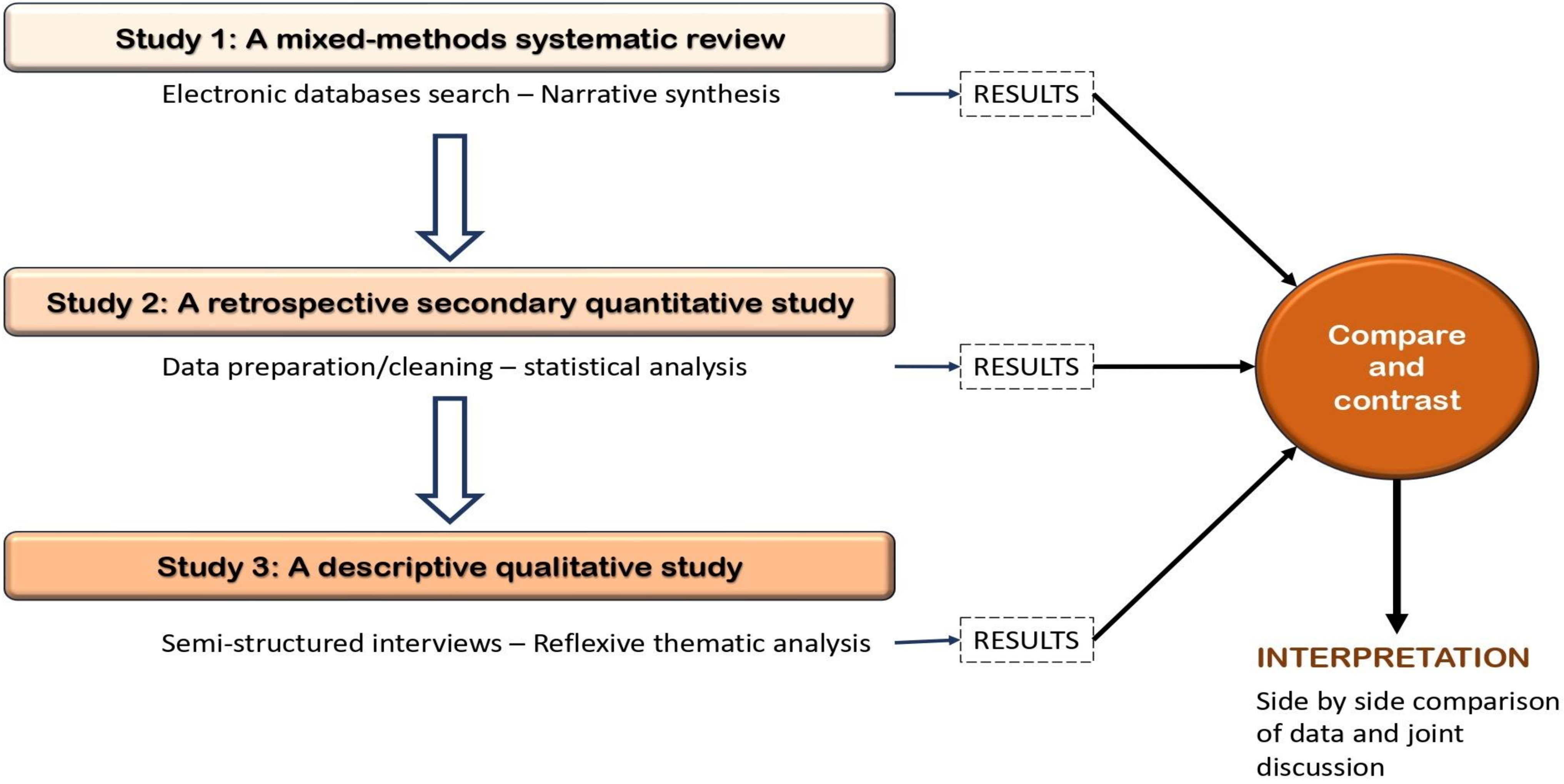


Figure 3-2: Sequential, multiple studies research

3.5. Rationale for Study I: Mixed-methods systematic review

Study 1 was a mixed-methods systematic review investigating the full spectrum of symptoms from existing literature among the heart failure cohort. According to Bleijenberg et al. (2018), identifying the evidence base in the literature is one of the core components for developing interventions. Systematic reviews are the most effective way to promote evidence-based practice (Lizarondo et al., 2022, Siddaway et al., 2019). A systematic review is a comprehensive search designed to bring together all primary studies relevant to a predefined research query. This requires careful evaluation of the research and synthesis of its results (Gopalakrishnan and Ganeshkumar, 2013).

Systematic reviews play a crucial role in minimising research inefficiency by guaranteeing that new primary research is conducted with a comprehensive understanding of existing studies, and that new research findings are analysed within the context of pre-existing knowledge (Siddaway et al., 2019). The value of a mixed-methods systematic review is unquestionable, as it integrates quantitative and qualitative evidence into a single review (Lizarondo et al., 2022). As mixed-methods systematic reviews maximise the effectiveness of review findings to support clinical and policy decision-making, they have been recognised as a significant step in evidence-based healthcare (Stern et al., 2020). Also, a review of the existing literature with a mixed-method systematic review can help to clarify how people's everyday lives and health are affected by living with multimorbidity (two or more chronic conditions) (González-González et al., 2021). A mixed-methods systematic review is the best way to provide the most reliable evidence base possible for the review questions being investigated from a critical realist point of view. As stated in Chapter 2, many studies use standard heart failure measurement instruments that focus on typical heart failure symptoms, rather than on less typical and non-ESC symptoms. Therefore, incorporating qualitative studies and the qualitative findings from mixed-method studies can help reveal additional symptoms. Therefore, a mixed-methods systematic review method was chosen to identify the evidence base from previously published literature of the full spectrum of symptoms and three associated factors (setting, age, and biological sex) in the typical and less typical ESC symptoms among people living with heart failure.

Systematic reviews have certain limitations, such as study selection issues, heterogeneity, and inappropriate subgroup analysis (Gopalakrishnan and Ganeshkumar, 2013). To minimise these limitations, researchers adopt the following actions: clear aims and research questions; comprehensive search strategy with relevant search terms and inclusion and exclusion criteria; a rigorous database search; critical appraisal of the research and papers; and appropriate data summarising techniques (Gopalakrishnan and Ganeshkumar, 2013, Siddaway et al., 2019, Impellizzeri and Bizzini, 2012). Searching multiple databases and grey literature is advised to capture relevant studies (Siddaway et al., 2019, Impellizzeri and Bizzini, 2012). To identify the relevant studies or publications related to research questions from the literature, a systematic search was carried out in electronic databases and then grey literature searches in this PhD thesis. Narrative synthesis was conducted to summarise the quantitative and qualitative findings based on converting synthesis design (Stern et al., 2020, Lizarondo L, 2020, Siddaway et al., 2019). This helps to present both quantitative and qualitative findings together, by using the same synthesis method. Since this current mixed-methods systematic review investigated the full spectrum of symptoms in heart failure, data transformation (Stern et al., 2020, Lizarondo L, 2020) can be involved. A narrative synthesis of both quantitative and qualitative data was performed. More details on this are provided in **Chapter 4: Methods**.

3.6. Rationale for Study II: Secondary quantitative data analysis research

Study II was a secondary data analysis of a previously published randomised control trial comparing two forms of nurse-led management in a real-world cohort of heart failure patients (the WHICH? II Trial: “Which Heart Failure Intervention Is Most Cost-effective in Reducing Hospital Stay”, (Scuffham et al., 2017). The researcher reused this comprehensive dataset and analysed it with a focus on the aims and objectives of the current study. More information on how the researcher used this dataset to answer the study research questions will be provided in **Chapter 4: Methods**.

Secondary data analysis involves examining and interpreting existing data collected for a purpose other than the current research. Secondary data analysis is a methodology for doing further analysis and interpretation of pre-existing statistical data to answer the original research question with better statistical techniques or new and different research question (McArt and McDougal, 1985, Stewart and Kamins, 1993, Sherif, 2018, Hakim, 1982, Johnston, 2014, Dale et al., 2008, Salkind, 2006, Devine, 2003). Researchers can use the secondary data analysis to re-analyse or re-use the quantitative and qualitative data (Dale et al., 2008, Heaton, 2008, Devine, 2003).

There are many advantages of doing secondary, rather than primary data analysis (Johnston, 2014, Salkind, 2006, Devine, 2003): (a) It saves the long and costly process of data collection; (b) Re-analysing data from a different perspective can create new knowledge and increase the quality of the existing data; (c) Large-scale datasets will often have a large sample size that may help researchers to achieve greater statistical reliability.

There are however also challenges and difficulties researchers can face in relation to secondary data analysis methodology: (a) Ethical considerations: the primary data collectors have a key responsibility to protect the data, and secondary researchers must respect the factors pertaining to this (Dale et al., 2008, Ruggiano and Perry, 2019, Devine, 2003); (b) Primary data is collected for a specific purpose and cannot always be applied to a new research question or answer different questions (Johnston, 2014, Salkind, 2006, Devine, 2003).

3.7. Retrospective quantitative research

Retrospective research has a place in science, and many of these studies have influenced medical practices. Retrospective studies might be analytical (cross-sectional, case-control, and cohort studies) or descriptive (case series and cross-sectional studies) (Ranganathan and Aggarwal, 2018). Cohort studies are used to estimate the likelihood that an outcome will occur in a group of people who have been exposed to a risk factor (Talari and Goyal, 2020). Cohort studies may be used to infer a correlation between the variable and the result over a period of follow-up time (Talari and Goyal, 2020, Ranganathan and Aggarwal, 2018).

There are a few advantages and disadvantages of retrospective studies of existing data. ***Advantages of retrospective studies*** (Hess, 2004, Talari and Goyal, 2020) are that they inexpensive; use existing records; allow for the investigation of unusual events; make it simpler to evaluate circumstances where there is a long lag time between exposure and sickness; and are able to produce hypotheses that are later retrospectively validated (quality improvement initiatives). ***Disadvantages of retrospective studies*** (Hess, 2004, Talari and Goyal, 2020, Tofthagen, 2012) are that they rely on a written record's accuracy or a person's memory (recall bias); there can be a lack of critical information; they pose a difficulty in controlling bias and confounders due to lack of blinding and randomisation; access to crucial information could be restricted (by a law or institutional rules); establishing causality and effect is challenging; and results are most useful for creating hypotheses.

The researcher accepts that the re-use or re-analysis of existing datasets (performed for different research purposes) poses the risk of certain biases. However, she took actions to reduce these biases in this retrospective secondary data analysis research, as listed below:

- ***Lack of comparison/Differences in baseline characteristics of groups.*** Differences in baseline characteristics of potential groups may have an impact on the outcome (Tofthagen, 2012). An appropriate comparison between groups and all significant variables were added to the logistic regression analysis to minimise this risk.
- ***The effects of the intervention/any other event.*** The intervention and other events can affect the findings (Tofthagen, 2012). The original study tested the effectiveness of an intervention in heart failure in Australia. A combination of intervention and control arms was added to the secondary data analysis. One potential limitation is the effects of the intervention on the results of the secondary data analysis.
- ***Missing data.*** Since the data was not collected specifically for this secondary data analysis, it is inevitable that there will be some missing information even in the original dataset included (Talari and Goyal, 2020). To address this, only participants with baseline and 12-month data were included in this secondary data analysis study – ensuring no missing information that affected the results of the study.
- ***Loss of follow-up in the original dataset.*** In retrospective research, the causes of missed follow-ups are frequently indeterminate and could bias the findings (Talari and Goyal, 2020). Participants who died before completing the 12-month follow-up data collection were therefore excluded. As the researchers needed to understand symptom changes over one year in men and women across heart failure subtypes, all incomplete 12-month data were excluded. This ensures that any missing follow-up data does not affect the results of our study.
- ***Generalising the results.*** Generalising the results to larger populations can be problematic (Tofthagen, 2012, Talari and Goyal, 2020). This is one of the external validity issues. This secondary data analysis investigated sex-stratified differences with regard to other factors to support the divergence of symptoms of heart failure. Basically, the findings can be generalised to highlight these stratified realities in symptoms.

3.8. Rationale for Study III: Qualitative research

Qualitative research involves the exploration of broad inquiries into human realities and experiences. Through ongoing interaction with subjects within their authentic contexts, qualitative research yields detailed and descriptive information that enhances our understanding of their experiences (Renjith et al., 2021). Specialised procedures within qualitative research allow for obtaining in-depth responses regarding individuals' thoughts and emotions (Dongre et al., 2009).

Qualitative inquiry, in contrast to quantitative methods, aims to investigate, describe, and elucidate phenomena while providing an in-depth understanding of complex realities (Renjith et al., 2021). Through qualitative data collection, researchers obtain rich insights into the phenomena of interest, emphasising the perspectives and voices of participants through direct quotations. This approach facilitates a comprehensive understanding of processes, particularly those that unfold over time. When quantitative measurements are insufficient, qualitative methods offer a valuable means to gather data and gain a deeper understanding of concepts (Creswell et al., 2011, Curry et al., 2009).

Grounded theory, case studies, phenomenology, descriptive qualitative, narrative studies and ethnography are examples of common interpretive research methods in health care (Johnston and Dowling, 2023, Renjith et al., 2021). Descriptive qualitative studies are used commonly in nursing (Johnston and Dowling, 2023). This approach is also widely employed in mixed-methods studies, where qualitative data can be utilised to validate and corroborate findings in convergent studies, as well as to explain quantitative findings in explanatory studies, construct questionnaires in exploratory studies, and explain quantitative findings in explanatory studies (Doyle et al., 2016). There has been an increase in the use of descriptive qualitative study in large-scale healthcare intervention studies (Doyle et al., 2020). This type of research can be used for a variety of purposes, including determining participants' perceptions of why an intervention worked or, more importantly, why it failed to work and how the intervention may have been enhanced (Doyle et al., 2016). Qualitative descriptive research can make the results of intervention studies more clinically relevant and meaningful (Doyle et al., 2020). Since this PhD research investigated the full spectrum of the symptoms and associated factors from the perspective of individuals with heart failure, the use of descriptive qualitative study design as a part of multiple method research provides a more in-depth understanding of these subjective symptom experiences and associated factors. A descriptive qualitative study was therefore considered appropriate, since the purpose of the qualitative data collection was to grasp individuals' perceptions of their breathlessness experiences and self-management strategies.

3.9. Descriptive qualitative design

A descriptive qualitative study is an appropriate choice to explore and describe the full spectrum of symptoms and experiences of breathlessness in a way that is grounded in the real-life context of the individuals involved insofar as it made possible the following outcomes: exploring the symptoms and breathlessness comprehensively; gaining a comprehensive and detailed understanding of them; providing findings from real-life experiences of individuals based on data collected rather than preconceived notions; and providing richer understanding of personal or subjective symptom experiences of individuals. Sandelowski (2000) description of the descriptive qualitative approach focused as its central idea on a broader summary of the context or event in the authentic everyday life of the subject(s). Descriptive qualitative approach allows for a deeper understanding of phenomena with an appropriate and rational combination of sampling, data collection, analysis, and representational techniques. Unlike high-inference qualitative methodologies (such as phenomenology or grounded theory), descriptive qualitative research needs a less conceptual or otherwise more abstract depiction of data, and calls for lower levels of interpretation (Sandelowski, 2000).

To establish conceptual categories and themes, researchers employ qualitative methodologies commonly referred to as “generic” procedures. These procedures include open coding, interviewing, and constant comparison, particularly in the context of descriptive qualitative studies (Sandelowski, 2010). According to Sandelowski and Barroso (2007, p.146), descriptive qualitative study occupies a location somewhere between exploratory and explanatory qualitative studies (**Figure 3-3**). They entail the development of conceptual or thematic descriptions derived from the data. Thematic descriptions involve narrative, phenomenological, or discursive interpretations of experiences, while conceptual descriptions encompass theoretical interpretations of phenomena, events, or situations, often associated with the social sciences and grounded theory research (Sandelowski and Barroso, 2007).

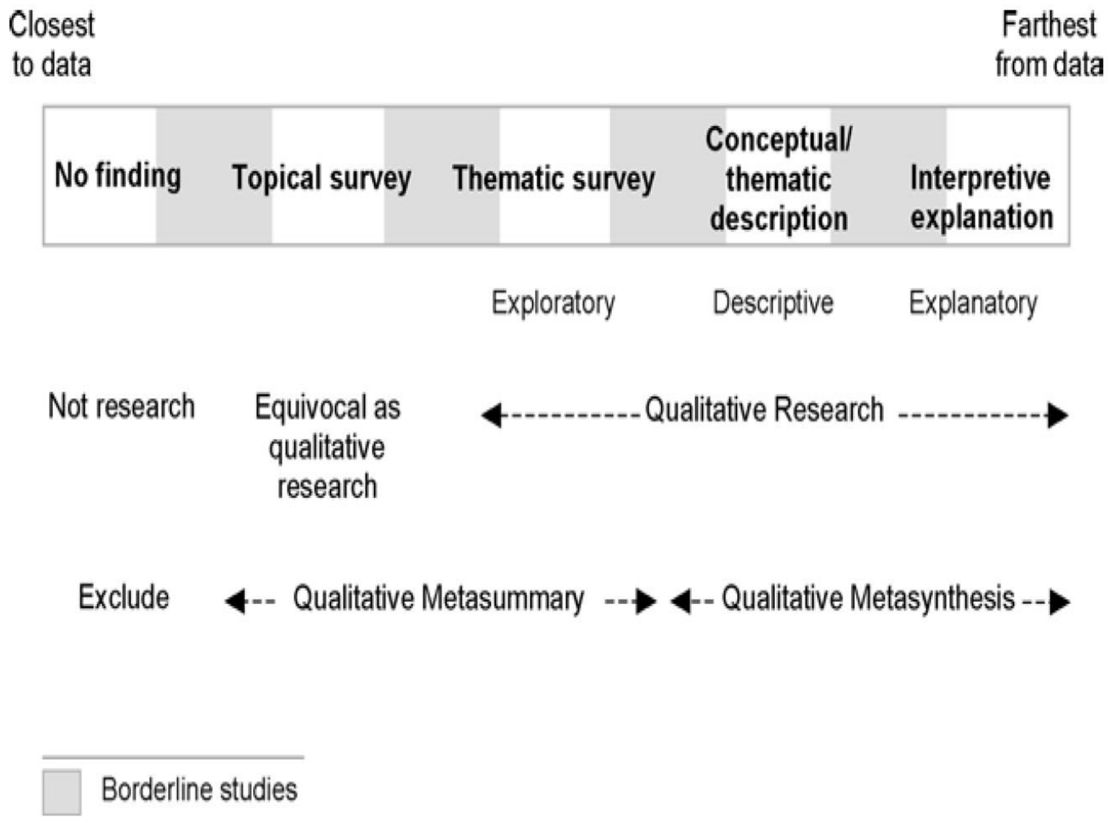


Figure 3-3: "Types of qualitative research findings by integration method" (Sandelowski and Barroso, 2007, p.134)

3.9.1. Rationale and challenges to descriptive qualitative study

Studies that are primarily descriptive in character are referred to as qualitative descriptions in qualitative research (Kim et al., 2017). This type of study is particularly prevalent in qualitative research on topics about healthcare and nursing because of their innate simplicity, adaptability, and usefulness in a variety of healthcare contexts (Polit and Beck, 2009, Doyle et al., 2020). One of the most frequent justifications for using a descriptive technique is to give evidence-based interpretations of feelings and perceptions, especially in fields where the subject under consideration is not well-known (Sandelowski, 2010). In descriptive qualitative studies, the findings are presented in a style that directly reflects or nearly approaches the terminology used in the original research question, recognising the subjective character of the problem and the varied experiences participants have (Bradshaw et al., 2017). The use of a descriptive qualitative approach in nursing is a good way to address significant clinical problems where the goal is to influence change and improve practice rather than to deepen theoretical or conceptual understanding (Chafe, 2017). Based on a realist perspective, the use of descriptive qualitative design helps to identify or generate themes for inductive and deductive reasoning regarding the phenomenon under investigation (Vaismoradi et al., 2013).

However, using descriptive qualitative design presents some challenges, as documented in the literature. Firstly, descriptive qualitative studies have been criticised for a lack of scientific rigour (Vaismoradi et al., 2013). This criticism of the descriptive qualitative design is exacerbated by the fact that it is not theory-driven or orientated, in contrast to other qualitative techniques such as phenomenology or grounded theory (Neergaard et al., 2009). Qualitative descriptive studies, on the other hand, frequently derive from naturalistic inquiry, which asserts a dedication to investigating something as close to its natural condition as is practical within the confines of the research setting (Lambert and Lambert, 2012). As a result, there can be no pre-selection of study factors, control of variables, and previous commitment to any one theoretical understanding of a given phenomenon. In other words, although the qualitative descriptive approach includes aspects of the other qualitative approaches, they are the least constrained by pre-existing philosophical or theoretical commitments. Another challenge is that the lack of transparency and inconsistent decision-making throughout the study process has undermined the credibility of this type of approach (Kahlke, 2014). According to Kim et al. (2017), more than half of researchers do not provide a rationale for the use of the descriptive qualitative design or clear justification for measurement and analysis technique decisions. Finally, it can be challenging to identify precisely what distinguishes a descriptive study design from the variety of other approaches available to qualitative researchers (Kim et al., 2017). Due to a lack of well-established methodological rules and boundaries for researchers, research texts and methodological papers become invisible (Kim et al., 2017, Kahlke, 2014). However, this may offer the flexibility and utility of a wide range of data collection and analysis methods to understand the phenomenon under investigation in-depth for the purpose of answering the research question (Neergaard et al., 2009).

Study III of this PhD research was a descriptive qualitative study including semi-structured interviews with people living with heart failure in Türkiye. We replicated a UK-nurse-based study (Walthall et al., 2017) in Türkiye to compare how symptom experiences are affected by the cultural and social context. Further information related to this is provided in **Chapter 4: Methods**.

3.9.2. Qualitative data collection: Semi-structured interviews

In qualitative research, the following data collection strategies are used: focus group discussions, one-on-one interviews, participant observation, simple observation, document analysis, narrative life history, videos or video footage, audio materials, and text analysis (Renjith et al., 2021). Interviews are the most prevalent techniques among these (Johnston and Dowling, 2023). There are three types of interviews: semi-structured, unstructured, and structured. Semi-structured interviews are a common qualitative data collection methods (Kallio et al., 2016).

Semi-structured interviews are utilised when there is enough objective information on an experience or phenomenon but insufficient subjective knowledge (McIntosh and Morse, 2015). Semi-structured interviews use a reasonably thorough interview guide or schedule that includes open-ended questions related to research questions and aims (Johnston and Dowling, 2023). Usually, these interview schedules (or guides) are based on the previous literature and consist of main questions (or themes) and then a few prompts or follow-up questions to cover the important areas of research interest being studied (Adams, 2015, Kallio et al., 2016). According to Kallio et al. (2016), a semi-structured interview guide goes through five stages: (1) identifying the requirements for using semi-structured interviews; (2) retrieving and utilising prior knowledge; (3) formulating the preliminary semi-structured interview guide; (4) pilot testing the guide; and (5) presenting the full semi-structured interview guide. All these stages increase the trustworthiness of the study, which includes credibility (accuracy), confirmability (researchers' objectivity), and dependability (repeatability).

The key benefit of semi-structured interviews is that they give participants the freedom to describe their experiences and give the researcher some control in ensuring the topic is explored in depth as planned during the interviews (McIntosh and Morse, 2015). Also, in mixed-methods research, semi-structured interviews can provide complementary and in-depth information to other methods (Adams, 2015).

These interviews can be administered face to face, via telephone and online (including electronic emails and electronic platforms/forums/software) (McIntosh and Morse, 2015, Saarijärvi and Bratt, 2021). In particular, online qualitative data collection increased during the Covid-19 pandemic (Saarijärvi and Bratt, 2021). Each meeting type has both advantages and disadvantages (Saarijärvi and Bratt, 2021).

Face-to-face meetings provide the benefits of synchronising in time and space, allowing the effective use of body language and facial expression and creating a safe and comfortable atmosphere for both participant and researcher. However, the disadvantages are that it is time-consuming, and poses a requirement of travel for the researcher (and occasionally the participants), as well as some potential safety risks (Saarijärvi and Bratt, 2021, McIntosh and Morse, 2015). Online chat or email interview removes any challenge posed by geographical distance, and is suitable for sensitive topics as it gives the interviewee time for reflection before answering, but it does require technical literacy and poses certain concerns related to confidentiality (Saarijärvi and Bratt, 2021, Davies et al., 2020, McIntosh and Morse, 2015). A video interview similarly resolves problems related to geographical distances, while being cost-effective and still providing the possibility to see body and facial expressions; but it also requires technical literacy and awareness of confidentially threats (Saarijärvi and Bratt, 2021, Davies et al., 2020, Mirick and Wladkowski, 2019). Finally, phone calls can also be used for longer geographic distances. They are shorter, less formal, and less tech-intensive than the previously mentioned options, but they may not be feasible if the participant has any hearing problems, and can also pose privacy issues (Saarijärvi and Bratt, 2021, McIntosh and Morse, 2015).

Sample size is also important for data adequacy in qualitative studies with semi-structured interviews. The "information power" is based on the study goal ("narrow or broad"), sample specificity ("dense or sparse"), theoretical foundations ("applied or not"), interview dialogue quality ("strong or poor"), and analysis technique ("case or cross-case") (Malterud et al., 2016). If researchers aim to understand common perceptions and experiences among a relatively homogenous group of individuals, 12 interviews can be sufficient (Guest et al., 2006). However, a large sample size is required when researchers aim to assess correlation among variables and to explore a heterogeneous group (Guest et al., 2006). Usually, a minimum of 30 participants is recommended for data adequacy in qualitative studies with semi-structured interviews (McIntosh and Morse, 2015). Also, in mixed-methods studies, sample size should be a minimum of 30 participants if the qualitative study carries greater weight in determining the findings than the quantitative study (Morse, 2012). However, in this PhD research, the quantitative and qualitative components represent equal weights. Therefore, sample size can be less than this required sample size. Additionally, the replicated study (Walthall et al., 2017) also had 25 participants.

To reach or identify the study sample, a purposive sampling method is usually used in qualitative studies with semi-structured interviews. Participants for semi-structured interviews are selected on the basis of their perspectives, experiences, and expertise to shed light on the phenomenon being studied. Purposive sampling develops a sample plan based on the research questions and the study objectives (Curtis et al., 2000). This technique also emphasises the importance of availability and willingness to participate and the ability to communicate experiences (Palinkas et al., 2015). The purposive sampling technique is appropriate for this qualitative study as it is pragmatically driven based on the research questions and study objectives. A “snowball sampling” approach was used, whereby the selection is made by referral from other participants or people who know potential participants (Tenny et al., 2017).

3.9.3. Qualitative data analysis: Reflexive thematic analysis

The researcher opted for thematic analysis in this PhD research due to its suitability for exploring the full spectrum of symptoms associated with heart failure. This approach provides a systematic and adaptable means of uncovering and interpreting patterns and themes within qualitative data, allowing for a comprehensive understanding of the diverse range of symptoms experienced by Turkish adults with heart failure.

Thematic analysis looks for hidden evidence behind text using interpretive techniques to identify, organise, and analyse themes developed from qualitative data (Johnston and Dowling, 2023, Braun and Clarke, 2022). Thematic analysis is a theoretically flexible method rather than a theoretically constrained technique, but various approaches are situated within broader paradigms shaping the method (Braun and Clarke, 2022). Thematic analysis also offers techniques for coding and theme development, the ability to capture semantic or latent meaning, and the ability to approach data inductively or deductively (Braun and Clarke, 2023). From a critical realist perspective, reflexive thematic analysis appears likely to provide the situated and interpreted realities related to symptoms and associated factors in heart failure, rather than simple and decontextualised lists.

Although thematic analysis was defined before Braun and Clarke, they have been perhaps the two best-known authorities on the thematic analysis method since their first publication on thematic analysis in 2006 (Braun and Clarke, 2006). They did not define any specific well-established approach at that time. However, recently, Braun and Clarke (2022) have offered “reflexive thematic analysis” to help with better practice using thematic analysis in qualitative studies. Reflexivity is the core concept for reflexive thematic analysis. Braun and Clarke (2022, p.5) argued that “reflexivity involves a disciplined practice of critically interrogating what we do, how and why we do it, and the impacts and influences of this on our research." An essential aspect of thematic analysis is the value placed on a reflexive researcher who is subjective, situated, aware, and asking questions (Braun and Clarke, 2019).

The process of reflexive thematic analysis includes six main phases (Braun and Clarke, 2022). *Familiarising yourself with the dataset* is the first phase, which includes re-reading the transcripts and re-listening to audio-recordings. The second stage is *coding*, in which the researcher focuses on capturing the single and specific meaning or concepts from the dataset. Following this, *generating initial themes* is the process to identify the candidate themes from the codes from the dataset. Then, stage four is *developing and reviewing themes*, in which one checks the themes against the dataset to confirm their suitability. The next phase is *refining, defining, and naming themes*, in which informative theme names and brief descriptions should be presented. The final stage is the *writing up* for a final analytical report of the findings of the analysis.

3.9.4. Reflexivity

Reflexivity is an important strategy for quality control in qualitative research. It is important to understand how the characteristics and experiences of researchers can affect reflectivity (Berger, 2015). As reflexivity encompasses the researcher, it affects the research process (including methodological choice, study population, collected data etc.) and outcomes. Reflective activities are also intricately linked to wider societal and social processes. Researchers must acknowledge the influence of broader society, recognising the potential social impacts that may emerge during analysis (Johnston et al., 2016). Braun and Clarke report researcher subjectivity and aligned practice of reflexivity as a key concept to successful reflexive thematic analysis (Braun and Clarke, 2022). However, in order to increase credibility and deepen understanding of the study, the contextual reflection between the researcher's own experience and the participants should be clearly defined by the researchers (Dodgson, 2019). In order to explain the similarities and differences between the researcher and the participants, the researcher should state his/her position as "insider" or "outsider" (Berger, 2015, Dodgson, 2019). Reviewing the same interview a few weeks later with a new lens/perspective allows the researcher to more accurately understand the participants' reports (by preventing the researcher's own experience from interfering with the participants' experience) (Berger, 2015). As mentioned earlier, reflexive thematic analysis (Braun and Clarke, 2022) includes the step of familiarising oneself with the dataset, which enables the researcher to gain an in-depth understanding of the dataset through reading, re-reading, listening to audio-recordings, and taking notes. Consulting with colleagues/advisors helps the researcher to get feedback on the reported results (Berger, 2015). (Further details related to reflexivity are provided in **Chapter 4: Methods**.)

3.10. Theoretical framework: Situation-Specific Theory of Heart Failure Self-care

This PhD research was theoretically underpinned by the Situation-Specific Theory of Heart Failure Self-care. The researcher chose this theory with a critical realist perspective to understand the full spectrum of heart failure symptoms because it focuses on individualised self-care in the context of varying symptom experiences. This approach allows for a comprehensive exploration of how people manage and experience heart failure symptoms, considering the societal and healthcare influences on self-care practices. The "Situation-Specific Theory of Heart Failure Self-care" (revised and updated in 2016) guided this study (Riegel et al. 2016). The theory describes the self-care process as a "Naturalistic Decision Making (NDM)" protocol and includes three constructs: (a) Self-care Maintenance, (b) Symptom Perception and (c) Self-care Management. This theory includes symptom perception and evaluation as one of the core concepts of heart failure management and self-care strategies (Riegel et al., 2016).

In heart failure, successful self-care management strategies influenced by a person's knowledge, skill, experience, and values start with symptom recognition (Riegel and Dickson, 2008, Riegel et al., 2022). The theory describes the typical direction of heart failure self-care as proceeding from situation to processing to action (**Figure 3-4**). The relevant situational characteristics (person, problem, and environment) and self-efficacy will affect the decision-making process (experience, knowledge, skills, and values), and both will contribute to the self-care actions (maintenance, symptom perception and management) in heart failure patients (Riegel et al. 2016). The situational characteristics and self-efficacy might make the heart failure self-care process unique to each person. Identification of symptoms in such situations might be affected by an individual's symptoms experiences and knowledge about their condition.

There are three main points in this framework:

1. "Successful heart failure self-care management requires well-structured symptom perception."
2. "Symptom perception can be impacted by the person, problem, and environmental factors."

3. “Self-care management strategies are shaped by one’s knowledge, experience, skill, and values related to heart failure.”

As has already been highlighted, several investigative teams describe how symptoms are experienced by people with heart failure as one symptom or symptom cluster (Luo et al., 2020, Lee et al., 2010). A study conducted in China to identify how Chinese patients with heart failure perceived their symptoms and their influencing factors showed that these patients’ perceptions of their symptoms was influenced by personal, physiological, and psychological factors (Luo et al., 2020). However, there is limited evidence for the link between individual factors (age, gender, culture, heart failure subtypes, and depressive symptoms) and heart failure symptom perception. This study addressed this issue by using a multiple method study design.

Self-care process

The links between the situational characteristics

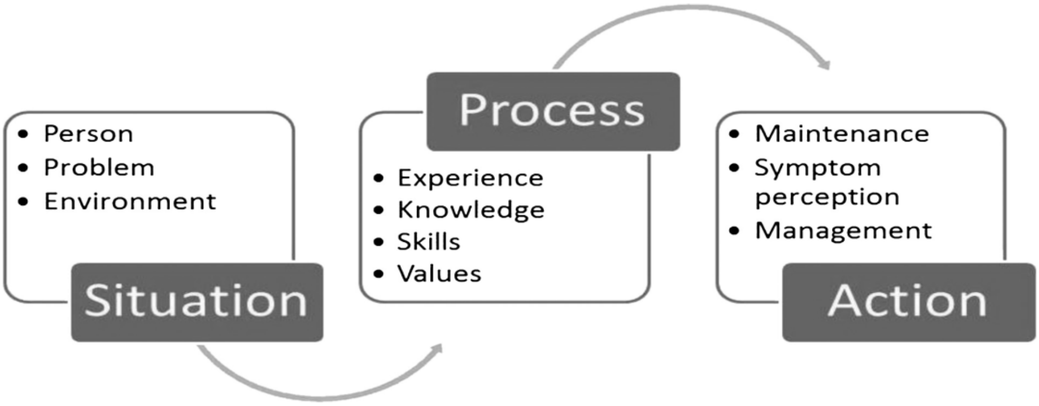


Figure 3-4: The Situation-Specific Theory of Heart Failure Self-care from Riegel et al. (2016)

In the “Example of How to Test the Theory” section (Riegel et al., 2016), provided detailed examples of a mixed-methods design (Dickson et al., 2013) testing the effects of moderators in self-care among adults with heart failure. Also, this theory had already been used in previously published qualitative (Li et al., 2019) and quantitative (Lee et al., 2010, Luo et al., 2020) research approaches. Therefore, this theory can be used in this PhD project to achieve research purposes. In the systematic review, the theory guided the synthesis of findings and the interpretation of results, ensuring a comprehensive understanding of the full spectrum of symptoms experienced by people with heart failure. In the secondary data analysis study, the theory underpinned the research questions and analysis, facilitating a deeper exploration of symptom experiences regarding biological sex and heart failure subtypes. In the descriptive qualitative study, the theory shaped the research design, providing a structured approach to uncovering and interpreting individual symptoms and breathlessness associated with heart failure. By incorporating theory into these research approaches, a more comprehensive and contextually relevant exploration of heart failure symptoms was achieved, enhancing the quality and relevance of the findings in this PhD research.

Application of the theory to the studies

This theory (Riegel et al., 2016) emphasises individualised self-care, recognising the unique symptom patterns, experiences, and self-care needs of each patient. The importance of personalising self-care strategies based on specific symptoms, demographic factors, and the context in which patients manage their condition highlights the importance of understanding each individual's unique symptom experiences and individual clinical and demographic factors in their symptom presentation to support their relevant self-care strategies within their culture.

Study 1 is a systematic review exploring the full spectrum of symptoms and symptom differences regarding sex, age, and setting. The theory (Riegel et al., 2016) guides this study by emphasising the need to understand individual differences in symptom presentation. By defining how symptoms vary across different demographic groups, this study aligns with the theory’s emphasis on personalised self-care. Understanding these variations is crucial for developing tailored self-care interventions that cater to the specific needs of diverse patient populations in heart failure.

Study 2 is a secondary data analysis assessing sex-stratified differences in symptoms and symptom changes over one year regarding LVEF-based heart failure subtypes. The theory (Riegel et al., 2016) is particularly relevant here as it underscores the importance of recognising and addressing sex-specific differences in symptom management. This study’s findings on gender-specific symptom trajectories provide valuable insights into the distinct self-care needs of men and women with heart failure, supporting the theory’s focus on individualised and gender-sensitive self-care practices.

Study 3 is a descriptive qualitative study exploring the full spectrum of symptoms and breathlessness experiences of individuals with heart failure. The theory (Riegel et al., 2016) is instrumental in this study by highlighting the significance of patients' subjective experiences and perceptions of their symptoms for their self-care strategies. By delving into the lived experiences of patients, this study provides a deeper understanding of the personal and contextual factors influencing self-care behaviours. This aligns with the theory's emphasis on tailoring self-care strategies to the unique experiences and needs of each patient.

These studies illustrate the applicability and relevance of the theory (Riegel et al., 2016) in understanding individual unique symptom patterns, experiences, and presentations to enhance heart failure self-care. Each study contributes to a deeper understanding of the theory by demonstrating its practical application in different research contexts, focusing on the importance of personalised symptom assessment for the diverse needs of the heart failure population. While the theory has been instrumental in guiding this research, it is essential to acknowledge the limited use of the theory domains in the first two studies, which mainly focus on symptom presentation and individual differences. Despite this limitation, the theory (Riegel et al., 2016) remains relevant to these studies, as it supports the identification of individual symptom patterns and presentations regarding their individual differences. This robust and valuable framework guides personalised self-care strategies effectively. See Table 8-4 on page 180.

3.11. Chapter summary

This chapter summarised and discussed the fundamentals underlying methodological choices made when designing the research through a comprehensive synthesis of the existing literature. Information was provided about the selected philosophical position (critical realism) and research design (sequential, multiple studies). Details regarding secondary data analysis and descriptive qualitative study methods for data collection and analysis were provided. Semi-structured interview techniques and six main phases of reflexive thematic analysis (Braun and Clarke, 2022) were discussed in this chapter. Finally, the theoretical framework, the Situation-Specific Theory of Heart Failure Self-care, was introduced and discussed.

The next chapter provides the details about each study design and patient and public engagement in the study.

Chapter Four - Methods

4.1. Introduction

In this chapter, the methods of mixed-method systematic review, secondary data analysis, and descriptive qualitative study designs are explained. Specifically, the details underpinning each study procedure are described, to answer questions such as “Where was the study carried out?”; “How was the study carried out?”; and “What stages were followed in the study?” While explaining each study, first, the purpose of the study and research questions are stated, and then information is provided about how the study was operationalised. Before describing each study process, the sequential design of the research is explained. Next, the principle of public and patient involvement (PPI) in research and how it applies to this research are discussed. PPI has been essential in the planning of every study in this thesis. PPI is compulsory for every PhD in the research group (all of which are supervised and guided by Professor Bridget Johnston), in order to encourage public involvement in nursing and healthcare research at the University of Glasgow. For this PhD research, the researcher had two PPI advisors.

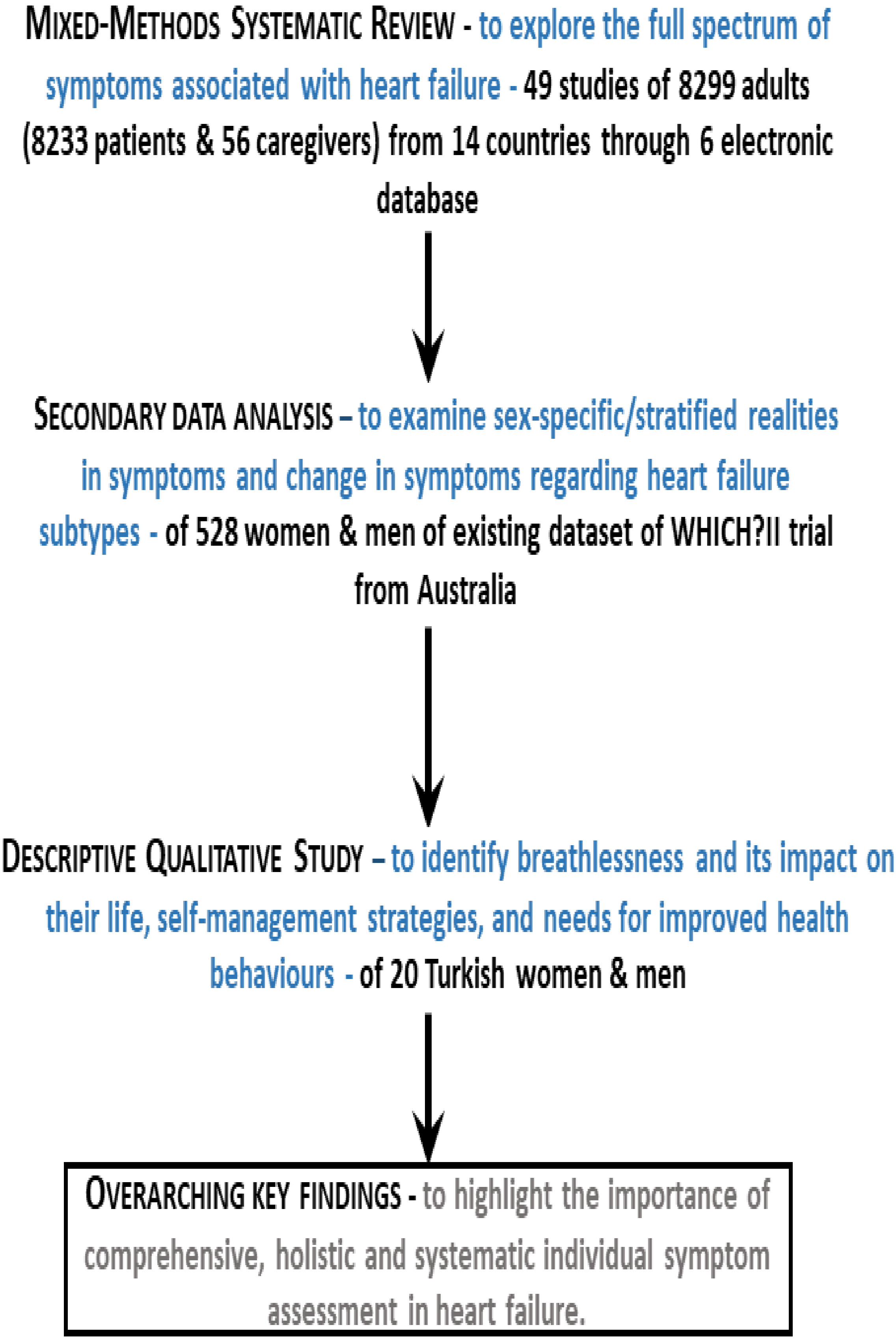
This research included three sequential studies: a mixed-methods systematic review (evidence base data), secondary data analysis (quantitative data), and descriptive qualitative study (qualitative data). After completion of these three distinct studies, side by side comparison of study findings were then used to generate an overarching set of key findings from all three studies of the research. The methods used for each study of the research are discussed and explained in brief summaries (including study settings and ethical considerations).

It is important to note that the programme of research described in this PhD research was affected by the Covid-19 pandemic. The researcher started her PhD just a few months before the Covid-19 pandemic began. During this period, her supervisory team and she decided to make some changes in the first research proposal due to unforeseen issues such as not being able to use the university facilities, to recruit the participants for studies, and to obtain ethical approval from the university or NHS institutions. Therefore, it was decided to perform a secondary data analysis of the WHICH?II Trial data. After these changes, the third study was redesigned, taking into account the first two studies.

4.2. Sequential design of the research

Between October 2019 and March 2023, the process and methods detailed in this chapter were performed sequentially. In sequential mixed designs, the qualitative and quantitative components are completed in sequence, and methods or questions at one stage can be derived from or built on from another (Schoonenboom and Johnson, 2017). This model intention was followed to use both quantitative and qualitative data, with an inclusion of mixed-methods systematic review of the existing literature, in order to answer the overarching research questions. The first study of the research was a mixed-methods systematic review investigating the full spectrum of symptoms associated with heart failure in relation to age, sex, and setting. The second study was a secondary data analysis of an existing research dataset (the WHICH?II Trial) to investigate sex-stratified differences in symptoms and symptom changes over one year with regard to LVEF-based heart failure subtypes. The third study was a thematic analysis of semi-structured interviews of Turkish individuals with self-reported heart failure exploring their breathlessness (and other symptoms) experiences, self-management strategies, and needs for improved health behaviours. This sequential design is presented in **Figure 4-1**.

After conducting three studies, a table was created and used for the PhD research. Presented in a tabular form, the findings of three studies (the mixed-methods systematic review, secondary data analysis, and descriptive study) were used to identify the overarching key findings. To ensure consistency and validity, PhD researcher’s supervisors and public advisors scrutinised the overarching findings. All overarching key findings are discussed in the **Chapter 8: Overall Discussion**.



Mixed-Methods Systematic Review - to explore the full spectrum of symptoms associated with heart failure - 49 studies of 8299 adults (8233 patients & 56 caregivers) from 14 countries through 6 electronic database

Secondary data analysis – to examine sex-specific/stratified realities in symptoms and change in symptoms regarding heart failure subtypes - of 528 women & men of existing dataset of WHICH?II trial from Australia

Descriptive Qualitative Study – to identify breathlessness and its impact on their life, self-management strategies, and needs for improved health behaviours - of 20 Turkish women & men

Overarching key findings - to highlight the importance of comprehensive, holistic and systematic individual symptom assessment in heart failure.

Figure 4-1: Sequential design of the project's studies

4.3. Patient and public involvement (PPI)

4.3.1. Introduction

PPI guided the studies of this research. The main purpose of this level of involvement/participation in the research was to guarantee a high level of findings and relevant recommendations for the target population (individuals with heart failure and their informal caregivers). PPI advisors helped to develop more relevant study protocols, designs, and findings. They checked the lay summaries of each study and final phase protocols and findings. The details about PPI of this PhD were published in 2023, in co-authorship with other members of Professor Bridget Johnston's research group in 2023 (McParland et al., 2023).

Three public advisors were involved at the beginning of this research. After one year, one advisor dropped out. Two public advisors helped to inform the studies' designs during the three years. Both public advisors provided input for each study design with their expertise and experiences, and reviewed lay summary and ethics application documents (including participant information sheet, consent form and privacy notice). In the descriptive qualitative study, three public advisors from Türkiye were involved to inform and confirm the readability and understandability of the documents for individuals in Türkiye. One specialist heart failure nurse from Glasgow was included to review the findings.

This section explains the importance of PPI in this project and summarises the contributions of the two public advisors. Robbie and Nikki, as my public advisors, assisted with the research. They provided written consent for me to share their contributions and stories in my thesis. (Please see **Appendix 1** for evidence of consent.)

4.3.2. Patient and public involvement in this PhD research

The public and patient engagement approach helped to ensure sufficient rigour, transparency, credibility, and effective study findings regarding users' needs, preferences, and wishes. Each study throughout this PhD project was carefully discussed, examined, and evaluated by those who agreed to participate as a public advisor.

Three public advisors took part in the first year of the project, while in the second year, one of the public advisors was diagnosed with cancer and left the research. These advisors were recruited through a developed public and patient involvement flyer posted on social media (Twitter and LinkedIn). Three public advisors were recruited from Twitter and met the eligibility criteria (adults with heart failure or informal caregivers of people with heart failure). This recruitment phase was carried out during the Covid-19 pandemic. For this reason, meetings were held via Zoom. After the pandemic, the researcher was able to meet one of her public advisors, Robbie, who lives near Glasgow, and she spoke to another public advisor, Nikki, via Zoom. Prior to meeting them, she explained the purpose and duration of her project, the importance of their participation in the project, and that participation was on a voluntary basis. They agreed to participate in the research as public advisors. Also, they provided their consent to share their story and contribution to this PhD project.

Expert contributions: Apart from these two public advisors, the descriptive qualitative study included nurse experts from Türkiye to ensure that the study method and findings support more comprehensive and real-world symptom experiences in Turkish individuals with heart failure. There were three nurses from Türkiye to review the Turkish version of the documents (including the participant information sheet, consent form, privacy notice and interview questions). They checked and confirmed the readability and intelligibility of the documents for individuals in Türkiye. The pilot interviews were performed with them to test the interview guide (from patient, caregiver, and healthcare perspectives) and the final version was achieved after these interviews. In addition, the findings of this descriptive qualitative study were reviewed and confirmed by a specialist heart failure nurse in Glasgow. This addition of expert assistance was used to increase the validity and reliability of the study.

The volunteer advisors and experts therefore comprised the following individuals: two Turkish nurses who had worked in cardiovascular wards for at least 5 years; one nurse researcher from a university in Türkiye; one person living with heart failure in Scotland; one family member of a person living with heart failure in England; and one specialist heart failure nurse in Scotland. They were included to develop it and make it more culturally relevant. The researcher met with the volunteers to discuss the interview questions and then the findings of the study.

Robbie's story and contribution to the project

Robbie has heart failure and dilated cardiomyopathy. He was diagnosed with heart failure at the age of 46. At the diagnostic stage, he felt breathlessness, fatigue, fluid retention, and stress. He was admitted to the hospital experiencing these ongoing symptoms. After the examination, he was found to have pulmonary oedema related to heart failure. He has an ICD and pharmacological treatment for heart failure. He actively contributes to many research and projects related to heart failure around the Glasgow area.

Robbie contributed to the design of each study by presenting his experience and expertise on the aims and objectives of the study. He reviewed every step of the different studies of this project.

Mixed-methods systematic review. He reviewed the symptoms identified in the review and compared them with his own experience. This has helped me to understand that each individual has their own symptom profile for heart failure.

Secondary data analysis study. Robbie and I discussed which factor should be evaluated to understand the differences in symptoms and symptom changes. After the data analysis, he reviewed the findings; and also evaluated the final version of the published article with his expertise.

Descriptive qualitative study. Robbie helped to formulate the ethics application document (including the English version of interview questions, the participant information sheet, content from, privacy notice, and flyer of the study). After the interviews, the findings of the qualitative studies were also reviewed by him.

Overarching themes of the project. After the triangulation phase of the project, the final overarching key themes were reviewed. Robbie was consulted at every stage of the project.

Nikki's story and contribution to the project

Nikki is a family caregiver for her husband who lives with heart failure. She is a mental health student nurse. She helped in my understanding of both psychological and physical symptoms and caregiver contributions in heart failure care.

Like Robbie, Nikki contributed to the design of each study, offering her experience and expertise in the study's aims and objectives by reviewing each stage of the project. She reviewed and provided her opinion on the findings of the mixed-methods systematic review, secondary data analysis, and descriptive qualitative study findings. The final version of the overarching key themes was also presented to her expertise.

4.4. Study I: A mixed-methods systematic review

4.4.1. Introduction

A mixed-methods systematic review (MMSR) was selected to examine the full spectrum of symptoms and then ESC (McDonagh et al., 2021) typical and less typical symptoms with respect to setting, age, and sex in heart failure. The rationale for choosing a mixed-method systematic review was provided in Chapter 3, page 43. The selection of the ESC Guidelines for heart failure (McDonagh et al., 2021) as the reference source for identifying symptoms listed in the clinical practice guidelines, as well as additional symptoms, was based its widespread use in numerous European countries, including Scotland and Türkiye.

4.4.2. Research aims/questions

This review sought to investigate the commonality of various symptoms in cases of heart failure. Symptoms included in the 2021 ESC Heart Failure Guidelines, as well as other symptoms, were reported. The researchers investigated whether or not there were differences in symptoms in hospitalised versus community-dwelling patients, in those aged <65 years versus ≥65 years, and in women versus men. Symptoms were investigated from both the perspective of those living with heart failure (patient perspective) and/or those caring for them (informal caregivers' perspective). Five main questions were addressed by this study of the project:

What is the full spectrum of symptoms experienced by people with heart failure?

1. How common were typical and less typical symptoms listed in the ESC Guidelines for heart failure?
2. Were there symptoms of heart failure that were not listed in the ESC Guidelines? How common were these?
3. Did ESC-defined typical and less typical symptoms vary from community to hospital?
4. How does age affect ESC typical and less typical symptoms?
5. How does sex affect ESC typical and less typical symptoms?

4.4.3. Design

This is a mixed-methods systematic review (MMSR) guided by the "Joanna Briggs Institute (JBI) Methodology" for MMSR (Lizarondo L, 2020) and the "Preferred Reporting Items for

Systematic Review and Meta-Analyses" (PRISMA) (Page et al., 2021). The protocol of this review was registered and published on PROSPERO (International Prospective Register of Systematic Review) under the number CRD42020185786 (**Appendix 2**).

4.4.4. Search strategy and study selection

The English literature search was conducted using six databases: CINAHL, MEDLINE, EMBASE, Web of Science, PsycINFO, and Cochrane Library. The search was conducted using the relevant search terms and strategy (**Appendix 3)**. Relevant search terms included relevant MeHS (Medical Subject Headings) (NIH, 2023) terms and synonymous keywords. The search was first conducted in 2020 and updated in February 2023. The Endnote software programme was used to de-duplicate the results. Then the titles and abstracts were reviewed with reference to the inclusion and exclusion criteria of the project (listed below). During the title and abstract screening, the researcher looked for papers that included "adult patient and/or (informal) caregiver population", "heart failure", and "symptoms". Studies were read in full independently by the primary researcher and one of the other researchers, and the results were compared and discussed for accuracy by all researchers. The reference sections of other relevant articles were searched manually by the primary author to ensure comprehensive inclusion for this research.

4.4.5. Inclusion criteria

The inclusion criteria were as follows: included self-reported symptoms of people with heart failure from patients and/or their informal caregivers' perspectives; studies that reported five or more physical and/or non-physical symptoms in individuals (adults) 18 years or older; qualitative, quantitative (not trials), or mixed-methods studies; primary and secondary analyses of data; informal (unpaid) caregivers; any setting including hospice and community-dwelling.

4.4.6. Exclusion criteria

Studies were excluded if they: included fewer than five symptoms; symptoms from medical records; symptoms not reported by patients or carers (e.g., reported by healthcare professionals including clinicians, nurses, and researchers); had a mixed/non-heart failure patient population; all formal (paid) caregivers; paediatric (i.e., younger than 18); patients with congenital heart disease/left ventricular assist device/cardiac transplants; less than ten participants as a study population; insufficient details about symptoms presence (for example, studies which gave only a total score of questionnaires, or they did not specify symptoms); self-care management of symptoms as main aim; conference papers; posters/abstracts; review/editorial reports etc.; book section/dissertation; and the relationship between symptoms of the patient and caregiver burden/stress/impact/support.

4.4.7. Data extraction

Data were extracted according to the main aims of the article. These included objectives, the characteristics of the research population (people with heart failure, age; and informal caregivers caring for someone with heart failure), sample size, research methods (interview, questionnaire, or both), and symptoms (prevalence and occurrence).

4.4.8. Quality assessment

The quality of the papers was evaluated using standard JBI critical appraisal instruments for assessing the methodological quality of the studies' outcomes (https://jbi.global/critical-appraisal-tools). The quality of the papers was assessed using the appropriate critical appraisal checklists for qualitative and quantitative studies. Three mixed-methods studies were assessed using the qualitative checklist for their qualitative components. Two other authors verified the first author's appraisal of the articles.

4.4.9. Synthesis of the results

Data interpretation was performed using a mixed-methods synthesis (convergent integrated) approach (Stern et al., 2020, Lizarondo L, 2020) for reporting the ESC and non-ESC symptom results across the included studies in NVivo software. Since the research question is addressed in both quantitative and qualitative research, combining qualitative and quantitative data with transformation is possible for synthesis and interpretation. The researchers were unable to carry out a meta-analysis due to the considerable heterogeneity among the studies included (including different outcome measures; and social, cultural, socio-demographic, and individual differences). Instead, narrative synthesis was carried out. This allowed for the inclusion of confounding variables (such as age, sex, and settings), which are frequently overlooked in meta-analysis (Popay et al., 2006). Each paper was described before being compared and synthesised. The papers were imported to NVivo, and symptom groups were categorised according to the following steps: (a) The results of qualitative and quantitative studies were analysed together by focusing on the self-reported symptoms of people with HF based on typical and less typical symptoms of ESC Guidelines

(McDonagh et al., 2021) and other (non-ESC) symptoms; (b) The typical and less typical symptoms were compared according to settings, age, and sex. Microsoft Excel was used to calculate descriptive statistics and to tabulate the figures. The studies included in this MMSR are different, so we cannot compare them directly. Therefore, we compare symptom percentage distributions in box plots. The Situation-Specific Theory of Heart Failure Self-care (Riegel et al., 2016) was chosen as the theoretical framework for this study to indicate ESC typical and less typical symptoms characteristics based on sex (men versus women), age (<65 versus ≥65 years old), and setting (hospital versus community settings).

4.4.10. Outcomes

4.4.10.1. Symptoms

Typical and less typical symptoms in the ESC HF Guidelines (2021)

Typical and less typical symptoms (**Table 2-1**: **in Background, page 9**) were defined according to the ESC Guidelines (2021) (McDonagh et al., 2021). Typical symptoms (n=6) included breathlessness, fatigue, and ankle swelling (McDonagh et al., 2021). Less typical symptoms (n=10) included dizziness, palpitations, bloated feeling, and loss of appetite (McDonagh et al., 2021).

Other (non-ESC) symptoms

People with heart failure experience more symptoms than those reported by the ESC HF Guidelines. Other symptoms not mentioned in ESC Guidelines (2021) were identified and termed “Non-ESC symptoms”.

4.4.10.2. Age, sex, and setting, and ESC typical and less typical symptoms

ESC typical and less typical symptoms were investigated according to age, sex, and setting.

Chapter 5 will present the findings of the mixed-methods systematic review.

4.5. Study II: A secondary data analysis

4.5.1. Introduction

The symptom profile is important for the maintenance of patient care, particularly in relation to clinical assessment, management, outcomes, and intervention development (DeVon et al., 2017, Graven et al., 2020, Heo et al., 2020, Lyons et al., 2020). In the literature, there were a few studies related to sex-specific differences in symptoms of heart failure (Heo et al., 2019b, Fischer and Bekelman, 2017). A secondary data analysis of the dataset from the "Which Heart Failure Intervention is most Cost-effective in Reducing Hospital Stays?" (WHICH?II) trial (Scuffham et al., 2017) was performed to investigate sex-stratified differences in symptoms regarding LVEF-based heart failures subtypes. Professor Simon Stewart, the researcher's supervisor, was the principal investigator of the WHICH?II Trial. The original trial was published in 2017 (Scuffham et al., 2017). Due to the Covid-19 pandemic's impacts on this PhD research, such as not being able to obtain ethical approval or to recruit participants from hospitals, the use of an existing dataset was judged the only option to increase the precision of the research. With the agreement of the supervisory team, a secondary analysis of this dataset was therefore performed in relation to the aim of this thesis.

In this section, the aims of the secondary data analysis, the data sharing and analysis, and the ethical application process are discussed.

4.5.2. Research aims/questions

A secondary data analysis of the dataset from the WHICH?II Trial (collating data from both study groups) was performed. Specifically, utilising comprehensive baseline (at hospital discharge) and follow-up profiling performed at 12 months in surviving patients, the study sought to answer the following research questions:

How do symptoms of heart failure differ between men and women, with respect to biological sex and heart failure types?

How do these symptoms change in the 12 months following a hospital admission in men and women, with respect to heart failure subtypes?

- What are sex-stratified differences in symptom changes over one year associated with heart failure with respect to LVEF-based heart failure subtypes?

- What are the baseline predictors of worsening heart failure symptoms in men and women separately?

4.5.3. The original WHICH?II Trial

The WHICH? II Trial (summarised in the table below) was a multicentre, randomised trial funded by the National Health & Medical Research Council of Australia (Scuffham et al., 2017). The primary results of the trial were reported in the *European Heart Journal*. Overall, there were minimal differences in the health outcomes of the two groups of patients, who were randomly grouped into a less intensive (control) versus more intensive form of disease management. Further details are provided in **Table 4-1**.

4.5.4. Study design: a retrospective secondary quantitative data analysis

This was a retrospective secondary analysis of quantitative data from a randomised control trial (WHICH?II Trial) that compared standard home-based and structured telephone support management of heart failure (Scuffham et al., 2017). The use of a secondary data analysis for this study had the following advantages. It eliminated any impact on research participants, because there was no data collection process for this study. With respect to the privacy and confidentially of participants, all data was transferred anonymously to the University of Glasgow server for secondary data analysis. There was no identification of participants, increasing the security of data protection and reducing the risk for participants. The results of the secondary data analysis were beneficial for future patients suffering from chronic heart failure when the feedback and recommendations were shared. There were no anticipated disadvantages of using secondary data analysis to answer the research questions to be developed by the secondary researchers. However, the original data was collected to answer the primary research question of the WHICH?II Trial and the secondary research questions were different from those questions. This could be a disadvantage for secondary analysis, but it was not thought to affect the results of this research. It is important to acknowledge that the follow-up data might underestimate the true prevalence of symptoms in the general population due to the experimental condition. Participants in the experimental arm were exposed to specific interventions that did not accurately reflect the experiences of the general population. These conditions may have influenced their symptom-reporting behaviour. For instance, participants aware of their involvement in a study might have been more motivated to report symptoms differently than in a non-research context.

Table 4-1: Details about the WHICH?II Trial

WHICH?II Trial (Scuffham et al., 2017)	
Aim	To test the hypothesis that structured telephone support interventions and home-based care intervention reduce the cost of healthcare in heart failure.
Years	2013–2017
Country	Four tertiary hospitals in Australia (Adelaide, Melbourne and Sydney)
Ethical approval	Central Northern Adelaide Health Service (HREC/13/TQEHLMH/99), Melbourne Health (HREC 2013.145), Prince of Wales Hospital, Sydney (HREC/13/SVH/313), and St Vincent's Hospital Sydney (HREC/13/SVS/313). Written informed consent was obtained from all participants.
Participants	People with chronic heart failure. Inclusion criteria for this study were: people aged 18 or older, with a diagnosis of chronic heart failure based on NYHA class II-IV, and more than one-year acute decompensated heart failure admission history. Exclusion criteria included having a terminal condition and being unable to provide fully informed consent.
Method of the study	Randomised control study. This study used blinded, computer-generated randomisation.
Follow-up duration of the study	The intervention follow-up time of the WHICH II Trial was 12 months.
Standard management and intervention	There were two groups, with a total of 400 participants for each group; the first group received the WHICH? II intervention, and the second group received the standard Australian management of heart failure.
Data collection	All study data were collected via online case-report forms. These forms included the following information of participants: (a) demographic and clinical baseline characteristics; (b) assessment of patients' depressive symptoms, cognition, physical strength, self-care abilities, and level of the multimorbidity.
Data collecting tools	The Montreal Cognitive Assessment (MoCA) Tool, European Self-Care Behaviour Scale, two-item ARROL Tool, and Charlson Comorbidity Index Score.
Details about outcome measures	***Demographic and clinical profiles:*** Demographic and clinical data were collected at the baseline via case-report form from the study – including socio-demographic (such as age, gender, ethnicity, marital status, living arrangements, education, occupation, and language) and clinical characteristics (such as heart failure duration, NYHA classes, LVEF range, and comorbid conditions). ***Heart failure symptoms:*** Heart failure symptoms were collected at baseline and 12 months later via the Kansas City Cardiomyopathy Questionnaire (KCCQ). ***Depressive symptoms:*** A two-item ARROL tool (Arroll et al., 2003) was used to measure depressive symptoms at baseline and at 12-months. ***Quality of life:*** Quality of life was measured by EQ-5D-5L (EuroQol 5-dimentions/5-levels questionnaire) and Heart Failure-specific KCCQ (Kansas City Cardiomyopathy Questionnaire) from baseline to 12 months.

4.5.5. Population, sample, and sample design

The target population was people living with chronic heart failure. The inclusion criteria were as follows (based on the original trial): (a) people aged 18 or over; (b) diagnosed with chronic heart failure (regardless type of heart failure, and including reduced or preserved ejection fraction) as confirmed by a cardiologist; (c) able to speak English; and (d) provided informed consent. Candidate participants were excluded if they had a) a terminal condition; and (b) significant confusion/delirium.

A total of 787 participants who participated in the original trial constituted the sample of this study. Based on this study aims, only patients who had experienced heart failure symptoms such as shortness of breath, swelling, fatigue etc., were considered for the analysis. However, 528 participants had baseline and 12-month follow-up data. For symptom change and worsening symptom experiences, these 528 people formed the study sample.

4.5.6. Ethical considerations and approval

Ethical approval for this study was obtained from the College of Medical, Veterinary & Life Sciences (MVLS) Ethics Committee at the University of Glasgow (Project no:200200145/13.07.2021) (**Appendix 4**). This was a secondary data analysis study of the anonymised dataset from the WHICH?II Trial. Therefore, ethical approval was obtained for research involving already available data based on the MVLS Ethics Committee for Non-Clinical Research Involving Human Participants. All documents for the ethical approval application were written by the researcher and cross-checked by the research team (including the three supervisors and co-author Yih-Kai Chen) and PPI advisors.

A range of training was undertaken in connection to research ethics and good practice: the NHS Research Good Clinical Practices Training; as well as courses provided by the University of Glasgow pertaining to issues such as data protection (GDPR); research data management; information security; research integrity; equality and diversity; and ethical approval for people working with human subjects.

Formal data sharing process: A formal data-sharing process was undertaken. Professor Simon Stewart, the researcher's supervisor, provided a formal letter for the data sharing process (**Appendix 4**). He was the principal investigator of the WHICH?II Trial. He was also the principal investigator of this secondary data analysis.

4.5.7. Data selection and cleaning

Co-author Yih-Kai Chen prepared the study data for analysis and sent it to the PhD researcher. After transferring the dataset to the server of the University of Glasgow, she checked and cleaned all data that did not help in answering the secondary analysis research questions. The original dataset was checked for the following factors:

- Biological sex (men versus women)
- LVEF-based heart failure subtypes (HFrEF, HFmrEF, and HFpEF)
- Typical heart failure symptoms (presence/absence at baseline and 12-month follow-up – shortness of breath, bilateral ankle oedema, orthopnoea, paroxysmal nocturnal dyspnoea, and nocturnal cough)
- Depressive symptoms (presence versus absence at baseline and 12-month follow-up)
- Other symptoms (presence/absence at baseline and 12-month follow-up – including sleep problems due to orthopnoea, pain, and walking problems)
- Quality of life scores (KCCQ and EQ-5D-5L)
- Sub-scores of KCCQ at baseline and 12-month follow-up to calculate the symptom changes over one year in men and women separately.

For this secondary data analysis, the PhD researcher excluded the participants with incomplete 12-month follow-up data. Handling the missing data is one of the important issues in data mining and analysis (Pratama et al., 2016, Lee and Yoon, 2017). In particular, missing values can happen unexpectedly in time series data collection like the original WHICH?II Trial. These missing data can distort the findings of the study (Alabadla et al., 2022). Therefore, it is important to deal with these missing values or data. Several simple (ignoring or deletion) or statistical (imputation) principles can be taken to deal with missing values or data (Pratama et al., 2016, Lee and Yoon, 2017). In the current secondary data analysis, to increase the credibility and generalisability of the findings among survivors with heart failure, exclusion of the incomplete data between baseline and 12-month follow-up times was chosen. Except for incomplete data that was deleted, less than 1% of participants had missing data on a few symptoms at 12-month follow-up. If the proportions of missing data is less than 5% of the total, which generally occurred in one of the compared groups at follow-up, it is valid to ignore missing data (Jakobsen et al., 2017).

4.5.8. Outcomes and measures

Demographic and clinical profiles: Demographic and clinical data were collected at the baseline via case-report form from the study. This secondary data analysis used demographic information such as age, gender, ethnicity, marital status, living arrangements, education, occupation, and language. It also looked at lifestyle factors, such as exercise and sleep quality. The patients' heart failure history and profile class (measured on the NYHA scores); and the LVEF range, and comorbid conditions and Charlson Comorbidity Index score (Sundararajan et al., 2004), were also used this analysis.

Heart failure symptoms: Heart failure symptoms were collected at baseline and 12 months later via the Kansas City Cardiomyopathy Questionnaire (KCCQ) (Green et al., 2000). This is a 23-item questionnaire and includes the following domains: "physical limitation" (Q1); "symptoms" (frequency (Q3,5,7&9); severity (Q4,6&8); and change over time (Q2)); "self-efficacy and knowledge" (Q11&12); "social interference" (Q16); and "quality of life" (Q13,14&15) (Green et al., 2000). The KCCQ total symptom score domain assesses symptom severity and frequency. Values for all domains range from 0 to 100, with higher scores indicating lower symptom burden and better quality of life.

Worsening, stable, and improved symptoms: To assess changes in symptoms over 12 months relative to the baseline, the researcher employed the KCCQ symptom stability score. A lower score in self-reported symptoms indicates deterioration, while a higher score suggests improvement (Green et al., 2000). The study results facilitated the classification of the symptomatic status of participants into three categories: a) "Improved" (with a positive score change ranging from 26 to 100), b) "Stable/persistent" (with an unchanged score ranging from -25 to +25), or c) "Worsened" (with a negative score change ranging from -26 to -100, including moderate worsening from -25 to -49 and severe worsening of ≥-50).

Depressive symptoms: The two-item ARROL tool (Arroll et al., 2003) was used to measure depressive symptoms at baseline and at 12 months. Question 1 is "During the past month, have you often been bothered by feeling down, depressed, or hopeless?" Question 2 is "During the past month, have you often been bothered by little interest or pleasure in doing things?" The questions are answered with a "yes" or "no". If the answer to both questions is "yes", the patient is considered to present depressive symptoms.

Quality of life: Quality of life was measured by the generic tool EQ-5D-5L (EuroQol 5-dimentions/5-levels questionnaire) and Heart Failure-specific KCCQ (Kansas City Cardiomyopathy Questionnaire) at baseline and 12 months. These scales have been shown to have adequate validity and reliability in heart failure populations. The EQ-5D-5L questionnaire is the self-report of generic health, and includes five domains: “mobility”, “self-care”, “usual activities”, “pain/discomfort”, “anxiety”, and “depression”. Each domain is measured on a five-point scale: “no problems”, “slight problems”, “moderate problems”, “severe problems”, and “unable to”/“extreme problems” (Herdman et al., 2011, Oppe et al., 2007). The EQ-5D-5L also includes an EQ-VAS (visual analogue scale) related to the patient’s health “today” (rated from 0 (worst) to 100 (best imaginable health). For domains, the label scores are between 0 (no pain/discomfort) to 100 (“I have extreme pain or discomfort”). The quality of life of KCCQ domains were mentioned in the heart failure symptoms section.

4.5.9. Statistical data analysis

Quantitative data: statistical analysis of data provided summaries of associations between variables among the groups and symptoms. Analyses were performed on a sex-specific basis.

All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences) V26.0 (SPSS Inc, IBM) software. Statistical significance was accepted at a 2-sided α of 0.05. Smaller “p” values gave the significance of the results. As this is a secondary analysis, no study power calculations were performed.

- ➢ Standard methods for describing and comparing continuous and grouped data, including means (± standard deviation) and medians (IQR), were applied for normally and non-Gaussian distributed continuous variables and proportions for categorical data according to baseline profiling. Descriptive analysis was performed to explore all data, and normality distributions were evaluated. Continuous variables were reported as mean and standard deviations, and categorical variables were reported as frequencies and percentages in the study.
- ➢ Percentage, mean, and standard deviation were used to summarise statistics. T-test was used to analyse mean difference for KCCQ sub-scores in men and women with respect to sex and heart failure subtypes to identify significant differences in men and women. ANOVA, Student’s T-test and chi-square analyses were used where appropriate, including comparisons of the inter-individual change in symptom scores recorded from baseline to 12-month follow-up, according to symptomatic status.
- ➢ Chi-square tests was used to investigate the association between symptoms and heart failure types in men and women to identify significant differences.

- A binary logistic regression was used to determine the correlates of worsening trajectory of symptoms. At the end of the analysis of data, the researchers were able to determine the effects of demographic and clinical factors in worsening trajectory of symptoms. A binary logistic regression examines the relationship between the categorical dependent (response) variables and (numerical or categorical) independent (predictor) variables. Therefore, the researcher chose the use of a binary logistic regression analysis to determine the significant correlates of worsening heart failure symptoms in men and women.

4.5.10. Data management and protection

The researcher took appropriate measures to ensure data protection. This is a secondary data analysis of the data from the WHICH?II Trial (Scuffham et al., 2017), and the primary researcher and her supervisors received the confidential/anonymous data record of the primary research. All data was electronic, and it was stored on a network drive with restricted access, in a folder with access limited to the first researcher and her supervisors. To reduce or eliminate risks, the researchers complied with The General Data Protection Regulations (GDPR) (2018).

The researchers stored the data at the University of Glasgow. All data came from the principal investigator of the WHICH?II Trial, Professor Simon Stewart, and was transferred directly to the University of Glasgow server through shared drive. All data was transferred into SPSS software and saved on an electronic encrypted device. During the analysis of data, the researcher stored the data the University of Glasgow server. All data was transferred as an online copy. Only the researcher and supervisors had access to the data on the university server. After completing the study, all data was deleted from the University of Glasgow's server by permission of the supervisors.

Chapter 6 will present the findings of secondary data analysis.

4.6. Study III: A descriptive qualitative study

6.6.1. Introduction

A descriptive qualitative study investigated a) breathlessness and other symptoms experiences of individuals with self-reported heart failure, b) the impact of breathlessness on daily life, c) self-management strategies, and d) needs for improved health behaviours.

A more comprehensive approach than the current clinical management guidelines, including physical, psychological, social, and economic issues, might be taken into consideration in heart failure management and symptoms assessment. The Situation-specific Theory of Heart Failure Self-care (Riegel et al., 2016) includes symptom perception and evaluation as one of the core concepts of heart failure management and self-care strategies. Symptoms of individuals are shaped by their subjective knowledge and experiences shaped by socio-cultural-behavioural context. This creates various methods of symptom management according to the individual's different interpretations of symptoms. It is important to know how each symptom is interpreted by individuals with reference to their cultural/social beliefs and values.

In this section, the aims of the descriptive study, mirroring study, data collection, data analysis, and ethics approvals process are explained.

4.6.2. Research aims/questions

The main purpose of this descriptive qualitative study was to explore how Turkish patients themselves describe their experiences of breathlessness, and how breathlessness affects their daily life and what they need for improved their health behaviours. The following research questions guided the study:

How is breathlessness described from a patient perspective in Türkiye?

What symptoms are experienced by Turkish individuals with heart failure?

- What are the impacts/consequences of breathlessness on daily life and health for people with heart failure in Türkiye?
- How do they manage their breathlessness?
- What are the health needs of individuals with heart failure in Türkiye?

4.6.3. Details about mirroring study

After the secondary data analysis study, a literature search was performed to identify qualitative studies related to symptoms in adults with heart failure. With the inclusion of the qualitative studies of the mixed-methods systematic review, relevant studies were listed and discussed with the principal supervisor, Professor Bridget Johnston. A final list included eight studies (investigating the experiences of people with heart failure), with nurse-led research and delimited to the UK and Ireland. With the decision to use the most up-to-date and relevant study, a time limit was added. Studies conducted after 2015 were discussed with the supervisor for the final decision. Consequently, it was decided to use the qualitative study of Walthall et al. (2017) as a mirroring study.

The mirroring study (Walthall et al., 2017) was an exploratory qualitative study that sought "to explore how patients themselves describe their experiences of breathlessness, how breathlessness affects their daily lives and how to adjust to and manage it." The study was conducted between November 2012 and June 2013 in England. The study sample included 25 individuals with heart failure reduced ejection fraction. The semi-structured interviews were conducted through home visits. Interviews duration was between 45–90 minutes. Based on thematic analysis (Braun and Clarke, 2006) of semi-structured interviews, four main themes were identified: the nature of breathlessness; the emotional impact of breathlessness; the impact of breathlessness on daily life; and managing breathlessness.

This current qualitative study was not designed to be exactly the same as the mirroring study. It was only a guide for formulating the research and semi-structured interview (main and prompt) questions. The rationale for following this mirroring study was to see the findings from a sample group from another country and to increase the credibility of the research. The researchers' aim was not to make a country comparison (between England and Türkiye) but to see differences in breathlessness with respect to the impact of cultural and social beliefs and values on individuals in Türkiye.

4.6.4. Study design and setting

A descriptive qualitative approach using the same methods of Sandelowski (2010) was followed. Semi-structured interview data were collected to describe the shortness of breath experienced by individuals with heart failure in Türkiye. The participants come from various settings, including hospital and community-dwelling, and from urban and rural areas of five different cities in Türkiye. This study complies with EQUATOR guidelines for reporting research that follows the "Consolidated Criteria for Reporting Qualitative Research" (COREQ), a 32-item checklist for interviews and focus groups (Tong et al., 2007) (**Appendix 5).**

4.6.5. Study procedure and population

Purposive and snowball sampling techniques were used to recruit the participants for one-on-one interviews. Participants were recruited via online research advertisements (including sharing research flyers and a video; see **Appendix 6** for the English version of these) in Türkiye. When potential participants contacted the first researcher (MS) to participate in the study via email or phone, MS checked the participants' compliance with the study's main inclusion criteria.

Eligibility criteria of the study were: being over 18 years old; able to understand and speak Turkish; having heart failure diagnosis; and experiencing shortness of breath. Exclusion criteria of the study were: being younger than 18 years old; having congenital heart disease; not able to understand or speak in Turkish language; not able to provide their informed consent; and having cognitive impairment, untreated current psychiatric symptoms, or serious long-term conditions that could impair the ability to provide informed consent.

All adult participants had been confirmed their heart failure diagnosis and breathlessness experiences. After an oral explanation of the study aim and procedure, if the participants were still interested in participating in the study, the details of the study information (including "Participant Information Sheet, Privacy Notice and Consent Form", **Appendix 6)** were sent to them by email or delivered by hand. Interviews were conducted with the participants who agreed to participate in the study and gave the required consent to participate. After consent forms had been provided, the researcher asked participants for their meeting preferences (face-to-face, telephone, or email). After deciding the meeting method, the researcher and participants decided on the interview time. For a face-to-face interview, a convenient time and place were scheduled. For telephone interviews, time was discussed with potential participants to arrange the interviews. After a participant was included in the study, the first researcher asked the participant to recommend others to participate in this research (snowball sampling).

Sampling frame/identification: Participants were selected with the intention of representing as diverse a mix of participants as possible in terms of gender, age, and duration of heart failure. These variables would help demonstrate the representativeness of the heart failure population with a sensitive, diverse, and comprehensive study sample. More details are provided in **Table 4-2** below.

Table 4-2: Sampling frame of qualitative study

Variable	Aim	Rationale	Achieved
Age ranges	Recruit >8 participants per age group below: Younger age (18–45) Middle age (45–65) Older age (65+)	Ensuring the inclusion of younger and middle age groups.	NO: 4 for 18–45; 9 for 45–65; and 6 participants for 65+ age groups
Gender	Recruit >10 participants per gender group for patients and caregivers as below: Female with heart failure Male with heart failure	Understanding of gender perspective in heart failure and care.	YES: 9 men and 11 women.
Ethnicity	Recruit >5 participants per ethnicity band as below: Turkish Kurdish Arabian Mixed ethnic background/others	Understanding of a diverse range of ethnic backgrounds in terms of cultural diversity.	NO: the majority of participants had Turkish background.
Duration of heart failure	Recruit >8 participants per group as below: 0 to 2 years 2 to 5 years >5 years	Understanding the needs of people who represent different duration of heart failure, so the full spectrum of needs can be determined.	NO: 13 participants had more than 5 years of heart failure duration.

4.6.6. Study sample

A total of 26 participants expressed interest in participating in the study. Six of them did not participate due to unmet inclusion criteria (n=4: atrial fibrillation (n=2); congenital heart disease (n=1); and hearing issues (n=1)) and wanting to participate with their spouses (n=2). Two people who were not available to participate claimed that their spouses (as a caregiver) know them well, and they did not want to talk without their participation. They were unable to answer even a simple question about their medical history on their own. 20 adults with self-reported heart failure voluntarily participated in this study in five different cities in southeast Türkiye.

Participants were selected based on their self-report heart failure diagnosis and experience of shortness of breath. Clinical heart failure diagnosis requires the following tests (McDonagh et al., 2021): electrocardiogram (ECG) for any abnormalities such as atrial fibrillation and left ventricular hypertrophy; measurements of plasma concentration of B-type natriuretic peptide (BNP, ≥35 pg/ml) and N-terminal pro-B-type natriuretic peptide (NT-proBNP, ≥125 pg/ml); echocardiography for assessment of cardiac function abnormalities; and LVEF measurement to define heart failure phenotype. However, this information of the participants could not be obtained due to the reasons stated below, and the self-reported heart failure diagnosis was used as the inclusion criterion.

- Not being able to use the hospital for participant recruitment: The first researcher is not currently working as a nurse in any hospital in Türkiye. Additionally, she is doing her PhD as a full-time student in Scotland. Although she obtained ethical approval from both Glasgow and Türkiye, it was not possible to obtain approval from any hospital or health centre for the recruitment phase of the study. She used online recruitment procedures instead.
- Advanced age and low education level: The prevalence of heart failure increases with advanced age. The literacy rate among older age people in Türkiye is very low. For example, six of the participants of this present qualitative study did not have any education. Therefore, they are not expected to be able to use or understand medical terminology/words for their diagnosis. This is also one of the factors that influence the way their doctors explain their heart failure condition to them. Therefore, it would not be expected to get information about the test results of the heart failure diagnosis mentioned above from them.

Table 4-3 presents several possible risk factors and ongoing treatments (specified during the interviews) for their clinic heart failure profile.

4.6.7. Study data collection

Semi-structured interviews were conducted to explore the experiences of individuals with heart failure from their own daily life stories between June and October 2022, with five main interview questions and socio-demographic questions (including age, sex, education level, heart failure duration etc.) (**Appendix 7**).

Table 4-3: Details about self-reported heart failure diagnosis of the participants

Participant		Breathlessness with walking/climbin	Pulmonary oedema	Heart attack	Hypertension	Arrythmias	Angina	Type 2 diabetes	Diuretic use	Pacemaker use
Ali	*HF diagnosis reported by his son (medical doctor) – interview at the hospital*	Yes	Yes	Yes	Yes			Yes	Yes	
Mert	*“I was shocked that I had heart failure. ... My doctor said that the infection directly affected my heart. That’s why he said you have this problem in your heart.”*	Yes			Yes				Yes	
Elif	*“Due to the late treatment of the infection in the body, deformation of the heart valve has occurred due to this infection. Especially since I never went to a doctor and did not use medication, my heart was adversely affected because of it. ... I was diagnosed with heart failure.”*	Yes								
Umut	*“I have heart failure. My mother also had heart failure. My mother also had bypass surgery and a stent was inserted.”*	Yes	Yes	Yes				Yes		
Canan	*“Also, the doctor said that you have heart failure; you should not tire [exert] yourself too much.”*	Yes	Yes	Yes	Yes			Yes	Yes	
Can	*“I was actually having a heart attack at the time. ... But at this stage, I lost a quarter of my heart. No, I lost a third of it. Because the heart was deprived of oxygen.”*	Yes		Yes						
Peri	*“The doctor told me that I have a problem with my heart valve.”*	Yes								
Oya	*“I had a leak in my heart after that, the doctor said, ‘That’s why you can’t breathe properly’.”*	Yes		Yes	Yes			Yes		
Emel	*HF diagnosis reported by his son*	Yes		Yes				Yes		
Alin	*HF diagnosis reported by her grandchild*	Yes	Yes	Yes	Yes			Yes		
Fulya	*“To the doctor: first I went to the respiratory ward, and they sent me to cardiology. So, I was diagnosed with arrhythmia at the age of 27. And then heart failure.”*	Yes		Yes		Yes				
Eymen	*HF diagnosis reported by his wife*	Yes	Yes	Yes	Yes					
Onur	*HF diagnosis reported by his wife*							Yes		
Leyla	*“The doctor said that my heart is working at 50%.”*	Yes		Yes						
Asya	*“The doctor said that you have a problem with your heart.”*			Yes	Yes					
Alp	*“My heart work capacity was below 20%.”*	Yes		Yes	Yes			Yes	Yes	Yes
Ayhan	*“I felt something like a heart spasm. I went to the doctor and was diagnosed. That’s how it started.”*	Yes					Yes			
Berk	*Email interview – “I was diagnosed with heart failure two years ago.”*	Yes								
Cansel	*Email interview – “I have a diagnosis of mitral valve - heart failure.”*	Yes	Yes					Yes		
Ela	*Email interview – “I was diagnosed with heart failure about 10 years ago.”*	Yes								

The main interview questions were:

1. Could you please tell me about your heart failure; what is that like for you?
2. Please tell me about a typical day for you in terms of feeling breathlessness?
3. How has the breathlessness you described affected your everyday life?
4. What coping mechanisms or strategies do you use to deal with your breathlessness?
5. Do you think you get enough education to manage your breathlessness from your doctors/nurses/other healthcare professionals?

These interview guides were developed on the basis of a previous qualitative study carried out in the UK (Walthall et al., 2017) and reviewed by the research team and public advisors. The interview covered the following issues:

- Understanding breathlessness and other symptoms in heart failure
- Impact of breathlessness on everyday life
- Breathlessness management strategies
- Needs for improved health behaviours.

Pilot interviews were conducted before starting the data collection. The researcher conducted pilot interviews with public advisors, consisting of two Turkish individuals and one English participant. Additionally, pilot interviews were conducted with her colleagues, specifically two PhD nurse researchers within the team. As this was the researcher's first experience conducting interviews, her principal supervisor, Professor Bridget Johnston – an expert in qualitative study designs – regularly met with her. They discussed how to conduct effective interviews and helped her develop her communication skills and interview techniques.

The face-to-face interviews (n=11) were conducted according to the participants' preferences with respect to time, place, and mode. Telephone (n=6) and email interviews (n=3) were also conducted. The average interview duration was 29.05 minutes (21–65 minutes) for telephone and face-to-face interviews. Three email interviews were conducted, using written answers to the interview questions. MS conducted all interviews in Turkish. Telephone and face-to-face interviews were audio-recorded, transcribed verbatim in Turkish, and translated into English. Each participant was assigned a (Turkish) pseudonym for the transcription. After these stages, English and Turkish transcripts were imported into NVivo 12 (Mac version) (Ltd., 2018).

4.6.8. Qualitative data analysis

The interview data was analysed using a reflexive thematic analysis developed by Braun and Clarke's (2022). This analysis included six phases ("familiarising; generating initial codes; generating initial themes; developing and reviewing themes; refining, defining, and naming themes; and writing-up") of the data analysis, which involves in-depth recording to combine codes and themes. **Table 4-4** describes these six phases of reflexive thematic analysis and how they were applied in this study.

4.6.9. Ethics approval and considerations

Ethical approval for this study was obtained from College of Medical, Veterinary and Life Sciences (MVLS) Ethics Committee (Project number: 200210076; 21 April 2022) and Kahramanmaraş Sütçü Imam University Ethics Committee (Project number: 143; 31 May 2022) (**Appendix 8**). The first ethical approval was obtained from the MVLS Ethics Committee. After the first submission of the ethical application documents to the committee, an amendment was submitted for clarity of recruitment and transcription stages. Then, the Turkish ethics application documents were submitted to Kahramanmaraş Sütçü Imam University Ethics Committee. All documents for the ethical approval application were written by the PhD researcher and cross-checked by the research team and PPI advisors. Informed verbal consent was given by all interviewees before starting the recorded interview.

After the ethical approval was obtained from the institutions in the two countries, an official/formal application was submitted to hospitals (recommended by Kahramanmaraş Sütçü Imam University Ethics Committee) to recruit participants for the research. However, the application was directed to the Turkish Ministry of Health and rejected. The reasons for the rejection were not detailed in the letter. Since the researcher added the online recruitment option to find participants as well, the study was continued by finding participants online.

As mentioned in the previous study's ethics section, various associated trainings were undertaken: the NHS Research Good Clinical Practices Training; as well as courses at the University of Glasgow on data controlling and governance, research data management; information security; research integrity; equality and diversity; and ethical approval for people working with human subjects.

Table 4-4 6 Phases of reflective thematic analysis in this present study

Phases of reflexive thematic analysis	Explanation	In this study
Phase 1: ***"Familiarising yourself with the dataset"***	Reflective thematic analysis starts with dataset familiarisation which is about gaining deep familiarity with the content of the dataset (immersion) and involves asking questions about the content of the dataset (critical engagement).	This phase included reading, re-reading, listening audio records, and making (brief) notes (at least two times). The researcher transcribed and translated the dataset. Each transcript was re-read, and notes were taken. Then, each audio-recording was listened to, and brief notes were taken on written transcripts.
Phase 2: ***"Coding"***	Coding is an engaged and systematic process. Codes need to capture specific and precise meanings with the dataset related to research questions/aims. The code labels then summarise the analytical ideas and data meaning captured by the codes.	After the data familiarisation stage, first initial codes were generated by the researcher through line-by-line inductive indexing of English and Turkish transcripts in NVivo 12. The codes created from Turkish and English transcripts were compared to reach the final version. The code labels were captured to summarise the codes.
Phase 3: ***"Generating initial themes"***	This involves clustering together potentially connected codes into the same candidate themes, and then exploring these initial meaning pattern.	Identified code labels were grouped into descriptive sub-themes and main themes based on a combination of the factors of the research questions.
Phase 4: ***"Developing and reviewing themes"***	This involves checking that themes make sense in relation to both the coded extracts and the full dataset associated with the research questions/aims.	Identified candidate themes (and sub-themes) were double-checked by one of research team members. This double-checked discussion helped researchers to ensure the themes (and sub-themes) highlighted the most important patterns across the dataset associated with research questions.
Phase 5: ***"Refining, defining, and naming themes"***	This involves analytically writing-up your theme definitions and naming related to research questions/aims.	After Phase 4, the identified themes (and sub-themes) were presented in a table with their definitions and names. The researcher discussed these themes and their definition with one heart failure specialist nurse and her two PPI participants for further consistency.
Phase 6: ***"Writing-up"***	This is the last analytic process of reflective thematic analysis, which involves telling a coherent and persuasive story about the dataset to the readers.	The final reports of the findings were written and presented as a thesis chapter.

4.6.10. Rigour

Rigour is a way to establish confidence in a research study's conclusions by establishing the objectivity and expertise of the study's methodology (Thomas and Magilvy, 2011, Tobin and Begley, 2004). According to Morse et al. (2002), a research study's credibility can be established through an approach of verification methods; this involves routinely verifying, confirming, and ensuring that the research's progress contributes to its ongoing validity and reliability, resulting in rigour. To help qualitative researchers guarantee the validity of their findings are applicable to practise, robust methodologies have been created (Porter, 2007, Rolfe, 2006). Trustworthiness and the components of reliability, dependability, transferability, and confirmability were taken into account in the study to make sure the research findings were "worth taking account of" (Lincoln and Guba, 1985). By analysing the data by many researchers and presenting detailed statements from those who participated to support the interpretation, it was possible to determine whether the appraisal of the findings represented a "credible" interpretation of the findings (Thomas and Magilvy, 2011).

The following actions were carried out to increase the trustworthiness of this study findings. After the interviews, all audio-recordings were professionally transcribed and translated from Turkish to English. Each English transcript was double-checked by one of the other researchers to assess the quality. The main aims of this stage were to correct any transcription errors and to remove any personal health information in the transcript. Themes were reviewed and refined by other researchers to reduce the risk of subjective judgements of the first researcher and improve the reliability and validity of the study. The coding followed an inductive or deductive orientation, and these were reviewed and refined by the research team to reach final themes and sub-themes.

4.6.11. Reflexivity

The practical measures listed below were taken to maintain the necessary balance between the researcher's own personal experiences and the participants included in this qualitative study; of course, the main purpose was not to exclude reflexivity but to explain the study.

- **Researcher position:** This descriptive qualitative research was undertaken by the primary researcher, a PhD researcher/nurse, with the guidance of three members of her supervisory team. Interviewing people living with heart failure on a one-on-one basis was a new experience for her. During the interviews, there was a professional researcher–participant relationship between the study participants and the researcher.

Her position was clearly as a researcher shaped by her academic and clinical nurse experience background. Although this could be seen as a personal bias, on the contrary, this allowed the researcher to understand the participants' real-life experiences in their own words and maintain the professional (researcher–participant) relationship. The research participants were recruited via online recruitment methods and information about the researcher was provided in the "Participant Information Sheet". This was another important factor that strengthened the researcher–participant professional relationship in this study, which in turn strengthened trust.

- **Repeated review:** To achieve this, the researcher repeatedly performed reading, listening, and note-taking in order to critically understand/interpret participants' interviews during the data analysis process. This stage was important, especially in order to understand how the reality of people's symptom experiences/self-management strategies are shaped by their cultural/social beliefs through their own words in Türkiye.
- **Peer consultation:** Apart from her supervisory team, the researcher discussed the findings of this study with a heart failure specialist nurse (UK) and two public advisors (UK) to evaluate its reliability and plausibility.

4.6.12. Data management and protection

The researcher ensured that all participants had enough time to read and understand the participation information sheet. Before signing the consent form, the researcher provided sufficient information about the research; and answered all questions and discussed any concerns that participants had. One-on-one interviews were carried out, and therefore each interview included only one participant and the researcher. The face-to-face interviews were conducted at the participants' preferred location and time, and according to their preferred mode. There was no risk for identifiable to other participants based on the locations.

The researchers were respectful of data protection requirements. During the analysis and reporting of the results, all participants' were anonymised and coded by participants' participation numbers, and a Turkish nickname was assigned. This process was explained to participants during their consent process. This ensured that participants' identities cannot be identified from the final written report (this thesis and possible published articles based on it). All transcripts of the interviews were also anonymised for data storage.

All data collected from this study were kept in accordance with General Data Protection Regulation (GDPR, 2018) laws. The University of Glasgow was a data holder, and the researchers were the data controller for this study. She was responsible for caring for and using participant information appropriately. The University of Glasgow will keep identifiable information about participants for 10 years after the study has been completed (as advised for participants with high risk) after which all information will be deleted permanently from the university server. All online documents (including Turkish and English transcript versions of the interviews, audio-recording files, and consent forms) of participants were password protected and only researchers of the study reached the study data.

This qualitative study was a low-risk study. The PhD researcher did not anticipate that it would cause any harm to participants. Participants talked about their experiences with heart failure. During the interview sessions, some participants had distress talking about death and dying because of their heart failure conditions and breathlessness experiences. She accepted that their emotions would be high when they talked about their concern and fear about death/dying and the future. With an acknowledgement of the difficulties/challenges of this kind of conversation for the participants, she allowed the participants to talk about their emotions and expression as much as they wished. They took a break until they felt ready and comfortable to talk about their experiences and stress.

Chapter 7 will present the findings of the descriptive qualitative study.

4.7. Chapter summary

This chapter provided details about methods of each study of this PhD research. The triangulation phase of the overarching key findings in the project was explained. PPI was described and explained for this research. The following three chapters will introduce the findings of the three studies of the research. Chapter 5 provides the findings of mixed-method systematic review.

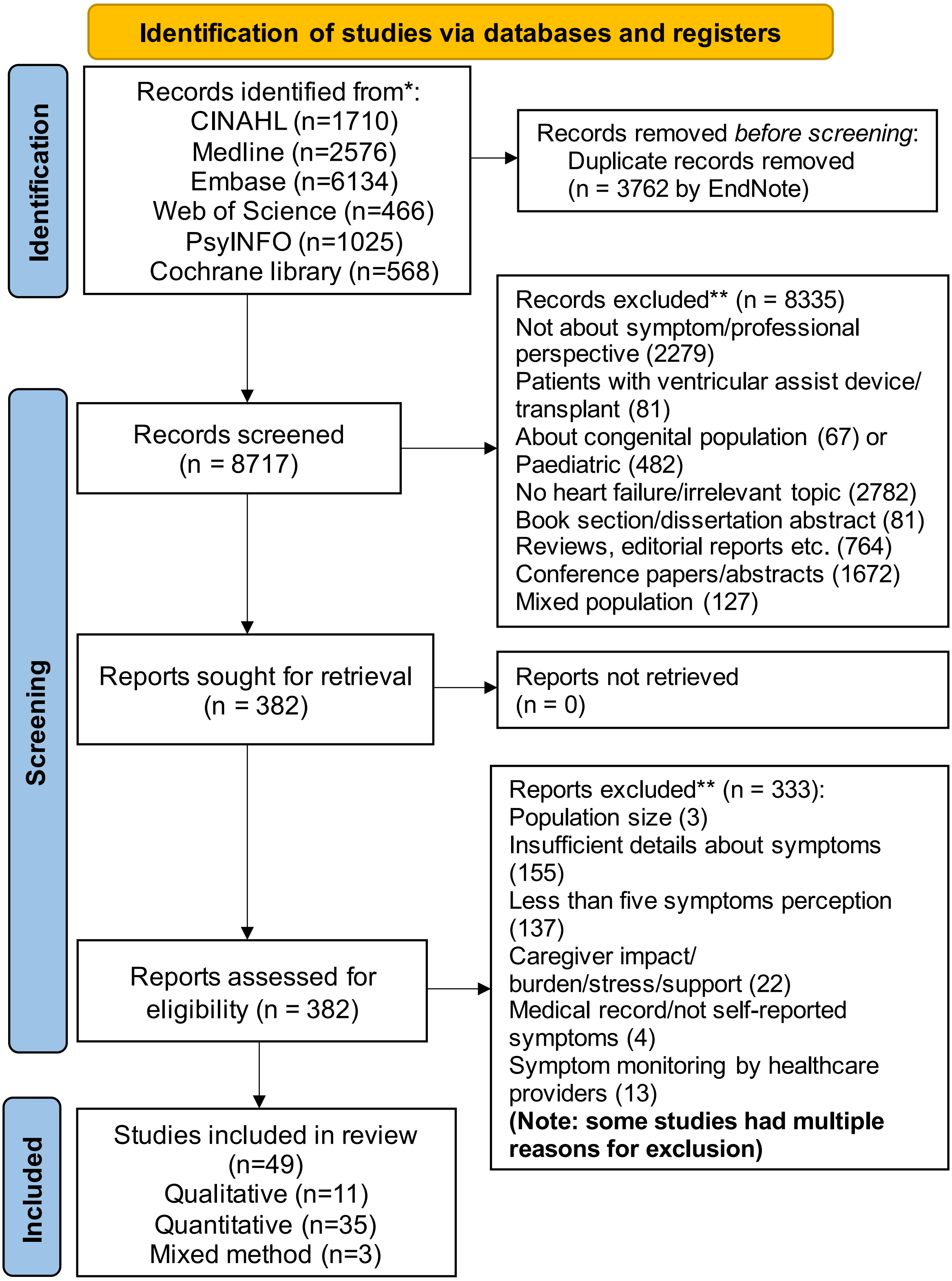
Chapter Five - Findings of mixed-methods Systematic review

5.1. Introduction

This chapter provides the findings of the mixed-method systematic review. Individuals living with heart failure encounter a variety of symptoms. However, existing clinical guidelines primarily concentrate on very limited number of symptoms, rather than comprehensively assessing and monitoring the full spectrum of symptoms. Thus, the full range of symptoms experienced in heart failure settings is under-appreciated. The objective of this review was to examine the full spectrum of heart failure symptoms based on the ESC heart failure guidelines, which categorise symptoms as “typical” or “less typical”, while also considering symptoms not listed in the guidelines. The investigation also considering setting, age, and gender differences.

As described on page 65-68, the methodology involved a mixed-method systematic review and narrative synthesis, employing the Joanna Briggs Institute’s framework for mixed-method systematic reviews (Lizarondo L et al., 2020). The literature search was conducted using the relevant MeSH terms and synonymous key words in six electronic databases. Symptoms were categorised as follows: 1) ESC-listed typical symptoms, 2) ESC-listed less typical symptoms, and 3) symptoms not listed by ESC. The study explored variations in symptom patterns across different scenarios: A) hospital versus community settings, B) age groups (individuals <65 years versus ≥65 years), and C) men versus women.

The search results of the combined six databases produced a total of 12479 publications (**Figure 5-1**). After duplicates were removed, 8717 papers were selected for the title and abstract screening. 8335 papers were excluded according to the research inclusion and exclusion criteria. 382 papers were screened for full text. In total, 49 papers were analysed for this review. The reference lists of these papers were also manually searched for additional records, and no additional paper was identified.



*Total n=12479
**Most studies had multiple reasons for exclusion

Figure 5-1: Prisma flow diagram

Table 5-1: Details of included studies

Details of included studies

		Total (n=49)
Summarised articles characteristics. (n) represents the number of papers with the characteristic		
Country	United States of America, n (%)	**27 (55)**
	South Korea, n (%)	**3 (6)**
	United Kingdom, n (%)	**3 (6)**
	China, n (%)	**3 (6)**
	Sweden, n (%)	**2 (4)**
	Türkiye, n (%)	**2 (4)**
	Australia, n (%)	**2 (4)**
	Canada, n (%)	**1 (2)**
	Japan, n (%)	**1 (2)**
	Italy, n (%)	**1 (2)**
	Spain, n (%)	**1 (2)**
	South Africa, n (%)	**1 (2)**
	Kenya, n (%)	**1 (2)**
	Vietnam, n (%)	**1 (2)**
Study design	Cross-sectional, n (%)	**26 (53)**
	Mixed-method, n (%)	**3 (6)**
	Descriptive qualitative, n (%)	**5 (10)**
	Phenomenological, n (%)	**4 (8)**
	Grounded theory, n (%)	**2 (4)**
	Other quantitative study design, n (%)	**9 (18)**
Setting	Hospital, n (%)	**18 (38)**
	Out-patient, n (%)	**19 (39)**
	Mixed, n (%)	**5 (10)**
	Other*, n (%)	**7 (14)**
Research population	Total number of participants, n (%)	**8298 (100)**
	Patients with heart failure, n (%)	**8233 (99)**
	Informal caregivers, n (%)	**56 (1)**
Participants characteristics	Aetiology of heart failure, n (%)	**12 (26)**
	Ejection fraction, n (%)	**26 (53)**
	<50%, n (%)	**20 (40)**
	≥50%, n (%)	**1 (2)**
	NYHA Functional Class, n (%)	**35 (71)**
	Comorbidities, n (%)	**27 (55)**
Summarised patients' descriptive for included 49 articles. (n) represented the number of participants		
Sample size	Total number of patients	**8233**
	Male, n (%)	**5080 (62)**
	Female, n (%)	**3153 (38)**
Age	Mean age**	**68.45**
	Mean Age range	**48–82**
Ejection Fraction	Mean ejection fraction range, %	**22%-54%**
NYHA Functional Class		**I-IV**

**Data collection very short after hospital discharge – hospital; **Two studies did not specify the mean age of their study population.*

5.2. Study characteristics

The 49 eligible studies identified (35 quantitative, 11 qualitative, and 3 mixed-methods research) were published between 2000 and 2022. 14 different countries were represented. More than half of these studies were conducted in the USA [27/49 (55%)] (**Table 5-1**). In 26 (53%) of the studies, the main study design was cross-sectional. Overall, 45 studies focused on the symptoms of people with heart failure, while four papers considered the perspectives of both caregivers and those living with heart failure. None of the studies includes patient symptom assessment from the perspective of caregivers only. 18 papers were conducted in hospitals.

5.3. Cohort characteristics

The mean age was 68 (48–82) years for people with heart failure [in two studies, age was not reported (Bekelman et al., 2007, Kimani et al., 2018)] (Table 5-1). In 42 studies most participants were men and in seven studies the (slight) majority were women. The total number of participants in the studies was 8298 (range 12–1271). This comprised 8233 people with heart failure, and the remainder (n=56) were informal caregivers. The majority of patients (62%, n=5080) were men. 26 studies reported ejection fraction, and one of them included participants with more than 50% of ejection fraction range. Only two studies included symptoms related to the end-of-life care phase for heart failure (Abshire et al., 2015, Wilson and McMillan, 2013), while eight studies focused on the advanced heart failure population (Blinderman et al., 2008, Checa et al., 2020, Haedtke et al., 2019, Kimani et al., 2018, Lokker et al., 2016, Opasich et al., 2008, Oriani et al., 2019, Yu et al., 2016) **(Figure 5-2)**.

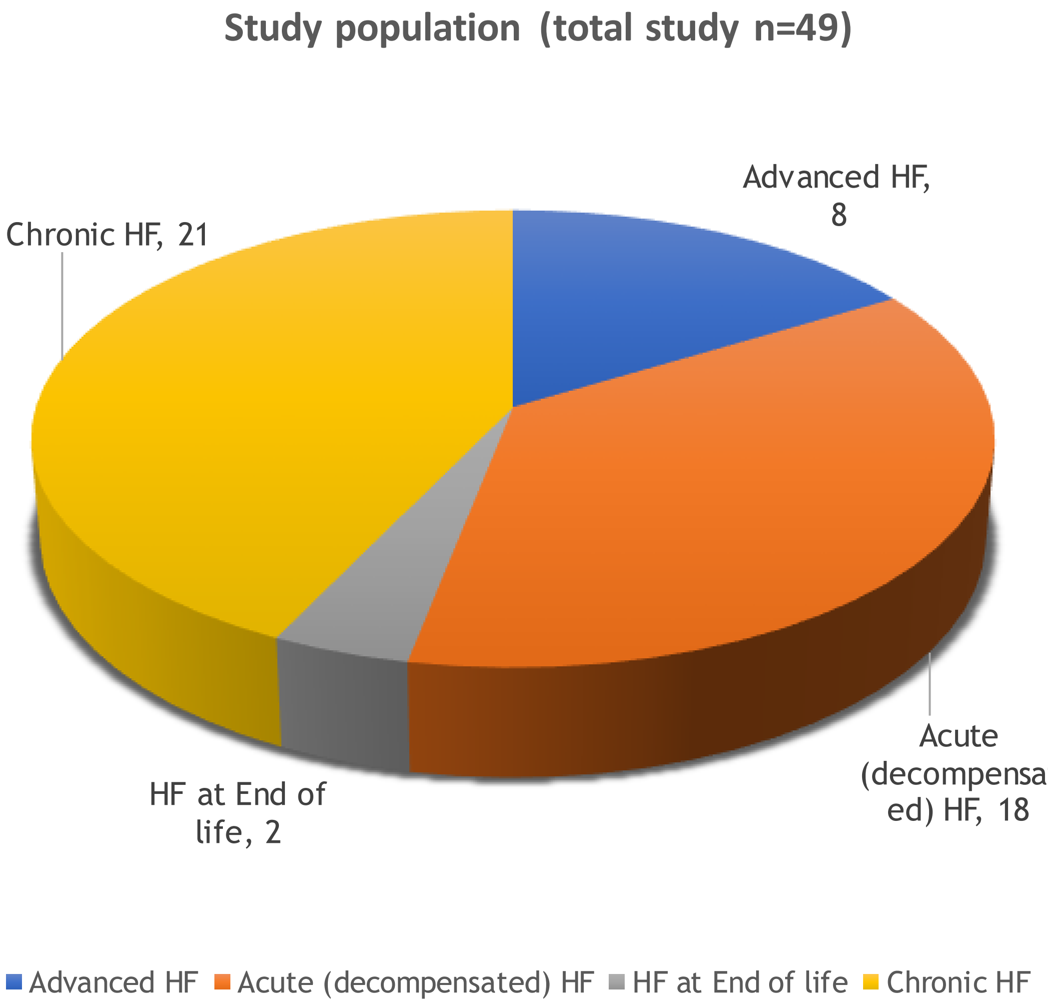


Figure 5-2: Study populations (n=49)

5.4. Quality assessment

Overall, only seven of 49 quantitative studies were of low quality (**Table 5-2**). Lack of clarity regarding the identification, evaluation of the risk of, and implementation of strategies to address the presence of confounding factors reduced the quality of papers in cross-sectional studies. Qualitative studies were of good quality, except for one study that has inconsistent reporting of gender percentage and insufficient details about inclusion criteria. One study had a high risk related to unclear ethical issues and study design. Two mixed-methods studies had good quality design, but one had insufficient details about demographic factors. No studies were excluded due to quality assessment.

Table 5-2: Joanna Briggs Institute Quality Appraisal Checklist for Studies (total number of studies, n=49)

Study's authors and date	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**Q6**	**Q7**	**Q8**	**Q9**	**Q10**	**Q11**	**Total Score**
Quantitative												
Albert et al. (2010)	Y	Y	U	U	Y	Y	Y	Y				6/8
Alkan and Nural (2017)	Y	Y	Y	Y	U	U	Y	Y				6/8
Altice and Madigan (2012)	Y	Y	Y	Y	Y	U	Y	Y				7/8
Bekelman et al. (2007)	Y	Y	U	Y	U	U	Y	Y				5/8
Blinderman et al. (2008)	Y	Y	U	Y	U	U	Y	Y				5/8
Darling et al. (2013)	Y	Y	U	Y	U	Y	Y	Y				6/8
Friedman and Quinn (2008)	Y	Y	Y	Y	Y	Y	Y	Y				8/8
Fischer and Bekelman (2017)	Y	Y	Y	Y	Y	Y	Y	Y				8/8
Flint et al. (2017)	Y	Y	U	Y	Y	Y	Y	Y				7/8
Gallagher et al. (2012)	N	Y	Y	Y	U	U	Y	Y				5/8
Graven et al. (2020)	Y	Y	U	Y	N	N	Y	Y				5/8
Haedtke et al. (2019)	Y	Y	Y	Y	U	U	Y	Y				6/8
Heo et al. (2019b)	Y	Y	Y	Y	Y	Y	Y	Y				8/8
Heo et al. (2020)	N/A	N/A	Y	Y	Y	Y	Y	Y	Y	Y	Y	9/11
Lokker et al. (2016)	Y	U	Y	Y	Y	Y	Y	Y				7/8
Lum et al. (2016)	N/A	N/A	Y	N	N	Y	Y	Y	Y	U	Y	6/11
Luo et al. (2020)	Y	Y	Y	Y	U	Y	Y	Y				7/8
Nguyen et al. (2022)	Y	Y	Y	Y	Y	U	Y	Y				7/8
Oguz and Enç (2008)	Y	Y	Y	Y	U	U	Y	Y				6/8
Okada et al. (2019)	Y	Y	Y	Y	Y	Y	Y	Y				8/8
Opasich et al. (2008)	Y	Y	Y	Y	N	N	Y	Y				6/8
Oriani et al. (2019)	Y	Y	Y	Y	Y	U	Y	Y				7/8
Reeder et al. (2015)	Y	Y	Y	Y	U	U	Y	Y				6/8
Salyer et al. (2019)	Y	Y	Y	Y	Y	U	Y	Y				7/8
Seckin et al. (2022)	Y	Y	Y	Y	Y	Y	Y	Y				8/8
Schiff et al. (2003)	U	Y	Y	Y	Y	Y	Y	Y				7/8
Shah et al. (2013)	Y	Y	Y	Y	U	U	Y	Y				6/8
Son and Won (2018)	Y	Y	Y	Y	Y	Y	Y	Y				6/8
Song et al. (2010)	N/A	N/A	Y	Y	Y	Y	Y	Y	Y	Y	Y	9/11
Todero et al. (2002)	N/A	N/A	Y	Y	N	N	Y	Y	Y	U	Y	6/11
Wang et al. (2020b)	N	Y	Y	Y	U	U	Y	Y				5/8
Wilson and McMillan (2013)	U	Y	Y	U	U	U	Y	Y				4/8
Yu et al. (2016)	Y	Y	Y	Y	Y	Y	Y	Y				8/8
Zambroski et al. (2005)	Y	Y	Y	Y	Y	Y	Y	Y				8/8
Qualitative and Mixed-methods (for qualitative components)												
Abshire et al. (2015)	U	Y	Y	Y	Y	N/A	N/A	Y	Y	Y		7/10
Aldred et al. (2005)	Y	Y	Y	Y	Y	U	Y	U	Y	Y		8/10
Bennett et al. (2000)	U	Y	Y	Y	Y	U	U	U	Y	Y		6/10
Checa et al. (2020)	Y	Y	Y	Y	Y	Y	Y	U	Y	Y		9/10
Hedemalm et al. (2008)	U	U	Y	Y	Y	U	U	Y	Y	Y		6/10
Heo et al. (2019a)	U	U	Y	Y	Y	Y	Y	Y	Y	Y		8/10
Jurgens et al. (2009)	Y	Y	Y	Y	Y	N/A	N/A	U	Y	Y		7/10
Kimani et al. (2018)	Y	Y	Y	Y	Y	U	U	U	Y	Y		7/10
Lin et al. (2021)	U	Y	Y	Y	Y	U	U	U	U	Y		5/10
McHorney et al. (2021)	Y	Y	Y	Y	Y	U	N	U	Y	Y		7/10
Patel et al. (2007)	Y	Y	Y	Y	Y	N	N	Y	Y	Y		8/10
Rodriguez et al. (2008)	U	Y	Y	Y	Y	U	U	U	U	Y		5/10
Rogers et al. (2002)	U	Y	Y	Y	Y	N	U	U	Y	Y		6/10
Schumacher et al. (2018)	N/A	Y	Y	Y	Y	U	Y	Y	Y	Y		8/10
Walsh et al. (2018)	U	Y	Y	Y	Y	N	Y	Y	Y	Y		8/10

Y-Yes; N-No; U-Unclear; N/A-Not applicable. Yes=1; No or not reported (U & N/A) =0

5.5. Symptoms

ESC typical (n=6) and less typical (n=10) symptoms were observed in 47 and 47 studies of the 49 studies, respectively (**Figure 5-4**). Participants in all 49 studies reported at least one of the non-ESC (n=37) symptoms. The numbers of symptoms ranged from 6–42 for all symptoms, 1–6 for the number of ESC typical symptoms, 1–8 for the numbers of ESC less typical symptoms, and 1–33 for non-ESC. 18 of 49 studies did not report any psycho-socio-behavioural symptoms. Symptom assessment (of at least six symptoms) was observed in all studies. These studies predominantly evaluated symptoms associated with hospitalisation (before or during hospital admission) (**Figure 5-3**). The main heart failure symptom assessed in the four included studies was depressive symptoms.

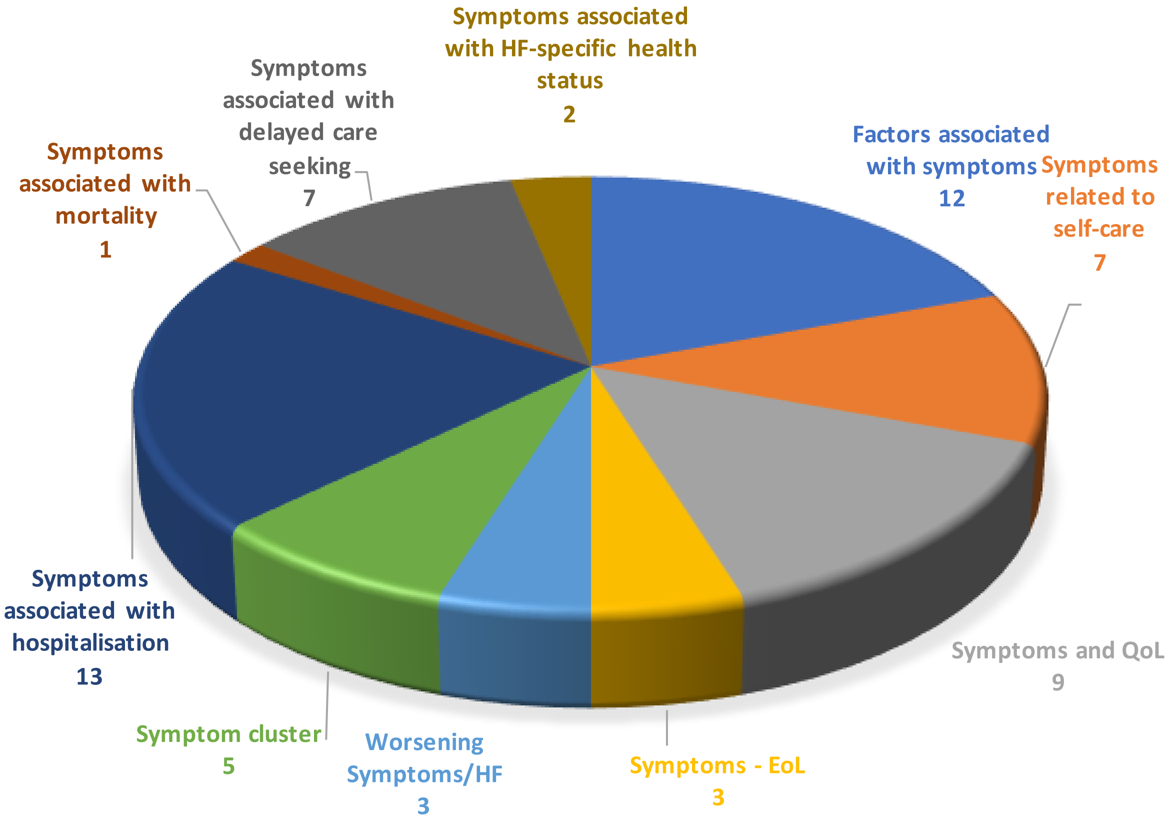
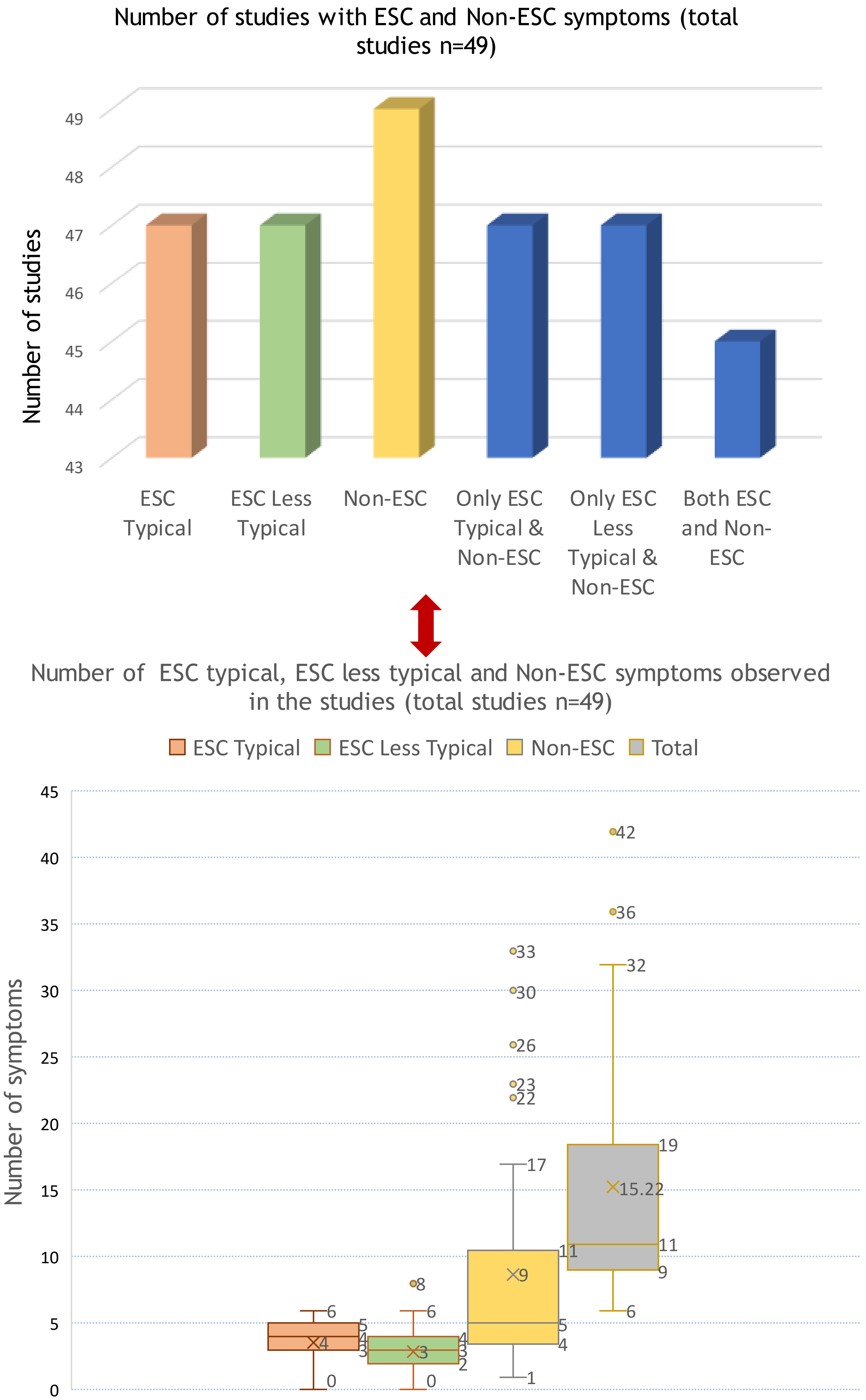


Figure 5-3: Reasons for symptoms evaluation/ assessment in the studies


Number of studies with ESC and Non-ESC symptoms (total studies n=49)

Number of ESC typical, ESC less typical and Non-ESC symptoms observed in the studies (total studies n=49)

Figure 5-4: Total number of studies with at least one of ESC and/or non-ESC symptoms

5.5.1. Typical heart failure symptoms from ESC Guidelines

ESC heart failure symptoms were the most observed (**Table 5-3**). Breathlessness was the most observed symptom in 44 out 49 studies. Fatigue was observed in 28 of 49. Tiredness was observed in 8 of 49 studies. Increased time to recover after exercise was not observed in any studies. Out of 49 studies, ankle swelling (including swelling lower extremities) was observed in 25; Orthopnoea in 13; paroxysmal nocturnal dyspnoea in 18; and reduced exercise tolerance in 13. The most common among ESC typical symptoms across all of the studies were as follows: breathlessness was experienced by 83% of 6265 participants from 36 studies, fatigue/tiredness was experienced by 69% of 5105 participants of 29 studies, and reduced exercise tolerance was experienced by 71% of 1720 participants of 11 studies were. (See **Table 5-4** for further details.)

5.5.2. Less typical heart failure symptoms from ESC Guidelines

Out of the 49 studies included, ESC (McDonagh et al., 2021) less typical symptoms were represented as follows: loss of appetite in 30; cough in 29; dizziness in 24; palpitations in 21; feeling depressed in 17; bloated feeling in 16; wheezing in 4; syncope in 3; confusion in 3; and bendopnea in 1 (**Table 5-3**). Among these symptoms, cough was the most common symptom, with 42% of 6209 participants of 28 studies. Feeling depressed was observed as the second most common less typical symptom, with 49% of 2319 participants of 12 studies. Please see **Table 5-4** for further details.

Table 5-3: Studies with ESC and non-ESC Symptoms

ESC and non-ESC symptoms in the studies (n=49)		
Symptoms	**No of studies**	**Studies**
ESC Typical symptoms		
Breathlessness (including at rest)	**44**	(Abshire et al., 2015, Albert et al., 2010, Alkan and Nural, 2017, Altice and Madigan, 2012, Bekelman et al., 2007, Bennett et al., 2000, Blinderman et al., 2008, Checa et al., 2020, Darling et al., 2013, Fischer and Bekelman, 2017, Graven et al., 2020, Haedtke et al., 2019, Hedemalm et al., 2008, Heo et al., 2019b, Heo et al., 2020, Heo et al., 2019a, Jurgens et al., 2009, Kimani et al., 2018, Lin et al., 2021, Lokker et al., 2016, Luo et al., 2020, McHorney et al., 2021, Nguyen et al., 2022, Oguz and Enç, 2008, Okada et al., 2019, Opasich et al., 2008, Oriani et al., 2019, Patel et al., 2007, Reeder et al., 2015, Rodriguez et al., 2008, Rogers et al., 2002, Salyer et al., 2019, Seckin et al., 2022, Schiff et al., 2003, Schumacher et al., 2018, Shah et al., 2013, Son and Won, 2018, Song et al., 2010, Todero et al., 2002, Walsh et al., 2018, Wang et al., 2020b, Wilson and McMillan, 2013, Yu et al., 2016, Zambroski et al., 2005)
Orthopnoea	**23**	(Albert et al., 2010, Alkan and Nural, 2017, Altice and Madigan, 2012, Darling et al., 2013, Friedman and Quinn, 2008, Graven et al., 2020, Haedtke et al., 2019, Hedemalm et al., 2008, Heo et al., 2019b, Heo et al., 2020, Jurgens et al., 2009, Lin et al., 2021, Luo et al., 2020, Okada et al., 2019, Patel et al., 2007, Reeder et al., 2015, Seckin et al., 2022, Schiff et al., 2003, Son and Won, 2018, Song et al., 2010, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
Paroxysmal nocturnal dyspnoea	**18**	(Albert et al., 2010, Alkan and Nural, 2017, Altice and Madigan, 2012, Darling et al., 2013, Friedman and Quinn, 2008, Gallagher et al., 2012, Graven et al., 2020, Haedtke et al., 2019, Lin et al., 2021, Luo et al., 2020, Patel et al., 2007, Reeder et al., 2015, Seckin et al., 2022, Son and Won, 2018, Song et al., 2010, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
Reduced exercise tolerance (including breathless with activity/ walking)	**13**	(Albert et al., 2010, Bennett et al., 2000, Friedman and Quinn, 2008, Gallagher et al., 2012, Graven et al., 2020, Hedemalm et al., 2008, Jurgens et al., 2009, Luo et al., 2020, Okada et al., 2019, Patel et al., 2007, Reeder et al., 2015, Schiff et al., 2003, Altice and Madigan, 2012)
Fatigue	**28**	(Abshire et al., 2015, Albert et al., 2010, Aldred et al., 2005, Darling et al., 2013, Friedman and Quinn, 2008, Graven et al., 2020, Hedemalm et al., 2008, Heo et al., 2019b, Heo et al., 2020, Heo et al., 2019a, Jurgens et al., 2009, Kimani et al., 2018, Lin et al., 2021, McHorney et al., 2021, Nguyen et al., 2022, Oguz and Enç, 2008, Okada et al., 2019, Oriani et al., 2019, Patel et al., 2007, Reeder et al., 2015, Rodriguez et al., 2008, Salyer et al., 2019, Seckin et al., 2022, Schumacher et al., 2018, Son and Won, 2018, Todero et al., 2002, Walsh et al., 2018, Yu et al., 2016)

Tiredness	8	(Altice and Madigan, 2012, Bennett et al., 2000, Checa et al., 2020, Gallagher et al., 2012, Luo et al., 2020, Opasich et al., 2008, Rogers et al., 2002, Shah et al., 2013)
Increased time to recover after exercise	0	
Ankle swelling (including swelling of lower extremities)	25	(Aldred et al., 2005, Alkan and Nural, 2017, Altice and Madigan, 2012, Bekelman et al., 2007, Bennett et al., 2000, Blinderman et al., 2008, Gallagher et al., 2012, Graven et al., 2020, Haedtke et al., 2019, Hedemalm et al., 2008, Kimani et al., 2018, Lokker et al., 2016, Luo et al., 2020, McHorney et al., 2021, Patel et al., 2007, Reeder et al., 2015, Rodriguez et al., 2008, Salyer et al., 2019, Seckin et al., 2022, Schumacher et al., 2018, Son and Won, 2018, Song et al., 2010, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
Oedema - general	18	(Abshire et al., 2015, Checa et al., 2020, Darling et al., 2013, Friedman and Quinn, 2008, Haedtke et al., 2019, Heo et al., 2019b, Heo et al., 2020, Heo et al., 2019a, Jurgens et al., 2009, Lin et al., 2021, Nguyen et al., 2022, Oguz and Enç, 2008, Okada et al., 2019, Oriani et al., 2019, Reeder et al., 2015, Schiff et al., 2003, Todero et al., 2002, Walsh et al., 2018)
ESC Less Typical Symptom		
Nocturnal cough/ cough	29	(Albert et al., 2010, Alkan and Nural, 2017, Altice and Madigan, 2012, Bekelman et al., 2007, Bennett et al., 2000, Blinderman et al., 2008, Darling et al., 2013, Friedman and Quinn, 2008, Fischer and Bekelman, 2017, Flint et al., 2017, Gallagher et al., 2012, Graven et al., 2020, Haedtke et al., 2019, Hedemalm et al., 2008, Lin et al., 2021, Lokker et al., 2016, Lum et al., 2016, Luo et al., 2020, McHorney et al., 2021, Oguz and Enç, 2008, Okada et al., 2019, Oriani et al., 2019, Patel et al., 2007, Rodriguez et al., 2008, Seckin et al., 2022, Schiff et al., 2003, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
Wheezing	4	(Albert et al., 2010, Bennett et al., 2000, Blinderman et al., 2008, McHorney et al., 2021)
Bloated feeling	16	(Albert et al., 2010, Alkan and Nural, 2017, Bekelman et al., 2007, Blinderman et al., 2008, Darling et al., 2013, Graven et al., 2020, Haedtke et al., 2019, Luo et al., 2020, McHorney et al., 2021, Reeder et al., 2015, Todero et al., 2002, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005, Lokker et al., 2016, Patel et al., 2007)
Loss of appetite (including anorexia)	30	(Abshire et al., 2015, Alkan and Nural, 2017, Bekelman et al., 2007, Bennett et al., 2000, Blinderman et al., 2008, Darling et al., 2013, Friedman and Quinn, 2008, Gallagher et al., 2012, Haedtke et al., 2019, Hedemalm et al., 2008, Lin et al., 2021, Lokker et al., 2016, Luo et al., 2020, McHorney et al., 2021, Nguyen et al., 2022, Okada et al., 2019, Opasich et al., 2008, Oriani et al., 2019, Reeder et al., 2015, Rogers et al., 2002, Salyer et al., 2019, Schumacher et al., 2018, Shah et al., 2013, Song et al., 2010, Todero et al., 2002, Wang et al., 2020b, Wilson and McMillan, 2013, Yu et al., 2016, Zambroski et al., 2005, Albert et al., 2010)
Confusion	3	(Albert et al., 2010, Heo et al., 2019a, Rogers et al., 2002)

Feeling depressed	17	(Bennett et al., 2000, Checa et al., 2020, Flint et al., 2017, Heo et al., 2019a, Kimani et al., 2018, Lum et al., 2016, Nguyen et al., 2022, Opasich et al., 2008, Oriani et al., 2019, Reeder et al., 2015, Salyer et al., 2019, Seckin et al., 2022, Shah et al., 2013, Todero et al., 2002, Walsh et al., 2018, Yu et al., 2016, McHorney et al., 2021)
Palpitations (irregular/ fluttering/ faster heartbeat)	21	(Alkan and Nural, 2017, Altice and Madigan, 2012, Bennett et al., 2000, Darling et al., 2013, Friedman and Quinn, 2008, Gallagher et al., 2012, Graven et al., 2020, Haedtke et al., 2019, Hedemalm et al., 2008, Heo et al., 2019a, Lin et al., 2021, Luo et al., 2020, McHorney et al., 2021, Oguz and Enç, 2008, Okada et al., 2019, Patel et al., 2007, Rodriguez et al., 2008, Todero et al., 2002, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
Dizziness/ light-headedness/ giddiness	24	(Albert et al., 2010, Alkan and Nural, 2017, Bekelman et al., 2007, Blinderman et al., 2008, Friedman and Quinn, 2008, Flint et al., 2017, Graven et al., 2020, Haedtke et al., 2019, Heo et al., 2019b, Heo et al., 2020, Heo et al., 2019a, Lin et al., 2021, Lokker et al., 2016, Lum et al., 2016, McHorney et al., 2021, Okada et al., 2019, Reeder et al., 2015, Rodriguez et al., 2008, Rogers et al., 2002, Schumacher et al., 2018, Walsh et al., 2018, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
Syncope (passing out/fainting)	3	(Lin et al., 2021, McHorney et al., 2021, Patel et al., 2007)
Bendopnea	1	(Bennett et al., 2000)
	Non-ESC symptoms (Other Symptoms)	
Lack of energy	11	(Alkan and Nural, 2017, Bekelman et al., 2007, Blinderman et al., 2008, Fischer and Bekelman, 2017, Gallagher et al., 2012, Haedtke et al., 2019, Lokker et al., 2016, Song et al., 2010, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
Weakness	5	(Bennett et al., 2000, Friedman and Quinn, 2008, McHorney et al., 2021, Rodriguez et al., 2008, Schumacher et al., 2018)
Need more rest during the day	3	(Altice and Madigan, 2012, Gallagher et al., 2012, Luo et al., 2020)
Excessive weight gain	15	(Alkan and Nural, 2017, Friedman and Quinn, 2008, Gallagher et al., 2012, Haedtke et al., 2019, Jurgens et al., 2009, Lin et al., 2021, Luo et al., 2020, Okada et al., 2019, Patel et al., 2007, Reeder et al., 2015, Rodriguez et al., 2008, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005, Altice and Madigan, 2012)
Chest pain/ discomfort	32	(Albert et al., 2010, Alkan and Nural, 2017, Altice and Madigan, 2012, Bennett et al., 2000, Blinderman et al., 2008, Checa et al., 2020, Darling et al., 2013, Friedman and Quinn, 2008, Gallagher et al., 2012, Graven et al., 2020, Haedtke et al., 2019, Heo et al., 2019b, Heo et al., 2020, Heo et al., 2019a, Jurgens et al., 2009, Lin et al., 2021, Lum et al., 2016, Luo et al., 2020, McHorney et al., 2021, Okada et al., 2019, Opasich et al., 2008, Patel et al., 2007, Rodriguez et al., 2008, Rogers et al., 2002, Salyer et al., 2019, Son

			and Won, 2018, Todero et al., 2002, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005, Reeder et al., 2015, Flint et al., 2017)
Pain	**General**	14	(Abshire et al., 2015, Bekelman et al., 2007, Bennett et al., 2000, Fischer and Bekelman, 2017, Hedemalm et al., 2008, Lokker et al., 2016, Nguyen et al., 2022, Oriani et al., 2019, Salyer et al., 2019, Seckin et al., 2022, Shah et al., 2013, Yu et al., 2016, Patel et al., 2007, Opasich et al., 2008)
	Other bodily pain (not chest pain)	13	(Alkan and Nural, 2017, Blinderman et al., 2008, Darling et al., 2013, Flint et al., 2017, Haedtke et al., 2019, Lum et al., 2016, McHorney et al., 2021, Patel et al., 2007, Rodriguez et al., 2008, Rogers et al., 2002, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
Difficulty sleeping (including due to orthopnoea and other sleeping problems)		26	(Alkan and Nural, 2017, Bennett et al., 2000, Bekelman et al., 2007, Blinderman et al., 2008, Fischer and Bekelman, 2017, Graven et al., 2020, Haedtke et al., 2019, Hedemalm et al., 2008, Heo et al., 2019b, Heo et al., 2020, Lin et al., 2021, Lokker et al., 2016, McHorney et al., 2021, Oriani et al., 2019, Patel et al., 2007, Reeder et al., 2015, Rogers et al., 2002, Seckin et al., 2022, Schumacher et al., 2018, Son and Won, 2018, Song et al., 2010, Todero et al., 2002, Walsh et al., 2018, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
Feeling drowsy		15	(Alkan and Nural, 2017, Bekelman et al., 2007, Blinderman et al., 2008, Fischer and Bekelman, 2017, Haedtke et al., 2019, Lokker et al., 2016, Nguyen et al., 2022, Opasich et al., 2008, Oriani et al., 2019, Salyer et al., 2019, Shah et al., 2013, Wang et al., 2020b, Wilson and McMillan, 2013, Yu et al., 2016, Zambroski et al., 2005)
Difficulty concentrating/ forgetfulness		15	(Alkan and Nural, 2017, Bekelman et al., 2007, Bennett et al., 2000, Blinderman et al., 2008, Graven et al., 2020, Haedtke et al., 2019, Lin et al., 2021, Lokker et al., 2016, Oriani et al., 2019, Reeder et al., 2015, Rodriguez et al., 2008, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005, McHorney et al., 2021)
Loss of balance/ falling		2	(Bennett et al., 2000, Hedemalm et al., 2008)
Gastrointestinal	**Changes in the way food tastes**	9	(Alkan and Nural, 2017, Bekelman et al., 2007, Blinderman et al., 2008, Haedtke et al., 2019, Lokker et al., 2016, Reeder et al., 2015, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
	Nausea/ vomiting/ indigestion	26	(Albert et al., 2010, Altice and Madigan, 2012, Alkan and Nural, 2017, Bekelman et al., 2007, Bennett et al., 2000, Blinderman et al., 2008, Darling et al., 2013, Friedman and Quinn, 2008, Fischer and Bekelman, 2017, Flint et al., 2017, Gallagher et al., 2012, Haedtke et al., 2019, Lin et al., 2021, Lokker et al., 2016, Lum et al., 2016, Nguyen et al., 2022, Oguz and Enç, 2008, Opasich et al., 2008, Oriani et al., 2019, Reeder et al., 2015, Shah et al., 2013, Son and Won, 2018, Wang et al., 2020b, Wilson and McMillan, 2013, Yu et al., 2016, Zambroski et al., 2005)
	Weight loss	9	(Alkan and Nural, 2017, Bekelman et al., 2007, Bennett et al., 2000, Blinderman et al., 2008, Haedtke et al., 2019, Lokker et al., 2016, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)

Constipation	**14**	(Alkan and Nural, 2017, Bekelman et al., 2007, Blinderman et al., 2008, Fischer and Bekelman, 2017, Flint et al., 2017, Haedtke et al., 2019, Hedemalm et al., 2008, Lokker et al., 2016, Lum et al., 2016, Reeder et al., 2015, Todero et al., 2002, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
Diarrhoea	**9**	(Alkan and Nural, 2017, Bekelman et al., 2007, Blinderman et al., 2008, Haedtke et al., 2019, Lokker et al., 2016, Reeder et al., 2015, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
Food cravings/ eating more	**2**	(Bennett et al., 2000, Salyer et al., 2019)
Dry mouth	**11**	(Alkan and Nural, 2017, Bekelman et al., 2007, Blinderman et al., 2008, Fischer and Bekelman, 2017, Flint et al., 2017, Haedtke et al., 2019, Lokker et al., 2016, Lum et al., 2016, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
Mouth sores	**3**	(Bekelman et al., 2007, Blinderman et al., 2008, Lokker et al., 2016)
Difficulty swallowing	**3**	(Bekelman et al., 2007, Blinderman et al., 2008, Lokker et al., 2016)
Sweats	**9**	(Alkan and Nural, 2017, Bekelman et al., 2007, Blinderman et al., 2008, Haedtke et al., 2019, Lokker et al., 2016, McHorney et al., 2021, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
Itching	**10**	(Alkan and Nural, 2017, Bekelman et al., 2007, Bennett et al., 2000, Blinderman et al., 2008, Haedtke et al., 2019, Lokker et al., 2016, Oriani et al., 2019, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
Problem with sexual interest/ activity	**9**	(Alkan and Nural, 2017, Bekelman et al., 2007, Bennett et al., 2000, Blinderman et al., 2008, Fischer and Bekelman, 2017, Haedtke et al., 2019, Lokker et al., 2016, Wilson and McMillan, 2013, Zambroski et al., 2005)
Numbness or tingling in hands and feet	**12**	(Alkan and Nural, 2017, Bekelman et al., 2007, Blinderman et al., 2008, Fischer and Bekelman, 2017, Flint et al., 2017, Haedtke et al., 2019, Lokker et al., 2016, Lum et al., 2016, McHorney et al., 2021, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
Problem with urination	**11**	(Alkan and Nural, 2017, Altice and Madigan, 2012, Bekelman et al., 2007, Blinderman et al., 2008, Haedtke et al., 2019, Lokker et al., 2016, Luo et al., 2020, Oguz and Enç, 2008, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
Muscle spasm/ cramps	**2**	(Bennett et al., 2000, McHorney et al., 2021)
Hair loss	**4**	(Bekelman et al., 2007, Blinderman et al., 2008, Lokker et al., 2016, McHorney et al., 2021)
Changes in skin	**3**	(Bekelman et al., 2007, Blinderman et al., 2008, Lokker et al., 2016)

Visual disturbance		1	(Bennett et al., 2000)
Walking problems		3	(Oriani et al., 2019, Patel et al., 2007, Seckin et al., 2022)
Feeling anxious/ nervous		19	(Alkan and Nural, 2017, Blinderman et al., 2008, Checa et al., 2020, Darling et al., 2013, Haedtke et al., 2019, Kimani et al., 2018, Lokker et al., 2016, Nguyen et al., 2022, Opasich et al., 2008, Oriani et al., 2019, Patel et al., 2007, Reeder et al., 2015, Salyer et al., 2019, Shah et al., 2013, Todero et al., 2002, Wang et al., 2020b, Wilson and McMillan, 2013, Yu et al., 2016, Zambroski et al., 2005)
Feeling isolated & lonely		4	(Aldred et al., 2005, Checa et al., 2020, Oriani et al., 2019, Wilson and McMillan, 2013)
Fear		7	(Abshire et al., 2015, Bennett et al., 2000, Blinderman et al., 2008, Checa et al., 2020, Hedemalm et al., 2008, Heo et al., 2019a, Patel et al., 2007)
Worrying		11	(Bennett et al., 2000, Alkan and Nural, 2017, Blinderman et al., 2008, Checa et al., 2020, Haedtke et al., 2019, Heo et al., 2019a, Kimani et al., 2018, Lokker et al., 2016, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
Negative emotions	**Feeling sad**	8	(Alkan and Nural, 2017, Blinderman et al., 2008, Checa et al., 2020, Haedtke et al., 2019, Lokker et al., 2016, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
	Feeling irritable	7	(Alkan and Nural, 2017, Blinderman et al., 2008, Haedtke et al., 2019, Lokker et al., 2016, Wang et al., 2020b, Wilson and McMillan, 2013, Zambroski et al., 2005)
	Feeling guilt, gloomy, unworthy, stigma, sorry etc.	13	(Abshire et al., 2015, Aldred et al., 2005, Bekelman et al., 2007, Blinderman et al., 2008, Darling et al., 2013, Hedemalm et al., 2008, Heo et al., 2019a, Kimani et al., 2018, Lokker et al., 2016, Patel et al., 2007, Rogers et al., 2002, Walsh et al., 2018, Wilson and McMillan, 2013)

Table 5-4: The percentages of ESC Typical and less typical, and (most-observed) non-ESC symptoms in the included 49 studies

Symptoms			N of studies	Total Sample	Male sex, n (%)	Mean age	Participants with symptom, n (%)	Min-Max %
ESC Guidelines FOR HF (2021)	Typical	Breathlessness	36	6265	3654 (58%)	68*	5233 (83%)	26%–100%
		Orthopnoea	22	5260	2987 (57%)	69	2631 (50%)	12%–81%
		Paroxysmal nocturnal dyspnoea	17	4978	2820 (57%)	70	1817 (36%)	9%–82%
		Reduced exercise tolerance**	11	1720	1012 (59%)	70	1228 (71%)	10%–93%
		Fatigue/Tiredness	29	5105	2823 (55%)	69	3527 (69%)	14%–94%
		Ankle swelling#	35	6534	3661 (56%)	69*	3462 (53%)	3%–81%
	Less typical	Nocturnal cough	28	6209	3928 (63%)	69*	2593 (42%)	1%–79%
		Wheezing	3	442	283 (64%)	62	63 (14%)	3%–19%
		Bloated feeling	15	3567	2055 (58%)	69*	1050 (29%)	2%–60%
		Loss of appetite	28	5491	3074 (56%)	69*	2092 (38%)	2%–86%
		Confusion	2	303	200 (66%)	62	74 (24%)	22%–44%
		Feeling depressed	12	2319	1612 (69%)	69	1137 (49%)	1%–69%
		Palpitation	20	4123	2354 (57%)	70	1169 (28%)	6%–78%
		Dizziness~	22	3578	2391 (67%)	66*	1360 (38%)	12%–80%
		Syncope	2	248	123 (49%)	61	21 (8%)	5%–10%
		Bendopnea	N/A	N/A	N/A	N/A	N/A	N/A
MOST OBSERVED NON-ESC SYMPTOMS		Chest pain	26	5550	3435 (62%)	69	2010 (36%)	15%–75%
		Difficulty sleeping	22	3850	2263 (59%)	68*	2026 (53%)	1%–78%
		Nausea	20	4953	3111 (63%)	69*	1303 (26%)	17%–55%
		Vomiting	8	1251	755 (60%)	66*	155 (12%)	7%–26%
		Difficulty concentrating	12	1910	1130 (59%)	66*	691 (36%)	2%–67%
		Feeling drowsy	14	2266	1395 (61%)	68*	1198 (53%)	1%–93%
		General pain	13	2118	1267 (60%)	69*	1279 (60%)	10%–91%
		Feeling anxious/nervous	17	3517	1985 (56%)	70	1546 (44%)	8%–92%
		Weight gain	14	2137	1253 (59%)	70	589 (27%)	7%–41%
		Lack of energy	11	2228	1390 (62%)	67*	1613 (72%)	24%–93%
		Constipation	13	2477	1820 (73%)	67*	868 (35%)	2%–72%
		Numbness/tingling in hands and feet	12	2397	1775 (74%)	66*	1353 (56%)	2%–86%
		Problem with urination	11	1598	955 (60%)	64*	650 (40%)	17%–88%
		Dry mouth	11	2333	1746 (75%)	66*	1369 (59%)	36%–87%
		Negative emotions	9	2208	1235 (55%)	68	554 (25%)	10%–90%

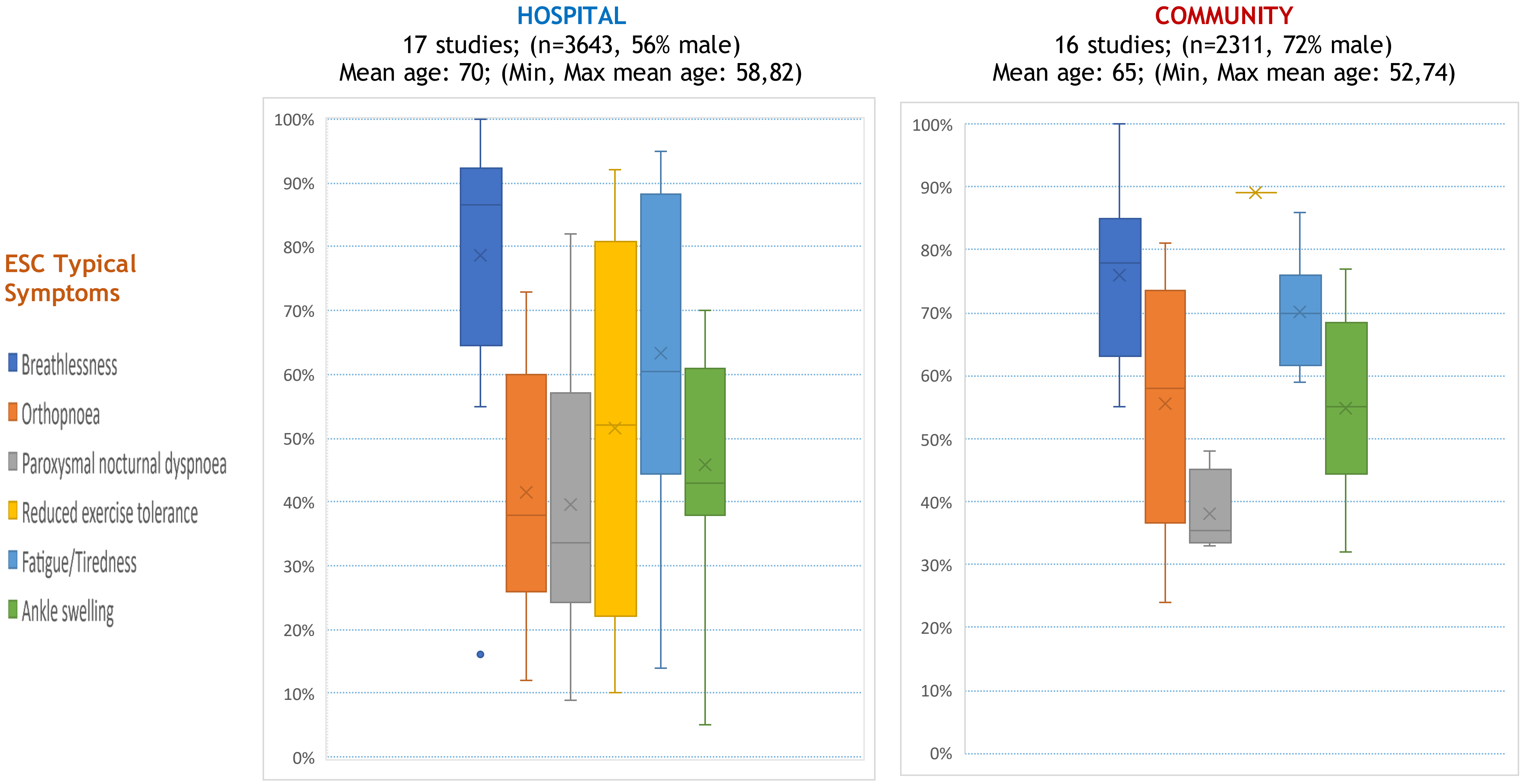
*1 study did not provide mean age; N/A, not applicable; **including the breathlessness with activity/walking; #Ankle swelling (including Swelling of lower extremities/general oedema); ~including light-headedness/giddiness.

5.5.3. Non-ESC symptoms

The rest of the symptoms (n=37) were non-ESC symptoms (**Table 5-3**). Nine symptoms were among the most observed symptoms, including: chest pain/discomfort (32/49); difficulty sleeping (26/49); nausea/vomiting/indigestion (26/49); feeling anxious/nervous (19/49); feeling drowsy (15/49); pain including other bodily pain (13/49; potentially also from other sources) and general pain (12/49); weight gain (15/49); difficulty concentrating/forgetfulness (15/49; potentially also related to the age of the population); and constipation (14/49). Among these symptoms (**Table 5-4**), the most common symptoms were lack of energy (72% of 2228 participants of 11 studies); general pain (60% of 2118 participants of 13 studies); dry mouth (59% of 2333 participants of 11 studies); feeling drowsy (53% of 2266 participants of 14 studies); numbness/tingling in hands and feet (56% of 2397 participants of 12 studies); difficulty sleeping (53% of 3850 participants of 22 studies); and feeling anxious/nervous (44% of 3517 participants of 17 studies).

5.6. ESC typical and less typical symptoms in hospital and community

Figure 5-5 and **Figure 5-6** show boxplots of the percentage distribution of individual studies for ESC typical and less typical symptoms in hospital (n=3643, 56% male with 70 mean age (range 58–82) in 17 studies) and community (n=2311, 72% male with 65 mean age (range 52–74) in 16 studies) settings. Among ESC typical symptoms, more paroxysmal nocturnal dyspnoea was observed in the hospital setting. Among ESC less typical symptoms, cough, palpitation, and dizziness were observed more in community settings, whereas wheezing was observed more in hospital settings.

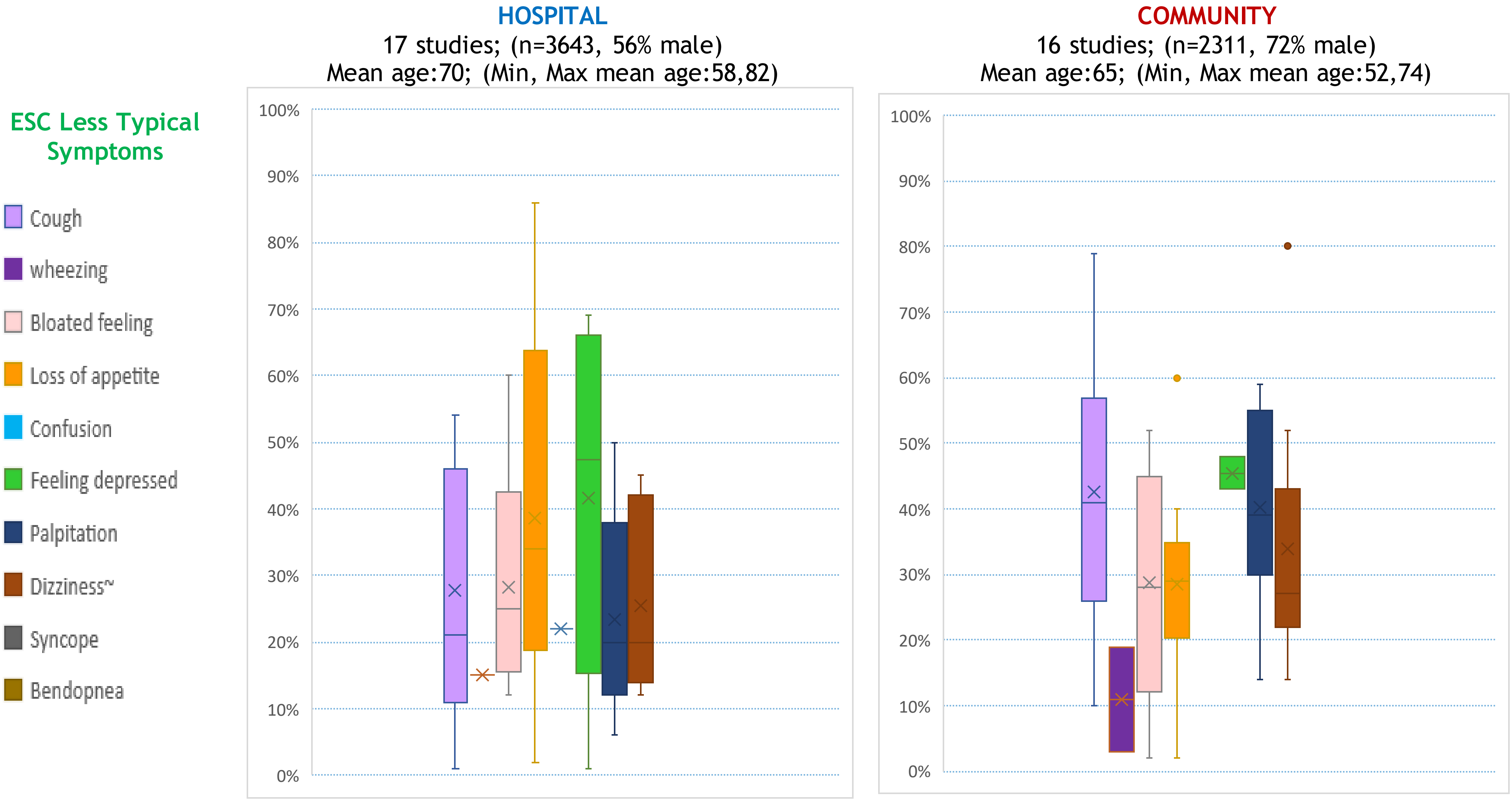


HOSPITAL
17 studies; (n=3643, 56% male)
Mean age: 70; (Min, Max mean age: 58,82)

COMMUNITY
16 studies; (n=2311, 72% male)
Mean age: 65; (Min, Max mean age: 52,74)

ESC Typical Symptoms

Figure 5-5: The percentage distribution of participants with ESC typical symptoms between hospital and community settings



HOSPITAL
17 studies; (n=3643, 56% male)
Mean age:70; (Min, Max mean age:58,82)

COMMUNITY
16 studies; (n=2311, 72% male)
Mean age:65; (Min, Max mean age:52,74)

Figure 5-6: The percentage distribution of participants with ESC less typical symptoms between hospital and community settings

5.7. ESC typical and less typical symptoms in <65 years old and ≥65 years old

Figure 5-7 and **Figure 5-8** show a boxplot of the percentage distribution of each study's findings for ESC typical and less typical symptoms between <65 years old (n=1761, 59% males with 60 mean age (range 52–63) in 14 studies) and ≥65 years old (n=6309, 62% males with 71 mean age (range 65–82) in 28 studies). More orthopnoea and ankle swelling were observed in those <65 years of age. Cough, dizziness, bloated feeling, and feeling depressed were more observed at ≥65 years, and palpitation at <65 years old age.

5.8. ESC typical and less typical symptoms in men and women

Table 5-5 indicates the percentages of each study's findings for ESC typical and less typical symptoms between men (n=619 with 68 mean age (range 64–67) in three studies) and women (n=342 with 72 mean age (range 62–76) in three studies), for some ESC typical and less typical symptoms. Among ESC typical symptoms, there was no difference between men and women in breathlessness and fatigue/tiredness. However, three ESC typical symptoms showed differences between men and women of 10% or more: orthopnoea (53% of 372 men versus 64% of 275 women); paroxysmal nocturnal dyspnoea (42% of 302 men versus 72% of 226 women); and ankle swelling (53% of 372 men versus 66% of 275 women).

No significant differences were observed between men and women in the ESC less typical symptoms cough (47% of 549 men versus 43% of 293 women) and dizziness (37% of 70 men versus 37% of 49 women). Other ESC typical and less typical symptoms are not observed in the studies regarding sex-related differences.

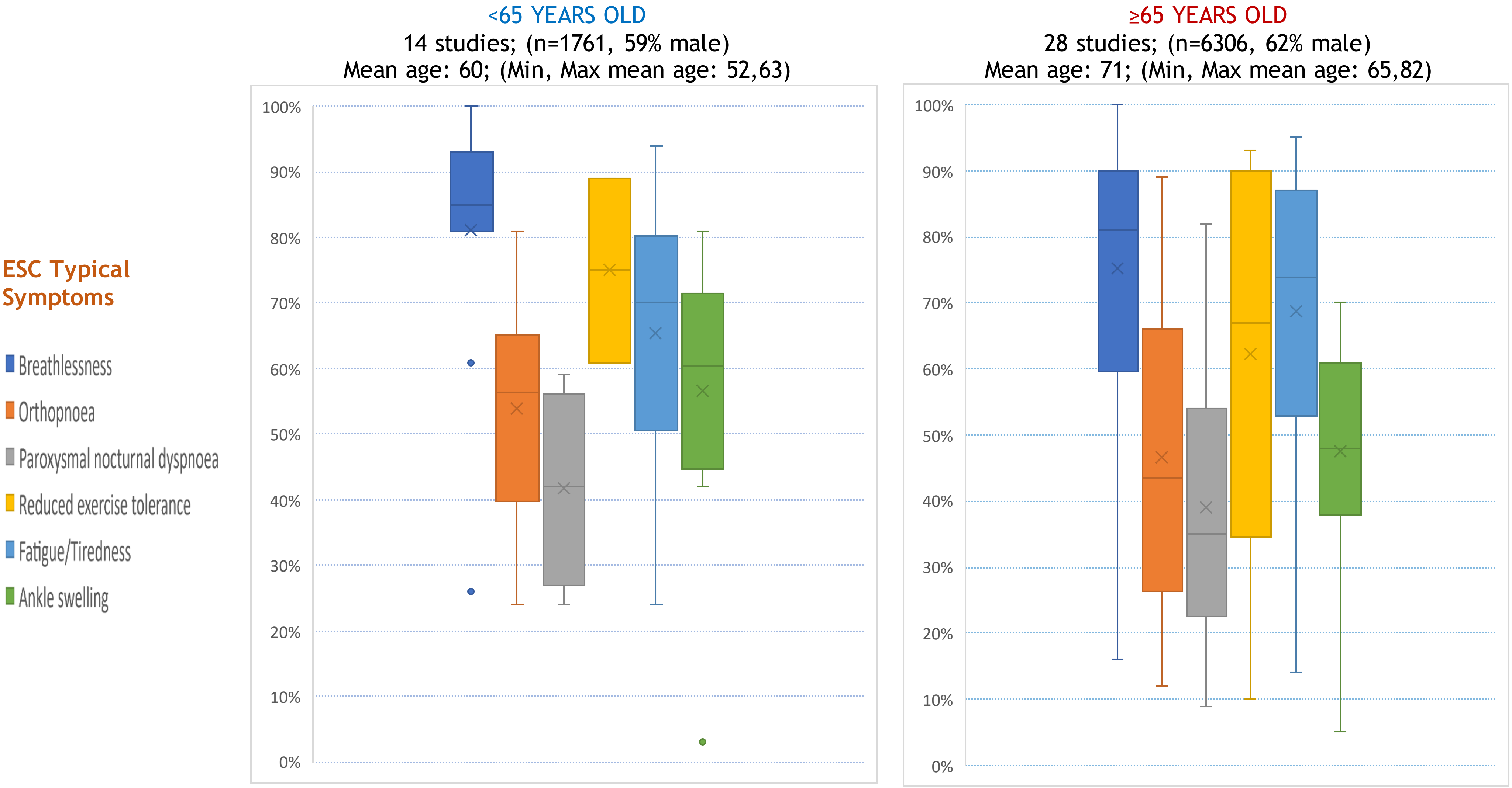


Figure 5-7: The percentage distribution of participants with ESC typical symptoms between <65 years old and ≥65 years old

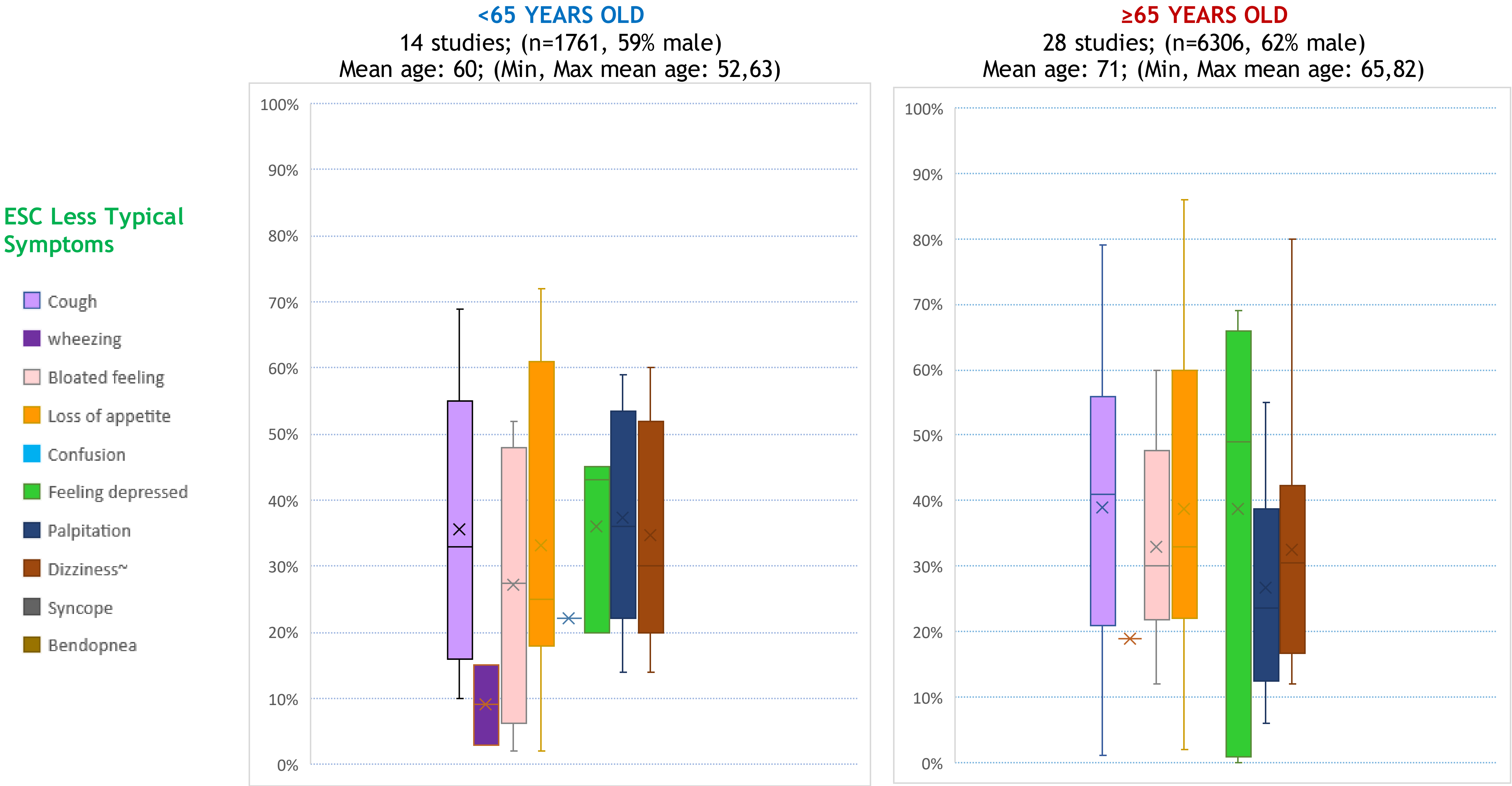


Figure 5-8: The percentage distribution of participants with ESC less typical symptoms between <65 years old and ≥65 years old

Table 5-5: The percentage distribution of participants with ESC typical and less typical symptoms between men and women

			MEN **3 studies; (n=619, 100% men)** **Mean age: 68; (min, max mean age: 64,71)**				**WOMEN** **3 studies; (n=342, 100% women)** **Mean age: 72; (min, max mean age: 62,76)**			
Symptoms			**Number of studies**	**Total sample**	**Participants with symptom, n (%)**	**Min-Max % between studies**	**Number of studies**	**Total sample**	**Participants with symptom, n (%)**	**Min-Max % between studies**
ESC Guidelines FOR HF (2021)	**Typical**	*Breathlessness*	3	619	530 (86%)	37%–92%	3	342	300 (88%)	53%–95%
		Orthopnoea	2	372	199 (53%)	21%–61%	2	275	177 (64%)	29%–72%
		Paroxysmal nocturnal dyspnoea	1	302	128 (42%)	42%	1	226	114 (72%)	72%
		Fatigue/Tiredness	2	372	313 (84%)	54%–91%	2	275	250 (90%)	69%–95%
		Ankle swelling[#]	2	372	193 (52%)	13%–61%	2	275	183 (66%)	39%–72%
	Less typical	*Cough*	2	549	257 (47%)	39%–56%	2	293	126 (43%)	39%–56%
		Dizziness	1	70	26 (37%)	37%	1	49	18 (37%)	37%

There was no observed percentage data for Reduced exercise tolerance, Wheezing, Bloated feeling, Palpitation, Loos of appetite, Confusion, Feeling depressed, Syncope, and Bendopnea in both sexes separately.

[#] *Including general oedema*

5.9. Strengths and limitations

This is the first systematic review to examine the self-reported ESC and non-ESC symptom experiences of the heart failure population and their influencing factors including setting, age, and sex, using a comprehensive PRISMA and six databases' search strategy methods. The symptoms represented a population with heart failure in 14 different countries. Typical and less typical symptom experiences of people with heart failure are comprehensively grouped in the review. People with heart failure and their informal caregivers' perspectives were included together to understand the full spectrum of symptom experiences of patients. PROSPERO registration was used for the protocol publication.

This review has several limitations. The major limitation of this review is cultural contexts and different healthcare systems; more than half of the included studies were conducted in the USA. Therefore, the results might not be applicable to other countries with advanced symptomology perspectives on heart failure. The second limitation is the mean age range of the participants included in the studies. In this review, there is no data to illustrate the younger patients' symptom perceptions of heart failure. Therefore, these results might not be generalisable to a younger age group, even if heart failure syndrome mostly affects older individuals. The female perspective is also limited in the studies, given that, in many studies, most participants were male. Although subjective symptom experiences are affected by clinical differences, there is a limitation for participants with HFpEF in the included studies.

The next limitation is the variety of outcomes measured in the symptoms, which limits comparability and the possibility of synthesising the results. Also, many studies mentioned typical symptoms of heart failure such as breathlessness, fatigue, ankle swelling, orthopnoea etc. Therefore, our results might not be sufficient to describe the less typical and non-ESC symptom perception of people with heart failure. In addition to this, many studies used standard heart failure measurement instruments such as the Memorial Symptom Assessment Scale-Heart Failure, Heart Failure Symptom Survey, and Edmonton Symptom Assessment Scale. These standard measures focus on typical heart failure symptoms rather than less typical and non-ESC symptoms. The addition of qualitative studies and the qualitative findings from mixed-method studies can help to reveal other symptoms and reduce this limitation. There is a limitation with respect to disease characteristics (ejection fraction range, and comorbid conditions) in the included studies. These are some of the effective concepts on symptom perception in heart failure. However, we are not able to analyse them to generalise the target population (people with heart failure). Another limitation is that of language: only papers written in English were selected for this MMSR. This means that relevant articles that are not published in English would have been omitted. This also affects the understanding of other cultures, insofar as the outcomes might be narrow or not culturally inclusive of symptom perceptions for people with heart failure.

5.10. Conclusion

This review highlighted that people with heart failure experienced many different symptoms (including ESC (typical/less typical) and non-ESC symptoms). Some non-ESC symptoms were more common than ESC typical/less typical symptoms. This review also highlighted that symptoms associated with heart failure are more likely to be influenced by individual differences. Further research is urgently needed to investigate different factors (especially for women, and different phases of heart failure such as palliative and end of life care)-related symptom experiences, including ESC and non-ESC symptoms associated with heart failure. (Please see **Box 5-1** for a summary of the research in context.)

5.11. Chapter summary: the perceived gap in the research

This chapter provided the results of a mixed-methods systematic review examining the full spectrum of symptoms and symptom experiences with reference to setting, age, and sex. The novel contributions of this review were:

- 37 non-ESC symptoms (not listed in the ESC Guidelines for heart failure) were identified.
- Some non-ESC symptoms were more common than some ESC (typical/less typical) symptoms.
- ESC typical and less typical symptoms were different in terms of setting and age.
- Symptom experiences of women were missing in the literature.
- Symptom experiences of individuals with HFpEF and HFmrEF were missing in the literature.

The main implications for the subsequent studies of this PhD research were that further studies are needed to understand the symptoms (regarding LVEF) of the heart failure sub-cohort comprised of women. The next chapter will provide the findings of the secondary data analysis study, investigating sex-stratified differences in symptoms.

Box 5-1: Mixed-methods systematic review research in context

Evidence before this study

Individuals living with heart failure often experience a wide range of symptoms, but current clinical guidelines tend to focus on a limited subset of these symptoms, failing to comprehensively assess and monitor the full spectrum of symptoms. As a result, the true scope of symptoms experienced in the context of heart failure is not adequately acknowledged.

The primary aim of this review was to systematically examine the full spectrum of heart failure symptoms, as reflected by the ESC heart failure guidelines, which classify symptoms as either "typical" or "less typical," while also considering symptoms that may not be explicitly listed in the guidelines. Additionally, the study investigated how these symptoms might vary according to factors such as the settings (hospital versus out-patient), age (younger versus older), and biological sex (women versus men).

A systematic search was conducted across six electronic databases, employing relevant search terms to uncover the full range of symptoms experienced by individuals with heart failure, as indicated by the ESC Guidelines for heart failure and other symptoms. To be eligible for inclusion, studies needed to involve adults diagnosed with heart failure or their informal caregivers, and must have reported on more than five distinct symptoms. We assessed the risk of bias by utilising the JBI critical appraisal tools.

Contribution of this study

To the best of our knowledge, this systematic review represents the first effort to comprehensively investigate the full spectrum of symptoms in the heart failure population. Our findings have revealed that individuals afflicted with heart failure commonly manifest a greater number of symptoms than those listed in the ESC clinical management guidelines. Notably, we have identified an additional 37 symptoms (e.g. chest pain/discomfort, difficulty sleeping, lack of energy, general pain, and dry mouth) beyond the scope of the ESC Guidelines. Among these symptoms, shortness of breath and fatigue are the most commonly observed symptoms. Some non-ESC symptoms demonstrated a consistent and higher presence across diverse study populations. Additionally, this review revealed disparities in symptom prevalence across age and care settings. However, it is essential to acknowledge a limitation in our analysis – due to the paucity of available data on female perspectives, we were unable to draw substantive conclusions regarding sex-based differences in symptoms.

Implications of all the available evidence

The findings of our study strongly demonstrate the need for enhanced awareness and acknowledgement of the full spectrum of symptoms experienced by individuals living with heart failure, whether within or outside hospital settings. More symptoms were identified than those listed in the ESC Guidelines. Some of these non-ESC symptoms were more commonly observed than some ESC symptoms. Furthermore, this review revealed distinctions in symptom prevalence with respect to clinical settings and age groups, underscoring the importance of tailoring symptom management strategies to specific contexts and characteristics. However, within the existing literature, there is a notable gap regarding the symptom experiences of women, as well as those individuals living with HFmrEF and HFpEF, and those of advanced age.

From a research standpoint, there is an urgent need to initiate investigations aimed at identifying the symptom experiences of women, diverse heart failure subtypes, and individuals of advanced age and various phases of heart failure. Such inquiries are crucial for advancing our understanding of heart failure and ensuring clinical management guidelines fit with the diverse symptom profiles experienced within this patient population. The acquisition of such data will serve to enhance our understanding of the symptom profiles among individuals, thereby facilitating the refinement of care strategies aimed at alleviating the burden of symptoms in heart failure management.

Chapter Six - Findings from a cohort of people hospitalised with heart failure in Australia

6.1. Introduction

In this chapter, sex-stratified differences in symptoms are examined. Based on the limitations of the systematic review findings (Chapter 5) due to the paucity of women in studies and different heart failure subtypes, the researchers were unable to identify differences in symptoms in men and women with heart failure. Therefore, this chapter provides a comprehensive exploration of symptom differences and symptom changes over one year according to the phenotypes of heart failure in men and women separately. In this chapter, two main factors were examined; biological sex (as a person factor-biological), and the phenotypes of heart failure based on LVEF (as a clinical factor).

The primary aim of this study was to examine how heart failure symptoms change over one year following a hospital admission according to sex and underlying phenotypes of heart failure based on LVEF. This study was published in 2022 in *European Journal of Cardiovascular Nursing* (**Appendix 9**) (Seckin et al., 2022). There are two main research questions of secondary data analysis: ***How do symptoms of heart failure differ between men and women, with respect to biological sex and heart failure types? and How do these symptoms change in the 12 months following a hospital admission in men and women, with respect to heart failure subtypes?***

As described on page 69-76, the methodology involved a secondary analysis of data obtained from hospitalised men and women diagnosed with heart failure who participated in the WHICH?II Trial in Australia. KCCQ symptom scores at baseline and 12-month follow-up were analysed along with individual symptom experiences. All statistical analyses were performed using the SPSS software programme between October 2021 and May 2022. A statistical analysis model was chosen in accordance with the research purpose and question.

Table 6-1: Baseline characteristics in men and women from Seckin et al. (2022)

Variables		Total (n=528)	Men (n=302)	Women (n=226)	Effect size	P-value
Socio-demographic profile						
Age, mean±SD (years)		73.05±11.98	70.88±12.03	76.60±11.06	0.065	**<0.0001**
Living alone, n (%)		228 (43.2)	105 (34.8)	123 (54.4)	0.196	**<0.0001**
Married – living with partner, n (%)		253 (47.9)	181 (59.9)	72 (31.9)	0.414	**<0.0001**
European/Caucasian ethnicity, n (%)		490 (92.8)	275 (91.1)	215 (95.1)	0.105	0.558
<12 years education, n (%)		454 (86.0)	253 (83.7)	201 (89.0)	0.252	**<0.0001**
English not first language, n (%)		98 (18.6)	48 (15.9)	50 (22.1)	0.079	0.068
Retired, n (%)		440 (83.3)	237 (78.5)	203 (89.8)	0.151	**<0.0001**
Risk profile						
BMI, mean±SD (kg/m^2)		30.00±6.66	29.51±5.62	30.81±8.03	0.004	0.145
>2.5-hour physical activity, n (%)		181 (34.3)	131 (22.1)	131 (43.4)	0.222	**<0.0001**
Non-smoker, n (%)		208 (39.4)	82 (27.2)	126 (55.8)	0.293	**<0.0001**
Diabetes, n (%)		235 (44.5)	144 (47.7)	91 (40.3)	0.074	0.090
Hypertension, n (%)		400 (75.8)	217 (71.9)	183 (81.0)	0.105	**0.016**
Heart failure profile						
HF duration, n(%)	0 to 2 years	224 (42.4)	118 (39.1)	106 (46.9)	0.079	0.195
	2 to 5 years	163 (30.9)	98 (32.5)	65 (28.8)		
	≥5 years	141 (26.7)	86 (28.5)	55 (24.3)		
LVEF, mean±SD (%)*		38.50±13.84	35.51±13.16	43.40±13.56	0.082	**<0.0001**
HF subtypes	HFrEF	**244 (46.2)**	**175 (57.9)**	**69 (30.5)**	**0.309**	**<0.0001**
	HFmrEF	**108 (20.5)**	**62 (20.5)**	**46 (20.4)**		
	HFpEF	**176 (33.3)**	**65 (21.5)**	**111 (49.1)**		
NYHA functional class III/IV, n (%)		109 (20.7)	57 (18.9)	52 (23.0)	0.058	0.623
Elevated BNP, n (%)		232 (45.1)	139 (47.3)	93 (42.3)	0.050	0.259
Raised JVP, n (%)		253 (48.1)	147 (49.0)	106 (46.9)	0.021	0.634
Prior HF admission (12 months), n (%)		299 (56.6)	167 (55.30)	132 (58.4)	0.031	0.476
Clinical profile						
Acute pulmonary oedema, n (%)		164 (31.1)	77 (25.5)	87 (38.7)	0.141	**0.001**
Atrial fibrillation, n (%)		279 (52.8)	162 (53.9)	117 (51.8)	0.019	0.670
Sleep Apnoea, n (%)		101 (19.1)	70 (23.2)	31 (13.7)	0.119	**0.006**
Heart rhythm disturbance, n (%)		96 (18.2)	75 (24.8)	21 (9.3)	0.199	**<0.0001**
Coronary artery disease, n (%)		312 (59.1)	197 (65.2)	115 (50.9)	0.144	**0.001**
Chronic pulmonary disease, n (%)		143 (27.1)	84 (27.8)	59 (26.1)	0.019	0.662
Cerebrovascular disease, n (%)		111 (21.0)	68 (22.5)	43 (19.0)	0.042	0.330
Cancer or tumour, n (%)		87 (16.5)	45 (14.9)	42 (18.6)	0.049	0.259
Charlson Comorbidity Score, mean±SD		6.69±2.39	6.48±2.48	7.03±2.19	0.011	**0.014**
Poor sleeping quality, n (%)		168 (31.8)	90 (29.8)	78 (34.5)	0.063	0.723
Acute pulmonary oedema, n (%)		343 (65.3)	190 (63.5)	153 (67.7)	0.043	0.322
KCCQ scores, mean±SD	Total symptom	45.10±24.72	48.08±24.99	40.22±23.56	0.020	**0.001**
	Symptom frequency	43.01±25.60	45.35±26.01	39.18±24.50	0.011	**0.016**
	Symptom burden	47.19±26.62	50.81±26.76	41.26±25.38	0.025	**<0.0001**
	Symptom stability	45.71±38.29	46.27±37.99	44.79±38.87	0.000	0.638
	Quality of life	38.09±22.63	40.18±23.10	34.67±21.47	0.009	**0.029**
EQ-5D-5L, mean±SD		0.68±0.20	0.71±0.19	0.64±0.20	0.030	**<0.0001**

Quality of life was assessed by KCCQ and EQ-5D-5L scales; depressive symptoms were calculated using a two-item ARROL tool; *n=178 for women and n=279 for men; HF=heart failure; BMI=Body mass index; LVEF=left ventricular ejection fraction; HFrEF=Heart failure with reduced ejection fraction (LVEF ≤40%);HFmrEF=Heart failure with mildly-reduced ejection fraction (LVEF 41%–49%); HFpEF=Heart failure with preserved ejection fraction (LVEF ≥50%); NYHA=New York Heart Association; BNP=b-type natriuretic peptide; elevated b-type natriuretic peptide (BNP) >6000pg/ml; JVP=jugular venous pressure; KCCQ=Kansan City Cardiomyopathy Questionnaire; EQ-5D-5L scale=EuroQol 5-level 5-dimensional scale; SD=standard deviation. ANOVA for continuous variables and chi-square (X^2) tests for categorical variables were used for a comparison between men and women.

6.2. A discussion around baseline characteristics and symptoms presence changes over one year in men and women

At baseline (**Table 6-1**), women (n=226) with heart failure differed from men (n=302) (who completed 12-month follow-up) in terms of 20 characteristics: they were older; less likely to be married and have a history of smoking; more likely to live alone, and be retired, active, and educated; had a higher likelihood of exhibiting hypertension and acute pulmonary oedema; a lower likelihood of exhibiting sleep apnoea, heart rhythm disturbance, coronary artery diseases; had higher comorbidity index score and LVEF range; had more HFpEF; had lower KCCQ total symptom, symptom frequency and burden scores; and lower KCCQ and EQ-5D-5L quality of life scores. As seen, women and men with heart failure had different baseline characteristic. These significant findings were used to determine the baseline predictors of worsening symptoms for statistical analysis later.

Regarding symptom changes (as %) over one year, there were significant differences between baseline and 12-month follow-up in men and women with heart failure. Pain/discomfort was not significantly different between sexes based on changes in the percentage of symptoms over one year. Also, walking problems for men did not change over one year. Eight other symptoms significantly changed in both sexes over one year: shortness of breath, fatigue, bilateral ankle oedema, nocturnal cough, orthopnoea, paroxysmal nocturnal dyspnoea, sleeping problems due to orthopnoea, and depressive symptoms (**Table 6-2**).

Table 6-2: Symptom changes (as %) in men and women over one year from Seckin et al. (2022)

	Men			**Women**		
Symptoms	Baseline	12-month	P-value	Baseline	12-month	P-value
Shortness of breath	278 (92.1%)	190 (62.9%)	**<0.0001**	216 (95.6%)	162 (71.7%)	**<0.0001**
Fatigue	275 (91.1%)	210 (69.5%)	**<0.0001**	216 (95.6%)	177 (78.3%)	**<0.0001**
Bilateral ankle oedema	184 (60.9)	72 (23.8%)	**<0.0001**	164 (72.6%)	57 (25.2%)	**<0.0001**
Nocturnal cough	119 (39.4%)	31 (10.3%)	**<0.0001**	89 (39.4%)	34 (15.0%)	**<0.0001**
Orthopnoea	184 (60.9%)	57 (18.9%)	**<0.0001**	163 (72.1%)	48 (21.2%)	**<0.0001**
Paroxysmal nocturnal dyspnoea	128 (42.4%)	27 (8.9%)	**<0.0001**	114 (50.4%)	17 (7.5%)	**<0.0001**
Pain/discomfort	125 (41.4%)	146 (48.3%)	0.053	101 (44.7%)	114 (50.4%)	0.184
Sleeping problems due to orthopnoea	137 (45.4%)	45 (14.9%)	**<0.0001**	102 (45.1%)	38 (16.8%)	**<0.0001**
Walking problems	170 (56.3%)	157 (52.0%)	0.271	165 (73.0%)	146 (64.5%)	**<0.0001**
Depressive symptoms	190 (62.9%)	136 (45.0%)	**<0.0001**	153 (67.7%)	105 (46.5%)	**<0.0001**

McNemar test was used to calculate differences of percentage between baseline and 12-month

6.3. Study sample

This study's sample comprised a total of 528 participants with chronic heart failure who completed baseline and 12-month follow-up from the WHICH?II Trial. From the study population, 57% of those were men (n=302) and the rest (43%) were women (n=226). 49% of women (n=111) had HFpEF diagnosis and 58% of men (n=175) had HFrEF diagnosis (**Figure 6-1**).

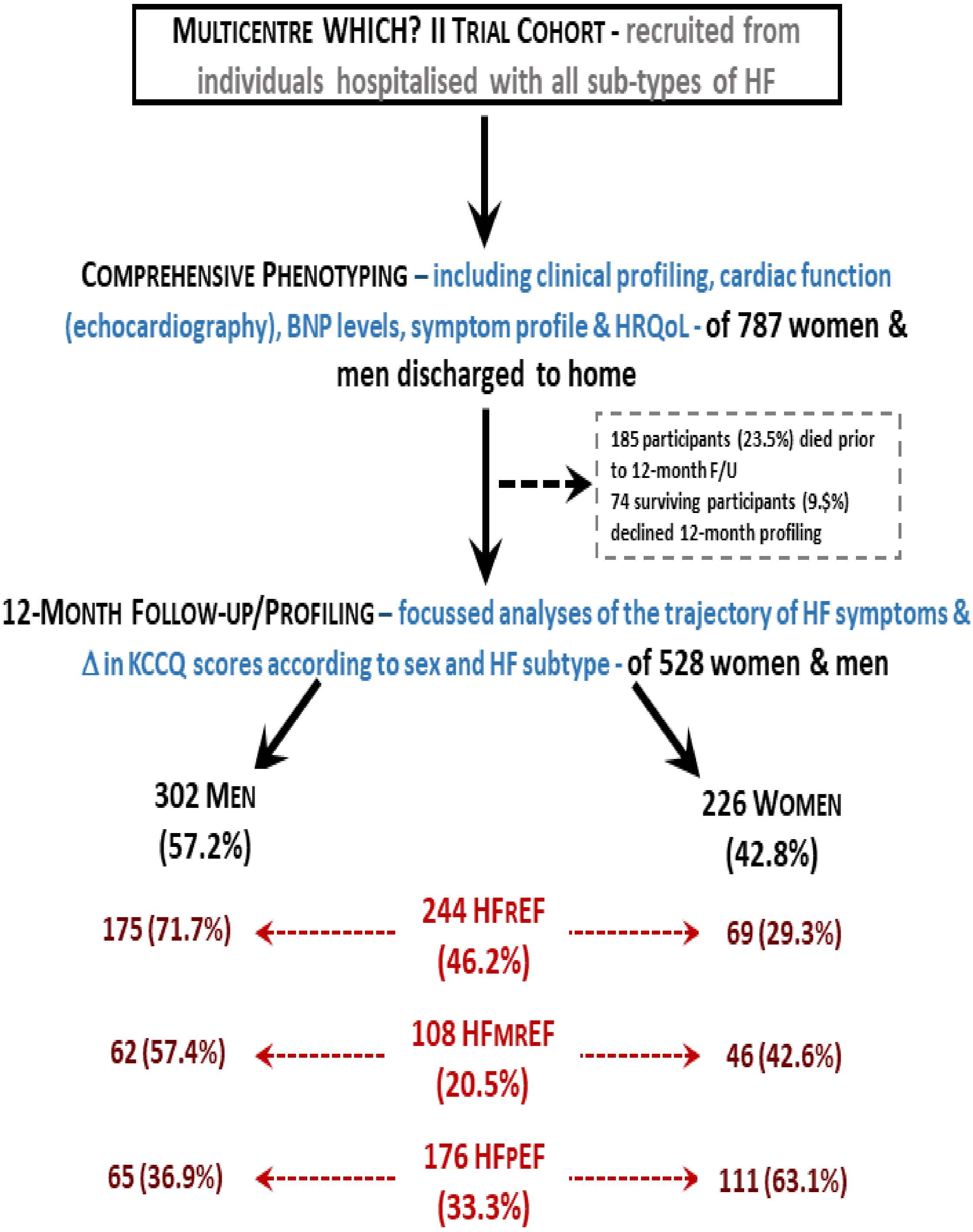


Figure 6-1: Study flow diagram from Seckin et al. (2022)

6.4. Baseline profile of women and men according to LVEF-based heart failure subtypes

Table 6-3 presents the sample characteristics of men and women according to left ventricular function. 528 people with chronic heart failure were included in the data analysis. 226 of those were women and 302 of those were men. 175 men had HFrEF, 65 men had HFpEF, and the rest of the men (n=62) had HFmrEF. The number of women was 111 for HFpEF, 69 for HFrEF, and 46 for HFmrEF. In the merged dataset, participants' ages ranged from 34 to 93 for women and from 37 to 98 for men. The average age of women was 79.51±9.22 for HFpEF, 75.63±10.35 for HFmrEF, and 74.48±12.24 for the HFrEF group. The average age of men was 74.52±11.60 years in HFpEF; 74.32±8.92 in HFmrEF; and 68.68±12.45 years in the HFrEF group.

At baseline assessment, in chronic heart failure, males with HFrEF differed from men with HFmrEF and HFpEF in terms of 11 characteristics: they were younger, less likely to be retired, had lower BMI (body mass index), had less raised JVP, less NYHA class III/IV, more likely to have elevated BNP, less Charlson comorbidity score, more depressive feelings symptoms, and less presence of atrial fibrillation, cerebrovascular disease and cancer/tumour (p-values<0.05). At baseline assessment, in chronic heart failure, women with HFpEF differed from women with HFrEF and HFmrEF in terms of 15 characteristics: they more likely to be older, married, not speak English as a first language, have higher BMI, have less history of smoking, have less elevated BNP, have prior hospital admission history, have higher KCCQ heart failure symptoms (total score, burden, frequency, and stability) scores, have lower EQ-5D-5L quality of life score, have a higher presence of hypertension and atrial fibrillation, and less presence of coronary artery disease (p-values<0.05).

Table 6-3: Baseline profiles of men and women from Seckin et al. (2022)

		Men (n=302)				**Women (n=226)**			
Variables		Reduced EF (n=175)	Mildly reduced EF (n=62)	Preserved EF (n=65)	P-value	Reduced EF (n=69)	Mildly reduced EF (n=46)	Preserved EF (n=111)	P-value
Socio-demographic profile									
Age (years) Mean (SD)		68.68±12.45	74.32±8.90	74.52±11.60	**<0.0001**	74.48±12.46	75.63±10.35	79.51±9.25	**0.004**
Living alone		56 (32.0%)	20 (32.3%)	29 (44.6%)	0.170	36 (52.2%)	28 (60.9%)	59 (53.2%)	0.612
Married – living with partner		107 (61.1%)	39 (62.9%)	35 (53.8%)	0.467	18 (26.1%)	14 (30.4%)	40 (36.0%)	**0.044**
Ethnicity n (%) – European/Caucasian		157 (89.7%)	57 (91.9%)	61 (93.8%)	0.831	63 (91.3%)	44 (95.7%)	108 (97.3%)	0.530
<12 years education level		114 (65.2%)	41 (66.1%)	42 (64.6%)	0.065	56 (81.2%)	39 (61.4%)	95 (85.6%)	0.070
Not English first language		27 (15.4%)	8 (12.9%)	13 (20.0%)	0.532	7 (10.1%)	11 (23.9%)	32 (28.8%)	**0.013**
Retired		127 (72.6%)	54 (87.1%)	56 (86.2%)	**0.014**	58 (84.1%)	42 (91.3%)	103 (92.8%)	0.158
Risk profile									
BMI		29.14±5.58	30.57±5.59	31.63±9.20	**0.024**	28.06±5.83	31.59±9.13	32.38±8.48	**0.002**
At least 2.5-hour physical activity – yes		82 (46.9%)	27 (43.5%)	22 (33.8%)	0.195	20 (29.0%)	12 (26.1%)	18 (16.2%)	0.130
No smoking history		43 (24.6%)	19 (30.6%)	20 (30.8%)	0.150	28 (40.6%)	19 (41.3%)	79 (71.2%)	**<0.0001**
Diabetes (type1&2)		77 (44.0%)	35 (56.5%)	32 (49.2%)	0.232	25 (36.2%)	15 (32.6%)	51 (45.9%)	0.215
Hypertension		119 (68.0%)	50 (80.6%)	48 (73.8%)	0.151	49 (71.0%)	36 (78.9%)	98 (88.3%)	**0.014**
Heart failure profile									
Heart failure duration	0 to 2 years	27 (15.4%)	13 (21.0%)	8 (12.3%)	0.291	21 (30.4%)	8 (17.4%)	22 (19.8%)	0.101
	2 to 5 years	100 (57.1%)	37 (59.7%)	45 (99.2%)		31 (44.9%)	26 (56.5%)	71 (64.0%)	
	≥5 years	48 (27.4%)	12 (19.4%)	12 (18.5%)		17 (24.6%)	12 (26.1%)	18 (16.2%)	
(LVEF %)*		27.25±6.61	43.17±2.75	58.35±5.90	<0.0001	30.29±6.47	42.80±2.32	58.29±6.90	<0.0001
NYHA functional class III/IV		31 (17.7%)	9 (14.5%)	17 (26.2%)$^{\#}$	**0.020**	15 (21.7%)$^{\#}$	8 (17.4%)$^{\#}$	29 (26.1%)	0.607
Elevated BNP		95 (56.2%)	22 (36.1%)	22 (34.4%)	**0.002**	39 (59.1%)	17 (37.8%)	37 (33.9%)	**0.004**
JVP raised		78 (44.8%)	29 (46.8%)	40 (62.5%)	**0.050**	32 (46.4%)	25 (54.3%)	49 (44.1%)	0.504
Prior HF admission (12 months)		94 (53.7%)	34 (54.8%)	39 (60.0%)	0.682	31 (44.9%)	29 (63.0%)	72 (64.9%)	**0.024**
Clinical profile									
Acute pulmonary oedema		40 (22.9%)	17 (27.4%)	20 (30.8%)	0.424	22 (32.4%)	16 (34.8%)	49 (44.1%)	0.242
Atrial fibrillation		81 (46.3%)	38 (61.3%)	43 (66.2%)	**0.009**	23 (33.3%)	24 (52.2%)	70 (63.1%)	**0.001**
Sleep Apnoea		40 (22.9%)	11 (17.7%)	19 (29.2%)	0.305	4 (5.8%)	7 (15.2%)	20 (18.0%)	0.065
Coronary artery disease		119 (68.0%)	41 (66.1%)	37 (56.9%)	0.274	40 (58.0%)	30 (60.2%)	45 (40.5%)	**0.007**
Chronic pulmonary disease		42 (24.0%)	19 (30.6%)	23 (35.4%)	0.185	20 (29.0%)	13 (28.3%)	26 (23.4%)	0.663
Cerebrovascular disease		29 (16.6%)	18 (29.0%)	21 (32.3%)	**0.013**	10 (14.5%)	9 (19.6%)	24 (21.6%)	0.493
Cancer or tumour		18 (10.3%)	14 (22.6%)	13 (20.0%)	**0.028**	19 (27.5%)	7 (15.2%)	16 (14.4%)	0.072
Charlson Comorbidity Score		5.99±2.30	7.19±2.81	7.08±2.16	**<0.0001**	6.80±2.32	6.78±2.10	7.15±1.93	0.432
Sleep quality – poor		56 (32.0%)	14 (22.6%)	20 (30.8%)	0.170	19 (27.5%)	20 (43.5%)	39 (35.1%)	0.132
Depressive symptoms		121 (69.9%)	36 (58.1%)	33 (51.6%)	**0.020**	48 (69.6%)	32 (69.6%)	73 (65.8%)	0.830
Heart failure symptoms	Total symptom score	49.06±24.75	47.44±25.57	43.76±25.30	0.347	45.92±23.68	43.31±24.75	40.62±23.69	**0.018**
	Symptom frequency	46.27±25.53	45.69±26.29	40.86±26.78	0.349	45.22±23.26	42.07±26.54	35.09±23.89	**0.020**
	Symptom burden	51.85±26.52	49.19±28.01	46.66±27.07	0.395	46.61±26.55	44.56±26.07	37.31±24.01	**0.039**
	Symptom stability	45.43±37.33	53.23±39.84	53.85±38.58	0.190	39.86±37.94	53.26±36.36	55.86±40.35	**0.025**
Quality of life	KCCQ	38.76±22.42	40.18±22.66	43.84±23.53	0.306	38.28±25.13	35.32±17.49	34.66±20.41	0.529
	EQ-5D-5L	0.72±0.19	0.72±0.18	0.69±0.20	0.672	0.70±0.17	0.64±0.19	0.61±0.22	**0.034**

*KCCQ was used for assessing HF symptom scores; QoL was assessed by KCCQ and EQ-5D-5L scales. depressive symptoms were calculated by a two-item ARROL tool; *n=261 for females and n=429 for males $^{\#}$No NYHA class IV; BNP: b-type natriuretic peptide; elevated BNP, >6000pg/ml; LVEF, left ventricular ejection fraction. NYHA, New York Heart Association; BMI, Body mass index*

6.5. Symptom differences in men and women based on LVEF-based heart failure subtypes

According to the different heart failure subtypes, we discovered that women reported significantly different KCCQ symptom scores (total, burden, frequency, and stability) and EQ-5D-5L quality of life scores (p-values<0.05), whereas males did not (with only minor symptom variations) (**Table 6-3**). Regardless of heart failure subgroups, fatigue and shortness of breath were the most common first symptoms in both sexes (**Table 6-4**). Yet in both sexes, bilateral ankle oedema was significantly more common in people with HFpEF than in people with HFmrEF or HFrEF (p=0.019 for men and p=0.0001 for women). Walking issues were reported by more HFpEF (p=0.019 for men and p=0.0001 for women). Walking issues were reported by more HFpEF women than HFrEF/HFmrEF women (p=0.019). Men with HFrEF had higher rates of depressive symptoms than men with HFmrEF/HFpEF (p=0.020).

6.6. KCCQ score changes in women and men according to LVEF-based heart failure subtypes

KCCQ total symptom, symptom frequency, and symptom burden mean scores increased over one year in both sexes with respect to the phenotypes of heart failure based on left ventricular ejection fraction (**Table 6-5**). However, there was an increase in the KCCQ symptom stability score in both sexes with HFrEF, while this score declined slightly for males and females with HFpEF and HFmrEF. Only KCCQ symptom stability mean score change was significant for females over one year.

Table 6-4: Baseline self-reported symptoms in men and women according to heart failure subtypes based on LVEF from Seckin et al. (2022)

	Men (n=302)				**Women (n=226)**			
Symptoms	**HFrEF (n=175)**	**HFmrEF (n=62)**	**HFpEF (n=65)**	**P-value**	**HFrEF (n=69)**	**HFmrEF (n=46)**	**HFpEF (n=111)**	**P-value**
Shortness of breath, n (%)	159 (90.9)	59 (95.2)	60 (92.3)	0.558	66 (95.7)	43 (93.5)	107 (96.4)	0.720
Fatigue, n (%)	161 (92.0)	57 (91.9)	57 (87.7)	0.562	66 (95.7)	43 (93.5)	107 (96.4)	0.720
Bilateral ankle oedema, n (%)	97 (55.4)	38 (61.3)	49 (75.4)	**0.019**	36 (52.2)	32 (69.6)	96 (86.5)	**<0.0001**
Nocturnal cough, n (%)	73 (41.7)	24 (38.7)	22 (33.8)	0.537	30 (43.5)	16 (34.8)	43 (38.7)	0.634
Orthopnoea, n (%)	108 (61.7)	35 (56.5)	41 (63.1)	0.707	51 (73.9)	28 (60.9)	84 (75.7)	0.157
Paroxysmal nocturnal dyspnoea, n (%)	80 (45.7)	20 (32.3)	28 (43.1)	0.182	38 (55.1)	23(50.0)	53 (47.7)	0.632
Pain/discomfort, n (%)	75 (43.1)	24 (38.7)	26 (40.0)	0.807	27 (39.7)	23 (50.0)	51 (46.4)	0.518
Sleep problems due to orthopnoea, n (%)	82 (46.9)	25 (40.3)	30 (46.2)	0.667	31 (44.9)	21 (45.7)	50 (45.0)	0.997
Walking problems, n (%)	91 (52.3)	35 (56.5)	44 (67.7)	0.102	43 (63.2)	32 (69.6)	90 (81.8)	**0.019**
Depressive symptoms, n (%)	121 (69.9)	36 (58.1)	33 (51.6)	**0.020**	48 (69.6)	32 (69.6)	73 (65.8)	0.830

HF=heart failure; LVEF=left ventricular ejection fraction; HFrEF=Heart failure with reduced ejection fraction (LVEF ≤40%); HFmrEF=Heart failure with mildly-reduced ejection fraction (LVEF 41%–49%); HFpEF=Heart failure with preserved ejection fraction (LVEF ≥50%). The chi-square (X^2) tests were used to compare the presence of symptoms in men and women separately.

Table 6-5: KCCQ heart failure symptoms score changes over one year from Seckin et al. (2022)

KCCQ Heart Failure Symptom Score Change		**Men (n=302)**									
		HFrEF (n=175)			**HFmrEF (n=62)**			**HFpEF (n=65)**			
		Baseline	**12-month**	**Baseline to 12 Months**	**Baseline**	**12-month**	**Baseline to 12 Months**	**Baseline**	**12-month**	**Baseline to 12 Months**	**P-value**
	Total Symptom	49.0±24.7	78.3±21.4	29.3(24.8,33.7)	47.4±25.5	76.8±23.8	29.4(21.2, 7.6)	43.7±25.3	72.9±24.0	29.3(22.50,36.2)	1.000
	Symptom Stability	45.4±37.3	52.2±19.1	6.8(0.8,12.8)	53.2±39.8	47.1±16.3	-6.0(-16.2,4.1)	53.8±38.5	52.3±18.2	-1.9(-12.1 8.2)	0.062
	Symptom Frequency	46.2±25.5	76.2±23.2	29.9(25.3,34.5)	45.6±26.2	75.5±23.9	29.8(21.4,38.3)	40.8±26.7	69.7±26.4	29.1(21.7,36.5)	0.934
	Symptom Burden	51.8±26.5	80.5±22.3	28.7(23.8,33.5)	49.1±28.0	78.2±25.3	29.0(20.3,37.7)	46.6±27.0	76.0±24.4	29.3(22.1,36.5)	0.990
		Women (n=226)									
		HFrEF (n=69)			**HFmrEF (n=46)**			**HFpEF (n=111)**			
		Baseline	**12-month**	**Baseline to 12 Months**	**Baseline**	**12-month**	**Baseline to 12 Months**	**Baseline**	**12-month**	**Baseline to 12 Months**	**P-value**
	Total Symptom	45.9±23.6	76.0±22.2	30.1(24.4,35.8)	43.3±24.7	74.7±23.2	31.4(21.7,41.1)	40.6±23.6	69.5±23.8	33.3(28.0,38.6)	0.749
	Symptom Stability	39.8±37.9	48.9±16.8	9.0(1.0,17.1)	53.2±36.3	48.3±20.6	-4.89(-17.5,7.7)	55.8±40.3	48.8±19.1	-6.9(-15.2,1.2)	**0.033**
	Symptom Frequency	45.2±23.2	75.4±22.3	30.2(24.3 36.1)	42.0±26.5	74.1±24.0	32.1(22.8,41.3)	35.0±23.8	66.4±25.3	31.3(25.4,37.2)	0.940
	Symptom Burden	46.6±26.5	76.6±24.2	30.0(23.4,36.7)	44.5±26.0	75.3±25.3	30.7(19.5,42.0)	37.3±24.0	72.5±25.6	35.2(29.6,40.9)	0.492

Symptom scores are presented as mean±SD (standard deviation) at baseline and 12-month; changes in symptom scores from baseline to 12-month are presented as mean difference (95% Confidence Interval [CI] upper and lower). HF=Heart failure; LVEF=Left ventricular ejection fraction; HFrEF=Heart failure with reduced ejection fraction (LVEF ≤40%); HFmrEF=Heart failure with mildly reduced ejection fraction (LVEF 41%–49%); HFpEF=Heart failure with preserved ejection fraction (LVEF ≥50%); KCCQ=Kansan City Cardiomyopathy Questionnaire. Repeated ANAVO was used to compare the symptom scores between baseline and 12-month in men and women separately.

6.7. Worsening heart failure symptoms groups

Worsening heart failure symptoms were calculated by the change in KCCQ symptoms stability over one year. There were four different groups, including improving heart failure, persistent heart failure, moderate worsening heart failure, and severe worsening heart failure groups (**Table 6-6**). 48% of males with HFrEF and 24% of females with HFmrEF exhibited improving heart failure. 22% of males with HFpEF and 55% of females with HFrEF had the same KCCQ symptom stability score between baseline and 12-month follow-up time.

Approximately 50% of females with HFpEF and 48% of males with HFmrEF were in the worsening heart failure group, including both severe and moderate worsening. However, 62 male participants were in the HFmrEF group. However, the percentage may not provide enough explanation in both sexes with the phenotypes of heart failure based on left ventricular ejection fraction, so differences in the number of participants in groups are also provided. In total, over one year, 59 males with HFrEF, 29 males with HFmrEF, and 26 males with HFpEF developed worse heart failure symptoms; while 55 females with HFpEF, 20 females with HFmrEF, and 16 females with HFrEF did so.

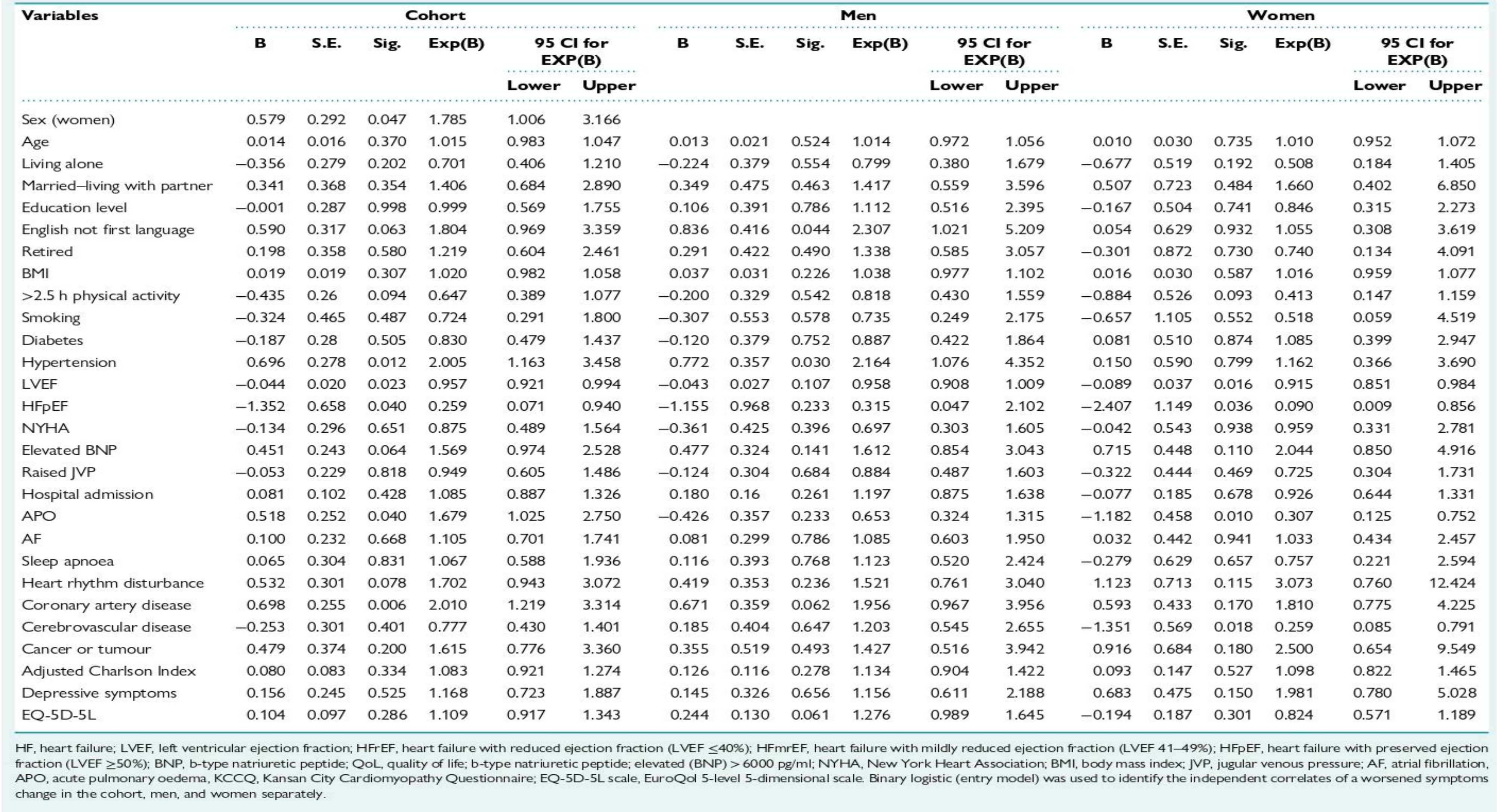
Table 6-6: Worsening heart failure symptoms group (KCCQ symptom stability score) from Seckin et al. (2022)

	Men (n=302)			**Women (n=226)**		
Symptoms change	HFrEF (n=175)	HFmrEF (n=62)	HFpEF (n=65)	HFrEF (n=69)	HFmrEF (n=46)	HFpEF (n=111)
Improving, n (%)	84 (48.0%)	23 (37.1%)	24 (37.5%)	38 (55.1%)	15 (32.6%)	39 (35.1%)
Persistent, n (%)	32 (18.3%)	10 (16.1%)	14 (21.9%)	15 (21.7%)	11 (23.9%)	17 (15.3%)
Moderate Worsening (25–49), n (%)	24 (13.7%)	10 (16.1%)	9 (14.1%)	5 (7.2%)	8 (17.4%)	20 (18.0%)
Severe Worsening (≥50), n (%)	35 (20.0%)	19 (30.6%)	17 (26.6%)	11 (15.9%)	12 (26.1%)	35 (31.5%)
		0.518			**0.025**	

6.8. Correlates of worsening heart failure symptoms over 12 months

As shown in **Table 6-7**, we tested a broad range of baseline correlates associated with worsened HF symptoms in men and women. Irrespective of gender, coronary artery disease (OR 2.01, 95% CI 1.21–3.31) and hypertension (OR 2.00, 95% CI 1.16–3.45) significantly correlated with worsened HF symptoms. Women were more likely to report worsening symptoms during the 12-month follow-up than men (OR 1.78, 95% CI 1.00–3.16). The higher LVEF range and those with HFpEF were more likely to report worsened symptoms in women, but not men. Moreover, these sex-specific differences extended to other baseline characteristics, with primary English-speaking status (OR 2.30, 95% CI 1.02–5.20) and the presence of hypertension (OR 2.16, 95% CI 1.07–4.35) also associated with worsening symptoms in men but not women; and acute pulmonary oedema (OR 0.30, 95% CI 0.12–0.75) and cerebrovascular disease (OR 0.25 95% CI 0.08–0.79) in women but not men.

Table 6-7: Correlates associated with worsening symptoms in the entire cohort, men, and women from Seckin et al. (2022)



Variables	**Cohort**						**Men**						**Women**					
	B	**S.E.**	**Sig.**	**Exp(B)**	**95 CI for EXP(B)**		**B**	**S.E.**	**Sig.**	**Exp(B)**	**95 CI for EXP(B)**		**B**	**S.E.**	**Sig.**	**Exp(B)**	**95 CI for EXP(B)**	
					Lower	**Upper**					**Lower**	**Upper**					**Lower**	**Upper**
Sex (women)	0.579	0.292	0.047	1.785	1.006	3.166												
Age	0.014	0.016	0.370	1.015	0.983	1.047	0.013	0.021	0.524	1.014	0.972	1.056	0.010	0.030	0.735	1.010	0.952	1.072
Living alone	−0.356	0.279	0.202	0.701	0.406	1.210	−0.224	0.379	0.554	0.799	0.380	1.679	−0.677	0.519	0.192	0.508	0.184	1.405
Married–living with partner	0.341	0.368	0.354	1.406	0.684	2.890	0.349	0.475	0.463	1.417	0.559	3.596	0.507	0.723	0.484	1.660	0.402	6.850
Education level	−0.001	0.287	0.998	0.999	0.569	1.755	0.106	0.391	0.786	1.112	0.516	2.395	−0.167	0.504	0.741	0.846	0.315	2.273
English not first language	0.590	0.317	0.063	1.804	0.969	3.359	0.836	0.416	0.044	2.307	1.021	5.209	0.054	0.629	0.932	1.055	0.308	3.619
Retired	0.198	0.358	0.580	1.219	0.604	2.461	0.291	0.422	0.490	1.338	0.585	3.057	−0.301	0.872	0.730	0.740	0.134	4.091
BMI	0.019	0.019	0.307	1.020	0.982	1.058	0.037	0.031	0.226	1.038	0.977	1.102	0.016	0.030	0.587	1.016	0.959	1.077
>2.5 h physical activity	−0.435	0.26	0.094	0.647	0.389	1.077	−0.200	0.329	0.542	0.818	0.430	1.559	−0.884	0.526	0.093	0.413	0.147	1.159
Smoking	−0.324	0.465	0.487	0.724	0.291	1.800	−0.307	0.553	0.578	0.735	0.249	2.175	−0.657	1.105	0.552	0.518	0.059	4.519
Diabetes	−0.187	0.28	0.505	0.830	0.479	1.437	−0.120	0.379	0.752	0.887	0.422	1.864	0.081	0.510	0.874	1.085	0.399	2.947
Hypertension	0.696	0.278	0.012	2.005	1.163	3.458	0.772	0.357	0.030	2.164	1.076	4.352	0.150	0.590	0.799	1.162	0.366	3.690
LVEF	−0.044	0.020	0.023	0.957	0.921	0.994	−0.043	0.027	0.107	0.958	0.908	1.009	−0.089	0.037	0.016	0.915	0.851	0.984
HFpEF	−1.352	0.658	0.040	0.259	0.071	0.940	−1.155	0.968	0.233	0.315	0.047	2.102	−2.407	1.149	0.036	0.090	0.009	0.856
NYHA	−0.134	0.296	0.651	0.875	0.489	1.564	−0.361	0.425	0.396	0.697	0.303	1.605	−0.042	0.543	0.938	0.959	0.331	2.781
Elevated BNP	0.451	0.243	0.064	1.569	0.974	2.528	0.477	0.324	0.141	1.612	0.854	3.043	0.715	0.448	0.110	2.044	0.850	4.916
Raised JVP	−0.053	0.229	0.818	0.949	0.605	1.486	−0.124	0.304	0.684	0.884	0.487	1.603	−0.322	0.444	0.469	0.725	0.304	1.731
Hospital admission	0.081	0.102	0.428	1.085	0.887	1.326	0.180	0.16	0.261	1.197	0.875	1.638	−0.077	0.185	0.678	0.926	0.644	1.331
APO	0.518	0.252	0.040	1.679	1.025	2.750	−0.426	0.357	0.233	0.653	0.324	1.315	−1.182	0.458	0.010	0.307	0.125	0.752
AF	0.100	0.232	0.668	1.105	0.701	1.741	0.081	0.299	0.786	1.085	0.603	1.950	0.032	0.442	0.941	1.033	0.434	2.457
Sleep apnoea	0.065	0.304	0.831	1.067	0.588	1.936	0.116	0.393	0.768	1.123	0.520	2.424	−0.279	0.629	0.657	0.757	0.221	2.594
Heart rhythm disturbance	0.532	0.301	0.078	1.702	0.943	3.072	0.419	0.353	0.236	1.521	0.761	3.040	1.123	0.713	0.115	3.073	0.760	12.424
Coronary artery disease	0.698	0.255	0.006	2.010	1.219	3.314	0.671	0.359	0.062	1.956	0.967	3.956	0.593	0.433	0.170	1.810	0.775	4.225
Cerebrovascular disease	−0.253	0.301	0.401	0.777	0.430	1.401	0.185	0.404	0.647	1.203	0.545	2.655	−1.351	0.569	0.018	0.259	0.085	0.791
Cancer or tumour	0.479	0.374	0.200	1.615	0.776	3.360	0.355	0.519	0.493	1.427	0.516	3.942	0.916	0.684	0.180	2.500	0.654	9.549
Adjusted Charlson Index	0.080	0.083	0.334	1.083	0.921	1.274	0.126	0.116	0.278	1.134	0.904	1.422	0.093	0.147	0.527	1.098	0.822	1.465
Depressive symptoms	0.156	0.245	0.525	1.168	0.723	1.887	0.145	0.326	0.656	1.156	0.611	2.188	0.683	0.475	0.150	1.981	0.780	5.028
EQ-5D-5L	0.104	0.097	0.286	1.109	0.917	1.343	0.244	0.130	0.061	1.276	0.989	1.645	−0.194	0.187	0.301	0.824	0.571	1.189

HF, heart failure; LVEF, left ventricular ejection fraction; HFrEF, heart failure with reduced ejection fraction (LVEF ≤40%); HFmrEF, heart failure with mildly reduced ejection fraction (LVEF 41–49%); HFpEF, heart failure with preserved ejection fraction (LVEF ≥50%); BNP, b-type natriuretic peptide; QoL, quality of life; b-type natriuretic peptide; elevated (BNP) > 6000 pg/ml; NYHA, New York Heart Association; BMI, body mass index; JVP, jugular venous pressure; AF, atrial fibrillation, APO, acute pulmonary oedema, KCCQ, Kansan City Cardiomyopathy Questionnaire; EQ-5D-5L scale, EuroQol 5-level 5-dimensional scale. Binary logistic (entry model) was used to identify the independent correlates of a worsened symptoms change in the cohort, men, and women separately.

6.9. Strengths and limitations

There are some limitations to this study. The nationally representative of men and women with chronic heart failure based on LVEF in Australia. It is important to state that not all heart failure symptoms and quality of life were assessed by the same group of people who participated in the primary research group. The participant did not receive telephone follow-up intervention, which may be influenced on the sample representativeness. Although there were no statistically significant differences between the experimental and control arms on KCCQ symptom scores over 12 months in the WHICH?II trial, the follow-up data might still underestimate the true symptom prevalence in the general population, as this is likely influenced by the effects of the experimental condition. Given that the study cohort was predominated by advancing age, Caucasian participants, and NYHA class II, there is a concern about the generalisability of the findings to the entire heart failure population. Another limitation is the presence of heart failure symptoms. Eight heart failure symptoms were evaluated; nevertheless, the study participants may have more symptoms than these. In section one, only seven independent factors related to heart failure symptoms were investigated in male and female chronic heart failure participants, which may not be sufficient from an individual perspective. In section two, KCCQ symptom stability score change was used to calculate worsening symptoms. KCCQ symptom stability score indicates the last two weeks' symptom change evaluation. This may bias the definition of worsening symptoms.

6.7. Conclusion and chapter summary

There were sex-stratified differences in symptoms and symptom changes according to heart failure subtypes in heart failure. Men and women were different with different phenotypes of heart failure based on LVEF. Only symptom stability declined for women and men with HFmrEF and HFpEF over one year. At least 20% of both sexes with any phenotypes of heart failure had worsening heart failure according to symptom stability score change. There are different factors associated with symptom stability change in men and women (please see **Box 6-1** for a summary of the research in context).

Implications of the findings of this PhD research

- There were sex-stratified differences in symptoms and symptom changes over one year according to the phenotypes of heart failure based on LVEF.

- Women and men with HFpEF had higher symptom burdens than those with HFrEF and HFmrEF.
- Regarding the KCCQ symptom stability score, women and men had different correlators associated with long-term worsening heart failure symptoms.

To this point, the current study has presented, first, the full spectrum of symptoms and setting- and age-related differences in ESC typical and less typical symptoms; and then stratified differences in symptoms and symptom changes with respect to LVEF-based heart failure subtypes in the heart failure cohort. In systematic review and secondary data analysis, breathlessness is the most observed symptoms. In the next chapter, symptoms (mainly breathlessness) experienced by Turkish individuals with respect to their cultural and social belief and values will be presented according to the findings of semi-structured interviews.

Box 6-1: Findings from a cohort of people hospitalised with heart failure – research in context

Evidence before this study

Individuals with heart failure often experience a variety of symptoms, and exacerbations and persistence of these symptoms are important indicators of the progressive nature of heart failure. The specific symptomatic profile and course are highly individual, according to the underlying pathophysiological aetiology of heart failure and LVEF. Additionally, it is important to consider that there might be differences in the types of heart failure and the symptoms associated with them between men and women. Surprisingly, there had not been any research conducted to explore these differences in symptom characteristics and changes based on heart failure types and gender. This research gap underscores the need for further research to better understand how various subgroups of heart failure patients experience their symptoms.

This study had two primary objectives: to explore sex-stratified differences in self-reported heart failure symptoms, and how these symptoms change within different heart failure subtypes and correlators of worsening heart failure symptoms between baseline and 12-month follow-up time.

This study undertakes a retrospective secondary data analysis of the data from a previously published randomised controlled trial that investigated the comparative efficacy of two nurse-led management approaches within a real-world cohort of patients diagnosed with heart failure (WHICH?II Trial). Statistical analyses were conducted using the SPSS software programme within the timeframe of October 2021 to May 2022. The selection of specific statistical models, such as T-tests, chi-square tests, and multiple logistic regression, was determined by the research objectives and the nature of the research questions. The KCCQ was used to calculate symptoms score stability and worsening symptom profile of men and women.

Contribution of this study

There was significant heterogeneity (with potential clinical implications) in symptoms and symptom changes by sex and LVEF-based heart failure subtype. There were 302 men (58% with HFrEF) and 226 women (49% with HFpEF). At baseline, shortness of breath and fatigue predominated; with key differences according to HF subtypes in bilateral ankle oedema (both sexes), walking problems (women) and depressive symptoms (men). At 12-month follow-up, most KCCQ scores had not significantly changed. However, 25% of individuals reported worse symptoms. In women, those with HFpEF had worse symptoms than those with HFmrEF/HFrEF. On an adjusted basis, women with coronary artery disease and baseline acute pulmonary oedema were most likely to report worsening symptoms. Among men, worsening symptoms correlated with a history of hypertension and a non-English-speaking background.

Implications of all the available evidence

The findings support that LVEF-based subtypes of heart failure were associated with different symptoms, symptom characteristics, and changes in men and women separately. Women with HFpEF were more likely to develop worsening symptoms over one year compared to women with HFrEF/HFmrEF. A better understanding of the differences in worsening symptoms of both sex-stratified and LVEF-based heart failure subtypes will help prevent the adverse outcomes of heart failure. Healthcare providers and researchers need to consider, develop, and then deliver tailored interventions and follow-up strategies to address a high underlying burden of severe and persistent symptoms in those hospitalised with the syndrome. Critically, the underlying LVEF-based heart failure subtype, sex, and likely factors influencing symptom changes of each affected individual need to be carefully considered.

From a research perspective, although this study reveals heterogeneity in symptoms and symptom changes in a hospitalised group, there is still a need to initiate research aimed at describing symptom experiences in heart failure from an individual perspective.

Chapter Seven - Personal experiences of Turkish individuals with self-reported heart failure

7.1. Introduction

The findings pertaining to the personal experiences of Turkish individuals with self-reported heart failure are presented in this current chapter. Breathlessness is one of the most prevalent symptoms of heart failure (in the MMSR and secondary data analysis of the WHICH?II Trial). However, there is a lack of research regarding this phenomenon among Turkish individuals. Therefore, this study sought to explore the experiences of Turkish individuals with heart failure, with a specific focus on elucidating their subjective descriptions of breathlessness and self-management strategies with reference to their socio-cultural-behavioural context. The following four research questions guided this study:

1. How is breathlessness described from a patient perspective in Türkiye?
2. What symptoms are experienced by Turkish individuals with heart failure?
3. What are the impacts/consequences of breathlessness on daily life and health for people with heart failure in Türkiye?
4. How do they manage their breathlessness?
5. What are the health needs of individuals with heart failure in Türkiye?

The details about study methods were provided in Chapter 4: Methods, page 77-87. In this present chapter, after a brief description of the methods, baseline socio-demographic and clinical characteristics are explained. Following this, identified themes and sub-themes are explored. Based on reflective thematic analysis (Braun and Clarke, 2022), the findings were identified from participants' interviews. The interpretation of the findings of this and the other two findings chapters (Chapter 5: Mixed-methods Systematic Review and Chapter 7: Findings of Secondary Data Analysis) will be presented in **Chapter 8: Overall Discussion**.

7.2. Brief overview of methods

A descriptive qualitative study was carried out in Türkiye. 20 adults (over 18 years old) with self-reported heart failure took part in the study. The primary limitation of this study was the inability to recruit participants directly from healthcare centres, which resulted in the absence of collected details regarding clinical diagnoses of heart failure, such as BNP, NT-proBNP, and LVEF range. This limitation was acknowledged and addressed in Chapter 4: Method. Consequently, the study was unable to distinguish between symptoms specific to different subgroups of heart failure and symptoms unrelated to heart failure. However, this study examines symptoms at an individual level, which is crucial. Individuals who self-reported heart failure also reported symptoms that align with those we have already identified in our systematic review. One-on-one semi-structured interviews were conducted with participants between June and October 2022. An interview guide based on the study of Walthall et al. (2017) was used, and the average length of audio-recorded face-to-face and telephone interviews was 29 minutes. Three email interviews were also conducted.

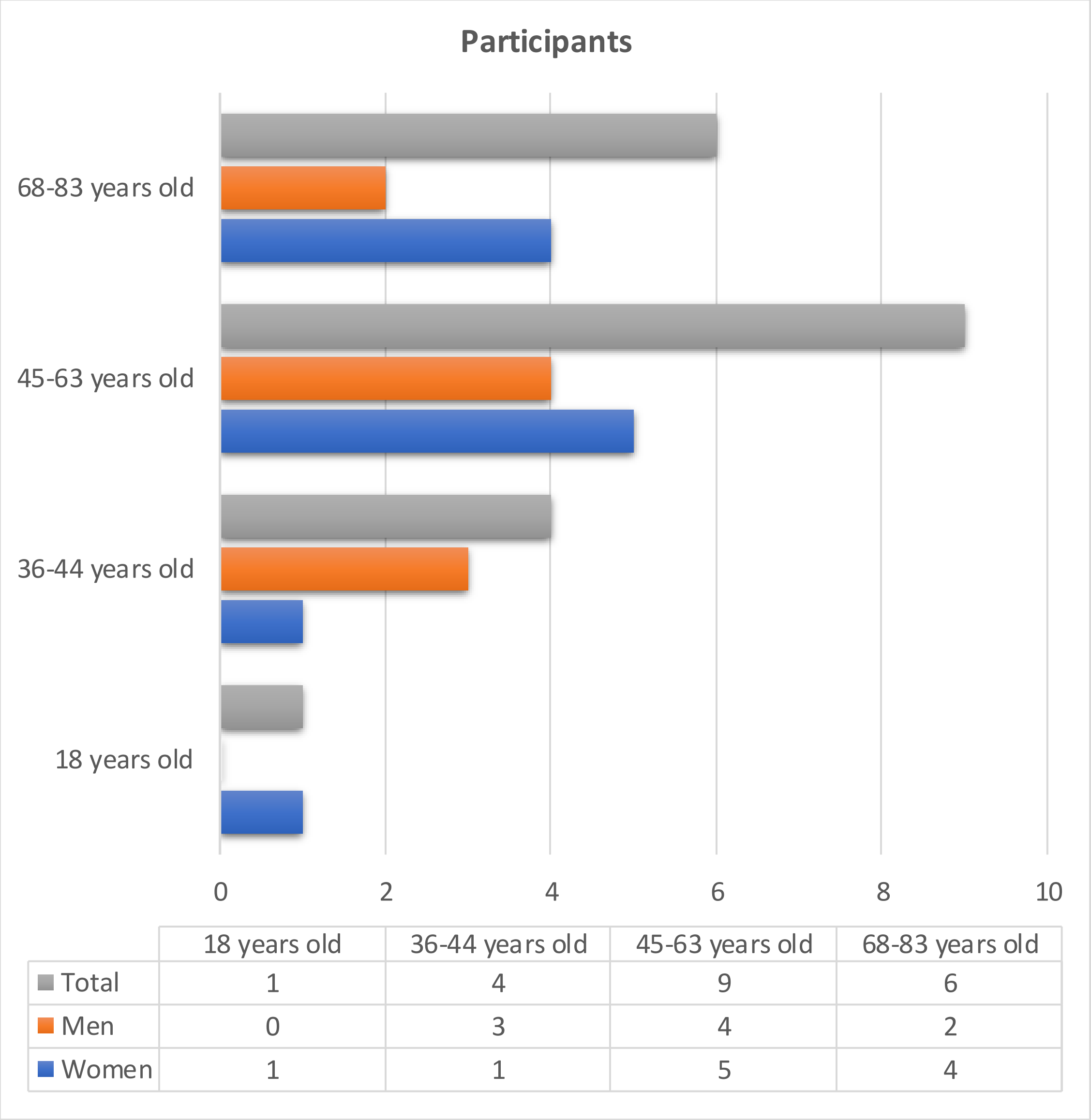
All interviews were conducted and transcribed in Turkish, and then translated into English. Each participant was assigned a pseudonym for the transcription. Transcripts (both English and Turkish versions) were separately imported into NVivo 12 to analyse through a reflective thematic analysis framework developed by Braun and Clarke (2022). Turkish transcripts were analysed to ensure that no cultural and social beliefs and perspectives of the participants were overlooked. After coding of both Turkish and English transcripts, identified codes were compared for consistency and credibility. All these stages were assessed and supervised by principal supervisor/researcher, Professor Bridget Johnston. Following these stages, the codes formed the candidate themes. The initial themes were reviewed and evaluated by the research team to identify the final themes. Following this phase, themes were defined and named in association with research questions and aims, and then final reports of the findings of participants' interviews are presented in this chapter.

This chapter presents the baseline profile of 20 participants and the identified six main themes with their sub-themes (with at least one supporting data from their interviews). Each exemplar from the participants' interviews was chosen based on the relevance of the themes and sub-themes. In general, when the participants described their experience of shortness of breath, they simultaneously described the causes and triggering factors. They were also strongly associated with physical and psychological management strategies, and participants often referred to all these stages together. For this reason, the interviews with the participants were slightly shorter than expected: numerous topics were covered in the same question, obviating the need for subsequent questions and exploration.

7.3. Baseline profile of participants

7.3.1. Socio-demographic characteristics

The 20 participants' mean age was 55.5±16.2 ranging between 18 and 83 years (**Figure 7-1** and **Table 7-1**). This study included one participant aged 18, four participants (three men, one woman) aged 36 to 44, nine participants (five women, four men) aged 45 to 63, and six participants (four women, two men) older than 67 years. The sample consisted of a total of 11 women and 9 men. Although sampling was purposive, and sought to recruit an equal number of women and men with heart failure, the prevalence of heart failure increases with older age and female sex in out-patient clinics (McDonagh et al., 2021). 15 participants were older than 44 years old, with female participants overrepresented in this group. 16 participants were Turkish. 13 participants had some education. Six participants did not have any education. Only four participants were retired. Nine of the women had home management as their employment status. Four of those women had no literacy and lived in the rural area of the cities. 17 participants were married and living with their partner. Although three participants were single, they lived with their family (including their mother/father/siblings or their son/daughter). 13 participants did not have a caregiver. The caregivers of the participants who were older and had restrictions on their movements in daily life were family members.



	18 years old	36-44 years old	45-63 years old	68-83 years old
Total	1	4	9	6
Men	0	3	4	2
Women	1	1	5	4

Figure 7-1: Study participants’ age range and biological sex

Table 7-1: Participants' characteristics (n=20)

Participants' characteristics (self-reported)	**Total (n=20)**
Socio-demographic characteristics	
Age (years)	
Mean±SD	**55.5±16.2**
Median (range)	**56.5 (18–83)**
IQR (lower quartile-upper quartile)	**24 (44.7–68.7)**
Gender, n	
Female	**11**
Male	**9**
Ethnicity, n – White (Turkish)	**16**
Turkish is not the first language – yes, n	**2**
Education status, n	
No education	**6**
Primary school	**6**
Secondary/high school	**4**
University degree	**3**
Postgraduate degree	**1**
Relationship status, n	
Single	**3**
Married	**17**
Employment status, n	
Employed full-time	**6**
Employed part-time	**1**
Retired	**4**
Homemaker	**9**
Caregivers, n	
Partner	**4**
Children/Grandchildren	**3**
No need	**13**
Clinical characteristics	
Heart failure duration (years)*	
Mean±SD	**8.1±5.0**
Median (range)	**6.5 (1–17)**
IQR (lower quartile-upper quartile)	**8.5 (3–11.5)**
Previous hospital admission (last 12 months) – yes, n	**9**
Clinical profile, n	
Acute myocardial infarction	**12**
Type 2 diabetes	**9**
Hypertension	**8**
Atrial fibrillation	**1**
Sleep apnoea	**1**
Acute pulmonary oedema	**6**
None – no comorbidities	**7**
Heart failure in family history – yes, n	**8**
Total individual self-reported symptom	
Mean±SD	**8.7±3.6**
Median (range)	**9 (3–15)**
IQR (lower quartile-upper quartile)	**5.2 (6–11.3)**

7.3.2. Clinical characteristics

Eight participants had a family history of heart failure (**Table 7-1**). The average duration of heart failure was 8.1±5.0 ranging between 1 and 17 years. One woman had recently been diagnosed with heart failure. Nine participants reported hospital admission in the last 12 months due to heart failure. 12 participants had a history of acute myocardial infarction. Eight participants had at least one comorbid condition with heart failure. Type 2 diabetes (n=9, 45%) was the comorbid condition most reported by participants. Those explained that they had type 2 diabetes before heart failure. The prevalence of heart failure was higher, and heart failure progress worse among people with diabetes than without diabetes (Lehrke and Marx, 2017). The next most commonly reported comorbidity was hypertension (n=9). Seven participants did not have any other conditions.

Regarding the second question of this study (***What symptoms are experienced by Turkish individuals with heart failure?***), the average of the total individual self-reported symptoms was 8.7±3.6 ranging between 3 and 15. Participants were provided with descriptions of various symptoms related to living with heart failure. Apart from breathlessness, 31 physical and 7 psycho-social behavioural symptoms were reported. Among these symptoms, fatigue/tiredness, difficulty sleeping, other body part pain, and fear about death and dying were reported more than other symptoms (**Table 7-2**). As can be seen in the following exemplars, the participants generally reported both physical and psycho-social behavioural symptoms together:

> *"Heart failure causes shortness of breath, chest pain, faster heartbeat, and faster breathing with intense activity. As a result, I suffer from decreased appetite, stress, and insomnia (sleeplessness)."* (Ela, 51 years old, woman)
>
> *"I feel heart failure with palpitations, chest pain, restlessness, and difficulty breathing. Lack of appetite, the constant feeling that this heart will stop, stress and some days sleeplessness."* (Cansel, 47 years old, woman)
>
> *"A situation of heart failure, breathing that feels like fainting, fainting with breathlessness, and fear about dying, especially effort and stress, and sleeplessness trigger this situation even more."* (Berk, 38 years old, man)

Table 7-2: Symptoms identified during the interviews with participants

Clusters	Symptoms		No of participants
Physical symptoms	Breathlessness		**20**
		Waking up breathlessness at night	**5**
		Difficulty breathing when lying flat	**4**
		Difficulty breathing when lying on the left/right side	**5**
		Breathlessness with exertion	**8**
		Breathlessness with walking/climbing stairs	**18**
		Breathlessness at rest	**1**
	Fatigue, tiredness		**13**
	Lack of energy, weakness		**2**
	Lack of appetite		**7**
	Swelling of arms or legs		**6**
	Dry mouth		**1**
	Sweats		**7**
	Problem with urination		**2**
	Constipation		**2**
	Feeling drowsy		**7**
	Dizziness		**2**
	Numbness/tingling hands, feet		**2**
	Pain (other bodily – back pain etc.)		**9**
	Chest pain		**7**
	Headache		**4**
	Nausea/vomiting		**3**
	Weight loss		**1**
	Weight gain		**1**
	Feeling bloated		**5**
	Difficulty sleeping		**10**
	Chest pressure/tightness		**4**
	Palpitations		**3**
	Irregular heartbeat		**1**
	Rapid heartbeat		**5**
	Shaking (body/hands)		**3**
	Wheezing		**3**
	Bendopnea		**2**
	Restlessness		**2**
	Poor mobility/walking problems		**3**
	Passing out		**1**
	Hair loss		**1**
	Bruises easily		**1**
Psycho-social behavioural symptoms	Fear (about death/dying)		**9**
	Stress		**6**
	Worry		**2**
	Feeling anxious/nervous		**4**
	Depression		**3**
	Concern about the uncertainty of future		**3**
	Negative emotions	Disturbing thoughts	**3**
		Loss of interest in life	**1**
		Unhappy	**1**
		Sad	**1**
		Angry	**2**
		Scared	**2**
		Boredom/bored	**3**
		Limited socialisation	**2**

7.4. Patient interviews

The findings in relation to the identification of themes associated with research questions are presented below. There are six themes and include several sub-themes, each representing a range of shortness of breath experiences by people with heart failure (**Table 7-3**).

Table 7-3: List of themes for breathlessness experiences, management, and needs for improved health behaviours

Themes	**Sub-themes**	**Research question**
1. Misconception & knowledge about breathlessness	***1.1-Knowledge and awareness of breathlessness*** ***1.2-Comparison with others***	1.How is breathlessness described from a patient perspective in Türkiye? 5.What are the health needs of individuals with heart failure in Türkiye?
2. Experience of breathlessness	***2.1-Psychological vulnerability*** ***2.2-Physical vulnerability*** ***2.3-Interactions with other symptoms*** ***2.4-Living with uncertainty & fear of death and dying***	1.How is breathlessness described from a patient perspective in Türkiye? 3.What is the impact/consequence of breathlessness on daily life and health for people with heart failure in Türkiye?
2. Cultural & religious considerations	***3.1-Religious life disruption*** ***3.2-Belief in Allah (God) & intuition*** ***3.3-Complementary and alternative strategies***	1.How is breathlessness described from a patient perspective in Türkiye? 3.What is the impact/consequence of breathlessness on daily life and health for people with heart failure in Türkiye? 4.How do people in Türkiye manage breathlessness themselves?
3. Breathlessness self-management strategies/ psychological	***4.1-Self-affirmation*** ***4.2- Avoiding undesirable situations*** ***4.3-Engaging with hobbies***	4. How do people in Türkiye manage breathlessness themselves?
4. Breathlessness self-management strategies/ physical	***5.1-Reliant on only their doctors*** ***5.2-Inputs from significant others*** ***5.3-Maintaining normality***	4. How do people in Türkiye manage breathlessness themselves?
5. Improved health behaviours	***6.1-Adequate education*** ***6.2-Psychological support*** ***6.3-Long-term evidence-based interventions***	5.What are the health needs of individuals with heart failure in Türkiye?

7.4.1. Theme 1: Misconceptions and knowledge about breathlessness

Awareness and knowledge about breathlessness (as a symptom) in heart failure (as a syndrome) and its outcomes were reported among the participants. There was a correlation between knowledge and breathlessness interpretation and management strategies. Knowledge about breathlessness (and heart failure) and comparison with others were the two main sub-themes of this main theme. Without understanding their condition and its impacts, it would be difficult to manage. Therefore, this theme formed the core concept of breathlessness experience and self-management strategies.

This theme included Knowledge about breathlessness (and heart failure) and Comparison with others sub-themes. Both these sub-themes explored, with relevant examples provided.

7.4.1.1. Knowledge about breathlessness (and heart failure)

Inaccurate knowledge (due to poor communication between healthcare providers and patients; financial/insurance issues; source of knowledge etc) and misconceptions were reported by the participants. Apart from those with a family history of heart failure, participants seemed to not have any information/knowledge about heart failure.

Lack of healthcare education: Most participants reported that they did not receive any information or education about their symptom experiences (including breathlessness) and management strategies associated with heart failure from their doctors or other healthcare professionals. As seen in the quotation below, a participant with a 14-year diagnosis of heart failure reported that heart failure information and management training had not been provided during this period.

> *"In other words, as I said, I stayed in the hospital due to diabetes, for example, they provide education on diabetes. They talk about education, which is about diabetes. A person can also do some of these things, but there is nothing like that about heart failure. I spent a lot of time in the hospital. I have been to many hospitals, and I have not received such training from doctors in any of them. But it would be better if they enlighten us. So, I haven't received any education and training until now."* (Alp, 61 years old, man – Heart failure duration: 14 years)

In addition, while some participants explained that private hospitals were good at providing information and training, some participants could not choose a private hospital due to their financial/insurance issues. The following exemplar illustrates this issue.

> *"Now I have no insurance, and because of it, I can never go there. ... I'm going to the state hospital too. But the doctor doesn't seem to know much about it in the state hospital. So, they don't know. So, they don't know as much as the doctor in that private hospital. Already, these drugs were prescribed to me in that private hospital."* (Peri, 63 years old, woman)

With the lack of healthcare education, participants did not seek to manage their breathlessness due to the uncertainty of the source of breathlessness related to heart failure and other risk factors/comorbid conditions/ageing/family background. As seen in the following exemplars, Umut expressed the belief that his shortness of breath was related to his weight, and Alp linked it to his diagnosis of diabetes.

> ***Exemplar 1:*** *"I'm overweight, and weight can be a thing, which affects walking too much with shortness of breath. I think this is the explanation for the shortness of breath on this walk because I am overweight."* (Umut, 53 years old, man)

> ***Exemplar 2:*** *"During sleep time, it is very rare. So, it has happened two or three times in 12 years, 13 years, and 14 years. I think it's due to diabetes. Caused by excessive glucose reduction. I mean, I can't do anything when it happens. So, I can't do anything; I cannot interfere with anything. Then I have shortness of breath at that time too."* (Alp, 61 years old, man)

Additionally, only typical heart failure symptoms were assessed in hospitals. In another exemplar below, when the researcher asked whether physical and emotional symptoms were evaluated by healthcare professionals, an 18-year-old participant stated that only swelling in the feet/hands was evaluated by her doctors.

> *"No. Actually, they don't ask much. At first, they checked my feet and hands. So, there was nothing else. [In the hospital,] they look at my heart valves and the working condition of the heart, that's all."* (Elif, 18 years old, woman)

Misconceptions: A major misconceptions was believing there was no education or care intervention to treat breathlessness, or that this was not their diagnosis. This shows why they do not need professional help in the management of breathlessness. Particularly, the participants evaluated shortness of breath separately from heart failure and thought that they could not get help from a health professional. This affected the reported breathlessness experience and management process. A 43-year-old male participant expressed that there was no training or treatment for breathlessness, which would be reflected in under-reporting or under-recognition of the symptom.

> *"Now, there is no training for this [shortness of breath]. Now everyone who plays sports knows this. Inevitably, after a certain period of time, you will be out of breath. So, I don't think there will be an education. It goes away after a certain time. If there was anything different, I would have told you. But that's it."* (Mert, 43 years old, man)

This sub-theme highlighted that recognition and appraisal of breathlessness were poor because of the lack of understanding and awareness of heart failure symptoms with the lack of adequate healthcare education.

7.4.1.2. Comparison with others

Some participants reported that their breathlessness experiences were normal or less problematic when they compared it to others. Most of the participants compared their breathlessness experiences with their healthy friends and concluded their breathlessness experiences were the same as those of their friend. Therefore, they did not think it was a main problem for their life or needed any special management strategies.

> *"You know, the person climbing the stairs next to me, in the same way, their hearts beat faster, and they also experience breathlessness."* (Leyla, 45 years old, woman)

7.4.1.3. Theme summary

This theme, Misconceptions and knowledge about breathlessness (and heart failure), expressed a lack of knowledge and awareness that is important in recognising and managing symptoms. This component is critically important for vulnerable individuals and communities to improve health-related outcomes in heart failure. Misinterpretation of symptoms may delay recognition of the worsening trajectory of heart failure. Many participants indicated that they did not receive any information or education on heart failure symptom management in Türkiye. This highlighted the importance of raising knowledge and awareness that heart failure symptoms and management should be a priority in Türkiye.

7.4.2. Theme 2: Experience of breathlessness

This theme title arose directly from participant quotes in relation to this study's first and second research questions. The experience of breathlessness was reported and explained by the participants. Each participant had a shortness of breath experience. As in previous published literature (Walthall et al., 2017, Walthall et al., 2023), most participants were able to describe their breathlessness experience, such as when it started or an acute episode that they experienced. The participants usually described their breathlessness in terms of when it is triggered (by simple activities such as walking a very short distance, climbing stairs, or doing any work in their everyday life). One participant experienced breathlessness at rest. They generally referred to the feeling of struggling to breathe, and not getting enough breath during the episodes. The following exemplars indicated these experiences of breathlessness.

> ***Exemplar 1:*** *"It is a very strange feeling when you have shortness of breath. You take a very deep breath, but the breath is not enough. Your heart beats faster, it suddenly suffocates, and you feel like you are going to faint. Your insides are burning like fire. And then you feel like it will never pass. Every time I do not feel well, I have shortness of breath."* (Cansel, 47 years old, woman)
>
> ***Exemplar 2:*** *"I actually do all the housework. Only when I do a lot at work, and also when I lift heavy things. When I use the vacuum cleaner, I get very short of breath, that's all. I'm out of breath. I'm short of breath, that's all."* (Fulya, 44 years old, woman)
>
> ***Exemplar 3:*** *"Shortness of breath – I feel it when climbing the hills and climbing stairs. Also, my knees hurt, and I can't climb stairs at all."* (Emel, 72 years old, woman)

However, the expression of when and how individuals experienced breathlessness would not be sufficient in and of itself to understand this experience or manage its impacts. The experience of breathlessness encompasses subjective assessment, evaluation, interpretation, and reporting, all of which are influenced by an individual's personal reality, beliefs about outcomes, and previous experiences. The concept of vulnerability, which connects physical, emotional, and cognitive phenomena, can aid in comprehensively understanding an individual's situation (Boldt, 2019). Individuals with (chronic) heart failure often experience physical impairment and emotional distress, including poor decision-making and a lack of empowerment for continuity of care/treatment regimes. An evaluation of a person's (physical and psychological) vulnerability in making decisions with serious and long-term effects is important in heart failure.

Therefore, the theme Experience of breathlessness indicated these aspects to promote the recognition of the factors to describe the situation from a wider to more narrow perspective. Psychological vulnerability; physical vulnerability; interactions with other symptoms; and living with uncertainty and fear of death/dying were the sub-themes identified from the interviews with the participants in this theme.

7.4.2.1. Psychological vulnerability

Participants who had lost a friend/family member to heart failure sometimes expressed their degree of breathlessness on the basis of their observations or inferences about their relative's/friend's experiences. These observations or inferences affected their decision-making process pertaining to their symptoms and self-management strategies, such as (1) a refusal of treatment options or not reporting their conditions, and (2) developing different strategies and thoughts due to misinterpretation.

Negative inferences from other people's experiences: The following quotation of a participant indicates how the participant refused surgery, and even though they made a wheezing sound when breathing in and out, they did not seek hospital admittance. However, the main issue was that, although the participant expressed that living on medication was better than surgery, she had not taken her medication recently.

> *"Look, our daughter-in-law's father has had open heart surgery, and her mother is already dead after a heart surgery. His father has just had surgery. He came home for a few days, then when he went to the control, they took him back to the intensive care unit. He was in intensive care because his lungs were always collecting water. It is because of this fear that I do not undergo surgery. Better to live with medicines."* (Alin, 78 years old, woman)

Incorrect interpretation of other people's experiences: Sometimes, participants interpreted their symptom experiences with reference to certain circumstances (such as eating more than normal) pertaining to their friends/relatives before dying or having a heart attack. The following quote indicates this type of reasoning:

> *"For example, a man at our university, so he was a teacher, but he went to play football one day. He ate a lot, telling his family he had to move to digest it. Suddenly he went to play football with friends. He just had dinner and then while he was playing, he had a heart attack. He had palpitation. He did not know if his veins were clogged before. What is the heart, what is food, and what is the food good for – does food make a person this way? As a society, we don't know them at all. We don't know, so a little bit more needs to be done. When we are healthy, we do not think about anything."* (Alp, 61 years old, man)

Also, **having more stressors** in daily life was one of the main factors described as increasing breathlessness experiences. Participants with more stressors (including family, job, and other stressors) reported more breathlessness experiences. The following quotations of the participants indicated that feeling stress increased the participant's breathlessness experience. In Example 1, a 36-year-old male participant working as a nurse expressed that work stress and heavy work caused more shortness of breath.

> ***Exemplar 1:*** *"Yes, differences in daily life cause shortness of breath. For example, wearing a mask during the Covid period, work stress and heavy work, and difficult seizures cause shortness of breath."* (Ayhan, 36 years old, man)

Example 2 explains shortness of breath due to family stressors, while Example 3 shows the effects of other stressors (e.g., bad news) on shortness of breath.

> ***Exemplar 2:*** *"If the children fight with each other a little – if they don't listen to you – that's when I lose myself more. Worrying, worrying, and then feeling shortness of your breath"* (Alin, 78 years old, woman)

> ***Exemplar 3:*** *"When I am very sad; I have bad news; I am very tired; I can't sleep, I feel short of breath and my heartbeat is getting faster."* (Cansel, 47 years old, woman)

The sub-theme, Psychological vulnerability, indicated that emotional distress was one of the factors affecting the recognition and appraisal of breathlessness among this population.

7.4.2.2. Physical vulnerability

Heart failure is a factor that increases the relative risk of susceptibility to adverse health outcomes (including infections, pain, fatigue, and further psychical decline). Most participants reported this type of vulnerability due to their heart failure condition. In the following exemplar, a 53-year-old participant expressed that he is susceptible to colds and experiences more coughing during the wintertime. This resulted in more breathlessness.

> *"It [breathlessness] happens a lot in the winter. It happens a lot in the winter because in the winter I get cold and cough a lot. I think it happens when I cough."* (Umut, 53 years old, man)

Another exemplar expressed that multimorbidity increases the risk of having more breathlessness. While this caused much more physical decline, it also increased hospital admissions for the participant.

> *"Both in shortness of breath: The combination of high blood pressure (hypertension), diabetes and heart failure affect me a lot. When all three of them relapse at the same time, they affect me a lot. They [the doctors/nurses] administer oxygen right away."* (Oya, 72 years old, woman)

Many participants expressed that they experienced more shortness of breath when they felt tired. Another exemplar from a 61-year-old man indicated that fatigue/tiredness was one of the factors that increase his breathlessness experiences in heart failure.

> *"For example, you get more tired when you are carrying something. Then you feel short of breath."* (Eymen, 61 years old, man)

Some participants reported that carrying anything in their hands increased their breathlessness. For this reason, activities like shopping, working, and doing housework were a problem for them. Several participants even expressed that choosing thick clothes in winter increases their experience of breathlessness. In the following exemplar, a 45-year-old woman expressed this interconnectivity between breathlessness and clothing.

> *"Now I can say this: we dress in layers in winter. You know. I feel breathlessness is more pronounced in the winter. It's not like that, but after all, we dress in layers, we dress more. In other words, when climbing stairs, we lift that load together. When we think about things. Inevitably, we move with a heavier load. We have boots, we have coats. In other words, if our weight is 70, it would be 80. It may be more of a feeling of shortness of breath, but I guess it's unclear whether I feel it more in winter or in the season itself than wearing more clothes."* (Leyla, 45 years old, woman)

In addition, a few participants expressed that they experienced more breathlessness in winter due to poor weather conditions or polluted air where they live. The following exemplar indicates this from one of the participant's own words.

> *"It happens more in the winter. It happens more in winter; we can't go out. In winter, it is both stale air and cold weather. You can still get some air in the summer. Even if it's summer, I wish we could get some air. Summer is still better for me than winter. I suffer more in winter. Look, we are using a stove now, the bad fumes of that stove, I can't stand them at all. There is the smell of those fumes, I can't stop. I can't stand the smoke and smell of that stove at all."* (Peri, 63 years old, woman)

A few participants reported that they also had breathlessness if they ate more than usual. The participants also indicated that this situation brought many other problems along with breathlessness. Following exemplars indicated this relationship.

> ***Exemplar 1:*** *"There is shortness of breath. So, it's also because of overeating, you have a lot of trouble after eating. ... Yes. It is very difficult to walk after eating. It increases the heartbeat and immediately causes shortness of breath. In addition, it increases sweating in the body too much, as well as increases fatigue and weakness. If I eat a lot, then it becomes a problem when I walk."* (Alp, 61 years old, man)

> ***Exemplar 2:*** *"For example, when my stomach is too full, it becomes a problem. For example, there is a pain in the heart. At that time there is shortness of breath. It is probably pressing when the stomach is full."* (Can, 71 years old, man)

> ***Exemplar 3:*** *"If I work, I feel shortness of breath. I feel it while eating. Especially when I eat a lot."* (Oya, 72 years old, woman)

This sub-theme expressed that the physical vulnerability of heart failure causes people to report more breathlessness. Especially advanced age and the presence of comorbidity were the main reasons for this.

7.4.2.3. Interactions with other symptoms

Most participants reported an interaction between breathlessness and other symptoms, such as fatigue/tiredness, sweating, sleep problems, and anxiety. Especially, sleep problems (difficulty sleeping and feeling drowsy during the day) were one of the most reported impacts of breathlessness. Several participants reported that they thought they might die while they slept. This impaired the quality of their sleep. The combination of those symptoms with breathlessness reduced their quality of life. Participants reported difficulty coping with all symptoms, not just breathlessness, due to their interactions. In the exemplar below, one participant expresses how he experienced breathlessness along with fatigue/tiredness, sweating, swelling, and weakness:

> *"Shortness of breath starts when you get a little tired. Fatigue begins. So, the body becomes weak. There is already excessive sweating. When I sweat excessively, I can't do anything. When you feel short of breath, fatigue turns into exhaustion. A swelling, especially in the area of the heart. I feel a swelling in the area where the pacemaker is."* (Alp, 61 years old, man)

Emotional representations refer to participants' emotional experiences related to breathlessness with heart failure. Although some participants reported generally feeling stressed and anxious when they had a breathlessness experience, some participants focused on their physical and emotional symptoms together. The following quotes demonstrate these symptom interactions in breathlessness.

> ***Exemplar 1 (breathlessness – feeling depressed):*** *"I feel like I'm drowning in shortness of breath. I feel like I am in such a grave that I am very depressed."* (Fulya, 44 years old, woman)
>
> ***Exemplar 2 (breathlessness – tachycardia –anxiety):*** *"During shortness of breath, there is a feeling of passing out, a feeling of fainting, a feeling of suffocation, and an increase in heart rate. There is panic anxiety, you feel crazy."* (Berk, 38 years old, man)

Breathlessness-related distress was one of the main problems for participants. Breathlessness was described as a stressful situation. A few participants described that when they had breathlessness, they experience more stress, which in turn increased the level and intensity of their breathlessness. This affected their daily lives in a kind of vicious circle. In the exemplar below, a 51-year-old woman expressed that she experienced breathlessness when she felt stressed as well.

> *"Shortness of breath is very stressful. My breathing rate increases, and I do not recognise myself. Where am I, what am I doing, I do not know. Significantly when I am stressed, my blood pressure rises, and my breathing becomes short."* (Ela, 51 years old, woman)

This sub-theme highlighted that breathlessness interacts with other symptoms, and that these symptom clusters are different for each individual. Evaluation of the presence of other symptoms in breathlessness would be important in terms of symptom management.

7.4.2.4. Living with uncertainty and fear of death/dying

This sub-theme arose from the participants' concerns about their life with breathlessness in heart failure. Many participants expressed that they worried about "what will happen". Worrying about "what will happen if they experience breathlessness" or "when and how their breathlessness will start" affected their work capacity and social functioning.

Living with an uncertainty future: The uncertainty of when they would experience shortness of breath or when the shortness of breath would worsen created a feeling of being unable to participate in social activities or enjoy life. In the exemplars below, the participants express their worry about what would happen to them and, as a result, their withdrawal from social life. In the following exemplar below, Mert expressed that the uncertainty about his future treatment influenced his life in many ways.

> ***Exemplar 1:*** *"Now you inevitably have a chronic disease. Now you are constantly in trouble; you always have expectations and thoughts about what will happen. Nothing else happens. ... Yes. Totally fearful. That is, you constantly ask yourself, 'I wonder what will happen; will there be any treatment?' I have been receiving treatment for seven years already. I just want to have an operation. They say you have time. They say wait. These are my fears, nothing more."* (Mert, 43 years old, man)

Fulya expressed that she would not leave her home city for vacations or travel because she was worried that something might happen, and she would not be able to get help on time. As a result, she withdrew from her social life.

> ***Exemplar 2:*** *"I can't go alone; I can't go anyway. Even if I go, I am afraid that something will happen in another city."* (Fulya, 44 years old, woman)

Fear of death and dying: Participants describes the feeling of dying and losing themselves, especially during acute episodes. These kinds of thoughts created more stress for the participants and make them uncomfortable. In the following exemplars, the participants expressed their fear/concern of death/dying when they experienced breathlessness.

> ***Exemplar 1:*** *"I immediately think of death. By Allah, when this happens, I immediately think of death. Such a sweat is coming. When I'm short of breath. I rest immediately, take a break, and then continue."* (Asya, 68 years old, woman)

> ***Exemplar 2:*** *"I feel the shortness of breath more. The reason why I say I am going to die is because of it. I'm afraid. There is fear. I'm looking, but I can't say I'm out of breath."* (Canan, 60 years old, woman)

Unwanted intrusive thoughts were unwanted and repetitive at any time and were influenced by their breathlessness experience. Without focusing on the level/degree of breathlessness, some participants explained that some unwanted thoughts came to their minds very quickly when they experienced breathlessness. They noted that due to their previous experience (mostly a history of heart attack), their fear of death and stress levels increased during breathlessness episodes. In the following exemplar, a 45-year-old woman expressed these unwanted thoughts related to breathlessness.

> *"When I feel shortness of breath, I feel like my heart is in my mouth. If at that moment the heart stops for a moment, I think the oxygen will not go to the brain. Here it will be, it will be like this. I mean, because we're studying biology, there are times when these processes work like machines. ... Possible scenarios occur in the minds."* (Leyla, 45 years old, woman)

This sub-theme highlighted the participants expressed their fear and its impacts on their lives in breathlessness.

7.4.2.5. Theme summary

The theme Experience of breathlessness expressed a better understanding of the experience of breathlessness with an in-depth interpretation of individual reality based on participants' emotional and physical phenomena. As explained in this theme, the recognition and interpretation of breathlessness is shaped by individuals' emotional and physical perspectives. Moreover, their previous experiences created more emotional distress. In addition to this, the combination/interactions of breathlessness and other symptoms should be considered for more comprehensive self-management strategies.

7.4.3. Theme 3: Cultural & religious considerations

This main theme included the following sub-themes: Religious life distribution, Belief in Allah (God) & intuition, and Complementary and alternative strategies. The theme highlighted how Turkish people's cultural and religious considerations shaped the way they live and cope with breathlessness in heart failure. Each sub-theme was illustrated by relevant exemplars from the interviews.

First of all, it was necessary to emphasise why this theme was chosen. An already-known fact is that culture is one of the core components affecting individuals' understanding of heart failure and its management (Alassoud et al., 2020). The importance of people's cultural and religious beliefs for symptom experiences and management/treatment strategies is emphasised by other healthcare researchers (Shahin et al., 2019, Noah, 2012, Helvaci et al., 2020). This theme was chosen to highlight the importance of culture and religion in heart failure self-management strategies in Türkiye. It formed the core of how people's religious lives were disrupted by breathlessness and how their beliefs/values helped them cope with their fears/concerns of heart failure. Another reason for choosing this theme was to highlight the importance of developing culture-tailored interventions for more achievable and comprehensive care and self-management strategies in heart failure. It should be noted that personal reality (including the subjectivity of symptom experiences) has a distinctive aspect shaped by culture, religion, and environmental factors. Therefore, the understanding of the role of cultural and religious considerations in heart failure symptoms was highlighted here.

7.4.3.1. Religious life distribution

Participants' religious needs such as praying five times a day, fasting, and attending mosque were interrupted in their lives because of the breathlessness they experienced. Such disruptions of religious life were emphasised especially by those who prioritise their religious life.

In the following exemplar, a 72-year-old woman expressed that she had more breathlessness experiences during her prayer time. Although there are sectarian differences in Islam, people living in Türkiye generally adhere to one of the four main sects of Islam, all of which require prayer five times a day. For this reason, she was suffering from breathlessness while praying five times a day.

> *"It's happening constantly. That is, when I pray, while bowing, where I pray. By Allah, it happens a lot while praying. I can't read everything silently inside of me. I can't read inside myself, I read everything out loud. So, if I read silently, I can't breathe. ... Exactly, I get better when I read aloud. They say only you can hear your voice; They say don't pray out loud. But I can't do that either, I have to read every prayer aloud."* (Oya, 72 years old, woman)

Another example is from a 71-year-old man who had breathlessness during and after prayers, because he moved very fast to catch the prayer times for a very short distance to the mosque.

> *"I said to my daughter, 'Take the car and go home'. Now, in the meantime, the distance between the mosque and me is only 30–40 meters. In the meantime, I looked like I'm going to be late for prayer, so I started running. Now I have arrived there, but until the end of the prayer, my heart rate and shortness of breath affected and disturbed me a lot. And that situation continued for two hours."* (Can, 71 years old, man)

This sub-theme, Religious life disruption, represented the way in which religious observances are affected by breathlessness in heart failure. As exemplified above, such considerations pertaining to the disruption of religious life distribution were more commonly expressed by older individuals.

7.4.3.2. Belief in Allah (God) and intuition

Belief in Allah (God) and intuition was one of the personal resources that individuals used to help them to manage their fear/concern about death and dying due to acute episodes of breathlessness in heart failure. In the following exemplars, two male participants express that their belief in Allah helped them to find a way to deal with their fear or negative emotions. This belief in Allah was especially effective in helping him achieve acceptance of death.

> ***Exemplar 1:*** *"God will protect you; nothing will happen. Ask my son why he is alive. He says he lives because he is religious. However, I am an ignorant man. You said I got the word from you; he said I got the word from him. If you have your religion, Allah will take care of you."* (Ali, 83 years old, man)

> ***Exemplar 2:*** *"I have no fear, thank Allah. Allah gave me this life. We are entrusted with the life that Allah has given us, so whenever Allah wants, Allah takes it. Besides, we have no such trouble or fear."* (Eymen, 61 years old, man)

Some participants expressed that their previous experiences (heart attack and pulmonary oedema) had caused them to focus more on their belief and religious observances. The following exemplar supports this experience, describing one of the coping mechanisms that the participant used to accept his situation and feel more secure.

> *"Now, thank Allah I passed that thing. I'm not that stressed. Even when I had a heart attack, the doctors said that I would not reach another city [for treatment]. Even though they say so, I believe this, because it is in our belief. I said that everyone will go one day, so that's my risk too. I didn't feel anything else. So, I accepted this situation. But when I had a heart attack, this thing happened: now my faith in Allah has increased a little more. Now, before this, I couldn't necessarily think like that. Now, even in the slightest trouble, the situation of going to the side of life is close. Inevitably, people do their prayers more. You take more care. It's such things. I'm saying, thank Allah, I don't have any problems in that respect."* (Can, 71 years old, man)

This sub-theme, Belief in God (Allah) and intuition, represented how people's belief in Allah helped them to cope with their fear of death/dying and other negative emotions.

7.4.3. Complementary and alternative strategies

Participants reported seeking an alternative way to reduce their shortness of breath by relaxing their bodies or de-stressing. These measures supported people in Türkiye to evaluate shortness of breath on a more emotional dimension. Therefore, they reported that shortness of breath was not primarily a physical problem for them, but rather an emotional concern, possibly due to their cultural beliefs/perspectives. In the following exemplar, a 36-year-old man expressed that he tried herbal tea to deal with his breathlessness. However, he did not see any benefits after a while and then gave up.

> *"Yes, I tried these for a while. It looks to be addictive after a while, but I have given up on it anyway. So, I tried things like Melissa tea and anise. For sure these are good. I would say psychological. But then it does not work."* (Ayhan, 36 years old, man)

Another exemplar mentioned below represented that the participant's doctor and friends also suggested some alternative strategies for managing his breathlessness. The participant specified that he tried these suggestions and continued to use them according to their effects.

> *"Friends brought something for shortness of breath, but I did not see any benefit. I don't know what they call it – a pinecone, they brought something like that. No, I did not see any benefit. No, the doctor told me to drink something ... he said to make hawthorn leaf tea and drink a glass or two. I used to drink at first, but now I don't. Maybe I'd better start back at him. I mean, it helps a little bit."* (Eymen, 61 years old, man)

The sub-theme Complementary and alternative strategies represented the ways participants tried alternative strategies for coping with breathlessness. This underlined the need for an evidence-based educational intervention in Türkiye.

7.4.3.4. Theme summary

The theme Cultural and religious consideration highlighted the importance of understanding cultural and religious belief/values of participants in heart failure symptom experiences. Breathlessness, one of the typical heart failure symptoms, affects Turkish people's religious life; and management of it is also affected by cultural and religious beliefs. Although religious consideration provided a means for people to cope with their emotional distress, alternative strategies used by people represented the ineffective aspect of heart failure symptom education and care in Türkiye.

7.4.4. Theme 4: Psychological strategies for managing breathlessness

After recognising and evaluating breathlessness, participants reacted to it through management strategies to reduce their breathlessness experience. These include pharmacological or non-pharmacological strategies (Asano et al., 2021).

This theme Breathlessness self-management strategies/psychological arose from participant quotes, and this study's third question, to understand how people manage their breathlessness psychologically at home. The theme included the following three sub-themes: Self-affirmation; Avoiding interaction with others; and Engaging with hobbies. These are explained in this section, along with relevant exemplars from the interviews.

7.4.4.1. Self-affirmation

Participants used self-affirmation to help them overcome their negative thoughts and mitigate the effects of stress to get better. Particularly, the participants who thought they could manage their breathlessness by themselves expressed they could easily cope with it. This type of positive thinking increased their mood and motivation to deal with their breathlessness. In the following exemplar, a participant expresses her self-affirmation to increase her well-being.

> *"For example, if I have a little argument with my husband – my everything at once: my heart, my brain. Do you understand? In other words, all my organs seem to be directly affected. So that's how I feel. But let's say when I experience something beautiful, my body feels everything – so it's like I feel that thing down to all my cells. So, it seems to me. That is why I want to go on the path of affirmation in my social life, my business life, and in my home life. I'm looking in that direction for myself."* (Leyla, 45 years old, woman)

7.4.4.2. Avoiding undesirable situations

Coping with the emotional burden of breathlessness experience was crucial for some participants. Because of the interaction of shortness of breath and stress, they tried to avoid unpredictable situations in their daily lives that increased their shortness of breath and stress levels. Therefore, they reported that they did not want to interact with others or pay attention to other things. However, this created self-isolation for them, because they do not want to see or talk with other people. In the exemplar below, this situation was expressed by a participant.

> *"So now, when someone says something to you, your whole mood breaks down; you're getting angry. That's why it's better. Something is said, I immediately get angry. As soon as I get bored, I'm not going anywhere. I'm looking at my jobs at home. If I can do my job, I do it. If I can't, I go to bed. If I can't lie down, I sit. Here's what I do."* (Peri, 63 years old, woman)

7.4.4.3. Engaging with hobbies

Having hobbies such as gardening helps participants to get involved in life. These activities distract their attention from their illness and positively affect the way they look at themselves. Having a hobby, in particular, has helped people get away from diseases by thinking about other things. In addition to this, their hobbies helped them participate in life. The following exemplars illustrated this. In the exemplars below, two participants over the age of 70 expressed that working or spending time in their garden helped them feel better.

> ***Exemplar 1:*** *"Now my children said to me, 'Mom doesn't do anything, Mom doesn't work, Mom doesn't do it like that, no, Mom doesn't do that.' But they don't know you listen to yourself as you sit, it's much worse when you listen to yourself. Look, I said to my husband, 'Get up, we'll go to the garden slowly. Maybe we can't dig, but we'll slowly clear the grass where we sit.' I said, 'Look, this is our garden. What can we do? We are working slowly. Here's what to do.', I'm like that too."* (Alin, 78 years old, woman)

> ***Exemplar 2:*** *"For example, some of my friends say that I am sick, but I do not consider myself sick. For example, I feel good right now. I go to XX city every week and come back. Our friends are sitting all the time because they have a heart condition. They have this thought. I don't have it, thank goodness. This is how I do my own small business. Now, for example, I work in the garden. Of course, I don't work with a pickaxe. Because digging is uncomfortable when working with a shovel. But when I work with the waist shovel, it is good. Now I make a garden, I plant in the ground there, here I plant vegetables. Now, when I deal with these slowly, it doesn't do anything to me. Then I feel better."* (Can, 71 years old, man)

7.4.4.4. Theme summary

The theme, Breathlessness self-management strategies/psychological, expressed how people tried to manage their breathlessness from their emotional perspective. This highlighted that people used different emotional coping strategies. Some tried to find a hobby to deal with their situation, while others avoided interacting with others to reduce their life stressors. This expresses that each individual has different emotional coping strategies based on their preferences and thinking. Considering this, more effective self-management strategies can be planned according to individual preferences and values in Türkiye.

7.4.5. Theme 5: Physical strategies for managing breathlessness

This theme, Breathlessness self-management strategies/physical, arose from participant quotes and this study's third question to understand how people manage their breathlessness psychically at home. The theme included the following three sub-themes: Reliant on only their doctors; Inputs from significant others; and Maintaining normality. These are explained in the following, along with exemplars.

7.4.5.1. Reliant on only their doctors

Many participants stated that they only followed what their doctor said (including prescribed medications and slowing down and resting). Many participants reported they used medications because the doctor said they would use them until they died. They experienced less shortness of breath because they used these meds regularly. The exemplar below shows a participant expressing that she only uses her medications prescribed by doctors.

> *"I take the medicines every doctor gives. The doctor ... prescribed the medicine. I said, 'For how long will I take this?' ... He says, 'You will take this medicine until you die, you have to take it'."* (Oya, 72 years old, woman)

7.4.5.2. Inputs from significant others

Input from significant others (including family members/friends) helped encourage their treatment and socialisation. In particular, the support of family members was important in managing symptoms. Many participants stated that their family members (including their children, spouses, and partners of their children) helped them at this stage. This support is clearly seen in the exemplars below.

> ***Exemplar 1:*** *"She is the best nurse for me. Because, when the time comes for my medicine, even when my wife is cooking or eating, she immediately reminds me that it's time for medicine. She says, 'Come on, it's time for the medicine.' She says, 'Take your medicine.' She says, 'These will be later, your medicines first. But if you fall, you cannot get up'."* (Ali, 83 years old, man)

> ***Exemplar 2:*** *"Better to live with meds. I say I take my medication; I don't tire myself out, thanks to my children, they support me every time."* (Alin, 78 years old, woman)

> ***Exemplar 3:*** *"My daughter-in-law took good care of me, I won't lie. That's how she looked after me like a child. I was like her kid."* (Canan, 60 years old, woman)

7.4.5.3. Maintaining normality

Maintaining normality was one of the core strategies for the participants. Especially in terms of the continuity of individual identity, people tried to continue their normal life as much as possible. This emphasised the participants' need to be valuable in life. For this reason, many have developed various strategies based on their physical limitations to continue their normal lives.

Preserving normality by doing things at a slower pace – Avoiding activities: Participants explained they would "slow down" or "avoid activities" to reduce the risk of feeling breathlessness. This is one of the most frequently used coping strategies for breathlessness by participants. Almost all of the participants expressed that they did their work slowly. The following exemplar supported this explanation.

> *"Secondly, I'm also doing something – while doing a job slowly, calmly, but I don't want to do this quickly so that it ends. I do all my work slowly, because when I try to do it fast, then ... shortness of breath begins, and I am affected."* (Onur, 46 years old, man)

Another physical self-management strategy for maintaining normality was avoiding activities that triggered their breathlessness. Some participants explained that doing sports (like swimming, jogging etc.) triggered their breathlessness. Therefore, they avoided this kind of activity in their daily life to reduce their breathlessness. In the exemplars below, the participants reported that they avoided doing some specific activity because they did not want to experience breathing difficulties later.

> ***Exemplar 1:*** *"I mean, there's a problem. So, you inevitably get nervous when you go into the sea. You can't stay in the sea for long. The sea is a little tiring. When you are*

> *tired, you have shortness of breath. Then shortness of breath is also experiencing body fatigue. That's why when I was last at the summer house, I couldn't stay in the sea long."* (Alp, 61 years old, man)

> **Exemplar 2:** *"Jogging. ... Things like that. After I was diagnosed. You know, I – humans inevitably pull back a little. You know, as one doesn't want to do anything wrong. Even if it's a sport. Because that's the heart side. I have a problem. For it. You know, mostly during walking, when I look at it, when I feel it while walking, I slow down directly. For example, when I go for a walk with my husband ... his strides are longer ... I try to catch up with him – then I say, 'Slow down a bit.' I feel it if I'm walking briskly."* (Leyla, 45 years old, woman)

Adjusting new strategies to the new normal (based on their limitations): Some participants reported that they took an action to reduce their breathlessness experiences, including adjusting new strategies to deal with their breathlessness. They were developing new strategies to continue their daily lives. In the following exemplar, a 78-year-old woman expressed that she used more pillows to reduce breathlessness when she slept.

> *"I can't sleep on my back. I have to use two pillows. I even put it aside for a while, at least I get up and sit down. Sometimes I get up and pray at night. I sit for a while, and when morning comes, I say, 'Thank Allah, it's morning.' It's good when I get some sleep, but I can't get enough sleep."* (Alin, 78 years old, woman)

7.4.5.4. Theme summary

The theme Breathlessness self-management strategies/physical expressed that participants tried to continue their daily life by implementing physical self-management strategies to reduce breathlessness. These strategies were especially important in terms of preserving the identity of the participants and maintaining their independence.

7.4.6. Theme 6: Prerequisites to improved health behaviours

This theme identified what individuals need to improve their health behaviours in respect of what is not provided by the current (routine) heart failure care in Türkiye. Four sub-themes included in this main theme were based on the participants' suggestions and study findings: Adequate education; Psychological support; Long-term evidence-based interventions; and Appropriate follow-up techniques.

7.4.6.1. Adequate education

Participants expressed a desire for more knowledge and awareness of heart failure and management strategies. As mentioned earlier, most participants reported that they had not received any information about their breathlessness experiences and management strategies, but also about the heart failure condition itself. To optimise their health and well-being, there is a need to raise awareness and information about heart failure and its symptoms among individuals with heart failure, their family members, and the community.

Participants often learned about heart failure through real-life experiences (especially after a heart attack). Knowledge and awareness of heart failure were mostly only for diagnostic terminology. Participants describe their need for adequate training/education for heart failure.

> *"For example, I didn't know anything about the heart until I experienced it. I learned it because I lived it. In other words, if an information education had been given, maybe some things would have been noticed earlier. We would be cautious. You realise that, but there is no such training. No, I have not come across such education or information about the disease being given in any of the hospitals."* (Alp, 61 years old, man)

> *"They say ..., 'It will be better for you if you use this while doing it; it would be better if you do this; you should not do this.' If they say, 'You better do this,' it would be better to enlighten us .... I think it is better to give such broad information. I think it would be better if they enlightened us, but as I said, none of them enlightened us."* (Onur, 46 years old, man)

> *"For example, we have a family doctor, and while I understand they can get a bit tired, I would really appreciate receiving weekly diet advice or something similar to stay more engaged. It would be great if the doctor could provide guidance such as "eat this this month" or "consume unsalted foods" or "eat more fruit." I'd love for them to give such advice. However, our family physicians don't seem to offer much in the way of proactive guidance (laughs). Generally, such training isn't provided. For instance, when I visit my family doctor, they ask about my complaints and what I need, then just prescribe the medication. They write the prescription right away. I would really like them to take a more active role in my health, especially by providing education on what to eat for heart failure and cancer patients."* (Fulya, 44 years old, woman)

7.4.6.2. Psychological support

Most participants (men and women, with a predominance among those slightly younger) expressed their need for psychological support in heart failure. They need psychological support at the beginning of their diagnosis, highlighting the continuity and motivation of heart failure care in Türkiye.

> *"I have shortness of breath. I think I should choose to participate in life instead of saying, 'Yes, I have shortness of breath,' and sitting on the side-lines. So, it's all in your head. So, psychology is the most important factor that affects everything. ... As I said, it might be a little more psychological. ... we can be referred directly to psychologists because we have heart disease. ... Yes, psychological support is very important. The heart is a sensitive organ – that is, our emotions, and our pain. In other words, it comes from the heart when I am unhappy, and it comes from the heart when I am happy. That's why you have to make it happy. I think like this."* (Leyla, 45 years old, man)

A few participants expressed a need for psychological and family support members in heart failure. This highlighted the importance of inclusion of their family members in their education and decision-making for heart failure self-care strategies.

> *"Emotionally, this dimension does not received enough attention because health professionals work hard. Supporting family members is not enough."* (Ayhan, 36 years old, man)

7.4.6.3. Long-term management strategies

Participants often described living with heart failure as something that lasts a lifetime rather than a very short time. They emphasised the need for relevant and appropriate follow-up care in heart failure. They wanted to ensure their treatment (mostly related to the medications they were using) was done correctly. In particular, this was linked to long-term management strategies in heart failure.

> ***Exemplar 1:*** *"There must be a set schedule, of course—everything is digital these days. But how many of us actually use these reminders or digital tools? And how many of us still use notebooks? How many of us stick to these methods of self-management? For this reason, I think my doctor should take on a more active role in managing my schedule, rather than relying on me to keep track. For instance, when I see my doctor, she might say, "I'm scheduling an appointment for you in six months'*

> *time." A week before the appointment, I would receive a reminder message, so I can adjust my work accordingly. This is a common practice for many people. For example, when going for a medical examination, it helps to have such reminders to ensure everything is managed smoothly … as I said, follow-up is very important."* (Leyla, 45 years old, woman)
>
> ***Exemplar 2:*** *"I have nothing to recommend to those who have shortness of breath and those who experience these symptoms. Since my condition is due to heart failure, it is not caused by asthma, allergies, lung problems or psychological reasons, it should be examined and treated for the cause."* (Ayhan, 36 years old, man)

7.4.6.4. Theme summary

The theme Improved health behaviours represented the importance of an urgent symptom assessment strategy (including well-established education about heart failure and culture-tailored evidence-based management strategies) in Türkiye.

7.5. Strengths and limitations

This study investigated how Turkish individuals who self-reported heart failure experienced breathlessness, how it affected them, and what self-management strategies they used. The findings indicated that cultural and behavioural factors in Türkiye played a significant role in shaping each person's unique experience of breathlessness.

It is important to acknowledge certain limitations in this study when interpreting the results. Firstly, this research focused on individuals who self-reported heart failure. Secondly, the participants were primarily from the southeast region of Türkiye, one of the country's seven geographic regions. This means that individuals from other parts of Türkiye might have different experiences and self-management approaches due to varying socio-cultural and behavioural contexts. In terms of ethnic diversity, the majority of those involved in this study had Turkish ancestry, with only one participant of Arab descent and three of Kurdish descent. Therefore, the findings may not fully represent the experiences of minority groups in Türkiye. Additionally, this study lacked representation of younger individuals, as there was only one participant aged 18, limiting the generalisability of our results to those between 18 and 30 years old with heart failure. Furthermore, given that the study involves 20 participants, it provides sufficient information power to ensure meaningful and reliable insights, offering a comprehensive understanding of the diverse individual differences in breathlessness experiences and self-management strategies. Despite these limitations, this study offers valuable insights into how individuals in the Turkish socio-cultural and behavioural context uniquely experience breathlessness and manage their condition.

7.6. Overall summary and conclusion

This chapter provided information about the findings of the descriptive qualitative study of Turkish people with self-reported heart failure. These findings demonstrated that the individual reality of subjective breathlessness experience was affected by socio-cultural-behavioural factors in heart failure. However, increasing "knowledge and awareness about breathlessness (and heart failure)" is the core concept for improving individuals' health behaviours in Türkiye. Without a good understanding of their heart failure spectrum, the other components of effective heart failure self-care (including recognition, reporting, monitoring, and management of their symptoms) could not be possible among Turkish people with heart failure. Overall, these findings highlighted the importance of the urgent need for nurse-led educational intervention for this population in Türkiye (please see **Box 7-1** for a summary of the research in context).

The next chapter presents the interpretation of the three studies of this PhD research: the mixed-methods systematic review, secondary data analysis, and descriptive qualitative study. The overarching key findings of these studies are provided and discussed in the next chapter.

Box 7-1: Personal experiences of Turkish individuals living with heart failure - research in context

Evidence before this study

Heart failure affects over 2.5 million individuals in Turkey. Compared to other Western countries, Turkish heart failure contexts are different in terms of risk patterns, more women, and younger age populations. Within the Turkish population, individuals with heart failure have reported a range of symptoms, mainly breathlessness, fatigue, ankle swelling, palpitations, and dizziness. Breathlessness is the most commonly observed symptom (in the mixed-method systematic review and secondary data analysis). Although understanding the subjective symptom experiences is the key for self-management strategies, there is insufficient research on the phenomenon of breathlessness among Turkish individuals with heart failure.

The main purpose of this descriptive qualitative study is to explore the experiences of Turkish individuals with heart failure, with a specific focus on elucidating their subjective descriptions of breathlessness and self-management strategies with respect to their socio-cultural-behavioural context.

A descriptive qualitative approach was carried out, underpinned by the Situation-Specific Theory of Heart Failure Self-care. Semi-structured one-on-one interviews were conducted with 20 Turkish individuals with self-reported heart failure. Reflexive thematic analysis was used to analyse the transcripts of interviews.

Contribution of this study

This study's findings indicated that breathlessness and self-management strategies are affected by individual perspectives in relation to their socio-cultural-behavioural context. The study participants reported 31 physical and 7 psycho-social-behavioural symptoms apart from breathlessness experiences. Based on reflexive thematic analysis of semi-structured interviews, six main themes were identified. Among them, knowledge and awareness of heart failure and breathlessness were poor. Experience of breathlessness was mostly related to their psychological and physical vulnerability perspective. The importance of cultural and religious perspectives on breathlessness, related to the Turkish socio-cultural-behavioural context, was also highlighted by them. There were physical and psychological breathlessness self-management strategies regarding their interpretation of their symptom experience. They needed more education, psychological support, and long-term evidence-based strategies in heart failure.

Implications of all the available evidence

This study explored heart failure-associated breathlessness in the Turkish socio-cultural-behavioural context, which has been never explored in the literature. Increasing "knowledge and awareness about breathlessness (and heart failure)" is the core concept for improving individuals' health behaviours in Turkey. Without a good understanding of their heart failure spectrum, effective heart failure self-care (including recognition, reporting, monitoring, and management of their symptoms) may not be possible. These findings highlight the urgent need for nurse-led educational intervention (tailored to Turkish culture) and heart failure specialist nurses to support this target population. Education should be personalised through good communication skills and the development of individualised advanced care plans, including specific recommendations to reduce each symptom (e.g., breathlessness), which help to improve health outcomes.

This study explored heart failure-associated breathlessness in the Turkish socio-cultural-behavioural context and indicated the uniqueness of each breathlessness based on their perspective. Therefore, more research is needed to explore differences in the full spectrum of symptoms with respect to the social-cultural-behavioural context.

From a research perspective, understanding individuals' unique breathlessness experiences with reference to their socio-cultural-behavioural context assists in the possible identification of individualised care strategies to reduce this symptom experience.

Chapter Eight - Overall discussion

8.1. Introduction

There is a need for research exploring and understanding the full spectrum of symptoms experienced by those living with heart failure, including people from diverse cultures (such as Türkiye) and individuals previously under-represented (e.g., women, those with HFpEF, and older age individuals). The primary aim of this PhD thesis, including three sequential research studies, was underpinned by two key research questions: *What is the full spectrum of symptoms experienced by people with heart failure?* and *Does an individual with heart failure experience the same symptoms regardless of any differences in their socio-demographic and clinical profile (including biological sex, age, heart failure subtypes, and Turkish culture)?*

The previous three chapters (5, 6, and 7) have presented the findings of three sequential research studies across the selected research methods. In this chapter, firstly, the overarching key findings with an overview of the studies is presented. This chapter provides a discussion and interpretation of the overarching key findings in a relation to previous literature and the importance and relevance of understanding and awareness of comprehensive and systematic symptom assessment in heart failure. The strengths and limitations of each research component described in this thesis are also discussed, and an overview of the next step in this research trajectory is discussed. Finally, the contribution of this research, in terms of knowledge gain and relevance to both future research and clinical practice to improve health outcomes, are presented and discussed.

Table 8-1: Main and novel findings related to each study research questions

Research questions	Main and novel findings
MIXED-METHODS SYSTEMATIC REVIEW	
Primary RQ: ***What is the full spectrum of symptoms experienced by people with heart failure?***	Main finding 1: There is a diverse range of symptoms experienced by people with heart failure. Current ESC HF clinical management guidelines do not represent the symptom profiles of individuals with heart failure. Current clinical practice guidelines should more fully consider the full spectrum of symptoms experienced by those affected in different phases of their journey with heart failure. This highlighted the need for more comprehensive and systematic symptom assessment in heart failure. Main finding 2: Two factors (age and setting) influence the symptom experiences of individuals. This highlighted the need for a more comprehensive symptom assessment that included factor assessment for each individual.
Sub-Q1: Were there symptoms of heart failure that were not listed in the ESC Guidelines? How common were these?	*37 non-ESC symptoms were identified (i.e., not listed in the ESC heart failure Guidelines).* *Some non-ESC symptoms were more common than some ESC (typical/less typical) symptoms.*
Sub-Q2: How common were typical and less typical symptoms listed in the ESC Guidelines for heart failure?	*Some ESC less typical symptoms were more common than some typical symptoms.*
Sub-Q3: Did ESC-defined typical and less typical symptoms vary from community to hospital?	*ESC typical and less typical symptoms were different with respect to setting.*
Sub-Q4: How does age affect ESC typical and less typical symptoms?	*ESC typical and less typical symptoms were different in <65 years old and ≥65 year old groups.*
Sub-Q5: How does sex affect ESC typical and less typical symptoms?	*More research is needed to explore sex-specific differences in this regard. – This is the main reason why sample groups of secondary data analysis were chosen.*
SECONDARY DATA ANALYSIS	
Primary RQ(s): ***How do symptoms of heart failure differ between men and women, with respect to biological sex and heart failure types?*** ***How do these symptoms change in the 12 months following a hospital admission in men and women, with respect to heart failure subtypes?***	Biological sex and LVEF-based heart failure subtypes were associated factors with different symptom experiences in heart failure. There were sex-stratified differences in symptoms with respect to heart failure subtypes in heart failure.

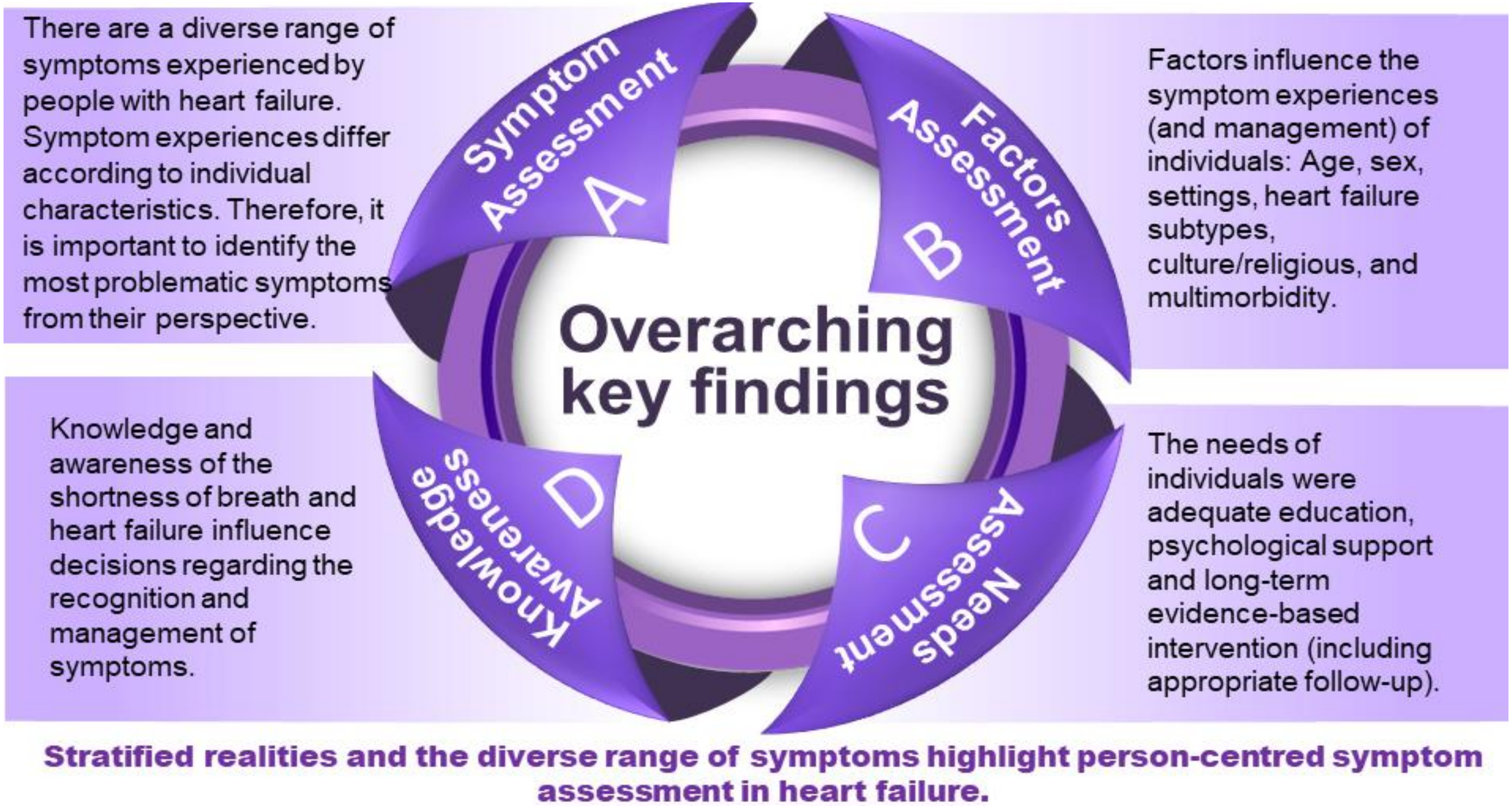
Sub-Q1: What are sex-stratified differences in symptom changes over one year associated with heart failure with respect to LVEF-based heart failure subtypes?	*There were sex-stratified differences in symptoms and symptom changes over one year according to the phenotypes of heart failure based on LVEF.* *Women and men with HFpEF had higher symptom burdens than those with HFrEF and HFmrEF.* *In women and men, different factors were associated with KCCQ symptom stability score changes over one year.*
Sub-Q2: What are the baseline predictors of worsening heart failure symptoms in men and women separately?	*Regarding the KCCQ symptom stability score, women and men had different correlators associated with long-term worsening heart failure symptoms.*
DESCRIPTIVE QUALITATIVE STUDY	
Primary RQ(s): ***How is breathlessness described from a patient perspective in Türkiye?*** ***What symptoms are experienced by Turkish individuals with heart failure?***	The findings indicated that the individual reality of subjective breathlessness experience was affected by socio-cultural-behavioural factors in heart failure. Increasing “knowledge and awareness about breathlessness (and heart failure)” is the core concept for improving individuals’ health behaviours in Türkiye. Individuals with a lack of knowledge and awareness about breathlessness and heart failure made inconsistent decisions about the recognition and management of their symptoms.
Sub-Q1: What are the impacts/consequences of breathlessness on daily life and health for people with heart failure in Türkiye?	*Physical (higher in people with multimorbidity and advanced age) and emotional (stress and anxiety) vulnerability was one of the factors that affected the experience and management of breathlessness.* *Environmental factors (linked with physical vulnerability) were effective in the interpretation of breathlessness.*
Sub-Q2: What symptoms are experienced by Turkish individuals with heart failure?	*There were various symptoms reported by Turkish individuals with self-reported heart failure.*
Sub-Q3: How do they manage their breathlessness?	*Breathlessness self-management (including both physical and psychological) was strongly associated with the following factors: knowledge of breathlessness; the way you experience and describe it; having sufficient ability to cope; and preferring coping mechanisms.* *Individuals’ previous experience was one of the recognition factors for reporting their experience of shortness of breath and continuing self-management strategies.* *They tried to cope with shortness of breath by developing strategies in emotional and physical dimensions.*
Sub-Q4: What are the health needs of individuals with heart failure in Türkiye?	*The needs of individuals for improved health behaviours in Türkiye were adequate education, psychological support, and long-term evidence-based intervention (including appropriate follow-up).*

8.2. Overarching key findings of this PhD research

Person-centred, comprehensive, and systematic symptom assessment are needed for the identification of appropriate management strategies.

This PhD thesis presents three individual but related studies. Firstly, a mixed-methods systematic review investigated the full spectrum of symptoms experienced by people with heart failure, and ESC typical and less typical symptom changes with respect to settings, age, and sex, as presented in Chapter 5. Following this, a secondary analysis of the data from the WHICH?II Trial examined sex-stratified differences in symptom and symptom changes with respect to LVEF-based heart failure phenotypes, as presented in Chapter 6. Thirdly, a descriptive qualitative study investigated the breathlessness experiences (along with other symptoms) and management strategies and needs of 20 individuals with self-reported heart failure in Türkiye, as presented in Chapter 7. **Table 8-1** presents the main and novel findings of each study of this PhD research.

Based on the results of three studies' findings, the overarching findings from the integrated programme of research described within this thesis are presented in **Table 8-1**. The summary of ***the overarching key findings of this PhD project*** **(Figure 8-1)** are as follows. There is a diverse range of symptoms experienced by individuals with heart failure – highlighting the need to ***"understand the full spectrum of symptoms"***. These symptoms differed according to individual characteristics, which highlights ***"stratified realities; complexity, unfamiliarity and unprioritised with symptoms"*** among this population. Knowledge and awareness of the condition/symptoms influence decisions regarding the recognition and management of symptoms. The importance of ***"knowledge and awareness about heart failure and symptoms"*** was associated with early detection of symptoms. Turkish individuals with self-reported heart failure expressed that heart failure is a long-term life condition and therefore needs long-term care as their ***"needs for improved health behaviours"***. Stratified realities and the diverse range of symptoms provide a need for "***the core concept: person-centred symptom assessment in heart failure"***. (Please see **Appendix 10** for further details on overarching key findings derived from three studies.)



There are a diverse range of symptoms experienced by people with heart failure. Symptom experiences differ according to individual characteristics. Therefore, it is important to identify the most problematic symptoms from their perspective.

Factors influence the symptom experiences (and management) of individuals: Age, sex, settings, heart failure subtypes, culture/religious, and multimorbidity.

Knowledge and awareness of the shortness of breath and heart failure influence decisions regarding the recognition and management of symptoms.

The needs of individuals were adequate education, psychological support and long-term evidence-based intervention (including appropriate follow-up).

Stratified realities and the diverse range of symptoms highlight person-centred symptom assessment in heart failure.

Figure 8-1: The overarching key findings of this PhD research

Table 8-2: Symptoms from three studies

	20 Turkish individuals	WHICH?II clinical trial	MMSR
Typical symptoms	Breathlessness (including at rest) Reduced exercise tolerance Orthopnoea Paroxysmal nocturnal dyspnoea Fatigue, tiredness Swelling of arms or legs	Shortness of breath Fatigue Bilateral ankle oedema Orthopnoea Paroxysmal nocturnal dyspnoea	Breathlessness (including at rest) Orthopnoea Paroxysmal nocturnal dyspnoea Reduced exercise tolerance (including breathless with activity/walking) Fatigue/ tiredness / increased time to recover after exercise Ankle swelling (including swelling of lower extremities)/ General oedema
Less typical symptom	Lack of appetite Dizziness Feeling bloated Palpitations (irregular heartbeat, rapid heartbeat) Wheezing Bendopnea Passing out Depression	Nocturnal cough Depressive symptoms	Nocturnal cough/ cough Wheezing Bloated feeling Loss of appetite (including anorexia) Confusion Feeling depressed Palpitations (irregular/ fluttering/ faster heartbeat) Dizziness/ light-headedness/ giddiness Syncope (passing out/ fainting) Bendopnea
Non-ESC symptoms (Other Symptoms)	Lack of energy Weakness Dry mouth Sweats Problem with urination Constipation Feeling drowsy Numbness/ tingling hand/ feet Pain (other bodily – back pain etc.) Chest pain Headache Nausea/ vomiting Weight loss Weight gain Difficulty sleeping Chest pressure/tightness **Shaking (body/ hands)** **Restlessness** Poor mobility/ walking problems Hair loss **Bruises easily** Fear (about death/ dying) Stress Worry Feeling anxious/ nervous **Concern about the uncertainty of future** Negative emotions (Disturbing thoughts, Loss of interest in life, Unhappy, Sad, Angry, Scared, Boredom/ bored, Limited socialisation)	Pain/ discomfort Sleeping problems due to orthopnoea Walking problems	Lack of energy Weakness **Need more rest during the day** Excessive weight gain Chest pain/ discomfort Pain (general and other bodily pain (not chest pain)) Difficulty sleeping (including due to orthopnoea and other sleeping problems) Feeling drowsy **Difficulty concentrating/ forgetfulness** **Loss of balance/ falling** Gastrointestinal (**Changes in the way food tastes**; Nausea/ vomiting/ indigestion; Weight loss; Constipation; **Diarrhoea;** **Food cravings/ Eating more**) Dry mouth **Mouth sores** **Difficulty swallowing** Sweats **Itching** **Problem with sexual interest/ activity** Numbness or tingling in hands/ feet Problem with urination **Muscle spasm/ cramps** Hair loss **Changes in skin** **Visual disturbance** Walking problems Feeling anxious/ nervous Feeling isolated & lonely Fear Worrying Negative emotions (Feeling sad, irritable, guilt, gloomy, unworthy, stigma, sorry, etc.)

8.2.1. Understanding the full spectrum of symptoms experienced by individuals with heart failure

Even in the absence of typical heart failure symptoms, it is important not to overlook the presence of other symptoms experienced by individuals.

As summarised in **Table 8-2**, there was a range of symptoms identified via the integrated programme of research described in this thesis. Compared to the clinical cohort symptoms assessed in the WHICH?II Trial, the full spectrum of symptoms identified from previous literature and individual perspectives was more diverse. The percentage of some non-ESC symptoms identified in the mixed-methods systematic review was also higher than typical and less typical symptoms listed in the current ESC Guidelines (McDonagh et al., 2021). If we consider individual symptom profiles and percentages, we also need to consider why these symptoms are not listed in the guidelines. Symptom-based treatments and research usually focus on the symptoms listed in the guidelines. Therefore, highlighting the assessment of the full spectrum of symptoms will be important in heart failure.

In a systematic review by Teunissen et al. (2007), 37 different symptoms were identified among individuals with cancer, fewer than the number of symptoms we identified among people with heart failure. Among these 37 symptoms, five (fatigue, pain, lack of energy, weakness, appetite loss) were experienced by over 50% of the participants (number of studies=40, total participants=25,074). When compared to cancer patients in the last one or two weeks of life (number of studies=6, total participants=2,219), four symptoms (fatigue, weight loss, weakness, and appetite loss) out of 24 were experienced by over 50% of them (Teunissen et al., 2007). However, in our review, 13 symptoms were experienced by over 50% of the general heart failure population. Although the samples and sizes of the studies varied, the evidence here emphasises the importance of person-centred symptom assessment, as well as the significance of palliative care for individuals living with heart failure.

Compared to the WHICH?II clinical trial, more symptoms were identified from existing literature and the Turkish individual perspective. Recent clinical guidelines/reports (McDonagh et al., 2021, Hollenberg et al., 2019, Lindenfeld et al., 2010, Tsutsui et al., 2019, SIGN, 2016) focus on heart failure-specific symptoms, which do not address the symptoms associated with comorbidity/multimorbidity in heart failure. Non-heart failure-specific symptoms are strongly associated with non-heart failure-related hospital admission (Khan et al., 2015, Davis et al., 2017) and overall reduced quality of life (Feng et al., 2021, Alikari et al., Omidzahir et al., 2021). Half of the symptoms selected for assessment in the heart failure population are not the typical symptoms of heart failure or congestion-related symptoms (Lawson et al., 2022). Although the purpose of clinical guidelines is to standardise and optimise disease treatment based on common heart failure symptoms, individualised clinical assessment prioritises the patient's unique symptomatology and experiences, ensuring that symptoms related to comorbidity/multimorbidity are not overlooked. Revising clinical guidelines to include 37 symptoms identified in this integrated programme of research can raise a critical discussion around the balance between practical implementation and personalised patient care. The risk is overwhelming clinical visits for both clinicians and patients during routine visits. A comprehensive symptom assessment using the Integrated Palliative Care Outcome Scale (IPOS) in hospitalised patients identified 17 items as important for supporting holistic symptom evaluation, without focusing on multimorbidity (Hamatani et al., 2022). A person-centred, comprehensive symptom assessment can enhance the understanding of patient experiences and complex symptom distress in the heart failure population. Effective use of electronic Patient-Reported Outcome Measures (ePROMs) can mitigate some of these challenges by facilitating continuous symptom monitoring and prioritisation, addressing potential data overload and integration issues (Warnecke et al., 2023). However, patients who are unfamiliar with electronic devices or vulnerable patients may be underrepresented, and using electronic devices as a single source of information may not be suitable for each subgroup of patients (Glenwright et al., 2023). A targeted approach that prioritises the most significant symptoms from the patient's perspective, supported by multidisciplinary teamwork and an advanced triage system, can ensure comprehensive yet practical patient care. If the full spectrum of symptoms is not considered, people will have no way to overcome their complex symptom distress and improve their quality of life with effective symptom monitoring.

Self-monitoring of symptoms is strongly associated with improving adherence to heart failure self-care (McDonagh et al., 2021). Assessing the full spectrum of symptoms of individuals will be the core component to overcome the challenges of the complex symptom distress in heart failure. Without a comprehensive and effective assessment, it will not be possible to monitor symptoms, symptom change, and correlates of the worsening trajectory of these symptoms (related to heart failure or not) to reduce these symptoms of distress in heart failure. Findings from the integrated programme of research described within this thesis expressed a diverse range of symptoms. Clinical assessment of the symptoms can be varied for each individual with heart failure. Therefore, the assessment of individual symptoms might be based on a person-centred approach. In the literature, telemonitoring (Inglis et al., 2015), patient-reported outcome measures (Hamatani et al., 2022), artificial intelligence (AI) (Leiter et al., 2020), and multidisciplinary care teams (Datla et al., 2019) have been highlighted as ways to improve precision and personalisation in heart failure symptom assessment. Continuous vital sign surveillance and follow-up methods with these approaches facilitate the early management of symptom exacerbations. In heart failure care, these improvements collectively enhance patient outcomes and symptom assessment.

8.2.2. Stratified realities: complexity, unfamiliarity, and unprioritised symptoms

There is no single reality to heart failure symptoms – personalised symptom assessment is required.

Statistically/strongly significant associations were found between symptoms and individual characteristics, consistent with previous reviews (Teunissen et al., 2007, Vuckovic et al., 2020, Santos et al., 2020). Identified factors associated with symptoms (and self-management) in this thesis are presented in **Table 8-3**. Unsurprisingly, symptoms changed according to a range of factors such as age, setting, sex, and heart failure subtypes. For example, based on the qualitative study findings, breathlessness, one of the typical and most common heart failure symptoms, was emphasised much more than any other of heart failure's significant physical and emotional impact on the daily life of individuals in Türkiye. This shows how symptom experiences differ individually/socially.

There are no single shared realities in individuals' symptom experiences. The symptom profiles of individuals (referring to self-management strategies) may consist of a combination of many factors rather than a combination of two, three, or four factors. Barbara Riegel and her colleagues expressed the same point in their recently published article as an update for the Situation-Specific Theory of Heart Failure Self-care (Riegel et al., 2022). This is the complexity and unfamiliarity with symptoms among the heart failure cohort. The evaluation of the symptoms should be from individual perspective.

In this qualitative study, the importance of people's cultural and religious considerations in heart failure became evident, as individuals reported disruptions in their religious life due to breathlessness in Turkiye. For example, during the Islamic calendar, Muslims observe fasting, and healthcare providers should engage in discussions and collaborate with patients to determine the most appropriate adjustments to medication and optimise self-care practices (Busolo and Woodgate, 2015). There is ethnocultural diversity in heart failure treatment provision and response (Hill et al., 2023, Beattie et al., 2024). The impact of culture on communication and the role of the family, end-of-life care decisions, the implications of medications, and self-care behaviours are significant (Beattie et al., 2024). Awareness of the cultural, social, and religious/spiritual preferences of patients and their families is required in a person-centred care approach (Hill et al., 2023). This entails the development of strategies to ascertain and address the bespoke needs of individuals across the cultural spectrum within the local population (Hill et al., 2023, Beattie et al., 2024). Indeed, the awareness of cultural diversity is essential to drive national and international initiatives to reduce healthcare inequalities in multicultural societies such as Turkiye, Scotland, and Australia.

Evidence around how individuals' religious and cultural consideration affect their symptoms and coping mechanisms in heart failure highlight a need for personalised assessment and care (Tyni-Lenné, 2004, Zambroski, 2003, Li et al., 2019, Warren-Findlow and Issel, 2010, Dickson et al., 2012). Person-centred care acknowledges the concept of personhood that is usually used in nursing care models such as palliative care (Sofronas et al., 2018, Johnston and Narayanasamy, 2016). Considering personhood from various aspects, including psycho-socio-cultural elements, allows for a comprehensive understanding of the individual, enabling a dignified and person-centred assessment (Sofronas et al., 2018). Personalised/individualised symptom assessment is important to understand the full spectrum of symptoms and coping mechanisms of individuals with heart failure.

Table 8-3: Factors associated with different symptom experiences in each study of the project

Associated factors with symptoms		**MMSR**	**Secondary data analysis**	**Descriptive qualitative study**
Person	Age	Yes		Yes
	Biological sex		Yes	Yes (related to education level)
	Knowledge/awareness			Yes
	Cultural/social beliefs/values			Yes
	Religious considerations			Yes
	Motivation/self-affirmation			Yes
Illness-Health	LVEF		Yes (Sex-stratified)	
	LVEF-based heart failure subtypes		Yes (Sex-stratified)	
	Quality of life		Yes (Sex-stratified)	
	NYHA classification		Yes (Sex-stratified)	
	Multimorbidity		Yes (Sex-stratified)	Yes
	Comorbidity type		Yes (Sex-stratified)	Yes
	Setting (hospital versus community)	Yes		
	Physical and psychological vulnerability (e.g., the experience of grief/bereavement due to heart failure)			Yes
Environment	Inputs from significant others (social support)			Yes
	Rural versus urban (accessibility of healthcare centres/information)			Yes
	Healthcare policies (public versus private hospitals)			Yes

8.2.3. Knowledge and awareness of symptoms and heart failure

A person's ability to report symptom, and preferences, motivation, and readiness to manage them, are related to knowledge and awareness of the condition and symptoms.

Patient education is essential because misconceptions, lack of awareness/knowledge, and other factors all contribute to inadequate self-care (Riegel et al., 2021, Jaarsma et al., 2021, Riegel et al., 2009). Many healthcare professionals think that if a patient can read and write, they are literate enough to practice good self-care. Although those with higher levels of education are more likely to practice self-care than people with lower levels of education (Rockwell and Riegel, 2001), having a low education level does not prevent one from developing the health literacy required to practise effective self-care (Smith et al., 2006, Redman, 2007). The findings of this project supported this view. In the descriptive qualitative study, misconceptions and knowledge about breathlessness (and heart failure) were strongly associated with poor symptom perception and management. This indicates that exploring a patient's knowledge and awareness of heart failure and its symptoms is important to establish better self-management goals. In addition to this, due to other reasons (such as inaccessibility to health centres, living outside the city, and different health systems/policies in different countries), people do not have enough information about their own situation and management strategies. Any education schedule created depending on the underlying cause will be sufficient to increase this level of knowledge in heart failure. Any training/education to be given in line with the wishes and preferences of the person will increase symptom observation, monitoring, reporting, and management.

However, despite the necessary knowledge regarding self-care, education alone is insufficient for fostering effective self-care behaviours in people with heart failure. A multifaceted, holistic, and patient-centred approach is imperative. Patient empowerment and activation have been associated with sustainable improvements in patients' outcomes including better clinical indicators, self-management knowledge and skills and compliance with care recommendations and treatments in chronic conditions (Stichler and Pelletier, 2023). The involvement of support networks, including families, friends, peer support groups, and caregivers is crucial (Wang et al., 2024, Yang et al., 2024). Building self-confidence and resilience through incremental progress, coping strategies for stress, anxiety, and other emotional challenges, and resilience training is essential (Rashid et al., 2023). Additionally, enhancing communication and follow-up through regular check-ins, and clear communication regarding care plans, medication schedules, and lifestyle modifications further supports effective self-care (Butler et al., 2023). From a nurse researcher's perspective, these comprehensive strategies are critical in addressing the complex needs of people with heart failure and promoting sustained self-care behaviours.

8.2.4. Needs assessment for improved health behaviours

Heart failure is a long-term life condition, highlighting the need for a long-term evidence-based intervention for everyone.

Symptom experience is associated with physical, psychological, social, and overall needs in heart failure (Schäfer-Keller et al., 2021). Quantifying demands not addressed in current management plans, needs assessment gives information on how patients perceive their current state of health. For planning education and care, this knowledge is helpful. This project's findings identified adequate education, long-term evidence-based care, and the psychological needs of people with heart failure. Some participants reported the need for long-term support and care strategies. They stated that they only received support during their stay in the hospital. These needs can differ according to individual perspectives and factors. Therefore, an individualised needs assessment will be important in heart failure.

The development of a treatment regimen and care plan based on patient-centred, evidence-based practice and multidimensional patient evaluation is necessary for the achievement of optimal outcomes (McDonagh et al., 2021, Grady et al., 2000). In nursing, the idea of needs assessment has been investigated as a method for assessing health status, determining patient satisfaction, and developing treatment strategies (Davidson et al., 2004). Evaluating the classification and segmentation of needs shaped by individual bio-psycho-social symmetry is strongly associated with quality of life and patient satisfaction (Davidson et al., 2004). There are a variety of unmet demands in heart failure, and unmet needs are correlated with a lower quality of life (Moser, 2002, Kavalieratos et al., 2014, Davidson et al., 2008). The ability to document demands at the level of the individual patient and their family is also necessary for providing appropriate care for patients with heart failure (Davidson et al., 2004, McIlfatrick et al., 2018).

8.2.5. The core concept: person-centred symptom assessment in heart failure

Person-centred symptom assessment is an approach in healthcare in which individuals take an active role in assessing and reporting their symptoms. As already discussed above, there is a diverse range of symptoms not considered by clinicians or other healthcare providers. Much of the current published information does not reflect the symptom profiles of the heart failure cohort in the real-world context. The importance of patient-reported outcomes in symptom monitoring and management is highlighted by other researchers (Lawson et al., 2022). Firstly, there is no such explanation about how an effective symptom assessment must be done as a first step. They usually provide standardised patient-reported symptoms lists (McDonagh et al., 2021), but the findings from the integrated programme of research described within this thesis indicated there are many various symptoms among the heart failure cohort. Additionally, the findings are consistent with those of previous studies (Hu et al., 2021, Sethares and Chin, 2021, Denfeld et al., 2020, Qiu et al., 2022), indicating that each symptom interacts with other symptoms. Therefore, any pre-established symptom profile list is unlikely to be representative of everyone. A comprehensive and systematic symptom assessment should be done as the first and core concept regarding the guidance of the person, and then effective self-monitoring and management can happen for patients. Secondly, patient-centred care has become a healthcare priority worldwide (World Health Organization, 2015, Pelzang, 2010, Santana et al., 2018) to monitor and manage patients with chronic diseases. Like person-centred care, person-centred symptom assessment strategies can be beneficial to improve patients' outcomes and reduce their symptom burden.

As mentioned in ***2.3.2. Assessing symptoms in heart failure***, the failure of PROMs to capture all relevant symptoms necessitates the implementation of a comprehensive symptom assessment. These structured and standardised measurements do not consider atypical symptoms experienced by patients, which could be of utmost importance to them. These measurements often miss the holistic perspective of symptomatology, as their main focus is on disease-specific symptom assessment rather than multimorbidity (Algurén et al., 2020). A comprehensive symptom assessment system for heart failure patients with multimorbidity can provide a structured and quantitative method to evaluate and monitor the full spectrum of symptoms. For instance, the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) offers a detailed framework for assessing adverse symptoms in cancer care, utilising robust measurement principles (Basch et al., 2014). While this framework could be adapted to assess symptom profiles in heart failure patients with multimorbidity, it may not fully support a person-centred approach in symptom assessment for this population. As vulnerable patients (such as advanced age, cognitive impairment and physical functioning and language proficiency) are also patient level of factors that affect the use of PROMs (Long et al., 2021, Glenwright et al., 2023).

Compared to standardised patient-reported outcomes, which are considered more reliable and valid in practice (Krogsgaard et al., 2021), open-ended questions have significant limitations in identifying symptoms due to recall bias, subjectivity, and lack of structure. However, care decisions made based on these standardised measurements are missing the patient values and preferences and lack an understanding of what matters to them the most as symptoms. As mentioned above, heart failure patients with comorbid conditions may not consider their shortness of breath as a main concern compared to those without comorbid conditions. Additionally, their cultural, social, and religious values and beliefs can be better understood when we ask individuals directly. Therefore, open-ended questions will support a more person-centred care approach in heart failure.

Open-ended questions should be combined with systematic assessments like PROMs to ensure accuracy and comprehensiveness to support person centredness. Comprehensive and systematic symptoms assessment require effective ***one-on-one (good) communication with person***. The person is the first and core element of understanding individual symptoms and associated factors in relation to the decision-making process. ***Identifying the full spectrum of symptoms*** (including typical and less typical symptoms associated with heart failure and other conditions/factors) is important. Identifying the full list of symptoms experienced by a person will be the key concept to reduce symptom burden.

To identify such a symptom list, the next question should be to ask the person "Do you have any symptoms that you want to share with us today?" It is important to note that the main purpose is to identify the full spectrum of symptoms they are experiencing, associated both with heart failure and other conditions. Understanding the most problematic one affecting their daily life is crucial to improve their health-related quality of life. The following simple question will help us find this: "Which of these affects your life more, and why?" The symptoms that the individual finds most problematic should be included in self-management strategies because these affect their daily life activities and life enjoyment. This symptom assessment process can be relevant and adaptable to all phases of heart failure (including palliative and end-of-life care). Therefore, identifying the full spectrum of symptoms, as well as the most problematic ones, is important for achieving better self-care strategies to reduce symptom burden.

Symptom experiences are affected by many different ***individual factors***, such as person-related (including age, sex, ethnicity etc.), illness-related (heart failure subtypes, multimorbidity, comorbid condition types etc.) and environment-related (seasons, air pollution, living in an area creating more stressors etc.) factors. The determination of the factors associated with the worsening trajectory of symptoms will be the main task at this stage. Regarding the findings of the second study of this PhD thesis (Chapter 6), biological sex and LVEF-based heart subtypes affect the symptom profiles and worsening trajectory of heart failure symptoms. At this stage, associated factors related to symptoms and their trajectory should be assessed/addressed.

The strengths of person-centred symptom assessment strategy are:

- ***Understanding the full spectrum of symptoms from the individual's perspective:*** Symptom assessment is key to success in reducing symptoms. This individualised symptom assessment strategy may help to understand the full spectrum of symptoms experienced by individuals with heart failure, which reduces the symptom burden and symptom-related adverse outcomes.

- ***Understanding the (unique) individual reality of symptom profile:*** Unique individual symptom profiles (associated with different factors) can be understood by healthcare providers.

- ***Adaptable and flexible for any individual and community:*** Symptom assessment and self-care management strategies are shaped by the person's own beliefs, values, previous experiences, and knowledge. They are affected by the cultural, social, and environmental structure of the society in which people live. A person-centred approach to symptom assessment aims to minimise adverse situations arising from these differences, which may be overlooked yet significantly impact their care.

These points listed above are from the researcher's perspective. Based on the organisational and individual level, these strengths and limitations can vary according to other factors. As with any strategy, it has some limitations. A person's level of knowledge and awareness are key to the success of this strategy. A lack of knowledge or awareness will distort the results and interpretation of any symptom assessment. Willingness and motivation are needed to formulate and talk about symptoms. Time-related issues can be important for both patients and healthcare providers.

8.3. The Situation-Specific Theory of Heart Failure Self-care as an explanatory framework

The overarching finding themes mapped onto the selected theory characteristics (Table 8-4). The Situation-Specific Theory of Heart Failure Self-care was developed as an explanation and understanding of the self-care management process in heart failure (Riegel et al., 2016). Particularly, the theory considered that self-care begins with maintenance (symptom monitoring and recognition), followed by symptom perception, and then management (symptom evaluation, treatment implementation and treatment evaluation) (Riegel and Dickson, 2008, Riegel et al., 2016). These three constructs of self-care are shown in this theory as being built on each other. Additionally, the decision-making process about self-care is influenced by situation (person, problem, and environment) and process (knowledge, experience, skill, and values) (Riegel et al., 2022, Riegel et al., 2016). Firstly, the findings of this thesis supported individual symptom assessment. Secondly, individual characteristics are strongly related and interconnected for symptoms. Stratified realities have been highlighted in symptoms linked with assessment (including recognising, monitoring, and reporting). Lastly, self-care maintenance generally includes heart failure-related symptoms monitoring, recognition, and treatment adherence. However, non-heart failure-related symptoms should also be considered, in order to improve overall health and well-being. Symptom assessment should be the first construct of self-care management in heart failure.

Table 8-4: Mapping the overarching key findings onto the selected theory's characteristics

	Situation-Specific Theory of Heart Failure Self-care characteristics		
Identified Overarching themes	**Situation** (person, illness, and environmental factors)	**Process** (knowledge, experiences, skill, and values)	**Action** (maintenance, symptom perception, and management)
Understanding the full spectrum of symptoms	A diverse range of symptoms (heart failure or non-heart failure-related) affected by ***individual differences***	***Knowledge/awareness/previous experiences/values etc.*** affect the symptom profile-distribution reporting and management	The diversity of individual symptoms calls for ***a wide variety of symptom reporting, evaluation, and management combinations***
Stratified realities: complexity, unfamiliarity, and unprioritised with symptoms	***Individual factors*** (setting, age, biological sex, heart failure subtypes, and socio-cultural-behavioural) affect symptom profiles	Situation-related factors influence the self-management ***decision-making process*** The patient's perspective is affected by individual ***socio-cultural-behavioural factors***	Differences in ***symptoms, symptom reporting, evaluation, and management*** with respect to stratified realities ***Symptom monitoring, recognition, and management*** with respect to a person's most problematic symptom description
Knowledge and awareness about heart failure and its symptoms	***Individual differences*** make a difference in understanding and awareness about conditions and symptoms	***Knowledge and awareness*** affect symptom monitoring, recognition, and management	***Symptom recognition, monitoring, evaluation, and management*** with respect to individual knowledge/awareness
Individuals need assessment for improved health behaviours	Individual needs change according to ***individual differences***	Needs for improved health behaviours can change regarding ***individual perspective/values***	Different symptom combinations and needs result in different **symptom reporting, monitoring, and management**

Final overarching convergent theme: The care concept – person-centred symptom assessment – is an approach in healthcare in which individuals take an active role in assessing and reporting their symptoms.

8.4. Overarching key strengths and limitations

8.4.1. Strengths

The overarching the key strengths reflected in this PhD research include:

- **Multiple methods approach including data triangulation**

The choice to conduct a sequential multiple methods study incorporating triangulation provided greater flexibility in how the various research topics explored within this PhD thesis could be addressed. The results of the two methods also showed some differences that could not be captured using a one-method approach. Additionally, triangulation provides a deeper understanding with further analysis of the findings to produce more accurate data regarding underlying factors narrowed down socio-cultural context. Based on the PhD researcher's own personal preference, understanding the stratified realities of symptoms underlying the socio-cultural-behavioural context would be possible through a combination of various methods.

- **Diverse cultural perspective on symptoms**

This PhD research began with a mixed-methods systematic review to explore and understand the full spectrum of symptoms being experienced and reported in the literature by people living with heart failure. This review included 14 different countries (including the USA, UK, Japan, China, Australia, Italy, Vietnam, Türkiye, Australia, South Korea, South Africa, and Iran). Furthermore, the research sample from which the data for the secondary data analysis was from Australia, and the qualitative study data was collected from Türkiye. The findings from the integrated programme of research described in this thesis therefore represent a diverse cultural perspective of symptoms among the heart failure population worldwide.

- **Comprehensive baseline data for symptoms in women and men**

The WHICH?II Trial provided valuable baseline data regarding heart failure symptoms and individual characteristics profiles of women and men across LVEF-based heart failure subtypes. The subsequent report represents the first of its kind, to indicate sex-stratified differences in symptoms and symptom changes across LVEF-based heart failure subtypes.

- **Theory-based approach**

The PhD researcher chose a heart failure self-care theory. The selected theory (Situation-Specific Theory of Heart Failure Self-care) helped to clarify the underexamined aspects of current self-care management in heart failure.

- **Patient and public involvement (PPI)**

PPI was included in this thesis at the beginning. The PPI advisors, Robbie and Nikki, were involved in three stages of the thesis (MMSR, secondary data analysis, and descriptive qualitative study), and provided feedback and comment on the studies and findings. Their valuable input helped me to understand the importance of comprehensive individual symptom assessment in heart failure. The PPI helped to enhance the reliability and relevance of this PhD thesis for individuals.

- **Mixed data collection (including face-to-face, telephone, and email interviews): a new trend in nursing**

During the Covid-19 pandemic, many nurse researchers tried to conduct interviews online or by telephone. Similarly, the researcher for the current study used a variety of data collection methods including face-to-face, telephone, and email. The inclusion of other interview techniques is also beneficial for the study. Firstly, she went to Türkiye for data collection for almost two months, and she recruited the participants via social media and flyers. It was difficult to obtain the desired number of participants within this short time. With the inclusion of telephone and email interviews (she also included online interview techniques, but nobody chose this option), she was able to recruit the participants after leaving Türkiye. Even though she was in Türkiye, some participants did not prefer face-to-face interviews as a first choice due to their work schedules and families. She did not feel any differences between interview options regarding the interview information. There was only one difficulty with the phone and email conversations, she was not able to observe the participants during the interview. Apart from this, the use of mixed interview technique options provided flexibility to follow the preferences of the participants.

- **Reflexive thematic analysis process of Turkish and English transcripts**

The use of reflexive thematic analysis provided more comprehensive information on the breathlessness experiences of individuals in Türkiye within the socio-cultural-behavioural context. This helped to explain deeply the phenomenon studied with the words of the participants. Also, Turkish and English transcripts were analysed separately, and their findings were compared for accuracy in order to obtain the final version of the themes of the interviews. This allowed us to capture the socio-cultural-behavioural effects of breathlessness. Sometimes, during translation, some words may lose their meaning and gain a new identity. Since this situation may distort the findings, both Turkish and English transcripts were analysed.

8.4.2. Limitations

The key limitations of this PhD are as follows:

- **Qualitative study: interview management**

Some areas for improvement of the interviews and reporting findings (including researcher bias) were explained in methods and analysis sessions. However, some of the issues are difficult to avoid, such as the literacy level of the participants, or living with their partners, children, or grandchildren. Family members of some participants interrupted the interview, which may have impacted the findings.

Another aspect is related to the number of interviews conducted. The PhD researcher planned to interview 25 participants to capture a more heterogenous group (including different ethnicity, age groups, and heart failure duration) for more comprehensive information. Although she reached data saturation with 11 participants, there is still a possibility that additional interviews (with different ethnicities, ages, and heart failure duration) may have provided a more comprehensive structure for symptoms. There were only four participants of Kurdish and Arab ethnic backgrounds among the participants.

The researcher was also not able to use the healthcare centres in Türkiye to recruit the participants, and she instead recruited them through social media or flyers. Therefore, participants were included according to their self-reported heart failure. This is another aspect of interview management.

In Turkish culture, discussion of death and dying is taboo. Some participants did not discuss or talk about their fear/concern about death/dying related to heart failure or their symptoms and experiences. The word death/dying was strong and unacceptable for some participants. They were uncomfortable discussing it, so the researcher was reluctant to dwell on the topic.

Furthermore, a few participants asked about the association between the study and healthcare centres. The researcher explained that there was no association between this study and their medical records or doctors; and that all data would be kept anonymous. These participants complained less about their situation and expressed that they received enough education/training (even though there is no such training for heart failure in Türkiye) although this research was not associated with any healthcare centres (their major concern).

- **Qualitative study: self-reported heart failure**

In this study, depending on self-reported heart failure status could present limitations, potentially resulting in under-reporting or over-reporting of symptoms, or recall bias. This might impact the accuracy, completeness, and comprehensiveness of the data.

- **Data collection instrument in systematic reviews**

Most of the studies in the systematic review were quantitative, and many data collection tools contained a limited number of symptoms. Especially, emotional symptoms were not included in several data collection instruments. Therefore, some symptoms might have been overlooked (for mainly non-ESC symptoms), potentially posing a barrier to the generalisability of the results.

- **Data collection instrument in secondary data analysis**

The KCCQ and EQ-5D-5L scale were chosen to quantify health-related quality of life in the WHICH?II Trial. The KCCQ includes only a few typical symptoms of heart failure (shortness of breath, fatigue, oedema, and sleeping problems due to orthopnoea). The WHICH?II investigators also used a brief symptom checklist including only typical symptoms of heart failure. Consequently, it was impossible to identify the full spectrum of symptoms experienced by those living with heart failure, when conducting secondary data analyses of trial data. However, we were able to identify that the typical symptoms of heart failure were influenced by sex-stratified differences with respect to heart failure subtypes.

8.5. Next step: Navigating heart failure - symptom spectrum exploration and assessment (NHF-SEA) study

Findings from the integrated programme of research described within this thesis indicated a diverse range of symptoms among individuals living with heart failure. Given the limitations of this PhD research, these results did not present a mapping of the full spectrum of symptoms regarding clinical characteristics for mainly LVEF-based heart failure symptoms, and mainly for HFpEF and HFmrEF, from the three studies. Clinically, there is need for assessment and exploration of the full spectrum of symptoms with respect to a variety of factors. The following study aim is to co-design and feasibility test a systematic and comprehensive person-centred symptom assessment strategy to explore the full spectrum of symptoms for clinical applications in heart failure. Regarding the identification of the full spectrum of symptoms, there will be three steps. ***Step 1*** will involve two phases. The first phase will be a mixed-methods approach including a symptom survey (identified symptoms from the integrated programme of research described within this thesis) and a qualitative interview study with Turkish individuals with HFpEF, HFmrEF, and HFrEF. The second phase will be a Delphi four-round study including patients, caregivers, and healthcare professionals (nurses, cardiologist, and family physicians) to identify the symptoms spectrum for each heart failure subtypes. ***Step 2*** will be a co-design of the person-centred symptom assessment strategy guided by the findings of the first step for enhanced in-patient and out-patient applications. ***Step 3*** will be a pre-post design, mixed-methods feasibility study to test the relevancy, usability, acceptability, and usefulness of the developed person-centred symptom assessment strategy, to be performed in a culturally diverse adult population with heart failure (in Türkiye). Following the feasibility study with positive results, a series of RCTs will be conducted to assess the effectiveness of the symptom assessment strategy in reducing hospital admissions by detecting the early worsening trajectory of heart failure.

8.6. Study contribution

This PhD research contributes the following to knowledge/literature:

- *A better understanding of the full spectrum of symptoms experienced by people living with heart failure regardless of their socio-demographic and clinical profile.*
- *The importance of understanding and exploring (with the affected individual and their family) the full range of symptoms associated with heart failure – particularly in respect to identifying those symptoms not currently listed/highlighted by clinical guidelines/reports.*
- *Insight into the stratified realities of symptom experiences shaped by socio-cultural-behavioural factors – highlighted individual symptom assessment.*
- *Sex-stratified differences and predictors of the worsening trajectory of heart failure symptoms across LVEF-based heart failure phenotypes.*
- *The increasing importance of expanding our collective knowledge and awareness of heart failure and the symptoms experienced by those living with the syndrome.*
- *Recommendations for best person-centred (comprehensive and systematic) symptom assessment for practice in improving health and reducing symptoms.*

8.7. Chapter Summary

Box 8-1 provides the PhD thesis research in context. This chapter provided a discussion and interpretation of the overarching key findings from three studies in this PhD research and person-centred symptom assessment strategy. This chapter highlighted the importance of understanding the full spectrum of symptoms and individual characteristics. Additionally, this chapter provided brief information on the next step in this research trajectory. The strengths and limitations of the present research were presented in this chapter. Finally, the contributions of this PhD research to the literature were presented.

The next chapter presents the conclusion to the thesis, including recommendations for practice, policy, and research.

Box 8-1: PhD research in context

Evidence before this study

Heart failure is a complex clinical syndrome characterised by multiple symptoms, including breathlessness, fatigue, ankle swelling, and depression. These symptoms can have adverse effects on the quality of life, mortality rates, and hospital admissions of individuals with heart failure and their families. However, there is a lack of comprehensive understanding of these symptoms for several reasons:

- Current clinical guidelines primarily focus on symptoms related to hospital admissions, resulting in a limited number of symptoms being addressed.
- Existing evidence on heart failure management is biased towards younger individuals, those with reduced ejection fraction, and males. This overlooks the majority of heart failure patients who are older, female, and have HFpEF. Research often fails to consider the unique symptom experiences of women, older individuals, and those with HFpEF, even though they constitute a significant portion of heart failure cases.
- Heart failure in Türkiye differs from Western countries due to varying risk patterns, a younger population, and a higher proportion of women. These differences may lead to distinct symptom experiences.

In summary, there is a need for more comprehensive research to understand and address the diverse symptom experiences of individuals with heart failure, particularly among women, older adults, and those with HFpEF, considering regional variations in contexts such as Türkiye. Thus, the primary aim of this PhD was to explore the full spectrum of symptoms of individuals with heart failure from their perspective.

A sequential, multiple methods approach consisting of three concurrent studies was applied to comprehensively explore the spectrum of heart failure symptoms. Study 1 involved a mixed-method systematic review of existing literature to examine the overall symptom spectrum. Study 2 analysed secondary data from the WHICH?II Trial, focusing on the clinical symptom perspective among hospitalised individuals with heart failure in Australia. Study 3 conducted a descriptive investigation into the personal experiences of Turkish individuals living with heart failure.

Contributions of this study

The findings of this PhD indicated the importance of understanding the full spectrum of symptoms experienced by individuals with heart failure from their own perspective. There were a diverse range of symptoms among the heart failure cohort, but many of them were not listed in the ESC Guidelines. Compared to the clinical cohort symptoms perspective (Study 2), there was a broad range of symptoms from the review (Study 1) and individual (Study 3) perspectives. These symptoms were also observed commonly among the study populations.

Additionally, symptoms were different according to age, setting, sex, heart failure subtypes, and cultural perspective of individuals. The assessment of individual symptoms can therefore not depend on a pre-established list across various patients and healthcare settings. Furthermore, while knowledge and awareness of heart failure and symptoms are important for individuals to report and manage their symptoms, among Turkish individuals, such knowledge and awareness about breathlessness related to heart failure were poor. Plus, Turkish individuals expressed a need for education, psychological support, and long-term evidence-based strategies to improve their health behaviours. These supported the need for person-centred symptom assessment strategies in heart failure.

Implications of all the available evidence

The findings of this thesis strongly emphasise the need for enhanced awareness and acknowledgement of the full spectrum of symptoms experienced by individuals living with heart failure. There was a diverse range of symptoms. Current clinical management guidelines should more fully consider the full spectrum of symptoms experienced by those affected in different phases of their journey with heart failure (such as advanced stage, palliative care, and end-of-life care). This highlighted the importance of person-centred symptom assessment strategies (adapted to culture or trans-cultural) as a fundamental idea for comprehensive, systematic, and holistic symptom assessment in heart failure.

Effective assessment of individual symptoms can be achieved through the use of open-ended questions. This approach allows a comprehensive examination of symptoms without restricting them to narrow limits. From a research perspective, there is a compelling need to initiate research aimed at identifying the holistic spectrum of symptom experiences among individuals. This effort will require the creation of comprehensive national and international cohort studies.

Chapter Nine - Conclusion and recommendations

9.1. Introduction

In the preceding chapters, we explored the subject, population, and problems studied (Chapters 1 and 2); outlined the general methods employed in this PhD research (Chapters 3 and 4); presented the findings from each study (Chapter 5: Mixed-Methods Systematic Review, Chapter 6: Secondary Data Analysis, and Chapter 7: Descriptive Qualitative Study); and discussed and interpreted the overarching key findings (Chapter 8). This final chapter provides the conclusion to the PhD research, presenting the main points of the overall conclusion, followed by recommendations for practice, policy, and research, respectively.

9.2. Overall conclusion

The integrated programme of research described in this PhD thesis aimed to understand the full spectrum of symptoms in people with heart failure. The researcher examined previous literature to identify the full spectrum of symptoms hitherto detailed to be experienced by people with heart failure, with a comparison of symptoms listed in ESC Guidelines for heart failure. Then, the symptoms of a real-world clinical cohort from Australia were explored with respect to biological sex and LVEF-based heart failure subtypes, followed by an individual symptoms perspective from a Turkish cohort. In conclusion, this project highlighted a diverse range of symptoms in heart failure, and the need for an individual, comprehensive and systematic symptom assessment.

The theoretical framework by Riegel et al. (2016) has been crucial in interpreting the findings. It highlighted individual symptom differences across various factors in Studies 1 and 2 while how patients' subjective experiences influence self-care behaviours in Study 3. Collectively, these findings underscore the theory’s focus on personalised, context-sensitive self-care strategies and a person-centred approach to symptom assessment.

Findings from the integrated programme of research described in this PhD thesis highlighted the need for person-centred symptom assessment in heart failure cohorts. As already discussed in previous chapters, understanding the full spectrum of symptoms experienced by people with heart failure is important to reduce symptom distress. The findings also demonstrate the important of understanding that stratified realities are shaped by the cultural beliefs and values of individuals. Specifically, education about heart failure and its symptoms could increase the chance of early recognition and reporting of symptoms among the Turkish population with heart failure.

Based on the findings of each individual study and the overarching key findings, this present project has a few recommendations for practice, policy, and research to improve the current symptom assessment (including the symptom management strategies) in the heart failure cohort.

9.3. Recommendations for practice

- The importance of ***comprehensive and person-centred symptom assessment*** must be highlighted in clinical guidelines and practice reports. One conclusion drawn from the integrated programme of research described in this PhD thesis is the need for ***comprehensive symptom assessment and strategies*** to support people with heart failure across diverse cultural and religious backgrounds. Various factors could be associated with different symptoms. Assumptions about what are typical and what less typical symptoms, of those listed in the guidelines, can be changed for individuals according to various associated factors such as age, biological sex, and heart failure subtypes. ***Individual symptom assessment*** may help to clarify this stratified reality of symptoms in heart failure. ***Person-centred symptom assessment*** may be required.
- Any care/maintenance and assessment created by incorporating only the acute (typical and less typical) symptoms listed in them have not been represented in the other phases of the heart failure cohort (such as palliative care, and end-of-life care). Therefore, clinical management guidelines/reports should be considered as symptoms in ***people with different stages of heart failure***.
- Focusing only on the symptoms people experience at the time of hospitalisation (including for a very short time before and after the admission) will not improve the care and life quality of individuals in the longer-term. Therefore, the ***symptoms experiences of those individuals living with heart failure in the community context*** should be considered by healthcare providers.
- The descriptive qualitative study indicated ***the lack of emotional/psychological symptom assessment*** in heart failure and the ***importance of routine psychological support***. This should be considered by healthcare providers.
- ***Individual symptom assessments*** are the most important element in understanding whether ***a person has adequate reporting skills and knowledge to manage symptoms***.

- To ***improve the person's ability*** to report their symptoms, ***education and training*** are the key concept in heart failure in **Türkiye**. ***Nurses*** can help assess the full spectrum of symptoms in ***clinics and communities***. Especially ***in Türkiye***, heart failure specialist nurses can help to assess and monitor the symptoms of people with heart failure. There is a need for trained heart failure specialist nurses or nurse practitioners.

9.4. Recommendation for policy

- ***Establish clinical principles for comprehensive and person-centred symptom assessment, with an emphasis on individual symptoms at different stages of the heart failure journey, to improve patient care.***
- People with heart failure are the core element for understanding their symptom experience. However, without adequate knowledge and awareness, they cannot help in the monitoring and reporting of these symptoms to prevent adverse outcomes of heart failure. ***Education and training*** will be the main component to increase the knowledge and awareness of individuals with heart failure in Türkiye.
- In addition, taking into ***consideration stratified realities of symptom experiences*** shaped by individuals' socio-cultural-behavioural factors, people with heart failure will be the key and first element in assessing their own symptoms. Any education/training should begin with a comprehensive symptom assessment tailored from ***individual perspectives***.
- To achieve the best care planning for the patients and their informal caregivers, any ***policy-making process should include patients and nurses*** in all countries. This can help create more realistic and logical policies for heart failure management in clinics and communities regarding symptom assessment, especially in Türkiye.

9.5. Recommendations for research

- There is a lack of research focused on ***the awareness of comprehensive symptom assessment*** in heart failure. This deficit includes understanding the full range of symptoms experienced by people ***in the different/distinctive phases of the heart failure journey*** (including palliative and end-of-life care). Thus, studies are needed to ***investigate the full spectrum of symptoms from an individual perspective*** among the heart failure cohort.
- Surprisingly, there is need to better understand psychological symptoms (other than depression and anxiety) in people with heart failure. Many symptom assessment tools in heart failure do not consider/measure these symptoms.

- Further research is needed to identify which ***symptom assessment strategy and/or method*** would be most effective for the identification of ***the full spectrum of (self-, proxy- or proxy-proxy-reported) symptoms*** at different phases of heart failure.
- The studies of this thesis included less ***women, non-white population (such as black ethnicity) and individuals with HFpEF and HFmrEF***. There is a need for symptom investigation of these populations.
- Also, symptom experiences and assessment strategies change due to cultural differences, so ***new research and interventions with a trans-cultural or culturally tailored dimension*** should be undertaken to develop the best symptom assessment and self-management strategies.
- ***Longitudinal studies*** are also needed to investigate the ***worsening trajectory of heart failure symptoms with an inclusion of non-ESC symptoms***.
- This thesis did not represent individuals ***such as the LGBTQ community, immigrants, and pregnant women.*** Therefore, new studies should consider these populations.

9.6. Chapter summary

This final chapter provided the details about the conclusion of the thesis, with recommendations for practice, policy, and research. This PhD thesis sought to explain the importance of understanding and assessment of the full spectrum of symptoms among the heart failure population. Healthcare professionals should consider the full spectrum of symptoms in people with heart failure to understand unique individual symptom profiles.

References

Abshire, M., Xu, J., Dennison Himmelfarb, C., Davidson, P., Sulmasy, D., Kub, J., Hughes, M. & Nolan, M. 2015. Symptoms and fear in heart failure patients approaching end of life: a mixed methods study. *Journal of Clinical Nursing,* 24**,** 3215-3223.

Adams, W. C. 2015. Conducting semi-structured interviews. *Handbook of practical program evaluation***,** 492-505.

Ågren, S., S Evangelista, L., Davidson, T. & Strömberg, A. 2013. Cost-effectiveness of a nurse-led education and psychosocial programme for patients with chronic heart failure and their partners. *Journal of clinical nursing,* 22**,** 2347-2353.

Alabadla, M., Sidi, F., Ishak, I., Ibrahim, H., Affendey, L. S., Ani, Z. C., Jabar, M. A., Bukar, U. A., Devaraj, N. K. & Muda, A. S. 2022. Systematic review of using machine learning in imputing missing values. *IEEE Access*.

Alassoud, B., Johnston, B. & Hogg, K. 2020. Culture and the understanding of advanced heart failure: a mixed-methods systematic review. *Collegian,* 27**,** 459-470.

Albert, N., Trochelman, K., Li, J. & Lin, S. 2010. Signs and symptoms of heart failure: are you asking the right questions? *American Journal of Critical Care,* 19**,** 443-452.

Alderson, P. 2021. *Critical realism for health and illness research: A practical introduction*, Policy Press.

Aldred, H., Gott, M. & Gariballa, S. 2005. Advanced heart failure: impact on older patients and informal carers. *Journal of advanced nursing,* 49**,** 116-124.

Algurén, B., Coenen, M., Malm, D., Fridlund, B., Mårtensson, J. & Årestedt, K. 2020. A scoping review and mapping exercise comparing the content of patient-reported outcome measures (PROMs) across heart disease-specific scales. *Journal of patient-reported outcomes,* 4**,** 1-10.

Ali, M. R., Freeman, S. C., Gray, L., Kadam, U., Lawson, C. & Group, C. H. 1996. Heart failure symptoms as predictors of hospital admission, readmission and all-cause mortality. *Cochrane Database of Systematic Reviews,* 2022.

Alikari, V., Platis, C., Alefragkis, D. & Theofilou, P. Assessing the quality of life and depression among patients with heart failure and heart attack.

Alkan, S. & Nural, N. 2017. Evaluation of symptoms and predictors in patients with heart failure in Turkey. *Journal of Hospice & Palliative Nursing,* 19**,** 404-412.

Allida, S., Du, H., Xu, X., Prichard, R., Chang, S., Hickman, L. D., Davidson, P. M. & Inglis, S. C. 2020. mHealth education interventions in heart failure. *Cochrane Database of Systematic Reviews*.

Alpert, C. M., Smith, M. A., Hummel, S. L. & Hummel, E. K. 2017. Symptom burden in heart failure: assessment, impact on outcomes, and management. *Heart failure reviews,* 22**,** 25-39.

Altice, N. F. & Madigan, E. A. 2012. Factors associated with delayed care-seeking in hospitalized patients with heart failure. *heart & lung,* 41**,** 244-254.

Altricher, H., Feldman, A., Posch, P. & Somekh, B. 1996. *Teachers investigate their work: An introduction to action research across the professions,* London, Routledge.

Ambrosy, A. P., Fonarow, G. C., Butler, J., Chioncel, O., Greene, S. J., Vaduganathan, M., Nodari, S., Lam, C. S., Sato, N. & Shah, A. N. 2014. The global health and economic burden of hospitalizations for heart failure: lessons learned from hospitalized heart failure registries. *Journal of the American College of Cardiology,* 63**,** 1123-1133.

Anderson, L. & Taylor, R. S. 2014. Cardiac rehabilitation for people with heart disease: an overview of Cochrane systematic reviews. *Cochrane database of systematic reviews*.

Anguera, M. T., Blanco-Villaseñor, A., Losada, J. L., Sánchez-Algarra, P. & Onwuegbuzie, A. J. 2018. Revisiting the difference between mixed methods and multimethods: Is it all in the name? *Quality & Quantity,* 52**,** 2757-2770.

Årestedt, K., Beattie, J. M., Evangelista, L. S., Liao, S., Motie, M., De Michelis, N. & Lombardo, D. 2014. On-going palliative care enhances perceived control and patient activation and reduces symptom distress in patients with symptomatic heart failure: a pilot study. *European journal of cardiovascular nursing,* 13**,** 116-123.

Armstrong, T. S. Symptoms experience: a concept analysis. Oncology nursing forum, 2003.

Arroll, B., Khin, N. & Kerse, N. 2003. Screening for depression in primary care with two verbally asked questions: cross sectional study. *Bmj,* 327**,** 1144-1146.

Asano, R., Newton, P. J., Currow, D. C., Macdonald, P. S., Leung, D., Phillips, J. L., Perrin, N. & Davidson, P. M. 2021. Rationale for targeted self-management strategies for breathlessness in heart failure. *Heart Failure Reviews,* 26**,** 71-79.

Atun, R., Aydın, S., Chakraborty, S., Sümer, S., Aran, M., Gürol, I., Nazlıoğlu, S., Özgülcü, Ş., Aydoğan, Ü. & Ayar, B. 2013. Universal health coverage in Turkey: enhancement of equity. *The Lancet,* 382**,** 65-99.

Austin, R. C., Schoonhoven, L., Clancy, M., Richardson, A., Kalra, P. R. & May, C. R. 2021. Do chronic heart failure symptoms interact with burden of treatment? Qualitative literature systematic review. *BMJ Open,* 11**,** e047060.

Aveyard, H. 2019. *Doing a Literature Review in Health and Social Care: A Practical Guide,* London, Open University Press.

Bahramnezhad, F., Shiri, M., Asgari, P. & Afshar, P. F. 2015. A review of the nursing paradigm. *Open Journal of Nursing,* 5**,** 17.

Bakitas, M. A., Dionne-Odom, J. N., Ejem, D. B., Wells, R., Azuero, A., Stockdill, M. L., Keebler, K., Sockwell, E., Tims, S. & Engler, S. 2020. Effect of an early palliative care telehealth intervention vs usual care on patients with heart failure: the ENABLE CHF-PC randomized clinical trial. *JAMA internal medicine,* 180**,** 1203-1213.

Barnason, S. A., Zimmerman, L. M., Brey, B., Catlin, S. & Nieveen, J. L. 2006. Patterns of recovery following percutaneous coronary intervention: a pilot study. *Applied Nursing Research,* 19**,** 31-37.

Basch, E., Reeve, B. B., Mitchell, S. A., Clauser, S. B., Minasian, L. M., Dueck, A. C., Mendoza, T. R., Hay, J., Atkinson, T. M. & Abernethy, A. P. 2014. Development of the National Cancer Institute's patient-reported outcomes version of the common terminology criteria for adverse events (PRO-CTCAE). *Journal of the National Cancer Institute,* 106**,** dju244.

Beattie, J. M., Castiello, T. & Jaarsma, T. 2024. The importance of cultural awareness in the management of heart failure: a narrative review. *Vascular Health and Risk Management*, 109-123.

Bekelman, D. B., Havranek, E. P., Becker, D. M., Kutner, J. S., Peterson, P. N., Wittstein, I. S., Gottlieb, S. H., Yamashita, T. E., Fairclough, D. L. & Dy, S. M. 2007. Symptoms, depression, and quality of life in patients with heart failure. *Journal of cardiac failure,* 13**,** 643-648.

Bender, M. S., Janson, S. L., Franck, L. S. & Lee, K. A. 2018. Theory of Symptom Management. *In:* Smith, M. J. & Liehr, P. R. (eds.) *Middle range theory for nursing.* Springer Publishing Company.

Bennett, J. A., Riegel, B., Bittner, V. & Nichols, J. 2002. Validity and reliability of the NYHA classes for measuring research outcomes in patients with cardiac disease. *Heart & Lung,* 31**,** 262-270.

Bennett, S. J., Cordes, D. K., Westmoreland, G., Castro, R. & Donnelly, E. 2000. Self-care strategies for symptom management in patients with chronic heart failure. *Nursing research,* 49**,** 139-145.

Berger, R. 2015. Now I see it, now I don't: Researcher's position and reflexivity in qualitative research. *Qualitative research,* 15**,** 219-234.

Bhaskar, R. 1978. *A Realist Theory of Science,* Brighton, Harvester Press.

Blecker, S., Paul, M., Taksler, G., Ogedegbe, G. & Katz, S. 2013. Heart failure–associated hospitalizations in the United States. *Journal of the American College of Cardiology,* 61**,** 1259-1267.

Bleijenberg, N., De Man-Van Ginkel, J. M., Trappenburg, J. C., Ettema, R. G., Sino, C. G., Heim, N., Hafsteindóttir, T. B., Richards, D. A. & Schuurmans, M. J. 2018. Increasing value and reducing waste by optimizing the development of complex interventions: Enriching the development phase of the Medical Research Council (MRC) Framework. *International journal of nursing studies,* 79**,** 86-93.

Bleumink, G. S., Knetsch, A. M., Sturkenboom, M. C., Straus, S. M., Hofman, A., Deckers, J. W., Witteman, J. C. & Stricker, B. H. C. 2004. Quantifying the heart failure epidemic: prevalence, incidence rate, lifetime risk and prognosis of heart failure: the Rotterdam Study. *European heart journal,* 25**,** 1614-1619.

Blinderman, C. D., Homel, P., Billings, J. A., Portenoy, R. K. & Tennstedt, S. L. 2008. Symptom distress and quality of life in patients with advanced congestive heart failure. *Journal of pain and symptom management,* 35**,** 594-603.

Blue, L., Lang, E., Mcmurray, J. J., Davie, A. P., Mcdonagh, T. A., Murdoch, D. R., Petrie, M. C., Connolly, E., Norrie, J. & Round, C. E. 2001. Randomised controlled trial of specialist nurse intervention in heart failure. *Bmj,* 323**,** 715-718.

Bogdan, R. & Biklen, S. K. 1997. *Qualitative research for education,* Boston, Allyn & Bacon.

Boldt, J. 2019. The concept of vulnerability in medical ethics and philosophy. *Philosophy, Ethics, and Humanities in Medicine,* 14**,** 1-8.

Bozkurt, B., Coats, A. J., Tsutsui, H., Abdelhamid, M., Adamopoulos, S., Albert, N., Anker, S. D., Atherton, J., Böhm, M. & Butler, J. 2021. Universal definition and classification of heart failure: a report of the heart failure society of America, heart failure association of the

European society of cardiology, Japanese heart failure society and writing committee of the universal definition of heart failure. *Journal of cardiac failure,* 27**,** 387-413.

Bradshaw, C., Atkinson, S. & Doody, O. 2017. Employing a qualitative description approach in health care research. *Global qualitative nursing research,* 4**,** 2333393617742282.

Bragazzi, N. L., Zhong, W., Shu, J., Abu Much, A., Lotan, D., Grupper, A., Younis, A. & Dai, H. 2021. Burden of heart failure and underlying causes in 195 countries and territories from 1990 to 2017. *European Journal of Preventive Cardiology,* 28**,** 1682-1690.

Braun, V. & Clarke, V. 2006. Using thematic analysis in psychology. *Qualitative research in psychology,* 3**,** 77-101.

Braun, V. & Clarke, V. 2019. Reflecting on reflexive thematic analysis. *Qualitative research in sport, exercise and health,* 11**,** 589-597.

Braun, V. & Clarke, V. 2022. *Thematic analysis: A practical guide.* , SAGE Publications.

Braun, V. & Clarke, V. 2023. Toward good practice in thematic analysis: Avoiding common problems and be (com) ing a knowing researcher. *International Journal of Transgender Health,* 24**,** 1-6.

Brewer, J. & Hunter, A. 2006. *Foundations of multimethod research: Synthesizing styles*, Sage.

Brush, S., Zambroski, C. H. & Rasmusson, K. 2006. Palliative Care for the Patient With End-Stage Heart Failure. *Progress in cardiovascular nursing,* 21**,** 166-170.

Buch-Hansen, H. & Nielsen, P. 2020. *Critical realism: Basics and beyond*, Bloomsbury Publishing.

Buck, H. G., Harkness, K., Wion, R., Carroll, S. L., Cosman, T., Kaasalainen, S., Kryworuchko, J., Mcgillion, M., O'keefe-Mccarthy, S. & Sherifali, D. 2015. Caregivers' contributions to heart failure self-care: a systematic review. *European Journal of Cardiovascular Nursing,* 14**,** 79-89.

Busolo, D. & Woodgate, R. 2015. Palliative care experiences of adult cancer patients from ethnocultural groups: a qualitative systematic review protocol. *JBI Evidence Synthesis,* 13**,** 99-111.

Butler, J., Braunwald, E. & Gheorghiade, M. 2014. Recognizing worsening chronic heart failure as an entity and an end point in clinical trials. *Jama,* 312**,** 789-790.

Butler, J., Petrie, M. C., Bains, M., Bawtinheimer, T., Code, J., Levitch, T., Malvolti, E., Monteleone, P., Stevens, P. & Vafeiadou, J. 2023. Challenges and opportunities for increasing patient involvement in heart failure self-care programs and self-care in the post–hospital discharge period. *Research Involvement and Engagement,* 9**,** 23.

Cameron, J., Worrall-Carter, L., Page, K. & Stewart, S. 2010. Self-care behaviours and heart failure: Does experience with symptoms really make a difference? *European Journal of Cardiovascular Nursing,* 9**,** 92-100.

Caruana, L., Petrie, M. C., Davie, A. P. & Mcmurray, J. J. 2000. Do patients with suspected heart failure and preserved left ventricular systolic function suffer from "diastolic heart failure" or from misdiagnosis? A prospective descriptive study. *BMJ,* 321**,** 215-9.

Cavusoglu, Y., Altay, H., Aras, D., Çelik, A., Ertas, F. S., Kilicaslan, B., Nalbantgil, S., Temizhan, A., Ural, D. & Yildirimturk, O. 2022. Cost-of-disease of Heart Failure in Turkey: A Delphi Panel-based Analysis of Direct and Indirect Costs.

Chafe, R. 2017. The value of qualitative description in health services and policy research. *Healthcare policy,* 12**,** 12.

Chan, Y.-K., Stickland, N. & Stewart, S. 2023. An inevitable or modifiable trajectory towards heart failure in high-risk individuals: insights from the nurse-led intervention for less chronic heart failure (NIL-CHF) study. *European Journal of Cardiovascular Nursing,* 22**,** 33-42.

Checa, C., Medina-Perucha, L., Muñoz, M.-Á., Verdú-Rotellar, J. M. & Berenguera, A. 2020. Living with advanced heart failure: A qualitative study. *Plos one,* 15**,** e0243974.

Cheng, R. K., Cox, M., Neely, M. L., Heidenreich, P. A., Bhatt, D. L., Eapen, Z. J., Hernandez, A. F., Butler, J., Yancy, C. W. & Fonarow, G. C. 2014. Outcomes in patients with heart failure with preserved, borderline, and reduced ejection fraction in the Medicare population. *American heart journal,* 168**,** 721-730. e3.

Chioncel, O., Lainscak, M., Seferovic, P. M., Anker, S. D., Crespo-Leiro, M. G., Harjola, V. P., Parissis, J., Laroche, C., Piepoli, M. F. & Fonseca, C. 2017. Epidemiology and one-year outcomes in patients with chronic heart failure and preserved, mid-range and reduced ejection fraction: an analysis of the ESC Heart Failure Long-Term Registry. *European journal of heart failure,* 19**,** 1574-1585.

Clark, A. M., Spaling, M., Harkness, K., Spiers, J., Strachan, P. H., Thompson, D. R. & Currie, K. 2014. Determinants of effective heart failure self-care: a systematic review of patients' and caregivers' perceptions. *Heart,* 100**,** 716-721.

Conrad, N., Judge, A., Tran, J., Mohseni, H., Hedgecott, D., Crespillo, A. P., Allison, M., Hemingway, H., Cleland, J. G. & Mcmurray, J. J. 2018. Temporal trends and patterns in heart failure incidence: a population-based study of 4 million individuals. *The Lancet,* 391**,** 572-580.

Cook, C., Cole, G., Asaria, P., Jabbour, R. & Francis, D. P. 2014. The annual global economic burden of heart failure. *International journal of cardiology,* 171**,** 368-376.

Coulter, A., Entwistle, V. A., Eccles, A., Ryan, S., Shepperd, S. & Perera, R. 2015. Personalised care planning for adults with chronic or long-term health conditions. *Cochrane Database of Systematic Reviews*.

Creber, R. M., Patey, M., Dickson, V. V., Decesaris, M. & Riegel, B. 2015. Motivational interviewing tailored interventions for heart failure (MITI-HF): study design and methods. *Contemporary clinical trials,* 41**,** 62-68.

Crespo-Leiro, M. G., Anker, S. D., Maggioni, A. P., Coats, A. J., Filippatos, G., Ruschitzka, F., Ferrari, R., Piepoli, M. F., Delgado Jimenez, J. F. & Metra, M. 2016. European Society of Cardiology Heart Failure Long-Term Registry (ESC-HF-LT): 1-year follow-up outcomes and differences across regions. *European journal of heart failure,* 18**,** 613-625.

Crespo-Leiro, M. G., Metra, M., Lund, L. H., Milicic, D., Costanzo, M. R., Filippatos, G., Gustafsson, F., Tsui, S., Barge-Caballero, E. & De Jonge, N. 2018. Advanced heart failure: a position statement of the Heart Failure Association of the European Society of Cardiology. *European journal of heart failure,* 20**,** 1505-1535.

Creswell, J. W. 2015. *A concise introduction to mixed methods research,* Thousand Oaks, California :bSAGE Publications, Inc.

Creswell, J. W. & Creswell, J. D. 2018. *Research design: Qualitative, quantitative, and mixed methods approaches*, Sage publications.

Creswell, J. W., Klassen, A. C., Plano Clark, V. L. & Smith, K. C. 2011. Best practices for mixed methods research in the health sciences. *Bethesda (Maryland): National Institutes of Health,* 2013**,** 541-545.

Creswell, J. W. & Plano Clark, V. L. 2018. *Designing and conducting mixed methods research,* London, SAGE Publications.

Cui, X., Zhou, X., Ma, L.-L., Sun, T.-W., Bishop, L., Gardiner, F. W. & Wang, L. 2019. A nurse-led structured education program improves self-management skills and reduces hospital readmissions in patients with chronic heart failure: a randomized and controlled trial in China. *Rural and remote health,* 19**,** 1-8.

Curry, L. A., Nembhard, I. M. & Bradley, E. H. 2009. Qualitative and mixed methods provide unique contributions to outcomes research. *Circulation,* 119**,** 1442-1452.

Curtis, S., Gesler, W., Smith, G. & Washburn, S. 2000. Approaches to sampling and case selection in qualitative research: examples in the geography of health. *Social science & medicine,* 50**,** 1001-1014.

Dale, A., Wathan, J. & Higgins, V. 2008. Secondary analysis of quantitative data sources. *The SAGE Handbook of Social Research Methods. London, United Kingdom: SAGE Publications Ltd***,** 520-535.

Darling, C., Saczynski, J. S., Mcmanus, D. D., Lessard, D., Spencer, F. A. & Goldberg, R. J. 2013. Delayed hospital presentation in acute decompensated heart failure: clinical and patient reported factors. *Heart & Lung,* 42**,** 281-286.

Datla, S., Verberkt, C. A., Hoye, A., Janssen, D. J. & Johnson, M. J. 2019. Multi-disciplinary palliative care is effective in people with symptomatic heart failure: a systematic review and narrative synthesis. *Palliative medicine,* 33**,** 1003-1016.

Davidson, P., Cockburn, J., Daly, J. & Fisher, R. S. 2004. Patient-centered needs assessment: rationale for a psychometric measure for assessing needs in heart failure. *Journal of Cardiovascular Nursing,* 19**,** 164-171.

Davidson, P. M., Cockburn, J. & Newton, P. J. 2008. Unmet needs following hospitalization with heart failure: implications for clinical assessment and program planning. *Journal of Cardiovascular Nursing,* 23**,** 541-546.

Davies, L., Leclair, K. L., Bagley, P., Blunt, H., Hinton, L., Ryan, S. & Ziebland, S. 2020. Face-to-face compared with online collected accounts of health and illness experiences: a scoping review. *Qualitative Health Research,* 30**,** 2092-2102.

Davis, J. D., Olsen, M. A., Bommarito, K., Larue, S. J., Saeed, M., Rich, M. W. & Vader, J. M. 2017. All-payer analysis of heart failure hospitalization 30-day readmission: comorbidities matter. *The American journal of medicine,* 130**,** 93. e9-93. e28.

Değertekin, M., Erol, Ç., Ergene, O., Tokgözoğlu, L., Aksoy, M., Erol, M. K., Eren, M., Sahin, M., Eroğlu, E. & Mutlu, B. 2012. Heart failure prevalence and predictors in Turkey: HAPPY study. *Turk Kardiyoloji Dernegi arsivi: Turk Kardiyoloji Derneginin yayin organidir,* 40**,** 298-308.

Denfeld, Q. E., Bidwell, J. T., Gelow, J. M., Mudd, J. O., Chien, C. V., Hiatt, S. O. & Lee, C. S. 2020. Cross-classification of physical and affective symptom clusters and 180-day event-free survival in moderate to advanced heart failure. *Heart & Lung,* 49**,** 151-157.

Denzin, N. K. 1978. *Sociological methods: A sourcebook,* NeW York, McGraw Hill.

Devine, P. 2003. Secondary Analysis. *The AZ of Social Research.* SAGE.

Devon, H. A., Vuckovic, K., Ryan, C. J., Barnason, S., Zerwic, J. J., Pozehl, B., Schulz, P., Seo, Y. & Zimmerman, L. 2017. Systematic review of symptom clusters in cardiovascular disease. *European Journal of Cardiovascular Nursing,* 16**,** 6-17.

Dickson, V. V., Buck, H. & Riegel, B. 2011. A qualitative meta-analysis of heart failure self-care practices among individuals with multiple comorbid conditions. *Journal of cardiac failure,* 17**,** 413-419.

Dickson, V. V., Buck, H. & Riegel, B. 2013. Multiple comorbid conditions challenge heart failure self-care by decreasing self-efficacy. *Nursing research,* 62**,** 2-9.

Dickson, V. V., Mccarthy, M. M., Alexandra Howe, B., Schipper, J. & Katz, S. M. 2012. Sociocultural Influences on Heart Failure Self-care Among an Ethnic Minority Black Population.

Dinatolo, E., Sciatti, E., Anker, M. S., Lombardi, C., Dasseni, N. & Metra, M. 2018. Updates in heart failure: what last year brought to us. *ESC heart failure,* 5**,** 989.

Dionne-Odom, J. N., Ejem, D. B., Wells, R., Azuero, A., Stockdill, M. L., Keebler, K., Sockwell, E., Tims, S., Engler, S. & Kvale, E. 2020. Effects of a telehealth early palliative care intervention for family caregivers of persons with advanced heart failure: the ENABLE CHF-PC randomized clinical trial. *JAMA network open,* 3**,** e202583-e202583.

Disertori, M., Masè, M., Rigoni, M., Nollo, G. & Ravelli, F. 2020. Declining clinical benefit of ICD in heart failure patients: Temporal trend of mortality outcomes from randomized controlled trials. *Journal of Cardiology,* 75**,** 148-154.

Ditewig, J. B., Blok, H., Havers, J. & Van Veenendaal, H. 2010. Effectiveness of self-management interventions on mortality, hospital readmissions, chronic heart failure hospitalization rate and quality of life in patients with chronic heart failure: a systematic review. *Patient education and counseling,* 78**,** 297-315.

Dodd, M., Janson, S., Facione, N., Faucett, J., Froelicher, E. S., Humphreys, J., Lee, K., Miaskowski, C., Puntillo, K. & Rankin, S. 2001a. Advancing the science of symptom management. *Journal of advanced nursing,* 33**,** 668-676.

Dodd, M. J., Miaskowski, C. & Paul, S. M. Symptom clusters and their effect on the functional status of patients with cancer. Oncology nursing forum, 2001b.

Dodgson, J. E. 2019. Reflexivity in qualitative research. *Journal of Human Lactation,* 35**,** 220-222.

Dongre, A. R., Deshmukh, P. R., Kalaiselvan, G. & Upadhyaya, S. 2009. Application of qualitative methods in health research: An overview. *Online J Health Allied Scs,* 8**,** 3.

Doyle, L., Brady, A.-M. & Byrne, G. 2016. An overview of mixed methods research–revisited. *Journal of Research in Nursing,* 21**,** 623-635.

Doyle, L., Mccabe, C., Keogh, B., Brady, A. & Mccann, M. 2020. An overview of the qualitative descriptive design within nursing research. *Journal of Research in Nursing,* 25**,** 443-455.

Driscoll, A., Currey, J., Tonkin, A. & Krum, H. 2015. Nurse-led titration of angiotensin converting enzyme inhibitors, beta-adrenergic blocking agents, and angiotensin receptor blockers for people with heart failure with reduced ejection fraction. *Cochrane Database of Systematic Reviews*.

Enç, N. & Öz Alkan, H. 2013. TKD Kalp Yetersizliği, Akut Koroner Sendromlar, Hipertansiyon, Perkütan Koroner ve Valvüler Girişimlerde Hemşirelik Bakım Kılavuzlarının Kullanımına Yönelik Değerlendirme.

Enç, N., Yigit, Z., Gün Altiok, M., Özer, S. & Oguz, S. 2007. *Kalp Yetersizligi, Akut Koroner Sendromlar ve Hipertansiyon Hemsirelik Bakim Kilavuzu* [Online]. Turkish Society of Cardiology. Available: https://file.tkd.org.tr/kilavuzlar/ulusal/2007_kalp_yetersizligi_akut_koroner_sendromlarda_hipertansiyon_hemsirelik_bakim_kilavuzu.pdf [Accessed July 2023].

Eriksen, T. E. & Risør, M. B. 2014. What is called symptom? *Medicine, Health Care and Philosophy,* 17**,** 89-102.

Erzberger, C. & Prein, G. 1997. Triangulation: Validity and empirically-based hypothesis construction. *Quality and quantity,* 31**,** 141-154.

Esc, E. S. O. C. 2022. *Turkish Society of Cardiology: The Turkish Society of Cardiology is a member of the European Society of Cardiology* [Online]. Available: https://www.escardio.org/The-ESC/Member-National-Cardiac-Societies/Turkish-Society-of-Cardiology [Accessed June 2023].

Fadol, A., Buitrago, J., Diaz, M. C., Shelton, V., Harty, C. & Mendoza, T. R. 2019. Validation of the Spanish version of the MD Anderson symptom inventory–heart failure (MDASI-HF-Spanish) module. *Cardio-Oncology,* 5**,** 1-7.

Fadol, A., Mendoza, T., Gning, I., Kernicki, J., Symes, L., Cleeland, C. S. & Lenihan, D. 2008. Psychometric testing of the MDASI-HF: a symptom assessment instrument for patients with cancer and concurrent heart failure. *Journal of cardiac failure,* 14**,** 497-507.

Farmer, T., Robinson, K., Elliott, S. J. & Eyles, J. 2006. Developing and implementing a triangulation protocol for qualitative health research. *Qualitative health research,* 16**,** 377-394.

Farquhar, M. C., Ewing, G. & Booth, S. 2011. Using mixed methods to develop and evaluate complex interventions in palliative care research. *Palliative medicine,* 25**,** 748-757.

Feng, K. Y., O'connor, C. M., Clare, R., Alhanti, B., Piña, I. L., Kraus, W. E., Whellan, D. J. & Mentz, R. J. 2021. Greater Pain Severity Is Associated with Worse Outcomes in Patients with Heart Failure. *Journal of Cardiovascular Translational Research***,** 1-8.

Ferguson, C., Inglis, S. C., Gallagher, R. & Davidson, P. M. 2020. Reflecting on the impact of cardiovascular nurses in Australia and new Zealand in the international year of the nurse and midwife. *Heart, Lung and Circulation,* 29**,** 1744-1748.

Fischer, S. & Bekelman, D. 2017. Gender differences in sexual interest or activity among adults with symptomatic heart failure. *Journal of palliative medicine,* 20**,** 890-894.

Flint, K. M., Schmiege, S. J., Allen, L. A., Fendler, T. J., Rumsfeld, J. & Bekelman, D. 2017. Health status trajectories among outpatients with heart failure. *Journal of pain and symptom management,* 53**,** 224-231.

Foster, R. L. 1997. Addressing epistemologic and practical issues in multimethod research: A procedure for conceptual triangulation. *Advances in Nursing Science,* 20**,** 1-12.

Friedman, M. M. & Quinn, J. R. 2008. Heart failure patients' time, symptoms, and actions before a hospital admission. *Journal of Cardiovascular Nursing,* 23**,** 506-512.

Gallagher, R., Sullivan, A., Hales, S., Gillies, G., Burke, R. & Tofler, G. 2012. Symptom patterns, duration and responses in newly diagnosed patients with heart failure. *International journal of nursing practice,* 18**,** 133-139.

Gbd 2018. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017.

Gerber, Y., Weston, S. A., Redfield, M. M., Chamberlain, A. M., Manemann, S. M., Jiang, R., Killian, J. M. & Roger, V. L. 2015. A contemporary appraisal of the heart failure epidemic in Olmsted County, Minnesota, 2000 to 2010. *JAMA internal medicine,* 175**,** 996-1004.

Glenwright, B. G., Simmich, J., Cottrell, M., O'leary, S. P., Sullivan, C., Pole, J. D. & Russell, T. 2023. Facilitators and barriers to implementing electronic patient-reported outcome and experience measures in a health care setting: a systematic review. *Journal of patient-reported outcomes,* 7**,** 13.

González-González, A. I., Brünn, R., Nothacker, J., Schwarz, C., Nury, E., Dinh, T. S., Brueckle, M.-S., Dieckelmann, M., Müller, B. S. & Van Den Akker, M. 2021. Everyday lives of middle-aged persons with multimorbidity: a mixed methods systematic review. *International Journal of Environmental Research and Public Health,* 19**,** 6.

Gopalakrishnan, S. & Ganeshkumar, P. 2013. Systematic reviews and meta-analysis: understanding the best evidence in primary healthcare. *Journal of family medicine and primary care,* 2**,** 9.

Grady, K. L., Dracup, K., Kennedy, G., Moser, D. K., Piano, M., Stevenson, L. W. & Young, J. B. 2000. Team management of patients with heart failure: a statement for healthcare professionals from the Cardiovascular Nursing Council of the American Heart Association. *Circulation,* 102**,** 2443-2456.

Graven, L. J., Higgins, M. K., Reilly, C. M. & Dunbar, S. B. 2020. Heart failure symptoms profile associated with depressive symptoms. *Clinical nursing research,* 29**,** 73-83.

Green, C. P., Porter, C. B., Bresnahan, D. R. & Spertus, J. A. 2000. Development and evaluation of the Kansas City Cardiomyopathy Questionnaire: a new health status measure for heart failure. *Journal of the American College of Cardiology,* 35**,** 1245-1255.

Greene, S. J., Butler, J., Albert, N. M., Devore, A. D., Sharma, P. P., Duffy, C. I., Hill, C. L., Mccague, K., Mi, X. & Patterson, J. H. 2018a. Medical therapy for heart failure with reduced ejection fraction: the CHAMP-HF registry. *Journal of the American College of Cardiology,* 72**,** 351-366.

Greene, S. J., Mentz, R. J. & Felker, G. M. 2018b. Outpatient worsening heart failure as a target for therapy: a review. *JAMA cardiology,* 3**,** 252-259.

Groenewegen, A., Rutten, F. H., Mosterd, A. & Hoes, A. W. 2020. Epidemiology of heart failure. *European journal of heart failure,* 22**,** 1342-1356.

Guba, E. G. & Lincoln, Y. S. 1994. Competing paradigms in qualitative research. *Handbook of qualitative research,* 2**,** 105.

Guest, G., Bunce, A. & Johnson, L. 2006. How many interviews are enough? An experiment with data saturation and variability. *Field methods,* 18**,** 59-82.

Haedtke, C. A., Moser, D. K., Pressler, S. J., Chung, M. L., Wingate, S. & Goodlin, S. J. 2019. Influence of depression and gender on symptom burden among patients with advanced heart failure: Insight from the pain assessment, incidence and nature in heart failure study. *Heart & Lung,* 48**,** 201-207.

Hakim, C. 1982. *Secondary analysis in social research: A guide to data sources and methods with examples.,* London, George Allen & Unwin.

Hamatani, Y., Iguchi, M., Ikeyama, Y., Kunugida, A., Ogawa, M., Yasuda, N., Fujimoto, K., Ichihara, H., Sakai, M. & Kinoshita, T. 2022. Comprehensive symptom assessment using Integrated Palliative care Outcome Scale in hospitalized heart failure patients. *ESC Heart Failure,* 9**,** 1963-1975.

Harkness, K., Buck, H. G., Arthur, H., Carroll, S., Cosman, T., Mcgillion, M., Kaasalainen, S., Kryworuchko, J., O'keefe-Mccarthy, S. & Sherifali, D. 2016. Caregiver contribution to heart failure self-care (CACHS). *Nursing Open,* 3**,** 51-60.

Harkness, K., Spaling, M. A., Currie, K., Strachan, P. H. & Clark, A. M. 2015. A systematic review of patient heart failure self-care strategies. *Journal of Cardiovascular Nursing,* 30**,** 121-135.

Heaton, J. 2008. Secondary analysis of qualitative data: An overview. *Historical Social Research/Historische Sozialforschung***,** 33-45.

Hedemalm, A., Schaufelberger, M. & Ekman, I. 2008. Symptom recognition and health care seeking among immigrants and native Swedish patients with heart failure. *BMC nursing,* 7**,** 1-7.

Heeks, R., Ospina, A. V. & Wall, P. Combining pragmatism and critical realism in ICT4D research: an e-Resilience Case Example. Information and Communication Technologies for Development. Strengthening Southern-Driven Cooperation as a Catalyst for ICT4D: 15th IFIP WG 9.4 International Conference on Social Implications of Computers in Developing Countries, ICT4D 2019, Dar es Salaam, Tanzania, May 1–3, 2019, Proceedings, Part II 15, 2019. Springer, 14-25.

Heidenreich, P. A., Albert, N. M., Allen, L. A., Bluemke, D. A., Butler, J., Fonarow, G. C., Ikonomidis, J. S., Khavjou, O., Konstam, M. A. & Maddox, T. M. 2013. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. *Circulation: Heart Failure,* 6**,** 606-619.

Helvaci, A., Izgu, N. & Ozdemir, L. 2020. Relationship between symptom burden, medication adherence and spiritual well-being in patients with chronic obstructive pulmonary disease. *Journal of Clinical Nursing,* 29**,** 2388-2396.

Henly, S. J., Kallas, K. D., Klatt, C. M. & Swenson, K. K. 2003. The notion of time in symptom experiences. *Nursing Research,* 52**,** 410-417.

Heo, S., Moser, D. K., Lennie, T. A., Fischer, M., Kim, J., Walsh, M. N., Ounpraseuth, S. & Turrise, S. 2020. Prediction of heart failure symptoms and health-related quality of life at 12 months from baseline modifiable factors in patients with heart failure. *Journal of Cardiovascular Nursing,* 35**,** 116-125.

Heo, S., Moser, D. K., Lennie, T. A., Grudnowski, S., Kim, J. & Turrise, S. 2019a. Patients' beliefs about causes and consequences of heart failure symptoms. *Western journal of nursing research,* 41, 1623-1641.

Heo, S., Moser, D. K., Riegel, B., Hall, L. A. & Christman, N. 2005. Testing a published model of health-related quality of life in heart failure. *Journal of cardiac failure,* 11, 372-379.

Heo, S., Shin, M.-S., Hwang, S. Y., An, M., Park, J.-K., Kim, S., Shim, J. L. & Kim, J. 2019b. Sex differences in heart failure symptoms and factors associated with heart failure symptoms. *Journal of Cardiovascular Nursing,* 34, 306-312.

Herdman, M., Gudex, C., Lloyd, A., Janssen, M., Kind, P., Parkin, D., Bonsel, G. & Badia, X. 2011. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Quality of life research,* 20, 1727-1736.

Herr, J. K., Salyer, J., Lyon, D. E., Goodloe, L., Schubert, C. & Clement, D. G. 2014. Heart failure symptom relationships: a systematic review. *Journal of Cardiovascular Nursing,* 29, 416-422.

Hess, D. R. 2004. Retrospective studies and chart reviews. *Respiratory care,* 49, 1171-1174.

Hill, L., Baruah, R., Beattie, J. M., Bistola, V., Castiello, T., Celutkienė, J., Di Stolfo, G., Geller, T. P., Lambrinou, E. & Mindham, R. 2023. Culture, ethnicity, and socio-economic status as determinants of the management of patients with advanced heart failure who need palliative care: A clinical consensus statement from the Heart Failure Association (HFA) of the ESC, the ESC Patient Forum, and the European Association of Palliative Care. *European journal of heart failure,* 25, 1481-1492.

Hill, L., Prager Geller, T., Baruah, R., Beattie, J. M., Boyne, J., De Stoutz, N., Di Stolfo, G., Lambrinou, E., Skibelund, A. K. & Uchmanowicz, I. 2020. Integration of a palliative approach into heart failure care: a European Society of Cardiology Heart Failure Association position paper. *European journal of heart failure,* 22, 2327-2339.

Hobbs, F. R., Roalfe, A. K., Davis, R. C., Davies, M. K. & Hare, R. 2007. Prognosis of all-cause heart failure and borderline left ventricular systolic dysfunction: 5 year mortality follow-up of the Echocardiographic Heart of England Screening Study (ECHOES). *European heart journal,* 28, 1128-1134.

Holden, R. J., Schubert, C. C. & Mickelson, R. S. 2015. The patient work system: an analysis of self-care performance barriers among elderly heart failure patients and their informal caregivers. *Applied ergonomics,* 47, 133-150.

Hollenberg, S. M., Warner Stevenson, L., Ahmad, T., Amin, V. J., Bozkurt, B., Butler, J., Davis, L. L., Drazner, M. H., Kirkpatrick, J. N. & Peterson, P. N. 2019. 2019 ACC expert consensus decision pathway on risk assessment, management, and clinical trajectory of patients hospitalized with heart failure: a report of the American College of Cardiology Solution Set Oversight Committee. *Journal of the American College of Cardiology,* 74, 1966-2011.

Houghton, C., Hunter, A. & Meskell, P. 2012. Linking aims, paradigm and method in nursing research. *Nurse researcher,* 20.

Hu, Y., Jiang, J., Xu, L., Wang, C., Wang, P., Yang, B. & Tao, M. 2021. Symptom clusters and quality of life among patients with chronic heart failure: A cross-sectional study. *Japan Journal of Nursing Science,* 18, e12366.

Hui, D. & Bruera, E. 2017. The Edmonton Symptom Assessment System 25 years later: past, present, and future developments. *Journal of pain and symptom management,* 53**,** 630-643.

Humphreys, J., Janson, S., Donesky, D., Dracup, K., Lee, K. A., Puntillo, K., Faucett, J. A., Aouizerat, B., Miaskowski, C., Baggott, C., Carrieri-Kohlman, V., Barger, M., Franck, L. & Christine, K. 2014. Theory of Symptom Management. *In:* Smith, M. J. & Liehr, P. R. (eds.) *Middle Range Theory for Nursing.* 3rd ed. New York: Springer.

Hung, Y., Cheung, N., Ip, S. & Fung, H. 2000. Epidemiology of heart failure in Hong Kong, 1997. *Hong Kong Medical Journal,* 6**,** 159-162.

Impellizzeri, F. M. & Bizzini, M. 2012. Systematic review and meta-analysis: A primer. *International journal of sports physical therapy,* 7**,** 493.

Imran, H. 2024. Pragmatic critical realism and Mixed methods in Inter-disciplinary Research—Management and Information systems. *Valley International Journal Digital Library***,** 5953-5962.

Inglis, S. C., Clark, R. A., Dierckx, R., Prieto-Merino, D. & Cleland, J. G. 2015. Structured telephone support or non-invasive telemonitoring for patients with heart failure. *Cochrane Database of Systematic Reviews*.

Inglis, S. C., Naismith, C., White, K., Hendriks, J. M., Bray, J., Hickman, L. D., Aldridge, C., Bardsley, K., Cameron, J. & Candelaria, D. 2020. CSANZ COVID-19 cardiovascular nursing care consensus statement: executive summary. *Heart, Lung and Circulation,* 29**,** 1263-1267.

Jaarsma, T., Hill, L., Bayes-Genis, A., La Rocca, H. P. B., Castiello, T., Čelutkienė, J., Marques-Sule, E., Plymen, C. M., Piper, S. E. & Riegel, B. 2021. Self-care of heart failure patients: practical management recommendations from the Heart Failure Association of the European Society of Cardiology. *European journal of heart failure,* 23**,** 157-174.

Jakobsen, J. C., Gluud, C., Wetterslev, J. & Winkel, P. 2017. When and how should multiple imputation be used for handling missing data in randomised clinical trials–a practical guide with flowcharts. *BMC medical research methodology,* 17**,** 1-10.

Janssen, D. J., Spruit, M. A., Uszko-Lencer, N. H., Schols, J. M. & Wouters, E. F. 2011. Symptoms, comorbidities, and health care in advanced chronic obstructive pulmonary disease or chronic heart failure. *Journal of palliative medicine,* 14**,** 735-743.

Jensen, J., Omar, M., Kistorp, C., Poulsen, M. K., Tuxen, C., Gustafsson, I., Køber, L., Gustafsson, F., Fosbøl, E. & Bruun, N. E. 2019. Empagliflozin in heart failure patients with reduced ejection fraction: a randomized clinical trial (Empire HF). *Trials,* 20**,** 374.

Jiang, Y., Koh, K. W. L., Ramachandran, H. J., Nguyen, H. D., Tay, Y. K., Shorey, S. & Wang, W. 2021. The effectiveness of a nurse-led home-based heart failure self-management programme (the HOM-HEMP) for patients with chronic heart failure: a three-arm stratified randomized controlled trial. *International journal of nursing studies,* 122**,** 104026.

Johansson, I., Joseph, P., Balasubramanian, K., Mcmurray, J. J., Lund, L. H., Ezekowitz, J. A., Kamath, D., Alhabib, K., Bayes-Genis, A. & Budaj, A. 2021. Health-related quality of life and mortality in heart failure: the global congestive heart failure study of 23 000 patients from 40 countries. *Circulation,* 143**,** 2129-2142.

Johnston, B. & Dowling, M. Qualitative Research and Cancer Nursing: A Guide for Novice Researchers. Seminars in Oncology Nursing, 2023. Elsevier, 151397.

Johnston, B., Mcgill, M., Milligan, S., Mcelroy, D., Foster, C. & Kearney, N. 2009. Self care and end of life care in advanced cancer: literature review. *European Journal of Oncology Nursing,* 13**,** 386-398.

Johnston, B. & Narayanasamy, M. 2016. Exploring psychosocial interventions for people with dementia that enhance personhood and relate to legacy-an integrative review. *BMC geriatrics,* 16**,** 1-25.

Johnston, B., Pringle, J. & Buchanan, D. 2016. Operationalizing reflexivity to improve the rigor of palliative care research. *Applied Nursing Research,* 31**,** e1-e5.

Johnston, B., Rogerson, L., Macijauskiene, J., Blaževičienė, A. & Cholewka, P. 2014. An exploration of self-management support in the context of palliative nursing: a modified concept analysis. *BMC nursing,* 13**,** 1-10.

Johnston, B. M., Milligan, S., Foster, C. & Kearney, N. 2012. Self-care and end of life care—patients' and carers' experience a qualitative study utilising serial triangulated interviews. *Supportive Care in Cancer,* 20**,** 1619-1627.

Johnston, M. P. 2014. Secondary data analysis: A method of which the time has come. *Qualitative and quantitative methods in libraries,* 3**,** 619-626.

Jones, M. C., Macgillivray, S., Kroll, T., Zohoor, A. R. & Connaghan, J. 2011. A thematic analysis of the conceptualisation of self-care, self-management and self-management support in the long-term conditions management literature. *Journal of Nursing and Healthcare of Chronic Illness,* 3**,** 174-185.

Jones, N. R., Roalfe, A. K., Adoki, I., Hobbs, F. R. & Taylor, C. J. 2019. Survival of patients with chronic heart failure in the community: a systematic review and meta-analysis. *European journal of heart failure,* 21**,** 1306-1325.

Jonkman, N. H., Westland, H., Groenwold, R. H., Ågren, S., Atienza, F., Blue, L., Bruggink-André De La Porte, P. W., Dewalt, D. A., Hebert, P. L. & Heisler, M. 2016. Do self-management interventions work in patients with heart failure? An individual patient data meta-analysis. *Circulation,* 133**,** 1189-1198.

Joseph, P., Dokainish, H., Mccready, T., Budaj, A., Roy, A., Ertl, G., Gomez-Mesa, J. E., Leong, D., Ezekowitz, J. & Hage, C. 2020. A multinational registry to study the characteristics and outcomes of heart failure patients: the global congestive heart failure (G-CHF) registry. *American Heart Journal,* 227**,** 56-63.

Jowsey, T., Jeon, Y.-H., Usherwood, T., Glasgow, N. J., Kljakovic, M. & Dugdale, P. 2009. Challenges for co-morbid chronic illness care and policy in Australia: a qualitative study. *Australia and New Zealand health policy,* 6.

Jurgens, C. Y. 2016. The value of patient perception of heart failure symptoms: commentary on physical and psychological symptom biomechanics in moderate to advanced heart failure. *Journal of Cardiovascular Nursing,* 31**,** 140-141.

Jurgens, C. Y., Fain, J. A. & Riegel, B. 2006. Psychometric testing of the heart failure somatic awareness scale. *Journal of cardiovascular nursing,* 21**,** 95-102.

Jurgens, C. Y., Hoke, L., Byrnes, J. & Riegel, B. 2009. Why do elders delay responding to heart failure symptoms? *Nursing research,* 58**,** 274-282.

Jurgens, C. Y., Lee, C. S. & Riegel, B. 2017. Psychometric analysis of the heart failure somatic perception scale as a measure of patient symptom perception. *The Journal of cardiovascular nursing,* 32**,** 140.

Kahlke, R. M. 2014. Generic qualitative approaches: Pitfalls and benefits of methodological mixology. *International journal of qualitative methods,* 13**,** 37-52.

Kallio, H., Pietilä, A. M., Johnson, M. & Kangasniemi, M. 2016. Systematic methodological review: developing a framework for a qualitative semi-structured interview guide. *Journal of advanced nursing,* 72**,** 2954-2965.

Kalogirou, F., Forsyth, F., Kyriakou, M., Mantle, R. & Deaton, C. 2020. Heart failure disease management: a systematic review of effectiveness in heart failure with preserved ejection fraction. *ESC heart failure,* 7**,** 195-213.

Karabulut, D., Günay, Ş., Sert Şekerci, S., Aydın, E., Köz, K., Katkat, F., Saraç, İ., Er, F., Öztürk, Ö. & Oktay, V. 2024. Heart Failure Awareness Survey in a Turkish Population: HFAS-TR. *Archives of the Turkish Society of Cardiology,* 52**,** 337-343.

Kavalieratos, D., Kamal, A. H., Abernethy, A. P., Biddle, A. K., Carey, T. S., Dev, S., Reeve, B. B. & Weinberger, M. 2014. Comparing unmet needs between community-based palliative care patients with heart failure and patients with cancer. *Journal of palliative medicine,* 17**,** 475-481.

Kelly, M., Dowling, M. & Millar, M. 2018. The search for understanding: The role of paradigms. *Nurse researcher,* 25**,** 9-13.

Khan, H., Greene, S. J., Fonarow, G. C., Kalogeropoulos, A. P., Ambrosy, A. P., Maggioni, A. P., Zannad, F., Konstam, M. A., Swedberg, K. & Yancy, C. W. 2015. Length of hospital stay and 30-day readmission following heart failure hospitalization: insights from the EVEREST trial. *European journal of heart failure,* 17**,** 1022-1031.

Kim, H., Sefcik, J. S. & Bradway, C. 2017. Characteristics of qualitative descriptive studies: A systematic review. *Research in nursing & health,* 40**,** 23-42.

Kimani, K. N., Murray, S. A. & Grant, L. 2018. Multidimensional needs of patients living and dying with heart failure in Kenya: a serial interview study. *BMC Palliative Care,* 17**,** 1-8.

Koh, A. S., Tay, W. T., Teng, T. H. K., Vedin, O., Benson, L., Dahlstrom, U., Savarese, G., Lam, C. S. & Lund, L. H. 2017. A comprehensive population-based characterization of heart failure with mid-range ejection fraction. *European journal of heart failure,* 19**,** 1624-1634.

Krethong, P., Jirapaet, V., Jitpanya, C. & Sloan, R. 2008. A causal model of health-related quality of life in Thai patients with heart-failure. *Journal of Nursing Scholarship,* 40**,** 254-260.

Kroenke, K., Spitzer, R. L. & Williams, J. B. 2001. The PHQ-9: validity of a brief depression severity measure. *Journal of general internal medicine,* 16**,** 606-613.

Krogsgaard, M. R., Brodersen, J., Christensen, K. B., Siersma, V., Kreiner, S., Jensen, J., Hansen, C. F. & Comins, J. D. 2021. What is a PROM and why do we need it? *Scandinavian journal of medicine & science in sports,* 31**,** 967-971.

Kutlay, M. & Öniş, Z. 2023. Liberal Democracy on the Edge? Anxieties in a Shifting Global (dis) order. *Alternatives,* 48**,** 20-37.

Kyriakou, M., Middleton, N., Ktisti, S., Philippou, K. & Lambrinou, E. 2020. Supportive care interventions to promote health-related quality of life in patients living with heart failure: a systematic review and meta-analysis. *Heart, Lung and Circulation,* 29**,** 1633-1647.

Lam, C. S., Arnott, C., Beale, A. L., Chandramouli, C., Hilfiker-Kleiner, D., Kaye, D. M., Ky, B., Santema, B. T., Sliwa, K. & Voors, A. A. 2019. Sex differences in heart failure. *European heart journal,* 40**,** 3859-3868c.

Lambert, V. A. & Lambert, C. E. 2012. Qualitative descriptive research: An acceptable design. *Pacific Rim international journal of nursing research,* 16**,** 255-256.

Lambrinou, E., Kalogirou, F., Lamnisos, D. & Sourtzi, P. 2012. Effectiveness of heart failure management programmes with nurse-led discharge planning in reducing re-admissions: a systematic review and meta-analysis. *International journal of nursing studies,* 49**,** 610-624.

Landrum, L. 2009. Description of symptom severity in heart failure: review of the literature. *Home Health Care Management & Practice,* 21**,** 158-170.

Larson, P. J., Carrieri-Kohlman, V., Dodd, M. J., Douglas, M., Faucett, J., Froelicher, E. S., Gortner, S. R., Halliburton, P., Janson, S., Lee, L. A., Miaskowski, C., Savedra, M. C., Stotts, N. A., Taylor, D. & Underwood, P. R. 1994. A model for symptom management. *IMAGE: Journal of Nursing Scholarship,* 26**,** 272–276.

Larson, P. J., Uchinuno, A., Izumi, S., Kawano, A., Takemoto, A., Shigeno, M., Yamamoto, M. & Shibata, S. 1999. An integrated approach to symptom management. *Nursing & Health Sciences,* 1**,** 203-210.

Lawson, C. A., Lam, C., Jaarsma, T., Kadam, U., Stromberg, A., Ali, M., Tay, W. T., Clayton, L., Khunti, K. & Squire, I. 2022. Developing a core outcome set for patient-reported symptom monitoring to reduce hospital admissions for patients with heart failure. *European Journal of Cardiovascular Nursing,* 21**,** 830-839.

Lawson, C. A., Solis-Trapala, I., Dahlstrom, U., Mamas, M., Jaarsma, T., Kadam, U. T. & Stromberg, A. 2018. Comorbidity health pathways in heart failure patients: A sequences-of-regressions analysis using cross-sectional data from 10,575 patients in the Swedish Heart Failure Registry. *PLoS medicine,* 15**,** e1002540.

Lawson, C. A., Zaccardi, F., Squire, I., Ling, S., Davies, M. J., Lam, C. S., Mamas, M. A., Khunti, K. & Kadam, U. T. 2019. 20-year trends in cause-specific heart failure outcomes by sex, socioeconomic status, and place of diagnosis: a population-based study. *The Lancet Public Health,* 4**,** e406-e420.

Lee, C. H. & Yoon, H.-J. 2017. Medical big data: promise and challenges. *Kidney research and clinical practice,* 36**,** 3.

Lee, C. S., Gelow, J. M., Mudd, J. O., Green, J. K., Hiatt, S. O., Chien, C. & Riegel, B. 2015. Profiles of self-care management versus consulting behaviors in adults with heart failure. *European journal of cardiovascular nursing,* 14**,** 63-72.

Lee, C. S., Mudd, J. O., Auld, J., Gelow, J. M., Hiatt, S. O., Chien, C. V., Bidwell, J. T. & Lyons, K. S. 2017. Patterns, relevance and predictors of heart failure dyadic symptom appraisal. *European Journal of Cardiovascular Nursing,* 16**,** 595-604.

Lee, K. S. & Moser, D. K. 2013. Heart failure symptom measures: critical review. *European Journal of Cardiovascular Nursing,* 12**,** 418-428.

Lee, K. S. & Oh, S. 2022. An integrative review of the symptom perception process in heart failure. *Journal of Cardiovascular Nursing,* 37**,** 122-133.

Lee, K. S., Song, E. K., Lennie, T. A., Frazier, S. K., Chung, M. L., Heo, S., Wu, J.-R., Rayens, M. K., Riegel, B. & Moser, D. K. 2010. Symptom clusters in men and women with heart failure and their impact on cardiac event-free survival. *Journal of Cardiovascular Nursing,* 25**,** 263-272.

Lee, S. & Riegel, B. 2018. State of the science in heart failure symptom perception research: an integrative review. *Journal of Cardiovascular Nursing,* 33**,** 204-210.

Lehrke, M. & Marx, N. 2017. Diabetes mellitus and heart failure. *The American journal of cardiology,* 120**,** S37-S47.

Leiter, R., Santus, E., Jin, Z., Lee, K., Yusufov, M., Moseley, E., Qian, Y., Guo, J. & Lindvall, C. 2020. An artificial intelligence algorithm to identify documented symptoms in patients with heart failure who received cardiac resynchronization therapy (s717). *Journal of Pain and Symptom Management,* 59**,** 537-538.

Lenz, E. R., Pugh, L. C., Milligan, R. A., Gift, A. & Suppe, F. 1997. The middle-range theory of unpleasant symptoms: an update. *Advances in nursing science,* 19**,** 14-27.

Li, C. C., Chang, S. R. & Shun, S. C. 2019. The self-care coping process in patients with chronic heart failure: A qualitative study. *Journal of clinical nursing,* 28**,** 509-519.

Lin, C.-Y., Hammash, M., Mudd-Martin, G., Biddle, M. J., Dignan, M. & Moser, D. K. 2021. Older and younger patients' perceptions, evaluations, and responses to worsening heart failure symptoms. *Heart & Lung,* 50**,** 640-647.

Lin, C.-Y., Miller, J. L., Lennie, T. A., Biddle, M., Mudd-Martin, G., Hammash, M. & Moser, D. K. 2020. Perceived control predicts symptom status in patients with heart failure. *The Journal of cardiovascular nursing,* 35**,** 530.

Lincoln, Y. S. & Guba, E. G. 1985. *Naturalistic inquiry*, sage.

Lindenfeld, J., Albert, N. M., Boehmer, J. P., Collins, S. P., Ezekowitz, J. A., Givertz, M. M., Katz, S. D., Klapholz, M., Moser, D. K. & Rogers, J. G. 2010. HFSA 2010 comprehensive heart failure practice guideline. *Journal of cardiac failure,* 16**,** e1-194.

Lindmark, K., Boman, K., Stålhammar, J., Olofsson, M., Lahoz, R., Studer, R., Proudfoot, C., Corda, S., Fonseca, A. F. & Costa-Scharplatz, M. 2021. Recurrent heart failure hospitalizations increase the risk of cardiovascular and all-cause mortality in patients with heart failure in Sweden: a real-world study. *ESC Heart Failure,* 8**,** 2144-2153.

Lizarondo L, S. C., Carrier J, Godfrey C, Rieger K, Salmond S, Apostolo J, Kirkpatrick P & H., L. 2020. Chapter 8: Mixed methods systematic reviews. . *In:* E, M. Z. E. A. (ed.) *JBI Manual for Evidence Synthesis.* JBI.

Lizarondo L, S. C., Carrier J, Godfrey C, Rieger K, Salmond S, Apostolo J, Kirkpatrick P, Loveday H. 2020. Chapter 8: Mixed methods systematic reviews. *In:* Aromataris E, M. Z. E. (ed.) *JBI Manual for Evidence Synthesis.* https://synthesismanual.jbi.global. https://doi.org/10.46658/JBIMES-20-09: JBI.

Lizarondo, L., Stern, C., Apostolo, J., Carrier, J., De Borges, K., Godfrey, C., Kirkpatrick, P., Pollock, D., Rieger, K. & Salmond, S. 2022. Five common pitfalls in mixed methods systematic reviews: lessons learned. *Journal of clinical epidemiology,* 148**,** 178-183.

Lokker, M. E., Gwyther, L., Riley, J. P., Van Zuylen, L., Van Der Heide, A. & Harding, R. 2016. The prevalence and associated distress of physical and psychological symptoms in patients with advanced heart failure attending a South African medical center. *Journal of Cardiovascular Nursing,* 31**,** 313-322.

Long, C., Beres, L. K., Wu, A. W. & Giladi, A. M. 2021. Patient-level barriers and facilitators to completion of patient-reported outcomes measures. *Quality of Life Research***,** 1-8.

Lourenco, A. P., Leite-Moreira, A. F., Balligand, J. L., Bauersachs, J., Dawson, D., De Boer, R. A., De Windt, L. J., Falcão-Pires, I., Fontes-Carvalho, R. & Franz, S. 2018. An integrative translational approach to study heart failure with preserved ejection fraction: a position paper from the Working Group on Myocardial Function of the European Society of Cardiology. *European journal of heart failure,* 20**,** 216-227.

Ltd., Q. I. P. 2018. NVivo qualitative data analysis software Version 12.

Lum, H. D., Carey, E. P., Fairclough, D., Plomondon, M. E., Hutt, E., Rumsfeld, J. S. & Bekelman, D. B. 2016. Burdensome physical and depressive symptoms predict heart failure–specific health status over one year. *Journal of pain and symptom management,* 51**,** 963-970.

Luo, H., Lindell, D. F., Jurgens, C. Y., Fan, Y. & Yu, L. 2020. Symptom perception and influencing factors in Chinese patients with heart failure: a preliminary exploration. *International journal of environmental research and public health,* 17**,** 2692.

Lyons, K. S., Sadowski, T. & Lee, C. S. 2020. The role of concealment and relationship quality on patient hospitalizations, care strain and depressive symptoms in heart failure dyads. *European Journal of Cardiovascular Nursing,* 19**,** 118-124.

Macdonald, M. R., Tay, W. T., Teng, T. H. K., Anand, I., Ling, L. H., Yap, J., Tromp, J., Wander, G. S., Naik, A. & Ngarmukos, T. 2020. Regional variation of mortality in heart failure with reduced and preserved ejection fraction across Asia: outcomes in the ASIAN-HF registry. *Journal of the American Heart Association,* 9**,** e012199.

Maddox, T. M., Januzzi Jr, J. L., Allen, L. A., Breathett, K., Butler, J., Davis, L. L., Fonarow, G. C., Ibrahim, N. E., Lindenfeld, J. & Masoudi, F. A. 2021. 2021 update to the 2017 ACC expert consensus decision pathway for optimization of heart failure treatment: answers to 10 pivotal issues about heart failure with reduced ejection fraction: a report of the American College of Cardiology Solution Set Oversight Committee. *Journal of the American College of Cardiology,* 77**,** 772-810.

Malgie, J., Clephas, P. R., Rocca, B.-L., De Boer, R. A. & Brugts, J. J. 2023. Guideline-directed medical therapy for HFrEF: sequencing strategies and barriers for life-saving drug therapy. *Heart Failure Reviews***,** 1-14.

Malterud, K., Siersma, V. D. & Guassora, A. D. 2016. Sample size in qualitative interview studies: guided by information power. *Qualitative health research,* 26**,** 1753-1760.

Mastenbroek, M. H., Versteeg, H., Zijlstra, W. P., Meine, M., Spertus, J. A. & Pedersen, S. S. 2014. Disease-specific health status as a predictor of mortality in patients with heart failure: a systematic literature review and meta-analysis of prospective cohort studies. *European Journal of Heart Failure,* 16**,** 384-393.

Mcart, E. W. & Mcdougal, L. W. 1985. Secondary data analysis–a new approach to nursing research. *Image: The Journal of Nursing Scholarship,* 17**,** 54-57.

Mcdonagh, T. A., Metra, M., Adamo, M., Gardner, R. S., Baumbach, A., Böhm, M., Burri, H., Butler, J., Čelutkienė, J. & Chioncel, O. 2021. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. *European heart journal,* 42**,** 3599-3726.

Mcevoy, P. & Richards, D. 2006. A critical realist rationale for using a combination of quantitative and qualitative methods. *Journal of research in nursing,* 11**,** 66-78.

Mchorney, C. A., Mansukhani, S. G., Anatchkova, M., Taylor, N., Wirtz, H. S., Abbasi, S., Battle, L., Desai, N. R. & Globe, G. 2021. The impact of heart failure on patients and caregivers: A qualitative study. *PLoS ONE,* 16(3 March).

Mcilfatrick, S., Doherty, L. C., Murphy, M., Dixon, L., Donnelly, P., Mcdonald, K. & Fitzsimons, D. 2018. 'The importance of planning for the future': burden and unmet needs of caregivers' in advanced heart failure: a mixed methods study. *Palliative medicine,* 32**,** 881-890.

Mcintosh, M. J. & Morse, J. M. 2015. Situating and constructing diversity in semi-structured interviews. *Global qualitative nursing research,* 2**,** 2333393615597674.

Mcmurray, J. J., Packer, M., Desai, A. S., Gong, J., Lefkowitz, M., Rizkala, A. R., Rouleau, J. L., Shi, V. C., Solomon, S. D. & Swedberg, K. 2014. Baseline characteristics and treatment of patients in prospective comparison of ARNI with ACEI to determine impact on global mortality and morbidity in heart failure trial (PARADIGM-HF). *European journal of heart failure,* 16**,** 817-825.

Mcparland, C., Johnston, B., Alassoud, B., Drummond, M., Farnood, A., Purba, C. I. H., Seckin, M. & Thanthong, S. 2023. Involving patients and the public in nursing PhD projects: practical guidance, potential benefits and points to consider. *Nurse Researcher,* 31.

Mendes, J. L., Dos Santos, C. M. & Sousa-Pinto, B. 2024. Assessment of patient-reported outcomes measures in heart failure: a systematic review. *Heart Failure Reviews***,** 1-15.

Miaskowski, C., Dodd, M. & Lee, K. 2004. Symptom clusters: the new frontier in symptom management research. *JNCI Monographs,* 2004**,** 17-21.

Mirick, R. G. & Wladkowski, S. P. 2019. Skype in qualitative interviews: Participant and researcher perspectives. *The Qualitative Report,* 24**,** 3061-3072.

Mo, Y., Wang, H., Huang, G. & Chu, M. 2020. Effectiveness of nurse-led program on mental health status and quality of life in patients with chronic heart failure. *Medicine,* 99.

Morgan, D. L. 1998. Practical strategies for combining qualitative and quantitative methods: Applications to health research. *Qualitative health research,* 8**,** 362-376.

Morse, J. M. 1991. Approaches to qualitative-quantitative methodological triangulation. *Nursing research,* 40**,** 120-123.

Morse, J. M. 2012. The implications of interview type and structure in mixed-method designs. *The SAGE handbook of interview research: The complexity of the craft***,** 193-204.

Morse, J. M., Barrett, M., Mayan, M., Olson, K. & Spiers, J. 2002. Verification strategies for establishing reliability and validity in qualitative research. *International journal of qualitative methods,* 1**,** 13-22.

Moser, D. K. 2002. Psychosocial factors and their association with clinical outcomes in patients with heart failure: why clinicians do not seem to care. *European Journal of Cardiovascular Nursing,* 1**,** 183-188.

Moser, D. K., Lee, K. S., Wu, J.-R., Mudd-Martin, G., Jaarsma, T., Huang, T.-Y., Fan, X.-Z., Strömberg, A., Lennie, T. A. & Riegel, B. 2014. Identification of symptom clusters among patients with heart failure: an international observational study. *International journal of nursing studies,* 51**,** 1366-1372.

Neergaard, M. A., Olesen, F., Andersen, R. S. & Sondergaard, J. 2009. Qualitative description–the poor cousin of health research? *BMC medical research methodology,* 9**,** 1-5.

Nguyen, T. T., Nguyen, T. X., Nguyen, T. T. H., Nguyen, T. N., Nguyen, H. T. T., Nguyen, H. T. T., Nguyen, A. T., Pham, T. & Vu, H. T. T. 2022. Symptom Burden among Hospitalised Older Patients with Heart Failure in Hanoi, Vietnam. *International Journal of Environmental Research and Public Health,* 19**,** 13593.

Nice, N. I. O. C. E. 2018. Chronic heart failure in adults: diagnosis and management (NG106). 2018 ed.

Nichols, G. A., Reynolds, K., Kimes, T. M., Rosales, A. G. & Chan, W. W. 2015. Comparison of risk of re-hospitalization, all-cause mortality, and medical care resource utilization in patients with heart failure and preserved versus reduced ejection fraction. *The American journal of cardiology,* 116**,** 1088-1092.

Nieveen, J. L., Zimmerman, L. M., Barnason, S. A. & Yates, B. C. 2008. Development and content validity testing of the Cardiac Symptom Survey in patients after coronary artery bypass grafting. *Heart & Lung,* 37**,** 17-27.

Nih, N. L. O. M. 2023. *Medical Subject Headings 2023* [Online]. Available: https://meshb.nlm.nih.gov/ [Accessed May 2023].

Nishiga, M., Wang, D. W., Han, Y., Lewis, D. B. & Wu, J. C. 2020. COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives. *Nature Reviews Cardiology,* 17**,** 543-558.

Noah, B. A. 2012. The role of race in end-of-life care. *J. Health Care L. & Pol'y,* 15**,** 349.

O'donoghue, T. & Punch, K. 2003. Qualitative Educational Research in Action: Doing and Reflecting. London: Routledge.

O'cathain, A., Murphy, E. & Nicholl, J. 2010. Three techniques for integrating data in mixed methods studies. *Bmj,* 341.

Ødegaard, K. M., Hallén, J., Lirhus, S. S., Melberg, H. O. & Halvorsen, S. 2020. Incidence, prevalence, and mortality of heart failure: a nationwide registry study from 2013 to 2016. *ESC heart failure,* 7**,** 1917-1926.

Oecd 2023. Social Protection Statistics.

Oguz, S. & Enç, N. 2008. Symptoms and strategies in heart failure in Turkey. *International nursing review,* 55**,** 462-467.

Okada, A., Tsuchihashi-Makaya, M., Kang, J., Aoki, Y., Fukawa, M. & Matsuoka, S. 2019. Symptom Perception, Evaluation, Response to Symptom, and Delayed Care Seeking in Patients With

Acute Heart Failure: An Observational Study. *Journal of Cardiovascular Nursing,* 34(1)**,** 36-43.

Omidzahir, S., Mansour-Ghanaei, R., Pourghane, P. & Atrkar-Roshan, Z. 2021. Quality of life and related demographic characteristics of elderly with heart failure admitted to hospitals of guilan university of medical sciences. *Health and Development Journal,* 10**,** 135-143.

Öniş, Z. 2015. Monopolising the centre: The AKP and the uncertain path of Turkish democracy. *The International Spectator,* 50**,** 22-41.

Öniş, Z. 2023. Türkiye'nin Yeni Cumhurbaşkanlığı Rejimi: Kırılganlık, Direnç, Tersine Dönebilirlik. *REFLEKTİF Sosyal Bilimler Dergisi,* 4**,** 159-179.

Onwuegbuzie, A. J. & Leech, N. L. 2005. On becoming a pragmatic researcher: The importance of combining quantitative and qualitative research methodologies. *International journal of social research methodology,* 8**,** 375-387.

Opasich, C., Gualco, A., De Feo, S., Barbieri, M., Cioffi, G., Giardini, A. & Majani, G. 2008. Physical and emotional symptom burden of patients with end-stage heart failure: what to measure, how and why. *Journal of Cardiovascular Medicine,* 9**,** 1104-1108.

Oppe, M., Devlin, N. J. & Szende, A. 2007. *EQ-5D value sets: inventory, comparative review and user guide*, Springer.

Oriani, A., Guo, P., Gadoud, A., Dunleavy, L., Kane, P. & Murtagh, F. E. M. 2019. What are the main symptoms and concerns reported by patients with advanced chronic heart failure?-a secondary analysis of the Palliative care Outcome Scale (POS) and Integrated Palliative care Outcome Scale (IPOS). *ANNALS OF PALLIATIVE MEDICINE,* 8**,** 775-780.

Owan, T. E., Hodge, D. O., Herges, R. M., Jacobsen, S. J., Roger, V. L. & Redfield, M. M. 2006. Trends in prevalence and outcome of heart failure with preserved ejection fraction. *New England Journal of Medicine,* 355**,** 251-259.

Packer, M. 2018. The future treatment of heart failure? : Oxford University Press.

Page, M. J., Mckenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A. & Brennan, S. E. 2021. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *International Journal of Surgery,* 88**,** 105906.

Palinkas, L. A., Horwitz, S. M., Green, C. A., Wisdom, J. P., Duan, N. & Hoagwood, K. 2015. Purposeful sampling for qualitative data collection and analysis in mixed method implementation research. *Administration and policy in mental health and mental health services research,* 42**,** 533-544.

Pandey, A., Omar, W., Ayers, C., Lamonte, M., Klein, L., Allen, N. B., Kuller, L. H., Greenland, P., Eaton, C. B. & Gottdiener, J. S. 2018. Sex and race differences in lifetime risk of heart failure with preserved ejection fraction and heart failure with reduced ejection fraction. *Circulation,* 137**,** 1814-1823.

Parker, M. 2006. Introduction to nursing theory. *Nursing theories and nursing practice***,** 268-280.

Parlour, R. & Mccormack, B. 2012. Blending critical realist and emancipatory practice development methodologies: making critical realism work in nursing research. *Nursing Inquiry,* 19**,** 308-321.

Patel, H., Shafazand, M., Schaufelberger, M. & Ekman, I. 2007. Reasons for seeking acute care in chronic heart failure. *European journal of heart failure,* 9**,** 702-708.

Pelzang, R. 2010. Time to learn: understanding patient-centred care. *British journal of nursing,* 19**,** 912-917.

Pereira Sousa, J., Neves, H. & Pais-Vieira, M. 2021. Does symptom recognition improve self-care in patients with heart failure? A pilot study randomised controlled trial. *Nursing Reports,* 11**,** 418-429.

Polit, D. F. & Beck, C. T. 2009. International differences in nursing research, 2005–2006. *Journal of Nursing Scholarship,* 41**,** 44-53.

Polit, D. F. & Beck, C. T. 2017. *Nursing Research: Generating and Assessing Evidence for Nursing Practice,* Philadelphia, Wolters Kluwer.

Polit, D. F., Beck, C. T. & Hungler, B. 2013. *Essentials of nursing research: Methods, appraisal, and utilization,* Philadelphia, Lippincott Williams & Wilkins.

Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., Britten, N., Roen, K. & Duffy, S. 2006. Guidance on the conduct of narrative synthesis in systematic reviews. *A product from the ESRC methods programme Version,* 1**,** b92.

Portenoy, R. K., Thaler, H. T., Kornblith, A. B., Lepore, J. M., Friedlander-Klar, H., Kiyasu, E., Sobel, K., Coyle, N., Kemeny, N. & Norton, L. 1994. The Memorial Symptom Assessment Scale: an instrument for the evaluation of symptom prevalence, characteristics and distress. *European Journal of Cancer,* 30**,** 1326-1336.

Porter, S. 2007. Validity, trustworthiness and rigour: reasserting realism in qualitative research. *Journal of advanced nursing,* 60**,** 79-86.

Posey, A. D. Symptom perception: a concept exploration. Nursing forum, 2006. Wiley Online Library, 113-124.

Potter, E. L., Hopper, I., Sen, J., Salim, A. & Marwick, T. H. 2019. Impact of socioeconomic status on incident heart failure and left ventricular dysfunction: systematic review and meta-analysis. *European Heart Journal-Quality of Care and Clinical Outcomes,* 5**,** 169-179.

Pozehl, B., Duncan, K. & Hertzog, M. 2006. Heart failure symptom survey: validity and reliability. *Journal of Cardiac Failure,* 12**,** S100.

Pratama, I., Permanasari, A. E., Ardiyanto, I. & Indrayani, R. A review of missing values handling methods on time-series data. 2016 international conference on information technology systems and innovation (ICITSI), 2016. IEEE, 1-6.

Pratschke, J. 2003. Realistic Models? Critical Realism and Statistical Models in the Social Scieces. *Philosophica,* 71**,** 13-38.

Public Health Agency of Canada 2018. Report from the Canadian Chronic Disease Surveillance System: Heart Disease in Canada, 2018. 2018 ed.

Public Health Scotland 2023. Scottish heart disease statistics - Year ending 31 March 2022.

Pucciarelli, G., Greco, A., Paturzo, M., Jurgens, C. Y., Durante, A., Alvaro, R. & Vellone, E. 2019. Psychometric evaluation of the Heart Failure Somatic Perception Scale in a European heart failure population. *European Journal of Cardiovascular Nursing,* 18**,** 484-491.

Qiu, C., Yu, D. S. F., Song, D. & Wang, X. 2022. The prognostic impact of symptom clusters in patients with heart failure: A systematic review and meta-analysis. *Journal of Advanced Nursing,* 78**,** 2713-2730.

Quinn, C., Dunbar, S. B. & Higgins, M. 2010. Heart failure symptom assessment and management: can caregivers serve as proxy? *The Journal of cardiovascular nursing,* 25**,** 142.

Raftery, J. P., Yao, G. L., Murchie, P., Campbell, N. C. & Ritchie, L. D. 2005. Cost effectiveness of nurse led secondary prevention clinics for coronary heart disease in primary care: follow up of a randomised controlled trial. *Bmj,* 330**,** 707.

Rahimi, K., Bennett, D., Conrad, N., Williams, T. M., Basu, J., Dwight, J., Woodward, M., Patel, A., Mcmurray, J. & Macmahon, S. 2014. Risk prediction in patients with heart failure: a systematic review and analysis. *JACC: Heart Failure,* 2**,** 440-446.

Ranganathan, P. & Aggarwal, R. 2018. Study designs: Part 1–An overview and classification. *Perspectives in clinical research,* 9**,** 184.

Rashid, S., Qureshi, A. G., Noor, T. A., Yaseen, K., Sheikh, M. a. A., Malik, M. & Malik, J. 2023. Anxiety and depression in heart failure: an updated review. *Current Problems in Cardiology,* 48**,** 101987.

Rector, T. S. & Cohn, J. N. 1992. Assessment of patient outcome with the Minnesota Living with Heart Failure questionnaire: reliability and validity during a randomized, double-blind, placebo-controlled trial of pimobendan. *American heart journal,* 124**,** 1017-1025.

Redman, B. K. 2007. Accountability for patient self-management of chronic conditions; ethical analysis and a proposal. *Chronic Illness,* 3**,** 88-95.

Reeder, K. M., Ercole, P. M., Peek, G. M. & Smith, C. E. 2015. Symptom perceptions and self-care behaviors in patients who self-manage heart failure. *The Journal of cardiovascular nursing,* 30**,** E1.

Reeder, K. M., Peek, G. M. & Nazir, N. 2022. Prehospitalization Symptom Perceptions, Lay Consultations, and Treatment-Seeking for Acute Decompensating Heart Failure: Implications for Nursing Practice. *Critical Care Nursing Clinics,* 34**,** 129-140.

Regitz-Zagrosek, V. 2020. Sex and gender differences in heart failure. *International Journal of Heart Failure,* 2**,** 157.

Renjith, V., Yesodharan, R., Noronha, J. A., Ladd, E. & George, A. 2021. Qualitative methods in health care research. *International journal of preventive medicine,* 12.

Rhodes, V. A. & Watson, P. M. Symptom distress—the concept: past and present. Seminars in Oncology Nursing, 1987. Elsevier, 242-247.

Richards, D. A. & Rahm Hallberg, I. (eds.) 2015. *Complex Interventions in Health: An overview of research methods*: Routledge.

Richer, M. C. & Ezer, H. 2000. Understanding beliefs and meanings in the experience of cancer: a concept analysis. *Journal of advanced nursing,* 32**,** 1108-1115.

Riegel, B., Bennett, J. A., Davis, A., Carlson, B., Montague, J., Robin, H. & Glaser, D. 2002. Cognitive impairment in heart failure: issues of measurement and etiology. *American Journal of Critical Care,* 11**,** 520-528.

Riegel, B. & Carlson, B. 2002. Facilitators and barriers to heart failure self-care. *Patient education and counseling,* 46**,** 287-295.

Riegel, B. & Dickson, V. V. 2008. A situation-specific theory of heart failure self-care. *Journal of cardiovascular Nursing,* 23**,** 190-196.

Riegel, B., Dickson, V. V. & Faulkner, K. M. 2016. The situation-specific theory of heart failure self-care: revised and updated. *Journal of Cardiovascular Nursing,* 31**,** 226-235.

Riegel, B., Dickson, V. V. & Vellone, E. 2022. The situation-specific theory of heart failure self-care: an update on the problem, person, and environmental factors influencing heart failure self-care. *Journal of Cardiovascular Nursing,* 37**,** 515-529.

Riegel, B., Dunbar, S. B., Fitzsimons, D., Freedland, K. E., Lee, C. S., Middleton, S., Stromberg, A., Vellone, E., Webber, D. E. & Jaarsma, T. 2021. Self-care research: where are we now? Where are we going? *International journal of nursing studies,* 116**,** 103402.

Riegel, B., Jaarsma, T., Lee, C. S. & Strömberg, A. 2019. Integrating symptoms into the middle-range theory of self-care of chronic illness. *ANS. Advances in nursing science,* 42**,** 206.

Riegel, B., Lee, C. S. & Dickson, V. V. 2011. Self care in patients with chronic heart failure. *Nature reviews cardiology,* 8**,** 644-654.

Riegel, B., Moser, D. K., Anker, S. D., Appel, L. J., Dunbar, S. B., Grady, K. L., Gurvitz, M. Z., Havranek, E. P., Lee, C. S. & Lindenfeld, J. 2009. State of the science: promoting self-care in persons with heart failure: a scientific statement from the American Heart Association. *Circulation,* 120**,** 1141-1163.

Robbins, J. M. & Kirmayer, L. J. 1991. Attributions of common somatic symptoms. *Psychological medicine,* 21**,** 1029-1045.

Rockwell, J. M. & Riegel, B. 2001. Predictors of self-care in persons with heart failure. *Heart & Lung,* 30**,** 18-25.

Rodriguez, K. L., Appelt, C. J., Switzer, G. E., Sonel, A. F. & Arnold, R. M. 2008. “They diagnosed bad heart”: a qualitative exploration of patients' knowledge about and experiences with heart failure. *Heart & Lung,* 37**,** 257-265.

Rogers, A., Addington-Hall, J. M., Mccoy, A. S., Edmonds, P. M., Abery, A. J., Coats, A. J., Simon, J. & Gibbs, R. 2002. A qualitative study of chronic heart failure patients’ understanding of their symptoms and drug therapy. *European journal of heart failure,* 4**,** 283-287.

Rolfe, G. 2006. Validity, trustworthiness and rigour: quality and the idea of qualitative research. *Journal of advanced nursing,* 53**,** 304-310.

Ruggiano, N. & Perry, T. E. 2019. Conducting secondary analysis of qualitative data: Should we, can we, and how? *Qualitative Social Work,* 18**,** 81-97.

Ryan, G. 2018. Introduction to positivism, interpretivism and critical theory. *Nurse researcher,* 25**,** 41-49.

Saarijärvi, M. & Bratt, E.-L. 2021. When face-to-face interviews are not possible: tips and tricks for video, telephone, online chat, and email interviews in qualitative research. Oxford University Press.

Sabouret, P., Attias, D., Beauvais, C., Berthelot, E., Bouleti, C., Genty, G. G., Galat, A., Hanon, O., Hulot, J. & Isnard, R. Diagnosis and management of heart failure from hospital admission to discharge: A practical expert guidance. Annales de Cardiologie et d'Angéiologie, 2022. Elsevier, 41-52.

Sağlik Hizmetleri Genel Müdürlüğü. 2023. *Sertifikalı Eğitim Programları* [Online]. Available: https://shgmesdb.saglik.gov.tr/TR-63589/sertifikali-egitim-programlari.html [Accessed March 2023].

Sahle, B. W., Owen, A. J., Mutowo, M. P., Krum, H. & Reid, C. M. 2016. Prevalence of heart failure in Australia: a systematic review. *BMC cardiovascular disorders,* 16**,** 1-6.

Salkind, N. J. 2006. Encyclopedia of measurement and statistics. SAGE publications.

Salyer, J., Flattery, M. & Lyon, D. E. 2019. Heart failure symptom clusters and quality of life. *Heart & Lung,* 48**,** 366-372.

Sandelowski, M. 2000. Whatever happened to qualitative description? *Research in nursing & health,* 23**,** 334-340.

Sandelowski, M. 2010. What's in a name? Qualitative description revisited. *Research in nursing & health,* 33**,** 77-84.

Sandelowski, M. & Barroso, J. 2007. *Handbook for Synthesizing Qualitative Research*, Springer Publishing Company.

Santana, M. J., Manalili, K., Jolley, R. J., Zelinsky, S., Quan, H. & Lu, M. 2018. How to practice person-centred care: A conceptual framework. *Health Expectations,* 21**,** 429-440.

Santas, E., De La Espriella, R., Palau, P., Miñana, G., Amiguet, M., Sanchis, J., Lupón, J., Bayes-Genís, A., Chorro, F. J. & Núñez Villota, J. 2020. Rehospitalization burden and morbidity risk in patients with heart failure with mid-range ejection fraction. *ESC heart failure,* 7**,** 1007-1014.

Santos, G. C., Liljeroos, M., Dwyer, A. A., Jaques, C., Girard, J., Strömberg, A., Hullin, R. & Schäfer-Keller, P. 2020. Symptom perception in heart failure: a scoping review on definition, factors and instruments. *European journal of cardiovascular nursing,* 19**,** 100-117.

Santos, G. C., Liljeroos, M., Dwyer, A. A., Jaques, C., Girard, J., Strömberg, A., Hullin, R. & Schäfer-Keller, P. 2021. Symptom perception in heart failure–Interventions and outcomes: A scoping review. *International journal of nursing studies,* 116**,** 103524.

Savarese, G., Becher, P. M., Lund, L. H., Seferovic, P., Rosano, G. M. & Coats, A. J. 2022. Global burden of heart failure: a comprehensive and updated review of epidemiology. *Cardiovascular research,* 118**,** 3272-3287.

Schäfer-Keller, P., Santos, G. C., Denhaerynck, K., Graf, D., Vasserot, K., Richards, D. A. & Strömberg, A. 2021. Self-Care, symptom experience, needs, and past health-care utilization in individuals with heart failure: results of a cross-sectional study. *European Journal of Cardiovascular Nursing,* 20**,** 464-474.

Schiff, G. D., Fung, S., Speroff, T. & Mcnutt, R. A. 2003. Decompensated heart failure: symptoms, patterns of onset, and contributing factors. *The American Journal of Medicine,* 114**,** 625-630.

Schoonenboom, J. & Johnson, R. B. 2017. How to construct a mixed methods research design. *Kolner Zeitschrift fur Soziologie und Sozialpsychologie,* 69**,** 107.

Schumacher, C., Hussey, L. & Hall, V. 2018. Heart failure self-management and normalizing symptoms: an exploration of decision making in the community. *Heart & Lung,* 47**,** 297-303.

Scuffham, P. A., Ball, J., Horowitz, J. D., Wong, C., Newton, P. J., Macdonald, P., Mcveigh, J., Rischbieth, A., Emanuele, N. & Carrington, M. J. 2017. Standard vs. intensified management of heart failure to reduce healthcare costs: results of a multicentre, randomized controlled trial. *European heart journal,* 38**,** 2340-2348.

Seckin, M., Johnston, B., Petrie, M. C., Stewart, S. & Chan, Y.-K. 2022. Characteristics of symptoms and symptom change across different heart failure subtypes: a sex-stratified analysis. *European Journal of Cardiovascular Nursing*.

Seckin, M., Johnston, B., Stewart, S. & Petrie, M. 2023. Full spectrum of symptoms associated with heart failure: a mixed-method systematic review and narrative synthesis. *European Journal of Cardiovascular Nursing,* 22.

Seferović, P. M., Vardas, P., Jankowska, E. A., Maggioni, A. P., Timmis, A., Milinković, I., Polovina, M., Gale, C. P., Lund, L. H. & Lopatin, Y. 2021. The heart failure association atlas: heart failure epidemiology and management statistics 2019. *European Journal of Heart Failure,* 23**,** 906-914.

Senni, M., Gavazzi, A., Oliva, F., Mortara, A., Urso, R., Pozzoli, M., Metra, M., Lucci, D., Gonzini, L. & Cirrincione, V. 2014. In-hospital and 1-year outcomes of acute heart failure patients according to presentation (de novo vs. worsening) and ejection fraction. Results from IN-HF Outcome Registry. *International journal of cardiology,* 173**,** 163-169.

Sethares, K. A. & Chin, E. 2021. Age and gender differences in physical heart failure symptom clusters. *Heart & Lung,* 50**,** 832-837.

Sezgin, D. & Mert, H. 2017. Self-care management of individuals with heart failure: A qualitative study. *International Journal of Caring Sciences,* 10**,** 285.

Shah, A. B., Udeoji, D. U., Baraghoush, A., Bharadwaj, P., Yennurajalingam, S. & Schwarz, E. R. 2013. An evaluation of the prevalence and severity of pain and other symptoms in acute decompensated heart failure. *Journal of palliative medicine,* 16**,** 87-90.

Shahin, W., Kennedy, G. A. & Stupans, I. 2019. The impact of personal and cultural beliefs on medication adherence of patients with chronic illnesses: a systematic review. *Patient preference and adherence***,** 1019-1035.

Sharifi, H., Rezaei, M. A., Khayat, N. H. & Mohammadinia, N. 2018. Agreement between heart failure patients and their primary caregivers on symptom assessment. *International journal of community based nursing and midwifery,* 6**,** 89.

Sherif, V. Evaluating preexisting qualitative research data for secondary analysis. Forum: qualitative social research, 2018. Freie Universität Berlin, 26-42.

Shfnf, S. H. F. N. F. 2018. Review of Specialist Heart Failure Nurse Services - Scotland 2018 2018 ed.

Shiga, T., Suzuki, A., Haruta, S., Mori, F., Ota, Y., Yagi, M., Oka, T., Tanaka, H., Murasaki, S. & Yamauchi, T. 2019. Clinical characteristics of hospitalized heart failure patients with preserved, mid-range, and reduced ejection fractions in Japan. *ESC heart failure,* 6**,** 475-486.

Siabani, S., Leeder, S. R. & Davidson, P. M. 2013. Barriers and facilitators to self-care in chronic heart failure: a meta-synthesis of qualitative studies. *Springerplus,* 2**,** 1-14.

Siddaway, A. P., Wood, A. M. & Hedges, L. V. 2019. How to do a systematic review: a best practice guide for conducting and reporting narrative reviews, meta-analyses, and meta-syntheses. *Annual review of psychology,* 70**,** 747-770.

Sign, S. I. G. N. 2016. *Management of chronic heart failure: a national clinical guideline*, Scottish Intercollegiate Guidelines Network.

Skotzko, C. E. 2009. Symptom perception in CHF:(why mind matters). *Heart failure reviews,* 14**,** 29-34.

Smith, B., Forkner, E., Krasuski, R. A., Galbreath, A. D. & Freeman, G. L. 2006. Educational attainment has a limited impact on disease management outcomes in heart failure. *Disease Management,* 9**,** 157-166.

Sofronas, M., Wright, D. K. & Carnevale, F. A. Personhood: An evolutionary concept analysis for nursing ethics, theory, practice, and research. Nursing Forum, 2018. Wiley Online Library, 406-415.

Solomon, S. D., Mcmurray, J. J., Anand, I. S., Ge, J., Lam, C. S., Maggioni, A. P., Martinez, F., Packer, M., Pfeffer, M. A. & Pieske, B. 2019. Angiotensin–neprilysin inhibition in heart failure with preserved ejection fraction. *New England Journal of Medicine,* 381**,** 1609-1620.

Son, Y.-J., Choi, J. & Lee, H.-J. 2020. Effectiveness of nurse-led heart failure self-care education on health outcomes of heart failure patients: a systematic review and meta-analysis. *International Journal of environmental research and public health,* 17**,** 6559.

Son, Y.-J. & Won, M. H. 2018. Symptom clusters and their impacts on hospital readmission in patients with heart failure: A cross-sectional study. *Research and Theory for Nursing Practice,* 32**,** 311-327.

Song, E. K., Moser, D. K., Rayens, M. K. & Lennie, T. A. 2010. Symptom clusters predict event-free survival in patients with heart failure. *The Journal of cardiovascular nursing,* 25**,** 284.

Stanek, E. J., Oates, M. B., Mcghan, W. F., Denofrio, D. & Loh, E. 2000. Preferences for treatment outcomes in patients with heart failure: symptoms versus survival. *Journal of cardiac failure,* 6**,** 225-232.

Stern, C., Lizarondo, L., Carrier, J., Godfrey, C., Rieger, K., Salmond, S., Apostolo, J., Kirkpatrick, P. & Loveday, H. 2020. Methodological guidance for the conduct of mixed methods systematic reviews. *JBI evidence synthesis,* 18**,** 2108-2118.

Stewart, D. W. & Kamins, M. A. 1993. Introduction. Secondary Research. Sage: London, UK.

Stewart, S., Carrington, M. J., Marwick, T. H., Davidson, P. M., Macdonald, P., Horowitz, J. D., Krum, H., Newton, P. J., Reid, C. & Chan, Y. K. 2012. Impact of home versus clinic-based management of chronic heart failure: the WHICH?(Which Heart Failure Intervention Is Most Cost-Effective & Consumer Friendly in Reducing Hospital Care) multicenter, randomized trial. *Journal of the American College of Cardiology,* 60**,** 1239-1248.

Stewart, S., Chan, Y. K., Wong, C., Jennings, G., Scuffham, P., Esterman, A., Carrington, M. & Investigators, N. C. 2015. Impact of a nurse-led home and clinic-based secondary prevention programme to prevent progressive cardiac dysfunction in high-risk individuals: the Nurse-led Intervention for Less Chronic Heart Failure (NIL-CHF) randomized controlled study. *European Journal of Heart Failure,* 17**,** 620-630.

Stewart, S., Riegel, B., Boyd, C., Ahamed, Y., Thompson, D. R., Burrell, L. M., Carrington, M. J., Coats, A., Granger, B. B. & Hides, J. 2016a. Establishing a pragmatic framework to optimise health outcomes in heart failure and multimorbidity (ARISE-HF): a multidisciplinary position statement. *International Journal of Cardiology,* 212**,** 1-10.

Stewart, S., Stewart, A. R., Waite, L. & Beilby, J. 2022. Out with the old and in with the new: primary care management of heart failure with preserved ejection fraction. *Cardiac Failure Review,* 8.

Stewart, S., Wiley, J. F., Ball, J., Chan, Y.-K., Ahamed, Y., Thompson, D. R. & Carrington, M. J. 2016b. Impact of nurse-led, multidisciplinary home-based intervention on event-free survival across the spectrum of chronic heart disease: composite analysis of health outcomes in 1226 patients from 3 randomized trials. *Circulation,* 133**,** 1867-1877.

Stichler, J. F. & Pelletier, L. R. 2023. Applying the Patient Empowerment, Engagement, and Activation Survey to Improve Patient Outcomes. *JONA: The Journal of Nursing Administration,* 53**,** 668-674.

Stockdill, M. L., Dionne-Odom, J. N., Wells, R., Ejem, D., Azuero, A., Keebler, K., Sockwell, E., Tims, S., Burgio, K. L. & Engler, S. 2023. African American recruitment in early heart failure palliative care trials: outcomes and comparison with the ENABLE CHF-PC randomized trial. *Journal of palliative care,* 38**,** 52-61.

Stockdill, M. L., Patrician, P. A. & Bakitas, M. 2019. Understanding and measuring symptom burden in heart failure: a concept analysis. *Western Journal of Nursing Research,* 41**,** 1423-1447.

Stolfo, D., Uijl, A., Vedin, O., Strömberg, A., Faxén, U. L., Rosano, G. M., Sinagra, G., Dahlström, U. & Savarese, G. 2019. Sex-based differences in heart failure across the ejection fraction spectrum: phenotyping, and prognostic and therapeutic implications. *JACC: Heart Failure,* 7**,** 505-515.

Strachan, P. H., Currie, K., Harkness, K., Spaling, M. & Clark, A. M. 2014. Context matters in heart failure self-care: a qualitative systematic review. *Journal of cardiac failure,* 20**,** 448-455.

Sumner, A. & Tribe, M. The nature of epistemology and methodology in development studies: what do we mean by 'rigour'. Development Studies Association Annual Conference, 2004. 1-27.

Sundararajan, V., Henderson, T., Perry, C., Muggivan, A., Quan, H. & Ghali, W. A. 2004. New ICD-10 version of the Charlson comorbidity index predicted in-hospital mortality. *Journal of clinical epidemiology,* 57**,** 1288-1294.

Talabani, N., Ängerud, K. H., Boman, K. & Brännström, M. 2020. Patients' experiences of person-centred integrated heart failure care and palliative care at home: an interview study. *BMJ supportive & palliative care,* 10**,** e9-e9.

Talari, K. & Goyal, M. 2020. Retrospective studies–utility and caveats. *Journal of the Royal College of Physicians of Edinburgh,* 50**,** 398-402.

Taniguchi, C., Okada, A., Seto, N. & Shimizu, Y. 2020. How visiting nurses detect symptoms of disease progression in patients with chronic heart failure. *International Journal of Qualitative Studies on Health and Well-being,* 15**,** 1735768.

Teerlink, J. R., Diaz, R., Felker, G. M., Mcmurray, J. J., Metra, M., Solomon, S. D., Adams, K. F., Anand, I., Arias-Mendoza, A. & Biering-Sørensen, T. 2021. Cardiac myosin activation with omecamtiv mecarbil in systolic heart failure. *New England Journal of Medicine,* 384**,** 105-116.

Tenny, S., Brannan, G. D., Brannan, J. M. & Sharts-Hopko, N. C. 2017. Qualitative study.

Teunissen, S. C., Wesker, W., Kruitwagen, C., De Haes, H. C., Voest, E. E. & De Graeff, A. 2007. Symptom prevalence in patients with incurable cancer: a systematic review. *Journal of pain and symptom management,* 34**,** 94-104.

Thd, T. H. D. 2023. TÜRK HEMŞİRELER DERNEĞİ HEMŞİRE GÖÇ EĞİLİM ÇALIŞMASI RAPORU.

Thomas, E. & Magilvy, J. K. 2011. Qualitative rigor or research validity in qualitative research. *Journal for specialists in pediatric nursing*.

Thurmond, V. A. 2001. The point of triangulation. *Journal of nursing scholarship,* 33**,** 253-258.

Tobin, G. A. & Begley, C. M. 2004. Methodological rigour within a qualitative framework. *Journal of advanced nursing,* 48**,** 388-396.

Todero, C. M., Laframboise, L. M. & Zimmerman, L. M. 2002. Symptom status and quality-of-life outcomes of home-based disease management program for heart failure patients. *Outcomes Management,* 6**,** 161-168.

Tofthagen, C. 2012. Threats to validity in retrospective studies. *Journal of the advanced practitioner in oncology,* 3**,** 181.

Tokgözoğlu, L., Yılmaz, M., Abacı, A., Altay, H., Atalar, E., Aydoğdu, S., Bozkurt, E., Çavuşoğlu, Y., Eren, M. & Sarı, İ. 2015. Türkiye'de kalp yetersizliği yol haritası kalp yetersizliğinin ve buna bağlı ölümlerin önlenmesi amacıyla geliştirilebilecek politikalara ilişkin öneriler. *Istanbul, Turkey: Türk Kardiyoloji Derneği*.

Tong, A., Sainsbury, P. & Craig, J. 2007. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International journal for quality in health care,* 19**,** 349-357.

Tromp, J., Ouwerkerk, W., Van Veldhuisen, D. J., Hillege, H. L., Richards, A. M., Van Der Meer, P., Anand, I. S., Lam, C. S. & Voors, A. A. 2022. A systematic review and network meta-analysis of pharmacological treatment of heart failure with reduced ejection fraction. *Heart Failure,* 10**,** 73-84.

Truby, L. K. & Rogers, J. G. 2020. Advanced heart failure: epidemiology, diagnosis, and therapeutic approaches. *Heart failure,* 8**,** 523-536.

Tsc, T. S. O. C. 2022. *Kalp Yetersizliği Belirtilerini Dikkate Alın, Kalp Yetersizliğinin Tedavisi Mümkün* [Online]. Available: https://tkd.org.tr/menu/201/kalp-yetersizligi-belirtilerini-dikkate-alin-kalp-yetersizliginin-tedavisi-mumk [Accessed August 2023].

Tsutsui, H., Ide, T., Ito, H., Kihara, Y., Kinugawa, K., Kinugawa, S., Makaya, M., Murohara, T., Node, K. & Saito, Y. 2021. JCS/JHFS 2021 guideline focused update on diagnosis and treatment of acute and chronic heart failure. *Circulation Journal,* 85**,** 2252-2291.

Tsutsui, H., Isobe, M., Ito, H., Okumura, K., Ono, M., Kitakaze, M., Kinugawa, K., Kihara, Y., Goto, Y. & Komuro, I. 2019. JCS 2017/JHFS 2017 guideline on diagnosis and treatment of acute and chronic heart failure—digest version—. *Circulation Journal,* 83**,** 2084-2184.

Türker, E. & Tanrıkulu, G. 2022. Türkiye'de kalp yetmezliği hastalarına yönelik yapılan hemşirelik tezlerinin incelenmesi. *Journal of Social and Analytical Health,* 2**,** 187-193.

Tyni-Lenné, R. 2004. Qualitative analysis of the male experience of heart failure. *Heart & Lung,* 33**,** 227-234.

Unhcr. 2023. *Refugees and Asylum Seekers in Turkey* [Online]. Available: https://www.unhcr.org/tr/en/refugees-and-asylum-seekers-in-turkey#:~:text=T%C3%BCrkiye%20currently%20hosts%20some%203.6,of%20concern%20from%20other%20nationalities. [Accessed July 2023].

Vaismoradi, M., Turunen, H. & Bondas, T. 2013. Content analysis and thematic analysis: Implications for conducting a qualitative descriptive study. *Nursing & health sciences,* 15**,** 398-405.

Vellone, E., Riegel, B. & Alvaro, R. 2021. The situation-specific theory of caregiver contributions to heart failure self-care. *Situation specific theories: Development, utilization, and evaluation in nursing***,** 193-206.

Vongmany, J., Hickman, L. D., Lewis, J., Newton, P. J. & Phillips, J. L. 2016. Anxiety in chronic heart failure and the risk of increased hospitalisations and mortality: a systematic review. *European Journal of Cardiovascular Nursing,* 15**,** 478-485.

Vuckovic, K. M., Bierle, R. & Ryan, C. J. 2020. Navigating symptom management in heart failure: the crucial role of the critical care nurse. *Critical Care Nurse,* 40**,** 55-63.

Walsh, A., Kitko, L. & Hupcey, J. 2018. The experiences of younger individuals living with heart failure. *Journal of Cardiovascular Nursing,* 33**,** E9-E16.

Walthall, H., Jenkinson, C. & Boulton, M. 2017. Living with breathlessness in chronic heart failure: a qualitative study. *Journal of clinical nursing,* 26**,** 2036-2044.

Walthall, H., Strickland, L. H. & Jenkinson, C. 2023. The development of a patient reported outcome measure for fatigue and breathlessness for patients with chronic heart failure (OxFAB). *Heart & Lung,* 58**,** 116-124.

Wang, D., Hu, B., Hu, C., Zhu, F., Liu, X., Zhang, J., Wang, B., Xiang, H., Cheng, Z. & Xiong, Y. 2020a. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *jama,* 323**,** 1061-1069.

Wang, G. P., Liu, X. Y. & Yang, Q. M. 2020b. Symptom clusters and quality of life in Chinese patients with heart failure. *COLLEGIAN,* 27**,** 521-528.

Wang, S.-P., Lin, L.-C., Lee, C.-M. & Wu, S.-C. 2011. Effectiveness of a self-care program in improving symptom distress and quality of life in congestive heart failure patients: a preliminary study. *Journal of Nursing Research,* 19**,** 257-266.

Wang, Y., Yang, Q., Liu, Y., Zheng, G., Fan, F., Tian, H. & Zhang, X. 2024. Psychosomatic mechanisms of heart failure symptoms on quality of life in patients with chronic heart failure: A multi-centre cross-sectional study. *Journal of Clinical Nursing,* 33**,** 1839-1848.

Wang, Z., Conley, S., Redeker, N. S. & Tocchi, C. 2023. An Evolutionary Concept Analysis in People With Heart Failure—Symptom Clusters or Symptom Cluster Profiles? *Advances in Nursing Science*, 10.1097.

Warnecke, E., Salvador Comino, M. R., Kocol, D., Hosters, B., Wiesweg, M., Bauer, S., Welt, A., Heinzelmann, A., Müller, S. & Schuler, M. 2023. Electronic patient-reported outcome measures (ePROMs) improve the assessment of underrated physical and psychological symptom burden among oncological inpatients. *Cancers,* 15**,** 3029.

Warren-Findlow, J. & Issel, L. M. 2010. Stress and coping in African American women with chronic heart disease: A cultural cognitive coping model. *Journal of Transcultural Nursing,* 21**,** 45-54.

Weaver, K. & Olson, J. K. 2006. Understanding paradigms used for nursing research. *Journal of advanced nursing,* 53**,** 459-469.

Welford, C., Murphy, K. & Casey, D. 2011. Demystifying nursing research terminology. Part 1. *Nurse Researcher,* 18.

Whitaker, K., Scott, S. & Wardle, J. 2015. Applying symptom appraisal models to understand sociodemographic differences in responses to possible cancer symptoms: a research agenda. *British journal of cancer,* 112**,** S27-S34.

Williams, D. M. & Evans, M. 2020. Dapagliflozin for heart failure with preserved ejection fraction: will the DELIVER study deliver? *Diabetes Therapy,* 11**,** 2207-2219.

Wilson, J. & Mcmillan, S. 2013. Symptoms Experienced by Heart Failure Patients in Hospice Care. *Journal of Hospice & Palliative Nursing,* 15**,** 13-21.

Wirta, S. B., Balas, B., Proenca, C. C., Bailey, H., Phillips, Z., Jackson, J. & Cotton, S. 2018. Perceptions of heart failure symptoms, disease severity, treatment decision-making, and side effects by patients and cardiologists: a multinational survey in a cardiology setting. *Therapeutics and clinical risk management***,** 2265-2272.

World Health Organization, W. H. O. 2015. *WHO global strategy on people-centred and integrated health services.* [Online]. World Health Organization. Available: https://apps.who.int/iris/bitstream/handle/10665/155002/WHO_HIS_SDS_2015.6_eng.pdf;jsessionid=CCA4E9FDB20767C694D61E9FB0C53838?sequence=1 [Accessed April 2023].

World Health Organization, W. H. O. 2022. *Health systems in action: Türkiye* [Online]. World Health Organization. Available: file:///C:/Users/XXXXXXX/Downloads/9789289059213-eng.pdf [Accessed July 2023].

Worldatlas. 2023a. *Middle East* [Online]. Available: https://www.worldatlas.com/webimage/countrys/me.htm [Accessed 18 July 2023].

Worldatlas. 2023b. *Turkey* [Online]. Available: https://www.worldatlas.com/maps/turkey [Accessed 18 July 2023].

Yancy, C. W., Jessup, M., Bozkurt, B., Butler, J., Casey, D. E., Jr., Drazner, M. H., Fonarow, G. C., Geraci, S. A., Horwich, T., Januzzi, J. L., Johnson, M. R., Kasper, E. K., Levy, W. C., Masoudi, F. A., Mcbride, P. E., Mcmurray, J. J., Mitchell, J. E., Peterson, P. N., Riegel, B., Sam, F., Stevenson, L. W., Tang, W. H., Tsai, E. J. & Wilkoff, B. L. 2013. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol,* 62**,** e147-239.

Yang, Z., Jia, H., Zhang, F., Huang, H., Hao, X. & Wang, A. 2024. A behavioural driving model of adherence to home-based cardiac rehabilitation exercise among patients with chronic heart failure: A mixed-methods study. *Journal of Clinical Nursing,* 33**,** 531-542.

Yılmaz, M. B., Aksakal, E., Aksu, U., Altay, H., Yıldırım, N., Çelik, A. & Akıl, M. A. 2020. Snapshot evaluation of acute and chronic heart failure in real-life in Turkey: A follow-up data for mortality.

You, J., Wang, S., Li, J. & Luo, Y. 2020. Usefulness of a nurse-led program of care for management of patients with chronic heart failure. *Medical Science Monitor: International Medical Journal of Experimental and Clinical Research,* 26**,** e920469-1.

Young, R. A. & Collin, A. 2004. Introduction: Constructivism and social constructionism in the career field. *Journal of vocational behavior,* 64**,** 373-388.

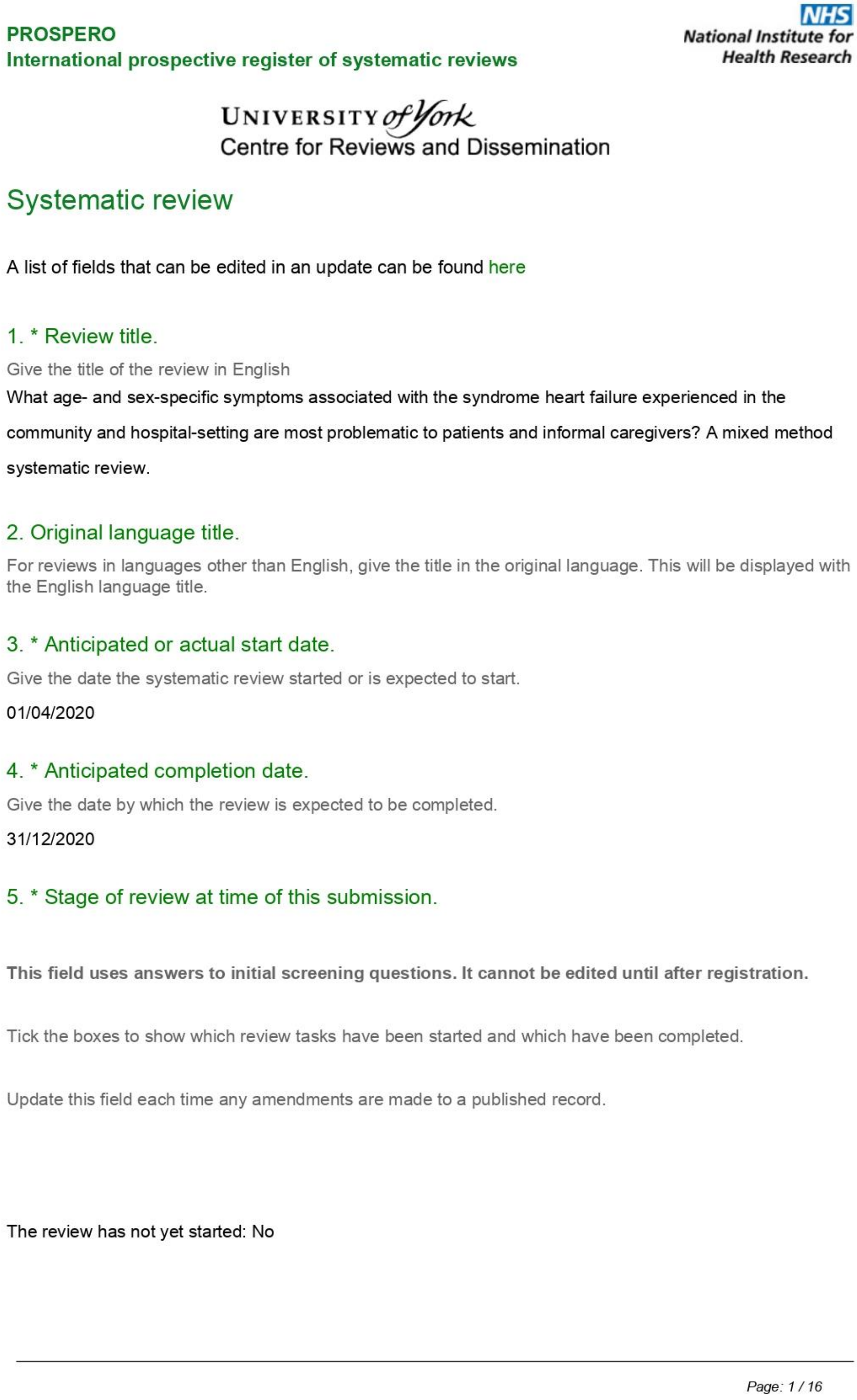
Yu, D. S. F., Chan, H. Y. L., Leung, D. Y. P., Hui, E. & Sit, J. W. H. 2016. Symptom clusters and quality of life among patients with advanced heart failure. *Journal of Geriatric Cardiology,* 13(5)**,** 408-414.

Zambroski, C. H. 2003. Qualitative analysis of living with heart failure. *Heart & Lung,* 32**,** 32-40.

Zambroski, C. H., Moser, D. K., Bhat, G. & Ziegler, C. 2005. Impact of symptom prevalence and symptom burden on quality of life in patients with heart failure. *European Journal of Cardiovascular Nursing,* 4**,** 198-206.

Zhang, J., Hobkirk, J., Carroll, S., Pellicori, P., Clark, A. L. & Cleland, J. G. 2016. Exploring quality of life in patients with and without heart failure. *International Journal of Cardiology,* 202**,** 676-684.

Appendix 2: PROSPERO registration



PROSPERO
International prospective register of systematic reviews

NHS
National Institute for Health Research

UNIVERSITY *of York*
Centre for Reviews and Dissemination

Systematic review

A list of fields that can be edited in an update can be found here

1. * Review title.

Give the title of the review in English

What age- and sex-specific symptoms associated with the syndrome heart failure experienced in the community and hospital-setting are most problematic to patients and informal caregivers? A mixed method systematic review.

2. Original language title.

For reviews in languages other than English, give the title in the original language. This will be displayed with the English language title.

3. * Anticipated or actual start date.

Give the date the systematic review started or is expected to start.

01/04/2020

4. * Anticipated completion date.

Give the date by which the review is expected to be completed.

31/12/2020

5. * Stage of review at time of this submission.

This field uses answers to initial screening questions. It cannot be edited until after registration.

Tick the boxes to show which review tasks have been started and which have been completed.

Update this field each time any amendments are made to a published record.

The review has not yet started: No

Review stage	**Started**	**Completed**
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

Provide any other relevant information about the stage of the review here.

6. * Named contact.

The named contact is the guarantor for the accuracy of the information in the register record. This may be any member of the review team.

Muzeyyen Seckin

Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:

Miss Seckin

7. * Named contact email.

Give the electronic email address of the named contact.

m.seckin.1@research.gla.ac.uk

8. Named contact address

Give the full institutional/organisational postal address for the named contact.

School of Medicine, Dentistry & Nursing,

University of Glasgow

57-61 Oakfield Avenue

9. Named contact phone number. [1 change]

Give the telephone number for the named contact, including international dialling code.

10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

University of Glasgow

Organisation web address:

11. * Review team members and their organisational affiliations.

Give the personal details and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong. **NOTE: email and country now MUST be entered for each person, unless you are amending a published record.**

Miss Muzeyyen Seckin. University of Glasgow, School of Medicine Dentistry and Nursing
Professor Bridget Johnston. University of Glasgow, School of Medicine Dentistry and Nursing
Professor Mark Petrie. University of Glasgow, Institute of Cardiovascular Medicine
Professor Simon Stewart. NHMRC of Australia Senior Principal Research Fellow, Torrens University, Australia Honorary Professor of Nursing, University of Glasgow

12. * Funding sources/sponsors.

Details of the individuals, organizations, groups, companies or other legal entities who have funded or sponsored the review.

None

Grant number(s)

State the funder, grant or award number and the date of award

13. * Conflicts of interest.

List actual or perceived conflicts of interest (financial or academic).

None

14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members. **NOTE: email and country must be completed for each person, unless you are amending a published record.**

15. * Review question.

State the review question(s) clearly and precisely. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS or similar where relevant.

Main research question:

What age- and sex-specific symptoms associated with the syndrome heart failure experienced in the community and hospital-setting are most problematic to patients and informal caregivers?

Sub questions:

· What are the symptoms experienced by people with heart failure?

· What is the prevalence of symptoms in the sub-populations?

· Do symptoms change over the age and gender?

. Are the symptoms experienced by the patients and observed by the caregiver concordant?

16. * Searches.

State the sources that will be searched (e.g. Medline). Give the search dates, and any restrictions (e.g. language or publication date). Do NOT enter the full search strategy (it may be provided as a link or attachment below.)

The search strategy of the review has been based on scoping current and previous relevant articles' key words, subject headings and strategies related to the review question. A librarian (PC) of the College of Medical, Veterinary and Life Science of the University helped to develop the literature searches. After defining the subject headings and text terms, a pilot electronic search was done to develop and to check the suitability of search terms in MEDLINE and CINAHL (between 01/04/2020 and 05/05/2020).

The search strategies will be conducted for a systematic search of six main databases (MEDLINE, EMBASE, CINAHL, Web of Science, PsycINFO and Cochrane Library Database), which will be comprehensive and appropriate for the review topic. All databases search will be completed untill end of the June. Unpublished/grey literature will also be conducted.

A systematic search will be conducted using the appropriate subject headings and free-text terms with using AND/OR Boolean in the databases. The search strategy will include the medical subject heading terms “heart failure” AND “patients” AND “caregivers” AND “symptoms” all of them will explode to encompass all subject headings with the term. Synonyms of these terms will be searched as free-text terms in the databases. Titles and abstracts search limitation will be contained for the text terms in the review. The English language limitation will be also used in the databases.

After all electronic databases search, Endnote (software programme) will be used for deduplication of the search results of databases.

The proposed systematic review will be conducted in accordance with the JBI methodology for mixed method systematic review (MMSR) (Chapter 8: Mixed methods systematic reviews (2019), Lucylynn L?zaronda, Cind Stern, Judith Carrier, Christina Godfrey, Kendra Rieger, Susan Salmond, Joao Apostob, Pamela Kirkpatrick, Heather Lavetay).

17. URL to search strategy.

Upload a file with your search strategy, or an example of a search strategy for a specific database, (including the keywords) in pdf or word format. In doing so you are consenting to the file being made publicly accessible. Or provide a URL or link to the strategy. Do NOT provide links to your search **results**.

https://www.crd.york.ac.uk/PROSPEROFILES/185786_STRATEGY_20200512.pdf

Alternatively, upload your search strategy to CRD in pdf format. Please note that by doing so you are consenting to the file being made publicly accessible.

Do not make this file publicly available until the review is complete

18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied in your systematic review.

Heart Failure People with heart failure experience severe physical and psychosocial symptoms. Especially, people who develop heart failure are old and have other chronic diseases. Although HFpEF and HFrEF share a similar clinical phenotype including symptoms, signs, outcomes and hemodynamic, studies indicate that patients with HFpEF have several different characteristics from people with HFrEF (Bhatia et al. 2006, Kitzman et al. 2002, Owan et al. 2006).

Caregivers

Patients with heart failure will require assistance in promotion of health and daily symptom management, by a family member (Kitko et al. 2015). Caregivers may be able to observe the patient during the day and have a key role to understand the importance of symptoms experienced by the patient.

Both caregivers' and patients' experiences are essential to understand the importance of patients' symptoms on their health status in heart failure.

Points to consider for this review

· Evaluating the prevalence of symptoms which are experienced by patients with heart failure.

· Assessment of problematic symptoms in terms of both patients' and caregivers' perspective.

· Understanding of the most problematic symptoms among different subgroups: including men versus women; young versus old age; HFrEF and HFpEF; and main pathology of heart failure.

19. * Participants/population.

Specify the participants or populations being studied in the review. The preferred format includes details of both inclusion and exclusion criteria.

Inclusion:

People who are over 18 years old age;

Heart failure is defined by HFrEF or HFpEF and NYHA class II, III and IV, and/or conventional diagnostic imaging results according to 2016 ESC HF Guidelines. We will look at the experiences of inpatient or outpatient with heart failure. The experiences of people with heart failure during end-of-life or palliative care phase will be also included.

Patients' unpaid caregivers (18+ age old) are primarily a family member of patients or friends, neighbours and relatives.

Exclusion:

Patients and caregivers are under 18 years old.

20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the interventions or the exposures to be reviewed. The preferred format includes details of both inclusion and exclusion criteria.

The review will identify physical and psychological symptoms of heart failure from patient and caregiver perspective. Also, we are interested in any symptoms which affect the life of people with heart failure whether these are cardiovascular or non-cardiovascular. Therefore, we will include studies which measure any kind of the symptoms from patients and their caregivers perspective in heart failure.

21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the intervention/exposure will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

We will compare patients and their caregivers viewpoints on symptom experiences within studies if it is applicable. A comparison will be also done between different groups; including sex, age, and main pathology of heart failure.

22. * Types of study to be included.

Give details of the study designs (e.g. RCT) that are eligible for inclusion in the review. The preferred format includes both inclusion and exclusion criteria. If there are no restrictions on the types of study, this should be stated.

Qualitative, quantitative and mixed method research designs will be measured the symptoms of heart failure from both patients and carers perspective, including; questionnaire, survey, interview, focus group, case study, observational study etc. Qualitative studies must include patients' and their caregivers' thoughts on their symptoms experiences. Quantitative data must include the symptom assessment of people with heart failure. Mixed method studies will only be considered if data from qualitative or quantitative components can be clearly extracted.

23. Context.

Give summary details of the setting or other relevant characteristics, which help define the inclusion or exclusion criteria.

This review will consider studies that investigate primary and secondary health care.

24. * Main outcome(s).

Give the pre-specified main (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

Following symptoms will be including for this review:

(a) Physical symptom of heart failure; shortness of breath, fatigue, oedema, sleeplessness, fall, headaches, pain/ chest pain etc.

(b) Other symptoms: psychological wellbeing, depression, anxiety, social isolation, spiritual etc.

(c) We are interested in all kinds of symptoms which have an effect on patients' life. We would also specify symptoms related to common comorbidities (eg COPD, diabetes, anaemia, arthritis, stroke etc.).

The aim of the review will be to assess the most problematic symptoms (any types of physical and psychological from patients and their caregiver perspective in heart failure. Qualitative and quantitative outcomes of these symptoms could be measured differently within studies included. Taking a consideration into any differences of measurement types used in the studies, we will evaluate these qualitative and quantitative outcomes to understand the most problematic symptoms of people with chronic heart failure. The symptoms of chronic heart failure will be assessed in terms of additional comorbid disease which can increase symptom burden.

Measures of effect

Please specify the effect measure(s) for you main outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

Not applicable

25. * Additional outcome(s).

List the pre-specified additional outcomes of the review, with a similar level of detail to that required for main outcomes. Where there are no additional outcomes please state 'None' or 'Not applicable' as appropriate to the review

Not applicable.

Measures of effect

Please specify the effect measure(s) for you additional outcome(s) e.g. relative risks, odds ratios, risk difference, and/or 'number needed to treat.

Not applicable

26. * Data extraction (selection and coding). [1 change]

Describe how studies will be selected for inclusion. State what data will be extracted or obtained. State how this will be done and recorded.

All data of the electronic search will be exported into Endnote for deduplication. The first author (MS) will screen all titles and abstracts against the prespecified inclusion/exclusion criteria, and one or more members of the supervisory team will cross-check the results for accuracy. This will include the full-text reading of relevant article to conduct considered evaluation of main themes of the article.

The reviewer will extract quantitative and qualitative data of studies included in the review using the standardised Joanna Bring Institute data extraction tool in JBI SUMARI. In this stage articles should include a strong relation to main themes of the review, including burden of symptoms and heart failure. If the article is strongly relevant to the research inclusion criteria, the article will code as clearly relevant. Or if article include possibly relation for the review, this will code as possibly relevant. However, if it not relevant for the review, it will code as unlikely relevant, and this article will not select for the review. After finding clearly relevant and possibly relevant papers, the first author and others will discuss the any uncertainty of selected article. After discussing any discrepancy by all reviews, a final decision will be recorded in a PRISMA flowchart (Moher et al. 2009).

Data extraction will be done with following information of each article found: year, author, country, objectives, and the characteristic of the research population (age, gender, heart failure types, caregivers' relationship, and comorbid burden and types), methods (interview or questionnaire), symptoms.

27. * Risk of bias (quality) assessment.

State which characteristics of the studies will be assessed and/or any formal risk of bias/quality assessment tools that will be used.

All included studies must be critically appraised using a standard JBI critical appraisal instruments to decide whether the studies can meet on all criteria or certain criteria, and it is also weight certain criteria differently (Joanna Briggs Institute 2014). The first author (MS) will read the articles and assess the quality of paper with using the Joanna Briggs Institute's qualitative/quantitative critical appraisal checklist. These critical appraisal tools will be used for assessing methodological quality of studies which has addressed any bias within research design, conduct and analysis. Other two authors of supervisory team will verify the appraisal of articles.

28. * Strategy for data synthesis. [1 change]

Describe the methods you plan to use to synthesise data. This **must not be generic text** but should be **specific to your review** and describe how the proposed approach will be applied to your data. If meta-analysis is planned, describe the models to be used, methods to explore statistical heterogeneity, and software package to be used.

Synthesis will take an integrated and a best fit narrative synthesis approach (Joanna Briggs Institute 2014). Narrative synthesis will be conducted for reporting the results of included studies in the review, which will provide an answer to the question of this review. A narrative synthesis approach can help to synthesis diverse studies in a structured way including following three main steps: (1) "developing a preliminary synthesis of the findings of the included studies"; (2) "exploring relationship in the findings"; and (3) "assessing the robustness of the synthesis produced" (Mays et al. 2005).

The results of the qualitative and quantitative studies will be analysed separately by focusing on the symptom perspective of the patients with heart failure and their informal caregivers. Data will be synthesized where they are reported in a minimum of one study to represent perceived importance of symptoms by included studies investigators. Finally, the results will be combined in a narrative synthesis.

Qualitative

A thematic analysis will be subject for analysing of findings from qualitative studies, which is outlined by Thomas and Harden (2008). Within narrative synthesis, thematic analysis is the most common method for producing a descriptive synthesis of the results across the included studies (Mays et al. 2005). In thematic analysis, data will be extracted using coding, groups similar codes and developing descriptive themes for the generation of the results.

Quantitative

Descriptive analysis will be subject for the analysing the findings of quantitative studies if it is applicable. A meta-analysis will be not expected for the quantitative results because included quantitative studies may include a variety of papers. Also, the intention is to look for symptom information and not to do a meta-analysis.

Combining the qualitative and quantitative finding

Qualitative and quantitative results components will be combined and reported according to the objective of the research. We will report results according to the relation between heart failure subtypes and any kind of symptoms experienced by patients.

29. * Analysis of subgroups or subsets.

State any planned investigation of 'subgroups'. Be clear and specific about which type of study or participant will be included in each group or covariate investigated. State the planned analytic approach.

Additional subgroup analyses will be carried out to identify if there are age, sex or pathology (coronary artery disease versus ischaemic cardiomyopathy) related differences in the way symptoms are perceived.

30. * Type and method of review.

Select the type of review, review method and health area from the lists below.

Type of review

Cost effectiveness

No

Diagnostic

No

Epidemiologic

No

Individual patient data (IPD) meta-analysis

No

Intervention

No

Living systematic review

No

Meta-analysis

No

Methodology

No

Narrative synthesis

Yes

Network meta-analysis

No

Pre-clinical

No

Prevention

No

Prognostic
No

Prospective meta-analysis (PMA)
No

Review of reviews
No

Service delivery
No

Synthesis of qualitative studies
No

Systematic review
Yes

Other
No

Mixed methods systematic review

Health area of the review

Alcohol/substance misuse/abuse
No

Blood and immune system
No

Cancer
No

Cardiovascular
Yes

Care of the elderly
No

Child health
No

Complementary therapies
No

COVID-19
No

Crime and justice
No

Dental

No

Digestive system

No

Ear, nose and throat

No

Education

No

Endocrine and metabolic disorders

No

Eye disorders

No

General interest

No

Genetics

No

Health inequalities/health equity

No

Infections and infestations

No

International development

No

Mental health and behavioural conditions

No

Musculoskeletal

No

Neurological

No

Nursing

Yes

Obstetrics and gynaecology

No

Oral health

No

Palliative care

Yes

Perioperative care

No

Physiotherapy

No

Pregnancy and childbirth

No

Public health (including social determinants of health)

No

Rehabilitation

No

Respiratory disorders

No

Service delivery

No

Skin disorders

No

Social care

No

Surgery

No

Tropical Medicine

No

Urological

No

Wounds, injuries and accidents

No

Violence and abuse

No

31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error.
English

There is not an English language summary

32. * Country.

Select the country in which the review is being carried out. For multi-national collaborations select all the countries involved.

Scotland

33. Other registration details.

Name any other organisation where the systematic review title or protocol is registered (e.g. Campbell, or The Joanna Briggs Institute) together with any unique identification number assigned by them. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

34. Reference and/or URL for published protocol.

If the protocol for this review is published provide details (authors, title and journal details, preferably in Vancouver format)

Add web link to the published protocol.

Or, upload your published protocol here in pdf format. Note that the upload will be publicly accessible.

No I do not make this file publicly available until the review is complete

Please note that the information required in the PROSPERO registration form must be completed in full even if access to a protocol is given.

35. Dissemination plans.

Do you intend to publish the review on completion?

Yes

Give brief details of plans for communicating review findings.?

This review will be publised in peer-review journal. This sudy will be a part of PhD thesis.

36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords help PROSPERO users find your review (keywords do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

Mixed method systematic review, heart failure, symptoms, caregiver, patients and symptom perspective.

37. Details of any existing review of the same topic by the same authors.

If you are registering an update of an existing review give details of the earlier versions and include a full bibliographic reference, if available.

38. * Current review status.

Update review status when the review is completed and when it is published.New registrations must be ongoing so this field is not editable for initial submission.

Please provide anticipated publication date

Review_Ongoing

39. Any additional information.

Provide any other information relevant to the registration of this review.

This review is the first part of a doctoral degree which be undertaken by the primary researcher at the University of Glasgow.

40. Details of final report/publication(s) or preprints if available.

Leave empty until publication details are available OR you have a link to a preprint (NOTE: this field is not editable for initial submission). List authors, title and journal details preferably in Vancouver format.

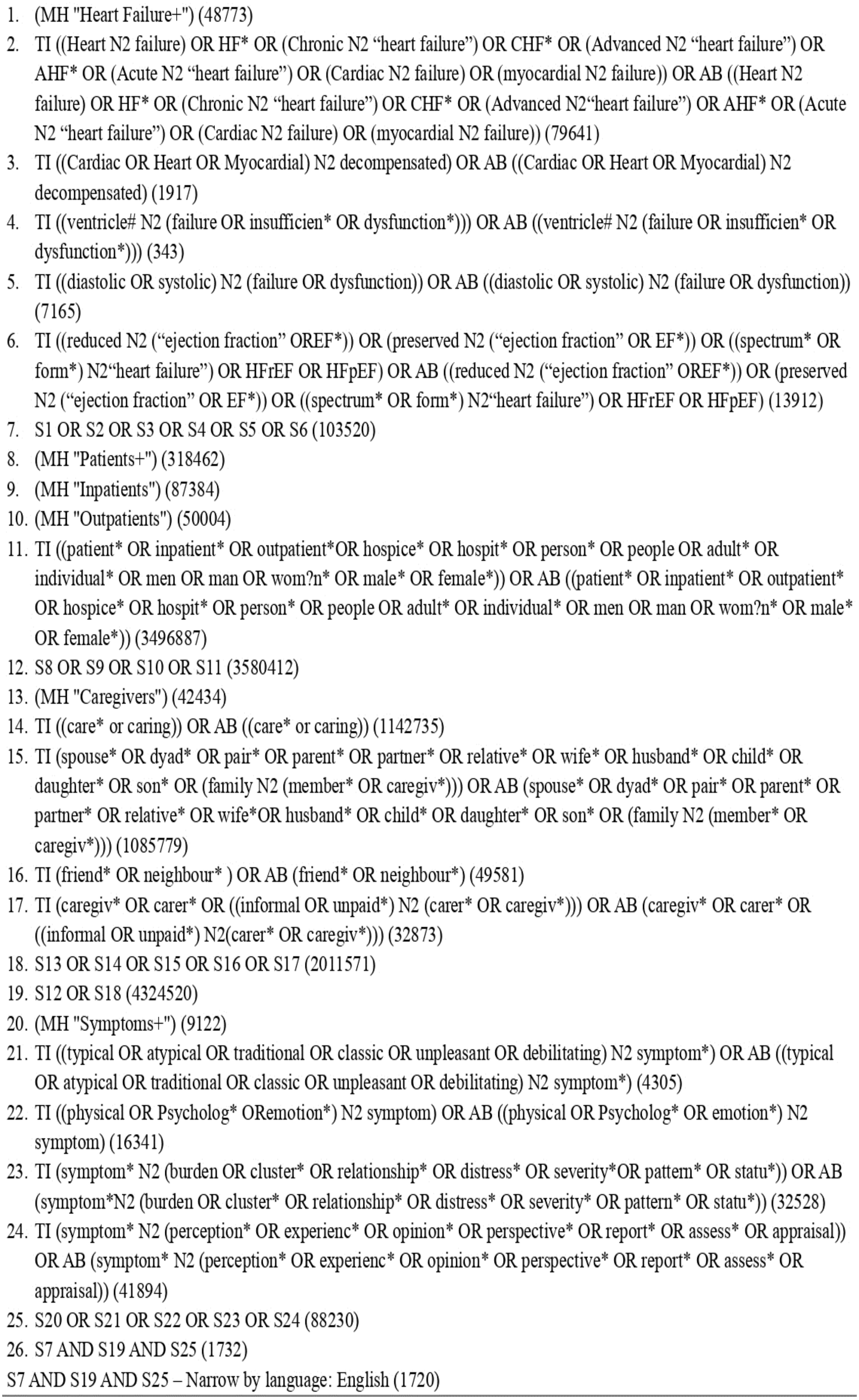
Give the link to the published review or preprint.

Appendix 3: Medline and CINAHL search syntax

```
Database: Ovid MEDLINE(R) ALL <1946 to February 23, 2023> Search Strategy:
--------------------------------------------------------------------------------

1 exp Heart Failure/ (144239)
2 (((advanced or chronic or acute) adj2 heart failure) or HF* or CHF* or AHF*).ti,ab. (160314)
3 ((heart or cardiac or myocardial) adj2 (failure or decompensated)).ti,ab. (213750)
4 (ventricle$ adj2 (failure or insufficien$ or dysfunction$)).ti,ab. (1095)
5 (((reduced or preserved) adj2 ("ejection fraction" or EF)) or HFrEF or HFpEF).ti,ab. (14467)
6 ((diastolic or systolic) adj2 (failure or dysfunction)).ti,ab. (22770)
7 ((spectrum* or form*) adj2 heart failure).ti,ab. (528)
8 1 or 2 or 3 or 4 or 5 or 6 or 7 (355521)
9 exp Patients/ (79162)
10 exp Inpatients/ (28585)
11 exp Outpatients/ (20786)
12 (patient* or inpatient* or outpatient* or hospice* or hospit* or person or people or adult* or individual or men or man
or wom#n or male* or female*).ti,ab. (12023869)
13 9 or 10 or 11 or 12 (12035204)
14 exp Caregivers/ (48704)
15 (care* or caring or caregiver* or carer*).ti,ab. (2035731)
16 (spouse* or dyad* or pair* or parent* or partner* or relative* or wife* or husband* or child* or daughter* or son* or
(family adj2 member*)).ti,ab. (4263706)
17 (Friend* or neighbour*).ti,ab. (152891)
18 ((informal or unpaid*) adj2 (carer* or caregiver*)).ti,ab. (5840)
19 14 or 15 or 16 or 17 or 18 (5962668)
20 exp Symptom Assessment/ (7056)
21 ((typical or atypical or traditional or classic or unpleasant or debilitateing) adj2 symptom$).ti,ab. (15045)
22 ((physical or psychology* or emotion*) adj2 symptom$).ti,ab. (17442)
23 (Symptom$ adj2 (cluster$ or burden or relationship$ or distress$ or severity$ or pattern$ or statu$)).ti,ab. (56328)
24 (symptom$ adj2 (perception$ or experienc$ or opinion$ or perspective$ or report$ or assess$ or appraisal$)).ti,ab.
(76786)
25 20 or 21 or 22 or 23 or 24 (156653)
26 8 and 13 and 19 and 25 (994)
27 limit 26 to english language (950)
```

Database: CINAHL-EBSCOhost - 24.02.2023



1. (MH "Heart Failure+") (48773)
2. TI ((Heart N2 failure) OR HF* OR (Chronic N2 “heart failure”) OR CHF* OR (Advanced N2 “heart failure”) OR AHF* OR (Acute N2 “heart failure”) OR (Cardiac N2 failure) OR (myocardial N2 failure)) OR AB ((Heart N2 failure) OR HF* OR (Chronic N2 “heart failure”) OR CHF* OR (Advanced N2“heart failure”) OR AHF* OR (Acute N2 “heart failure”) OR (Cardiac N2 failure) OR (myocardial N2 failure)) (79641)
3. TI ((Cardiac OR Heart OR Myocardial) N2 decompensated) OR AB ((Cardiac OR Heart OR Myocardial) N2 decompensated) (1917)
4. TI ((ventricle# N2 (failure OR insufficien* OR dysfunction*))) OR AB ((ventricle# N2 (failure OR insufficien* OR dysfunction*))) (343)
5. TI ((diastolic OR systolic) N2 (failure OR dysfunction)) OR AB ((diastolic OR systolic) N2 (failure OR dysfunction)) (7165)
6. TI ((reduced N2 (“ejection fraction” OREF*)) OR (preserved N2 (“ejection fraction” OR EF*)) OR ((spectrum* OR form*) N2“heart failure”) OR HFrEF OR HFpEF) OR AB ((reduced N2 (“ejection fraction” OREF*)) OR (preserved N2 (“ejection fraction” OR EF*)) OR ((spectrum* OR form*) N2“heart failure”) OR HFrEF OR HFpEF) (13912)
7. S1 OR S2 OR S3 OR S4 OR S5 OR S6 (103520)
8. (MH "Patients+") (318462)
9. (MH "Inpatients") (87384)
10. (MH "Outpatients") (50004)
11. TI ((patient* OR inpatient* OR outpatient*OR hospice* OR hospit* OR person* OR people OR adult* OR individual* OR men OR man OR wom?n* OR male* OR female*)) OR AB ((patient* OR inpatient* OR outpatient* OR hospice* OR hospit* OR person* OR people OR adult* OR individual* OR men OR man OR wom?n* OR male* OR female*)) (3496887)
12. S8 OR S9 OR S10 OR S11 (3580412)
13. (MH "Caregivers") (42434)
14. TI ((care* or caring)) OR AB ((care* or caring)) (1142735)
15. TI (spouse* OR dyad* OR pair* OR parent* OR partner* OR relative* OR wife* OR husband* OR child* OR daughter* OR son* OR (family N2 (member* OR caregiv*))) OR AB (spouse* OR dyad* OR pair* OR parent* OR partner* OR relative* OR wife*OR husband* OR child* OR daughter* OR son* OR (family N2 (member* OR caregiv*))) (1085779)
16. TI (friend* OR neighbour*) OR AB (friend* OR neighbour*) (49581)
17. TI (caregiv* OR carer* OR ((informal OR unpaid*) N2 (carer* OR caregiv*))) OR AB (caregiv* OR carer* OR ((informal OR unpaid*) N2(carer* OR caregiv*))) (32873)
18. S13 OR S14 OR S15 OR S16 OR S17 (2011571)
19. S12 OR S18 (4324520)
20. (MH "Symptoms+") (9122)
21. TI ((typical OR atypical OR traditional OR classic OR unpleasant OR debilitating) N2 symptom*) OR AB ((typical OR atypical OR traditional OR classic OR unpleasant OR debilitating) N2 symptom*) (4305)
22. TI ((physical OR Psycholog* ORemotion*) N2 symptom) OR AB ((physical OR Psycholog* OR emotion*) N2 symptom) (16341)
23. TI (symptom* N2 (burden OR cluster* OR relationship* OR distress* OR severity*OR pattern* OR statu*)) OR AB (symptom*N2 (burden OR cluster* OR relationship* OR distress* OR severity* OR pattern* OR statu*)) (32528)
24. TI (symptom* N2 (perception* OR experienc* OR opinion* OR perspective* OR report* OR assess* OR appraisal)) OR AB (symptom* N2 (perception* OR experienc* OR opinion* OR perspective* OR report* OR assess* OR appraisal)) (41894)
25. S20 OR S21 OR S22 OR S23 OR S24 (88230)
26. S7 AND S19 AND S25 (1732)

S7 AND S19 AND S25 – Narrow by language: English (1720)

Appendix 4: Data sharing letter and Ethics approval from University of Glasgow for secondary data analysis of WHICH?II Trial

Data sharing letter

TORRENS UNIVERSITY AUSTRALIA

8th May 2021

Muzeyyen Seckin
PhD Student (Nursing),
School of Medicine, Dentistry & Nursing,
College of Medical, Veterinary & Life Sciences,
University of Glasgow

Dear Muzeyyen,

In accordance with the original ethics approval (including the Patient Information and Consent Form) of the NHMRC of Australia funded "**Which Heart failure Intervention is most Cost-effective in reducing Hospital stay (WHICH? II) Trial [ANZCTR 12613000921785]**", I can confirm (as the Principal Investigator and Grant Holder) that pending relevant ethics approval from the University of Glasgow, we are in a position to share with you de-identified data on the pattern of symptoms within the trial cohort, under the supervision of your PhD supervisors – Professor Bridget Johnston and Professor Mark Petrie.

Original ethics approval was provided the HREC of Australian Catholic University (ACU), Melbourne, Australia, and study data remains housed at the Mary MacKillop Institute for Health Research (of which I was the founding Director). As per our discussions, my colleague at ACU (Dr Yih-Kai Chan who was a Co-Investigator on the trial and continues to co-publish reports from the trial) is able to share anonymised study data (via secure password file transfer) with you once institutional ethics approval is obtained.

Please note that we strictly adhere to the *Australian Code for the Responsible Conduct of Research* – please make yourself aware of these.

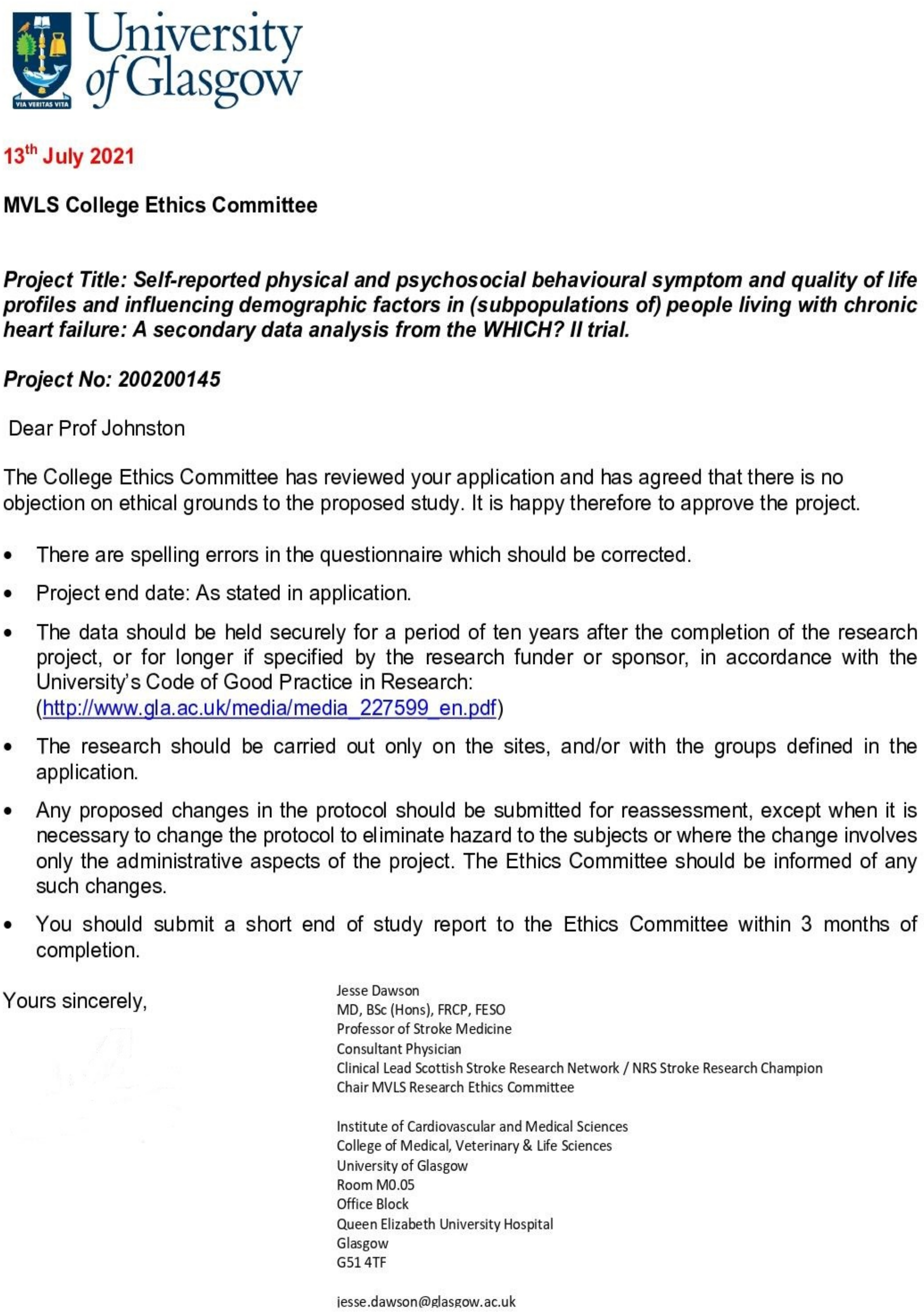
National Health and Medical Research Council (2018). Australian Code for the Responsible Conduct of Research. https://www.nhmrc.gov.au/about-us/publications/australian-code-responsibleconduct-research-2018

Please remember (due to a potential conflict of interest) to note in your ethics application that I am also your Co-Supervisor and have an Adjunct appointment at the University of Glasgow. Both me and Dr Chan will need to remain involved in the analyses and reporting as part of our "data sharing" (highly encouraged by the NHMRC) plans for the trial.

With best wishes

Professor Simon Stewart
NHMRC Senior Principal Research Fellow
Tel:
E: simon.stewart@torrens.edu.au

Ethics approval



University of Glasgow

13th July 2021

MVLS College Ethics Committee

Project Title: Self-reported physical and psychosocial behavioural symptom and quality of life profiles and influencing demographic factors in (subpopulations of) people living with chronic heart failure: A secondary data analysis from the WHICH? II trial.

Project No: 200200145

Dear Prof Johnston

The College Ethics Committee has reviewed your application and has agreed that there is no objection on ethical grounds to the proposed study. It is happy therefore to approve the project.

- There are spelling errors in the questionnaire which should be corrected.
- Project end date: As stated in application.
- The data should be held securely for a period of ten years after the completion of the research project, or for longer if specified by the research funder or sponsor, in accordance with the University's Code of Good Practice in Research: (http://www.gla.ac.uk/media/media_227599_en.pdf)
- The research should be carried out only on the sites, and/or with the groups defined in the application.
- Any proposed changes in the protocol should be submitted for reassessment, except when it is necessary to change the protocol to eliminate hazard to the subjects or where the change involves only the administrative aspects of the project. The Ethics Committee should be informed of any such changes.
- You should submit a short end of study report to the Ethics Committee within 3 months of completion.

Yours sincerely,

Jesse Dawson
MD, BSc (Hons), FRCP, FESO
Professor of Stroke Medicine
Consultant Physician
Clinical Lead Scottish Stroke Research Network / NRS Stroke Research Champion
Chair MVLS Research Ethics Committee

Institute of Cardiovascular and Medical Sciences
College of Medical, Veterinary & Life Sciences
University of Glasgow
Room M0.05
Office Block
Queen Elizabeth University Hospital
Glasgow
G51 4TF

jesse.dawson@glasgow.ac.uk

Appendix 5: ***Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist***

No	Item	Guide questions/description	Page and heading/details
Domain 1: Research team and reflexivity			
Personal characteristics			
1.	Interviewer/facilitator	Which author/s conducted the interview or focus group?	Page 81 - data collection
2.	Credentials	What were the researcher's credentials? *E.g. PhD, MD*	PhD-student
3.	Occupation	What was their occupation at the time of the study?	-Nurse researcher
4.	Gender	Was the researcher male or female?	- Female
5.	Experience and training	What experience or training did the researcher have?	- Educated in Motivational Interviewing
Relationship with participants			
6.	Relationship established	Was a relationship established prior to study commencement?	- Yes
7.	Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. *personal goals, reasons for doing the research*	Page 86
8.	Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g. *Bias, assumptions, reasons and interests in the research topic*	Page 86
Domain 2: study design			
Theoretical framework			
9.	Methodological orientation and Theory	What methodological orientation was stated to underpin the study? *e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis*	Page 77 and 78
Participant selection			
10.	Sampling	How were participants selected? *e.g. purposive, convenience, consecutive, snowball*	Page 51 and 79
11.	Method of approach	How were participants approached? e.g. *face-to-face, telephone, mail, email*	Page 79
12.	Sample size	How many participants were in the study?	Page 80
13.	Non-participation	How many people refused to participate or dropped out? Reasons?	Page 80
Setting			
14.	Setting of data collection	Where was the data collected? e.g. *home, clinic, workplace*	Page 78
15.	Presence of non-participants	Was anyone else present besides the participants and researchers?	Page 78
16.	Description of sample	What are the important characteristics of the sample? *e.g. demographic data, date*	Page 79

Data collection			
17.	Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	Page 81
18.	Repeat interviews	Were repeat interviews carried out? If yes, how many?	No (N/A)
19.	Audio/visual recording	Did the research use audio or visual recording to collect the data?	Page 81
20.	Field notes	Were field notes made during and/or after the interview or focus group?	No (N/A)
21.	Duration	What was the duration of the interviews or focus groups	Page 81
22.	Data saturation	Was data saturation discussed?	No (N/A)
23.	Transcripts returned	Were transcripts returned to participants for comment and/or correction?	No (N/A)
Domain 3: analysis and findings			
Data analysis			
24.	Number of data coders	How many data coders coded the data?	Page 84
25.	Description of the coding tree	Did authors provide a description of the coding tree?	Page 84
26.	Derivation of themes	Were themes identified in advance or derived from the data?	Page 84
27.	Software	What software, if applicable, was used to manage the data?	Page 81 and 84
28.	Participant checking	Did participants provide feedback on the findings?	No (N/A)
Reporting			
29.	Quotations presented	Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.g. *participant number*	Page 86 and Chapter 7
30.	Data and findings consistent	Was there consistency between the data presented and the findings?	Chapter Seven -
31.	Clarity of major themes	Were major themes clearly presented in the findings?	Chapter Seven -
32.	Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	Chapter Seven -

*N/A, not applicable

Appendix 6: Participant recruitment phase (advertisement documents and Participant Information Sheet, Privacy Notice and Consent Form of the study)

1

Do you experience breathlessness due to heart failure?

CALL FOR PARTICIPANTS!

Muzeyyen Seckin is a Turkish Nurse and PhD researcher in Nursing at University of Glasgow. Her research interest is about developing a person-led care intervention for people living with heart failure and their family members. She is looking at symptoms experienced by people with heart failure and the impacts of symptoms on everyday life.

Volunteers are needed to take part in nursing research which aims to help exploring the impacts of breathlessness in heart failure.

This study involves **individual interview** via **face-to-face, telephone call or online platform. We are interested in recruiting potential participants. Participants must be;**

- **Over 18 years of age**
- **Diagnosed with heart failure**
- **Experiencing breathlessness**
- **Fluent in the Turkish language**

If you want to participate or have some more information, please contact us

m.seckin.1@research.gla.ac.uk

@SeckinMuzeyyen

University of Glasgow

Scotland, UK

V 1.2 02/02/2022

2

Are you interested in sharing your experiences of having breathlessness targeted for people with heart failure?

University of Glasgow

Scotland, UK

Volunteers are needed to take part in nursing research which aims to help exploring the impacts of breathlessness in heart failure.

CALL FOR PARTICIPANTS!

This study involves **individual interview via face-to-face, telephone call or online platform.** We are interested in recruiting potential participants. Participants must be;

- Over 18 years of age
- Diagnosed with heart failure
- Experiencing breathlessness
- Fluent in the Turkish language

If you want to participate or have some more information, please contact us

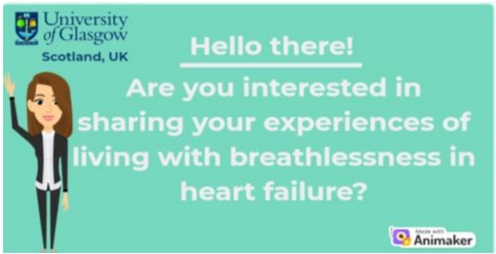
m.seckin.1@research.gla.ac.uk

@SeckinMuzeyyen

V 1.2 02/02/2022

Video content →

3



University of Glasgow

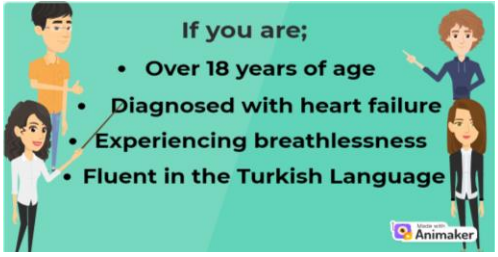
Scotland, UK

Hello there!

Are you interested in sharing your experiences of living with breathlessness in heart failure?

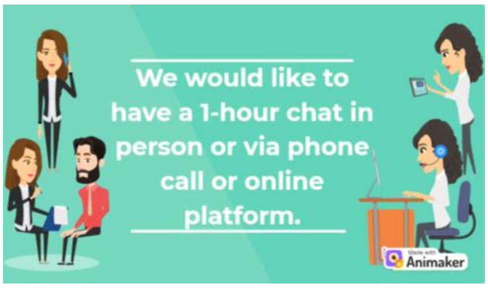
We are researchers from University of Glasgow.

The research is exploring the impacts of breathlessness on everyday life from your perspective.



If you are;

- **Over 18 years of age**
- **Diagnosed with heart failure**
- **Experiencing breathlessness**
- **Fluent in the Turkish Language**



We would like to have a 1-hour chat in person or via phone call or online platform.

If you want to find out more, please contact us!

m.seckin.1@research.gla.ac.uk

@SeckinMuzeyyen

WhatsApp: [redacted]

University of Glasgow

Scotland, UK

Participant Information Sheet

University of Glasgow | College of Medical, Veterinary & Life Sciences

Scotland, UK

Participant Information Sheet (PIS)

Please note this was translated into Turkish

1. Study title

Peoples experience of breathlessness in heart failure (in Turkey): a qualitative study

2. Invitation paragraph

My name is Muzeyyen Seckin, a Turkish nurse and a PhD student in Nursing at the **University of Glasgow, Scotland, UK.** My research interest is to improve the life and care quality of people living with heart failure and their family caregivers. My research will look at breathlessness experiences of people living with heart failure in their everyday lives.

I would like to invite you to take part in a one-to-one interview as a part of my PhD project. Your participation is voluntary. Before you decide to join in this research, it is important for you to understand why this research is important for us and what it will include.

Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. If you decide to take part in this study, you will be given a copy of this Participant Information Sheet and the signed consent form to keep. If you would like to participate in this study, then please complete the enclosed/attached consent form and return it to the researcher, Muzeyyen Seckin.

3. What is the purpose of this study?

The primary aim of this research is to explore the experience of living with breathlessness in people with heart failure from the patient perspective. This study will contribute towards a PhD degree that is due to be completed by October 2022.

We will have an online/ in person chat with you that will take no more than 1 hour. The topic is about your experiences of breathlessness, the impact of breathlessness on your everyday life, and how you manage your breathlessness. This study requires participants who live with heart conditions. Your participation will provide us with insights into what it is like to live with breathlessness in heart failure or care for someone with heart failure.

4. Why have I been invited to participate?

We want to involve an equal number of female and male participants for patient groups in as much as possible. You have been chosen because you fit the profile of the population being studied that is:

- You are over the age of 18 years.
- You are living with heart failure condition and experiencing breathlessness.
- You are from Turkey.

5. Do I have to take part?

No, your participation is entirely voluntary. If you do not want to take part or enrol and decide to withdraw later, your care or legal rights will not be affected by these decisions. If you decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. However, you are still free to withdraw at any time and without giving any reason. If you decide to withdraw consent, information related to you will not be kept. If you wish to withdraw, any information about you and your interview transcript will be deleted. Please note that if we have already disseminated the overall findings (in the thesis or published article) before your withdrawal, it will not be possible to delete your information, such as quotes.

6. What will happen to me if I take part?

- You will have a one-to-one meeting with the researcher (Muzeyyen Seckin).
- We can have a physical meeting (face-to-face meeting) and/or we can use any online communication software (FaceTime, Skype, and Zoom); or telephone call; or email option.
- The time of the meeting will depend on your preference and schedule. We will discuss this via email or telephone. This interview meeting will do around your schedule and at a time and place that is convenient for you.
- This interview will be no more than one hour on the date provided by you.
- Sociodemographic questions (including your age, duration of heart failure and symptoms you are experiencing) will be asked verbally at the interview.
- It is an opportunity for you to share your thoughts, feeling and ideas related to heart failure.
- You will not have anything to prepare, you just need to be willing to talk during the interview with the researcher.
- There are no right or wrong answers for us. We would like to learn your thoughts and experiences related to breathlessness in heart failure.
- The interview will be voice-recorded. However, your personal information will not be made public.
- Our meetings notes/data will be used for developing a person-led care intervention.
- Your personal information will be kept anonymous.

7. What do I have to do?

If you decide to take part, you will be asked to contact Muzeyyen Seckin via phone or email. We will ask you to (a) provide some basic demographic information about yourself and (b) have an up to 1-hour chat with the researcher (Muzeyyen Seckin) about your life experiences related to heart failure. You can change your mind at any time.

What are the possible disadvantages of taking part?

There is not any direct disadvantage or risk of taking part in this study. We understand that your time is valuable, and we acknowledge that participating may reduce your free time. There is no personal risk to taking part as the interview will be kept private and you will not be identifiable. You will only be identifiable to the research team and study organisers. We do not expect you to feel stressed during and after the interview. However, we will present a list of mental health support organizations for you. If you need any psychological support, you can contact them.

8. What are the possible benefits of taking part?

There are no direct benefits for you. However, the main benefit of taking part in this study is that your thoughts about your conditions and health outcomes are valuable to help develop more relevant and convenient care for people living with heart failure and their family members in the future. This will help us to make this research more relevant to patients, carers, and professionals.

Will my taking part in this study be kept confidential?

You will meet with only one researcher, Muzeyyen Seckin. All information that we collected about you and your responses will be kept anonymous and confidential. Only the researcher and her supervisors. And study orginiser (University of Glasgow) will be able to access the original information. You will be identified by a code number and any information about you will have your name and contact details removed. You will not be identifiable on any reports and publications. You can rest assured that the audio recordings will be stored securely and used only for this research. Audio recordings will be destroyed after the work is completed. Your information will be stored on a password-protected computer. Any information in paper form will be stored in a locked cabinet within a restricted access office at the University of Glasgow. No one other than the research team can learn your name or other personally identifiable information. Please note that confidentiality will be strictly adhered to as long as no risk or evidence of serious harm is discovered. In such cases, the University may have to apply to the relevant legal institutions.

9. What will happen to my data?

The researcher will type up the transcripts of the audio-recorded interview in Turkish and translate them into English. This means that they will be made into a complete document of what was said by you in the interview. This document will be analysed by the research team, who will prepare a report on the themes related to the interview findings. Results will be published in scientific journals, presentations, and student dissertations (if applicable). None of these publications will contain any information that can identify you

Information will be retained in archiving facilities in accordance with Glasgow University retention policy of up to 10 years. After this period, further storage can be agreed, or your data will be securely destroyed by the relevant standard procedures. Researchers from the University of Glasgow collect, store, and process all personal information in collaboration with the Data Management Team and in accordance with the General Data Protection Regulation (May 2018). The audio recordings will be stored securely and used only for this research. Audio recordings will be destroyed after the work is completed. Other researchers may access anonymous data only if they have scientific and ethical approval (with the permission of the researcher team) and agree to maintain the confidentiality of this information as stated in this form.

10. What will happen to the results of the research study?

The overall results of the study will be written up as a part of Muzeyyen Seckin's thesis for the requirements for the degree of Doctor of Philosophy (PhD) in Nursing at the University of Glasgow. It is expected that the study will be written up and submitted for publication in a relevant research journal between 2022 and 2024. Although we may quote you in these reports, your details will not be identified in the written or published materials.

11. Who is organising and funding the research?

I am **Muzeyyen Seckin** (PhD Student), responsible for organising this PhD project. I am an international doctoral student from Turkey. I am doing my PhD at the University of Glasgow, Scotland, UK. I completed my nursing bachelor's degree in my home country (Turkey), and I also have a master's degree in clinical nursing from Kings' College London. I have support and guidance from three supervisors.

Professor Bridget Johnston, University of Glasgow, School of Medicine, Dentistry & Nursing (Scotland, UK). She is a principal researcher and primary supervisor of Muzeyyen Seckin (PGR). She is a Clinical Professor of Nursing and Palliative Care at the University of Glasgow. In her current clinical role, she has a role with NHS Greater Glasgow and Clyde as Chief Nurse Research

Professor Mark Petrie, University of Glasgow, Institute of Cardiovascular & Medical Sciences (Scotland, UK). He is a PhD supervisor of Muzeyyen Seckin (PGR). He is a Clinical Professor of Cardiology and Consultant cardiologist within NHS Greater Glasgow and Clyde and the Institute of Cardiovascular & Medical Sciences at the University of Glasgow.

Professor Simon Stewart, NHMRC of Australia Senior Principal Research Fellow, Torrens University, Adelaide Australia is one of the PhD supervisors of Muzeyyen Seckin (PGR). He is also an Honorary Professor of Nursing at the University of Glasgow (Scotland, UK).

This project is not a funded research project.

12. Who has reviewed the study?

This project has been reviewed by the University of Glasgow College of Medical, Veterinary & Life Sciences Ethics Committee (Scotland, UK) and Kahramanmaraş Sütçü Imam University Ethics Committee (Turkey).

13. Contact for further information

Muzeyyen Seckin (PhD Nursing)
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Twitter: @SeckinMuzeyyen
Mobile:
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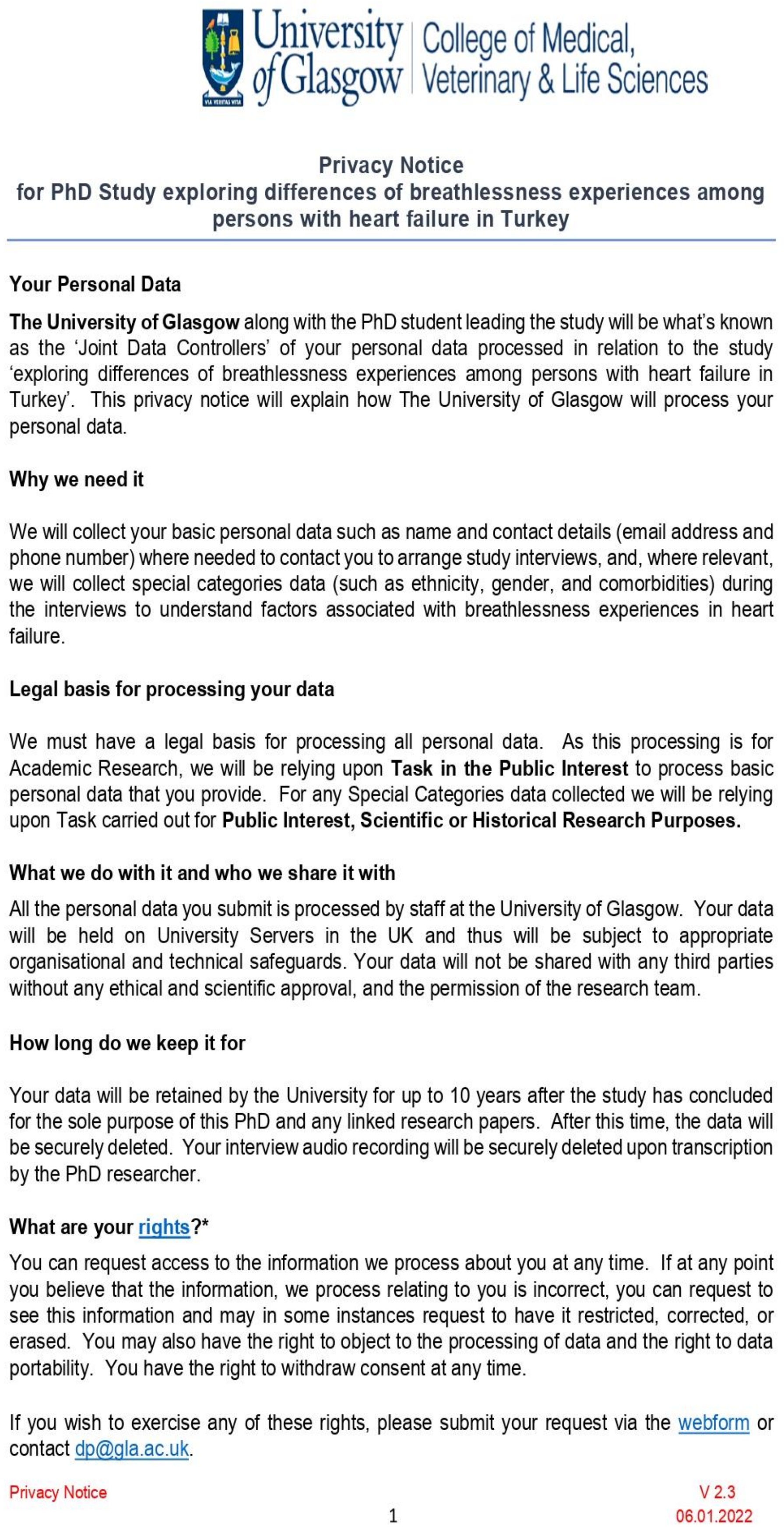
University of Glasgow, Scotland, UK

Professor Bridget Johnston (Principal supervisor)
Email: Bridget.Johnston@glasgow.ac.uk
Professor Mark Petrie (2. supervisor)
Email: Mark.Petrie@glasgow.ac.uk
Professor Simon Stewart (3. Supervisor)
Email: simon.stewart@Torrens.edu.au

Thank you for taking the time to read this Participant Information Sheet.
Please do not hesitate to contact us if you require any further information.

Privacy Notice



University of Glasgow | College of Medical, Veterinary & Life Sciences

Privacy Notice
for PhD Study exploring differences of breathlessness experiences among persons with heart failure in Turkey

Your Personal Data

The University of Glasgow along with the PhD student leading the study will be what's known as the 'Joint Data Controllers' of your personal data processed in relation to the study 'exploring differences of breathlessness experiences among persons with heart failure in Turkey'. This privacy notice will explain how The University of Glasgow will process your personal data.

Why we need it

We will collect your basic personal data such as name and contact details (email address and phone number) where needed to contact you to arrange study interviews, and, where relevant, we will collect special categories data (such as ethnicity, gender, and comorbidities) during the interviews to understand factors associated with breathlessness experiences in heart failure.

Legal basis for processing your data

We must have a legal basis for processing all personal data. As this processing is for Academic Research, we will be relying upon **Task in the Public Interest** to process basic personal data that you provide. For any Special Categories data collected we will be relying upon Task carried out for **Public Interest, Scientific or Historical Research Purposes.**

What we do with it and who we share it with

All the personal data you submit is processed by staff at the University of Glasgow. Your data will be held on University Servers in the UK and thus will be subject to appropriate organisational and technical safeguards. Your data will not be shared with any third parties without any ethical and scientific approval, and the permission of the research team.

How long do we keep it for

Your data will be retained by the University for up to 10 years after the study has concluded for the sole purpose of this PhD and any linked research papers. After this time, the data will be securely deleted. Your interview audio recording will be securely deleted upon transcription by the PhD researcher.

What are your rights?*

You can request access to the information we process about you at any time. If at any point you believe that the information, we process relating to you is incorrect, you can request to see this information and may in some instances request to have it restricted, corrected, or erased. You may also have the right to object to the processing of data and the right to data portability. You have the right to withdraw consent at any time.

If you wish to exercise any of these rights, please submit your request via the webform or contact dp@gla.ac.uk.

*Please note that the ability to exercise these rights will vary and depend on the legal basis on which the processing is being carried out.

Complaints

If you wish to raise a complaint on how we have handled your personal data, you can contact the University Data Protection Officer who will investigate the matter.

Our Data Protection Officer can be contacted at dataprotectionofficer@glasgow.ac.uk

If you are not satisfied with our response or believe we are not processing your personal data in accordance with the law, you can complain to the Information Commissioner's Office (ICO) https://ico.org.uk/

Please note this was translated into Turkish

Consent Form

University of Glasgow | College of Medical, Veterinary & Life Sciences

Centre Number:

Project Number:

Participant Identification Number for this trial:

Title of Project: Persons experiences of breathlessness in heart failure (in Turkey): a qualitative study

Name of Researcher(s): Muzeyyen Seckin
Professor Bridget Johnston
Professor Simon Stewart
Professor Mark Petrie

CONSENT FORM

	Please initial box
I confirm that I have read and understood the Participant Information Sheet version 3.1 dated 02/02/2022.	☐
I confirm that I have read and understood the Privacy Notice version 2.3 dated 06/01/2022.	☐
I have had the opportunity to think about the information and ask questions, and understand the answers I have been given.	☐
I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected.	☐
I confirm that I agree to the way my data will be collected and processed and that data will be stored for up to 10 years in University archiving facilities in accordance with relevant Data Protection policies and regulations.	☐
I understand that all data and information I provide will be kept confidential and will be seen only by study researchers and regulators whose job it is to check the work of researchers.	☐
I agree that my name, contact details and data described in the information sheet will be kept for the purposes of this research project.	☐
I understand that if I withdraw from the study, my data collected up to that point will be deleted and not used for the remainder of the study.	☐
I agree to take part in the study.	☐
I agree to my interview being audio-recorded.	☐

I understand that the recorded interview will be transcribed word by word and the transcription stored for up to 10 years in University archiving facilities in accordance with Data Protection policies and regulations. ☐

I understand that my information and things that I say in an interview may be quoted in reports and articles that are published about the study, but my name or anything else that could tell people who I am will not be revealed. ☐

I agree for the data I provide to be anonymously archived in the UK data archive or other approved archiving facilities, and that other researchers can have access to this data only if they have scientific and ethical approval, and agree to preserve the confidentiality of this information as set out in this form. ☐

I agree that should significant concerns regarding my mental or physical health arise during my participation in the study that a member of an appropriate clinical team will be immediately informed. ☐

Name of participant	Date	Signature
Name of Person taking consent (if different from researcher)	Date	Signature
Researcher	Date	Signature

(1 copy for participant; 1 copy for researcher)

Please note this was translated into Turkish

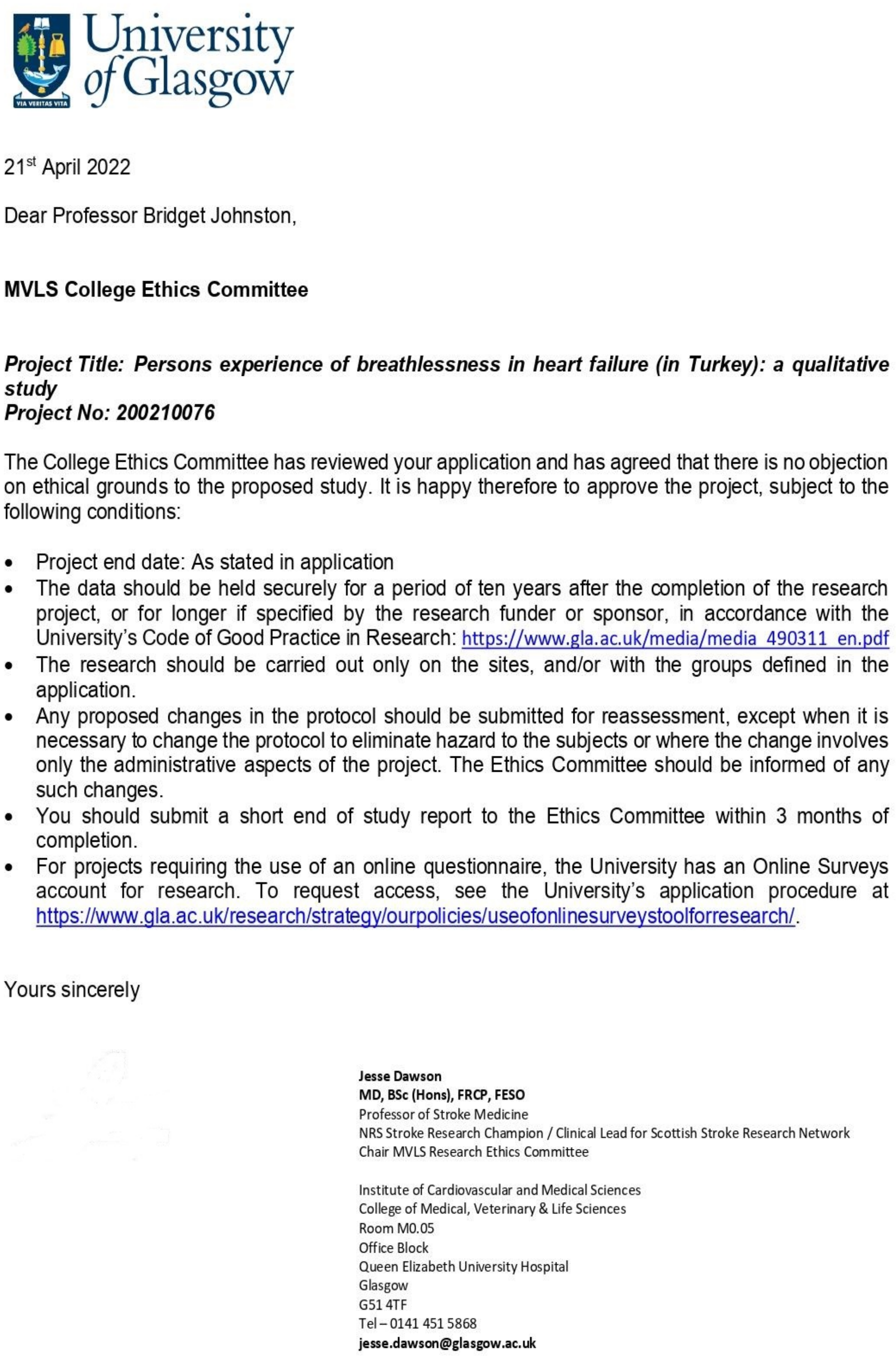
Appendix 7: Socio-demographic and semi-structured interview questions

Sociodemographic questions		
What is your age? (In year at next birthday)		
How long have you had heart failure? (In years)		
Do you have another disease apart from heart failure?	☐ Yes (written in); ___________________________ ☐ No	
Have you had recent hospital admission due to heart failure (last 12 months)?	☐ Yes (How many times);______________________ ☐ No	
Does anyone else in your family have heart failure?	☐ Yes (Whom? ____________________) ☐ No	
What is your relationship status?	☐ Single ☐ Married	☐ Widowed ☐ In a relationship
Do you have any children?	☐ Yes (How many children do you have?__________) ☐ No	
How do you describe your ethnicity?	☐ White Turkish ☐ White others ☐ Asian ☐ Mixed ethnic group	☐ Kurdish ☐ Black African ☐ Arabian ☐ Any other ethnic group
What is your highest educational qualification?	☐ Primary school ☐ Secondary school ☐ College degree/diploma	☐ University degree ☐ Postgraduate degree ☐ Others (written in) ____
Are you currently working?	☐ Employed full-time ☐ Employed part-time ☐ Home duties ☐ Unemployed	☐ Retired ☐ Unable to work ☐ Student ☐ Others (written in) ____
Breathlessness	☐Whole day ☐At night	☐During exercise

No	Interview Questions
1.	Could you please tell me about your heart failure; what is that like for you?
2.	Please tell me about a typical day of you in terms of feeling breathlessness?
3.	How has the breathlessness you described affected your everyday life?
4.	What coping mechanisms or strategies do you use to deal with your breathlessness?
5.	Do you think you get enough education to manage your breathlessness from your doctors/nurses/other healthcare professionals?

Appendix 8: Ethics approval from University of Glasgow and Kahramanmaraş Sütçü Imam University

Ethics approval from MVLS College Ethics Committee (University of Glasgow) (UK)



21st April 2022

Dear Professor Bridget Johnston,

MVLS College Ethics Committee

Project Title: Persons experience of breathlessness in heart failure (in Turkey): a qualitative study
Project No: 200210076

The College Ethics Committee has reviewed your application and has agreed that there is no objection on ethical grounds to the proposed study. It is happy therefore to approve the project, subject to the following conditions:

- Project end date: As stated in application
- The data should be held securely for a period of ten years after the completion of the research project, or for longer if specified by the research funder or sponsor, in accordance with the University's Code of Good Practice in Research: https://www.gla.ac.uk/media/media_490311_en.pdf
- The research should be carried out only on the sites, and/or with the groups defined in the application.
- Any proposed changes in the protocol should be submitted for reassessment, except when it is necessary to change the protocol to eliminate hazard to the subjects or where the change involves only the administrative aspects of the project. The Ethics Committee should be informed of any such changes.
- You should submit a short end of study report to the Ethics Committee within 3 months of completion.
- For projects requiring the use of an online questionnaire, the University has an Online Surveys account for research. To request access, see the University's application procedure at https://www.gla.ac.uk/research/strategy/ourpolicies/useofonlinesurveystoolforresearch/.

Yours sincerely

Jesse Dawson
MD, BSc (Hons), FRCP, FESO
Professor of Stroke Medicine
NRS Stroke Research Champion / Clinical Lead for Scottish Stroke Research Network
Chair MVLS Research Ethics Committee

Institute of Cardiovascular and Medical Sciences
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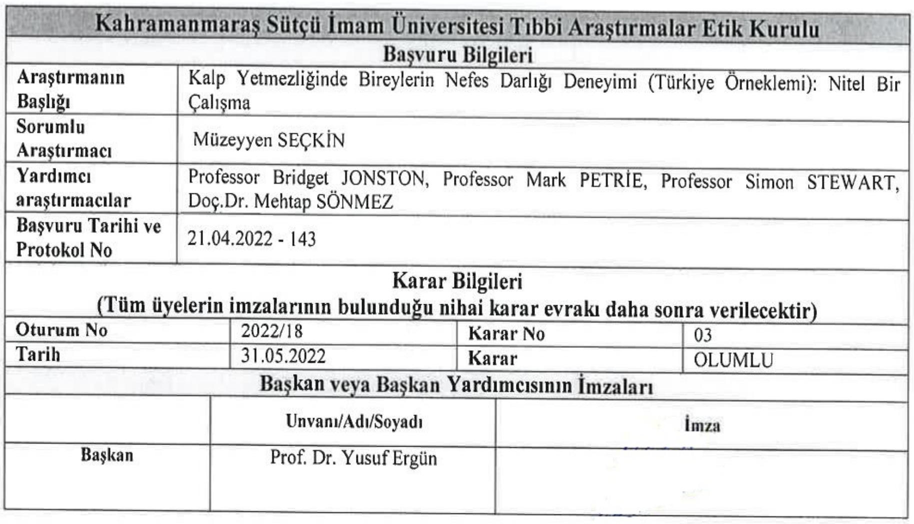
Kahramanmaraş Sütçü Imam University Ethics Committee (Türkiye)



Kahramanmaraş Sütçü İmam Üniversitesi Tıbbi Araştırmalar Etik Kurulu

Başvuru Bilgileri

Araştırmanın Başlığı	Kalp Yetmezliğinde Bireylerin Nefes Darlığı Deneyimi (Türkiye Örneklemi): Nitel Bir Çalışma
Sorumlu Araştırmacı	Müzeyyen SEÇKİN
Yardımcı araştırmacılar	Professor Bridget JONSTON, Professor Mark PETRİE, Professor Simon STEWART, Doç.Dr. Mehtap SÖNMEZ
Başvuru Tarihi ve Protokol No	21.04.2022 - 143

Karar Bilgileri

(Tüm üyelerin imzalarının bulunduğu nihai karar evrakı daha sonra verilecektir)

Oturum No	2022/18	**Karar No**	03
Tarih	31.05.2022	**Karar**	OLUMLU

Başkan veya Başkan Yardımcısının İmzaları

	Unvanı/Adı/Soyadı	**İmza**
Başkan	Prof. Dr. Yusuf Ergün	

Appendix 9: Publication in EJCN (Chapter six -secondary data analysis)

ESC
European Society
of Cardiology

European Journal of Cardiovascular Nursing (2022) **00**, 1–11
https://doi.org/10.1093/eurjcn/zvac099

ORIGINAL RESEARCH

Characteristics of symptoms and symptom change across different heart failure subtypes: a sex-stratified analysis

Muzeyyen Seckin [1], Bridget Johnston [1,2], Mark C Petrie [2,3], Simon Stewart [1,4], and Yih-Kai Chan [5]*

[1]School of Medicine, Dentistry & Nursing, University of Glasgow, 57-61 Oakfield Avenue, Glasgow, G12 8LL, UK; [2]NHS Greater Glasgow and Clyde, 1055 Great Western Rd, Glasgow, G12 0XH, UK; [3]School of Cardiovascular & Metabolic Health, University of Glasgow, 126 University Place, Glasgow, G12 8TA, UK; [4]Institute of Health Research, Notre Dame University of Australia, 32 Mouat St, Fremantle, WA 6160, Australia; and [5]Mary MacKillop Institute for Health Research, Australia Catholic University, 215 Spring Street, Melbourne, VIC 3000, Australia

Received 22 May 2022; revised 13 October 2022; accepted 20 October 2022; published 27 October 2022

Aims To examine sex-stratified differences in the association of left ventricular ejection fraction-based heart failure (HF) subtypes and the characteristics and correlates of self-reported changes in HF symptoms.

Methods and results We report a secondary data analysis from 528 hospitalized individuals diagnosed with HF characterised by a reduced, mildly reduced, or preserved ejection fraction [HF with reduced ejection fraction (HFrEF), HF with mildly reduced ejection fraction (HFmrEF), or HF with preserved ejection fraction (HFpEF)] who completed 12-month follow-up within a multicentre disease management trial. There were 302 men (71.1 ± 11.9 years, 58% with HFrEF) and 226 women (77.1 ± 10.6 years, 49% with HFpEF). The characteristics of self-reported symptoms measured by the Kansas City Cardiomyopathy Questionnaire (KCCQ) at baseline and 12-month were analysed. At baseline, shortness of breath and fatigue predominated; with key differences according to HF subtypes in bilateral ankle oedema (both sexes), walking problems (women) and depressive symptoms (men). At 12-month follow-up, most KCCQ scores had not significantly changed. However, 25% of individuals reported worse symptom. In women, those with HFpEF had worse symptoms than those with HFmrEF/HFrEF ($P = 0.025$). On an adjusted basis, women [odds ratios (OR): 1.78, 95% confidence interval (CI): 1.00–3.16 vs. men], those with coronary artery disease (OR: 2.01, 95% CI: 1.21–3.31) and baseline acute pulmonary oedema (OR: 1.67, 95% CI: 1.02–2.75) were most likely to report worsening symptoms. Among men, worsening symptoms correlated with a history of hypertension (OR: 2.16, 95% CI: 1.07–4.35) and a non-English-speaking background (OR: 2.30, 95% CI: 1.02–5.20).

Conclusion We found significant heterogeneity (with potential clinical implications) in the symptomatic characteristics and subsequent symptom trajectory according to the sex and HF subtype of those hospitalized with the syndrome.

Trial Registration ANZCTR12613000921785

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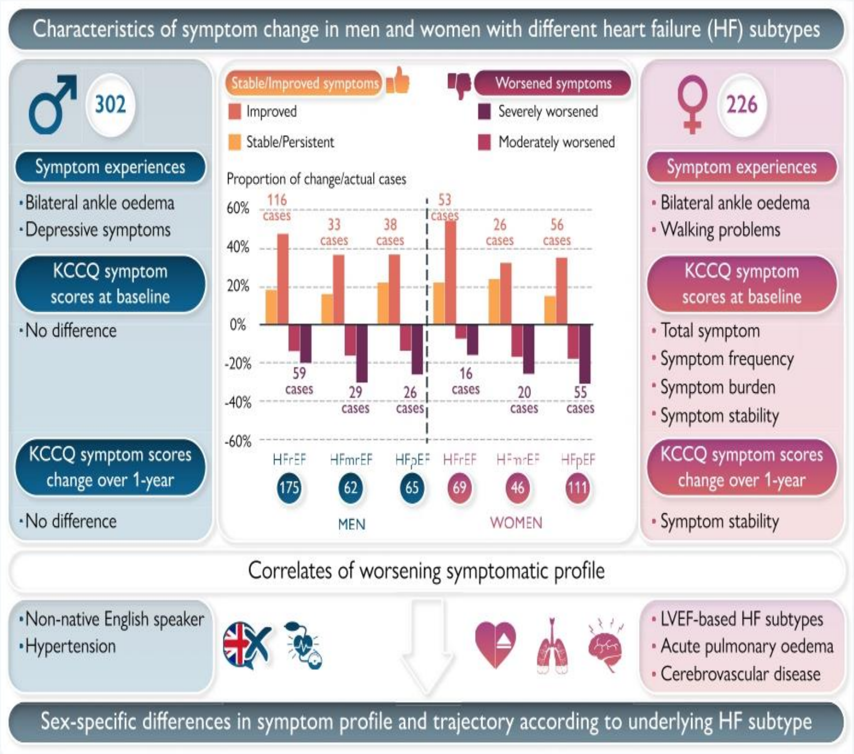
* Corresponding author. Email: YihKai.Chan@acu.edu.au

Graphical Abstract



Keywords Heart failure • Symptom • Sex • Left ventricular ejection fraction • Secondary data analysis

Novelty

- There are potentially important differences in the initial characteristics and post-hospitalisation trajectory of symptoms according to left ventricular ejection fraction (LVEF)-based heart failure (HF) subtypes in men and women.
- HF with preserved ejection fraction (HFpEF) was associated with worsening symptoms at 12 months in women.
- Women and men appear to have different baseline correlates for worsening HF symptoms associated with an acute hospitalisation.
- Individualized assessment and clinical care are needed to reduce potentially debilitating HF symptoms related to LVEF-based HF subtypes in both sexes.

Introduction

Heart failure (HF) is one of the most common diagnoses made in clinical practice, with increased prevalence and rising medical costs as a result of an ageing population and advances in medical treatment.[1] Consequently, HF is a leading cause of unplanned hospitalization among older individuals. Unplanned hospitalizations are one of the major components of its burden on the healthcare systems worldwide.[2] Clinically, a higher probability of hospital admission and death is linked to worsening symptoms.[3–5] People living with HF may experience a broad range of symptoms[1,6] that are often become severe, prolonged, and persistent[7] this combination being a marker of worsening progression of HF.[7] Thus, addressing worsening of symptoms represents an important therapeutic goals for targeted therapies in HF.[8,9]

The type and progression of symptoms may differ on an individual basis according to the underlying pathophysiology of their HF and left ventricular ejection fraction (LVEF). According to the recently updated European Society of Cardiology (ESC) guidelines,[1] HF can be categorized into three distinct phenotypes based on the measurement of LVEF. This includes HF with reduced ejection fraction (HFrEF–LVEF ≤40%); HF with mildly reduced ejection fraction (HFmrEF–LVEF 41–49%); and HF with preserved ejection fraction (HFpEF–LVEF ≥50%). Previous studies have found symptom differences across LVEF-based HF subtypes in some symptoms such as palpitation (HFpEF > HFmrEF),[10] peripheral oedema (HFpEF > HFrEF),[11] and pain (HFpEF > HFrEF).[12] Within the broad HF patient population, the sex-specific distribution of HF subtypes and associated symptoms are potentially different in men and women.[13–17] For example, in the primary care setting, it has been reported that 52% of women are managed for HFpEF and 41% of men for HFrEF (age group 65–79 years).[18] Although symptom characteristics appear to differ by sex and HF subtypes, sex-stratified differences in symptom characteristics and change according to HF subtypes remain under-investigated and reported—something this study seeks to address.

We have developed a research framework based on Riegel's 'The Situation-Specific Theory of Heart Failure Self-care',[19] which includes 'Symptom perception' as the core concept of self-care and is influenced by problem, person, and environmental factors. In this recent study, we have formed the related factors associated with symptoms characteristics and changes over one year (as problem factors) according to LVEF-based HF subtypes (as problem factors) in men and women (as person factors).

Given the paucity of data exploring this important issue, the primary aims of this study were (i) to examine differences in baseline characteristics by LVEF-based HF subtypes in men and women separately; (ii) to examine differences in baseline symptoms and symptom change between LVEF-based HF subtypes in men and women separately; and (iii) to identify factors associated with worsening symptoms in cohort, men and women separately.

Methods

This is a retrospective secondary data analysis of a previously published randomized controlled trial comparing two forms of nurse-led management in a real-world cohort of HF patients (the WHICH? II Trial-'the Which Heart failure Intervention is most Cost-effective in reducing Hospital stay').[20] The WHICH? II Trial had been prospectively registered at the Australian New Zealand Clinical Trial Registry (*ANZCTR12613000921785*).[20] Ethics approval of the WHICH? II Trial[20] was obtained from Central Northern Adelaide Health Service (*HREC/13/TQEHLMH/99*), Melbourne Health (*HREC 2013.145*), St Vincent's Hospital Sydney (*HREC/13/SVH/313*) and Prince of Wales Hospital, Sydney (*HREC/13/SVH/313*). For the present secondary analysis, an approval was obtained from the University of Glasgow Medical, Veterinary & Life Sciences College Ethics Committee (Project no:*200200145/13.07.2021)*. This investigation conforms with the principles outlined in the Declaration of Helsinki.[21] Written informed consent for participation was provided by all participants.

Study setting

The WHICH? II Trial,[20] was a multicentre, randomized controlled trial that tested the hypothesis that an intensified HF management programme (INT-HF-MP) would be superior to gold-standard HF management (SM) in reducing healthcare costs for 12 months following an acute hospitalization. Participants allocated to the INT-HF-MP group received a combination of face-to-face and structured telephone support (STS) based on their location and underwent a Green, Yellow, Red Risk and Need for HF (GARDIAN-HF) assessment.[22] As originally reported,[20] data were obtained from participants with chronic HF randomized to the 'INT-HF-MP' vs. 'SM' groups from four geographically dispersed hospitals in Australia by trained personnel applying a standardized study protocol of profiling and follow-up.

Study cohort

In the original trial,[20] 787 study participants met the following eligibility criteria: (i) aged ≥18 years, (ii) chronic HF as confirmed by a cardiologist with NYHA Class II-IV, and (iii) discharged to home following an acute index hospitalization. Majority (59%) were men aged 71.7 ± 12.0 years while women were significantly older (77.5 ± 10.7 years) (see Supplementary material online, *Table S1*). Overall, HFrEF and HFpEF were most common in men (59%) and women (49%), respectively. For our analyses, we excluded 259 participants (185/23.5% died and 74/9.4% did not return for reprofiling) who did not complete 12-month follow-up according to the study protocol (*Figure 1*). Consequently, comprehensive baseline and 12-month follow-up data were available for 528 participants.

Study data

As part of the WHICH? II Trial protocol,[20] baseline data collection included sociodemographic factors, symptoms (shortness of breath, fatigue, bilateral ankle oedema, nocturnal cough, paroxysmal nocturnal dyspnoea, sleeping problems due to orthopnoea, walking problems, and pain), depressive symptoms, and quality of life using standardized case report forms administered by trained personnel. At subsequent 12-month follow-up of surviving participants, the same profiling was repeated. Charlson Comorbidity Index score[23] was also calculated to reflect each participant's underlying comorbid burden of disease.

Outcomes and measures

As originally reported, there was no difference between the two study groups for any of the primary or secondary outcome measures at 12-month.[20] This included the pattern of readmission, mortality, and healthcare costs on an intention-to-treat basis. It also included responses to the Kansas City Cardiomyopathy Questionnaire (KCCQ), which used to measure self-reported HF symptoms and quality of life scores from baseline to 12-month.[24] The KCCQ is a 23-item questionnaire and includes the following domains: 'physical limitation'; 'symptoms' (total; frequency; burden and stability); 'self-efficacy and knowledge'; 'social limitation'; and 'quality of life'.[24] Values for all domains range from 0 to 100, with higher scores indicating lower symptom burden and better quality of life. The sensitivity, reproducibility, and validity of the KCCQ to clinical changes have been previously evaluated in subjects with HF.[24] A two-item ARROL tool was also used to measure depressive symptoms at baseline and 12-month,[25] whilst the EQ-5D-5L questionnaire was used to assess general quality of life of study participants over the same 12-month timeframe.[26]

Heart failure subtypes

As originally reported,[20] the WHICH? II Trial purposefully sought to recruit a real-world clinical cohort with a range of different HF subtypes and comorbid profiles (consequently increasing the potential to recruit more eligible women into the trial). For this secondary analysis study, we have grouped the study cohort according to the recently updated ESC criteria[1] for categorising HF cases according to their LVEF (assessed and confirmed by echocardiography prior to trial randomization)-HF with reduced ejection fraction (HFrEF–LVEF ≤40%); HF with mildly reduced ejection fraction (HFmrEF–LVEF 41–49%); and HF with preserved ejection fraction (HFpEF–LVEF ≥50%)[1] In our analyses, these three different HF subtypes are predominately described and compared on a sex-specific basis.

Worsened, stable, and improved symptoms

The KCCQ symptom stability score was used to determine the presence/absence of worsening symptoms at 12-month follow-up (compared with baseline). A lower symptom stability score indicates worsening symptoms, while a higher score indicates an improvement in self-reported symptoms.[24] Using these data, the study cohort's symptomatic status was categorized as follows, based on their baseline to 12-month KCCQ symptom stability score—(i) improved (positive score change = 26 to 100), (ii) stable/persistent (score unchanged = −25 to +25), or (iii) worsened (negative score change = −26 to −100 including −25 to −49, moderate and ≥ −50, severe).

Study endpoints

The primary endpoint was the change in self-reported symptom scores from baseline to 12-month as reflected by the participants' responses to the KCCQ (according to the three pre-specified groups outlined above), according to sex and their underlying three LVEF-based HF subtypes.

Statistical analysis

Summary statistics are presented as means (± standard deviation, SD) for normally distributed or median (interquartile range, IQR) for non-gaussian distributed continuous variables, and number of cases (percentages, %) for categorical variables. Baseline characteristics were compared among three LVEF groups in men and women separately using one-way ANOVA for continuous variables and chi-square (χ^2) tests for categorical variables. Chi-square (χ^2) test was also used to examine the differences of symptom presences in men and women according to LVEF-based HF subtypes at baseline. Repeated measures ANOVA was used to assess changes in KCCQ symptom scores between baseline and 12-month for men and

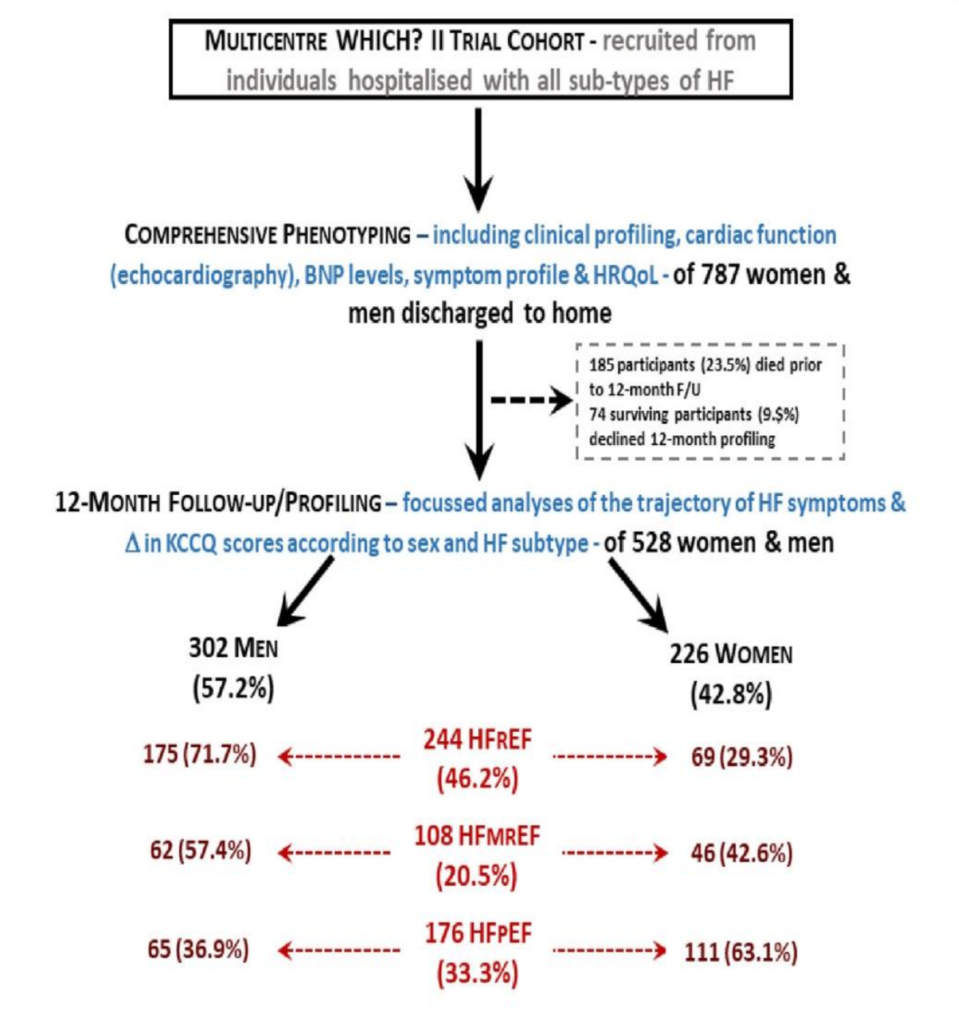


Figure 1 Study flow diagram. HF, heart failure; HFrEF, heart failure with reduced ejection fraction (LVEF ≤40%); HFmrEF, heart failure with mildly reduced ejection fraction (LVEF 41–49%); HFpEF, heart failure with preserved ejection fraction (LVEF ≥50%).

women separately. Binary logistic regression (entry model) was used to identify the independent correlates of a worsened symptomatic characteristic changes at 12-month (vs. those with stable or improved symptoms), with inclusion of all baseline variables associated with a univariate *P*-value <0.1 (from *Table 1* and Supplementary material online, *Table S1*) when comparing baseline differences across HF subtypes on a sex-specific basis. Three different multivariate models were constructed to derive adjusted odds ratios (OR) and 95% confidence interval (95% CI) for men and women combined (with the inclusion of sex in the model) and then separately for men and women. Statistical significance was accepted at a two-sided α of 0.05. All statistical analyses were performed using SPSS V25.0 (SPSS Inc, IBM).

Patient and public involvement

Patient and public involvement (PPI) were included in this study. To refine these study findings and make the research more relevant to patients, caregivers, and healthcare professionals, two volunteer advisors (one person with HF and one informal caregiver) were included. This involvement supported a more comprehensive person-centred care research from their own perspective in this study. The first author (M.S.) brought together and discussed the study findings to arrive at the final version.

Results

Study cohort

As shown in *Figure 1*, the underlying distribution of HF subtypes was significantly different among men and women. In men, 58% had HFrEF, while, in women, only 31% had HFrEF. In contrast, only 22% of men had HFpEF, while 49% of women had HFpEF.

Table 1 summarizes the baseline characteristics of men and women according to the three HF subtypes. Men with HFrEF were typically younger with a lower body mass index (BMI), were more likely to be employed and had less comorbidity including atrial fibrillation (AF), cerebrovascular disease, and a history of malignancy than men with HFmrEF/HFpEF. They also had less severe functional impairment according to their NYHA Class whilst recording a higher brain natriuretic peptide (BNP) level than those with HFmrEF and HFpEF ($P < 0.05$ for all comparisons). Women with HFpEF were significantly older, had a higher BMI, and were more likely to be married, from a non-English-speaking environment, and a history of hypertension, AF, and prior hospital episodes than women with HFrEF/HFmrEF.

Table 1 Baseline characteristics of men and women according to heart failure subtypes based on left ventricular ejection fraction

Variables		Men ($n = 302$)				Women ($n = 226$)			
		HFrEF ($n = 175$)	HFmrEF ($n = 62$)	HFpEF ($n = 65$)	*P*-value	HFrEF ($n = 69$)	HFmrEF ($n = 46$)	HFpEF ($n = 111$)	*P*-value
Sociodemographic characteristics									
Age, mean ± SD (years)		68.6 ± 12.4	74.3 ± 8.9	74.5 ± 11.6	<0.0001	74.4 ± 12.4	75.6 ± 10.3	79.5 ± 9.2	0.004
Living alone, *n*(%)		56 (32.0)	20 (32.3)	29 (44.6)	0.170	36 (52.2)	28 (60.9)	59 (53.2)	0.612
Married–living with partner, *n*(%)		107 (61.1)	39 (62.9)	35 (53.8)	0.467	18 (26.1)	14 (30.4)	40 (36.0)	0.044
European/Caucasian ethnicity, *n*(%)		157 (89.7)	57 (91.9)	61 (93.8)	0.831	63 (91.3)	44 (95.7)	108 (97.3)	0.530
<12 years education, *n*(%)		114 (65.2)	41 (66.1)	42 (64.6)	0.065	56 (81.2)	39 (61.4)	95 (85.6)	0.070
English not first language, *n*(%)		27 (15.4)	8 (12.9)	13 (20.0)	0.532	7 (10.1)	11 (23.9)	32 (28.8)	0.013
Retired, *n*(%)		127 (72.6)	54 (87.1)	56 (86.2)	0.014	58 (84.1)	42 (91.3)	103 (92.8)	0.158
Risk characteristics									
BMI, mean ± SD (kg/m^2)		29.1 ± 5.5	30.5 ± 5.5	31.6 ± 9.2	0.024	28.0 ± 5.8	31.5 ± 9.1	32.3 ± 8.4	0.002
>2.5 h physical activity, *n*(%)		82 (46.9)	27 (43.5)	22 (33.8)	0.195	20 (29.0)	12 (26.1)	18 (16.2)	0.130
Non-smoker, *n*(%)		43 (24.6)	19 (30.6)	20 (30.8)	0.150	28 (40.6)	19 (41.3)	79 (71.2)	<0.0001
Diabetes, *n*(%)		77 (44.0)	35 (56.5)	32 (49.2)	0.232	25 (36.2)	15 (32.6)	51 (45.9)	0.215
Hypertension, *n*(%)		119 (68.0)	50 (80.6)	48 (73.8)	0.151	49 (71.0)	36 (78.9)	98 (88.3)	0.014
Heart failure characteristics									
HF duration, *n*(%)	0–2 years	27 (15.4)	13 (21.0)	8 (12.3)	0.291	21 (30.4)	8 (17.4)	22 (19.8)	0.101
	2–5 years	100 (57.1)	37 (59.7)	45 (99.2)		31 (44.9)	26 (56.5)	71 (64.0)	
	≥5 years	48 (27.4)	12 (19.4)	12 (18.5)		17 (24.6)	12 (26.1)	18 (16.2)	
LVEF, mean ± SD (%)[a]		27.2 ± 6.6	43.1 ± 2.7	58.3 ± 5.9	<0.0001	30.2 ± 6.4	42.8 ± 2.3	58.29 ± 6.90	<0.0001
NYHA functional Class III/IV, *n*(%)		31 (17.7)	9 (14.5)	17 (26.2)	0.020	15 (21.7)	8 (17.4)	29 (26.1)	0.607
Elevated BNP, *n*(%)		95 (56.2)	22 (36.1)	22 (34.4)	0.002	39 (59.1)	17 (37.8)	37 (33.9)	0.004
Raised JVP, *n*(%)		78 (44.8)	29 (46.8)	40 (62.5)	0.050	32 (46.4)	25 (54.3)	49 (44.1)	0.504
Prior HF admission (12 months), *n*(%)		94 (53.7)	34 (54.8)	39 (60.0)	0.682	31 (44.9)	29 (63.0)	72 (64.9)	0.024
Clinical characteristics									
Acute pulmonary oedema, *n*(%)		40 (22.9)	17 (27.4)	20 (30.8)	0.424	22 (32.4)	16 (34.8)	49 (44.1)	0.242
Atrial fibrillation, *n*(%)		81 (46.3)	38 (61.3)	43 (66.2)	0.009	23 (33.3)	24 (52.2)	70 (63.1)	0.001
Sleep apnoea, *n*(%)		40 (22.9)	11 (17.7)	19 (29.2)	0.305	4 (5.8)	7 (15.2)	20 (18.0)	0.065
Heart rhythm disturbance, *n*(%)		46 (26.3)	18 (29.0)	11 (16.9)	0.227	6 (8.7)	4 (8.7)	11 (9.9)	0.952
Coronary artery disease, *n*(%)		119 (68.0)	41 (66.1)	37 (56.9)	0.274	40 (58.0)	30 (60.2)	45 (40.5)	0.007
Chronic pulmonary disease, *n*(%)		42 (24.0)	19 (30.6)	23 (35.4)	0.185	20 (29.0)	13 (28.3)	26 (23.4)	0.663
Cerebrovascular disease, *n*(%)		29 (16.6)	18 (29.0)	21 (32.3)	0.013	10 (14.5)	9 (19.6)	24 (21.6)	0.493
Cancer or tumour, *n*(%)		18 (10.3)	14 (22.6)	13 (20.0)	0.028	19 (27.5)	7 (15.2)	16 (14.4)	0.072
Charlson Comorbidity Score, mean ± SD		5.99 ± 2.30	7.19 ± 2.81	7.08 ± 2.16	<0.0001	6.80 ± 2.32	6.78 ± 2.10	7.15 ± 1.93	0.432
Poor sleeping quality, *n*(%)		56 (32.0)	14 (22.6)	20 (30.8)	0.170	19 (27.5)	20 (43.5)	39 (35.1)	0.132

Continued

Table 1 ***Continued***

Variables		Men ($n = 302$)				Women ($n = 226$)			
		HFrEF ($n = 175$)	HFmrEF ($n = 62$)	HFpEF ($n = 65$)	*P*-value	HFrEF ($n = 69$)	HFmrEF ($n = 46$)	HFpEF ($n = 111$)	*P*-value
KCCQ scores, mean ± SD	Total symptom score	49.0 ± 24.7	47.4 ± 25.5	43.7 ± 25.3	0.347	45.9 ± 23.6	43.3 ± 24.7	40.6 ± 23.6	0.018
	Symptom frequency	46.2 ± 25.5	45.6 ± 26.2	40.8 ± 26.7	0.349	45.2 ± 23.2	42.0 ± 26.54	35.0 ± 23.8	0.020
	Symptom burden	51.8 ± 26.5	49.1 ± 28.0	46.6 ± 27.0	0.395	46.6 ± 26.5	44.5 ± 26.0	37.3 ± 24.0	0.039
	Symptom stability	45.4 ± 37.3	53.2 ± 39.8	53.8 ± 38.5	0.190	39.8 ± 37.9	53.2 ± 36.3	55.8 ± 40.3	0.025
	Quality of life	38.7 ± 22.4	40.1 ± 22.6	43.8 ± 23.5	0.306	38.2 ± 25.1	35.3 ± 17.4	34.6 ± 20.4	0.529
EQ-5D-5L, mean ± SD	Quality of life	0.7 ± 0.1	0.7 ± 0.1	0.6 ± 0.2	0.672	0.7 ± 0.1	0.6 ± 0.1	0.6 ± 0.2	0.034

[a] $n = 178$ for women and $n = 279$ for men; HF, heart failure; BMI, body mass index; LVEF, left ventricular ejection fraction; HFrEF, heart failure with reduced ejection fraction (LVEF ≤40%); HFmrEF, heart failure with mildly reduced ejection fraction (LVEF 41–49%); HFpEF, heart failure with preserved ejection fraction (LVEF ≥50%); NYHA, New York Heart Association; BNP, b-type natriuretic peptide; elevated b-type natriuretic peptide (BNP) > 6000 pg/ml; JVP, jugular venous pressure; SD, standard deviation; KCCQ, Kansan City Cardiomyopathy Questionnaire; EQ-5D-5L scale, EuroQol 5-level 5-dimensional scale; Quality of life was assessed by KCCQ and EQ-5D-5L scales; depressive symptoms were calculated by a two-item ARROL tool. ANOVA for continuous variables and chi-square (X^2) tests for categorical variables were used for a comparison between men and women.

Women with HFpEF were also less likely to have a history of smoking, coronary artery disease, and recorded lower BNP levels than at least one of the other groups ($P < 0.05$ for all comparisons).

Symptom differences based on LVEF-based HF subtypes in men and women

We found women reported significant differences in KCCQ symptom (total, burden, frequency, and stability) scores and EQ-5D-5L quality of life scores ($P < 0.05$) according to HF subtypes but no significant differences in men (with minimal symptom differences across HF subtypes) (*Table 1*). At baseline, shortness of breath and fatigue were the most prominent symptoms in both sexes irrespective of HF subgroups (*Table 2*). However, bilateral ankle oedema was proportionally higher in those with HFpEF compared to HFmrEF/HFrEF in both sexes ($P = 0.019$ for men and $P < 0.0001$ for women). More women with HFpEF than HFrEF/HFmrEF reported walking problems ($P = 0.019$). Men with HFrEF experienced more depressive symptoms than those with HFmrEF/HFpEF ($P = 0.020$).

Symptom scores change based on LVEF-based HF subtypes in men and women

Overall, KCCQ total symptom, symptom frequency and symptom burden scores did not change significantly during the 12 months of follow-up in both sexes irrespective of their HF subtypes (*Table 3*). Only symptom stability score change was statistically significant in women only across the three HF subgroups ($P = 0.03$).

Worsened, stable, and improved symptoms

Within the HFrEF subgroup, 48% of men and 55% of women improved their symptoms, a further 18% of men and 22% of women reported no change during the 12 months period (*Table 4*). Approximately 47% of men with HFmrEF and 50% of women with HFpEF self-reported worsened symptoms. Overall, there were no statistical differences for worsened symptoms vs. improved/stable in men according to HF subtypes ($P = 0.518$). However, it was statistically significant in women (especially for women with HFpEF) ($P = 0.025$). Based on the sensitivity analysis, sex and LVEF-based HF subtypes did not significantly interact with baseline and 12-month KCCQ symptom scores—see Supplementary material online, *Table S2* for more descriptive data.

Correlates of worsening HF symptoms over 12-month

As shown in *Table 5*, we tested a broad range of baseline correlates associated with worsened HF symptoms in men and women. Irrespective of gender, coronary artery disease (OR: 2.01, 95% CI: 1.21–3.31) and hypertension (OR: 2.00, 95% CI: 1.16–3.45) significantly correlated with worsened HF symptoms. Women were more likely to report worsening symptoms during the 12-month follow-up than men (OR: 1.78, 95% CI: 1.00–3.16). The higher LVEF range and those with HFpEF were more likely to report worsened symptoms in women but not men. Moreover, these sex-specific differences extended to other baseline characters, with primary English-speaking status (OR: 2.30, 95% CI: 1.02–5.20) and the presence of hypertension (OR: 2.16, 95% CI: 1.07–4.35) in men not women vs. acute pulmonary oedema (OR: 0.30, 95% CI: 0.12–0.75) and cerebrovascular disease (OR: 0.25, 95% CI: 0.08–0.79) in women not men also associated with worsening symptoms.

Table 2 Baseline self-reported symptoms in men and women according to heart failure subtypes based on left ventricular ejection fraction

Symptoms	Men ($n = 302$)				Women ($n = 226$)			
	HFrEF ($n = 175$)	HFmrEF ($n = 62$)	HFpEF ($n = 65$)	*P*-value	HFrEF ($n = 69$)	HFmrEF ($n = 46$)	HFpEF ($n = 111$)	*P*-value
Shortness of breath, *n*(%)	159 (90.9)	59 (95.2)	60 (92.3)	0.558	66 (95.7)	43 (93.5)	107 (96.4)	0.720
Fatigue, *n*(%)	161 (92.0)	57 (91.9)	57 (87.7)	0.562	66 (95.7)	43 (93.5)	107 (96.4)	0.720
Bilateral ankle oedema, *n*(%)	97 (55.4)	38 (61.3)	49 (75.4)	0.019	36 (52.2)	32 (69.6)	96 (86.5)	<0.0001
Nocturnal cough, *n*(%)	73 (41.7)	24 (38.7)	22 (33.8)	0.537	30 (43.5)	16 (34.8)	43 (38.7)	0.634
Orthopnoea, *n*(%)	108 (61.7)	35 (56.5)	41 (63.1)	0.707	51 (73.9)	28 (60.9)	84 (75.7)	0.157
Paroxysmal nocturnal dyspnoea, *n*(%)	80 (45.7)	20 (32.3)	28 (43.1)	0.182	38 (55.1)	23(50.0)	53 (47.7)	0.632
Pain/discomfort, *n*(%)	75 (43.1)	24 (38.7)	26 (40.0)	0.807	27 (39.7)	23 (50.0)	51 (46.4)	0.518
Sleeping problems due to orthopnoea, *n*(%)	82 (46.9)	25 (40.3)	30 (46.2)	0.667	31 (44.9)	21 (45.7)	50 (45.0)	0.997
Walking problems, *n*(%)	91 (52.3)	35 (56.5)	44 (67.7)	0.102	43 (63.2)	32 (69.6)	90 (81.8)	0.019
Depressive symptoms, *n*(%)	121 (69.9)	36 (58.1)	33 (51.6)	0.020	48 (69.6)	32 (69.6)	73 (65.8)	0.830

HF, heart failure; LVEF, left ventricular ejection fraction; HFrEF, heart failure with reduced ejection fraction (LVEF ≤40%); HFmrEF, heart failure with mildly reduced ejection fraction (LVEF 41–49%); HFpEF, heart failure with preserved ejection fraction (LVEF ≥50%). The chi-square (χ^2) tests were used to compare the presence of symptoms in men and women separately.

Discussion

This study examined multifaceted factors associated with changes in symptoms in men and women living with different HF subtypes not typically examined in previously conducted studies. Subsequently, we report on three key findings relevant to the clinical management of those hospitalized with the syndrome. Firstly, we observed baseline differences across LVEF-based HF subtypes for men and women, Secondly, here were potentially important differences in the symptom experiences and trajectory of symptom change among women across all HF subtypes (especially for HFpEF). Thirdly, different baseline characteristics correlated with a worsening symptomatic change at 12 months across the entire cohort and for both sexes. Overall, without being definitive, these findings suggest potentially important sex-stratified and LVEF-based HF subtypes differences in the symptomatic characteristics and symptom trajectory of those admitted and then discharged from hospital with the syndrome.

Previous studies that examined sex-related differences within HF subtypes[15–17,27,28] or HF subtypes in cohorts[18] have reported inconsistent findings. However, the present study showed that there are some key baseline differences by LVEF-based HF subtypes stratified by sex. Several baseline characteristics, including age, BMI, NYHA classification, elevated BNP, atrial fibrillation, and presence of comorbidities were different in the LVEF-based HF subtypes stratified by sex. In the ESC Guidelines,[1] the medical management of HF differs by LVEF-based subtypes (noting that many elements and objective of multidisciplinary HF management/support remains the same). Building on the need for tailored treatment, our findings indicate that a combination of the sex and LVEF-based HF subtypes need to be considered when designing individualized treatment and follow-up/management strategies.

Reinforcing the above points, differences in symptom status at baseline were associated with LVEF-based HF subtypes in men and women separately. Also at baseline, KCCQ sub-category symptom scores were significantly different among women based on LVEF-based HF subtypes, and the presence of bilateral ankle oedema was significantly different across HF subtypes in both sexes. Walking problems were significantly different in women and depressive symptoms in men according to LVEF-based HF subtypes. In this study, these sex-stratified outcomes according to the three common HF phenotypes cannot be compared to any other studies due to the paucity of data available. Although there is a lack of information on how HF subtypes stratified by sex affect HF symptom status overall, some evidence has shown that sex and HF subtypes affect HF symptoms. Women with HFpEF have worse symptoms and lower quality of life than men with HFpEF.[13,14,17] Women also self-report worse KCCQ overall summary scores than men.[29] Men with HFrEF have higher median KCCQ total symptom, symptom frequency and symptom burden scores than women with HFrEF. This collectively suggests that men have less HF symptom burden than women.[15] Consequently, it is very likely that LVEF-based HF subtypes are associated with different symptom characteristics for women and men.

Based on symptom changes over one year, KCCQ sub-category symptom scores (except symptom stability score for women) did not change significantly according to LVEF-based HF subtypes irrespective of sex. Women with HFpEF were more likely to have worsening symptoms compared to women with HFrEF and HFmrEF. The majority of HF patients in the high-risk community were women with HFpEF, particularly those over 70 years of age.[18] Consistent with the findings reported in our study, women with HFpEF were older and had a longer-term severe worsened symptom than women with HFrEF/HFmrEF. Additionally, we found that women with HFpEF had higher comorbidity scores (according to Charlson Comorbidity Index). Comorbidities (but not the only explanation) are more common in patients with HFpEF, making diagnosis difficult in patients with this type of HF and non-specific HF symptoms (including shortness of breath and fluid retention such as chronic obstructive pulmonary disease).[1,18] Lastly, lower quality of life has also been shown to be associated with being a woman, geographical region, greater number of comorbidities, severe symptom burden in HFpEF.[29] In this present study, women with HFpEF had more comorbid conditions and worsening symptoms. In older patients with multimorbidity, symptoms of both men and women with HFpEF can be misclassified or overlooked because of inadequate assessment of this HF subtype in both in- and out-patient settings. This is important because current strategies to support women with HF may be misdirected by findings (such as symptoms, medications, self-care management etc.) generated from a minority of women living with HFrEF as opposed to those with a preserved EF.[18,28] Given the differences in the symptom characteristics and changes of HFpEF in women, there is heterogeneity among this patient population, which requires greater clinical attention for treatment and diagnosis.[18]

Table 3 Changes in KCCQ sub-category symptom scores from baseline according to heart failure subtypes based on left ventricular ejection fraction

	Men ($n = 302$)									
	HFrEF ($n = 175$)			HFmrEF ($n = 62$)			HFpEF ($n = 65$)			
	Baseline	12-month	Baseline to 12 months	Baseline	12-month	Baseline to 12 months	Baseline	12-month	Baseline to 12 months	*P*-value
Total symptom	49.0 ± 24.7	78.3 ± 21.4	29.3(24.8,33.7)	47.4 ± 25.5	76.8 ± 23.8	29.4(21.2, 7.6)	43.7 ± 25.3	72.9 ± 24.0	29.3(22.50,36.2)	1.000
Symptom stability	45.4 ± 37.3	52.2 ± 19.1	6.8(0.8,12.8)	53.2 ± 39.8	47.1 ± 16.3	−6.0(−16.2,4.1)	53.8 ± 38.5	52.3 ± 18.2	−1.9(−12.1 8.2)	0.062
Symptom frequency	46.2 ± 25.5	76.2 ± 23.2	29.9(25.3,34.5)	45.6 ± 26.2	75.5 ± 23.9	29.8(21.4,38.3)	40.8 ± 26.7	69.7 ± 26.4	29.1(21.7,36.5)	0.934
Symptom burden	51.8 ± 26.5	80.5 ± 22.3	28.7(23.8,33.5)	49.1 ± 28.0	78.2 ± 25.3	29.0(20.3,37.7)	46.6 ± 27.0	76.0 ± 24.4	29.3(22.1,36.5)	0.990

	Women ($n = 226$)									
	HFrEF ($n = 69$)			HFmrEF ($n = 46$)			HFpEF ($n = 111$)			
	Baseline	12-month	Baseline to 12 Months	Baseline	12-month	Baseline to 12 Months	Baseline	12-month	Baseline to 12 Months	*P*-value
Total symptom	45.9 ± 23.6	76.0 ± 22.2	30.1(24.4,35.8)	43.3 ± 24.7	74.7 ± 23.2	31.4(21.7,41.1)	40.6 ± 23.6	69.5 ± 23.8	33.3(28.0,38.6)	0.749
Symptom stability	39.8 ± 37.9	48.9 ± 16.8	9.0(1.0,17.1)	53.2 ± 36.3	48.3 ± 20.6	−4.89(−17.5,7.7)	55.8 ± 40.3	48.8 ± 19.1	−6.9(−15.2,1.2)	0.033
Symptom frequency	45.2 ± 23.2	75.4 ± 22.3	30.2(24.3 36.1)	42.0 ± 26.5	74.1 ± 24.0	32.1(22.8,41.3)	35.0 ± 23.8	66.4 ± 25.3	31.3(25.4,37.2)	0.940
Symptom burden	46.6 ± 26.5	76.6 ± 24.2	30.0(23.4,36.7)	44.5 ± 26.0	75.3 ± 25.3	30.7(19.5,42.0)	37.3 ± 24.0	72.5 ± 25.6	35.2(29.6,40.9)	0.492

Symptom scores are presented as mean ± SD (standard deviation) at baseline and 12-month; changes in symptom scores from baseline to 12-month are presented as mean difference [95% confidence interval (CI) upper and lower]. HF, heart failure; LVEF, left ventricular ejection fraction; HFrEF, heart failure with reduced ejection fraction (LVEF ≤40%); HFmrEF, heart failure with mildly reduced ejection fraction (LVEF 41–49%); HFpEF, heart failure with preserved ejection fraction (LVEF ≥50%); KCCQ, Kansan City Cardiomyopathy Questionnaire. Repeated ANOVA was used to compare the symptom scores between baseline and 12-month in men and women separately.

Table 4 Baseline to 12-month symptoms change in men and women according to heart failure subtypes based on left ventricular ejection fraction

Symptoms change	Men ($n = 302$)			Women ($n = 226$)		
	HFrEF ($n = 175$)	HFmrEF ($n = 62$)	HFpEF ($n = 65$)	HFrEF ($n = 69$)	HFmrEF ($n = 46$)	HFpEF ($n = 111$)
Improving, *n*(%)	84 (48.0%)	23 (37.1%)	24 (37.5%)	38 (55.1%)	15 (32.6%)	39 (35.1%)
Persistent, *n*(%)	32 (18.3%)	10 (16.1%)	14 (21.9%)	15 (21.7%)	11 (23.9%)	17 (15.3%)
Moderate Worsening (25–49), *n*(%)	24 (13.7%)	10 (16.1%)	9 (14.1%)	5 (7.2%)	8 (17.4%)	20 (18.0%)
Severe Worsening (≥50), *n*(%)	35 (20.0%)	19 (30.6%)	17 (26.6%)	11 (15.9%)	12 (26.1%)	35 (31.5%)
		0.518			0.025	

Symptoms change is calculated by change in KCCQ symptom stability scores from baseline to 12-month. LVEF, left ventricular ejection fraction; HF, heart failure; HFrEF, heart failure with reduced ejection fraction (LVEF ≤40%); HFmrEF, heart failure with mildly reduced ejection fraction (LVEF 41–49%); HFpEF, heart failure with preserved ejection fraction (LVEF ≥50%); KCCQ, Kansan City Cardiomyopathy Questionnaire. The chi-square (χ^2) tests were used to compare the presence of stable/improved/worsened symptoms change between baseline and 12-month.

Correlates of worsening symptoms were different among the entire cohort as well as among men and women. At baseline, we found that HFpEF significantly predicted worsening symptoms at 12 months for the entire cohort and for women. In a previous study, there were significant differences in BNP level, HF symptoms (dyspnoea and fatigue), and pulmonary oedema presence between worsening HF groups and complicated and uncomplicated hospital groups.[4] Another study found that older age, increased LVEF, and higher BNP were independently related to the development of worsening HF among hospital inpatients.[30] Compared to our finding, this suggested that influencing factors of worsening HF progression can be different among different study cohorts. However, in our cohort, men and women also had different correlates of worsening HF symptoms. Therefore, factors influencing symptom changes in men and women in each cohort should be considered.

Early detection of worsening symptoms in out-patient settings could help improve long-term outcomes and reduce healthcare cost.[5,8,9] Post-hospital discharge, severe episodes of worsening HF may be prevented with prompt and targeted follow-up care (according to sex and HF subtypes). Due to a lack of research data reporting HFmrEF/HFpEF symptom profiles in men and women, we need be cautious in applying a homogenous maintenance and follow-up care (including telemonitoring tools) to manage individuals with different LVEF-based subtypes. If we can identify who, and at what point women and men with different HF phenotypes would need more care (pharmacological/device therapy), and with early detection of worsening symptomatic profile, then we can apply timely interventions to reduce severe episodes of worsening HF and the potential for unplanned admissions and even death.[31] At this stage, in out-patient settings, HF specialist nurses need to improve person-centred care (including patient education, treatment, symptom monitoring, and follow-up care) by identifying sex-specific predictors of long-term worsening symptomatic course to prevent disease progression. Addressing the subjective needs of men and women in their specific socio-cultural worldviews will support well-structured patient-centred care in HF.[32] Finally, assessment of symptoms should adapt to both sexes perspectives to reduce the risk of worsening symptomatic profile and improve quality of life. Further research is needed to understand sex differences that drive symptom changes and progressive worsening of HF.

Limitations

The study sample included older adults with HF, which limits the generalizability of its findings to the broader population. Although the original WHICH? II trial enrolled a nationally representative of women and men with chronic HF in Australia, not all participants were assessed at both time points, which may influence the sample representativeness. Our results also may not be generalisable due to inherent participant characteristic bias, such that most participants were in the NYHA Class II, mainly of European/Caucasian descent (>90%) and had high BMI. Also, participants may have under-reported their symptoms and quality of life because their activity level was limited, and their age was older which may influence their symptom experiences and quality of life. Self-reported symptom experiences and quality of life may be influenced by the contribution of the other cardiometabolic risk factors or concurrent comorbid conditions. In addition, we were blinded from the original intervention allocation during the secondary data analysis, hence we analysed the two groups together. This may have influenced the symptom score changes among the LVEF-based HF subgroups. Lastly, the definition of worsening symptoms was based on the change in KCCQ symptom stability score, and this score only includes the main symptoms (shortness of breath, swelling and fatigue). The KCCQ symptom stability score includes the last 2 weeks' evaluation of symptom changes, and this can be controversial in terms of time.

Conclusion

The current study showed that LVEF-based subtypes of HF were associated with different symptoms, symptom characteristics, and changes in men and women separately. Women with HFpEF were more likely to develop worsening symptoms over one year compared to women with HFrEF/HFmrEF. A better understanding of the differences in worsening symptoms of both sex-stratified and LVEF-based HF subtypes will help prevent the adverse outcomes of HF. Healthcare providers and researchers need to consider, develop, and then deliver tailored interventions and follow-up strategies to address a high underlying burden of severe and persistent symptoms in those hospitalized with the syndrome. Critically, the underlying LVEF-based HF subtype, sex, and likely factors influencing symptom changes of each affected individual need to be carefully considered.

Author contributions

S.S. conceived and designed the study, Y.K.C. prepared the study data for analyses; M.S. analysed the data and drafted the main body of the

Table 5 Correlates associated with worsening symptoms in the entire cohort, men, and women

Variables	Cohort						Men						Women					
	B	S.E.	Sig.	Exp(B)	95 CI for EXP(B)		B	S.E.	Sig.	Exp(B)	95 CI for EXP(B)		B	S.E.	Sig.	Exp(B)	95 CI for EXP(B)	
					Lower	Upper					Lower	Upper					Lower	Upper
Sex (women)	0.579	0.292	0.047	1.785	1.006	3.166												
Age	0.014	0.016	0.370	1.015	0.983	1.047	0.013	0.021	0.524	1.014	0.972	1.056	0.010	0.030	0.735	1.010	0.952	1.072
Living alone	−0.356	0.279	0.202	0.701	0.406	1.210	−0.224	0.379	0.554	0.799	0.380	1.679	−0.677	0.519	0.192	0.508	0.184	1.405
Married–living with partner	0.341	0.368	0.354	1.406	0.684	2.890	0.349	0.475	0.463	1.417	0.559	3.596	0.507	0.723	0.484	1.660	0.402	6.850
Education level	−0.001	0.287	0.998	0.999	0.569	1.755	0.106	0.391	0.786	1.112	0.516	2.395	−0.167	0.504	0.741	0.846	0.315	2.273
English not first language	0.590	0.317	0.063	1.804	0.969	3.359	0.836	0.416	0.044	2.307	1.021	5.209	0.054	0.629	0.932	1.055	0.308	3.619
Retired	0.198	0.358	0.580	1.219	0.604	2.461	0.291	0.422	0.490	1.338	0.585	3.057	−0.301	0.872	0.730	0.740	0.134	4.091
BMI	0.019	0.019	0.307	1.020	0.982	1.058	0.037	0.031	0.226	1.038	0.977	1.102	0.016	0.030	0.587	1.016	0.959	1.077
>2.5 h physical activity	−0.435	0.26	0.094	0.647	0.389	1.077	−0.200	0.329	0.542	0.818	0.430	1.559	−0.884	0.526	0.093	0.413	0.147	1.159
Smoking	−0.324	0.465	0.487	0.724	0.291	1.800	−0.307	0.553	0.578	0.735	0.249	2.175	−0.657	1.105	0.552	0.518	0.059	4.519
Diabetes	−0.187	0.28	0.505	0.830	0.479	1.437	−0.120	0.379	0.752	0.887	0.422	1.864	0.081	0.510	0.874	1.085	0.399	2.947
Hypertension	0.696	0.278	0.012	2.005	1.163	3.458	0.772	0.357	0.030	2.164	1.076	4.352	0.150	0.590	0.799	1.162	0.366	3.690
LVEF	−0.044	0.020	0.023	0.957	0.921	0.994	−0.043	0.027	0.107	0.958	0.908	1.009	−0.089	0.037	0.016	0.915	0.851	0.984
HFpEF	−1.352	0.658	0.040	0.259	0.071	0.940	−1.155	0.968	0.233	0.315	0.047	2.102	−2.407	1.149	0.036	0.090	0.009	0.856
NYHA	−0.134	0.296	0.651	0.875	0.489	1.564	−0.361	0.425	0.396	0.697	0.303	1.605	−0.042	0.543	0.938	0.959	0.331	2.781
Elevated BNP	0.451	0.243	0.064	1.569	0.974	2.528	0.477	0.324	0.141	1.612	0.854	3.043	0.715	0.448	0.110	2.044	0.850	4.916
Raised JVP	−0.053	0.229	0.818	0.949	0.605	1.486	−0.124	0.304	0.684	0.884	0.487	1.603	−0.322	0.444	0.469	0.725	0.304	1.731
Hospital admission	0.081	0.102	0.428	1.085	0.887	1.326	0.180	0.16	0.261	1.197	0.875	1.638	−0.077	0.185	0.678	0.926	0.644	1.331
APO	0.518	0.252	0.040	1.679	1.025	2.750	−0.426	0.357	0.233	0.653	0.324	1.315	−1.182	0.458	0.010	0.307	0.125	0.752
AF	0.100	0.232	0.668	1.105	0.701	1.741	0.081	0.299	0.786	1.085	0.603	1.950	0.032	0.442	0.941	1.033	0.434	2.457
Sleep apnoea	0.065	0.304	0.831	1.067	0.588	1.936	0.116	0.393	0.768	1.123	0.520	2.424	−0.279	0.629	0.657	0.757	0.221	2.594
Heart rhythm disturbance	0.532	0.301	0.078	1.702	0.943	3.072	0.419	0.353	0.236	1.521	0.761	3.040	1.123	0.713	0.115	3.073	0.760	12.424
Coronary artery disease	0.698	0.255	0.006	2.010	1.219	3.314	0.671	0.359	0.062	1.956	0.967	3.956	0.593	0.433	0.170	1.810	0.775	4.225
Cerebrovascular disease	−0.253	0.301	0.401	0.777	0.430	1.401	0.185	0.404	0.647	1.203	0.545	2.655	−1.351	0.569	0.018	0.259	0.085	0.791
Cancer or tumour	0.479	0.374	0.200	1.615	0.776	3.360	0.355	0.519	0.493	1.427	0.516	3.942	0.916	0.684	0.180	2.500	0.654	9.549
Adjusted Charlson Index	0.080	0.083	0.334	1.083	0.921	1.274	0.126	0.116	0.278	1.134	0.904	1.422	0.093	0.147	0.527	1.098	0.822	1.465
Depressive symptoms	0.156	0.245	0.525	1.168	0.723	1.887	0.145	0.326	0.656	1.156	0.611	2.188	0.683	0.475	0.150	1.981	0.780	5.028
EQ-5D-5L	0.104	0.097	0.286	1.109	0.917	1.343	0.244	0.130	0.061	1.276	0.989	1.645	−0.194	0.187	0.301	0.824	0.571	1.189

HF, heart failure; LVEF, left ventricular ejection fraction; HFrEF, heart failure with reduced ejection fraction (LVEF ≤40%); HFmrEF, heart failure with mildly reduced ejection fraction (LVEF 41–49%); HFpEF, heart failure with preserved ejection fraction (LVEF ≥50%); BNP, b-type natriuretic peptide; QoL, quality of life; b-type natriuretic peptide; elevated (BNP) > 6000 pg/ml; NYHA, New York Heart Association; BMI, body mass index; JVP, jugular venous pressure; AF, atrial fibrillation, APO, acute pulmonary oedema, KCCQ, Kansan City Cardiomyopathy Questionnaire; EQ-5D-5L scale, EuroQol 5-level 5-dimensional scale. Binary logistic (entry model) was used to identify the independent correlates of a worsened symptoms change in the cohort, men, and women separately.

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Supplementary material

Supplementary material is available at *European Journal of Cardiovascular Nursing* online.

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Data availability

Deidentified aggregated data that support the findings of this study are available from the corresponding author, upon reasonable request.

References

1. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, Burri H, Butler J, Čelutkienė J, Chioncel O, Cleland JGF, Coats AJS, Crespo-Leiro MG, Farmakis D, Gilard M, Heymans S, Hoes AW, Jaarsma T, Jankowska EA, Lainscak M, Lam CSP, Lyon AR, McMurray JJV, Mebazaa A, Mindham R, Muneretto C, Francesco Piepoli M, Price S, Rosano GMC, Ruschitzka F, Kathrine Skibelund A, ESC Scientific Document Group. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European society of cardiology (ESC) with the special contribution of the heart failure association (HFA) of the ESC. *Eur Heart J* 2021;**42**:3599–3726.
2. Giles L, Freeman C, Field P, Sörstadius E, Kartman B. Humanistic burden and economic impact of heart failure–a systematic review of the literature. *F1000Res* 2020;**8**:859.
3. Butler J, Gheorghiade M, Kelkar A, Fonarow GC, Anker S, Greene SJ, Papadimitriou L, Collins S, Ruschitzka F, Yancy CW. In-hospital worsening heart failure. *Eur J Heart Fail* 2015;**17**:1104–1113.
4. DeVore AD, Hammill BG, Sharma PP, Qualls LG, Mentz RJ, Waltman Johnson K, Fonarow GC, Curtis LH, Hernandez AF. In-hospital worsening heart failure and associations with mortality, readmission, and healthcare utilization. *J Am Heart Assoc* 2014;**3**:e001088.
5. Butler J, Djatche LM, Sawhney B, Chakladar S, Yang L, Brady JE, Yang M. Clinical and economic burden of chronic heart failure and reduced ejection fraction following a worsening heart failure event. *Adv Ther* 2020;**37**:4015–4032.
6. Alpert CM, Smith MA, Hummel SL, Hummel EK. Symptom burden in heart failure: assessment, impact on outcomes, and management. *Heart Fail Rev* 2017;**22**:25–39.
7. Heo S, Moser DK, Pressler SJ, Dunbar SB, Martin GM, Lennie TA. The psychometric properties of the symptom status questionnaire-heart failure. *J Cardiovasc Nurs* 2015;**30**:136.
8. Cooper LB, DeVore AD, Felker GM. The impact of worsening heart failure in the United States. *Heart Fail Clin* 2015;**11**:603–614.
9. Greene SJ, Mentz RJ, Felker GM. Outpatient worsening heart failure as a target for therapy. *JAMA Cardiol* 2018;**3**:252.
10. Özlek B, Özlek E, Ağuş HZ, Tekinalp M, Kahraman S, Çil C, Çelik O, Başaran Ö, Doğan V, Kaya BC. Patients with HFpEF and HFmrEF have different clinical characteristics in Turkey: a multicenter observational study. *Eur J Intern Med* 2019;**61**:88–95.
11. Edelmann F, Musial-Bright L, Gelbrich G, Trippel T, Radenovic S, Wachter R, Inkrot S, Loncar G, Tahirovic E, Celic V. Tolerability and feasibility of beta-blocker titration in HFpEF versus HFrEF: insights from the CIBIS-ELD trial. *JACC Heart Fail* 2016;**4**:140–149.
12. Shah AB, Udeoji DU, Baraghoush A, Bharadwaj P, Yennurajalingam S, Schwarz ER. An evaluation of the prevalence and severity of pain and other symptoms in acute decompensated heart failure. *J Palliat Med* 2013;**16**:87–90.
13. Lam CS, Arnott C, Beale AL, Chandramouli C, Hilfiker-Kleiner D, Kaye DM, Ky B, Santema BT, Sliwa K, Voors AA. Sex differences in heart failure. *Eur Heart J* 2019;**40**:3859–3868c.
14. Heo S, Shin MS, Hwang SY, An M, Park JK, Kim S, Shim JL, Kim J. Sex differences in heart failure symptoms and factors associated with heart failure symptoms. *J Cardiovasc Nurs* 2019;**34**:306–312.
15. Dewan P, Rørth R, Jhund PS, Shen L, Raparelli V, Petrie MC, Abraham WT, Desai AS, Dickstein K, Køber L. Differential impact of heart failure with reduced ejection fraction on men and women. *Je Am Coll Cardiol* 2019;**73**:29–40.
16. Stolfo D, Uijl A, Vedin O, Strömberg A, Faxén UL, Rosano GM, Sinagra G, Dahlström U, Savarese G. Sex-based differences in heart failure across the ejection fraction spectrum: phenotyping, and prognostic and therapeutic implications. *JACC Heart Fail* 2019;**7**:505–515.
17. Dewan P, Rørth R, Raparelli V, Campbell RT, Shen L, Jhund PS, Petrie MC, Anand IS, Carson PE, Desai AS. Sex-related differences in heart failure with preserved ejection fraction. *Circ Heart Fail* 2019;**12**:e006539.
18. de Boer AR, Vaartjes I, Gohar A, Valk MJ, Brugts JJ, Boonman-de Winter LJ, van Riet EE, van Mourik Y, Brunner-La Rocca H, Linssen GC. Heart failure with preserved, mid-range, and reduced ejection fraction across health care settings: an observational study. *ESC Heart Fail* 2022;**9**:363–372.
19. Riegel B, Dickson VV, Faulkner KM. The situation-specific theory of heart failure self-care: revised and updated. *J Cardiovasc Nurs* 2016;**31**:226–235.
20. Scuffham PA, Ball J, Horowitz JD, Wong C, Newton PJ, Macdonald P, McVeigh J, Rischbieth A, Emanuele N, Carrington MJ. Standard vs. Intensified management of heart failure to reduce healthcare costs: results of a multicentre, randomized controlled trial. *Eur Heart J* 2017;**38**:2340–2348.
21. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. 2013.
22. Carrington MJ, Kok S, Jansen K, Stewart S. The green, amber, red delineation of risk and need (GARDIAN) management system: a pragmatic approach to optimizing heart health from primary prevention to chronic disease management. *Eur J Cardiovasc Nurs* 2013;**12**:337–345.
23. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghali WA. New ICD-10 version of the charlson comorbidity index predicted in-hospital mortality. *J Clin Epidemiol* 2004;**57**:1288–1294.
24. Green CP, Porter CB, Bresnahan DR, Spertus JA. Development and evaluation of the Kansas city cardiomyopathy questionnaire: a new health status measure for heart failure. *J Am Coll Cardiol* 2000;**35**:1245–1255.
25. Arroll B, Khin N, Kerse N. Screening for depression in primary care with two verbally asked questions: cross sectional study. *BMJ* 2003;**327**:1144–1146.
26. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, Bonsel G, Badia X. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res* 2011;**20**:1727–1736.
27. Beale AL, Meyer P, Marwick TH, Lam CS, Kaye DM. Sex differences in cardiovascular pathophysiology: why women are overrepresented in heart failure with preserved ejection fraction. *Circulation* 2018;**138**:198–205.
28. Lainščak M, Milinković I, Polovina M, Crespo-Leiro MG, Lund LH, Anker SD, Laroche C, Ferrari R, Coats AJS, McDonagh T. Sex-and age-related differences in the management and outcomes of chronic heart failure: an analysis of patients from the ESC HFA EORP heart failure long-term registry. *Eur J Heart Fail* 2020;**22**:92–102.
29. Chandra A, Vaduganathan M, Lewis EF, Claggett BL, Rizkala AR, Wang W, Lefkowitz MP, Shi VC, Anand IS, Ge J. Health-related quality of life in heart failure with preserved ejection fraction: the PARAGON-HF trial. *JACC Heart Fail* 2019;**7**:862–874.
30. DeVore AD, Greiner MA, Sharma PP, Qualls LG, Schulte PJ, Cooper LB, Mentz RJ, Pang PS, Fonarow GC, Curtis LH. The ADHERE risk model for in-hospital worsening heart failure. *Circ Cardiovasc Qual Outcomes* 2015;**8**:A168.
31. Wierda E, Dickhoff C, Handoko ML, Oosterom L, Kok WE, de Rover Y, de Mol B, van Heerebeek L, Schroeder-Tanka JM. Outpatient treatment of worsening heart failure with intravenous and subcutaneous diuretics: a systematic review of the literature. *ESC Heart Fail* 2020;**7**:892–902.
32. Hill L, Prager Geller T, Baruah R, Beattie JM, Boyne J, de Stoutz N, Di Stolfo G, Lambrinou E, Skibelund AK, Uchmanowicz I. Integration of a palliative approach into heart failure care: a European society of cardiology heart failure association position paper. *Eur J Heart Fail* 2020;**22**:2327–2339.

Supplementary data of the publication

SUPPLEMENTARY MATERIALS:

Table S1 Baseline characteristics in men and women

Variables		Total (n=528)	Men (n=302)	Women (n=226)	Effect size	P-value
Sociodemographic profile						
Age, mean±SD (years)		73.05±11.98	70.88±12.03	76.60±11.06	0.065	**<0.0001**
Living alone, n(%)		228 (43.2)	105 (34.8)	123 (54.4)	0.196	**<0.0001**
Married-living with partner, n(%)		253 (47.9)	181 (59.9)	72 (31.9)	0.414	**<0.0001**
European/Caucasian ethnicity, n(%)		490 (92.8)	275 (91.1)	215 (95.1)	0.105	0.558
<12 years education, n(%)		454 (86.0)	253 (83.7)	201 (89.0)	0.252	**<0.0001**
English not first language, n(%)		98 (18.6)	48 (15.9)	50 (22.1)	0.079	0.068
Retired, n(%)		440 (83.3)	237 (78.5)	203 (89.8)	0.151	**<0.0001**
Risk profile						
BMI, mean±SD (kg/m^2)		30.00±6.66	29.51±5.62	30.81±8.03	0.004	0.145
>2.5-hour physical activity, n(%)		181 (34.3)	131 (22.1)	131 (43.4)	0.222	**<0.0001**
Non-smoker, n(%)		208 (39.4)	82 (27.2)	126 (55.8)	0.293	**<0.0001**
Diabetes, n(%)		235 (44.5)	144 (47.7)	91 (40.3)	0.074	0.090
Hypertension, n(%)		400 (75.8)	217 (71.9)	183 (81.0)	0.105	**0.016**
Heart failure profile						
HF duration, n(%)	0 to 2 years	224 (42.4)	118 (39.1)	106 (46.9)		
	2 to 5 years	163 (30.9)	98 (32.5)	65 (28.8)	0.079	0.195
	≥5 years	141 (26.7)	86 (28.5)	55 (24.3)		
LVEF, mean±SD (%)*		38.50±13.84	35.51±13.16	43.40±13.56	0.082	**<0.0001**
HF subtypes	HFrEF	**244 (46.2)**	**175 (57.9)**	**69 (30.5)**		
	HFmrEF	**108 (20.5)**	**62 (20.5)**	**46 (20.4)**	**0.309**	**<0.0001**
	HFpEF	**176 (33.3)**	**65 (21.5)**	**111 (49.1)**		
NYHA functional class III/IV, n(%)		109 (20.7)	57 (18.9)	52 (23.0)	0.058	0.623
Elevated BNP, n(%)		232 (45.1)	139 (47.3)	93 (42.3)	0.050	0.259
Raised JVP, n(%)		253 (48.1)	147 (49.0)	106 (46.9)	0.021	0.634
Prior HF admission (12 months), n(%)		299 (56.6)	167 (55.30	132 (58.4)	0.031	0.476
Clinical profile						
Acute pulmonary oedema, n(%)		164 (31.1)	77 (25.5)	87 (38.7)	0.141	**0.001**
Atrial fibrillation, n(%)		279 (52.8)	162 (53.9)	117 (51.8)	0.019	0.670
Sleep Apnoea, n(%)		101 (19.1)	70 (23.2)	31 (13.7)	0.119	**0.006**
Heart rhythm disturbance, n(%)		96 (18.2)	75 (24.8)	21 (9.3)	0.199	**<0.0001**
Coronary artery disease, n(%)		312 (59.1)	197 (65.2)	115 (50.9)	0.144	**0.001**
Chronic pulmonary disease, n(%)		143 (27.1)	84 (27.8)	59 (26.1)	0.019	0.662
Cerebrovascular disease, n(%)		111 (21.0)	68 (22.5)	43 (19.0)	0.042	0.330
Cancer or tumour, n(%)		87 (16.5)	45 (14.9)	42 (18.6)	0.049	0.259
Charlson Comorbidity Score, mean±SD		6.69±2.39	6.48±2.48	7.03±2.19	0.011	**0.014**
Poor sleeping quality, n(%)		168 (31.8)	90 (29.8)	78 (34.5)	0.063	0.723
Acute pulmonary oedema, n(%)		343 (65.3)	190 (63.5)	153 (67.7)	0.043	0.322
KCCQ scores, mean±SD	Total symptom	45.10±24.72	48.08±24.99	40.22±23.56	0.020	**0.001**
	Symptom frequency	43.01±25.60	45.35±26.01	39.18±24.50	0.011	**0.016**
	Symptom burden	47.19±26.62	50.81±26.76	41.26±25.38	0.025	**<0.0001**
	Symptom stability	45.71±38.29	46.27±37.99	44.79±38.87	0.000	0.638
	Quality of life	38.09±22.63	40.18±23.10	34.67±21.47	0.009	**0.029**
EQ-5D-5L, mean±SD		0.68±0.20	0.71±0.19	0.64±0.20	0.030	**<0.0001**

Legend Quality of life was assessed by KCCQ and EQ-5D-5L scales; depressive symptoms were calculated by a two-item ARROL tool; *n=178 for women and n=279 for men; HF, heart failure; BMI, Body mass index; LVEF, left ventricular ejection fraction; *HFrEF,Heart failure with reduced ejection fraction (LVEF ≤40%);HFmrEF, Heart failure with mildly-reduced ejection fraction (LVEF 41-49%); HFpEF, Heart failure with preserved ejection fraction (LVEF ≥50%);* NYHA, New York Heart Association; BNP, b-type natriuretic peptide; elevated b-type natriuretic peptide (BNP) >6000pg/ml; JVP, jugular venous pressure; KCCQ, Kansan City Cardiomyopathy Questionnaire; EQ-5D-5L scale, EuroQol 5-level 5-dimensional scale; SD: standard deviation. *ANOVA for continuous variables and chi-square (X^2) tests for categorical variables were used for a comparison between men and women.*

Table S2 Interaction analysis of sex and LVEF-based HF subtypes in KCCQ symptom scores at baseline and 12-month

	Variables		F statistic	p-values	Partial eta squared	Adjusted R squared
At Baseline	Total symptom	*Sex*	4.500	**0.034**	0.009	0.028
		LVEF-based HF subtypes	4.382	**0.013**	0.017	
		*Sex*LVEF-based HF subtypes*	0.387	0.679	0.001	
	Symptom burden	*Sex*	6.511	**0.011**	0.012	0.031
		LVEF-based HF subtypes	3.475	**0.032**	0.013	
		*Sex*LVEF-based HF subtypes*	0.367	0.693	0.001	
	Symptom frequency	*Sex*	2.071	0.151	0.004	0.020
		LVEF-based HF subtypes	4.421	**0.012**	0.017	
		*Sex*LVEF-based HF subtypes*	0.395	0.674	0.002	
	Symptom stability	*Sex*	0.102	0.749	0.000	0.012
		LVEF-based HF subtypes	5.238	**0.006**	0.020	
		*Sex*LVEF-based HF subtypes*	0.469	0.626	0.002	
At 12-month follow-up	Total symptom	*Sex*	0.487	0.486	0.001	0.070
		LVEF-based HF subtypes	1.680	0.187	0.006	
		*Sex*LVEF-based HF subtypes*	0.005	0.995	0.000	
	Symptom burden	*Sex*	0.834	0.361	0.002	0.052
		LVEF-based HF subtypes	0.623	0.537	0.002	
		*Sex*LVEF-based HF subtypes*	0.033	0.967	0.000	
	Symptom frequency	*Sex*	0.212	0.646	0.000	0.071
		LVEF-based HF subtypes	3.123	**0.045**	0.012	
		*Sex*LVEF-based HF subtypes*	0.052	0.949	0.000	
	Symptom stability	*Sex*	1.035	0.310	0.002	0.016
		LVEF-based HF subtypes	1.246	0.288	0.005	
		*Sex*LVEF-based HF subtypes*	0.605	0.547	0.002	

Legend LVEF: left ventricular ejection fraction, HF: Heart failure, KCCQ, Kansan City Cardiomyopathy Questionnaire. Two-way ANOVA was used to calculate the interaction of sex and LVEF-based HF subtypes in KCCQ symptom scores at baseline and 12-month. Baseline KCCQ symptom scores were used as covariates in each model of 12-month KCCQ symptom scores evaluation.

Baseline: There is a significant interaction between sex and KCCQ total symptom and symptom burden scores but not symptom frequency and stability scores at baseline. Whereas LVEF-based HF subtypes interacted significantly with all KCCQ symptom scores (including total symptom, symptom burden, frequency, and stability scores). Both sex and LVEF-based HF subtypes did not reach the significance level for any of the KCCQ scores. At this point, it can be said that sex and LVEF-based HF subtypes can be influence the symptom scores separately but not together. An interaction between sex and LVEF-based HF subtypes could not be demonstrated for baseline KCCQ symptom scores (total symptom scores F (2.522) =0.387, p=0.679; symptom burden F (2.522) =0.367, p=0.693; symptom frequency F (2.522) =0.395, p=0.674; and symptom stability F (2.522) =0.469, p=0.626).

12-month: An interaction between sex and LVEF-based HF subtypes could not be demonstrated for 12-month KCCQ symptom scores (total symptom scores F (2.519) =0.005, p=0.995; symptom burden F (2.520) =0.033, p=0.967; symptom frequency F (2.520) =0.052, p=0.946; and symptom stability F (2.519) =0.605, p=0.547).

Appendix 10: Overarching key findings from the findings of the studies

Meta-themes	MMSR – supplementary data	Secondary data analysis (Quantitative data)	Descriptive qualitative (Qualitative data)	Triangulated interpretation -findings show
Full spectrum of symptoms	16 ESC (typical and less typical) + 37 non-ESC symptoms		Identified 31 physical and 7 psychological symptoms	-Regarding the findings of MMSR and qualitative study, each individual has their unique symptom profile (including a diverse range of symptoms). -Though more than half of the symptoms did not list in the guidelines. But people with heart failure experience both heart failure and non-heart failure-related symptoms together. -Symptoms related to diagnosis or congestion listed but symptoms experienced by those in the community was missing. - **Convergence**
			The average of the total individual self-reported symptoms was 8.7±3.6 ranging between 3 and 15.	
			Breathlessness interacts with other symptoms -creating different symptom cluster	
Identifying the most problematic symptoms	Different percentage of each symptom in each study			-Each individual has a unique symptom experiences and profiles. -Not only heart failure symptoms but other symptoms were also associated with individuals' life and care quality. -Same symptom (breathlessness) can affect the individuals differently. -The importance of the symptoms can be changed regarding individual differences. - **Complementarity**
	Higher percentage of some non-ESC symptoms than ESC symptoms			
			Different degree of the breathlessness among participants	
			A few participants expressed that their other symptoms (including depressive symptoms, and fatigue) were more problematic than breathlessness for them.	

Stratified realities in symptoms and associated factors	Different symptom range between hospice versus community dwelling.			-Different factors (such as age, sex, setting, and culture) had a different effect on different symptom experiences in heart failure. -If one more factor is added, symptom experiences are still affected – highlighting that different factor combinations create different symptom profiles for individuals. - There are stratified realities in symptoms shaped by individual characteristics based on socio-cultural-behavioural context – highlighting the uniqueness of symptom profile for each individual. -Worsening trajectory of symptoms is also associated with stratified factors. -Participants with multimorbidity (heart failure + other comorbidities) represent more symptoms than those with only heart failure – highlighting the recognition of non-heart failure-related symptoms. This also increases the physical and psychological vulnerability of the participants in symptomology. - **Complementarity**
	Different symptom range between less than 65 years old versus over 65 years old age			
	Slightly supported - Different symptom range between men versus women	Different symptom presence between men and women: Dyspnoea, dyspnoea type (at rest or on exertion), fatigue, orthopnoea, and paroxysmal nocturnal dyspnoea statistically different between men and women *(all p-values <0.05).* LV function, Charlson Comorbidity Index, and quality of life were associated with KCCQ total symptom score in women but NYHA class, Comorbidity index, and quality of life in men *(all p-values <0.05).*		
		Sex-stratified differences in symptom across heart failure subtypes: bilateral ankle oedema and depressive symptoms were statistically different in men across heart failure subtypes, and bilateral ankle oedema and walking problems in women regarding LVEF-based heart failure subtypes *(all p-values <0.05).*		
		Sex-stratified differences in symptom changes across heart failure subtypes: Women had different worsening symptom profile (based on KCCQ symptom stability score) across LVEF-based heart failure subtypes *(p-value<0.05).* Age, orthopnoea, chronic pulmonary disease, coronary artery disease, KCCQ		

		total symptom, symptom frequency, and stability score, and quality of life were associated with worsening trajectory of heart failure symptoms *(all p-values <0.05).*		
		Different correlates associated with worsening trajectory of symptoms in men and women Non-native English speaking (OR 2.30, 95% CI 1.02–5.20) and hypertension (OR 2.16, 95% CI 1.07–4.35) were correlated with worsening trajectory over one year in men, whereas LVEF range, HFpEF type, acute pulmonary oedema (OR 0.30, 95% CI 0.12–0.75), and cerebrovascular disease (OR 0.25 95% CI 0.08–0.79) in women *(all p-values <0.05)*.		
			Participant with multimorbidity (heart failure + other comorbidity) expressed more symptom experiences than those without comorbidity.	
			Cultural and religious consideration affect the breathlessness experiences and management.	
			Individuals' psychological and physical vulnerabilities influence their interpretation/report/experience of breathlessness.	

Knowledge/awareness about symptoms/heart failure	Not assessed	Not quantitatively assessed	Misconception & knowledge about breathlessness (and heart failure) affect the symptom reporting, interpretation, and management.	-Knowledge and awareness of symptoms and heart failure condition were significantly associated with symptom assessment and management. Without correct interpretation of their symptoms, participants will not be able to manage or report it. -And this can be affected by individual differences. - **Silence**
			Each individual has own management strategies regarding own understanding and abilities.	
Needs assessment	Not assessed but regarding identified symptoms not listed in the ESC Guidelines, symptom assessment is needed in community to find the non-congestion-related symptoms	Not quantitatively assessed		-Needs assessment is the main concept of the effective symptom self-management strategies with a comprehensive and systematic symptom assessment in heart failure. -From holistic care perspective, participant expressed the need of psychological and long-term evidence-based care management strategies apart from the education needs in Türkiye. -Also, apart from the symptom related to congestion/diagnosis, other symptoms should be assessed for those in the different stage of their heart failure journey in community. - **Silence**
			People express the need of adequate education, psychological support and long-term evidence-based management strategies.	
Person-centred symptom assessment: Unique individual symptom profile and diverse associated factors	Diverse range of symptoms and symptom changes regarding setting, sex, and age	Sex-stratified differences in symptom and symptom changes across heart failure subtypes in Australia	Unique symptom experiences regarding socio-cultural-behavioural context – differences of breathlessness description/experience/interpretation among individuals in Türkiye. And knowledge/awareness and needs assessment are important to achieve the best practice and management strategies.	-This is the overarching theme of the overarching findings of the project from the findings of each study (MMSR, Secondary data analysis and descriptive qualitative), which indicates the uniqueness of symptom profile of each individual regarding socio-cultural-behavioural context. -if person lead his/her assessment/management, identified these unique symptom profile and associated factors will be possible. - **Convergence**