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A mixed-method investigation to understand symptom burden and needs in individuals with or at risk of cardiac disease

Dissertation

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1. INTRODUCTION

"It is more important to know what sort of person has a disease than to know what sort of disease a person has."
Hippocrates

This quote underlines the significance of subjectivity in health and illness which has been recognised for many centuries. Around the world, diseases are categorized into diagnoses and codes, such as ICD-10 and DSM-V. These diagnoses are used to create guidelines that support healthcare professionals and standardize treatment. The diagnosis a person receives depends on the measured or described symptoms. However, research has shown that not all diseases are the same, even when they share the same diagnosis. Diseases can have different stages and levels of severity, and sometimes, individuals in a clinical setting suffer from similar symptoms but perceive these and respond to them very differently. Or as an example given by one of my colleagues from cardiology states: "Why can two individuals have the same level of heart failure and similar symptoms, but one of them goes and mows the lawn while the other does not?"

Research has shown that factors beyond biomedical markers can influence an individual's health. Symptom experience is affected by the perception and evaluation of symptoms, as well as the response to them (Dodd et al., 2008; Stockdill et al., 2019). To put it simply, when the perception, evaluation, or response to symptoms is negative, it is referred to as symptom burden (Gapstur, 2007). Studies have demonstrated that symptom burden, regardless of biomedical markers, is associated with poorer well-being. Higher symptom burden is associated with increased mortality, more frequent hospitalizations, and lower functional status (Almutary et al., 2013; Lee et al., 2014; Löwe et al., 2022a; Melhem et al., 2021; Ryan et al., 2007).

Over the past few decades, a more holistic view of somatic diseases has been adopted. The biopsychosocial model, which suggests that biological, psychological, and social factors all contribute to the development of symptoms and diseases, was a starting point (Engel, 1977). In clinical diagnosis, there has also been a shift towards this biopsychosocial approach. For example, the introduction of the somatic symptom disorder (SSD) diagnosis, which replaced the previous somatoform disorder diagnosis, allows for the coexistence of a somatic disease and psychological symptoms (American Psychiatric Association, 2013). Furthermore, studies have already indicated that psychological factors significantly influence the experience of symptom burden (Kitselaar et al., 2023a). However, research focusing on individuals with somatic diseases, such as cardiac disease, and examining differences in experienced symptom burden despite similar symptoms, remains limited.

The phenomenology of increased symptom burden and the phenomenology of medical predispositions, such as symptoms of cardiac disease, show a high degree of overlap. At the same time, the etiology explaining the origins of what the individuals experience can differ markedly. To better understand the differences in experienced symptom burden among individuals with similar symptoms and disease stages, and to identify factors beyond biomedical markers that are influential, this dissertation closely examines the symptom burden and needs of individuals with or at risk of cardiac disease. Specifically, groups at similar disease stages (e.g., individuals at risk for heart failure) were analyzed to identify potential subgroups regarding experienced symptom burden. Additionally, it was investigated whether differences in biomedical or psychological factors could be found that might explain the variations in experienced symptom burden. To gain further insight into the needs of these individuals and to explore potential improvements in treatment, individuals who underwent cardiac surgery were asked for an evaluation of a psychological support intervention. This dissertation aims to provide new empirical evidence on symptom burden in individuals with or at risk of cardiac disease and therefore contributes to understanding how to adapt treatment approaches to better meet the needs of this population.

2. THEORETICAL BACKGROUND

2.1 Characteristics of symptom burden

A symptom is defined as "a subjective experience reflecting changes in the biopsychosocial functioning, sensations, or cognition of an individual" (Dodd et al., 2008). Unlike symptoms, which are subjective, a sign is "any abnormality indicative of disease that is detectable by the individual or others" (Dodd et al., 2008; Löwe et al., 2024). Symptoms can only be reported by the person experiencing them and often serve as warning signals (Cleeland, 2007; Dodd et al., 2008). Approximately 80% of the general population experiences one or more symptoms during a month, and acute symptoms turn into persistent somatic symptoms (PSS) in about one in four individuals (Acevedo-Mesa et al., 2021; Hinz et al., 2017; Kroenke, 2014; Löwe et al., 2022a). Understanding the underlying mechanisms of symptoms can be challenging for both, individuals and healthcare professionals, and there seems to be a risk of over- or underestimating disease processes based on the interpretation of symptoms (Cleeland, 2007; Löwe et al., 2024).

Symtom experience is shaped by the way symptoms are perceived, evaluated, and responded to, as well as the interaction among these processes (Dodd et al., 2008; Stockdill et al., 2019). Symptom perception involves the individual noticing changes from their usual feelings and behaviors. The evaluation of symptoms includes the individual assessing their severity, cause, treatability, and effects. Whereas the response to symptoms describes physiological, psychological, sociocultural, and behavioral reactions (Dodd et al., 2008). Additionally, symptom experience is influenced by other factors, such as demographic, disease-related, and individual characteristics (Armstrong, 2003).

In comparison, symptom burden is a more specific aspect of symptom experience, defined as the "subjective, quantifiable prevalence, frequency, and severity of symptoms placing a physiological burden on patients and producing multiple negative, physical, and emotional responses" (Gapstur, 2007). It is characterized by symptoms – whether physical, psychological, or other – which negatively impact an individual's life, quality of life, or functioning (Evangelista et al., 2012; Flint et al., 2017; Stockdill et al., 2019). Symptom burden can be understood as a negative symptom experience and is considered a fluid phenomenon (Stockdill et al., 2019).

It is also important to distinguish between symptom prevalence and symptom burden. A symptom can be very prevalent without being perceived as burdensome, and conversely, a less common symptom can be experienced as highly burdensome, highlighting the subjectivity of symptom experience (Zambroski et al., 2005). Research aiming at understanding factors influencing symptom burden generally shows the importance of psychosocial and biomedical factors rather than focusing on biomedical factors alone (Ladwig et al., 2022). In a clinical setting, symptom burden is amongst other reasons relevant because experienced symptoms often prompt individuals to seek healthcare (Dodd et al., 2008). In order to better understand the development of symptom burden, it is crucial to gain a deeper understanding of the multidimensional nature of symptoms and how they interact with each other (Stockdill et al., 2019).

Within this dissertation symptom burden is mainly portrayed through the terms of persistent somatic symptoms (PSS) and somatic symptom disorder (SSD). Therefore, the following sections will provide explanations and definitions of PSS and SSD.

Persistent somatic symptoms (PSS) are defined as "distressing somatic complaints, regardless of cause, that are present on most days for at least several months" (Löwe et al., 2024). These symptoms are often accompanied by excessive health-related concerns and are assessed through individuals' reports of their subjective somatic symptom severity (Löwe et al., 2024). The symptoms are heterogeneous and can include pain, cardiovascular, gastroenterological, and neurological symptoms, which may or may not be linked to an underlying medical condition (Fränkl et al., 2024). While the initial development of somatic symptoms is often driven by disease-specific and biomedical mechanisms, persistent symptoms involve additional cross-disease mechanisms, as well as psychological and social factors (Boersma & Linton, 2005; Löwe et al., 2024). Symptom persistence is typically defined as a duration of three to six months (Löwe et al., 2024).

Explanations for the development of persistent somatic symptoms (PSS) include a process where the brain predicts sensory input and then compares these predictions with actual sensory input to minimize prediction errors (Henningsen et al., 2018). This indicates that constructs such as expectations may play a crucial role in the perception of PSS (Henningsen et al., 2018). Previous studies have shown that when PSS are present, they contribute to a greater disease burden for both the individual and the healthcare system (Kitselaar et al., 2023a). The diagnostic process and the identification of appropriate treatments for individuals with PSS are often described as challenging (Fränkl et al., 2024; Kitselaar et al., 2023a).

Persistent somatic symptoms also play a role regarding the somatic symptom disorder (SSD). The diagnosis of SSD differs from the previous diagnosis of somatoform disorder by allowing for the presence of a comorbid somatic disease (American Psychiatric Association, 2013; Löwe et al., 2022b). The diagnostic criteria for SSD are as follows: the A-criterion requires the presence of distressing somatic symptoms; the B-criterion involves excessive thoughts, feelings, and/or behaviors related to the somatic symptoms or associated health concerns; and the C-criterion specifies that the symptoms must be persistent (American Psychiatric Association, 2013). The B-criterion does not provide a concrete definition of "excessiveness" which is why recent research has attempted to quantify this. Findings suggest that spending three to four hours daily on thoughts related to symptoms may indicate excessiveness (Toussaint et al., 2021).

Individuals with somatic symptom disorder (SSD) experience both physical and psychological impairments. Research shows a strong association between SSD and conditions such as depressive and anxiety disorders, as well as other physical conditions and functional somatic disorders (Löwe et al., 2022b). A scoping review by Löwe et al. (2022b) aimed to show the prevalence of SSD and illustrate its variation depending on the healthcare setting. According to these results, the prevalence of SSD in the general population ranges from 6.7% to 17.4%, with a mean frequency of 12.9% (Lehmann et al., 2022; Löwe et al., 2022b). In non-specialized general medicine settings, the prevalence of SSD ranges from 3.5% to 45.5%, with a mean frequency of 35%. In various specialized care settings, the prevalence ranges from 5.8% to 52.9%, with a mean frequency of 23.6%. In mental health care settings, the prevalence ranges from 40.3% to 77.7%, with a mean frequency of 60.1% (Löwe et al., 2022b). One study which specifically examined individuals with cardiac disease found a prevalence of 18.5% for SSD in this group (Guidi et al., 2013).

The ability to diagnose SSD alongside a comorbid somatic disease supports a biopsychosocial approach. However, it also presents a challenge due to the overlap in symptom phenomenology between SSD and somatic diseases (Löwe et al., 2022b). This dissertation focuses on individuals with or at risk of cardiac disease because of its high prevalence and significant impact. The development of cardiac disease is primarily attributed to biological factors, while the etiology of symptom burden-related concepts like SSD involves a complex interplay of biological, psychological, and social factors (Glattacker et al, 2022). Additionally, since one-third of persistent somatic symptoms (PSS) cannot be linked to a recognized disease, exploring symptoms beyond diagnostic categories could offer valuable insights (Kohlmann et al., 2013a; Löwe et al., 2024).

2.2 Characteristics of cardiac disease

Individuals with cardiac disease often experience multiple symptoms which are characterized by a wide diversity (Blinderman et al., 2008; Jurgens et al., 2009; Snipelisky et al., 2019). While the interactions between these symptoms are not fully understood, it is possible that they may act as catalysts for one another (Armstrong, 2003). Symptoms in individuals with cardiac disease range from disease-specific symptoms (e.g., dyspnea, drowsiness, chest pain) to non-specific symptoms (e.g., fatigue, sleep problems, pain) or psychological symptoms (e.g., increased anxiety, depressive mood, difficulty concentrating) (Al-Sutari & Abdalrahim, 2024; Blinderman et al., 2008; Zambroski et al., 2005). Studies have shown that these symptoms are associated with a higher risk of hospitalization and mortality, as well as a decrease in functional status and quality of life (Alpert et al., 2017; Al-Sutari & Abdalrahim, 2024; Ladwig et al., 2022; Locatelli et al., 2024; Retrum et al., 2013; Salyer et al., 2019; Schopfer et al., 2016).

Overall, individuals with cardiac disease frequently experience an increased symptom burden (Stockdill et al., 2019). However, the subjective nature of symptoms must be taken into account. While symptoms such as shortness of breath and lack of energy are commonly reported, other less prevalent symptoms, such as sleep problems and increased anxiety, may be perceived as more burdensome (Blinderman et al., 2008; Zambroski et al., 2005). Stockdill and colleagues (2019) attribute this variation in perceived burden to the greater negative impact these symptoms have on daily functioning and activities.

Research identified a range of risk factors for developing cardiac disease. Behavioral factors include physical inactivity, poor diet, smoking, excessive alcohol consumption, and poor sleep hygiene (Albus et al., 2022; Mesa-Vieira et al., 2021; Schmidt-Trucksäss et al., 2024). Psychosocial risk factors encompass depression, anxiety, social isolation, work-related stress, relationship and family stress, socioeconomic disadvantages, and certain personality traits (Albus et al., 2022; Ladwig et al., 2022; Mesa-Vieira et al., 2021; von Känel et al., 2022). Conversely, factors that can help prevent cardiac disease include increased physical activity and fitness, a heart-healthy diet, maintaining a normal weight, adequate sleep, stress reduction, addressing psychosocial risk factors, and health education (Gerber et al., 2021; Schmidt-Trucksäss et al., 2024).

2.3 Symptom burden in individuals with or at risk of cardiac disease

2.3.1 Consequences

There are several factors which have been identified as significant predictors of quality of life in individuals with cardiac disease such as functional status, sociodemographic, and psychological factors, symptom experience and symptom management strategies (Al-Sutari & Abdalrahim, 2024; Blinderman et al., 2008; Thida et al., 2021; Zambroski et al., 2005).

Additionally, increased symptom prevalence and higher symptom burden are associated with poorer physical and mental quality of life (Al-Sutari & Abdalrahim, 2024; Auschra et al., 2024; Löwe et al., 2022b; Zambroski et al., 2005). Specific symptoms identified as predictors for worse physical and mental quality of life include tiredness, nausea, loss of appetite, and anxiety (Al-Sutari & Abdalrahim, 2024).

Apart from the correlation between increased symptom burden and worse quality of life, there are further consequences related to experienced symptom burden. Higher symptom burden in individuals with cardiac disease is associated with increased morbidity and mortality, regardless of biomedical markers (Flint et al., 2017; Janssen et al., 2011; Stockdill et al., 2019). Furthermore, a higher symptom burden is accompanied by more severe disease progression, higher rates of re-hospitalization, greater physical impairment, and consequently lower functional status (Almutary et al., 2013; Lee et al., 2014; Löwe et al., 2022a; Melham et al., 2021; Ryan et al., 2007). Research on whether higher symptom burden correlates with increased healthcare utilization shows mixed results (Löwe et al., 2022b).

2.3.2 Risk and protective factors

After understanding which consequences are associated with increased symptom burden, it seems relevant which factors influence whether and how severe symptom burden is experienced by individuals. Biomedical factors contributing to greater symptom burden include physical impairment, the presence of infections or other somatic disorders, as well as certain epigenetic profiles and dysregulation in immune, metabolic, and microbiome systems (Kitselaar et al., 2023a; Li et al., 2023; Löwe et al., 2024). Psychological risk factors include heightened general and illness-related anxiety, increased depression severity, and alexithymia (Kitselaar et al., 2023a; Löwe et al., 2022b; Smakowski et al., 2024). Additionally, issues such as sleep problems, deficits in emotion regulation, and perceived stigmatization further exacerbate symptom burden (Barsky & Wyshak., 1990; Löwe et al., 2022a; Mayou et al., 2005; Sharpe et al., 2006).

In addition to biomedical and psychological factors, according to the literature, health behaviors, as well as contextual, interpersonal, and cognitive-perceptual factors, seem to contribute to the development of symptom burden. Health behaviors linked to increased symptom burden include cardiac risk factors such as physical inactivity, irregular or non-adherent medication use, smoking, and alcohol abuse (Kitselaar et al., 2023a; Li et al., 2023). Furthermore, behaviors such as increased body checking and avoidance are also associated with a higher symptom burden (Barsky & Wyshak, 1990; Hüsing et al., 2023; Löwe et al., 2022a; Mayou et al., 2005; Sharpe et al., 2006).

Contextual factors associated with increased symptom burden include sociodemographic characteristics such as age, gender, employment and education level, socioeconomic status, and healthcare utilization (Kitselaar et al., 2023a; Löwe et al., 2022a). Recent studies have also identified a migration background, either personally or in the previous generation, as a risk factor (Barbek et al., 2024; von dem Knesebeck et al., 2023). Additionally, interpersonal risk factors such as life events, childhood adversity, interpersonal stress, and personality traits like neuroticism and perfectionism have been linked to a higher symptom burden (Hüsing et al., 2023; Kitselaar et al., 2023a).

Recent research has increasingly focused on cognitive-perceptual factors that influence the development of symptom burden. Such risk factors for increased symptom burden include catastrophizing, somatosensory amplification, somatic illness attributions, and intolerance of bodily complaints (Hüsing et al., 2023; Löwe et al., 2022a; Löwe et al., 2022b; Müller-Tasch et al., 2024). Additional risk factors seem to be a heightened focus on symptoms and negative treatment expectations, which may be shaped by an individual's attitude towards their disease or previous experiences (Hüsing et al., 2023; Li et al., 2023; Löwe et al., 2022a; Löwe et al., 2024). Perceptions and expectations regarding symptoms and the disease are also linked to symptom burden, with negative expectations being associated with an increase in symptom burden (Hüsing et al., 2023; Löwe et al., 2024). Previous studies have developed interventions aiming at an improvement of expectations for individuals undergoing cardiac surgery, resulting in positive effects on personal control and recovery (Rief et al., 2017; Salzmann et al., 2020).

2.3.3 Needs

So far, research has highlighted the significant role that symptom burden plays, independently of biomedical markers, affecting factors such as physical impairment, hospitalization, and quality of life. Further investigation is required to better understand what individuals need to avoid developing a high symptom burden or to reduce an existing one. Many studies have emphasized the subjectivity of symptom experience, noting that the perception of the same symptoms differ between both individuals and healthcare professionals (Blinderman et al., 2008; Stockdill et al., 2019). It is not sufficient to merely assess the presence or absence of symptoms; treatment should also involve the perspectives of those experiencing them (Gill et al., 2012; Zambroski et al., 2005). Treatment approaches should be tailored to the specific symptoms described by the individual, taking into account the subjective nature of symptom experience (Al-Sutari & Abdalrahim, 2024; Sarenmalm et al., 2014). To improve outcomes such as quality of life, research supports to focus on reducing symptom burden rather than solely targeting the symptoms themselves (Al-Sutari & Abdalrahim, 2024).

To understand the needs of individuals with cardiac disease better, Kohlmann and colleagues (2013b) conducted a qualitative study, revealing a desire for more support, such as receiving additional health information and increased assistance with psychological needs. Many studies that compare new interventions with standard treatment show improvements in measured outcomes like functional status or quality of life. However, to successfully implement an intervention, it seems relevant to understand the needs of the individuals who shall benefit from it and incorporate those needs into the intervention design (Bonevski et al., 2000; Cushing & Metcalfe, 2007; Epstein, 2006; Kohlmann et al., 2013b)

Identifying individuals with increased symptom burden seems crucial for improving health-related outcomes, and early identification can significantly enhance health (Berezowski et al., 2022; Löwe et al., 2022b). Conversely, research indicates concerning the actual circumstances that the symptom burden of many individuals is frequently not recognized, resulting in fragmented treatment and a lack of specialized care (Hüsing et al., 2023; Kitselaar et al., 2023a; Kohlmann et al., 2018).

Typically, treatment focuses on improving biomedical markers or reducing symptoms. However, even when the underlying pathophysiology is addressed, symptom burden often remains unchanged (Joustra et al., 2015; Kumar et al., 2013). This highlights the need to incorporate psychological factors more thoroughly in treatment. For instance, studies have shown that individuals who deny the reality of their disease tend to have lower adherence to treatment, such as medication non-adherence, physical inactivity, poor dietary control, and inadequate self-care (Ladwig et al., 2022).

One important aspect that supports the needs of individuals receiving treatment seems to be person-centeredness. Studies have shown that a greater focus on person-centeredness in treatment is associated with reduced symptom burden and lower healthcare utilization (Little et al., 2001). When asked about their needs for feeling involved in their treatment, individuals emphasized the importance of person-centered communication and a personal relationship with healthcare professionals (Little et al., 2001; Löwe et al., 2024). This involves feeling supported, validated, and in control, as well as perceiving engagement and a positive approach towards the diagnosis from healthcare professionals (Little et al., 2001; Fränkl et al., 2024). Individuals also expressed a desire for education that includes a biopsychosocial explanation and self-help strategies as part of their treatment (Fränkl et al., 2024; Löwe et al., 2024). Incorporating a biopsychosocial approach in treatment has demonstrated positive effects on shared decision-making, improved diagnostic and treatment processes, and reduced binary thinking, which may ultimately lead to reducing stigmatization experienced (Löwe et al., 2024). Additionally, providing education helps individuals better interpret their symptoms, which can be particularly challenging if they lack experience with the disease or if the disease progression is inconsistent (Song et al., 2010).

In addition to support from healthcare professionals, individuals value social support highly, which has been shown to positively impact health-related outcomes (Richardson, 2003; Zahedifard et al., 2024). A recent approach trying to enhance social support involves supplementing the assistance provided by family and friends with peer support programs (Zahedifard et al., 2024).

Some factors have been identified as negatively impacting treatment success. These include issues related to the evaluation and management of symptoms, such as symptom catastrophizing, excessive worrying, somatosensory amplification tendencies, low symptom acceptance, and low self-efficacy (Löwe et al., 2024; Sarter et al., 2021; Sarter et al., 2022). Furthermore, lower levels of physical and social functioning, comorbid depressive and anxiety disorders as well as longer reported symptom duration also seem to influence treatment outcomes negatively (Löwe et al., 2024; Sarter et al., 2021; Sarter et al., 2022).

2.3.4 Expectations

As previously noted, individuals' expectations significantly influence symptom perception, with negative expectations often linked to increased symptom burden (Hüsing et al., 2023; Löwe et al., 2024). While defining a consistent construct of expectations can be challenging, in healthcare, expectations are generally described as “future-directed beliefs that focus on the incidence or non-incidence of a specific event or experience” (Kube et al., 2017; Laferton et al., 2013). Beyond symptom perception, numerous studies have demonstrated that expectations play a crucial role in both physical and mental health (Laferton et al., 2017). Research indicates that expectations impact treatment outcomes irrespective of medical conditions, demographic factors, experienced stress, socioeconomic status, and health behaviors (Auer et al., 2016; Barefoot et al., 2011; Habibovic et al., 2014; Jurgens et al., 2009; Kohlmann et al., 2012; Laferton et al., 2016; Petrie et al., 1996; Salzmann et al., 2022).

The integrative model of expectations serves as the foundation for interventions designed to improve the expectations of individuals undergoing surgery. According to this model, treatment outcomes – including symptoms, functional status, and quality of life – are shaped by both expectations about the treatment and the individual's treatment-related behavior. Additionally, broader expectations such as optimism, generalized self-efficacy, and perceptions of the treatment timeline also influence these outcomes (Laferton et al., 2016).

Several key factors have been identified for developing effective expectation-focused interventions. One of these concerns the importance of communication that addresses the individual's beliefs and concepts (Laferton et al., 2013). This communication should be empathetic and emphasize the benefits of the treatment for the individual (Bingel et al., 2011; Kam-Hansen et al., 2014; Kaptchuk et al., 2008). A notable example of a successful expectation-focused intervention is the PSY-HEART trial, which demonstrated positive effects for individuals undergoing cardiac surgery (Rief et al., 2017; Salzmann et al., 2020). This intervention involved optimizing expectations by emphasizing the benefits of the surgery and correcting any misconceptions about the disease. It also included planning positive future activities, addressing risk factors such as health behaviors, preparing coping strategies for potential side effects, and visualizing a positive outlook on post-surgery recovery.

Research indicates that expectation-focused interventions can lead to better health outcomes across a range of medical conditions, including cardiac disease, when compared to standard treatments or those emphasizing only emotional support (Broadbent et al., 2009; Löwe et al., 2024; Rief et al., 2017). These expectation-focused interventions have been shown to reduce stress-related biomarkers, alleviate post-surgery pain, enhance functional status, and speed up return to work (Broadbent et al., 2009; Holmes et al., 2016; Petrie et al., 2002; Powell et al., 2016; Rief et al., 2017). Individuals who underwent such interventions also tended to report improved coping mechanisms and a greater sense of personal control (Glattacker et al., 2022; Rief et al., 2017; Salzmann et al., 2020). Furthermore, these approaches seem to be linked to lower symptom burden, reduced cardiac anxiety, and improved quality of life (Hlubocky et al., 2011; Rief et al., 2017).

2.4 Aims of this dissertation

Overall, numerous studies highlight the significance of symptom burden and its serious consequences, such as increased mortality, higher rates of hospitalization, and diminished quality of life. Understanding these consequences, along with the risk factors and underlying causes of symptom burden, is a crucial starting point. In clinical practice, the diagnosis and prevalence of symptoms often take precedence for healthcare professionals and can influence treatment decisions. However, research has shown that the severity or stage of a disease does not always align with the subjective experience of symptom burden (Conqay et al., 2011; Hansen et al., 2022; Löwe et al., 2022a). Therefore, the conducted studies aim to shift focus towards the subjective nature of symptoms, emphasizing individuals' perceptions of symptom burdensomeness rather than exclusively their prevalence.

Research has demonstrated that early identification of individuals with increased symptom burden is crucial for providing timely and effective treatment. However, there is currently a lack of sufficient knowledge to identify these individuals at an early stage. In particular the high diversity of symptoms and the overlap within the phenomenology in individuals with medical predispositions is challenging. To improve early identification, a deeper understanding of how symptoms develop and how individuals perceive them is needed which will be approached by understanding characteristics and predictors of increased symptom burden better.

In this dissertation, the aim was to deepen the understanding of symptom burden in individuals with cardiac disease. To explore the impact of the medical condition more comprehensively, individuals with different medical predispositions and treatment settings were included. More precisely, individuals with cardiac disease, those at risk of developing cardiac disease, and individuals undergoing cardiac surgery were the target groups within the studies. The goal was to identify characteristics and predictors of symptom burden in these groups and to recognize distinct subgroups. Additionally, the needs of individuals with or at risk of cardiac disease were examined, using existing knowledge on the benefits of expectation-focused interventions. The goal was to gain insights into the experiences of those receiving such interventions, ultimately enhancing knowledge to effectively disseminate these strategies.

From these objectives, the following research questions derive:

1. Can subgroups be defined concerning symptom burden in individuals with or at risk of cardiac disease?
2. Which biomedical and psychological factors are associated with symptom burden in individuals with or at risk of cardiac disease?
3. How is symptom burden associated with healthcare utilization and quality of life?
4. What are the needs of individuals with or at risk of cardiac disease?

3. METHODS

3.1 The projects

The data for this cumulative dissertation was drawn from three distinct projects: RiskAct, the Hamburg City Health Study (HCHS), and INCREASE. The following sections will outline each of these projects and detail the specific data used for the analyses relevant to this dissertation.

RiskAct

RiskAct was a randomized controlled trial designed to compare the risk perception of individuals from the cardiac outpatient clinic of the University Medical Center Hamburg-Eppendorf and a non-university cardiac outpatient clinic in Hamburg, Germany. The study involved providing individualized, patient-oriented feedback on physical activity levels to some individuals, while others did not receive such feedback. The hypotheses were that individuals who received feedback would demonstrate an increased risk perception after one month and a higher level of physical activity after three months. The study was funded by the Werner Otto Stiftung and received ethical approval from the Ethics Committee of the Medical Chamber (reference number PV5199).

Hamburg City Health Study (HCHS)

The Hamburg City Health Study (HCHS) was a population-based cohort study including individuals aged 45 to 74 from the general population of Hamburg, Germany. Its primary objective was to identify critical risk and prognostic factors for major chronic diseases through ongoing follow-up measurements (Jagodzinski et al., 2020). Data collection started in February 2016, with 10,000 individuals enrolled and their data systematically recorded. Assessments were conducted at the epidemiological study center at the University Medical Center Hamburg-Eppendorf. The funding for the study was provided by the euCanSHare grant agreement, Joachim Herz Foundation, Foundation Leducq, Innovative Medicine Initiative, Deutsche Gesetzliche Unfallversicherung, Deutsches Krebsforschungszentrum, Deutsches Zentrum für Herz-Kreislauf-Forschung, Deutsche Stiftung für Herzforschung, Seefried Stiftung, Bayer, Amgen, Novartis, Schiller, Siemens, Topcon, Unilever, and donations from the Förderverein zur Förderung der HCHS e.V. and TePe. The project was approved by the independent Ethics Committee of the Medical Chamber (reference number PV5131).

INCREASE

The full title of the INCREASE project is: Interdisciplinary and cross-sectoral perioperative care model in cardiac surgery: implementation in the setting of minimally invasive heart valve surgery (Klotz et al., 2022). It was conducted as a randomized controlled trial at two centers: the University Medical Center Hamburg-Eppendorf and the University Hospital Augsburg. The primary goal was the improvement of treatment for individuals undergoing heart valve surgery (Klotz et al., 2022). The study involved a minimally invasive heart valve surgery within an interprofessional enhanced recovery after surgery (ERAS) program. This ERAS program included surgical, anesthesiological, physiotherapeutic, advanced nursing, and psychosomatic components throughout the pre-, peri-, and postoperative phases. Individuals in the intervention group received a psychosomatic intervention based on the EXPECT manual developed in the PSY-HEART trial, with adaptations for heart valve surgery (Laferton et al., 2013; Rief et al., 2017; Salzmann et al., 2020). This intervention aimed to develop positive and realistic post-surgery expectations as well as individual coping strategies for potential side effects, and to address emotional concerns such as surgery-related anxiety. In contrast, the control group received standard care and no expectation-focused intervention. Hypotheses of the study were that individuals receiving the interprofessional ERAS program would experience greater effectiveness in terms of reduced hospital days due to cardiac causes within the first year post-surgery and improved functional performance, as measured by the six-minute walk test. Secondary outcomes included assessments of health-related quality of life, depression and anxiety, health literacy, and other relevant health-related measurements (Klotz et al., 2022). The INCREASE study was funded by the Innovationsausschuss in the Gemeinsamer Bundesausschuss with resources of the Innovationsfonds (funding code: 01NVF19028). It received approval from the Ethics Committee of the Medical Association Hamburg (reference number 2020-10276-BO-ff) and additional approval for the qualitative study from the Ethics Committee of the University Medical Center (reference number LPEK-0358).

3.2 Outcomes and participants

Study I (RiskAct)

The primary analysis of the RiskAct study revealed no significant results regarding the impact of feedback on physical activity and risk perception, nor was there any observed association between risk perception and increased physical activity. Given that this dissertation focuses on symptom burden, a secondary analysis to explore the characteristics and predictors of symptom burden in individuals with cardiac disease was conducted. This analysis included 95 individuals with cardiac disease from the RiskAct trial. The Somatic Symptom Scale-8 (SSS-8) was used to assess experienced symptom burden (Gierk et al., 2014). The longitudinal design of the study, with follow-up measurements over a three-month period, allowed to identify individuals with persistent somatic symptoms (PSS) by analyzing SSS-8 results throughout this time. The characteristics and predictors of PSS were examined by exploring its association with sociodemographic, biomedical, and psychological factors. Sociodemographic factors included age, gender, language, living situation, education, and employment status. Biomedical factors encompassed the number of cardiac diseases, comorbidities, medications, cardiac risk factors, and the presence of angina pectoris (Campeau, 1976). Psychological factors included depression and anxiety severity (Kroenke et al., 2010; Löwe et al., 2004; Löwe et al., 2008; Spitzer et al., 2006). Additionally, healthcare utilization based on the number of visits to general practitioners and cardiologists was analyzed.

Study II (HCHS)

The primary objective of this secondary analysis was to identify clusters of individuals based on symptoms of the somatic symptom disorder (SSD) and to gain a deeper understanding of these subgroups by examining associated biomedical and psychological factors. Especially when medical predispositions or somatic comorbidities are present it poses a challenge to identify whether experienced symptom burden indicates SSD. For this reason, the focus was on individuals at risk for heart failure, as their symptoms may not yet be as pronounced as in those with established heart failure, potentially providing valuable insights. The analysis included 412 individuals at risk for heart failure, each showing a minimum of 5% risk of heart failure-related hospitalization within the next ten years (Agarwal et al., 2012; Jagodzinski et al., 2020). To assess SSD symptoms, the Somatic Symptom Scale-8 (SSS-8) and the Somatic Symptom Disorder-B Criteria Scale (SSD-12) were utilized. The characteristics of identified SSD symptom clusters were analyzed by examining their associations with sociodemographic, biomedical, cardiac, and psychological factors. Sociodemographic factors included age, gender, family status, living situation, education, and employment status. Biomedical factors encompassed the ARIC score (which assesses the risk of heart failure-related hospitalization within the next ten years), the number of cardiac diseases, somatic comorbidities, medications, and cardiac risk factors (Agarwal et al., 2012). Cardiac factors included assessments of angina pectoris and dyspnea, left ventricular ejection fraction (LVEF), left atrial diameter, and NT-proBNP levels (Campeau, 1976; Levin et al., 1994). Psychological factors included the depression and anxiety severity as well as the number of mental disorders (Kroenke et al., 2010; Löwe et al., 2004; Löwe et al., 2008; Spitzer et al., 2006). Additionally, physical and mental quality of life, as well as healthcare utilization based on the number of visits to general practitioners were analyzed.

Study III (INCREASE)

The aim of this study was to evaluate individuals' perceptions of an expectation-focused intervention in the context of heart valve surgery. To achieve this, 18 individuals from the INCREASE trial participated in qualitative interviews. Recruitment occurred between November 2021 and July 2022 and involved participants from the University Medical Center Hamburg-Eppendorf. Of these individuals, eleven received the expectation-focused intervention, while seven were in the control group and had not received the intervention. A purposive sampling strategy was used to ensure diversity in age, gender, and disease duration. To describe the study sample, sociodemographic and clinical characteristics were assessed. Sociodemographic data included age, gender, group affiliation, living situation, marital status, education, and employment status. Clinical characteristics encompassed disease duration, the number of cardiac diseases, somatic comorbidities, cardiac risk factors, and assessments of angina pectoris and dyspnea (Campeau, 1976; Levin et al., 1994). The semi-structured interview guide was developed to cover topics addressed in the expectation-focused intervention, including feasibility, acceptance, barriers, effectiveness, and experiences of adverse effects.

3.3 Overview of studies

This dissertation comprises three publications. Studies I and II focus on symptom burden in individuals with or at risk of cardiac disease. Study I has a longitudinal study design including individuals with cardiac disease and aimed at identifying characteristics and predictors of those experiencing persistent somatic symptoms. Study II is a cross-sectional population-based cohort study aiming at identifying symptom clusters related to somatic symptom disorder (SSD) in individuals at risk for cardiac disease, and comparing these clusters based on sociodemographic, biomedical, cardiac, and psychological factors. Study III examines the needs of individuals undergoing heart valve surgery by evaluating their experiences with an expectation-focused intervention. A detailed description of the methods used in these studies is provided in section 4 (Summary of Articles).

4. SUMMARY OF ARTICLES

4.1 Summary Study I

Clifford, C., Löwe, B. & Kohlmann, S. Characteristics and predictors of persistent somatic symptoms in patients with cardiac disease. *Scientific reports, 14*(1), 1-10.

Background and aims

Approximately 23% of individuals visiting general practitioners in Germany are diagnosed with somatic symptom disorder (SSD), where the persistence of somatic symptoms is a key diagnostic criterion. Identifying SSD in individuals with cardiac disease poses challenges due to ambiguous definitions of symptom persistence. However, this is crucial given the high prevalence and its associations with increased mortality and hospitalization. Studies have highlighted that persistent somatic symptoms are associated with severe disease progression, higher clinical treatment needs, and an elevated risk of mortality (Almutary et al., 2013; Lee et al., 2014; Löwe et al., 2022a). This study aimed to define and estimate the prevalence of persistent somatic symptoms (PSS) in individuals with cardiac disease. The aim was to identify characteristics and potential predictors of PSS in this target group by examining sociodemographic, biomedical, and psychological factors. Additionally, healthcare utilization was investigated to better understand the impact of persistent somatic symptoms.

Methods

Outpatients from the University Heart Center and a non-university cardiac outpatient clinic in Hamburg, Germany, were recruited by telephone. To be included in the study, participants needed to have a confirmed cardiac disease, be at least 18 years old, have telephone access, and possess adequate language skills. Exclusion criteria included a restricting somatic or psychiatric condition or the lack of written informed consent. Over a three-month period, participants underwent one assessment in person and three telephone assessments. Somatic symptoms were evaluated at each assessment using the Somatic Symptom Scale-8 (SSS-8), which measures the presence and severity of common somatic symptoms (Gierk et al., 2014). A cut-off score of 4 points on the SSS-8 is recommended to identify the presence of somatic symptom burden (Gierk et al., 2014). Since there is no established empirical cut-off score for defining the persistence of somatic symptoms in individuals with cardiac disease, the aim was to validate the definition of persistent somatic symptoms (PSS) using both a psychometric approach, based on the SSS-8 cut-off score, and a data-driven approach through cluster analysis (Ward method). Sociodemographic factors (e.g., age, gender, employment), biomedical factors (e.g., number of cardiac diseases, medication, angina pectoris), and psychological factors (e.g., depression and anxiety severity) were also measured. To assess healthcare utilization, participants were asked during the final follow-up how frequently they had visited a general practitioner and a cardiologist in the preceding three months. Characteristics of individuals with cardiac disease experiencing PSS were examined using descriptive analyses, t-tests, and chi-squared tests. Predictors of PSS were analyzed through multivariable logistic regression analyses.

Results

Using both methodological approaches, it was identified that approximately one-third of individuals with cardiac disease exhibited persistent somatic symptoms (32% using the psychometric-driven approach and 28% using the data-driven approach). Characteristics associated with persistent somatic symptoms (PSS) included female gender, unemployment, greater impairment from angina pectoris, and higher levels of depression and anxiety (all with $p \leq 0.05$). The study identified several predictors for PSS in individuals with cardiac disease: female gender, older age, increased depression severity, and greater angina pectoris impairment (all with $p \leq 0.015$). Individuals with PSS demonstrated significantly higher healthcare utilization, indicated by more frequent visits to general practitioners and cardiologists.

Discussion

This study reveals that approximately one-third of individuals with cardiac disease report persistent somatic symptoms, which is a key criterion for somatic symptom disorder (SSD). The phenomenology of SSD often overlaps with that of cardiac conditions, and there is limited evidence on how to accurately assess symptom persistence – a core criterion of SSD – when somatic comorbidities are present. This exploratory study supports a biopsychosocial perspective on the factors influencing and predicting persistent somatic symptoms (PSS). Future research should examine additional variables, such as interpersonal factors and health behaviors, and further explore the impact of psychological aspects. Incorporating psychological considerations in clinical practice seems crucial for the early identification of individuals with cardiac disease at risk for SSD.

4.2 Summary Study II

Clifford, C., Twerenbold, R., Hartel, F., Löwe, B. & Kohlmann, S. (2024). Somatic symptom disorder symptoms in individuals at risk for heart failure: A Cluster analysis with cross-sectional data from a population-based cohort study. *Journal of Psychosomatic Research, 184,* 111848.

Background and aims

Somatic symptom disorder (SSD) is characterized by the following criteria: distressing somatic symptoms (Criterion A), excessive thoughts, feelings, and/or behaviors related to these symptoms (Criterion B), and persistent symptomatic states (Criterion C) (American Psychiatric Association, 2013). The diagnosis of SSD can be made even if a comorbid somatic disease is present alongside the psychological symptoms. Identifying whether the symptom burden in individuals with medical predispositions indicates SSD is challenging due to the significant overlap in symptom phenomenology within these groups. To deepen the understanding of SSD, the goal was to examine SSD at the symptomatic level in individuals at risk for heart failure. Additionally, this study aimed to explore the complex interplay of biomedical and psychological factors, as well as the association between symptom burden and general practitioner visits as well as quality of life.

Methods

This study utilized data from the Hamburg City Health Study (HCHS), a population-based cohort study examining risk factors for major chronic diseases (Jagodzinski et al., 2020). Among the 10,000 participants, 412 individuals with at least a 5% risk of hospitalization due to heart failure, as determined by the ARIC score were identified (Agarwal et al., 2012). A cluster analysis using items from the Somatic Symptom Scale-8 (SSS-8) and the Somatic Symptom Disorder-B Criteria Scale (SSD-12) was performed. ANOVAs were employed to compare sociodemographic, biomedical, and psychological factors across clusters. Additionally, linear regressions, adjusted for sociodemographic, biomedical, and psychological variables, were used to explore associations between clusters and healthcare utilization as well as quality of life.

Results

Among the 412 individuals at risk for heart failure, three distinct clusters were identified based on the SSS-8 and the SSD-12: cluster 1 (n = 215), cluster 2 (n = 151), and cluster 3 (n = 46). The SSS-8 sum scores for clusters 1,2 and 3 were 3.4 (SD = 2.7), 6.5 (SD = 3.4), and, 12.5 (SD = 3.6) respectively. The SSD-12 sum scores for clusters 1,2 and 3 were 3.1 (SD = 2.6), 12.1 (SD = 4.3), and, 23.4 (SD = 6.4) respectively. Significant differences between clusters were observed in biomedical factors (having diabetes: $p = .005$; dyspnea: $p \leq .001$), psychological factors (depression severity: $p \leq .001$; anxiety severity: $p \leq .001$), and the persistence of somatic symptoms for at least six months ($p \leq .001$). Comparing biomedical and psychological factors concerning the identified clusters showed that individuals with a medical predisposition experienced biomedical symptoms but those with higher symptom burden were more likely to suffer additionally from psychological factors. Independently of sociodemographic, biomedical, and psychological factors, increased symptom burden was associated with more frequent general practitioner visits ($\beta = .172$; $p = .002$) and worse physical quality of life ($\beta = -.417$; $p \leq .001$). However, cluster affiliation was not associated with mental quality of life ($\beta = .023$; $p = .565$).

Discussion

This study aimed to enhance the understanding of somatic symptom disorder (SSD) symptoms in individuals at risk for heart failure. Three distinct clusters based on SSD criteria were identified, representing a range from none to moderate and severe SSD symptoms. Both biomedical and psychological factors were found to significantly influence the severity of SSD symptoms, regardless of the individual's risk for heart failure. Increased severity of SSD symptoms was linked to more frequent general practitioner visits. This result supports previous research that underscores the challenge of diagnosing SSD in individuals with medical predispositions due to the diversity and overlap of symptoms. A longitudinal study could provide valuable insights into prognostic factors and disease progression. Future research should focus on the diagnosis and prevalence of SSD in individuals with somatic comorbidities. Additionally, efforts to improve healthcare utilization should include identifying the specific needs of subgroups with SSD symptoms and addressing the needs of healthcare professionals to reduce uncertainties in the diagnostic process.

4.3 Summary Study III

Clifford, C., Girdauskas, E., Klotz, S.G., Kurz, S., Löwe, B. & Kohlmann, S. (2024). Patient-centered evaluation of an expectation-focused intervention for patients undergoing heart valve surgery: a qualitative study. *Frontiers in Cardiovascular Medicine, 11,* 1338964.

Background and aims

Research has demonstrated that expectations significantly impact treatment outcomes, irrespective of the individual's medical condition or type of surgical procedure. Negative expectations are linked to more complications, decreased quality of life, greater illness-related disability, increased depressive symptoms, and longer periods of inability to work. To address these challenges, randomized controlled trials have compared the effects of expectation-focused interventions with emotion-focused interventions or standard treatments. Findings have shown that expectation-focused interventions can enhance personal control beliefs, improve quality of life, and reduce postoperative pain and hospital stays. Understanding the perspective of affected individuals seems crucial for effective integration into routine healthcare. This qualitative study aimed to explore individuals' evaluations of an expectation-focused intervention within the context of heart valve surgery.

Methods

Eighteen individuals from a multicenter randomized controlled trial aimed at improving treatment for heart valve surgery were included in this qualitative study. Eleven of these individuals received an expectation-focused intervention as part of an Enhanced Recovery After Surgery (ERAS) program, the other seven participants were part of the control group. Both, individuals of the intervention and control group were included to minimize potential bias related to treatment experiences. A purposive sampling strategy was applied, considering factors such as age, gender, and disease experience, to ensure diverse representation. Semi-structured interviews were conducted approximately six weeks after heart valve surgery, covering topics such as feasibility, acceptance, barriers, benefits, and side effects. The interviews were transcribed and analyzed using Kuckartz's qualitative content analysis methodology (Kuckartz, 2014).

Results

Through qualitative content analysis, five key themes emerged as particularly relevant to the individuals: personal needs, expectations and emotions, relationship, communication, and individuality. Individuals' personal needs showed considerable variation, ranging from no perceived need for the intervention to strong recommendations for incorporating an expectation-focused approach into routine care. Regarding expectations and emotions, individuals valued the opportunity to express their feelings and the preparation for potential side effects of the surgery. They reported an increased sense of self-efficacy but noted challenges in aligning their expectations with the actual outcomes post-surgery. Establishing a trusting relationship was seen as challenging, with some individuals feeling stigmatized by the involvement of a psychologist in their heart valve surgery process. In terms of communication, individuals highlighted the importance of clear and transparent dialogue, as well as the sensitivity of language used. While some desired a more personalized approach, others felt the intervention was effectively tailored to their needs. Additionally, individuals appreciated the interprofessional approach and the involvement of their relatives. Almost all of them (94%) expressed a willingness to participate in an expectation-focused intervention (again) if offered. To enhance the intervention, individuals suggested incorporating stress management and breathing exercises. A further idea would be the introduction of a buddy system where they could share experiences with others who have already successfully underwent heart valve surgery.

Discussion

Overall, individuals found the expectation-focused intervention to be beneficial, with no adverse effects reported. The identified themes suggest that they appreciated both the content of the intervention and the presence of a psychologist as a contact person. However, challenges included stigmatization, establishing a trusting relationship within a limited timeframe and clarifying the individuals' benefits at the beginning of the intervention. To enhance the intervention and make it more personalized, future research should consider taking sociodemographic, disease-specific, and psychosocial variables into account. Developing a modular approach that allows for a participatory decision-making process regarding the intervention's content could be a valuable direction for future studies.

5. DISCUSSION

The overall aim of this dissertation was to gain a deeper understanding of the symptom burden in individuals with or at risk of cardiac disease, as well as identifying the needs of this target group. Specifically, the goal was to determine whether distinct subgroups based on symptom burden exist within this population (research question I) and to explore which biomedical and psychological factors are associated with symptom burden (research question II). Additionally, the aim was to understand the relationship between symptom burden, and healthcare utilization as well as quality of life in individuals with or at risk of cardiac disease (research question III), and to learn more about their specific needs (research question IV). To address these objectives, three studies were conducted: a longitudinal study examining the characteristics and predictors of individuals with cardiac disease who experience persistent somatic symptoms (Study I), a cross-sectional, population-based cohort study investigating symptoms of somatic symptom disorder in individuals at risk for heart failure (Study II), and a qualitative study evaluating an expectation-focused intervention from the perspective of individuals undergoing heart valve surgery (Study III).

5.1 Summary and critical reflection of the results

With respect to research question I, Studies I and II aimed to identify subgroups of individuals with or at risk of cardiac disease who experience an increased symptom burden. The findings revealed that among individuals with cardiac disease, one-third of the study sample exhibited persistent somatic symptoms over a three-month period (Study I). In individuals at risk for heart failure, distinct subgroups were identified differing by the severity of somatic symptom disorder symptoms (Study II). These results suggest that varying levels of symptom burden can exist, even among individuals with similar medical predispositions to cardiac disease.

Addressing the research question II, biomedical and psychological factors between individuals with lower and higher symptom burden were compared in Studies I and II. Regarding biomedical factors, increased symptom burden was associated with subjectively reported symptoms such as more severe angina pectoris and dyspnea. However, objective biomedical markers such as the number of cardiac diseases, comorbidities, or medications did not show a significant association with symptom burden. All psychological factors included in the analyses in both studies were significantly associated with symptom burden. Higher symptom burden was linked to increased severity of depression and anxiety and a greater number of mental disorders. Study II further explored the overlap between individuals suffering from biomedical and psychological factors. The findings showed that while all individuals with a medical predisposition experienced biomedical symptoms, those with higher symptom burden were more likely to also suffer from psychological factors. In contrast, individuals with lower symptom burden primarily experienced biomedical symptoms without accompanying psychological issues.

Regarding research question III, the Studies I and II found that increased symptom burden was associated with a higher number of outpatient visits. Additionally, in Study II, there was a significant negative association between physical quality of life and symptom burden in individuals at risk for cardiac disease, independent of sociodemographic, biomedical, and psychological factors. However, no such association was observed between symptom burden and mental quality of life in the sample.

Research question IV focused on the needs of individuals with or at risk of cardiac disease. Based on the findings from Studies I and II, it seems crucial for a successful dissemination to engage the target group in understanding what is important to them. In Study III, individuals' perspectives on an expectation-focused intervention which they received during their heart valve surgery were evaluated. Overall, the intervention was perceived as helpful, with no adverse effects reported. The individuals appreciated the preparation for the surgery, awareness of potential side effects, the space to express emotions, and clear and transparent communication. However, establishing a trustful relationship between healthcare professionals and the individuals receiving the intervention seemed challenging but vital for the intervention's perceived effectiveness. A participatory approach that emphasizes the personal benefits of the treatment for the individuals, along with a tailored strategy, appears to be essential for meeting personal needs. A key takeaway from all three studies seems to be that needs can vary greatly, even among individuals who are medically similar, such as those with the same disease, risk for a disease, or undergoing the same treatment.

In the conducted studies, subgroups based on symptom burden within individuals with or at risk of cardiac disease were found. A recently published review aligns with these findings, highlighting the variability of symptom burden among individuals with the same symptoms, underscoring the subjective nature of symptom experience (Löwe et al., 2024). Other studies also support the results, indicating that symptoms are primarily grouped by severity (DeVon et al., 2017). However, one study examining individuals with chronic obstructive pulmonary disease found that increased symptom burden was associated with a more severe stage of the disease (Melhem et al., 2021). While that study focused on a different population, it contrasts with the found results, where individuals experienced varying levels of symptom burden even with similar medical predispositions.

Regarding research question II, the findings of the conducted studies highlighted the association of primarily psychological and also biomedical factors with symptom burden in individuals with or at risk of cardiac disease which seems consistent with findings of other studies (Gierk et al., 2014; Kohlmann et al., 2013a; Ladwig et al., 2022). Those have additionally observed associations between symptom burden and functional status, as well as the impact of migration background (Abbott et al., 2010; Barbek et al., 2024; DeVon et al., 2017). Future research should consider these factors, along with a broader range of biomedical and psychological variables, to better understand symptom burden in individuals with medical predispositions like cardiac disease.

The relationship between symptom burden and quality of life is a main focus of research question III. Quality of life is inherently tied to the concept of symptom burden, as symptom burden is often defined by the negative impact it has on an individual's quality of life (Evangelista et al., 2012; Flint et al., 2017; Stockdill et al., 2019). Consistent with the findings of the conducted studies, others also demonstrated that symptom burden, regardless of sociodemographic, biomedical, or psychological factors, significantly affects quality of life, particularly physical quality of life (Kohlmann et al., 2013a). When it comes to mental quality of life, psychological factors, especially anxiety, are more commonly associated, along with other somatic symptoms (Alpert et al., 2017; Al-Sutari & Abdalrahim, 2024). Recent studies have highlighted fatigue and sleep problems as significant factors influencing both physical and mental quality of life (Al-Sutari & Abdalrahim, 2024). Additionally, some research suggests that symptom burden may be a better measure for evaluating interventions than quality of life, arguing that while quality of life is a more stable construct, symptom burden could more accurately reflect the effectiveness of an intervention (Cleeland, 2007; Zambroski et al., 2005).

The other focus of research question III was the association between symptom burden and healthcare utilization. While previous research has not been entirely consistent, some studies have found an association between higher symptom burden and increased healthcare utilization (Gierk et al., 2014; Löwe et al., 2022b). The findings of the conducted studies also support the association between individuals with or at risk of cardiac disease who experience higher symptom burden and more frequent healthcare utilization. A tailored approach to treatment, including its extent, seems crucial in managing symptom burden effectively. Specialized care has shown significant positive outcomes for treating symptom burden, but in clinical settings, late recognition and fragmented treatment often seem to hinder the process (Fränkl et al., 2024; Kustra-Mulder et al., 2023; Löwe et al., 2022a). The conducted studies suggest that individuals with similar medical predispositions often experience varying levels of symptom burden. However, determining which individuals would benefit most from specific treatments and at what intensity – aiming to avoid over-, under-, or mistreatment – remains an important area for further investigation.

With respect to research question IV, Study III identified several needs expressed by individuals undergoing cardiac surgery regarding expectation-focused interventions. These needs align with those identified in other studies on disseminating person-centered care, which often emphasizes individuality, a holistic approach, effective communication, and shared decision-making (Grover et al., 2022). Additionally, these studies explored the broader impacts on the healthcare system, including the training required for healthcare professionals and the cultural changes necessary within the healthcare system (Grover et al., 2022). Another study examined the needs of individuals with cardiac disease alongside those of healthcare professionals, categorizing these needs into so called personas that represent different attitudes from the target group: a) those who need and want support, b) those who have accepted their situation and seek help as needed, and c) those who feel neglected by the healthcare system (Engelmann et al., 2023). That study, which incorporated perspectives from healthcare professionals in the interviews, similarly demonstrates that individuals with the same medical condition can have markedly different needs and responses, just as the findings of the conductes studies seem to reveal.

Theoretical frameworks define symptom burden in terms of prevalence, frequency, and severity of symptoms (Gapstur, 2007). Despite evidence from numerous studies, including those discussed above, indicating a notable impact of psychological factors on the experience of symptom burden, these factors are often not part of conceptual models explaining the development of symptom burden (Ladwig et al., 2022; Müller-Tasch et al., 2024; Stockdill et al., 2019). This suggests that current definitions of symptom burden may not fully capture its complexity or the range of influencing factors. Some studies have attempted a more nuanced approach, such as Sarenmalm et al. (2014), who introduced categories like emotional, gastrointestinal, and general symptom burden. However, it remains uncertain whether such distinctions can be effectively maintained, particularly in clinical settings. Further research indicates that vital exhaustion, defined by excessive fatigue, increased irritability, and feelings of demoralization, seems to be a relevant psychological risk factor for cardiac disease (Appels et al., 1987; Cohen et al., 2017; Frestad & Prescott, 2017).

Considering this construct into the evaluation of symptom burden in individuals with cardiac disease seems valuable.

Measuring as well as understanding the development of symptom burden is challenging due to the need to account for various relevant factors, particularly the subjective nature of symptoms and their perceived burdensomeness. While validated instruments, such as the SSS-8 and SSD-12, which we used in our studies, exist, other tools vary in the symptoms they assess and sometimes do not include psychological factors, despite their importance. Involving the target group in the development or evaluation of instruments is recommended to improve feasibility. Additionally, adjusting cut-off values for groups with medical predispositions may enhance the accuracy of interpretations.

In addition to exploring ways to identify individuals with increased symptom burden and addressing their needs within the healthcare system, it also seems important to better understand how individuals make decisions when experiencing symptoms or increased symptom burden. For example, it could be valuable to investigate the circumstances and time points when individuals choose to seek help from healthcare professionals and which other strategies they consider (Kalantar-Zadeh et al., 2022). Previous studies showed that different self-management strategies are influenced by factors such as the individual's concept of their disease, the perceived level of uncertainty, personal attributes, and how they communicate with healthcare professionals (Wingham et al., 2014). Research indicates that poor self-management is associated with increased symptom burden, while greater self-care helps individuals to better recognize changes in their symptoms, including their frequency and severity (Ladwig et al., 2022; Li et al., 2023; Zambroski et al., 2005). Promoting effective self-care without fostering excessive focus on somatic symptoms or related health concerns might be beneficial. To enhance self-care behaviors, studies have identified that educating individuals about their conditions and setting realistic expectations, along with interventions aiming at improving self-confidence and self-efficacy, are effective strategies (Humphreys et al., 2014; McGreal et al., 2014; Salzmann et al., 2020; Song et al., 2010; Zambroski et al., 2005).

There are probably additional factors that influence symptom perception, decision-making, and healthcare utilization. One such factor could be stigmatization. It is well-known that stigmatization reduces the likelihood of individuals seeking help, while increased acceptance of symptoms and conditions is associated with higher remission rates (Eger Aydogmus, 2020; Löwe et al., 2022b; Naskar et al., 2020). Allowing for somatic comorbidity within the SSD diagnosis and adopting a standardized, holistic treatment approach appears to reduce stigma (Löwe et al., 2022b; Ohanyan et al., 2021). Based on the findings in Study III, it also seems possible that stigmatization is an underlying but significant factor influencing the decision-making process of individuals seeking healthcare. This suggests that further integration of holistic treatment approaches could be beneficial. Moreover, effective communication, the choice of words, and the establishment of a trustful relationship appear to influence experiences of stigmatization, which should be taken into account when interacting with individuals receiving treatment (Löwe et al., 2024; Zipfel et al., 2016).

5.2 Strengths and limitations

This dissertation contributes empirical evidence to the understanding of symptom burden and needs in individuals with a medical predisposition. Two different methodological approaches to examine persistent somatic symptoms (PSS) in individuals with cardiac disease were employed. Particularly valuable was the ability to gain deeper insights into the characteristics and predictors associated with individuals with cardiac disease and PSS, as the data was collected longitudinally over three months (Study I). While somatic symptom disorder (SSD) has been increasingly studied in the general population and to some extent in individuals with somatic comorbidities, Study II expands on this by closely examining SSD symptoms in individuals at risk for cardiac disease. This "at-risk" group is of special interest, as early identification of SSD is linked to higher remission rates. Finally, a qualitative study was conducted in which individuals undergoing cardiac surgery who received an expectation-focused intervention were asked about their experiences and needs (Study III). Although expectation-focused interventions have shown positive health-related outcomes in other studies, understanding the perspectives of those receiving the intervention seems critical for a successful dissemination.

One limitation arises from the fact that Study I was a secondary analysis and Study II utilized a pre-existing dataset from a population-based cohort study. Consequently, no clinical interviews were conducted to confirm the diagnosis of SSD, preventing the estimation of SSD prevalence rates within the target group. In Study I, the secondary analysis restricted the longitudinal data collection to a three-month period. Extending the assessment period to six months could enhance the understanding of the development of somatic symptoms in this population.

The analyses were primarily based on questionnaires, which are known for their validity and reliability, yet they depend on self-reported data. Given that the studies focused on symptom burden, a concept characterized by its subjective nature, this approach likely did not introduce significant bias into the results. In Study II, the persistence of symptoms experienced by participants was also examined. Due to the cross-sectional design of the study, the persistence was measured through a single item asking whether individuals had experienced symptoms for at least six months. Comparing the results found in the cross-sectional data with follow-up data from a longitudinal design would be beneficial in understanding how symptom persistence, cardiac disease progression, and symptom burden evolve over time. Such an approach would also provide valuable insights into the stability of the results and the consistency of the identified subgroups.

In all three studies, we cannot confidently assert that there was no bias among the participating individuals. Each study had certain advantages, such as health examinations or newly developed treatment approaches, which may have attracted health-conscious individuals to participate. Furthermore, the sample in Study III was drawn from a randomized controlled trial (RCT) that involved repeated assessments for all participants and enhanced interprofessional treatment for the intervention group. This may have made it challenging for participants to differentiate between the various interprofessional components of the treatment. To mitigate these challenges, individuals from the control group were also included in the study sample, and the interviews included a section that reiterated the specific elements of the expectation-focused intervention being evaluated.

5.3 Practice implications

Beyond its research value, the findings hopefully provide beneficial information for clinical practice. Understanding symptom burden and its predictors, could help to identify individuals and to develop tailored treatment approaches. Involving individuals in the development and dissemination of interventions designed to benefit them allows to recognize challenges and make necessary improvements. Often, symptom burden persists even after the underlying pathophysiology has been treated, highlighting the importance of further exploring symptom burden and individuals' needs (Joustra et al., 2015; Kumar et al., 2013; Löwe et al., 2022a; Löwe et al., 2024). It also seems crucial for healthcare professionals to deepen their understanding and develop clear clinical decision-making guidelines (Kitselaar et al., 2023b).

Based on the literature and the findings of the conducted studies, several key considerations emerge for treating individuals with or at risk of cardiac disease who experience increased symptom burden. Given the subjective nature of symptom burden, a person-centered approach is essential, focusing on the individual's specific symptoms and their impact rather than solely on the clinical diagnosis. Understanding how symptoms interact and what factors contribute to their development or change seems crucial in the clinical setting. Rather than aiming to eliminate all symptoms, prioritizing the most burdensome ones and improving symptom management can be a more realistic goal, ultimately enhancing the individual's quality of life and sense of control. To ensure person-centered treatment, healthcare professionals could gain insights from the perspectives of those experiencing increased symptom burden. From this understanding, a personalized biopsychosocial explanatory model should be collaboratively developed with the individual (Löwe et al., 2024; Wingham et al., 2014). Additionally, literature and the results of the conducted studies suggest potential areas for person-centered treatment, including: addressing dysfunctional symptom and treatment expectations, managing illness-related anxiety, modifying catastrophizing thoughts and somatosensory amplifications, enhancing emotion regulation skills, and addressing early childhood trauma (Behm et al., 2021; Löwe et al., 2024).

The biopsychosocial approach should be integrated not only in interactions with individuals experiencing increased symptom burden but also in the design of their treatment plans. This is particularly important given that research indicates that biomedical, psychological, and potentially additional factors such as health behaviors, contextual influences, and cognitive-perceptual elements are associated with and may predict increased symptom burden (Hüsing et al., 2023; Kitselaar et al., 2023a; Löwe et al., 2024). Future studies could explore how psychological factors and individual needs can be incorporated alongside biomedical assessments in the diagnostic process.

In addition to depression, which is a recognized psychological factor related to symptom burden, functional status also appears to be a significant factor (Schopfer et al., 2016). Creating an environment that supports individuals – by involving family members and healthcare professionals – can help facilitate and sustain lifestyle changes, such as improving exercise capacity or achieving smoking cessation, which in turn can enhance functional status (Schmidt-Trucksäss et al., 2024; Schopfer et al., 2016). It seems important to assess symptoms within the context of the disease stage, as some symptoms, like pain, are often unrecognized or undertreated (Alpert et al., 2017; Al-Sutari & Abdalrahim, 2024; Ladwig et al., 2022). These symptoms, when inadequately addressed, can negatively impact functional status and are closely linked to the individual's overall quality of life (Al-Sutari & Abdalrahim, 2024).

A collaboration among different professions seems important for implementing a holistic treatment approach (Löwe et al., 2024). Building a strong relationship between individuals with increased symptom burden and healthcare professionals seems to enhance adherence and openness. Training programs that emphasize effective communication techniques and validation skills have been shown to be beneficial (Fryer et al., 2023; Löwe et al., 2024). Additionally, the consideration of cultural differences is supported by the literature as an important factor (Kustra-Mulder et al., 2024). Beyond interactions with healthcare professionals, individuals with increased symptom burden also gain significant benefits from support within their social environment, such as from family and friends (Al-Sutari & Abdalrahim, 2024; Schmidt-Trucksäss et al., 2024). The results of the conducted studies also highlight the positive impact of support from relatives.

A key debate in the treatment of somatic diseases is whether psychosocial factors should be screened as routinely as somatic markers. To better understand individuals with or at risk of cardiac disease, screening for psychosocial risk factors – such as low socio-economic status, stress, social isolation, and negative emotions – is recommended, given their association with cardiac disease outcomes (Mesa-Vieira et al., 2021). Early identification of individuals with increased symptom burden through psychosocial screening has furthermore been associated with better remission rates (Kitselaar et al., 2023b). However, arguments against such screening include increased costs, time inefficiency, and potential reluctance of individuals to share personal information during somatic disease treatment. Despite these concerns, qualitative research by Ohanyan et al. (2021) indicated that screening for depressive symptoms was generally well-received by individuals with cardiac disease. The conducted studies also suggest that integrating psychosocial aspects into routine treatment can reduce stigmatization and allow individuals to recognize the personal benefits of these additional efforts.

Evaluations of interventions for individuals with increased symptom burden have shown positive outcomes for those based on cognitive behavioral therapy (CBT) and those incorporating emotion regulation training (Kleinstäuber et al., 2019; Löwe et al., 2024). Additionally, mindfulness-based and acceptance-based CBT have demonstrated improvements in symptom burden (Löwe et al., 2024; Maas genannt Bermpohl et al., 2023). Successful treatment approaches appear to be tailored to the specific needs of individuals with increased symptom burden and often involve an interprofessional approach (Löwe et al., 2024; Schmidt-Trucksäss et al., 2024). Multi-behavioral interventions which combine health education, physical exercise, psychological therapy, stress management, and integration of the social environment, such as the expectation-focused intervention described above, address both biomedical and psychological aspects of the disease (Rief et al., 2017; Salzmann et al., 2020; Schmidt-Trucksäss et al., 2024). The aim of such treatments is to improve biomedical and psychological factors, as both are linked to symptom burden. Positive results from interventions with an interprofessional approach have already been observed in individuals with somatic symptom disorder (Wijnen et al., 2023).

Since somatosensory amplification seems to contribute to the development of increased symptom burden, an intervention known as interoceptive differentiation training was developed to enhance the perceptual differentiation of these interoceptive sensations (Henningsen et al., 2018). The therapeutic relationship is also highlighted as a crucial part of the training, with supportive and trustful interactions providing opportunities for corrective experiences (Henningsen et al., 2018). Enhanced awareness of the mind-body interaction has been supported in the literature, particularly for individuals with increased symptom burden (Hennemann et al., 2023; Löwe et al., 2024; Wortman et al., 2022).

Another potential approach includes the integration of e-health strategies into treatment. While experts advise against replacing direct personal support with e-health solutions, these technologies could help optimize resource allocation within the healthcare system (Ladwig et al., 2022). For instance, interoceptive differentiation training could benefit from virtual reality techniques, which allow individuals to work on interoceptive perceptions while simultaneously receiving exteroceptive input in augmented or virtual reality environments (Henningsen et al., 2018).

Based on the evaluation of individuals receiving expectation-focused interventions, several ideas for further development have emerged. Given the significant emphasis placed by individuals on their personal needs, a modular approach could be beneficial. This would allow individuals, in collaboration with healthcare professionals, to select which aspects of the intervention are most relevant to them personally. To address the potential stigmatization associated with making use of psychological support, it would be beneficial to offer a core set of modules while providing additional options based on individual interests or goals. Research indicates that tailoring content for individuals with specific issues such as increased depression or anxiety is effective (Auer et al., 2016). Additionally, the intervention could be expanded to include more detailed information about the surgical process, stress management education, and breathing exercises. The aim would be to provide a comprehensive yet manageable amount of information (Wingham et al., 2014). Another promising idea is the implementation of a buddy system, where individuals preparing for surgery are paired with those who have successfully completed the process (Klein et al., 2021). For future research, focusing on identifying subgroups of individuals with varying needs related to cardiac surgery could offer relevant benefits for clinical practice. Understanding which individuals would benefit from specific types, extents, and frequencies of expectation-focused interventions may lead to more efficient resource utilization within the healthcare system. Considering sociodemographic, disease-related, and psychosocial factors in subgroup identification could enhance the effectiveness of these interventions.

While research helps to identify factors associated with or increasing the risk of symptom burden, it is important not to overinterpret these findings. The aim is to recognize patterns and subgroups to enhance healthcare efficiency and tailor treatments to individual needs. However, maintaining a focus on individual differences is essential. This consideration is crucial when individuals interact with healthcare professionals and becomes even more complex as their conditions evolve and progress, which can be challenging to predict (Ladwig et al., 2022).

Several studies have identified factors linked to poor treatment outcomes in individuals with increased symptom burden. These factors included psychological issues such as comorbid depressive and anxiety disorders, catastrophizing, tendencies towards somatosensory amplification, low symptom acceptance, and low self-efficacy (Löwe et al., 2024; Sarter et al., 2021; Sarter et al., 2022). Social factors also contributed to poor treatment results, including low educational attainment, low socioeconomic status, and inadequate access to healthcare (Löwe et al., 2024). Additionally, a longer duration of reported symptoms, high symptom intensity prior to treatment, and low physical functioning have also been highlighted as significant factors (Löwe et al., 2024). Regarding the role of healthcare professionals, dismissive attitudes toward the individuals' concerns, overly pessimistic outlooks on health-related outcomes, or exaggeration of treatment of rare side effects have been associated with negative treatment results (Elsenbruch & Enck, 2015; Löwe et al., 2024; Stone et al., 2020).

Future research on characteristics and predictors of increased symptom burden, should include a broader range of biomedical, psychological, and other contributing factors (Kitselaar et al., 2023a). The classification proposed by Kitselaar et al. (2023a) could serve as a useful starting point for identifying which factors to assess. This classification includes not only biomedical and psychological factors but also interpersonal, contextual, and health behavior factors that are associated with increased symptom burden. Initial findings suggest that factors such as age at onset, duration of untreated illness, sleep problems, illness anxiety, alexithymia, emotion regulation difficulties, and avoidance behaviors may be linked to increased symptom burden (Kitselaar et al., 2023a; Löwe et al., 2022b; Smakowski et al., 2024). Additionally, risk factors identified in the literature include catastrophizing, heightened symptom focus, migration background, and loneliness (James et al., 2022; von dem Knesebeck et al., 2023; Vos et al., 2023). It also seems important to consider the influence of culture and social support on the experience of symptom burden (Al-Sutari & Abdalrahim, 2024; DeVon et al., 2017). Given that beliefs about illness and stigmatization appear to play significant roles, future research should focus on these aspects when studying symptom burden and developing interventions for individuals experiencing increased symptom burden (von dem Knesebeck et al., 2023).

Assessing and diagnosing increased symptom burden seems to be an important aspect in the clinical setting. Therefore it may be beneficial to explore how symptoms interact and form clusters, as these dynamics could impact the development of symptom burden. There is a scarcity of studies investigating the prevalence of conditions associated with increased symptom burden, such as somatic symptom disorder, in individuals with or at risk of somatic diseases (Löwe et al., 2022b). Measuring symptom burden presents challenges, as various instruments are currently used without a standardized approach. Future research could focus on determining a more effective way to measure symptom burden and assess whether screening for symptoms would be advantageous in a clinical setting.

In addition to the expectation-focused intervention previously described, some other findings concerning interventions designed for individuals with increased symptom burden were mentioned. Continuing to refine these approaches by involving the affected individuals in the dissemination process seems a promising strategy. Developing a deeper understanding of subgroups, while still recognizing the individuality and providing personalized approaches, is likely to be beneficial. Furthermore, considering the economic aspects of healthcare utilization in future research could also be valuable.

5.4 Conclusion

The aim of this dissertation was to better understand symptom burden and needs in individuals with or at risk of cardiac disease. Numerous studies have demonstrated that increased symptom burden is associated with higher mortality rates, more frequent hospitalizations, and reduced quality of life, regardless of biomedical markers. Additionally, research indicates that factors such as the presence of somatic disorders or elevated psychosocial risk factors are linked to increased symptom burden. Identifying increased symptom burden in individuals with or at risk of cardiac disease presents a challenge, as the etiology of cardiac disease and increased symptom burden differs significantly, yet their phenomenologies often overlap. Beyond gaining a deeper understanding of the characteristics and predictors of increased symptom burden, this dissertation also aimed to better understand the needs of these individuals.

The dissertation included three studies: Study I focused on identifying characteristics and predictors of increased symptom burden in individuals with cardiac disease. The longitudinal study design allowed for an analysis of the predictive value of the included factors over time. Study II used data from a population-based cohort study of individuals at risk for cardiac disease. By examining the symptoms of somatic symptom disorder, this study identified different levels of symptom burden and explored the differences in characteristics, quality of life, and healthcare utilization among these groups. Finally, Study III provided insights into the needs of individuals undergoing cardiac surgery by evaluating an expectation-focused intervention using a qualitative approach.

Through this combination of studies, the aim was to identify subgroups related to symptom burden in individuals with or at risk of cardiac disease and determine which biomedical and psychological factors are associated with symptom burden in this population. Additionally, the relationship between increased symptom burden and healthcare utilization as well as quality of life was explored. And finally, the goal was to provide insights into the needs of individuals with or at risk of cardiac disease.

In the conducted studies, the identified subgroups related to symptom burden among individuals with or at risk of cardiac disease. These subgroups primarily differed in the severity of symptom burden experienced, rather than in the specific symptoms themselves. Both biomedical and psychological factors appear to be important in relation to increased symptom burden. Notably, subjectively experienced factors, such as the severity of depression and anxiety, as well as self-reported functional impairments like increased dyspnea and angina pectoris, were associated with higher levels of symptom burden. However, other biomedical factors, such as the increased risk of developing cardiac disease, the number of comorbidities, or medication use, were not significantly associated. Findings also showed that, regardless of sociodemographic, biomedical, and psychological factors, there was a significant association between increased symptom burden and higher healthcare utilization, as well as a decrease in physical quality of life. A decrease in mental quality of life was better explained by psychological factors than the increased symptom burden itself. Regarding the needs of individuals with or at risk of cardiac disease, the findings highlight the high degree of individuality in this population. Even among those with similar symptoms, the experienced symptom burden seemed to vary greatly, and individuals receiving the same treatment described different needs from one another. However, some aspects appear to be universally important, such as transparent communication, building a trusting relationship, and the benefits of an interprofessional, holistic treatment approach.

Future research could explore more deeply the biomedical and psychological factors associated with increased symptom burden, as well as incorporate additional factors to better understand their relationship and predictive value. Gaining insight into the etiology, development, and prevalence of increased symptom burden in individuals with or at risk of cardiac disease would be beneficial for the clinical setting. Studies that focus on the economic aspects of healthcare utilization in treating individuals with increased symptom burden might provide new perspectives on the potential over- or undertreatment of these individuals. To support a successful dissemination of developed treatment approaches, involving the individuals receiving the interventions in the process seems advantageous. The findings of the conducted studies and the existing literature support a biopsychosocial and interprofessional approach, which is person-centered and includes educational aspects. Additionally, understanding the impact of stigmatization and strategies to potentially mitigate it could prove valuable. Lastly, future research should consider evaluating the construct of symptom burden itself, exploring methods for measuring it, and determining whether screening for symptom burden would be beneficial in clinical settings.

Overall, this dissertation supports the idea of a holistic view including biomedical and psychological aspects in diagnosis and treatment. The findings suggest a more individualized approach that emphasizes the symptoms and experiences of individuals rather than focusing on the diagnosis or biomedical markers only. Additionally, it highlights the importance of involving individuals in their treatment and its development to better address their personal needs.

6. LIST OF ABBREVIATIONS

ARIC	Atherosclerosis Risk in Communities
CBT	Cognitive behavioral therapy
CCS	Canadian Cardiovascular Society Angina Grading Scale
ERAS	Enhanced Recovery After Surgery
GAD-7	Generalized Anxiety Disorder Scale-7
HCHS	Hamburg City Health Study
LVEF	Left ventricular ejection fraction
NT-proBNP	N-terminal pro B-type Natriuretic Peptide
PHQ-9	Patient Health Questionnaire-9
PSS	Persistent Somatic Symptoms
RCT	Randomized Controlled Trial
SSD	Somatic Symptom Disorder
SSD-12	Somatic Symptom Disorder – B Criteria Scale
SSS-8	Somatic Symptom Scale-8

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8. APPENDIX

8.1 Studies

Study I

Characteristics and predictors of persistent somatic symptoms in patients with cardiac disease.

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Characteristics and predictors of persistent somatic symptoms in patients with cardiac disease

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Persistent somatic symptoms (PSS) are a diagnostic core criterion of the somatic symptom disorder. This longitudinal study aims to determine the frequency of PSS in patients with cardiac disease, identify potential predictive factors, and investigate its impact on healthcare utilization. Somatic symptoms were assessed with the Somatic Symptom Scale-8 four times over the course of three months in consecutively approached cardiac outpatients. Patients were grouped having PSS vs. not having PSS following a psychometric-driven approach based on the SSS-8 cut-off score and a data-driven approach applying cluster analysis. T-tests were performed to compare the characteristics between patients having vs. not having PSS. To identify predictors of group affiliation, we conducted multivariable logistic regressions. Additionally, analyses of covariance were used to further examine associations between healthcare utilization and group affiliation. The study included 95 patients (30.5% female) with a mean age of 60.5 years ($SD=8.7$). All patients had at least one of the following cardiac diseases recorded in their medical history: coronary heart disease ($n=51$), myocardial infarction ($n=21$), valve disease ($n=22$), cardiomyopathy ($n=15$), cardiac dysrhythmia ($n=43$), and heart failure ($n=12$). 30 (32%) were grouped having PSS according to the psychometric-driven approach and 27 (28%) according to the data-driven approach. For both approaches, patients with PSS were more likely to be female, unemployed, reporting angina pectoris, having higher depression, and higher anxiety severity (for all: $p\leq 0.05$). Predictors of PSS group affiliation were female gender, higher age, depression severity, and angina pectoris (for all: $p\leq 0.015$). Patients with PSS more frequently visited general practitioners and cardiologists compared to patients without PSS ($p\leq 0.013$). Enhancing our knowledge of PSS in patients with cardiac disease could help to improve identification of patients' specific needs and the factors to consider in diagnosis and individualized treatment.

Keywords Cardiac disease, Cluster analysis, Depression, Healthcare utilization, Somatic Symptom Scale-8, Persistent somatic symptoms

Abbreviations

CCS	Canadian Cardiovascular Society
GAD-7	Generalized Anxiety Disorder Scale-7
PHQ-9	Patient Health Questionnaire-9
PSS	Persistent somatic symptoms
SSD	Somatic symptom disorder
SSS-8	Somatic Symptom Scale-8

Approximately 23% of patients visiting general practitioners in Germany are affected by somatic symptom disorder (SSD)[1]. One of the diagnostic criteria for somatic symptom disorder, as outlined in the DSM-5, is the persistence of somatic symptoms[2]. Identifying SSD in individuals with cardiac disease poses a particular challenge due to the high diversity of symptoms and the overlap of phenomenology with SSD. Given the lack of evidence regarding persistent somatic symptoms (PSS) in patients with cardiac diseases, the objective of this longitudinal study is to approach a definition, approximate the prevalence, and examine the associated characteristics of PSS.

The prevalence of subjective somatic symptoms in patients with cardiac disease is high and comparable to those of patients with cancer[3,4]. Independent of cardiac disease markers, subjective somatic symptoms are

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associated with death and hospitalization[5–7]. From other somatic diseases, it is well known that, in particular, the persistence of somatic symptoms carries far-reaching consequences such as a more severe course of the disease, increased need of clinical treatment, and increased mortality risk[8–10]. Persistent somatic symptoms (PSS) are defined as "subjectively distressing somatic complaints, irrespective of their etiology, that are present on most days for at least several months"[10]. Löwe et al.[10] described the operationalization of PSS through somatic symptom severity experienced by the patient. PSS predict functional impairment, disability, decreased quality of life, and a higher probability of developing affective disorders[3,11,12].

Somatic symptoms result from a complex interplay of biological, psychological, and social processes[13]. According to the model by Löwe et al., which describes risk factors and mechanisms for somatic symptom persistence, sociodemographic, psychosocial, and biomedical factors play a key role in developing short-term somatic symptoms[10]. Other psychosocial and biomedical factors such as cognitive-perceptual and emotional mechanisms or disease-specific factors as well as personal expectations, increase the chances of developing PSS[10]. According to the model, it could be valuable to understand the development of PSS in patients with cardiac disease. So far, the model has already been applied to other somatic diseases such as chronic kidney disease, primary biliary cholangitis, irritable bowel syndrome, and ulcerative colitis[14–16].

From a healthcare perspective, it also appears essential to examine PSS in patients with cardiac disease: Unsatisfactory encounters with the healthcare system and adverse treatment experienced by patients with PSS often result in unnecessary, frequent, and potentially harmful overuse of healthcare which engenders substantial costs[17–19]. It is understood that individuals with PSS commonly seek assistance from their general practitioners[20]. Further research into the actual healthcare situation of patients with cardiac disease and PSS is warranted to facilitate early identification and the development of patient-oriented interventions[18,21].

To date, predicting the occurrence of PSS in patients with cardiac disease remains a challenge. By gaining insight into the predictors for group affiliation, specifically identifying which patients develop PSS and which do not, we can infer the underlying factors and needs of this patient group. Research has so far focused on the consequences of PSS in different patient groups such as increased mortality and higher probability of developing affective disorders[3,10]. This study will focus on the characteristics and predictors of patients with PSS.

The objective of this longitudinal study is to determine PSS in patients with cardiac disease over a time period of three months. In addition to approximating a definition of PSS in this longitudinal study, the aim is also to approximate the prevalence of PSS in patients with cardiac disease. Associations of psychological factors, as well as cardiac characteristics and comorbidities with somatic symptoms, are tested as predictors for PSS. The following research questions are examined exploratively:

1. Which biomedical and psychological factors characterize patients with cardiac disease who report persistent somatic symptoms?
2. Which biomedical and psychological factors predict persistence of somatic symptoms over the course of three months in patients with cardiac disease?
3. Do patients with cardiac disease with persistent somatic symptoms report more healthcare utilization compared to patients without persistent somatic symptoms?

Materials and methods

Design

Outpatients from the University Heart Center and from a non-university cardiac outpatient clinic in Hamburg (Germany) who had a regular consultation appointment were approached by telephone. Patients with a cardiac disease according to medical records, or with at least two risk factors for developing coronary heart disease were contacted. Data from patients was included in the analyses if a cardiac disease had been confirmed during consultation. Further inclusion criteria were 18 years or older, access to a telephone, and sufficient language skills (German). Exclusion criteria were life-threatening health status, a severe somatic or psychiatric disorder requiring urgent treatment, severe cognitive, motoric, or visual difficulties, hospitalization within the previous week, a surgical procedure with at least a three-day hospitalization within the last two months, myocardial infarction within the last three months, any skeletal disease or no written informed consent.

The longitudinal study consisted of four assessments: Two weeks before a regular cardiac consultation, the first data assessment took place via telephone (T0). On the day of the cardiac consultation (T1), the second data assessment was conducted in person. One month (T2) and three months (T3) after consultation, further assessments were conducted by telephone. At each timepoint the following data was collected: the Somatic Symptom Scale (SSS-8), the Patient Health Questionnaire (PHQ-9), the Generalized Anxiety Disorder Scale (GAD-7), and the Canadian Cardiovascular Society (CCS) class. Sociodemographic data was gathered at baseline, while healthcare utilization was assessed at three months after baseline assessment by asking the patients about their visits to a general practitioner and cardiologist over the previous three months. Biomedical factors, including the number of cardiac diseases, were obtained from medical records and had to be confirmed during the cardiac consultation. In the psychometric- and data-driven approach to identify patients with PSS, we included the SSS-8 sum scores from two weeks to three months after baseline assessment (T1 to T3). Data was assessed as part of the Risk Act study (Clinicaltrials.gov identifier: NCT02802254). The study was approved by the Ethics Committee of the Medical Chamber, Hamburg, Germany (PV5199). All methods were carried out in accordance with relevant guidelines and regulations.

Measurements

Sociodemographic data

Patients completed questionnaires assessing sociodemographic data, including age, gender, language, living situation, education, and employment.

Somatic symptom severity

Somatic symptom severity was measured with the Somatic Symptom Scale (SSS-8), which assesses the presence and severity of common somatic symptoms (e.g. back pain, stomach or bowel problems, chest pain, and fatigue)[22]. The SSS-8 is brief, valid, and reliable (*alpha* = 0.81). A cut-off score for identifying somatic symptom burden is set at 4 points[22]. This cut-off score has been validated in cross-sectional studies; there is no empirical cut-off score to define the persistence of somatic symptoms.

Biomedical factors

To measure biomedical factors, the number of cardiac diseases was assessed. Therefore, medical records were screened and the diagnoses had to be confirmed during the cardiac consultation including coronary heart disease, myocardial infarction, valve disease, cardiomyopathy, cardiac dysrhythmia, and heart failure. Furthermore, the number of comorbidities and medications were obtained from medical records. Comorbidities were defined as non-cardiac diagnoses such as liver or kidney diseases, cancer, epilepsy, etc., but also included mental illnesses such as depression, anxiety disorder, or addiction. Additionally, cardiac risk factors such as hypertension, diabetes, hyperlipidemia, smoking, obesity, and positive family history were assessed through self-report.

Cardiac factors

The impairment caused by angina pectoris was rated according to the Canadian Cardiovascular Society (CCS) class[23]. This classification system is an established marker of the functional severity of heart diseases[24]. According to the impairment level, four classes are determined, ranging from 'no impairment at all' to 'impairment even at resting'. As symptom impairment increases, the classes are rated higher.

Psychological factors

The Patient Health Questionnaire (PHQ-9) was used to measure depression severity. The PHQ-9 assesses how often patients have experienced the nine most common depressive symptoms over the previous two weeks. The score range is 0–27 points. Cut-off scores are 5 (mild depression), 10 (moderate depression), and 15 points (severe depression). The PHQ-9 is a valid and reliable instrument[25,26].

The Generalized Anxiety Disorder Scale (GAD-7) was used to evaluate the severity of anxiety over the last two weeks. The score range is 0–21 points. Cut-off scores are 5 (mild anxiety), 10 (moderate anxiety), and 15 points (severe anxiety). The GAD-7 has valid and reliable case-finding properties for the most common anxiety disorders[27,28].

Healthcare utilization

To quantify healthcare utilization, patients were asked at the last follow-up how often they visited a general practitioner and a cardiologist during the previous three months.

Statistical analysis

To define PSS in patients with cardiac disease, two methodological approaches were applied: (a) psychometric-driven approach, based on the cut-off of the SSS-8, and (b) data-driven approach, applying a cluster analysis on the SSS-8 sum scores. By applying two approaches, we aimed to cross-validate our findings concerning PSS. According to the psychometric-driven approach, patients were grouped as having PSS if they scored four points or more on the SSS-8 at all assessment points except for the baseline measurement (PSS group vs. no PSS group). The predictive variables were derived from the baseline data, which is why the baseline measurement of the SSS-8 was not considered in developing the group affiliations. Applying the data-driven approach, patients were grouped according to the results of a cluster analysis (PSS cluster vs. no PSS cluster). Given the exploratory nature of our research question, we opted for a hierarchical cluster analysis using the Ward method, without pre-specifying the number of clusters to be identified. The cluster analysis was conducted using the SSS-8 sum scores for each patient, incorporating data from two weeks to three months after baseline assessments (T1 to T3). Data from the baseline assessment (T0) of the SSS-8 was not included in the cluster analysis, as variables from this time point were used as predictors. Based on the dendrogram and the explained variance observed in the cluster analysis, we identified a two-cluster solution as meaningful regarding the presence of PSS in our population of patients with cardiac disease (see Supplement A and B).

Firstly, descriptive analyses as well as t-tests and chi-squared tests were conducted to identify sociodemographic, biomedical, and psychological characteristics that differentiate between patients with and without PSS longitudinally according to the psychometric- and data-driven approach. Analyses were conducted for both approaches and group affiliation was treated as independent variable in each case.

Secondly, multivariable logistic regression was performed to identify predictors of group affiliation (PSS vs. no PSS). Concerning the biomedical factors, the following predictors were entered into the model: the number of cardiac diseases, cardiac risk factors, comorbidities, and medication, as well as angina pectoris defined by the CCS class. As psychological factors depression severity (PHQ-9) and anxiety severity (GAD-7) were entered. To understand which factors contributed to predicting PSS, we used group affiliation based on the SSS-8 sum scores as the dependent variable in the logistic regression. The model was adjusted for age and gender. Two models, according to the psychometric-driven and the data-driven approach, were analyzed.

As a third step, correlations and analyses of covariance (ANCOVA) were performed to test the association between PSS group affiliation (predictor) and healthcare utilization (outcome). Direct maximum likelihood estimation was applied to handle missing follow-up data. Missings were at random, ranging between one and fifteen percent. Two-tailed p-values < 0.05 were considered significant. We used SPSS 27 for statistical analyses. Multicollinearity and further statistical prerequisites were tested. As a sensitivity analysis, the groups of patients with and without PSS were formed, excluding three items from the SSS-8 which are related to cardiac disease (chest pain or shortness of breath, dizziness, feeling tired or having low energy)[3]. Excluding these items did not show differences in the results. The data that supports the findings of this study is available on request from the corresponding author.

Results

Sample

In total, 270 outpatients having a regular cardiac consultation were approached via telephone and were asked to participate in a regular data assessment over a three-month time period. Of those, 95 were eligible and gave informed consent. Others were excluded due to missing informed consent ($n=120$), language difficulties ($n=18$), missing contact details ($n=9$), severe somatic disease ($n=9$), skeletal disease ($n=9$), no cardiac disease ($n=6$), an operation within the last two months ($n=2$), a myocardial infarction within the last three months ($n=1$) or a life-threatening status ($n=1$). There was no drop-out during the longitudinal study and all 95 patients participated in the three-month assessment. As the data derives as a secondary analysis, we conducted a post-hoc power analysis to determine the statistical power. Given a sample size of $n=95$, our analyses showed a power of $1-\beta=0.70$ to detect medium-sized effects ($R^2=0.13$) on identifying groups (with PSS vs. without PSS) when testing nine predictors in logistic regression models[29]. Given a sample size of $n=95$, our analyses showed a power of $1-\beta=0.67$ to detect medium-sized effects ($f=0.25$) in the conducted ANCOVAs. Regarding the recommended sample size for conducting cluster analysis, research suggests that traditional assumptions about statistical power only apply partially. However, a range of 20–30 observations per expected subgroup is generally advised to ensure meaningful and stable results[30].

According to the psychometric-driven approach, $n=30$ (32%) of the patients had 4 points or above on the SSS-8 at all assessment points included. According to the data-driven definition of PSS, $n=27$ (28%) of the patients were assigned to the PSS cluster. The overlap concerning group membership between both approaches was 95%.

Table 1 summarizes the characteristics of the sample for all patients and according to the psychometric-driven and data-driven approach for PSS definitions.

In addition, we took a closer look at the distribution of the somatic symptom severity according to the Somatic Symptom Scale (SSS-8) in the sample for all patients and according to the psychometric-driven and data-driven approach for PSS definition. The scale for each item stretches from 0 (“not at all”) to 4 (“very much”) describing how much the patient has been disturbed by the somatic symptom during the previous seven days. The average sum score calculated through the eight items for all patients is 6.5 points ($SD=5.2$ points). For patients with PSS, the sum score is between 11.6 points ($SD=4.6$ points) for the psychometric-driven approach and 12.7 points ($SD=4.0$ points) for the data-driven approach. For patients without PSS, the sum score is between 4.1 points ($SD=3.3$ points) and 4.2 points ($SD=3.6$ points). The results show a higher symptom severity in patients with PSS for every assessed symptom except headache. Further details can be seen in Table 1.

Biomedical and psychological characteristics of patients with and without PSS

Patients with and without PSS differed at baseline concerning gender, employment status, angina pectoris (CCS class), somatic symptom severity, and psychological factors. Patients with PSS were more likely to be female, unemployed, to suffer from more severe angina pectoris, to describe higher somatic symptom severity, and to show higher depression and anxiety scores (for all tests; $p<0.005$). These differences could be found both in the psychometric-driven and data-driven grouping approach. Groups did not differ significantly regarding age, further sociodemographic information, and clinical characteristics such as cardiac diseases, comorbidities, medication, and cardiac risk factors. Further details can be seen in Table 1.

Biomedical and psychological factors as predictors of PSS

To visualize the differential effects of biomedical and psychological factors in patients with PSS, the unstandardized regression coefficients and confidence intervals are displayed in Fig. 1. Predictors entered in the model were age, gender, cardiac risk factors, number of cardiac diseases, comorbidities, and medication as well as depression, anxiety, and angina pectoris scores. To predict group membership for PSS for patients according to the psychometric-driven approach, the regression model showed good prediction abilities (*-2 Log-Likelihood* = 54.9; *Cox & Snell* $R^2=0.488$; *Nagelkerkes* $R^2=0.685$). Positive prediction abilities were also seen in the prediction of PSS for patients according to the data-driven approach (*-2 Log-Likelihood* = 49.2; *Cox & Snell* $R^2=0.491$; *Nagelkerkes* $R^2=0.705$). Stable predictors for PSS according to the psychometric-driven approach were age ($OR=1.18$; $p=0.005$), gender ($OR=0.04$; $p=0.001$), PHQ-9 depression score ($OR=1.58$; $p=0.001$) and CCS class indicating the severity of angina pectoris ($OR=2.99$; $p=0.010$). Stable predictors for PSS according to the data-driven approach were similar: age ($OR=1.16$; $p=0.015$), gender ($OR=0.06$; $p=0.002$), PHQ-9 depression score ($OR=1.68$; $p=0.001$) and CCS class indicating the severity of angina pectoris ($OR=3.21$; $p=0.005$). To adjust for multiple comparisons, the significance level was interpreted according to the Benjamini Hochberg formula[31].

Association of persistent somatic symptoms with healthcare utilization

As can be seen in Fig. 2, the groups with and without PSS according to the psychometric-driven and data-driven approach, were compared regarding outpatient visits.

Based on the psychometric-driven approach, patients with PSS showed a mean of 2.9 ($SD=3.0$) visits to a general practitioner within a three-month period compared with 1.3 ($SD=1.5$) visits on average for patients without PSS ($p=0.008$). Patients with PSS showed a mean of 2.2 ($SD=2.1$) visits to a cardiologist within a three-month period compared with 0.9 ($SD=0.8$) visits on average for patients without PSS ($p=0.003$). The ANCOVA

Characteristics	All patients	Groups based on psychometric-driven approach			Groups based on data-driven approach		
		PSS group	No PSS group		PSS cluster	No PSS cluster	
	(n = 95)	(n = 30)	(n = 65)	p value	(n = 27)	(n = 68)	p value
Sociodemographics, n (%)							
Age, mean (SD), years	60.5 (8.7)	60.2 (8.9)	60.7 (8.6)	0.798	59.1 (8.7)	61.1 (8.6)	0.327
Gender, female	29 (30.5)	17 (56.7)	12 (18.5)	< 0.001	16 (59.3)	13 (19.1)	< 0.001
German mother tongue	90 (94.7)	29 (96.7)	61 (93.8)	0.567	27 (100.0)	63 (92.6)	0.148
Living alone	15 (15.8)	6 (20.0)	9 (13.8)	0.445	5 (18.5)	10 (14.7)	0.646
≥ 10 years of formal education	62 (65.3)	20 (66.7)	42 (64.6)	0.845	19 (70.4)	43 (63.2)	0.510
Employed	37 (38.9)	7 (23.3)	30 (46.2)	0.034	6 (22.2)	31 (45.6)	0.035
Clinical characteristics, n (%)							
Coronary heart disease	51 (53.7)	12 (40.0)	39 (60.0)	0.069	10 (37.0)	41 (60.3)	0.040
Myocardial infarction	21 (22.1)	7 (23.3)	14 (21.5)	0.845	6 (22.2)	15 (22.1)	0.986
Valve disease	22 (23.2)	10 (33.3)	12 (18.5)	0.110	7 (25.9)	15 (22.1)	0.687
Cardiomyopathy	15 (15.8)	5 (16.7)	10 (15.4)	0.873	5 (18.5)	10 (14.7)	0.646
Cardiac dysrhythmia	43 (45.3)	16 (53.3)	27 (41.5)	0.283	15 (55.6)	28 (41.2)	0.204
Heart failure	12 (12.6)	6 (20.0)	6 (9.2)	0.142	6 (22.2)	6 (8.8)	0.076
Number of cardiac diseases, mean (SD)	2.1 (1.3)	2.5 (1.6)	2.0 (1.1)	0.125	2.4 (1.6)	2.0 (1.2)	0.246
Number of comorbidities, mean (SD)	2.5 (1.5)	2.5 (1.5)	2.6 (1.6)	0.775	2.5 (1.5)	2.5 (1.6)	0.897
Number of medication, mean (SD)	5.2 (2.7)	6.0 (2.8)	4.9 (2.6)	0.066	5.8 (2.7)	5.0 (2.7)	0.170
Somatic symptoms, mean (SD)							
Somatic symptom severity [SSS-8]	6.5 (5.2)	11.6 (4.6)	4.2 (3.6)	< 0.001	12.7 (4.0)	4.1 (3.3)	< 0.001
Stomach or bowel problems	0.5 (1.0)	1.1 (1.5)	0.2 (0.5)	0.002	1.1 (1.5)	0.2 (0.6)	0.005
Back pain	1.2 (1.2)	1.9 (1.3)	0.8 (1.0)	< 0.001	2.2 (1.3)	0.8 (1.0)	< 0.001
Pain in the arms, legs, or joints	1.1 (1.1)	1.8 (1.2)	0.8 (0.9)	< 0.001	2.0 (1.0)	0.7 (1.0)	< 0.001
Headaches	0.5 (1.0)	0.7 (1.1)	0.4 (0.9)	0.255	0.7 (1.1)	0.4 (0.9)	0.164
Chest pain or shortness of breath	0.9 (1.1)	1.8 (1.1)	0.6 (0.9)	< 0.001	1.8 (1.0)	0.6 (1.0)	< 0.001
Dizziness	0.4 (0.8)	1.0 (1.1)	0.2 (0.5)	0.001	1.0 (1.1)	0.2 (0.5)	0.001
Feeling tired or having low energy	1.0 (1.1)	1.7 (1.1)	0.7 (0.9)	< 0.001	1.9 (1.2)	0.6 (0.8)	< 0.001
Trouble sleeping	0.9 (1.2)	1.6 (1.4)	0.5 (0.9)	< 0.001	1.9 (1.4)	0.5 (0.8)	< 0.001
Cardiac risk factors, n (%)							
Hypertension	68 (71.6)	22 (73.3)	46 (70.8)	0.797	19 (70.4)	49 (72.1)	0.869
Diabetes	21 (22.1)	5 (16.7)	16 (24.6)	0.385	2 (7.4)	19 (27.9)	0.030
Hyperlipidemia	43 (45.3)	16 (53.3)	27 (41.5)	0.283	15 (55.6)	28 (41.2)	0.204
Smoking	30 (31.6)	10 (33.3)	20 (30.8)	0.803	10 (37.0)	20 (29.4)	0.471
Obesity	44 (46.3)	16 (53.3)	28 (43.1)	0.351	13 (48.1)	31 (45.6)	0.821
Family history	32 (33.7)	9 (30.0)	23 (35.4)	0.606	8 (29.6)	24 (35.3)	0.598
Number of risk factors, mean (SD)	2.5 (1.1)	2.6 (0.9)	2.5 (1.2)	0.571	2.5 (0.9)	2.5 (1.2)	
Angina pectoris, n (%)							
CCS Class 1	67 (70.5)	11 (36.7)	56 (86.2)	< 0.001	9 (33.3)	58 (85.3)	< 0.001
CCS Class 2	11 (11.6)	6 (20.0)	5 (7.7)	0.081	5 (18.5)	6 (8.8)	0.183
CCS Class 3	6 (6.3)	5 (16.7)	1 (1.5)	0.005	5 (18.5)	1 (1.5)	0.002
CCS Class 4	11 (11.6)	8 (26.7)	3 (4.6)	0.002	8 (29.6)	3 (4.4)	0.001
Psychological factors, mean (SD)							
Depression severity [PHQ-9]	4.5 (4.5)	7.5 (5.1)	3.1 (3.3)	< 0.001	8.4 (5.2)	2.9 (3.0)	< 0.001
Anxiety severity [GAD-7]	2.9 (3.4)	4.5 (3.5)	2.2 (3.2)	0.003	5.1 (3.9)	2.1 (2.9)	0.001

Table 1. Baseline characteristics of $n = 95$ patients with cardiac disease. SSS-8 = Somatic Symptom Scale-8; CCS = Canadian Cardiovascular Society; PHQ-9 = Patient Health Questionnaire-9. GAD-7 = Generalized Anxiety Disorder Scale-7; SD = Standard deviation.

adjusted for age and gender showed differences between patients with and without PSS for visits to the general practitioner ($F = 7.22$; $p = 0.009$) and the cardiologist ($F = 12.9$; $p = 0.001$).

Based on the data-driven approach, patients with PSS showed a mean of 3.0 ($SD = 3.1$) visits to a general practitioner within a three-month period compared with 1.4 ($SD = 1.5$) visits on average for patients without PSS ($p = 0.013$). Patients with PSS showed a mean of 2.3 ($SD = 2.2$) visits to a cardiologist within a three-month period compared with 0.9 (SD = 0.8) visits on average for patients without PSS ($p = 0.003$). The ANCOVA

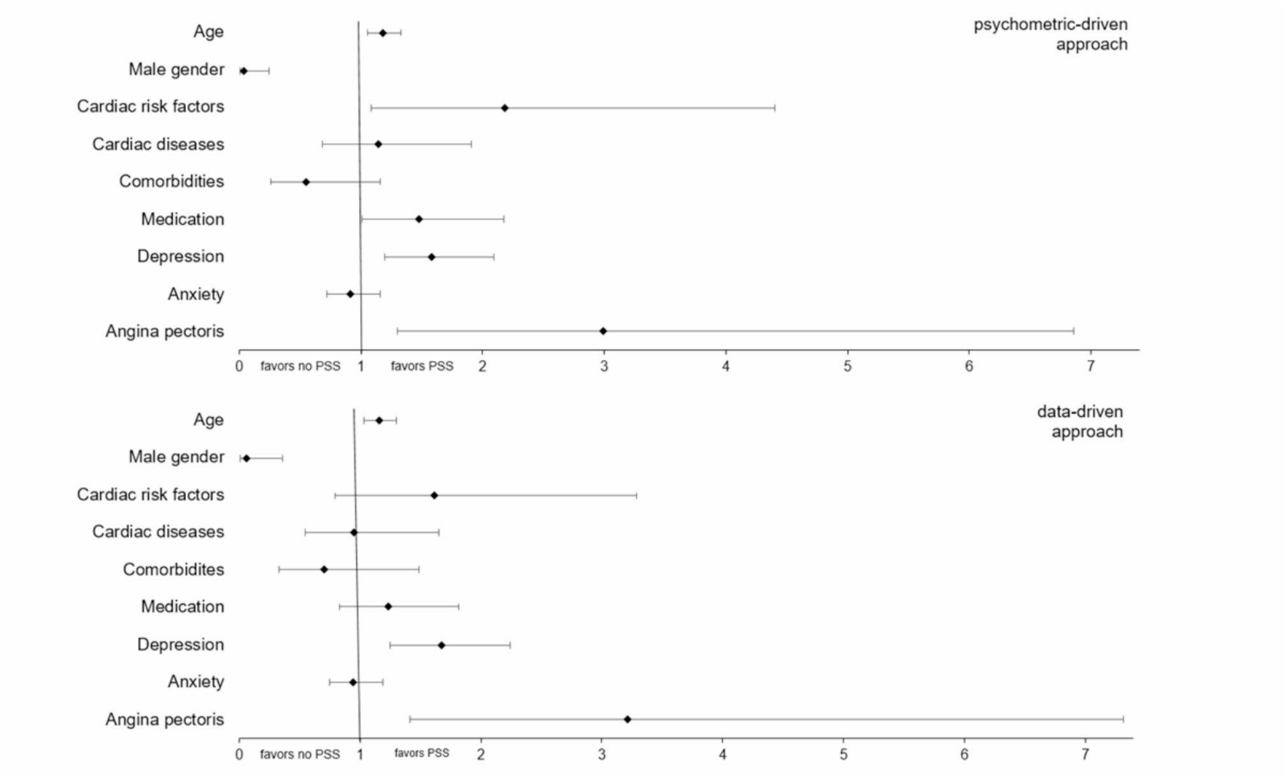

Fig. 1. Biomedical, psychological, and sociodemographic predictors for the occurrence of persistent somatic symptoms in patients with cardiac disease based on both the psychometric- and the data-driven approach.

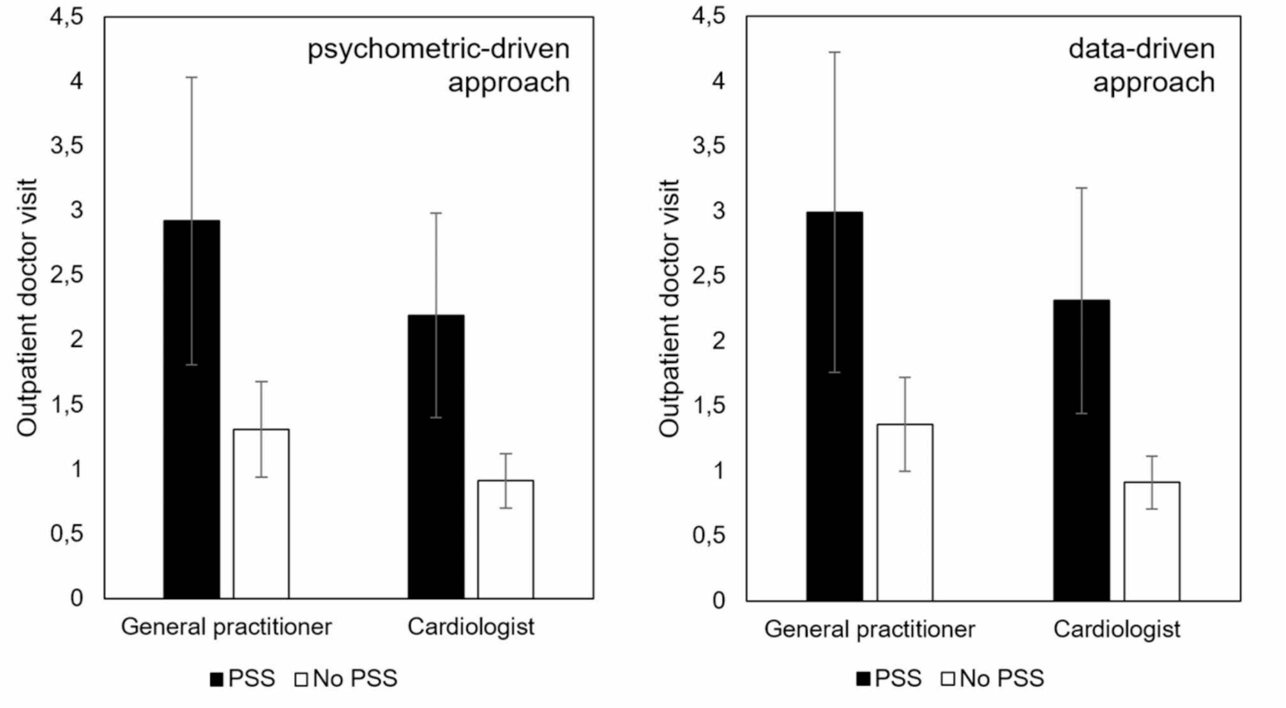

Fig. 2. Healthcare utilization comparison of patients with cardiac disease with and without persistent somatic symptoms according to the psychometric-driven and data-driven approach. The total number of outpatient visits to a general practitioner and to a cardiologist are compared.

adjusting for age and gender showed significant differences between patients with and without PSS for visits to the general practitioner ($F = 6.53$; $p = 0.012$) and the cardiologist ($F = 14.45$; $p < 0.001$).

Discussion and conclusion

Discussion

To the best of our knowledge, this is the first longitudinal study identifying characteristics and predictors of persistent somatic symptoms (PSS) in patients with cardiac disease. Over the course of three months, one-third of the study population showed PSS. The psychometric- and the data-driven approach, revealed similar rates of PSS. Patients with cardiac disease showing PSS were more likely to be female, to be unemployed, and to suffer from more severe angina pectoris. Additionally, they also showed higher depression and anxiety severity. Higher age, female gender, more severe angina pectoris, and higher depression severity were significant and stable predictors for PSS over the course of three months. Biomedical factors such as the number of cardiac diseases, comorbidities, cardiac risk factors, or number of medications could not be identified as predictors for PSS. Both the psychometric-driven as well as the data-driven approach indicate that patients with PSS showed a higher number of outpatient visits.

These results enabled us to gain more differentiated insights into which factors from the bio-psycho-social model play a role, especially for patients with cardiac disease[10]. Concerning biomedical factors angina pectoris seems to be relevant while somatic comorbidities, cardiac risk factors, and the number of medications do not play a major role in predicting PSS. Depression, as a psychological factor predicting PSS, appears to be a risk factor in cardiac disease while anxiety does not seem to predict PSS. The results underline the importance of an integrated assessment of biomedical and psychological factors for patients with cardiac disease. Future research should examine how psychological needs in addition to biomedical examinations can be included in diagnostics and patient-oriented treatment to reduce symptom severity and persistence as well as improve the quality of life of patients with cardiac disease.

The main focus of this longitudinal study was to gain knowledge about which patients with cardiac disease develop PSS and which characteristics and predictors play a role. DeVon et al. (2017) published a systematic review examining symptom profiles in individuals with cardiac disease[32]. The findings revealed variability in both the number and structure of identified profiles. While some studies classified symptoms based on severity, others emphasized symptom quality. Additionally, the identified profiles often included both somatic and psychological factors across different studies[32]. Riegel et al. (2010) provided one example of symptom profiles for patients with cardiovascular disease[33]. They identified four clusters (classic acute coronary syndrome, pain symptoms, stress symptoms, and diffuse symptoms) and were able to find correlations between symptom profile and mortality. Further examples of identified symptom profiles in individuals with cardiac disease include the six distinct symptom clusters found by Hu et al. (2020): fatigue, dyspneic, discomfort, congestive, ischemic, and emotional clusters[34]. Denfeld et al. (2020) identified profiles such as congruent-mild, incongruent, and congruent-severe, also including both physical and affective heart failure symptoms[35]. As yet there is no knowledge about the persistence within these symptom profiles. In future research increased differentiated knowledge can be gained by forming symptom profiles and analyzing these regarding persistence. Additionally, it could be of interest to focus on patients at risk prior to developing a cardiac disease. This could be helpful for the early identification and may be used to develop individualized interventions such as screening or interdisciplinary support.

Given the high overlap in phenomenology between cardiac diseases and SSD, we aimed to explore PSS as a substantial component of SSD in a population of patients with cardiac disease. Previous research has indicated that subjective symptom burden is not directly associated to the severity of the disease itself[10]. Instead, psychological factors play a key role in the persistence of symptoms, which then contributes to maintaining the overall disease burden[36]. Research on individuals at risk for heart failure has demonstrated varying levels of symptom burden, independent of disease stage or risk, highlighting the importance of adopting a bio-psycho-social perspective[37]. A recent study by Müller-Tasch et al. (2024) also demonstrated that somatic symptoms are significantly associated with depressive comorbidity in patients with chronic heart failure[38].

Löwe et al.[10] stated that patients with PSS show frequent and potentially harmful overuse of healthcare. Our results showed a significantly higher number of visits to general practitioners as well as cardiologists for patients with PSS. Former studies showed an overuse of invasive cardiac procedures especially in Germany[39]. This study does not give an insight into whether the significantly higher healthcare utilization is appropriate, protective, or harmful. Considering the absence of significant differences in cardiac disease, comorbidities, or the number of medications as biomedical characteristics among patients with and without PSS, it would be valuable to investigate the direction and causality in future studies. These could analyze whether there is an association between invasive overuse and PSS in patients with cardiac disease. This knowledge could be helpful in efficiently guiding patients through the healthcare system. Konnopka et al. (2013) showed which costs are associated with somatic symptom severity in patients with medically unexplained symptoms[17]. Along the lines of these results, the costs due to PSS in patients with cardiac disease could be quantified.

Limitations

Even though the study is exploratory it is important to note that the statistical power to detect predictors of PSS group affiliation and associations with healthcare utilization was only moderate. By defining the inclusion criteria to select patients with cardiac disease, we can ensure the focus on the target group of interest. However, given that this study involves secondary analysis, the sample exhibits high heterogeneity in terms of cardiac diseases. This diversity is valuable for an initial exploratory analysis aimed at defining PSS and enhancing our understanding of this patient group. Future studies should consider a larger sample size to test for replicability and should focus on a more differentiated approach of cardiac disease. This approach would allow for the identification of variations in characteristics, predictors, and specific needs among different subgroups within the population of patients with cardiac disease.

In this study, different approaches were used to define patients with and without PSS. Due to the study design of this secondary analysis, we were limited to utilizing longitudinal data spanning a 3-month period. Within criteria of related diagnoses such as the somatic symptom disorder according to the DSM-5, persistence is defined as six months or longer[2]. An extension of assessments over a longer period of time, such as six months, would improve our knowledge on the development of somatic symptoms in this patient group. Additionally, this study compares two approaches (psychometric-driven and data-driven) to define PSS in patients with cardiac disease in an explorative way. Further research should continue analyzing and specifying a definition of PSS in this patient group.

Finally, the study is based mainly on self-reporting. Biomedical factors, including cardiac disease, comorbidities, and medications, were assessed by screening the medical records of the patients and confirming the diagnoses during the cardiac consultation. Nevertheless, this study aimed to increase knowledge about factors characterizing and predicting PSS, which are based on subjective and individual perceptions[10]. The self-report questionnaires utilized were chosen as they have been shown to have reasonable psychometric properties in cardiology and primary care. In future research, social factors such as working circumstances and social interactions could be of interest against the background of the bio-psycho-social model[13].

Conclusion

To the best of our knowledge, this is the first study reporting on characteristics and predictors of patients with cardiac disease with PSS compared to those without PSS. Biomedical factors, except for angina pectoris as a cardiac factor, did not show significant differences in characteristics and prediction of patients with cardiac disease showing PSS. Additionally, psychological factors such as higher depression severity as well as sociodemographic factors such as higher age and female gender seemed to predict the development of PSS in this patient group. Due to these identified predictors, it could be advisable to evaluate PSS, especially in patients with cardiac disease at a higher age, female gender, significant angina pectoris, and elevated depression severity.

This longitudinal study provides insights into an initial exploration of defining PSS in patients with cardiac disease while describing its characteristics and predictors. PSS is one of the diagnostic criteria for somatic symptom disorder (SSD) as outlined in the DSM-5[2]. By expanding our knowledge about PSS in this patient group, we are also progressing towards the challenge of identifying somatic symptom disorder in patients with cardiac disease. It is noteworthy that approximately one-third of patients with cardiac disease exhibits PSS. Given the exploratory nature of this study, specific conclusions regarding changes in routine care cannot be drawn. However, suggestions for future research include focusing on patient-oriented treatment approaches or implementing screening measures, such as the assessment of depression severity, to enhance healthcare for patients with cardiac disease experiencing PSS and to support early identification. To comprehensively address the needs and appropriate healthcare, it is crucial to expand knowledge about PSS within this patient group. This can be achieved by analyzing patients with distinct cardiac diseases, other somatic diseases, or individuals at risk of developing cardiac diseases in future studies. Such research would enable the generalization and evaluation of initial findings observed in this longitudinal study.

Data availability

The data that supports the findings of this study is available on request from the corresponding author.

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Author contributions

Conceptualization: C.C., S.K., B.L. Data curation: C.C., S.K. Formal analysis: C.C., S.K. Funding acquisition: S.K., B.L. Investigation: S.K. Methodology: C.C., S.K. Project administration: C.C., S.K. Resources: S.K., B.L. Software: C.C., S.K. Supervision: S.K., B.L. Validation: C.C., S.K. Visualization: C.C., S.K. Roles/Writing—original draft: C.C. Writing – review and editing: S.K., B.L.

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Declarations

Competing interests

The authors declare no competing interests.

Ethical approval

The study was approved by the Ethics Committee of the Medical Chamber, Hamburg, Germany (PV5199).

Additional information

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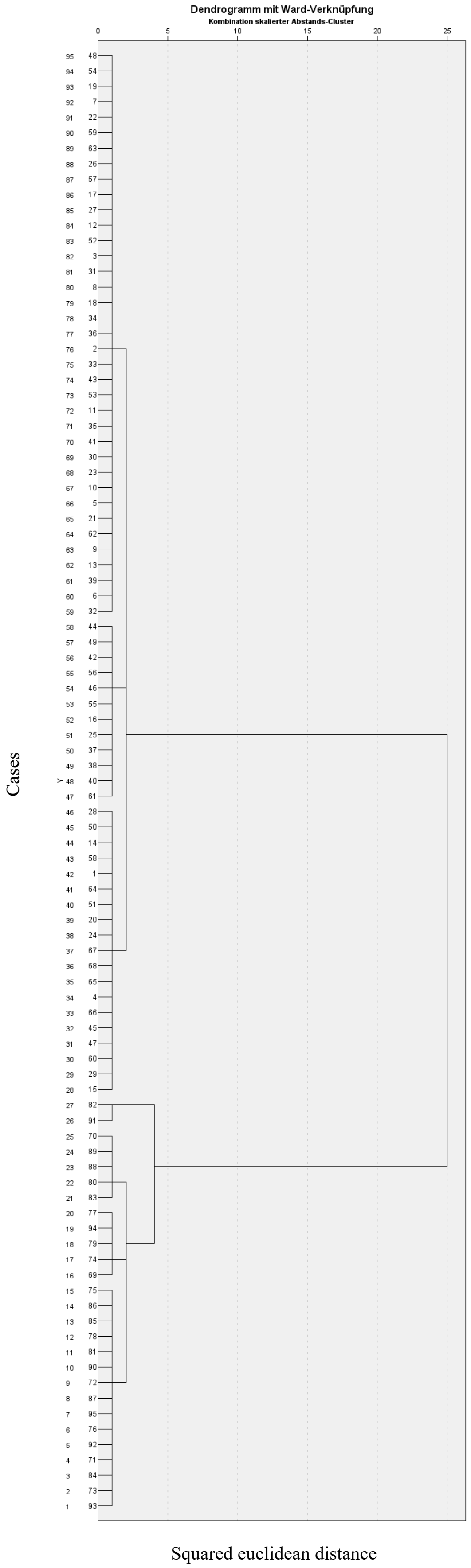
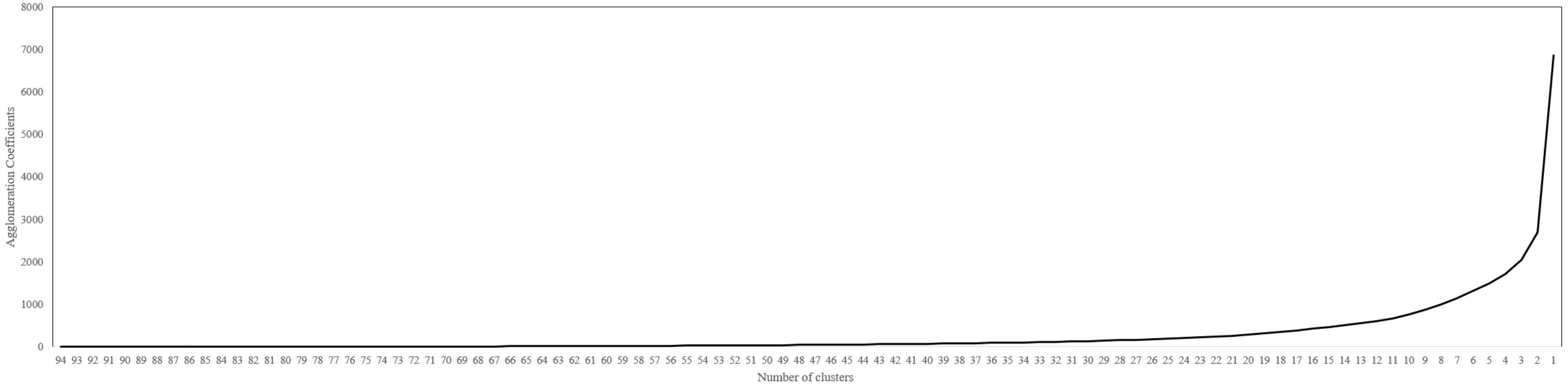
Supplement A

Dendrogram displaying hierarchical clustering results for group assignment.



Supplement B

Elbow plot for determining optimal clusters using Ward’s method.



Study II

Somatic symptom disorder symptoms in individuals at risk for heart failure: A cluster analysis with cross-sectional data from a population-based cohort study.

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Somatic symptom disorder symptoms in individuals at risk for heart failure: A cluster analysis with cross-sectional data from a population-based cohort study

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ABSTRACT

Objective: Identifying whether experienced symptom burden in individuals with medical predisposition indicates somatic symptom disorder (SSD) is challenging, given the high overlap in the phenomenology of symptoms within this group. This study aimed to enhance understanding SSD in individuals at risk for heart failure.

Subjects and methods: Cross-sectional data from the Hamburg City Health Study was analyzed including randomly selected individuals from the general population of Hamburg, Germany recruited from February 2016 to November 2018. SSD symptoms assessed with the Somatic Symptom Scale-8 and the Somatic Symptom Disorder-12 scale were categorized by applying cluster analysis including 412 individuals having at least 5% risk for heart failure-related hospitalization within the next ten years. Clusters were compared for biomedical and psychological factors using ANOVA and chi-square tests. Linear regressions, adjusting for sociodemographic, biomedical, and psychological factors, explored associations between clusters with general practitioner visits and quality of life.

Results: Three clusters emerged: none ($n = 215$; 43% female), moderate ($n = 151$; 48% female), and severe ($n = 46$; 54% female) SSD symptom burden. The SSS-8 mean sum scores were 3.4 ($SD = 2.7$) for no, 6.4 ($SD = 3.4$) for moderate, and 12.4 ($SD = 3.7$) for severe SSD symptom burden. The SSD-12 mean sum scores were 3.1 ($SD = 2.6$) for no, 12.2 ($SD = 4.2$) for moderate, and 23.5 ($SD = 6.7$) for severe SSD symptom burden. Higher SSD symptom burden correlated with biomedical factors (having diabetes: $p = .005$ and dyspnea: $p \leq .001$) and increased psychological burden (depression severity: $p \leq .001$; anxiety severity: $p \leq .001$), irrespective of heart failure risk ($p = .202$). Increased SSD symptoms were associated with more general practitioner visits ($\beta = 0.172$; $p = .002$) and decreased physical quality of life ($\beta = -0.417$; $p \leq .001$).

Conclusion: Biomedical factors appear relevant in characterizing individuals at risk for heart failure, while psychological factors affect SSD symptom experience. Understanding SSD symptom diversity and addressing subgroup needs could prove beneficial.

1. Introduction

In comparison to the previous somatoform disorder diagnoses, the diagnosis of somatic symptom disorder (SSD) allows for a comorbid somatic disease alongside the psychological symptoms [1]. The diagnostic criteria of SSD define distressing somatic symptoms (Criterion A) accompanied by excessive thoughts, feelings, and/or behaviors (Criterion B) as well as the persistence of symptomatic states (Criterion C) [1]. Due to the high overlap with medical conditions identifying which symptom-related thoughts, feelings, and behavior indicate SSD is challenging [2,3]. Uncertainties arise in applying diagnostic criteria, especially when using the same standards for individuals both with and

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without pathophysiological diseases [4,5]. These uncertainties pose difficulties for healthcare professionals when managing patients with SSD symptoms [6,7] which in some cases leads to inadequate diagnostics preventing patients from receiving appropriate treatment or resulting in unwarranted patient investigations, potentially resulting in iatrogenic harm [2,8].

Patients with heart failure report a variety of symptoms ranging from cardiac-associated ones (e.g. dyspnea or chest pain) to disease-unspecific symptoms (e.g. sleep disturbance, loss of energy, or pain). Often these symptoms are not acute but persistent [9,10], have implications for function and quality of life and are linked to heightened risks of hospitalization and mortality [11–14]. Research has shown that individuals often report a range of somatic symptoms months or even years before heart failure is formally diagnosed [15]. These early-stage symptoms can closely resemble those of SSD, which makes the population of individuals at risk for heart failure a crucial group for investigation. By examining individuals at risk for heart failure, we aim to understand their experiences concerning symptom burden in the stage of symptom onset.

Although the phenomenology of symptoms in SSD and heart failure can overlap (i.e. persistence of symptoms, fatigue, pain), the etiologies differ significantly. Heart failure development is primarily explained by biological factors, whereas SSD etiology involves a complex interplay of biological, psychological, and social factors [16,17]. Psychosocial factors, including patients' beliefs, expectations, and illness anxiety, contribute to the development of SSD [17,18]. The significance of these psychosocial factors is underscored by the observation that symptom burden often remains despite optimal treatment of the underlying pathophysiology [18–20]. To address the knowledge gaps regarding developmental aspects, a closer examination of SSD symptoms in individuals at risk for heart failure, where symptoms are not yet as strongly pronounced as in individuals with heart failure, could provide valuable insights concerning early detection and distinguishing features [2,12,21,22].

We are interested in understanding the diverse presentation of SSD symptoms rather than focusing on diagnosis prevalence. Therefore, we aimed to identify clusters of individuals based on the SSD symptoms using an explorative approach without predefined structures (e.g. symptom groups) or numbers concerning the cluster solution. We intended to gain a deeper understanding of these subgroups by closely examining biomedical and psychological factors, and assessing their distribution among the clusters. Furthermore, we sought to explore the impact of SSD symptoms on the number of general practitioner (GP) visits and the quality of life. From these considerations, we derived the following research questions:

1. Can clusters of somatic symptom disorder (SSD) symptoms be identified in individuals at risk for heart failure?
2. What characteristics do these clusters show concerning sociodemographic, biomedical, and psychological factors?
3. How are biomedical and psychological burden distributed among the clusters?
4. Are these clusters associated with the number of general practitioner visits and the quality of life beyond sociodemographic, biomedical, and psychological factors?

2. Subjects and methods

2.1. Design

In this study, we used the data from the Hamburg City Health Study, a population-based cohort study involving individuals aged 45 to 74 years from the general population of Hamburg, Germany [23]. The participants invited to the study were identified by a random sample from the official inhabitant data file divided into age and gender strata [23]. The primary objective was to understand critical risk and prognostic factors for major chronic diseases through ongoing follow-up measurements [23]. Data collection of the first cohort took place from February 2016 to November 2018, with 10,000 individuals currently enrolled and their data systematically recorded. According to the study protocol of the Hamburg City Health Study, this sample size and recruitment strategy was selected to represent the population aged 45 to 74 years in Hamburg, Germany.

The assessment took place at the epidemiological study center at the University Medical Center Hamburg-Eppendorf (Germany). Following explanation of the study's purpose by a study nurse, each participant provided consent. The assessment included a 7-h examination of different organ systems, along with self-report questionnaires. After completion, participants received a letter containing relevant results and recommendations based on the examination outcomes [23].

To gain a better understanding of SSD symptoms in individuals at risk for heart failure, we included those with a minimum 5% risk for heart failure-related hospitalization within the next ten years, as determined by the Atherosclerosis Risk in Communities study (ARIC score) [24]. We selected a 5% cut-off, a relatively low threshold, to include a broad range of risk for heart failure, enhancing our ability to examine its association with symptom burden. Exclusion criteria were an ARIC score below 5% or a prior diagnosis of heart failure as indicated by medical records, assessments within the Hamburg City Health Study, or self-report. From the 10,000 study participants of the Hamburg City Health Study, 1328 met the criteria of a minimum 5% risk based on the ARIC score. Additionally, we had to exclude participants who, due to the study design, did not complete the questionnaires needed to assess SSD symptoms (Somatic Symptom Scale-8 and Somatic Symptom Disorder-B Criteria Scale), resulting in a study sample size of $n = 412$.

The Hamburg City Health Study has been registered at ClinicalTrial.gov (NCT03934957). The study protocol was approved by the local ethics committee of the Landesärztekammer Hamburg (State of Hamburg Chamber of Medical Practitioners, PV5131) as well as by the Data Protection Commissioner of the University Medical Center of the University Hamburg-Eppendorf and the Data Protection Commissioner of the Free and Hanseatic City of Hamburg (D4/17.06–22).

2.2. Measurements

2.2.1. Sociodemographic data

Patients completed questionnaires assessing sociodemographic data, including age, gender, family status, living situation, employment, and education.

2.2.2. SSD symptoms

Distressing somatic symptoms (Criterion A) and associated psychological symptoms (Criterion B), were assessed according to SSD criteria using two recommended questionnaires [25]. The Somatic Symptom Scale-8 (SSS-8) evaluated somatic symptoms, such as back pain, stomach or bowel problems, chest pain, and fatigue [26]. The Somatic Symptom Disorder-B Criteria Scale (SSD-12) assessed psychological symptoms related to patients' perception of their symptom-related thoughts, feelings, and behavior [27]. The SSS-8 scores range from 0 to 32 points, with the following classification: 0–3 indicating no to minimal somatic symptom severity, 4–7 low, 8–11 medium, 12–15 high, and 16–32 very high [26]. SSD-12 scores range from 0 to 48 points, with a sum score of 23 points or above indicating somatic symptom burden [27]. Additionally, the SSD-12 allows an interpretation across three subscales describing cognitive, affective, and behavioral aspects [27]. Both questionnaires are characterized by brevity, validity, and reliability [26,27]. In our study, we found the validity of the questionnaires to be sufficient, as indicated by a Pearson correlation between each item of the SSS-8 and SSD-12 and their respective sum score (all items $p \leq .001$). Furthermore, we assessed the reliability using Cronbach's alpha, which yielded $\alpha = 0.78$ for the SSS-8 and $\alpha = 0.93$ for the SSD-12, indicating adequate reliability for both measures.

Previous research combined results from both questionnaires to identify individuals at risk for SSD. Using a cut-off score of 9 points in the SSS-8 and 23 points in the SSD-12 showed moderate sensitivity and specificity (69% and 70%) in identifying at-risk individuals [25]. Due to the lack of information on cut-off scores for individuals at risk for heart failure, we employed an exploratory cluster analysis approach in this study to examine SSD symptoms in this population. Additionally, Criterion C, regarding the persistence of symptoms, was assessed by asking if reported somatic symptoms had lasted at least six months.

2.2.3. Biomedical factors

The ARIC score predicts the likelihood of hospitalization due to heart failure within the following ten years [24]. It takes into account factors like heart rate, antihypertensive medication, NT-proBNP, coronary heart disease, blood pressure, diabetes, body mass index, and smoking, both recently and in the past.

Further biomedical factors related to cardiac diseases were assessed, including prior myocardial infarction, existence of coronary heart disease, valve disease, cardiomyopathy, cardiac dysrhythmia, and aortic aneurysm. Cardiac risk factors, such as diabetes, hyperlipidemia, hypertension, obesity, positive family history, and smoking were evaluated. Assessment also extended to non-cardiac somatic diseases diagnosed currently or in the past including cancer ($n = 112$), kidney diseases ($n = 62$), stroke ($n = 15$), sleep apnea ($n = 28$), and chronic obstructive pulmonary disease ($n = 40$). Additionally, medication usage was documented.

Angina pectoris and dyspnea were evaluated to measure clinical symptoms linked to cardiac diseases. Angina pectoris severity was determined using the Canadian Cardiology Society (CCS) class [28], while dyspnea was assessed using the New York Heart Association (NYHA) class [29]. Both classification systems are established indicators of the functional severity of cardiac diseases [30,31], categorizing impairment into four classes from '*no impairment at all*' to '*impairment even at resting*', with higher classes indicating greater symptom impairment.

Left ventricular ejection fraction (LVEF), left atrial diameter, and NT-proBNP were evaluated as clinical markers relevant to heart failure diagnosis. According to guidelines, LVEF values of 60% and above are normal, 50–60% are borderline, and below 50% indicate a reduced ejection fraction. Left atrial diameter measurements below 34 ml/m^2 are normal, 34–38 ml/m^2 are borderline, and above 38 ml/m^2 indicate dilatation. NT-proBNP-levels below 125 ng/l are normal, 125–300 ng/l are borderline, and values above 300 ng/l are elevated [32].

2.2.4. Psychological factors

The Patient Health Questionnaire-9 (PHQ-9) assessed depression severity by evaluating the frequency of experiencing the nine most common depressive symptoms over the past two weeks. Scores range from 0 to 27 points, with cut-off values of 5 indicating mild, 10 indicating moderate, and 15 indicating severe depression. The PHQ-9 is a valid and reliable instrument [33,34].

The Generalized Anxiety Disorder Scale-7 (GAD-7) assessed anxiety severity by evaluating the frequency of anxiety symptoms over the past two weeks. Scores range from 0 to 21 points, with cut-off values of 5 indicating mild, 10 indicating moderate, and 15 indicating severe anxiety. The GAD-7 has valid and reliable case-finding properties for the most common anxiety disorders [35,36].

Further, the following mental disorders were assessed through self-reporting: depression ($n = 24$), bipolar disorder ($n = 0$), anxiety disorders ($n = 5$), obsessive-compulsive disorders ($n = 0$), addictive disorders ($n = 0$), personality disorders ($n = 0$), eating disorders ($n = 0$), post-traumatic stress disorder ($n = 0$), dementia ($n = 1$), and schizophrenia ($n = 0$).

2.2.5. General measure of biomedical and psychological burden

We chose a comprehensive approach beyond quantitative comparison of individual variables to examine the distribution of biomedical and psychological factors. We established binary definitions for biomedical and psychological burden based on the assessed variables. Biomedical burden was considered present if any of the following conditions were met within an individual: having at least two cardiac risk factors, a minimum impairment level of 2 in NYHA or CCSC, the presence of cardiac or other somatic diseases, or regular medication use. Psychological burden was considered present if any of the following conditions were met within an individual: a minimum PHQ-9 sum score of 5, a minimum GAD-7 sum score of 5, or the presence of a mental disorder.

2.2.6. Quality of life

We used the Short-Form Health Survey-8 (SF-8) to assess health-related quality of life which measures eight profile dimensions, including physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions. Each item is rated on a 5- or 6-point Likert scale, and scores are aggregated to derive physical (PCS-8) and mental scores (MCS-8), with higher scores indicating better quality of life [37]. The SF-8 is considered a valid and reliable instrument [38,39].

2.2.7. General practitioner visits

To measure the number of GP visits, individuals reported their frequency of visits to a GP during the past 12 months.

2.3. Statistical analysis

We conducted a hierarchical cluster analysis (Ward method) based on the individual score of each item of the SSS-8 and the SSD-12 to form clusters based on SSD symptoms. The number of clusters was determined using the elbow method which identifies a meaningful number of clusters that best represent the data [40]. To validate our cluster solution, we conducted a two-step cluster analysis.

We conducted ANOVAs and chi-squared tests to explore sociodemographic, biomedical, and psychological differences among the clusters. All data measured on a continuous scale were analyzed accordingly. To adjust for multiple comparisons, significance levels were interpreted using the Benjamini-Hochberg formula [41]. Pairwise comparisons between clusters were conducted using Tukey post hoc analysis for the ANOVAs and a z-test of two proportions with a Bonferroni correction for the chi-squared tests. The distribution of biomedical and psychological burden between clusters was compared descriptively. Linear regression, adjusting for sociodemographic, biomedical, and psychological factors, examined associations between clusters and the number of GP visits, as well as physical and mental quality of life. Dummy coding was used to transform categorical variables into binary ones, facilitating the integration of categorical data into linear regression.

Missings ranged from 0% to 27% and were addressed through multiple imputations. Statistical significance was set at a two-tailed p-value $<.05$. All statistical analyses, including tests for multicollinearity and other statistical prerequisites, were conducted using SPSS 27.

3. Results

3.1. Sample

Among the $n = 412$ individuals at risk for heart failure, three clusters were identified based on SSS-8 and SSD-12: cluster A (no SSD symptoms, $n = 215$), cluster B (moderate SSD symptoms, $n = 151$), and cluster C (severe SSD symptoms, $n = 46$). The SSS-8 mean sum scores for clusters A, B, and C were 3.4 ($SD = 2.7$), 6.4 ($SD = 3.4$), and 12.4 ($SD = 3.7$). The SSD-12 mean sum scores for clusters A, B, and C were 3.1 ($SD = 2.6$), 12.2 ($SD = 4.2$), and 23.5 ($SD = 6.7$). These clusters were labeled according to the SSS-8 and SSD-12 cut-off scores. Significant differences were observed among the clusters for all items and sum scores of SSS-8 and SSD-12 (all tests: $p \leq .001$). All subscales of the SSD-12 revealed significant differences both among the clusters and between each individual cluster (all tests: $p \leq .001$). Descriptive information on SSS-8 and SSD-12 items can be found in Table 1 and in the supplementary material (A).

The sensitivity analysis, comprising a two-step cluster analysis, revealed a slight variance with 90% overlap in cluster affiliation, yet it produced congruent results in the analyses. Further details on the outcomes of the two-step cluster analysis are provided in the supplementary materials (B and C).

Within the study sample, $n = 19$ individuals met the criteria for being at risk for SSD based on the cut-off scores of the SSS-8 and the SSD-12 [25].

3.2. Sociodemographic, biomedical, and psychological characteristics of the clusters

Regarding sociodemographic factors, the clusters did not show significant differences except for age ($p = .014$). In terms of biomedical factors, significant differences between the clusters were observed for having diabetes ($p = .005$), the number of cardiac diseases ($p = .014$), and dyspnea ($p \leq .001$). Other biomedical factors, such as the ARIC score, angina pectoris, left ventricular ejection fraction, left atrial diameter, NT-proBNP, or medication use, did not show significant differences. Regarding psychological factors, significant differences between the clusters were evident in depression severity ($p \leq .001$), anxiety severity ($p \leq .001$), and the number of mental disorders ($p = .014$).

The Tukey post hoc analysis and the z-test of two proportions with a Bonferroni correction revealed specific differences between clusters. On average, individuals in cluster A ($m = 70.9$; $SD = 4.8$) were older compared to those in cluster C ($m = 68.5$; $SD = 5.9$; $p = .011$), while cluster B ($m = 70.3$; $SD = 5.0$) did not significantly differ from either cluster A ($p = .448$) or C ($p = .106$) in age. Individuals in cluster B ($m = 0.7$; $SD = 0.7$) had significantly fewer cardiac diseases than those in cluster C ($m = 1.0$; $SD = 0.9$; $p = .012$), whereas cluster A ($m = 0.8$; $SD = 0.7$) did not significantly differ from either cluster B ($p = .227$) or C ($p = .138$). Individuals in cluster A ($n = 25$; 11.6%) had significantly fewer cases of diabetes than those in cluster C ($n = 25$; 16.6%), while cluster B ($n = 14$; 30.4%) did not significantly differ from either cluster A or C. Individuals in cluster C ($m = 0.2$; $SD = 0.5$) showed significantly more mental disorders than those in cluster A ($m = 0.0$; $SD = 0.2$; $p \leq .001$) or cluster B ($m = 0.1$; $SD = 0.3$; $p = .010$), while cluster A and B did not significantly differ in terms of mental disorders ($p = .071$). Regarding dyspnea (cluster A and B: $p = .014$; cluster B and C: $p = .006$; cluster A and C: $p \leq .001$), depression severity (cluster A and B: $p \leq .001$; cluster B and C: $p \leq .001$; cluster A and C: $p \leq .001$), and anxiety severity (cluster A and B: $p \leq .001$; cluster B and C: $p \leq .001$; cluster A and C: $p \leq .001$), significant differences were observed among all clusters, with individuals in cluster C exhibiting the highest burden and those in cluster A the lowest.

Upon examining the persistence of symptomatic states, significant differences emerged between the clusters. In cluster A (no SSD symptoms), 41.4% of individuals reported persistent somatic symptoms, whereas in cluster B (moderate SSD symptoms) this increased to 74.8%, and in cluster C (severe SSD symptoms), it rose to 97.8% ($p \leq .001$). Table 1 summarizes the characteristics of the entire sample and distinguishes between the three identified clusters.

Table 1
Characteristics of $n = 412$ individuals at risk for heart failure.

Characteristics	Total sample	Cluster A	Cluster B	Cluster C	p-value
	$n = 412$	$n = 215$	$n = 151$	$n = 46$	
Sociodemographics, n (%)					
Age, mean (SD), age	70.4 (5.0)	70.9 (4.8)	70.3 (5.0)	68.5 (5.9)	0.014
Gender, female	190 (46.1)	93 (43.3)	72 (47.7)	25 (54.3)	0.348
Family status, married	289 (70.1)	148 (68.8)	110 (72.8)	31 (67.4)	0.648
Living alone	108 (26.2)	58 (27.0)	36 (23.8)	14 (30.4)	0.629
Employed	96 (23.3)	47 (21.9)	35 (23.2)	14 (30.4)	0.458
≥ 10 years of formal education	391 (94.9)	206 (95.8)	142 (94.0)	43 (93.5)	0.672
SSD symptoms, mean (SD)					
Somatic symptom severity [SSS-8]	5.5 (4.2)	3.4 (2.7)	6.4 (3.4)	12.4 (3.7)	<0.001
Somatic symptom disorder-B criteria scale [SSD-12]	8.7 (7.8)	3.1 (2.6)	12.2 (4.2)	23.5 (6.7)	<0.001
Subscale: cognitive aspects [SSD-12]	3.1 (2.7)	1.3 (1.3)	4.4 (1.9)	7.3 (2.4)	<0.001
Subscale: affective aspects [SSD-12]	3.1 (2.8)	1.2 (1.2)	4.3 (1.8)	8.2 (2.6)	<0.001
Subscale: behavioral aspects [SSD-12]	2.5 (2.8)	0.6 (0.8)	3.5 (1.5)	8.1 (2.6)	<0.001
Symptom persistence, n (%)					
Persistence of somatic symptoms (> 6 months)	252 (61.2)	92 (42.8)	115 (76.2)	45 (97.8)	<0.001
Cardiac risk factors, n (%)					
Diabetes	65 (15.8)	25 (11.6)	26 (17.2)	14 (30.4)	0.005
Hyperlipidemia	152 (36.9)	77 (35.8)	55 (36.4)	20 (43.5)	0.613
Hypertension	359 (87.1)	186 (86.5)	128 (84.8)	45 (97.8)	0.063
Obesity	114 (27.7)	56 (26.0)	42 (27.8)	16 (34.8)	0.485
Family history	141 (34.2)	72 (33.5)	54 (35.8)	15 (32.6)	0.877
Smoking	91 (22.1)	43 (20.0)	39 (25.8)	9 (19.6)	0.379
Number of risk factors, mean (SD)	2.2 (1.1)	2.1 (1.1)	2.3 (1.1)	2.6 (1.4)	0.053
Clinical characteristics, mean (SD)					
ARIC score	11.3 (8.2)	10.9 (7.4)	11.3 (8.0)	13.3 (11.8)	0.202
Number of cardiac diseases	0.8 (0.7)	0.8 (0.7)	0.7 (0.7)	1.1 (0.9)	0.014
Number of other somatic diseases	0.6 (0.7)	0.6 (0.7)	0.7 (0.7)	0.8 (0.9)	0.071
Number of medication	1.2 (1.2)	1.1 (1.1)	1.3 (1.2)	1.5 (1.3)	0.159
Left ventricular ejection fraction, mean (SD) %	58.8 (5.3)	58.5 (5.6)	59.1 (4.9)	59.1 (4.8)	0.496
Left atrial diameter, mean (SD) ml	46.6 (18.5)	46.3 (17.9)	48.1 (20.1)	43.7 (16.2)	0.362
NT-proBNP, mean (SD) ng/l	196.5 (213.5)	198.7 (220.5)	184.6 (189.7)	225.4 (252.8)	0.516
Angina pectoris, (%)					
CCS Class 1	405 (98.3)	211 (98.2)	150 (99.3)	44 (95.7)	
CCS Class 2	3 (0.7)	2 (0.9)	1 (0.7)	0 (0.0)	
CCS Class 3	2 (0.5)	2 (0.9)	0 (0.0)	0 (0.0)	
CCS Class 4	2 (0.5)	0 (0.0)	0 (0.0)	2 (4.3)	0.019
Dyspnea, n (%)					
NYHA Class 1	358 (86.9)	201 (93.5)	126 (83.4)	31 (67.5)	<0.001

(*continued on next page*)

Fig. 1 illustrates the distribution of biomedical and psychological burden across the three identified clusters. In cluster A, 13% of individuals experienced biomedical and psychological burden, 86% experienced only biomedical burden, and 1% experienced only psychological burden. In cluster B, 44% described biomedical and psychological burden, while 56% reported only biomedical burden; no

Table 1 (*continued*)

Characteristics	Total sample	Cluster A	Cluster B	Cluster C	p-value
	n = 412	*n* = 215	*n* = 151	*n* = 46	
NYHA Class 2	38 (9.2)	11 (5.1)	17 (11.3)	10 (21.7)	
NYHA Class 3	13 (3.2)	3 (1.4)	7 (4.6)	3 (6.5)	
NYHA Class 4	3 (0.7)	0 (0.0)	1 (0.7)	2 (4.3)	
Psychological characteristics, mean (SD)					
Depression severity [PHQ-9]	3.1 (3.1)	1.8 (1.8)	4.0 (3.1)	6.6 (3.8)	<0.001
Anxiety severity [GAD-7]	2.3 (2.7)	1.2 (1.6)	3.0 (2.9)	5.1 (3.3)	<0.001
Number of mental disorders	0.1 (0.3)	0.0 (0.2)	0.1 (0.4)	0.2 (0.5)	<0.001
Physical quality of life [SF-8 PCS]	48.9 (7.8)	52.0 (5.7)	47.4 (7.4)	39.0 (8.1)	<0.001
Mental quality of life [SF-8 MCS]	54.9 (6.5)	56.7 (3.7)	53.9 (7.7)	49.1 (8.4)	<0.001
Healthcare utilization, mean (SD)					
Number of visits to the general practitioner	3.4 (3.2)	2.7 (3.1)	3.8 (3.3)	5.0 (2.9)	<0.001

Abbreviations: SSS-8 = Somatic Symptom Scale-8; SSD-12 = Somatic Symptom Disorder-B Criteria Scale; CCS = Canadian Cardiovascular Society Angina Grading Scale; NYHA = New York Heart Association Scale; PHQ-9 = Patient Health Questionnaire-9; GAD-7 = Generalized Anxiety Disorder Scale-7; SF-8 PCS = Short-Form Health Survey-8; SD = Standard deviation. The indicated p-value refers to the comparison between all three groups.

individuals experienced only psychological burden. In cluster C, 100% of individuals experienced psychological burden, with 76% additionally reporting biomedical burden.

3.3. *Association between clusters and GP visits as well as quality of life*

Linear regression analysis tested associations between cluster affiliation and the number of GP visits as well as quality of life, adjusting for sociodemographic, biomedical, and psychological factors. Regardless of these factors, higher symptom burden was associated with an increased number of GP visits ($\beta = 0.172$; $p = .002$) and decreased physical quality of life ($\beta = -0.417$; $p \leq .001$), but not with mental quality of life ($\beta = 0.023$; $p = .565$). Further details are provided in Table 2.

4. Discussion and conclusion

4.1. *Discussion*

Among our sample of 412 individuals at risk for heart failure, we distinguished three distinct clusters not differing by specific somatic symptoms but by symptom severity: cluster A ($n = 215$) showing no SSD symptoms, cluster B ($n = 151$) showing moderate SSD symptoms, and cluster C ($n = 46$) showing severe SSD symptoms. These findings support the hypothesis that individuals with similar medical predisposition experience varying levels of symptom burden. Notable differences emerged among the clusters concerning sociodemographic (age), biomedical (having diabetes, number of cardiac diseases, dyspnea), and psychological factors (depression severity, anxiety severity, number of mental disorders). Biomedical and psychological burden distribution revealed that individuals with no SSD symptoms (Cluster A) primarily experienced biomedical burden, while those with more frequent SSD symptoms (Cluster B & C) experienced psychological burden in addition to medical burden. With respect to GP visits, there was an almost linear increase from no to moderate to severe SSD symptom cluster. While physical quality of life showed a similar association, mental quality of life was not linked with cluster affiliation. To the best of our knowledge, this is the first study identifying clusters of individuals at risk for heart failure based on SSD symptoms.

Research so far has shown that psychological factors, besides biological and social aspects, play a key role in the development of SSD [17,18]. Depression, anxiety, illness anxiety, and alexithymia appear to be particularly linked to SSD [1,2,42]. Additionally, according to a meta-analysis looking into psychological risk factors for SSD, factors such as emotion regulation and avoidance behavior are understudied and warrant further investigation [42]. Our findings support the idea that while biomedical factors are relevant for individuals at risk for heart failure, psychological factors play a more prominent role in influencing SSD symptoms. Despite a similar risk for heart failure-related hospitalization, individuals exhibited varying SSD symptom severities, whereas clinical markers for heart failure remained consistent across the group. Understanding which psychological or additional factors act as predictors or mediators of increased symptom burden in individuals with medical predisposition is crucial for enhancing our comprehension and providing knowledge necessary to address SSD symptoms in a clinical context.

Furthermore, we noted an association between more individuals reporting persistent somatic symptoms and increased severity of SSD symptoms. Former research has identified predictors of persistent somatic symptoms across biological, psychological, interpersonal, and contextual domains, as well as health behavior [43]. While our study focused on biomedical, psychological, and contextual factors, future research could expand on interpersonal aspects, such as life events and social support, and further explore health behavior, including physical activity and illness behavior.

Previous studies have primarily focused on identifying SSD within the general population [2,25]. Our explorative approach, which focused on symptomatic levels and labeled the clusters based on SSS-8 and SSD-12 cut-off scores, precluded us from providing insights into SSD diagnosis in individuals at risk for heart failure. So far, only one study has been conducted on patients with cardiac disease, showing a prevalence of the SSD diagnosis in 18.5% of patients suffering from congestive heart failure [44]. Future research aiming at approximating SSD diagnosis prevalence rather than solely focusing on symptomatic levels could prove beneficial by providing a more detailed and individualized understanding of the diagnostic criteria, particularly for individuals with a

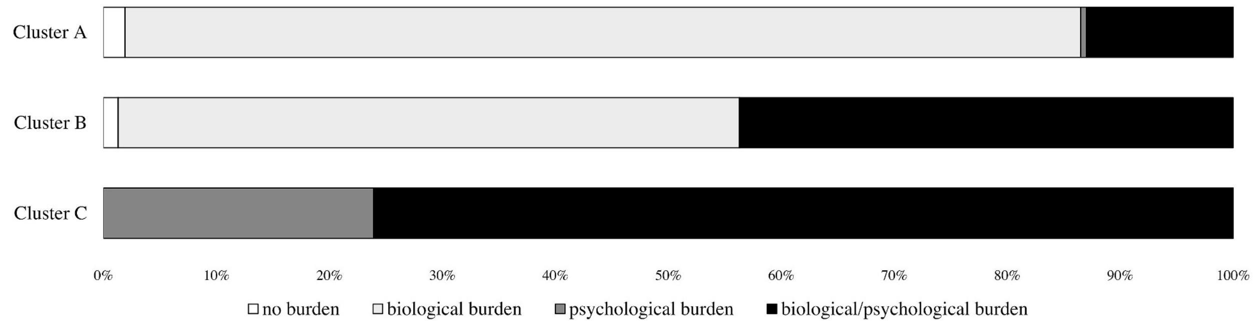

Fig. 1. Distribution of biomedical and psychological burden according to clusters based on SSD symptoms in individuals at risk for heart failure.

Table 2
Linear regression analysis to examine the association between cluster affiliation and the number of general practitioner visits, as well as physical and mental quality of life.

Variables	B	SE B	Beta	F-value - adjusted R^2
Number of general practitioner visits during the previous year				6.34–0.15**
Sociodemographic factors				
Age	−0.005	0.004	−0.074	
Gender	0.020	0.031	0.031	
Family status	−0.058	0.055	−0.082	
Living situation	0.089	0.058	0.121	
Employment	0.054	0.037	0.071	
Education	−0.105	0.068	−0.071	
Biomedical factors				
ARIC score	0.003	0.002	0.086	
Number of risk factors	0.012	0.017	0.044	
Number of medication	0.041	0.016	0.149*	
Number of cardiac diseases	−0.048	0.021	−0.109*	
Number of other somatic diseases	0.028	0.021	0.063	
Psychological factors				
Depression severity [PHQ-9]	0.016	0.008	0.151	
Anxiety severity [GAD-7]	−0.005	0.009	−0.045	
Cluster affiliation	0.082	0.026	0.172**	
Physical quality of life [SF-8]				16.06–0.34**
Sociodemographic factors				
Age	−0.072	0.076	−0.047	
Gender	−1.741	0.659	−0.112**	
Family status	1.289	1.174	0.076	
Living situation	−1.696	1.229	−0.096	
Employment	−0.117	0.793	−0.006	
Education	3.008	1.448	0.085*	
Biomedical factors				
ARIC score	−0.065	0.042	−0.068	
Number of risk factors	−0.579	0.364	−0.088	
Number of medication	0.224	0.339	0.034	
Number of cardiac diseases	0.069	0.443	0.007	
Number of other somatic diseases	−0.953	0.436	−0.091*	
Psychological factors				
Depression severity [PHQ-9]	−0.892	0.175	−0.352**	
Anxiety severity [GAD-7]	0.674	0.191	0.231**	
Cluster affiliation	−4.753	0.547	−0.417**	
Mental quality of life [SF-8]				34.38–0.53
Sociodemographic factors				
Age	0.11	0.054	0.085*	
Gender	1.005	0.464	0.077*	
Family status	−1.502	0.826	−0.106	
Living situation	1.307	0.865	0.089	
Employment	0.244	0.557	0.016	
Education	1.199	1.018	0.041	
Biomedical factors				
ARIC score	0.001	0.03	0.002	
Number of risk factors	−0.132	0.256	−0.024	
Number of medication	0.360	0.238	0.065	
Number of cardiac diseases	0.107	0.311	0.012	
Number of other somatic diseases	0.647	0.307	0.074*	
Psychological factors				
Depression severity [PHQ-9]	−0.798	0.123	−0.377**	
Anxiety severity [GAD-7]	−1.007	0.134	−0.413**	
Cluster affiliation	0.221	0.385	0.023	

Abbreviations: PHQ-9 = Patient Health Questionnaire-9; GAD-7 = Generalized Anxiety Disorder Scale-7; SF-8 PCS = Short-Form Health Survey-8.

[*] Significant at $p < .05$.

[**] Significant at $p < .01$.

medical predisposition. Additionally, examining how to detect individuals with increased SSD symptoms and adjusting cut-off scores for subgroups with medical predisposition could be beneficial in the clinical context. Advantages of more accurately identifying individuals with heightened SSD symptoms include the ability to tailor treatment approaches and better allocate clinical resources, ensuring that those who would benefit most from specific treatments are effectively targeted.

The uncertainties surrounding the manifestation of SSD symptoms in individuals with a medical predisposition pose challenges for healthcare professionals and may result in inadequate diagnostics, hindering patients from receiving appropriate treatment [2,3,6–8]. Our study identified an association between increased GP visits and greater severity of SSD symptoms. Initial efforts to develop treatments particularly for individuals experiencing SSD symptoms, such as cognitive behavioral group treatment, have demonstrated positive effects [45]. Future research should delve into understanding existing treatment approaches for varying severity levels of SSD symptoms, developing preventive strategies and tailored treatments, as well as addressing the needs of healthcare professionals to overcome these uncertainties.

Early identification of SSD symptoms and increased acceptance of the diagnosis are associated with improved remission rates [2]. However, interpersonal issues, somatic symptom severity, stress, and SSD-related stigma can impede individuals from seeking help [2,46,47]. Acknowledging the heterogeneity of SSD symptoms and identifying subgroups, may facilitate a more nuanced understanding of SSD symptoms and help reduce stigma by recognizing its multifaceted nature and variability. To gain a more differentiated understanding, future studies could furthermore profit from contrasting our findings with those of individuals diagnosed with heart failure.

Research has shown a connection between heart failure and quality of life [11,12,14]. In this study, an increase in SSD symptoms was associated with a decrease in physical quality of life. There was no observed association between cluster affiliation and mental quality of life; however, psychological factors appeared to be relevant. These results suggest SSD symptoms contributing to the association between a medical predisposition and decreased physical quality of life. The association between increased symptom burden and reduced physical quality of life might be attributed to functional impairment [37]. Considering the correlation between functional impairment and adverse prognosis in individuals with heart failure, future research could explore factors affecting functionality among those at risk for heart failure, including managing illness perception, enhancing self-efficacy, and adopting improved self-care strategies [48–51].

4.2. Limitations

This study used the baseline data from the Hamburg City Health Study, benefiting from its large and diverse population-based sample. However, a potential selection bias may exist, as individuals more conscious about their health might have been more inclined to participate, attracted by the thorough health examination provided.

As only the baseline measurement and no follow-up had been conducted yet, we could not make any assumptions about the development of heart failure or SSD symptoms. Analyzing pre-existing data limited flexibility in individual measurements, resulting in excluding individuals from the analysis due to incomplete questionnaire responses, including the SSS-8 and SSD-12.

Additionally, persistence was assessed by relying solely on a self-reported item inquiring whether any of the experienced symptoms had persisted over the past six months. Future studies should consider a longitudinal design when follow-up data becomes available.

Furthermore, the exact structure of SSD symptoms remains uncertain, and it is conceivable that a continuous dimension would better capture this structure. In future studies, exploring methods to represent the combination of different SSD criteria in a continuous manner (such as including criteria A, B, and C of SSD diagnosis in one questionnaire) and analyzing associations and predictors using such a continuous dimension would be intriguing.

5. Conclusion

This study aimed to enhance comprehension of SSD at a symptomatic level in individuals with medical predispositions, such as the risk for heart failure, and to provide insights into the complex interplay of somatic and psychological factors. Three clusters were identified among these individuals, ranging from no SSD symptoms to varying severity levels. Regardless of the individual's risk for heart failure, both biomedical and psychological factors significantly contributed to the SSD symptoms. However, the differences in the severity of symptom burden appeared more apparent concerning psychological factors than biomedical ones. Increased SSD symptom severity was associated with more GP visits, aligning with previous research that highlighted the difficulty of identifying SSD in individuals with somatic comorbidities due to symptom diversity and overlap. Future research should focus on the diagnosis and prevalence of SSD in individuals with somatic comorbidities.

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CRediT authorship contribution statement

Caroline Clifford: Writing – original draft, Visualization, Validation, Software, Methodology, Formal analysis, Data curation, Conceptualization. **Raphael Twerenbold:** Writing – review & editing, Resources, Formal analysis. **Friederike Hartel:** Writing – review & editing, Formal analysis. **Bernd Löwe:** Writing – review & editing, Supervision, Project administration, Conceptualization. **Sebastian Kohlmann:** Writing – review & editing, Visualization, Validation, Supervision, Software, Project administration, Methodology, Formal analysis, Data curation, Conceptualization.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the author used ChatGPT in order to improve the wording. After using this tool, the author reviewed and edited the content as needed and takes full responsibility for the content of the publication.

The study was approved by the Ethics Committee of the Landesärztekammer Hamburg (State of Hamburg Chamber of Medical Practitioners, PV5131).

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychores.2024.111848.

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Study III

Patient-centered evaluation of an expectation-focused intervention for patients undergoing heart valve surgery: a qualitative study.

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Patient-centered evaluation of an expectation-focused intervention for patients undergoing heart valve surgery: a qualitative study

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Objective: Randomized controlled trials demonstrate the effectiveness of expectation-focused interventions in improving recovery outcomes following cardiac surgery. For dissemination in routine health care, it is important to capture the perspective of affected individuals. This qualitative study explores the perceived benefits and intervention-specific needs of patients who received expectation-focused intervention in the context of heart valve surgery. In addition, it explores potential barriers and adverse effects.
Methods: As part of an Enhanced Recovery After Surgery (ERAS) program within a multicentered randomized controlled trial, patients undergoing minimally invasive heart valve surgery received an intervention focused on their expectations. Six weeks after the intervention, semi-structured interviews were conducted with 18 patients to assess its feasibility, acceptance, barriers, benefits, and side effects. The transcribed interviews were analyzed using qualitative content analysis.
Results: The results indicate that both the intervention and the role of the patient and psychologist are key aspects in evaluating the expectation-focused intervention. Five key themes emerged from the patients' perspective: personal needs, expectations and emotions, relationship, communication, and individuality. Patients valued the preparation for surgery and recovery and the space for emotions. Establishing a trustful relationship and addressing stigmatization were identified as primary challenges within the intervention.
Conclusion: Overall, patients experienced the expectation-focused intervention as helpful and no adverse effects were reported. Perceived benefits included enhanced personal control throughout the surgery and recovery, while the potential barrier of stigmatization towards a psychologist may complicate establishing a trustful relationship. Addressing personal needs, as a relevant topic to the patients, could be achieved through additional research to identify the specific needs of different patient subgroups. Enhancing the expectation-focused intervention could involve the implementation of a modular concept to address individual needs better.

KEYWORDS

enhanced recovery after surgery (ERAS), evaluation, expectations, heart valve surgery, preoperative psychological intervention, qualitative research

1 Introduction

Numerous research findings indicate that patient expectations significantly influence treatment outcomes, irrespective of factors such as demographic variables, experienced stress, socioeconomic status, and health behavior (1, 2). This influence remains consistent regardless of the patient's medical condition or the type of surgical procedure (3). Negative expectations are associated with more complications, lower quality of life, higher illness-related disability, depressive symptoms, and prolonged inability to work (4, 5). Interventions to optimize patients' expectations before undergoing heart surgery have been developed in the past (5–7). Former studies showed an association between expectation-focused interventions and a faster recovery, including a reduced hospital stay and quicker return to work (8–10). Patients reported less postoperative pain and showed better physical health outcomes (10, 11). Furthermore, expectation-focused interventions were associated with greater personal control beliefs, increased quality of life, and reduced cardiac anxiety (12–14).

As research showed the advantages of expectation-focused interventions, Rief and colleagues developed a standardized preoperative intervention known as EXPECT within the PSY-HEART trial. The EXPECT intervention aims at optimizing the patients' expectations in the context of a coronary artery bypass graft surgery (6, 7, 13). This expectation-focused intervention was based on the integrative model of expectations which includes generalized self-efficacy, treatment outcome expectations (benefit expectations), timeline expectations, and personalized outcome expectancy (3).

To further illustrate the effectiveness of expectation-focused interventions in different medical contexts and as the need for psychological support for patients undergoing heart valve surgery was identified in former studies, an expectation-focused intervention based on the EXPECT intervention and adapted for patients with heart valve surgery was conducted (6, 7, 15). The intervention was implemented into an interprofessional Enhanced Recovery After Surgery (ERAS) program within a randomized controlled trial (RCT) on the improvement of treatment for patients undergoing heart valve surgery (16, for the study protocol; main manuscript under preparation). As the ERAS program was part of an RCT, a comparison between patients receiving the expectation-focused intervention and those receiving treatment as usual was possible. The expectation-focused intervention involved sessions led by a psychologist and included the development of realistic expectations about the benefits of the surgery and the recovery process. Relevant steps to achieve the personal goals as well as strategies to handle unpleasant symptoms were discussed (13). The first sessions took place four to six weeks before the surgery, followed by sessions one day before the surgery and during the hospital stay after the surgery. Relevant information and worksheets in a diary designed interprofessionally complemented the intervention and a last follow-up via telephone was conducted six weeks after the operation.

To date, the evaluation of expectation-focused interventions has primarily focused on quantifiable measures such as the duration of hospital stays or patient-reported outcomes such as anxiety (8, 13). To effectively disseminate an intervention, it is crucial to gain insights into the personal needs of patients (17–19). By including patients, we can identify which resources were experienced as needed, which needs were assessed as unmet and we can identify personal needs on a subgroup level (20).

In this study, we aimed to capture the evaluation of patients regarding an expectation-focused intervention in the context of heart valve surgery. Specifically, through a qualitative interview study, we intended to explore which aspects of the expectation-focused intervention are perceived as beneficial by patients undergoing heart valve surgery, whether they encounter any adverse effects, and how the intervention could be further enhanced.

2 Material and methods

2.1 Study context

The study was conducted as a qualitative follow-up of a randomized controlled trial (RCT) on the improvement of treatment for patients undergoing heart valve surgery (16, for the study protocol; main manuscript under preparation). In this trial, $N = 186$ patients undergoing minimally invasive heart valve surgery were randomized to treatment as usual or to an interprofessional treatment following an Enhanced Recovery After Surgery (ERAS) protocol. Part of the ERAS protocol for the intervention group was an expectation-focused intervention aiming at the development of realistic expectations concerning the surgery and its outcome, preparing for side effects (e.g., pain), and addressing emotions (e.g., anxiety). The medical clarification and decision-making processes such as heart valve choice occurred with the cardiac surgeon and were not part of the expectation-focused intervention. The Department of Psychosomatic Medicine and Psychotherapy conducted the expectation-focused intervention. An interprofessional approach involving surgical, anesthesiological, physiotherapeutic, and advanced nursing components was also part of the ERAS program.

2.2 Sampling

Recruitment for the qualitative study took place in Hamburg (Germany) between November 2021 and July 2022. Patients were recruited through a randomized controlled trial on the improvement of treatment for patients undergoing heart valve surgery at the University Medical Center Hamburg-Eppendorf. Inclusion criteria were an indication for elective minimally invasive aortic or mitral valve surgery and a functional status classification as "FIT" or "Pre-Frail" with the LUCAS functional index derived from the Longitudinal Urban Cohort Ageing Study (21). Furthermore, written informed consent, sufficient German language skills, and the ability to adequately understand the nature and extent of the individual's requirement for participation in the ERAS model of care were required. Exclusion criteria were severe chronic obstructive pulmonary disease, dialysis-dependent renal failure, advanced liver cirrhosis, residual neurological impairment following a prior stroke, predicted life expectancy of less than one year, previous cardiac surgery, severe depressive disorder, substance-related addictive disorders or a lack of a social environment that ensures adequate supportive care during the perioperative time.

As a second step, participants received information about the qualitative study before participation and were free to decide whether they wished to participate independently of their participation within the randomized controlled trial on the improvement of treatment for patients undergoing heart valve surgery. All participants gave written informed consent regarding the qualitative study. In addition, patients received an expense allowance of 15 € for participating in the interviews. The qualitative study was conducted in accordance with the Helsinki Declaration and was approved by the Ethics Committee of the University Medical Center (reference number: LPEK-0358).

We applied a purposive sampling strategy to ensure that variations in gender, age, and disease duration were accounted for. We included patients of both, the intervention and control groups, to compare how patients received the expectation-focused intervention and how patients would evaluate their motivation in participating. Considering a high variation of age, gender, and disease duration, we collected a sample size of $N = 18$ patients, based on findings on saturation of themes (22).

2.3 Study design and data collection

We used an exploratory, qualitative framework, applying a semi-structured interview guide. The semi-structured interviews with $N = 18$ patients were conducted by the first author (CC). Interviews were split into two parts in order not to overstrain the patients, each lasting between 35 and 45 min. The interviews took place after rehabilitation, about six weeks after the operation, and were conducted virtually via video-telephony as patients lived at various locations across Northern Germany. The semi-structured interview guide included topics addressed in the expectation-focused intervention, such as feasibility, acceptance, barriers, and effectiveness plus the experience of adverse effects. Further key issues regarding the combination of psychology and cardiology in treatment and the perception of the interprofessional approach were also included in the interview guide. The different topics were supplemented by more structured questions based on pre-identified themes. Prompting questions were used to encourage patients to elaborate on their experiences and reduce possible bias by expressing both positive and negative accounts. Interviews were audiotaped, pseudonymized, and transcribed verbatim by trained student research assistants. Transcription followed the rules of Dresing and Pehl, with all transcripts being checked for correctness by CC (23).

2.4 Study variables

In addition to demographic data such as age, gender, marital status, living situation, employment status, and education, patients were asked about their disease duration. Cardiac risk factors including smoking, obesity, hypertension, hyperlipidemia, diabetes, and positive family history as well as the presence of any further cardiac or somatic comorbidity were assessed. The severity of cardiac symptoms was measured through the New York Heart Association (NYHA) classification (24) and the Canadian Cardiovascular Society Classification (CCSC) (25). Both are self-reporting questionnaires: in the NYHA classification, patients rate the severity of their dyspnea, whereas the CCSC assesses chest pain. Both classifications categorize patients into four classes, ranging from "no impairment at all" to "impairment even at resting". With increasing symptom severity, patients are assigned to higher classes. The determination of these classes is based on the criteria outlined in the questionnaires, which consider the reported symptoms, limitations in daily activities, and the impact of the symptoms on the patient's overall well-being.

2.5 Data analysis

Data was analyzed according to the qualitative content analysis by Kuckartz (26) and using the software MAXQDA (version 2022). The analysis was conducted by identifying themes at the semantic (explicit) rather than latent (interpretative) level, as we were interested in evaluating the expectation-focused intervention from the patient's perspective. Given the exploratory nature of the research interest, we predominantly used an inductive approach, after initially formulating deductive themes derived from the interview guide and intervention. The analysis process involved multiple stages and collaborative efforts among the research team. The first author (CC) and co-author (SKU) independently conducted an initial data screening. During this phase, we focused on the formulated deductive themes. Gradually, both coders (CC and SKU) began identifying new themes and interesting features not anticipated in the deductive phase. These new themes emerged through an inductive coding process. Subsequently, CC, SKU, and SKO (as the last author) engaged in discussions to create a preliminary codebook. This codebook served as a guide for the subsequent coding process. CC and SKU then systematically coded the entire dataset multiple times, referring to the preliminary codebook. During this process, they engaged in ongoing discussions to resolve any ambiguities or discrepancies in the interpretation of the data. In the final stage of coding, the research team merged or redefined subthemes as needed to ensure the coding accurately reflected the nuances and variations present in the data. This iterative process allowed for a more nuanced and differentiated coding of the material.

3 Results

3.1 Sample description

Within the sample ($N = 18$), age ranged from 19 to 71 years with a mean of 51.3 years (SD = 15.5). We included $n = 11$ patients of the intervention group who had received the expectation-focused intervention and $n = 7$ patients of the control group who had not received the intervention. Within the sample, 61% of patients ($n = 11$) experienced a long disease duration (more than three years), whereas 39% of patients ($n = 7$) described a short disease duration (less than three years). Of the 18 patients, $n = 5$ patients experienced complications from the heart valve surgery including sternal rewiring, retroperitoneal hematoma, pseudoaneurysm, increased levels of inflammatory markers, single postoperative tachycardic atrial fibrillation, and rethoracotomy. Regarding the type of surgery, $n = 8$ underwent reconstruction, $n = 9$ received a bioprosthetic valve replacement, and $n = 1$ received a mechanical valve replacement. Regarding gender, there was an overrepresentation with 78% male patients ($n = 14$) compared to 22% female patients ($n = 4$). Further relevant characteristics are shown in Table 1.

3.2 Patients' evaluation of an expectation-focused intervention in the context of heart valve surgery

The main aim of this qualitative study was to gain insights into how patients undergoing heart valve surgery evaluate an expectation-focused intervention. During the analysis, it became apparent that patients evaluated not only the intervention itself but also assigned importance to the roles of both the patient and the psychologist conducting the intervention. We identified five main themes in the patients' evaluation of the expectation-focused intervention: personal needs, expectations and emotions, relationship, communication, and individuality. As seen in Figure 1, the patient who played a pivotal role in evaluating the expectation-focused intervention was involved in all identified themes. Moreover, certain themes, such as personal needs or expectations and emotions, influenced the content and design aspects of the intervention significantly. Conversely, the psychologist conducting the intervention notably influences the relationship theme. The evaluation of communication and individuality could be observed as being influenced collectively by the patient, the psychologist, and the intervention.

TABLE 1 Description of the study sample ($N = 18$).

Characteristics ($N = 18$)	
Sociodemographics, *n* (%)	
Age, mean (SD), years	51.3 (15.5)
Gender, female	4 (22.2)
Group affiliation, intervention group	11 (61.1)
Living alone	4 (22.2)
Married	9 (50.0)
≥10 years of formal education	17 (94.4)
Employed	12 (66.7)
Clinical characteristics, *n* (%)	
≥3 years of disease duration	11 (61.1)
No cardiac comorbidities, mean (SD)	17 (94.4)
No somatic comorbidities, mean (SD)	12 (66.7)
Cardiac risk factors, *n* (%)	
Hypertension	6 (33.3)
Diabetes	1 (5.6)
Hyperlipidemia	11 (61.1)
Smoking	1 (5.6)
Obesity	3 (16.7)
Positive family history	14 (77.8)
Angina pectoris, *n* (%)	
CCS Class 1	4 (22.2)
CCS Class 2	2 (11.1)
CCS Class 3	5 (27.8)
CCS Class 4	7 (38.9)
Dyspnea, *n* (%)	
NYHA Class 1	11 (61.1)
NYHA Class 2	5 (27.8)
NYHA Class 3	2 (11.1)
NYHA Class 4	0 (0.0)

CCS, Canadian Cardiovascular Society Classification; NYHA, New York Heart Association Classification.

3.2.1 Personal needs

One of the themes most discussed by patients undergoing heart valve surgery was the personal need for an expectation-focused intervention. Patients expressed a range of views on this theme, from feeling no personal need for such an intervention to recommending its implementation for every surgery:

> *'Perhaps it could be different with a more difficult operation or if I'm not doing well, but now in the course of this operation, I didn't really feel the need to get help through personal conversation.'*

> *'Yes, I think that this should happen for every operation. Because every operation is worrying for the patient and their anxiety levels may vary. Therefore, I think it's always appropriate to have such a conversation.'*

Patients' views on the need for an expectation-focused intervention varied, based on how well they were coping with the surgery themselves. For some patients, the decision depended on their individual experiences and symptoms:

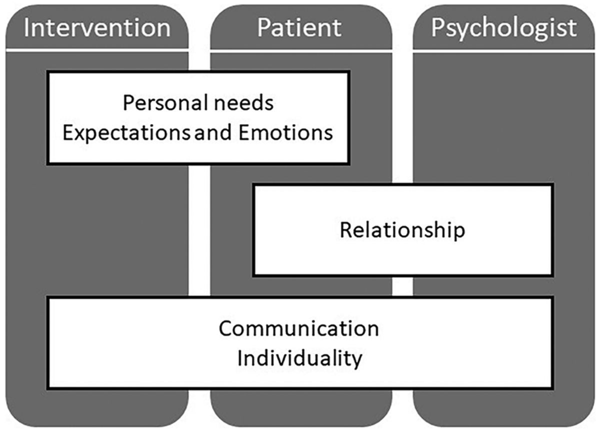

FIGURE 1
Identified themes from patients' evaluation of an expectation-focused intervention in the context of heart valve surgery.

> *'When I'm not well, it depends on why I'm feeling that way. If it's due to nausea or pain, I wouldn't necessarily want to talk to a psychologist. If anxiety would overwhelm me, then it would be more likely. It depends on what the symptoms are.'*

The evaluation concerning the time frame of the expectation-focused intervention was one further aspect of personal needs. One patient experienced the session after the surgery too early and recommended more time to focus on themselves. The majority supported the given time frame, including the length and frequency of sessions:

> *'Well-arranged at excellent intervals. Both, before the operation, you were there on the day before and then again afterwards, and again after Christmas. I must say that I found the intervals perfect. Because the phases I was in were very different. My perspective regarding the occurrence changed after the operation.'*

3.2.2 Expectations and emotions

The theme of expectations and emotions primarily focused on content-related aspects of the intervention. In accordance with the aim of the expectation-focused intervention, patients described the preparation for the surgery as helpful. Building up strategies such as how to deal with side effects following the surgery increased the experienced personal control:

> *'I remember our first conversation really well. You advised me to prepare for possible pain and shortness of breath during my treatment but assured me that these symptoms can be managed. Your words helped me understand what to expect and made me feel better prepared for it.'*

Although the patients experienced increased personal control, it seemed difficult for them to build up realistic expectations. Some patients described a discrepancy between their expectations and the perceived reality after the surgery, which was not communicated clearly enough in the intervention.

During the pre- and postoperative phases, patients experienced different emotions such as overburdening, helplessness, and anxiety but also confidence and hope. In addition to preparing for potential somatic side effects, patients found it beneficial to be mentally prepared for the emotional aspects before and after surgery. One example is the relief experienced by the space given for emotions:

> *'It was positive because for me, when talking about critical points or difficult things and then for example an emotion comes through like crying it feels like a release. So it's definitely been positive.'*

3.2.3 Communication

Patients regarded transparent communication as a positive factor and emphasized the importance of language which is not perceived as banalizing throughout the treatment. Concerning the feasibility, the content of the expectation-focused intervention was assessed to be clear and comprehensible. While the content was straightforward to follow, patients encountered uncertainty regarding the purpose of the intervention, leading them to question what personal benefits they could expect:

> *'I'm not quite sure about the objective [of the expectation-focused intervention], so I'm not sure of the best way to achieve it.'*

3.2.4 Relationship

Within the theme of relationship, the perception of the relationship between the psychologist and the patient was evaluated. Patients described a trustful relationship with the psychologist as supportive, viewing them as a contact person with whom they can openly discuss difficulties and worries. Patients deemed a trusting relationship crucial for discussing sensitive and challenging topics without fear of judgment. However, they evaluated the process of establishing this trustful bond with the psychologist as challenging:

> *'[Building up trust towards the psychologist] is not something that can be accomplished in ten or fifteen minutes. You first have to build up a basis of trust in order to show your inner self in a conversation or to show your direct feelings or what is bothering you before the operation. I don't think you can build up this trust in such a short time.'*

Patients described inconsistent evaluations regarding the inclusion of a psychologist into the pre- and postoperative treatment of heart valve surgery. Some patients felt that it carried a sense of stigmatization, while others evaluated the psychologist as an integral part of an interprofessional team, contributing to a holistic treatment approach:

> *'I thought, well, why do I need a psychologist now? […] That was a bit surprising for me.'*

> *'This process of talking to a psychologist is a matter of course for me in the process of good health treatment and even if there is no need, it is still good to have checked it as maybe something is hidden where there is still a need. That's why I approached the conversation with a positive attitude.'*

3.2.5 Individuality

The theme of individuality encompassed patients' evaluation of feeling individually addressed and understood within the intervention. Patients evaluated the individuality of the expectation-focused intervention differently. Some patients felt it catered to their individual needs, while others did not experience this personalization:

> *'No, I didn't really feel personally addressed.'*

> *'I felt like I was receiving totally personalized care. [The psychologist] also knew exactly what my weak points were,*

> *which worried me initially. And later they asked if I felt better [concerning the weak points]. And I found that very individual.'*

3.2.6 Additional findings

During the interviews, we encountered results that piqued our interest but were not directly related to the research question. These findings are discussed in the following section, which presents additional findings.

One further aspect of the expectation-focused intervention was to involve close relatives in the process. They could join during the preoperative session, which included the management of expectations concerning the surgery and recovery as well as building up strategies to handle unpleasant symptoms. The participation of close relatives was experienced as supportive by the patients, especially in the sense of having somebody to exchange experiences and emotions with. Additionally, some patients suggested offering sessions with a psychologist to relatives of patients undergoing heart valve surgery.

The expectation-focused intervention was embedded into an interprofessional treatment approach. The interprofessional exchanges, especially during ward rounds where experts from various professions participated, were evaluated as a particularly positive aspect when it comes to a holistic treatment approach.

Within the sample, we identified patients who experienced complications related to heart valve surgery. Their evaluation of the expectation-focused intervention was similar with those of patients without complications.

In addition to the evaluation through patients who had received the expectation-focused intervention, we conducted interviews with patients of the control group. The main challenge was that these patients had not received an expectation-focused intervention and therefore could not evaluate the intervention. To overcome this challenge, we adjusted the interview guide. Instead of evaluating the actual intervention, the control group patients were asked to evaluate the contents and aims which would typically be addressed in the expectation-focused intervention. We were interested in the opinion of patients of the control group as they had not been biased by receiving the expectation-focused intervention beforehand but at the same time were able to assess the experience of a heart valve surgery itself. Concerning the themes of expectations and emotions, relationship, communication, and individuality, the evaluation was congruent with the evaluation described by patients of the intervention group. In respect of personal needs, patients of the control group also varied between no personal need and the view of implementing an expectation-focused intervention in routine care. Without experiencing the interventions, some patients evaluated a higher personal need after the surgery than they would have expected in a preoperative stage.

3.2.7 Overall evaluation of the expectation-focused intervention

All patients ($N = 18$) were asked whether they (a) would themselves participate (again) and (b) would recommend others to participate in the expectation-focused intervention if they were undergoing heart valve surgery. Of the intervention group, 100% of the patients ($n = 11$) agreed they would participate again and would also recommend it to others. Of the control group, 86% of the patients ($n = 6$) stated they would have participated if they had been given the possibility. All patients of the control group ($n = 7$) reported they would recommend the expectation-focused intervention to others undergoing heart valve surgery.

Furthermore, patients were asked about any adverse effects they may have experienced due to the expectation-focused intervention. All patients responded negatively, indicating an absence of any adverse effects. Overall, the patients evaluated the expectation-focused intervention as helpful:

> *'I found the sessions [with the psychologist] really useful because they changed my approach to the whole process of the operation. I also knew that I had support when I wasn't doing well. That's why I wouldn't do without it under any circumstances.'*

3.3 Optimization of the expectation-focused intervention

A key consideration in enhancing the expectation-focused intervention for patients undergoing heart valve surgery revolved around addressing personal needs. The aim would be to find strategies to provide support for those who benefit from optimizing expectations while streamlining the intervention for those who do not experience the same level of benefit. According to the patients interviewed, a higher need for support would be relevant for patients with anxiety or negative attitudes towards life, patients of higher age, patients with little social support or self-care, or those experiencing acute symptoms. The patients interviewed assessed patients who knew about their surgery far in advance as having less need for an expectation-focused intervention compared to patients with less preparation time or less experience when it comes to surgery in general.

Concerning the time frame of the intervention the patients evaluated it as helpful that the psychologist took the first step in approaching the patient, offering the expectation-focused intervention. At the same time, they suggested adapting the amount and length of appointments individually, based on what the psychologist and the patient mutually judge to be beneficial:

> *'I would definitely offer this to every patient before and after the operation at certain intervals. And also approach the patient directly, as I think that many patients have an inhibition to seek help and it's easier to accept help when it's offered.'*

Furthermore, the patients evaluated the content of the expectation-focused intervention as well-suited for the context of a heart valve surgery and that none of the addressed topics should have been omitted. To enhance personal control, patients recommend more participation in the surgical process as an integral component of the expectation-focused intervention. This could include options like watching a video of the surgery in advance. Furthermore, the patients addressed the topic of acceptance. They proposed including breathing and relaxation exercises to better handle emotions such as anxiety and helplessness. Apart from discussing the current situation of heart valve surgery, patients expressed a desire to focus on health-related behavior. This could be achieved by including stress management and nutritional information in the intervention. While some patients recommended including discussions about the topic of death within the intervention, others strongly disapproved of this idea. Adding any decision-making processes such as heart valve choice was not mentioned as a topic relevant to the patient in the context of the expectation-focused intervention.

4 Discussion and conclusion

4.1 Discussion

Overall, the patients experienced the expectation-focused intervention as helpful and none of the patients reported experiencing any adverse effects from it. The results indicate that not only the intervention but also the role of the patient and psychologist play a major part in evaluating the expectation-focused intervention. One of the most discussed themes by the patients is the assessment of personal needs and how these needs vary among patients. As positive aspects, the preparation concerning the surgery and recovery including how to handle unpleasant symptoms as well as the space for emotions are mentioned. It is evaluated positively that the expectation-focused intervention aligned with topics that were individually relevant to the patient. Concerning communication patients assume they would benefit from a clearer understanding of the advantages they can gain from the intervention. Establishing a trustful relationship within the limited time frame before the surgery also appears to be a challenging task.

According to Holmes and colleagues, it is important that patients' discrepancies between pre- and postoperative expectations are as small as possible (10). The patients in this study describe the development of realistic expectations as challenging as the surgery and its consequences could take different courses and individual perceptions seem relevant. Within the expectation-focused intervention, the patients evaluated the preparation and development of strategies to cope with difficulties before and after the surgery as helpful and associated with increased personal control. Kube and colleagues shift the focus toward postoperative expectations when it comes to improving the clinical outcome after surgery (27). Further development of the expectation-focused intervention could focus on postoperative expectations. Furthermore, patients could experience higher personal control by receiving additional insights into the surgery process. Klein and colleagues interviewed patients undergoing radical cystectomy and urinary diversion concerning their perioperative experiences (28). These patients expressed a desire for the implementation of a buddy system. Such a buddy system where patients in the perioperative phase are paired with patients who have undergone successful heart valve surgery for an experience exchange could be considered as a helpful additional element to the expectation-focused intervention.

Patients describe establishing a trustful relationship within the limited time frame before the surgery as a challenge. We deduct that stigmatization associated with sessions with a psychologist is a contributing factor that complicates building up trust and admitting personal needs. Some patients additionally reflected that the purpose of the intervention and their possible personal benefit were not easy to identify. During the initial session of the expectation-focused intervention, the psychologist introduces and discusses the concept and purpose. To align the purpose with the individual needs of the patient, it could be beneficial to provide a more detailed and stronger differentiated explanation about the topics encompassed within the intervention. Furthermore, the psychologist's role could be introduced in a manner that avoids the use of language or terminology that might contribute to stigmatization.

When it comes to the experienced individuality of the expectation-focused intervention, the majority of patients perceive it as addressing their individual needs. Table 1 illustrates variations among the patients undergoing heart valve surgery, including variances in disease duration, comorbidities, cardiac risk factors, as well as other clinical characteristics like angina pectoris and dyspnea. However, it remains unclear which patients derive the greatest benefit from the intervention. Future research should place a greater emphasis on understanding the specific needs of various patient subgroups while actively involving patients in the process of the intervention.

The patients in this study suggested incorporating additional elements into the expectation-focused intervention, such as including breathing exercises and learning new strategies to cope with stress. To face the challenge of maintaining an efficient time schedule, it could be valuable to organize the expectation-focused intervention as a modular concept. The choice of modules on which to focus could be determined by the patient's preferences and what appears relevant from the psychologist's perspective, possibly, for example through the use of screening tools. Auer and colleagues provided initial insights into tailored approaches within expectation-focused interventions (12). Their study revealed that patients seeking to alleviate depressive symptoms should focus on different aspects of expectations, whilst focusing on expected consequences is particularly beneficial in reducing anxiety (12). In future studies, to obtain a more comprehensive perspective, it is essential to include a diverse range of patients with varying sociodemographic, disease-related, and psychosocial variables. Quantitative measures related to the identified themes could be used to test associations between these variables and the evaluation of the expectation-focused intervention. A more nuanced understanding of which patient subgroups profit from specific intervention focuses and frequencies could also lead to a more efficient allocation of resources within the healthcare system.

4.2 Limitations

The results of this study should be interpreted in light of the following limitations. Firstly, the interview subsample was self-selected. The patients of the intervention group were asked during the initial session of the expectation-focused intervention whether they would like to participate in the interview to evaluate the intervention, whereas patients of the control group were approached after the surgery. All patients provided informed consent and retained the option to withdraw from the study at any stage. Although no patients chose to withdraw, it is possible that those who participated may have had a higher level of motivation to invest effort in evaluating and improving expectation-focused interventions. Furthermore, the sample included more male patients (78%) in comparison to female patients (22%). An overrepresentation of male patients is a recognized characteristic in the context of heart valve surgery, which is why we consider the collected data sufficient in terms of achieving a balanced sample, based on pre-defined criteria (29).

Secondly, the sample was recruited from an RCT which included repeated assessments for all patients and increased interprofessional treatment for the intervention group. The assessments comprised surveys including questions about mental health which might have induced heightened self-reflection when compared to patients not participating in the study. By including patients of the control group in the qualitative study, we obtained insights into patients who did not receive enhanced interprofessional treatment but nevertheless underwent heart valve surgery. These patients did not receive the expectation-focused intervention which helps mitigate bias but also poses a challenge in envisioning the potential impact of such an intervention. Moreover, the patients may have faced challenges in distinguishing between the various interprofessional aspects of the treatment. To assist patients in identifying the components associated with the expectation-focused intervention, we revised the specific elements linked to this intervention at the beginning of the interview.

Thirdly, due to the protection of data, the interviews were solely conducted with patients from the University Medical Center Hamburg-Eppendorf. This limits the choice of psychologists performing the expectation-focused interventions with the patients. Both the performance of the intervention and the evaluation process were executed by the Department of Psychosomatic Medicine and Psychotherapy at the University Medical Center Hamburg-Eppendorf. By involving different members of the department in the process of conducting the intervention and interviews, transcribing, coding, and analyzing the interviews, we aimed to reach the highest possible validity within our resources.

5 Conclusion

Overall, our analysis generated first insights into patients' views on expectation-focused intervention in the context of heart valve surgery. This qualitative study shows an overall endorsement of the intervention and appears to address holistic care demands. Establishing a trustful relationship and perceived stigmatization of treatment by a psychologist pose the main challenges. Stigmatization could be reduced by framing the role of the psychologist differently and implementing an expectation-focused intervention as part of routine care. The initiation of initial contact could be beneficial in reducing stigmatization and lowering the barrier to seeking help. To address individual needs in the best possible way, the introduction of a modular concept, where patients and psychologists in collaboration determine the most suitable focus and frequency of the intervention, could be considered. Certain topics, such as preparing for unpleasant symptoms and providing space for emotions, should be integral components of every intervention. Innovative enhancements, such as providing sessions for relatives, and expanding the range of topics to include breathing exercises and stress-coping strategies, could be considered as additions. Introducing a buddy system, pairing patients in the preoperative phase with those who have successfully undergone heart valve surgery to enhance experience exchange, could also be of great value. Future research should concentrate on developing the expectation-focused intervention within a modular concept and investigate the influence of sociodemographic, disease-related, and psychosocial variables in identifying specific personal needs among patient subgroups.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, upon reasonable request.

Ethics statement

The underlying INCREASE RCT involving humans was approved by the Ethics Committee of the Hamburg Medical Association (reference number: 2020-10276-BO-ff). The present qualitative study was approved by the Ethics Committee of the University Medical Center (reference number: LPEK-0358). The studies were conducted in accordance with the local legislation and institutional requirements. The participants proved their written informed consent to participate in this study.

Author contributions

CC: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing – original draft. EG: Conceptualization, Funding acquisition, Resources, Writing – review & editing. SGRK: Conceptualization, Funding acquisition, Resources, Writing – review & editing. SKu: Formal Analysis, Methodology, Software, Validation, Visualization, Writing – review & editing. BL: Conceptualization, Funding acquisition, Writing – review & editing. SKo: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

EG declares that he was an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

Publisher's note

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9. ABSTRACT / ZUSAMMENFASSUNG

9.1 Abstract

Symptom burden refers to the negative impact on an individual's life or functional status caused by their experienced symptoms. **Research has shown that an increased symptom burden is associated with severe consequences, such as higher morbidity, mortality, hospitalization rates, and poorer quality of life, regardless of biomedical markers.** Some studies also indicate a link between increased symptom burden and greater healthcare utilization. Risk factors for an increased symptom burden include biomedical factors, such as infections or somatic diseases, and psychological factors, such as higher levels of depression and anxiety or deficits in emotion regulation. This dissertation focused on the symptom burden and needs of individuals with or at risk of cardiac disease due to the significant overlap in the phenomenology (i.e., experienced symptoms) between individuals with increased symptom burden and those with cardiac disease, despite their differing etiologies. While the development of cardiac disease is primarily explained by biological factors, the etiology of increased symptom burden involves a complex interplay of biological, psychological, and social factors. Often, the subjective symptom burden persists even after the underlying pathophysiology has been treated.

The objectives of this dissertation were to examine whether there are distinct subgroups of individuals with or at risk of cardiac disease based on their symptom burden and to analyze which biomedical and psychological factors are associated with increased symptom burden in this population. Additionally, the dissertation aimed to explore the relationship between increased symptom burden and both healthcare utilization and quality of life. An evaluation of an expectation-focused intervention was also conducted to better understand the needs of individuals with cardiac disease. Study I is a longitudinal study involving individuals with cardiac disease, focusing on identifying characteristics and predictors associated with increased symptom burden. Study II is a population-based, cross-sectional cohort study including individuals at risk for heart failure, where symptom burden and its associated factors were assessed. In Study III, an expectation-focused intervention within a randomized controlled trial aiming at improving the treatment of individuals undergoing heart valve surgery was evaluated.

The results of Study I and II demonstrated that subgroups could be identified based on experienced symptom burden. **Biomedical factors associated with increased symptom burden in individuals with or at risk of cardiac disease included angina pectoris and dyspnea**, while factors such as the number of cardiac diseases, comorbidities, and medication use did not show significant differences. **Psychological factors linked to increased symptom burden included higher severity of depression and anxiety as well as the presence of mental disorders.** When comparing biomedical and psychological burden, it was evident that individuals with a medical predisposition, such as an elevated risk for heart failure, primarily experienced biomedical burden, whereas psychological burden was more prevalent among those with increased symptom burden. **The conducted studies found a consistent association between increased symptom burden and both higher healthcare utilization and lower physical quality of life,** regardless of sociodemographic, biomedical, and psychological factors. Decreased mental quality of life was better explained by psychological factors than by symptom burden itself. The evaluation of an expectation-focused intervention for individuals undergoing heart valve surgery (Study III) identified key needs, including **transparent communication, the establishment of a trustful relationship with healthcare professionals, and a desire for an interprofessional treatment approach.** The individuals reported benefiting from enhanced personal control through education and preparation regarding the surgery and its potential side effects, as well as having a supportive environment to express and reflect on their emotions.

The findings suggest that individuals with similar diseases and symptoms seem to experience different levels of symptom burden. Similarly, the needs of individuals with the same diagnosis and treatment approach differ between one another. Psychological factors, in particular, appear to play a crucial role in increased symptom burden, whereas objectively measured biomedical factors do not show a strong association. The importance of recognizing the subjective nature of symptom experience and burden is emphasized, and this individuality should also be reflected in treatment approaches. **The findings advocate a personalized approach that focuses more on the symptoms and experiences of individuals, rather than strictly on diagnosis or biomedical markers.** In doing so, psychological factors should be considered and individuals should be involved in their treatment to better meet their personal needs. Future research should further explore the factors that influence the development of symptom burden in individuals with or at risk of cardiac disease. This could be achieved by incorporating additional biomedical and psychological factors, as well as considering health behavior, contextual, interpersonal, and cognitive-perceptual factors. In the clinical setting, the development of modular treatment concepts or the implementation of screening tools to address needs and to identify individuals at risk for increased symptom burden at an early stage could be highly beneficial.

9.2 Zusammenfassung

Der Begriff der Symptombelastung bezieht sich auf die negativen Auswirkungen, die Symptome auf das Leben oder die Funktionsfähigkeit eines Individuums haben. **Forschungen haben gezeigt, dass eine erhöhte Symptombelastung, unabhängig von biomedizinschen Markern, mit schwerwiegenden Folgen assoziiert ist, wie beispielsweise einer höheren Morbidität, Mortalität, einer erhöhten Anzahl an Krankenhausaufenthalten und einer schlechteren Lebensqualität.** Einige Studien weisen zudem einen Zusammenhang zwischen erhöhter Symptombelastung und einer stärkeren Inanspruchnahme des Gesundheitssystems auf. Risikofaktoren für eine erhöhte Symptombelastung umfassen biomedizinische Faktoren wie Infektionen oder somatische Erkrankungen, sowie psychologische Faktoren wie höhere Depressions- und Angstniveaus oder Defizite in der Emotionsregulation. Der Fokus dieser Dissertation lag auf der Symptombelastung und den Bedürfnisse von Individuen mit oder einem Risiko für Herzerkrankungen. Dies scheint relevant, da es bei Individuen mit erhöhter Symptombelastung und solchen mit Herzerkrankungen oftmals eine Überlappung in der Phänomenologie (d.h. der erlebten Symptome) gibt, wohingegen die Ätiologie sich grundlegend unterscheidet. Während die Entstehung von Herzerkrankungen in erster Linie durch biologische Faktoren erklärt wird, basiert die Ätiologie einer erhöhten Symptombelastung auf einem komplexen Zusammenspiel von biologischen, psychologischen und sozialen Faktoren. Oftmals besteht die subjektive Symptombelastung auch nach der Behandlung der zugrunde liegenden Pathophysiologie fort.

Ziele dieser Dissertation waren, zu untersuchen, ob es unterschiedliche Subgruppen von Individuen mit Herzerkrankung oder einem Risiko für Herzerkrankung auf Basis ihrer Symptombelastung gibt, und zu analysieren, welche biomedizinischen und psychologischen Faktoren mit einer erhöhten Symptombelastung in dieser Population verbunden sind. Darüber hinaus zielte die Dissertation darauf ab, den Zusammenhang zwischen erhöhter Symptombelastung und sowohl der Inanspruchnahme des Gesundheitssystems als auch der Lebensqualität zu untersuchen. Die Evaluation einer erwartungsfokussierten Intervention wurde ebenfalls im Rahmen der Dissertation durchgeführt, um die Bedürfnisse von Individuen mit Herzerkrankungen besser zu verstehen. Studie I ist eine longitudinale Studie, welche das Ziel verfolgte Charakteristika und Prädiktoren bei Individuen mit Herzerkrankung zu identifizieren, die mit einer erhöhten Symptombelastung assoziiert sind. Studie II ist eine bevölkerungsbasierte, querschnittliche Kohortenstudie in der die Symptombelastung und deren assoziierte Faktoren bei Individuen mit einem Risiko für Herzinsuffizienz analyisiert wurden. In Studie III wurde eine erwartungsfokussierte Intervention als Teil einer randomisierten, kontrollierten Studie evaluiert, die darauf abzielte, die Behandlung von Individuen, die sich einer Herzklappenoperation unterziehen, zu verbessern.

Die Ergebnisse aus den Studien I und II zeigten, dass Subgruppen auf Basis der erlebten Symptombelastung identifiziert werden konnten. **Biomedizinische Faktoren, die mit erhöhter Symptombelastung bei Individuen mit Herzerkrankung oder mit einem Risiko für Herzerkrankung assoziiert waren, umfassten Angina pectoris und Dyspnoe,** während Faktoren wie die Anzahl der Herzerkrankungen, Komorbiditäten und Medikamenteneinnahme keine signifikanten Unterschiede aufwiesen. **Psychologische Faktoren, die mit erhöhter Symptombelastung verbunden waren, umfassten eine höhere Schwere von Depressionen und Ängsten, sowie das Vorliegen psychischer Störungen.** Beim Vergleich von biomedizinischer und psychologischer Belastung zeigte sich, dass Individuen mit einer medizinischen Prädisposition, wie einem erhöhten Risiko für Herzinsuffizienz, hauptsächlich biomedizinische Belastungen erfuhren, während psychologische Belastungen insbesondere bei Individuen mit erhöhter Symptombelastung vorkamen. Die durchgeführten Studien zeigten, unabhängig von soziodemografischen, biomedizischen und psychologischen Faktoren, **einen Zusammenhang zwischen erhöhter Symptombelastung und sowohl einer höheren Inanspruchnahme des Gesundheitssystems als auch einer geringeren physischen Lebensqualität auf.** Eine verminderte mentale Lebensqualität ließ sich besser durch psychologische Faktoren als durch die Symptombelastung selbst erklären. Die Evaluation der erwartungsfokussierten Intervention für Individuen, die sich einer Herzklappenoperation unterzogen (Studie III), identifizierte zentrale Bedürfnisse, darunter eine **transparente Kommunikation, den Aufbau einer vertrauensvollen Beziehung zu den Behandler:innen und den Wunsch nach einem interprofessionellem Behandlungsansatz.** Die Individuen berichteten, dass sie von einer verbesserten persönlichen Kontrolle durch Aufklärung und Vorbereitung auf die Operation und deren mögliche Nebenwirkungen, sowie von einer unterstützenden Umgebung, in der sie ihre Emotionen ausdrücken und reflektieren konnten, profitierten

Die Ergebnisse deuten darauf hin, dass Individuen mit vergleichbaren Erkrankungen und Symptomen unterschiedliche Niveaus der Symptombelastung zu erleben scheinen. Ebenso unterscheiden sich die Bedürfnisse von Individuen mit derselben Diagnose und demselben Behandlungsansatz voneinander. Insbesondere psychologische Faktoren scheinen eine entscheidende Rolle bei einer erhöhten Symptombelastung zu spielen, während objektiv gemessene biomedizinische Faktoren weniger Relevanz bezüglich der Symptombelastung zeigen. Die Anerkennung der subjektiven Natur des Symptomempfindens und der

Symptombelastung scheint relevant und diese Individualität sollte sich auch in den Behandlungsansätzen widerspiegeln. **Die Ergebnisse sprechen für einen personalisierten Ansatz, der sich stärker auf die Symptome und Erfahrungen der Betroffenen konzentriert, anstatt sich strikt an den Diagnosen oder biomedizinischen Markern zu orientieren.** Hierbei sollten auch psychologische Faktoren berücksichtigt und die Betroffenen in ihre Behandlung einbezogen werden, damit persönlichen Bedürfnisse erfüllt werden können. Zukünftige Forschung sollte weiter untersuchen, welche Faktoren die Entwicklung der erhöhten Symptombelastung bei Individuen mit Herzerkrankung oder einem Risiko für Herzerkrankung beeinflussen. Dies könnte durch die Einbeziehung zusätzlicher biomedizinischer und psychologischer Faktoren, sowie durch die Berücksichtigung von Gesundheitsverhalten, kontextuellen, zwischenmenschlichen und kognitiv-perzeptuellen Faktoren erreicht werden. Im klinischen Kontext könnte die Entwicklung modularer Behandlungskonzepte oder die Implementierung von Screening-Tools von Nutzen sein, um Bedürfnisse zu adressieren und Individuen mit einem Risiko für eine erhöhte Symptombelastung frühzeitig zu identifizieren.

10. AUTHOR CONTRIBUTION STATEMENT

Financial support for Study I was given by the Werner Otto Stiftung, Hamburg, Germany (project ID 12/87),. Study II was funded by the euCanSHare grant agreement (Grant Number 825903-euCanSHare H2020), Joachim Herz Foundation, Foundation Leducq (Grant Number 16 CVD 03), Innovative Medicine Initiative (Grant Number 116074), Deutsche Gesetzliche Unfallversicherung (DGUV), Deutsches Krebsforschungszentrum (DKFZ), Deutsches Zentrum für Herz-Kreislauf-Forschung (DZHK), Deutsche Stiftung für Herzforschung, Seefried Stiftung, Bayer, Amgen, Novartis, Schiller, Siemens, Tocon, Unilever, TePe and by donations from the "Förderverein zur Förderung der HCHS e.V.". Financial support for Study III was given by the Innovationsausschuss in the Gemeinsamer Bundesausschuss with resources of the Innovationsfonds for the promotion of new forms of care. All studies were supervised by Prof. Dr. Sebastian Kohlmann. In all three studies, Caroline Clifford was involved in conceptualization, methodology, data curation, data analysis, visualization, validation, software and writing of the manuscript.

Study I: Clifford, C., Löwe, B. & Kohlmann, S. Characteristics and predictors of persistent somatic symptoms in patients with cardiac disease. *Scientific reports, 14*(1), 1-10.

Caroline Clifford was involved in the conceptualization of the study, data curation, formal analysis, methodology, project administration, software, validation, visualization, and wrote the original draft of the manuscript. Bernd Löwe was involved in the conceptualization of the study, funding acquisition, provided resources, supervision, and gave input for the draft of the manuscript. Sebastian Kohlmann was involved in the conceptualization of the study, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, software, provided resources, supervision, validation, visualization, and contributed to the preparation of the manuscript by reviewing and editing.

Study II: Clifford, C., Twerenbold, R., Hartel, F., Löwe, B. & Kohlmann, S. (2024). Somatic symptom disorder symptoms in individuals at risk for heart failure: A Cluster analysis with cross-sectional data from a population-based cohort study. *Journal of Psychosomatic Research, 184,* 111848.

Caroline Clifford was involved in the conceptualization of the study, data curation, formal analysis, methodology, software, validation, visualization, and wrote the original draft of the manuscript. Raphael Twerenbold was involved in the formal analysis, provided resources, and gave input for the draft of the manuscript. Friederike Hartel was involved in the formal analysis, and gave input for the draft of the manuscript. Bernd Löwe was involved in the conceptualization of the study, project administration, supervision, and gave input for the draft of the manuscript. Sebastian Kohlmann was involved in the conceptualization of the study, data curation, formal analysis, methodology, project administration, software, supervision, validation, visualization, and contributed to the preparation of the manuscript by reviewing and editing.

Study III: Clifford, C., Girdauskas, E., Klotz, S.G., Kurz, S., Löwe, B. & Kohlmann, S. (2024). Patient-centered evaluation of an expectation-focused intervention for patients undergoing heart valve surgery: a qualitative study. *Frontiers in Cardiovascular Medicine, 11,* 1338964.

Caroline Clifford was involved in the conceptualization of the study, data curation, formal analysis, investigation, methodology, project administration, provided resources, software, validation, visualization, and wrote the original draft of the manuscript. Evaldas Girdauskas was involved in the conceptualization of the study, funding acquisition, provided resources, and gave input for the draft of the manuscript. Susanne G. Klotz was involved in the conceptualization of the study, funding acquisition, provided resources, and gave input for the draft of the manuscript. Saskia Kurz was involved in the formal analysis, methodology, software, validation, visualization, and gave input for the draft of the manuscript. Bernd Löwe was involved in the conceptualization of the study, funding acquisition, and gave input for the draft of the manuscript. Sebastian Kohlmann was involved in the conceptualization of the study, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, provided resources, supervision, validation, visualization, and contributed to the preparation of the manuscript by reviewing and editing.

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12. CURRICULUM VITAE

Lebenslauf aus datenschutzrechtlichen Gründen nicht enthalten.

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13. EIDESSTATTLICHE VERSICHERUNG

Ich versichere ausdrücklich, dass ich die Arbeit selbständig und ohne fremde Hilfe verfasst, andere als die von mir angegebenen Quellen und Hilfsmittel nicht benutzt und die aus den benutzten Werken wörtlich oder inhaltlich entnommenen Stellen einzeln nach Ausgabe (Auflage und Jahr des Erscheinens), Band und Seite des benutzten Werkes kenntlich gemacht habe.

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Ich erkläre mich einverstanden, dass meine Dissertation vom Dekanat der Medizinischen Fakultät mit einer gängigen Software zur Erkennung von Plagiaten überprüft werden kann.

C. Clifford

Unterschrift: ....