

PATIENTS WITH WORSENING CHRONIC HEART FAILURE – SYMPTOMS AND ASPECTS OF CARE

A Descriptive and Interventional study

Harshida Patel

Institute of Health and Care Sciences Göteborg University



The Sahlgrenska Academy
AT GÖTEBORG UNIVERSITY

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ISBN 13 978-91-628-7356-1
Printed in Sweden by Intellecta DocuSys AB,
Västra Frölunda 2008

The road to the *Dissertation* is not straight. There is a curve called *Planning*, speed bumps called *Data collection*, a confusion loop called *Data analysis*, caution lights called *Publication*. But, with a spare called Determination, an engine called Perseverance, an insurance called Faith, Inspiration, Support and Courage from Family and Friends, a driver called good Supervisor, the goal is not far to a place called Dissertation (Success).

To,
My parents
loving husband Kirit
beloved Mainak, Seema, Keval and Kevin

ABSTRACT

The aims of this thesis are to (1) explore the factors related to seeking care (Paper I), (2) describe the association between fatigue and selected symptoms (Paper II), (3) validate a method to detect the symptoms (Paper III) and (4) evaluate home care with respect to health-related quality of life (HRQL), medical safety, and cost-effectiveness in patients with worsening chronic heart failure (CHF) (Paper IV).

All studies utilise data on patients with worsened CHF who sought care at the emergency department (ED) or heart failure (HF) clinic. Semi-structured interviews were performed (Paper I), and the questionnaires were administered in the form of interviews (Papers II – IV). Eligible patients (Paper IV) were randomised either to home care (HC) or conventional care (CC). Patients in the home care group were initially treated in the emergency department or in the ward and thereafter sent home. Follow-up took place the next day by a specialist nurse and thereafter every day or every other day for 5 -7 days, determined by patient's health status. The Patients in the CC group were treated according to hospital treatment guidelines. The patients were followed-up after 1, 4, 8 and 12 months in both groups.

The patients reasons for seeking emergency attention were mainly because of symptoms they experienced (58%), followed by recommendations from either relatives or caregivers (42%). Reasons for not seeking care earlier were attribution of their symptoms to the external factors, uncertainty, old age, previous unpleasant experiences with health care, and hopelessness. Only 5% could relate their current symptoms to worsening CHF. Anxiety was associated with mental fatigue, whereas depression was associated with general fatigue, a decrease in activity and reduced motivation. The Kansas City Cardiomyopathy Questionnaire (KCCQ) was valid, reliable and more responsive than the Short Form-36. Health care cost differed significantly between the HC and the CC group ($p < 0.001$ after initial intervention and $p = 0.04$ at the end of the study and $p = 0.05$ including costs from HF clinic visits, which occurred after termination of the intervention and during study period). The groups did not differ in HRQL or medical safety.

The findings from this thesis suggest that, emotional distress may influence patients' ability to identify symptoms and response for seeking care. KCCQ can be helpful in measuring symptoms in patients with CHF. HC evaluated in this study might play an important role in future care and treatment of patients with CHF. The important aspect is to identify crucial elements in individual needs and provide care accordingly. The significance of being cared for at home and factors influencing symptom reporting are discussed in this thesis.

Key words: Chronic heart failure; Deterioration; Signs and symptoms; Psychometric properties; Kansas City Cardiomyopathy Questionnaire; Quality-adjusted life years; Cost-utility analysis; emotional distress; health care costs

LIST OF ORIGINAL PAPERS

This thesis is based on the following papers:

- I.** Patel, H., Shafazand, M., Schaufelberger, M., Ekman, I. Reasons for seeking acute care in Chronic Heart Failure.
European Journal of Heart Failure 2007;9:702-708
- II.** Falk, K., Patel, H., Swedberg, K., Ekman, I. Fatigue in patients with Chronic Heart Failure – a burden associated with emotional distress.
(Submitted for publication)
- III.** Patel, H., Ekman, I., Wasserman, S., Spertus, J., Persson, LO. Psychometric properties of a Swedish version of the Kansas City Cardiomyopathy Questionnaire in a Chronic Heart Failure population.
(Epublished ahead of print in European Journal of Cardiovascular Nursing 2007)
- IV.** Patel, H., Shafazand, M., Ekman, I., Höjgård, S., Swedberg, K., Schaufelberger, M. Home care as an option in worsening chronic heart failure – A pilot study with aspects on Medical safety, Quality Adjusted Life Years and Cost-Effectiveness.
(Submitted for publication)

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ABBREVIATIONS

CC	Conventional Care (Control group)
CHF	Chronic Heart Failure
CEA	Cost-effectiveness analysis
CHQ	Chronic Heart failure Questionnaire
COPD	Chronic obstructive pulmonary disease
CUA	Cost-utility analysis
ESC	European Society of Cardiology
ED	Emergency Department
EMEA	European Medicines Agency
EQ-5DVAS	EuroQol 5 dimension with Visual Analogue Scale
FDA	Food and Drug Administration
HAD	Hospital Anxiety and Depression Scale
HF	Heart Failure
HC	Home Care (Intervention group)
HRQL	Health-Related Quality of Life
KCCQ	Kansas City Cardiomyopathy Questionnaire
LVEF	Left ventricular ejection fraction
MFI 20	Multi dimension Fatigue Inventory – 20 items
MLHFQ	Minnesota Living with Heart Failure questionnaire
NYHA	New York Heart Association classification system
QALY	Quality-Adjusted Life Years
QLQ-SHF	Quality of Life Questionnaire- Severe Heart Failure
QoL	Quality of Life
SDS	Symptom Distress Scale
SF	Symptom Frequency
SF-36	MOS Survey short form 36
SG	Standard Gamble
SS	Symptom Severity
SMM	Symptom Management Model
WHO	World Health Organisation
WHOQoL	World Health Organisation Quality of Life questionnaire

DEFINITIONS

Assessment	The process of determining the meaning of measurement(s), <i>i.e.</i> evaluation of patient's problems [181]
Care	Intervention to alleviate consequences of illness [181]
Chronic heart failure	Chronic heart failure is defined as a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood [10]
Deterioration/Worsening Disease	The process of becoming worse [12] Disorder of body function, system or organ; a morbid entity characterised by recognised etiologic agent, identifiable group of symptoms and signs or consistent anatomic alteration [14]
Health-related quality	The subjective perception of the impact on health of life status, including disease and treatment on physical, psychological, social functioning and well-being [111, 112]
Illness	Illness means experienced reduction in states of well-being and social function manifesting as symptoms [14]
Measurement	Quantification of an observation to establish patients' health status, symptom severity and to evaluate outcome [181]
Perception	The mental process of becoming aware of or recognising something [12]
Sign	Any abnormal observation indicative of disease, discoverable on examination of the individual; an objective indication of disease [12]
Syndrome	The aggregate of symptoms and signs associated with any morbid process, and constituting together the picture of the disease [12]
Symptom	Any morbid phenomenon or departure from the normal, in structure, function or sensation experienced by an individual, it is a subjective indication of disease [12]
Symptom cluster	Symptom clusters are defined as three or more symptoms that occur together and are related to each other [60]
Treatment	Intervention to reduce illness [181]

INTRODUCTION

As a nurse specialised in care for patients with coronary disease, a strong wish to increase well-being in patients with chronic heart failure (CHF) has evolved over the years. The economic impact associated with the care of these patients is staggering, with rising epidemiology of increment in an elderly population surviving the acute condition. Previous research has indicated that it would probably be more suitable for an older, fragile population of patients with CHF to receive care and treatment in their homes rather than at hospital-based out-patient clinics [1]. However, it was challenging to evaluate care for these patients with a deteriorating condition in order to increase their well-being by providing care in their homes.

The condition is chronic, difficult to cure, associated with poor health-related quality of life (HRQL), considerable distress and disability. Despite advancement in pharmacological and non-pharmacological care and extensive research, patients with CHF experience roller coaster pathway in their lives, characterised by episodic deterioration, symptom burden, affected functional capacity and recurrent hospital admissions. Patients diagnosed with CHF have a mortality rate comparable to those with cancer. Stewart *et al.* [2] studied the prognostic impact of CHF relative to that of cancer. Their data showed that patients admitted to hospital with a diagnosis of cancer often survived longer than those with a diagnosis of CHF. They concluded that, with the notable exception of lung cancer, CHF is as 'malignant' as many common types of cancer and is associated with a comparable number of expected life-years lost. While much has been done to improve the pharmacological treatment and non-pharmacological management of CHF in recent years, the patients still experience a high level of symptoms and symptom burden with impact on quality of life (QoL) [3]. Such a condition continues to be associated with frequent, and often prolonged, hospitalisations [4], translating into spiralling health care costs. Because of the high prevalence and the high costs involved in caring for these patients, improvements in care and treatment could have a significant impact on the costs as well as the outcomes. The nurse-led heart failure (HF) outpatient clinics have contributed in improving patients care management, reducing rehospitalisation and mortality through education and counselling [5] and improving the cost-effectiveness of treatment [6, 7]. However, patients with worsening CHF still do seek care at the emergency department (ED) when their condition has deteriorated. We know from previous research that patients hesitate to go to the hospital and prefer to stay in their homes, even when they become impaired [8]. Thus, we need to develop knowledge about care and treatment in the patients' home when their health has deteriorated. In summary, the epidemiology and economics of CHF have begun to exert considerable demands on the health care system. In response, health care providers have to implement alternative approaches to meet the diverse, yet resource-intensive, health care needs of patients with worsening CHF.

BACKGROUND

Chronic heart failure

Definition and pathophysiology

There is no uniform and widely accepted characterisation and definition of CHF, probably because of the complexity of the syndrome. The definition of the condition reflects our knowledge of its pathophysiology [9]. CHF is “a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood” [10 p.1119]. According to the European Society of Cardiology (ESC) guidelines [4], CHF is diagnosed by symptoms, such as fatigue and dyspnoea, either at rest or during exertion, or signs, such as ankle swelling and evidence of cardiac dysfunction at rest verified preferably by echocardiography and response to the treatments in which a relatively fast symptomatic improvement could be anticipated (*e.g.*, diuretic or nitrate administration) strengthens the diagnosis.

Strauss [11] described chronic disease as being of long duration and often episodic or remitting, *i.e.* acute phases alternating with resting phases. HF occurs because of impairment in the heart's working capacity [4]. CHF is most common among elderly, referring to better survival after myocardial infarction because of advancement in medical treatment, ineffective valve function, rhythm disturbances and hypertension [4]. The aetiology or pathophysiology depends on underlying causes, including decreased blood supplies to the heart muscle because of coronary artery disease and problems within the heart structure itself (*e.g.*, cardiomyopathy, left ventricular dysfunction or the dysfunction of valves) [10].

Deterioration

The concept of “deterioration or worsening”, used interchangeably in this thesis, has the same meaning in congruence with a definition: “A process of changing to the inferior state” [12]. CHF can be distinguished as “compensated” or “decompensated”. Compensated CHF implies that symptoms and signs are stable, whereas decompensated CHF implies an insidious gradual worsening, which may present either as an acute episode of pulmonary congestion or as lethargy and malaise, a reduction in physical activity and increased dyspnoea on exertion (or exertional dyspnoea). Common causes for deterioration are ischemia, arrhythmia and infections [4, 13].

From the patient perspective, deterioration of CHF is referred to as illness. Illness is not necessarily disease. Eisenberg [14] defined disease as an abnormality in the structure and functions of body organs and systems and can often be identified by signs of bodily disorder such as oedema or reduced ejection fraction. Illness, on the other hand, refers to an experienced reduction in states of well-being and social function manifesting as symptoms. This message conveys that an illness experience is imbued with meaning specific to the individual, and a patient with worsening of CHF is not necessarily experiencing any emergency to revoke deterioration.

Scope of the problem

Almost 4% of the population aged over 55 years and up to 13% of those aged over 75 was affected with CHF in the general population from the Rotterdam study [15]. Moreover, it is estimated that there are at least 10 million cases in Europe with a yearly incidence of 0.4 to 2% [4]. In the USA, 5 million people have CHF and the incidence of new diagnosed cases is 550 000 each year [16].

In Sweden, the prevalence is 2-3%, *i.e.* 180 000 – 300 000 Swedes aged ≥ 75 years have CHF. The incidence of new diagnosed cases is about 30 000 yearly [17]. Almost one third of these patients are in New York Heart Association (NYHA) functional class III or IV. CHF, often characterised by progressive deterioration and frequent hospital admissions, prognosis is very poor where 4 year-mortality is 50%; among those with severe HF, more than 50% die within a year [18]. Individuals 55 years and over are reported to have a 5-year survival of 35% following diagnosis [19]. In a retrospective study one-year mortality following hospitalisation was between 24 and 61% in the oldest co-morbidity-laden patients with first time hospital admission for HF [20]. Recently, studies from Sweden and the UK have concluded improved survival trends in CHF [21, 22]. Because of a trend in age and gender changes in the population structure, a substantial number of incidents of new cases have been predicted by year 2020 (31% of the men and about 17% of the women with CHF in the community). The hospital admissions associated with a principle diagnosis of CHF is expected to increase by 34% in men and 12% in women by the year 2020 [23].

The increasing prevalence in CHF is due to the increasing aging population as well as the marked increase in survival after improved treatment of cardiovascular diseases [17, 18]. Conservative estimates suggest that over 50% of the cases have an ischemia origin while up to 75% of the cases had hypertension as a contributing factor [17]. About 38% of patients have signs of HF after myocardial infarction during hospitalisation and 35% develop CHF syndrome within a five-year timeline [24].

Economic aspects

CHF is the most common cause of hospitalisation in patients over 65 years of age. The annual costs in Sweden is about 2.0-2.6 billion SEK, which is about 2% of the Swedish health care budget [25], where 70-75% of the budget is used in institutional care [25 - 27]. A Substantial number of HF hospitalisations are not initial admissions but readmissions. CHF is a growing problem and hospital admissions have doubled during the past two decades, with a hospital readmission rate of 30-50% within six months after discharge [4, 28 - 31] and 11% within 3 months after discharge [32].

Literature over health care costs for CHF has stressed the importance of reducing readmission rates to minimise costly hospital stay [6, 23, 33 - 36]. Ryden-Bergsten *et al.* [25] evaluated costs for care on CHF in Sweden. They found that institutional care (hospital and nursing home) represented 64-75% of the annual expenditure (2.6 billion SEK). Total ambulatory Care (hospital outpatient and primary care) accounted for 15% of total costs. Patients aged 80 years and older represented 50% of all CHF

hospital discharges. In a retrospective study in a primary health care setting Agvall *et al.* [33] found that hospital care accounted for 47% of the total cost, whereas primary care accounted for 22%, with medication, nursing home and examinations accounting for the rest. These figures demonstrate that the health care costs of CHF are primarily a function of the cost of hospitalisations, which occur more frequently in elderly patients. In another Swedish study [35] a retrospective analysis was undertaken of the total cost of care of all CHF patients. The authors concluded that hospitalisation was the largest part of the total cost. Hence, efforts to reduce health care costs should focus on hospitalisation.

Failure to seek prompt medical treatment because of the inability of recognising changing symptoms, inadequate attention to diet and drug therapies has been associated with hospital readmissions [4, 27, 37]. Earlier research with multidisciplinary patient management included patients either from HF clinics or patients after hospital discharge, *i.e.* stable patients in either home-based or predominantly polarised towards clinic-based intervention. These studies have consistently shown that CHF patients receiving this type of care experience a reduction in subsequent hospitalisations and hospital days, a higher QoL and an improvement in functional status [5 - 7, 23, 36, 38 - 44]. Stewart *et al.* [6, 7] found a reduction in cost with home-based intervention with nurse follow-up after hospital discharge. Furthermore, substantial cost savings could be found in an economic analysis of specialist HF nurse management [26]. However, some studies did not reveal any significant differences between groups in resource utilisation [1, 45, 46]. Bruce *et al.* [47, 48] found a “hospital at home” model feasible, efficacious, safe and related to patient satisfaction in patients who required acute hospital care. In this model nurses and a study physician made at least one home visit daily. Strömberg *et al.* [5] evaluated the effect of follow-up at a nurse-led HF-clinic and noted fewer readmissions and days in hospital after 12 months. The impact of a hybrid clinic-based and home-based intervention programme of care was found to be equally beneficial on hospital utilisation in patients with CHF on recurrent readmission and event-free survival [49]. Kasper *et al.* [40] demonstrated better QoL with multidisciplinary approach to CHF management at a similar cost in recently hospitalised high-risk patients with CHF.

A recent meta-analysis review of 29 randomised studies involved more than 5000 patients from the USA [50]. In this study the mean patient age was between 56 and 80 years and the intervention range was between 1 visit and 30 months. This review demonstrated that patient management with multidisciplinary programmes was associated with a 27% reduction in readmissions related to CHF and 43% in all-cause hospitalisations. Although none of these trials incorporated formal cost-effectiveness analysis (CEA), a majority of the trials reported cost savings by interventions, whereas few reported cost neutrality. Phillips [51] reviewed studies with miscellaneous multidisciplinary patient management programmes (telephone follow-up, home- or clinic-based, involvement of pharmacist and cardiologists) and found that the common component in 83% of the studies was nurse-led patient education. Thus, the literature provides convincing evidence that it is possible to significantly reduce rehospitalisation rates and costs and increase QoL for CHF patients using the clinic- and home-based post discharge care models. Bearing in mind the great significance of hospital costs, it is essential to find ways of treating CHF that reduce the need for in-hospital care.

Symptoms

The word Symptom comes from the Greek word *symptoma*, which means “*anything that has befallen one*” [52]. Wilson and Cleary [53, p 61] explained a symptom as an indication of disorder or illness and defined it as a “*patient’s perception of an abnormal physical, emotional or cognitive state*”. The distinction between ‘disease’ and ‘illness’ has been made by Eisenberg [14], where disease is defined as any detectable abnormality followed by physiological changes (*e.g.*, leg oedema) and illness is the experience of reduced well-being followed by symptoms. Illness (*i.e.* symptoms) is a patient’s subjective experience of changes in the body that may occur in the absence of signs; disease (*i.e.* signs) is an objectively observable abnormality of the body and can be detected without experience of symptoms [54, 55]. Symptoms reflect more than physical aspects of disease, such as impact on lifestyle and expectations from the patient with individual variation and from one time to another. Moreover, worsening CHF makes patients emotionally affected by symptoms [54]. Therefore, the study of symptoms should be based on the perception of the individual experiencing the symptom and his or her self-report [56]. Further, recognition and appreciation of the importance of symptoms should be the reason for a structured assessment in order to provide optimal care for patients with CHF [54]. Because measuring symptoms is a complex procedure, which might be the reason for poor documentation in patients’ medical records, reliable methods for documentation of the symptoms need to be evolved [57, 58]. It is now the recognised strategy by EMEA [31] as well as the American Food and Drug Administration [59] and ESC guidelines [4] that relief of symptoms is an important target for treatment of patients with CHF. Symptom assessment is a valid, easy and inexpensive measure that closely mirrors the patients’ reality and that reflects the patients’ own experience of medical therapy [54].

Symptom clusters are defined as three or more symptoms that occur together and are related to each other [60]. Symptom clusters address problems from a broader perspective and enable one to look at interactions among the mechanisms involved in the symptomatology. The symptom cluster in patients with CHF often comprises shortness of breath, leg swelling and fatigue and has been recognised as an indication of worsening CHF. However, the origin of the symptoms of CHF is not fully understood [54]. Other symptoms, such as cough, palpitation and nausea, loss of appetite, thirst, constipation, depression, anxiety, dizziness and confusion have also been reported [3, 17, 61 - 64]. Zambroski *et al.* [3] found that symptom prevalence and symptom burden were the greatest predictors of diminished HRQL. Kroenke [65] stated that symptoms are ubiquitous and that presenting complaints are but a fraction of the symptoms. Symptoms produce impairment in patients functioning and HRQL, and generate a great amount of health care expenditures in terms of clinical visits, medications, other therapies (*e.g.*, physiotherapy) and laboratory testing. Symptoms, especially fatigue and dyspnoea, are important factors in clinical diagnosis and assessment of the severity of CHF [4]. The studies have shown a poor relationship between symptoms and the severity of cardiac dysfunction, gauged as LVEF [66 - 69], but symptoms may be a prognostic marker [4, 70]. The severity of symptoms is highly dependent on patient expectations and medical interpretation. The diagnosis of the condition is notoriously difficult [4] because the principal symptoms (breathlessness, oedema and fatigue) are common to several other disease states, such as anaemia, chronic obstructive pulmo-

nary disease (COPD) and other cardiovascular diseases. The fact that as many as 50% of patients in primary care have been originally misdiagnosed with CHF diagnosis reflects this difficulty [54, 71 - 73].

Fatigue

Fatigue is a prominent symptom in patients with CHF and, together with dyspnoea, is known to have a significant negative effect on HRQL [3, 67, 74, 75]. Fatigue is one of the most distressing symptoms in patients with CHF [74] and a predictor of worsening CHF [70]. In a qualitative study [76] describing experiences of fatigue in elderly patients with severe CHF the main causes identified were illness, old age and loneliness. In several studies [77 - 79] fatigue and lack of energy were the main causes of physical limitation. Stanek *et al.* [80] found that many patients, if given the choice, express a greater desire for QoL (symptom improvement) than for quantity of life (longer survival). The patients in this study assigned 30% of the weight for relief of tiredness *versus* only 18% of the weight for survival in their rating decisions, reinforcing the importance of applying an adequate symptom management strategy to relieve symptoms. Little is known about the pathophysiological causes of fatigue though theories include low cardiac output, peripheral hypoperfusion and skeletal muscle deconditioning [4]. It has been suggested that chronic, low grade haemodynamic stress as seen in CHF may lead to dominance of catabolic processes, which in turn leads to skeletal myopathy, causing the sensation of fatigue [81]. Recently, Smith *et al.* [82] identified predictors of both exertion and general fatigue. The physical characteristics (dyspnoea, hypertension and depressive symptoms) predicted exertion fatigue, whereas general fatigue was predicted by both physical and psychological characteristics (dyspnoea, depressive symptoms and sleep problems).

Depression & Anxiety

The prevalence of depression in patients with CHF has been reported to be from 9 – 60% in a recent review, with more women than men and higher prevalence rates in higher NYHA classes [83]. This fact is illuminated by findings from qualitative research in which an experience of being a burden was described by women with depressive symptom [77, 79] but not by men [78]. In another study the feeling of burden was found in both women and men among elderly patients with severe CHF [84]. Qualitative studies have described that people with CHF experience immense emotional problems [77, 84, 85]. Difficulties with psychological functions has been reported as over 50% of patients experienced anxiety, depression, stress or cognitive functions impairment [63]. In a qualitative study patients with CHF reported that their sleep disturbances led to a variety of symptoms, including loss of concentration, fatigue, anxiety and depression [86]. Depression is a common symptom in patients with CHF and poses a significant problem to distinguish it from fatigue [87]. It is strongly associated with fatigue and dyspnoea [88 - 91], and depression is a decline in health status and a predictor for worsening CHF [70, 92, 93]. Furthermore, depression may result in delay in treatment-seeking behaviour and increased hospital utilisation [83, 94 - 96]. Depression has commonly been described [85] among patients with less disease severity [77] and has been related to non-adherence [97]. Although a strong association exists between anxiety and depression, no evidence of anxiety and related

prognosis in CHF has been found [98], but increased medical cost has been reported by Sullivan *et al.* [99]. Anxiety has shown to be correlated with chest pain in patients with impaired functional status [88, 92] and depression predicted mortality independent of clinical status [88]. In a recent study Phil *et al.* [100] found that patients with severe CHF were more likely to experience depression. Katon *et al.* [101] found that patients with CHF and depression or anxiety compared to those with chronic medical illness alone reported a significantly higher number of medical symptoms when controlling for severity of disease. Koenig [102] found that the majority of depressed CHF patients did not receive treatment for their depression. Because depression is associated with lack of physical activity and patients' HRQL, these findings have important implications for the care of older patients with CHF.

Symptom Management Model (SMM)

The International Council of Nurses (ICN) has identified patients' symptoms as one of the research priorities for nursing research [103]. Because symptom is the main focus here, the Symptom Management Model (SMM) [56, 104] has been a source of inspiration in the construction of the research questions, in the design of the intervention and in the collection of data. According to SMM, symptoms experienced in worsening CHF can be assessed, managed and evaluated through the use of three dimensions: symptom experience, management and outcomes.

The concept of symptoms includes an individual's perception of a symptom, evaluation of the meaning of a symptom and response to a symptom. For a valid self-report of symptoms, the person reporting must be responding to a perception of a symptom. Symptom management strategies are highly dependent on the symptom experience phase. The goal of symptom management is to control, prevent or treat the symptoms through the use of different strategies. Symptom management is a dynamic process that requires interventional changes in response to the outcome. The model proposes questions that formulate a design for caring strategies. These are: of what (the nature of the strategy), when, where, why, how much (intervention dose), to whom (recipient of intervention) and how delivered. The outcome reflects the consequences of caring strategies. In worsening CHF a patient's perception and evaluation of a symptom is highly influenced by personal variables (*e.g.*, socio-demographics, psychological, sociological and physiological factors) as well as health status and the physical environment.

New York Heart Association (NYHA)

The New York Heart Association functional classification is a nomenclature to describe an overall clinical appraisal of the status of a patient with CHF. It was developed in 1928 for use as an essential criterion for a comprehensive cardiac diagnosis. The NYHA is widely used in research to categorise the degree of cardiac disability based on symptoms and activity limitations, but is also influenced by knowledge of LVEF, prior medical history and the physician's perception of prognosis [66, 105]. The NYHA class measures the physical dimension of functional performance in four classes (Table 1), which should inherently reflect the patient's clinical status [106].

The NYHA functional classification is correlated to HRQL and a higher functional class (I - IV) is associated with a poorer QoL [69, 107, 108] and mortality [4, 109].

Table 1. New York Heart Association classification of heart failure

NYHA Class I	No limitation, ordinary physical activity does not cause undue fatigue, dyspnoea or palpitation
NYHA Class II	Slight limitation of physical activity, comfortable at rest but ordinary activities results in fatigue, dyspnoea or palpitation
NYHA Class III	Marked limitation of physical activity, comfortable at rest but less than ordinary activities result in fatigue, dyspnoea or palpitations
NYHA Class IV	Unable to carry out any physical activity without discomfort, symptoms of heart failure are present even at rest with increased discomfort with any physical activity

Health-related quality of life

The World Health Organisation (WHO) defined QoL in its constitution in 1948 to include physical, mental and social well-being, and not just the absence of disease or illness. Although its definition raised questions as to whether or not QoL could be measured, the comprehensiveness of the definition has set a standard by which many measurement efforts have been judged. Increasingly, however, experts have come to realise that QoL is subjective and individual, and the final determination will always be made by the patient [59].

The term QoL is global and covers both private and professional aspects of living, such as satisfaction with social network, job, living style and health perception [110]. QoL refers to the individual's own values, expectations and satisfaction with life, whereas HRQL is defined as the subjective perception of the impact on health status, including disease and treatment on physical, psychological, social functioning and well-being [111, 112]. Further, HRQL is a multidimensional concept defined as functional capacity, involving physical performance, social, intellectual and emotional functioning [113]. The FDA [59] defines HRQL as an individual's perceptions of how an illness and its treatment affect, at a minimum, the physical, mental and social aspects of a patient's life. Thus, HRQL refers to the narrower aspects of QoL related to a disease-specific health status, influenced by expectations and experiences [110] and measures the effects of treatment on illness from the patient's perspective. HRQL has been shown to be strongly associated with self-rated disease severity [114].

HRQL is impaired in patients with CHF in comparison to the general population, with more severe physical and emotional symptoms, poorer functional status and worse health perceptions [69, 108, 115, 116]. Furthermore, HRQL is more impaired in CHF than in other chronic medical conditions (*e.g.*, chronic haemodialysis, chronic hepatitis C and depression) [69]. It is strongly related to the symptoms of CHF, especially

fatigue and dyspnoea, but also to social isolation and lack of energy for leisure activities [3] and increasing dependency [117]. The poor relationship between LVEF and HRQL [69, 117] and prolonged and frequent hospital admissions have been reported [30]. Although the NYHA functional class and patients self-assessed symptoms are not in congruence, both are related to HRQL, whereas clinical “objective” measurements, such as LVEF are not [66, 117, 118].

Why measure health-related quality of life in patients with CHF?

Quantity and QoL are the two basic outcome components of a given treatment in clinical studies. The quantity of life, expressed in terms of survival, is a traditional outcome measure and widely accepted in clinical studies with few problems of comparison. QoL, on the other hand, embraces a whole range of different facets of people’s lives, not just their HRQL. Even restricting the focus on HRQL will result in a number of dimensions relating to both physical and mental capacity, even though sharing a common grade of disease severity. It has been recognised that the patient’s perspective is as legitimate and valid as the clinician’s in monitoring health care outcomes [31, 59]. The measurement of health, the effects of disease and the impact of health care include an indication of changes in disease frequency and severity but also an estimate of the patients’ perception of HRQL before and after treatment. This has led to the development of instruments to quantify the patients’ perceptions of their HRQL [119]. These instruments are important in assessing HRQL outcomes [4] and in nursing interventions [120]. Improvement in HRQL is one of the main economic benefits in care and treatment and therefore needs to be incorporated in economic evaluation [121].

Types of HRQL instrument

Three basic categories of instruments are used in different circumstances and for different purposes to measure QoL, as well as to express the HRQL to address treatment effects important to clinical management.

Generic instrument

Generic instruments attempt to measure the core dimension of HRQL. They are multi-dimensional, containing sets of items on physical, mental and general health, vitality, QoL and social dimensions (*e.g.*, SF-36, WHOQOL, EQ-5D). Major advantages of these instruments include applicability to a variety of areas and populations, regardless of the underlying condition. However, a potential drawback of these measurements is that they may fail to capture small effects specific to a disease and thus not always responsive to changes in specific conditions [75, 122].

Disease-Specific Instrument

The second basic approach to HRQL measurement focuses on aspects of health that is specific to the area of CHF. The instrument measures the distinctive aspects of CHF and provides valuable information on changes over time in the patient’s condition. For example, dyspnoea and fatigue are the two most common symptoms of CHF patients and therefore condition-specific instruments for CHF focus on these symptoms in assessing HRQL. In addition to the likelihood of improved responsiveness, specific

measures have the advantage of relating closely to areas routinely analysed by clinicians [122]. Further, these instruments are perceived as more relevant than generic measures by both patients and health care professionals because of their ability to discriminate. The Minnesota Living with Heart Failure Questionnaire (MLHFQ), the Chronic Heart Failure Questionnaire (CHQ) and the Quality of Life Questionnaire in Severe Heart failure (QLQ-SHF) are scales used to measure HRQL in patients with CHF. Leidy *et al.* [123] reviewed 41 randomised controlled trials published in English between 1990 and 1998 that evaluated HRQL as an explicitly designated treatment outcome. The authors of this review reported that the most frequently used instruments were the QLQ-SHF and the MLHFQ. However, important to note is that none of the studies using QLQ-SHF produced significant results and only one study that used the MLHFQ reported significant results. The authors of the review concluded that no single scale was sufficient to evaluate HRQL outcomes in patients with CHF. This has been confirmed in a review article by Berry and McMurray [119] who reported that none of the existing instruments measured QoL in CHF trials in a reliable or reproducible fashion and therefore an obvious need exists for the development of a valid and reliable instrument for this specific group of patients. Further, the impact of chronic disease and therapeutic interventions must be evaluated from the patient's perspective in addition to traditional measures of clinical outcome.

Preference-based measures

The third category of instruments, utility measures, yield a set of weights from which quality adjusted life years (QALYs) can be estimated. Preference-based measures summarise a broad range of relevant outcomes among patients into an overall HRQL outcome called "utility" or "preference" [124]. Individual preference is represented as a single number along a continuum from 0 (anchored as death) to 1 (anchored as full health). Some generic instruments, (*e.g.*, the EuroQoL-5 dimensions, EQ-5D) yield an overall QoL score in an index and can therefore be treated as utility measures suitable for generating QALYs [121]. Other generic measure (*e.g.*, SF-36) allows only comparison of health within each dimension independently. An overall single index from the different dimensions cannot be created, because neither the scores within each dimension are comparable with one another nor the relative weight attached to each dimension is known. Thus, neither condition-specific nor general health profile measures are suitable for QALY calculation.

The key elements of utility measures are that they incorporate preference measurements and relate health states to death, as well as reflect both the health status and the value of that health status to the patient [122]. Utility instruments provide an alternative way of measuring HRQL that can be used for economic analysis. The usefulness of utility measures in economic analysis is important for health care providers to justify the resources devoted to treatment. Utility measures provide a single summary score of the net change in HRQL: the gains in HRQL from the treatment effect minus the burdens of side effects influencing HRQL [122]. Hence, utility measures enable comparisons across different interventions and disease or conditions evaluating HRQL, which is not possible with generic or disease-specific instruments because of the multi-dimensional nature of the instruments, except the EQ-5D with the Visual Analogue Scale (VAS).

Utility values can be derived through a standard gamble (SG) technique directly from individual patients alternatively; patients can rate their health status using a multi-attribute, health-status classification system such as the EQ-5DVAS [122]. Utilities are valid measures of HRQL in patients with CHF and CEA of CHF treatments incorporating utilities in the outcome measure can be meaningful. Valuations from the VAS are elicited in a choiceless context, and thus do not require people to make trade-offs between different arguments in their utility function, whereas SG has been advocated on the grounds that almost all decisions about health care are made under conditions of uncertainty [121, 125]. Although VAS is commonly regarded by economists as theoretically inferior to the SG method, it has the practical advantages of being simpler to complete and cheaper to administer than SG [125].

Quality Adjusted Life Year

Klarman and colleagues [126] first introduced the concept of QALY, which is defined as a life year adjusted for QoL. Weinstein and Stason [127] described the QALY gained as the appropriate measure of effectiveness. QALY is a common unit of measure of health gain related to health economics and that is designed to aid priority setting in health care and to take into account QoL in addition to survival [128], which are the important aspects from the perspective of the patient. The utility assessment and the concept of a QALY are relatively recent developments in health care research; to our knowledge, there are no published studies evaluating outcomes within the context of utility in deteriorated CHF until now. The basic concept of QALY gained is displayed in Figure 1. The figure shows a life profile of a patient with and without intervention. The advantage of the QALY as a measure of health outcome is that it can simultaneously capture gains from reduced morbidity (quality gains) and reduced mortality (quantity gains) and combine this into a single measure [121] and then aggregate these improvements across individuals, which is a goal of the intervention. For example, an intervention that would extend the life of patient A with 1 year with a quality level of 0.5 and would improve the QoL for patient B with 0.25 for one year would be said to produce 0.75 QALYs gained. The fundamental ethical judgement inherent in this approach is that 1 full healthy year gained counts as 1.0, regardless of the patient's socio-demographic background [128].

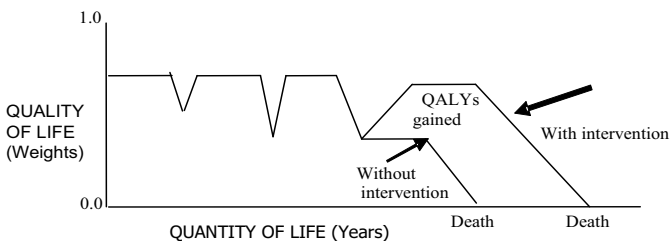


Figure 1. Quality-adjusted life years gained (adapted from Torrance 1989).

QALYs combined with the costs of provided intervention results in a cost-utility ratio, which indicates the additional costs required to generate a year of perfect health (one QALY). Comparisons can be made between interventions, and priorities can be established based on those alternatives of care that are relatively inexpensive (low cost/QALY) [121].

Subjective measures (such as HRQL, suffering, pain and anxiety) are difficult to measure, but the development of a health index and health profiles have made it possible to analyse effects relevant to the individual as QALY [121, 128]. It is also important for the health care sector with increasing specialisation to measure the efficacy of the provided care. Output can be measured as QALYs and then compared with cost (“cost/QALY”). The main purpose with QALY is to make explicit individuals preferences in order to allow ranking while compared across different alternative treatments [121].

Methods of cost-effectiveness analysis

The essence of cost-effectiveness evaluation is a comparison of the costs and consequences of health care alternatives [121]. The aim is to increase the effectiveness of health care. However, effectiveness means cost-effectiveness to the decision makers, treatment outcome to the physician and well-being, convenience and being able to maintain a normal life to the patient [129]. Economic costs include direct costs (professional fees, drugs, hospitalisation, diagnostic tests, personnel and interventions), indirect costs (earning of a patient forgone as a result of treatment) and tangible costs (suffering) [121].

Incorporation of HRQL in economic evaluation is a form of cost-utility analysis (CUA). Both CEA and CUA measure cost compared with effect, but differ in how effect is measured. CEA measures effects of an intervention in natural units, whereas CUA measures effects as gained QALYs. The difference between the two is that outcomes in CEA are single, programme specific and unvalued. In contrast, outcomes in CUA may be single or multiple, are generic as opposed to programme specific and incorporate the notion of value [121]. From a holistic perspective, capturing the long time effects are often difficult in an intervention. Hence, HRQL is an important aspect in health economics research. HRQL captures the effect of treatment from a patient perspective and can be applied to estimate QALY, which can be implicated in the CUA. QALYs in CUA are understudied outcomes in pharmacological and non-pharmacological CHF research [123]. Economic analysis in the health care sector is a tool for resource allocation and evaluation of different treatment alternatives. CUA can be used to compare resources used for different treatment strategies and gained health effects in terms of improved QoL and prolonged life (QALY). According to WHO [130], the ambition of the health provider should be maximum health status in consideration with length and HRQL.

RATIONALE OF THE STUDY

Symptoms are the most common reason people seek health care. Treatment and care for patients with CHF frequently depend on clinical judgement informed by symptom assessment. Although self-care education has been provided in clinics and evaluated in research [50, 51], little is known about how patients evaluate their condition, how they monitor change and how they decide to seek help. Hence, it is of utmost importance to explore what makes a patient seek emergent care. Further, patients with CHF are burdened with an array of symptoms. Worsening conditions often provoke emotional responses that make the patients feel even more severely affected by their symptoms. Common prevalent symptoms, such as anxiety and depression, are difficult to distinguish from fatigue. Symptoms are important for the interpretation and understanding of patients with CHF. They reflect the patients' perception of illness [54]. There is a need to recognise patients' perception of experienced and reported symptoms and explore the association between them.

Efficacy of provided care and treatment is crucial for clinical management of symptoms. Haemodynamic surrogate measures used in research have shown poor concordance to symptoms or NYHA class [55]. Therefore, the effect of care should be evaluated from the perspective of those who benefit from it, *i.e.* the patients. For this purpose, valid and reliable response to clinical change and culturally adapted measures are important to consider. There are few instruments measuring symptoms and HRQL in patients with CHF, and those that do exist fail to capture relevant information in different dimension of symptoms in the way that the Kansas City Cardiomyopathy Questionnaire (KCCQ) does. The KCCQ is an instrument that has been translated into Swedish, but has not been psychometrically tested. An important aspect in the validation of KCCQ was to improve a method for detecting clinically important changes in relevant dimensions and to investigate and compare the effects of interventions from a similar context from different cultures.

One of the central aspects in nursing is to provide individualised care in order to alleviate suffering and increase HRQL from the patient perspective. Another aspect is to minimise costs from the health care sector's perspective. Based on clinical experience, a clear distinction should be made between the perspectives of patients and health providers. Patient expectations about and demand for specific types of care are strongly influenced by several factors, including patient perceptions of the intensity and perceived seriousness of the symptoms, their vulnerability to illness and their experience with health care [131]. Thus, new feasible models of care to patients with worsened CHF are required. Already today patients who are reluctant regarding hospitalisation are sent home after a few hours of observation in the hospital. Does this approach improve a patient's well-being? Is it medically safe? Is it cost-saving for health care? Systematic analysis of the association between input of resources and output as effects on health status is still lacking in the field of CHF. Given that the CHF epidemic is likely to be sustained [23], it is time to evaluate different methods of care in terms of well-being, safety and costs.

AIMS OF THE THESIS

The overall aim of this thesis was to improve our understanding of factors related to seeking acute care, explore symptoms and to evaluate home care in patients with deteriorated CHF.

The specific aims were:

1. To explore factors related to seeking acute care in patients with deteriorated CHF (Paper I).
2. To examine the association between fatigue and anxiety, depression and symptom distress, further to explore the relationships between symptoms and fatigue as a multidimensional experience in patients with CHF (Paper II).
3. To evaluate the validity, reliability and responsiveness of the Swedish version of the KCCQ in patients with worsening CHF (Paper III).
4. To evaluate effects of an intervention (home care vs. conventional care) in patients with worsening CHF with aspects on medical safety, HRQL in terms of QALYs and cost-effectiveness (Paper IV).

METHODS

Design and settings

In this thesis a triangulation of research designs were used [132]: descriptive (Papers I and II), methodological (Paper III) and experimental (Paper IV).

All studies utilised empirical data from patients with worsening CHF, who sought care at the emergency department (ED) or the HF outpatient clinic (Figure 2). The study was conducted at Sahlgrenska University Hospital/Östra, a hospital serving 250 000 inhabitants in Göteborg, Sweden. Patients were identified either at the ED or within 72 hours after hospital admission (Papers I, II, III). The sole inclusion criterion was exacerbation of CHF (Papers I, II, III). Known dementia, communicative limitations (*e.g.*, loss of hearing and speech) and unwillingness to participate in the study were exclusion criteria. The diagnosis of CHF was validated according to ESC guidelines [4] and verified from electronic medical records. Discrepancies were reviewed and resolved by a senior cardiologist. The study was conducted between April 2004 and January 2006 (Paper I), May 2006 (Papers III, IV) and June 2006 (Paper II).

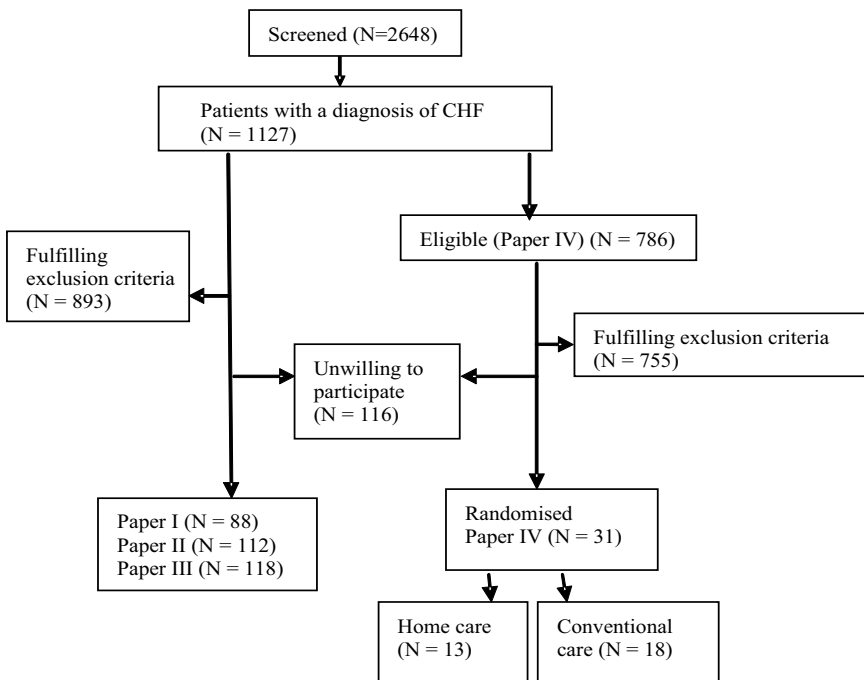


Figure 2. Patient flow and data availability for all Papers.

Table 2. Inclusion and exclusion criteria for Paper IV.

Inclusion criteria

1. Earlier diagnosed CHF with diastolic or systolic left ventricular dysfunction
 2. Deterioration of HF \geq 3 days with symptoms of increasing dyspnoea, orthopnea, Weight gain \geq 2 kg, debuting peripheral oedema or abdominal swelling
 3. Clinical signs, *e.g.*, extended jugular vein, leg oedema, tachypnea, pulmonary crackles, ascites, 3rd sound
 4. At least one symptom and one sign should be present
 5. New York Heart Association class II – IV
-

Exclusion Criteria

1. Unwillingness to participate
 2. Deterioration of CHF < 3 days
 3. Newly onset of HF
 4. Pulmonary or pre-pulmonary oedema
 5. Need for monitoring of arrhythmia
 6. Other morbidities indicating need for hospitalisation
 7. Living at an institution
 8. Inability to follow instructions
 9. S-Haemoglobin < 100 g/L or decrease of S-haemoglobin > 20g/L
 10. S-Creatinine > 250 μ mol/L
 11. S-Potassium > 5.5 mmol/L or < 3.4 mmol/L
 12. S-Troponin T > 0.05 ug/L
 13. Creatine Kinase-MB > 5 ug/L
 14. ASAT & ALAT > thrice above the normal value
 15. Systolic blood pressure < 95 mmHg
 16. Heart rate < 45 or > 110 beats/minute
-

Paper IV is a randomised, controlled trial. All patients with a clinical diagnosis of CHF and that sought care at the ED, HF outpatient clinic or the medical ward were identified within 24 hours from admission. After one year, the protocol was amended, with an extension of time to inclusion to 48 hours. Eligible patients were those who were assessed as in need of hospital care by their consulting physician, fulfilled all of the inclusion criteria and none of the exclusion criteria (Table 2). An overview of the study design is presented in Table 3.

Descriptive studies (Papers I - III)

Subjects (Papers I - III)

Totally, 1127 patients with CHF were screened over a 23-month period with clinical symptoms similar to worsening CHF (no screening took place during official holidays). A flow chart with data availability is presented in Figure 2.

Paper I

Totally, 117 patients were approached of which 6 declined to participate and 23 others were excluded from data analyses because of a discharge diagnosis other than CHF exacerbation. The final study sample comprised 88 patients.

Table 3. Presentation of design and methods for data collection and data analysis.

Study	N	Objectives	Design	Methods for data collection	Methods for data analysis
I	88	Explore the factors related to seeking acute care	Descriptive	Semi-structured interviews	Content analysis
II	112	Examine the association between fatigue and anxiety, depression and symptom distress. To explore the relationships between symptoms and fatigue as a multidimensional experience in patients with CHF	Descriptive and Correlational.	Questionnaires - <ul style="list-style-type: none"> ▪ MFI 20 – Fatigue ▪ SDS – Symptom distress ▪ HAD – Depression and anxiety 	Descriptive Regression Chi-square Students t-test
III	118	Evaluate the psychometric properties of a Swedish version of the KCCQ	Methodological - validation	Questionnaires – <ul style="list-style-type: none"> ▪ KCCQ – symptoms and HRQL ▪ SF-36 - generic ▪ NYHA classification 	Validity, reliability, responsiveness
IV	31	Evaluate home care vs. conventional care	Randomised controlled trial	Clinical variables <ul style="list-style-type: none"> ▪ EQ-5DVAS – value measure ▪ SG – utility measure ▪ KCCQ ▪ SF-36 Health care utilisation related to CHF	Descriptive Mann-Whitney Wilcoxon signed rank test CUA Kaplan-Meier Sensitivity analysis

Paper II

Initially, 128 consecutive patients hospitalised for worsening CHF were eligible for the study, but 16 patients were excluded from data analysis (8 because of the extent of incomplete data from the interviews and 8 because of a discharge diagnosis other than CHF). Thus, the final study sample consisted of 112 patients.

Paper III

Initially, 125 patients were approached and consented to participate in the study. Seven patients were excluded because of being too feeble to answer the questionnaire. At baseline, 118 patients were interviewed while 51 and 83 patients were assessed at 1 month and 4 months, respectively. The lower number of patients attending the follow-up visit at 1 month as compared with 4 months was often due to the patients' unwillingness to return for an interview soon after hospital discharge.

Instruments

Short Form 36 (SF-36)

The SF-36 is a well-established generic and global health status-measuring instrument [133, 134]. The SF-36 includes eight multi-item scales (domains) containing 2 to 10 items each plus a single item to compare the current health with a person's health one year earlier (health transition). The SF-36 measures health status in eight domains: physical functioning, role physical, body pain, general health, vitality, social functioning, role emotional, mental health and two summary score domains – physical component summary and mental component summary. The SF-36 is a 36-item Likert scale, where the scores on each subscale and the two main dimensions are converted to a scale ranging from 0 to 100. A higher score indicates better health. The SF-36 scale is well tested and has proven to have satisfactory psychometric properties and international comparability with internal consistency, with a Cronbach alpha > 0.8. The cross-cultural stability of the SF-36 in a Swedish population was established in a study by Persson *et al.* [135].

In a study by Stewart *et al.* [136] the SF-36 discriminated patients with different levels of severity of CHF ranked with the NYHA classification system. The conclusion reached was that the SF-36 is a general HRQL instrument suitable for use in CHF patients and can be optimally used in combination with a disease-specific instrument. Further, administration of the SF-36 via interview has been suggested as the best way to use this instrument in an elderly population [137]. Cronbach's alpha in Paper III was 0.82.

Symptom Distress Scale (SDS)

Symptom distress is defined as, "the degree of discomfort from the specific symptom being experienced as perceived by the patient" [138, 139] in the present time. The Swedish version of the scale [140] measures severity of symptom distress in 13 symptoms (Nausea, Appetite, Insomnia, Pain, Fatigue, Mobility, Bowel pattern, Mood, Concentration, Appearance, Breathing, Outlook and Cough). In addition, it measures the frequency of pain and nausea. A score of 1 indicates the least and 5 indicates the most amount of distress associated with the symptom. Items in the SDS are summed to arrive at a total score ranging from 15 to 75, with higher scores indicating a higher

degree of symptom distress. Because the scale was developed to study distress in patients with cancer, the selection of symptoms consisted of those symptoms with the most physical distress associated with the cancer disease. It has been used within many clinical populations and in various settings where it has been shown to be a reliable and valid measure. Reliability scores with Cronbach's alpha have been reported between 0.70 and 0.92, mainly in cancer populations using the English version [139], and 0.81 in a Swedish study with cancer patients [141]. The SDS was chosen here because there is no existing valid version of SDS in patients with CHF and because patients with CHF experience similar symptoms in accordance to the questionnaire. Cronbach's alpha in the Paper II was 0.79.

Hospital Anxiety and Depression Scale (HAD)

Anxiety and depression were measured using a Swedish version of Zigmond & Snaith's [142] Hospital Anxiety and Depression scale. It includes 14 Likert-scale items intended to determine the state of anxiety (seven items) and depression (seven items) in hospital patients. The scale provides information about the patients' emotional state with a one-week window of self-assessments. The statements are rated on a 4-point Likert scale and the summed scores on each subscale range between 0 and 21. A scale score between 0 and 7 is considered within the normal range; a score between 8 and 10 indicates a "possible" case of clinical anxiety and depression; and a score between 11 and 21 indicates a "probable" case of anxiety and depression. The item to subscale reliability correlations ranged from 0.41 to 0.76 for the anxiety items and 0.30 to 0.60 for the depression items [142]. Cronbach's alpha values for the anxiety and depression sub-scales were 0.77 and 0.78 respectively (Paper II).

Multi Fatigue Inventory – 20 items (MFI-20)

In this thesis fatigue was measured with the Swedish version [143] of the MFI-20. The MFI was developed as a tool to assess fatigue in a comprehensive way [144]. MFI is a 20-item self-report instrument designed to measure subjective fatigue. It covers five dimensions of fatigue: General Fatigue, Physical Fatigue, Reduced Activity, Reduced Motivation and Mental Fatigue. General Fatigue includes general statements about fatigue, such as "I am tired" and decreased functioning. Physical Fatigue concerns physical sensations related to feelings of tiredness. Reduced Activity refers to a possible consequence of fatigue, namely a decreased level of activity. Reduced Motivation relates to lack of motivation to start any activity. Mental Fatigue pertains to cognitive functions, including difficulties to focus and concentrate. The patient rates his or her experiences on a 5-point Likert scale, summed for each dimension to yield a range between 4 and 20, where higher scores indicate a higher level of fatigue. The instrument has demonstrated good reliability in different patient populations undergoing radiotherapy, patients with chronic fatigue syndrome, psychology students, medical students, army recruits and junior physicians [144].

The Swedish version of the MFI-20 scale demonstrated good internal consistency (Cronbach's coefficient alpha ranged from 0.75 to 0.94) in measuring fatigue in radiotherapy patients [143]. In two recent Swedish studies that included patients with CHF Cronbach's alpha for the different sub-scales ranged from 0.56 – 0.87 [145] and 0.63 to 0.88 [115]. In Paper II, Cronbach's alpha ranged from 0.60 to 0.78.

Kansas City Cardiomyopathy Questionnaire (KCCQ)

The KCCQ was developed in 2000 by Green & co-workers [146]. This questionnaire is a condition-specific instrument sensitive to clinical changes and designed to capture specific distinct features of CHF. The KCCQ was used to cover specific aspects (e.g., symptoms and HRQL), which have a great impact on patient's with deteriorating CHF. The KCCQ is made up of 23 items that are grouped into the following six domains (scales): Physical Limitation, Symptoms (Frequency and Severity), Symptom Changes, Self-efficacy, Social Interference and QoL. In addition, there are two summary score domains: Overall Summary Score and Clinical Summary Score. The responses on the KCCQ consist of a Likert scale, with a range of 5 – 7 alternative answers for each item. Higher scores indicate better health status (fewer symptoms, better function and higher HRQL). Information obtained is from two preceding weeks. The reliability coefficient has ranged from 0.62 – 0.99 in English, Norwegian and Italian translated versions [146 - 148]. The KCCQ has shown greater sensitivity to changes over time than the SF-36, the MLHFQ [146] and the EuroQoL-5D, Short Form-12 [149]. The KCCQ has also shown acceptable cross-sectional validity and reliability in patients with post-myocardial infarction [147]. An Italian validation of the KCCQ has also reported higher sensitivity than the MLHFQ [148]. The KCCQ has been estimated as a method for identifying high-risk patients with CHF [150].

Data collection procedure (Papers I - III)

All patients were approached in a consecutive manner and informed orally and in writing about the study. Baseline characteristics and demographic data for all four papers were collected from the patients and, if needed, completed from the patients' medical record. Information was collected about age, gender, education, marital status, aetiology, co-morbidities, weight, height, blood pressure and data about various symptoms. Information about clinical data such as left ventricular ejection fraction, pharmacological treatment and previous hospitalisations related to CHF and HF clinic utilisation was obtained from the patients' medical record. Disease severity was graded on the basis of the NYHA classification system [106] by a physician or specialist HF nurse.

All the questionnaires were administered by interview and all items were read to the patients to standardise data collection and minimise missing data. Inter-observer reliability was assessed by comparing the extent to which the interviewers agreed in their understanding of the questions and the patients' answers to the questions.

Paper I

The face-to-face, semi-structured interviews [132] were conducted after obtaining written consent from the patients. The method emanates from ontology, where health and ill-health are regarded as a personal experience, as a process and as a way of being [151]. The interviews lasted approximately 15–30 minutes and took place either at the ED or in the ward. The following open-ended questions were used: "Could you please explain why you sought care at the ED today?" "Did you consider seeking care at an earlier time?" "Did you have any idea what your condition was?" The patients' responses were written down verbatim.

Papers II and III

Structured interviews were performed using the following questionnaires: the MFI-20, HAD, SDS [Paper II] and the KCCQ and SF-36 (Paper III) during the patients' hospitalisation, and at 1 and 4 months after the first questionnaire (Paper III). The US version of the KCCQ was translated into Swedish according to the forward and backward translation procedure (Paper III) [134, 152].

Data analysis (Papers I – III)

All statistical analyses were performed using SPSS version 11.5, 12.0.1 and 14.0 for windows (SPSS Inc., Chicago, ILL, USA). The weight of evidence was quantified using statistical significant tests and the p-value was set at < 0.05 (two-tailed).

Paper I

The interview analysis was inspired by Krippendorff's content analysis technique [153].

Content analysis (I)

When data are semi-structured, data analysis begins with content analysis [153]. Krippendorff defined content analysis as, "a research technique for making replicable and valid inferences from data to their context" [a. a., p.18]. This technique was found to be suitable because it is unobtrusive, accepts unstructured material and is context sensitive and thus able to process symbolic forms. Content analysis has its roots in journalism and was used primarily to analyse documents, producing counts of words or phrases. In content analysis, issues surrounding coding are important, where the identification of these codes is central to obtain as good a description as possible of the studied problem. This is the start of a process of exploring information, identifying relationships between data and understanding the meaning emerging from the data. The data analysis starts with reading all answers to each question several times to establish a "feel" for the answers [154]. As each answer is read, and a "general sense" of the implication of the answers is established, separating the answers to each question into mutually exclusive categories of similar content. In Paper I, the unit of analysis (statements) that were observed in the text were coded into units. Similar coding units were then classified into content categories according to the patients' answers to the open-ended questions. Once the data had been analysed and categories derived, we were able to report the most common prevalent factors related to seeking acute care in worsening CHF. One of the co-authors (IE) read one third of the interview text and validated this process by coding independently. Because the narratives were short, disagreements in coding were rare, and when they did occur, they were discussed until consensus was reached. Also basic to this design are descriptive statistics, *i.e.* frequencies, modes and percentages for nominal data were calculated.

Paper II

Descriptive statistics were used to characterise the sample. A Chi-square test was performed to compare proportions in discrete variables. Ordinal and continuous variables were compared using independent sample t-tests. Multicollinearity was tested using Pearson's correlation coefficient and tolerance diagnosis performed using the

SPSS. Hierarchical regression analyses were used to examine the individual contribution of anxiety, depression and symptom distress to the variance in the five fatigue dimensions described earlier as measured with the MFI-20. To evaluate predictors of fatigue, multiple stepwise regression analyses were conducted using different dimensions of fatigue as the dependent variables. Symptoms were tested as the independent variables (fatigue was excluded).

Paper III

The data from the KCCQ questionnaire was analysed using classical psychometric methods [152].

Psychometric methods

The scale and item distributions of the KCCQ were examined, including proportions of missing values. Construct validity was tested with item convergent and discriminatory validity as well as by the known groups comparisons (a combination of tests for validity and responsiveness assessment) with the NYHA classification system (analysis of variance, ANOVA). Criterion validity was examined using SF-36 scores (correlation). Reliability was tested with the Cronbach's alpha coefficient for each of the hypothesised scales of the KCCQ. Test-retest reliability was tested by intra-class correlations (ICC) in patients with stable NYHA. Responsiveness was examined by computing t-test statistics and standardised response means (SRM).

Reliability

In brief, reliability refers to the consistency of assessment scores and is necessary in establishing the usefulness of a scale. Because the magnitude of the reliability coefficient is directly related to the variability among subjects, the coefficient reflects the extent to which a scale can differentiate among individuals. This was assessed by internal consistency, which involves testing for homogeneity of the items contained in the questionnaire and was determined by Cronbach's alpha. The ICC was used to measure the strength of agreement between repeated measurements [152].

Validity

Validity determines if the scale is measuring what it is intended to measure [152]. The ability of an instrument to discriminate between different grades of severity of disease is an important form of validity. These attributes are important for measuring change in symptoms and HRQL and hence the outcome of an intervention [152].

Validity of the KCCQ was measured as follows: (1) Content validity refers to the appropriateness of the content of the instrument to measure what it is intended to and face validity refers to the researchers subjective assessment of the relevance of the questionnaire. This was determined by experts in the area (2) Criterion validity refers to the extent to which an assessment tool correlates with some form of external criterion. This was assessed with an established scale, *i.e.* the SF-36 (3) Construct validity refers to the ability of the instrument to measure the underlying concept it claims to measure. This was measured with convergent and discriminatory validity using multi-trait multi-method analysis [155]. Further, known groups comparisons were performed using the NYHA classification system.

Responsiveness

Responsiveness reflects the ability of the KCCQ to detect clinically meaningful changes in a patient's subjective health status, which is critical to both patient management and the interpretation of outcome. To be a valid scale of clinical change it must be capable of capturing both improvements and deterioration in clinical status. SRM was used to measure responsiveness of KCCQ.

The experimental study (Paper IV)

Subjects (Paper IV)

Totally, 1127 patients with CHF and clinical symptoms comparable to worsening CHF were screened over a period of 23 months (no screening took place during official holidays). The inclusion criteria were fulfilled by 785 (70%) patients, and only 31 (4%) of these patients had no exclusion criteria and could be included in the study. Twenty-four (77%) completed the 12-month follow-up. Four patients, two from each group, died during the study because of stroke and cardiac arrest, and three from the conventional care (CC) group withdrew their consent. In the home care (HC) group, seven patients were sent home directly from the ED, five were recruited within 24 hours and one within 48 hours from the medical ward.

Instruments (Paper IV)

The European Quality Of Life 5-Dimension with VAS (EQ-5DVAS)

The EQ-5D was developed in Europe [156]. It is a simple generic questionnaire with a two-part measure that provides both a compact descriptive profile and a single index value. The descriptive part addresses five dimensions of health: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The dimensions are rated on a 3-point scale in terms of perceived problems: 1 (no problem), 2 (some problems) and 3 (severe problems). The VAS scale maps weights of levels of functioning on several health state domains to derive an overall score for a health state. It is useful in clinical studies as a method of describing the health status of patients and tracking changes over time. Furthermore, the VAS has been recommended in measuring HRQL in cardiac patients. Repeated observation provides cardinal data on changes in HRQL and thus on health outcome. It can be used for CUAs and for the comparison of therapeutic effects across different diseases [156]. In Paper IV, Cronbach's alpha was 0.75.

Standard Gamble technique (SG)

The SG is a simple framework for eliciting utilities, *i.e.* for analysing the strength of an individual's preference for different health states after considering both benefits and risks [121, 157]. The SG technique is based directly on the Von Neumann-Morgenstern utility theory (when future health outcomes are uncertain, uncertainty should be incorporated into decision making) and is the original technique for measuring utilities [157]. This technique is useful in measuring HRQL because it is a generic instrument that takes into account past experience, attitudes towards taking risks, beliefs and health values with reliability coefficients reported between 0.80-0.90 [157]. The focus for the SG technique is a paired comparison between two alternative choices: choice A is to take the relevant health state with certainty, whereas choice B is to take a gamble on a treatment with the possibility of a better outcome. The application of this

approach is illustrated in Figure 3. The probability p is then varied until the patient is indifferent between choices A and B. Consider that state A in patient's perspective means better than death but worse than perfect health. When probability (p) is 1.0, the patient will prefer choice B because that gives perfect health with certainty. When p is 0.0, the patient will prefer choice A because choice B now leads to immediate death with certainty. Somewhere between $p = 1.0$ and $p = 0.0$ there is a value of indifference, p , at which the patient must switch from choice B to choice A [121, 128].

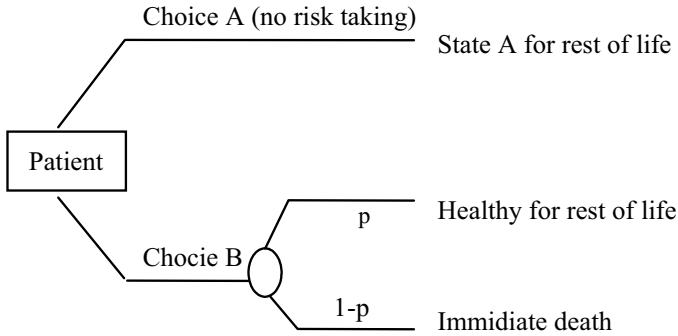


Figure 3. SG technique for eliciting utilities for a chronic state (adapted from Torrance 1989)

Data collection procedure (Paper IV)

All patients with CHF that sought care for exacerbation at the ED or HF clinic and patients who had already been admitted to the medical ward within 24 hours up to 48 hours (time from ED visit) were eligible if they fulfilled all the inclusion and none of the exclusion criteria, *i.e.* in need of hospital care, unwillingness to participate, abnormal laboratory status and communication problems (Table 2). The patients were asked about study participation upon identification, and were given oral and written information. Patients were randomised either into the HC group (intervention by a specialist nurse) or into the CC group (hospital admission).

Baseline

Baseline data collection was similar in both groups, *i.e.* demographics and baseline characteristics, an interview and questionnaires were performed in the same sequence for all patients in both groups to avoid order effect. A complete history and physical examination, including the NYHA classification, weight, blood pressure, heart rate, breathing frequency, jugular venous distension, peripheral oedema, pulmonary auscultation and symptoms were conducted. Additional blood samples were drawn if not covered by those already prescribed by the patient's physician or as stated in the exclusion criteria. All data were recorded in a case record form (CRF). Four questionnaires [KCCQ (symptoms & HRQL domain), EQ-5DVAS, SG and SF-36 (global question 1)] were administered by interview to assess HRQL while awaiting the results of the blood samples. Echocardiography was considered valid if less than one-year old otherwise a new echocardiography was performed.

Intervention (home care, HC) group

Patients in the HC group were initially treated in the ED or up to 48 hours in the ward (time limit was extended from 24 to 48 hours after one year because of the few number of patients recruited). The treating physician in the ED or in the ward assessed patients for eligibility. Drug adjustment was done by either the study investigator (cardiologist) or by the patients' physician at the ED or in the ward. Patients could return to their homes instead of hospital admissions followed by an ED visit or from the medical ward after agreeing on a follow-up visit. The follow-up took place the next day by a specialist nurse from the HF clinic. After the follow-up, a specialist HF nurse visited the patients every day or every other day for 5 -7 days, the intensity of the visits being determined by the patient's health status. After each home visit, the cardiologist was informed about the patient's health status.

Home visits were terminated when patients had regained their health status as before the deterioration. This was considered to have occurred if the patient: (1) was in the same or improved NYHA class as before deterioration, (2) had the same weight or a weight loss of at least one kg, (3) exhibited no pulmonary rales and (4) exhibited no leg oedema or oedema up to the ankles. If needed, patients could contact the specialist nurse by telephone during office hours. During out of office hours, the nurses at the intensive cardiac care unit could be reached by telephone. A cardiologist was always available for telephone consultation. Up to one month after the last home visit, the specialist nurse was also available for telephone counselling. If needed, the patients were referred to the HF clinics for drug up titration after termination of home visits.

Assessments

At each visit, clinical signs and symptoms were assessed according to the study protocol. Samples for blood electrolytes were drawn and medication was adjusted after consulting the study cardiologist. If no improvement was noted in dyspnoea, orthopnea, leg oedema and weight, or if rales persisted, intravenous diuretics could be administered and drug adjustments were performed according to the study protocol or after consultation with the cardiologist.

Information was offered about the treatment and the condition (*e.g.*, the importance of regularly taking prescribed drugs and how to recognise symptoms of worsening CHF). All information took place in the form of a dialogue, which was individualised and tailored for the particular patient and in consideration with the patient's current medical condition. The routines for weighing were established, with the goal of weighing at least twice a week. To establish weighing routines we helped the patients to locate their old scale and if that scale was not in usable condition, the patients were advised to buy a new one. Some of the patients were provided with a weighing scale, because they had not used a scale for many years.

The principle point in the dialogues with patients was to relate information to their daily lives. For example, noticing the symptoms of worsening CHF was explained by relating them to different daily tasks. Patients were advised to notice changes in their condition by simply observing whether their trousers had become too tight around their waist, whether markings appeared after the sock ankle band, whether they could

not carry out activities that could be performed with little or no problem a few days ago, poor appetite, coughing, increasing tiredness, feebleness and difficulty getting on their shoes. Other conditions to look for included weight gain >2 kg in 2 days, swollen legs, difficulty lying down, the need for more than two pillows while going to bed because of breathing difficulty, forced to sit and sleep during the night and feelings of nausea or other symptoms of a bad appetite. The uniqueness of this study was that each patient was individually cared for in his/her familiar environment and was informed in relation to his/her personal experiences, resources and barriers.

Medical safety

It was considered medically safe to treat patients at home if they had a S-Potassium between 3.4 and 5.5 mmol/L, systolic blood pressure > 95 mmHg, S – Creatinine < 250 µmol/L and less than a 50% increase from the baseline value during drug adjustment. To ensure medical safety the specialist nurse responsible for patients in the HC group had a memo to follow written by cardiologists involved in the study; however, in case of uncertainty, a cardiologist could be consulted.

Conventional Care (CC) group

The patients randomised to the CC group were treated according to hospital guidelines. Data were collected in a similar manner as in the HC group.

Follow-up

Follow-ups by a specialist nurse were performed after 1, 4, 8 and 12 months after study enrolment, either at hospital or at the patients' home. Assessments were done in the same manner in both groups. All patients completed the questionnaire package and repeated examinations were performed according to the study protocol. Patients' clinical status was documented and information about events was elicited by patient-interviews and completed, if necessary, by their medical record. Patients from both groups were treated in a similar manner after initial intervention.

Resource utilisation

All resource utilisation is considered from a health care perspective. Information on all health care utilisation specific to CHF was elicited by patient interviews and complemented with data from their medical record. Costs for the patients in the CC group were based on compensation charged by the hospital for each patient based on diagnose-related group (DRG) values.

Costs for the patients in the HC group included time costs for the specialist nurses (e.g., home visits and time for pre- and post-visit preparation and transportation). Time cost for physicians included consultation, prescriptions, referrals or any other practical task performed. Further, the laboratory tests and the costs for intravenous diuretics administered to patients in the HC group were also included in the costs for the HC. Information on the number of visits and telephone contacts to the HF clinics, emergency visits and hospitalisations that were caused by HF was elicited by patient interviews at follow-up, again complemented by data from their medical record. Only direct costs were considered as the majority of patients were retired in this study. Costs for patients in the CC group and readmissions for patients in both groups were derived from the financial department in hospital, based on DRG system.

Data analysis (Paper IV)

Descriptive statistics [mean (SD) for continuous variables, proportions for categorical (baseline data) variables and median for non-normally distributed variables] were used to characterise the groups. The Wilcoxon signed-rank test was used to determine clinical improvement (weight, NYHA, NT- proBNP) over time within groups. The Mann-Whitney test was used to compare between group differences for ordinal data (from the SF-36 and the KCCQ), categorical variables (from the NYHA) and continuous data (from the QoL, QALYs, hospital-days, costs, weight and NT- ProBNP as analysed with Electro Chemi Luminescent Immuno Assay). The significance level was set at $p < 0.05$.

The CUA assessed the HC and CC groups based on monetary costs and QALYs elicited by the VAS and SG techniques. Spearman's correlation was used to assess the association between QALYs derived from the SG and VAS techniques. Because HRQL might be affected by the choice of technique used (VAS vs. SG) to elicit QALYs, cost-utility ratios (CUR) were calculated using both techniques. An incremental cost-effectiveness ratio (ICER) was calculated by the mean difference between HC and CC groups in the cost, divided by the mean difference between the HC and CC groups in the QALYs. Further, survival analysis (Kaplan-Meier non-parametric analysis and a Cox proportional hazards model) was done to analyse whether the probability of re-hospitalisation differed between treatment groups [158]. The Cox proportional hazards model was used to investigate the effects of treatment regimen while simultaneously controlling for confounding factors.

Sensitivity analysis

Sensitivity analysis was performed for cost and HRQL with last value carried forward (LWCF) for patients who dropped out during the study. Finally, because information on HRQL is only available at inclusion and at the follow-ups (*i.e.* at 1, 4, 8, and 12 months), the number of QALYs for the patients in each group was calculated using three assumptions: (1) Any change in HRQL between two measurement points occurred immediately after the first measurement point, (2) any change in HRQL occurred immediately before the second measurement point and (3) any change in HRQL occurred exactly half way between the two measurement points.

ETHICAL CONSIDERATIONS

Nurses have a responsibility to the patient to conform to the appropriate professional and ethical conduct of the research. Important considerations in all studies were respect for the individual's autonomy and to avoid the risk of causing emotional and psychological problems because of exposure to the interviews and questionnaires. All patients received both oral and written information, including that their participation was voluntary and that they could withdraw consent at any time without affecting their treatment and without the need to provide any reason for withdrawal. Confidentiality was guaranteed by coding the questionnaires. Collected data and personal data were stored separately according to the Swedish Data Protection Act [159]. The principles of "doing well and no harm" were considered as a medical safety in the intervention group, since this type of care was not a standard before. The right of privacy could be a potential issue, while visiting and treating patients in their homes. The visiting nurses ensured that the visit was not more intrusive than necessary. The patient's welfare is paramount in the nurse-patient relationship. To care for patients in the home, first necessitates understanding the patient's values, and then spending time discussing the condition and how to deal with the deterioration. Approval was obtained from The Regional Ethical Review Board, and participants gave their written, informed consent. This thesis was guided by international research-ethical principles outlined in the World Medical Association Declaration of Helsinki [160, 161].

The questions posed to patients were routine questions that are typically asked in this kind of context and thus were not considered an additional burden on the patients (Paper I). The questions were interview administered to decrease the burden on patients (Paper II, Paper III). To send home patients (Paper IV) with worsening of CHF with a potential need for hospitalisation after initial treatment needs careful assessment. However, in this study only patients with worsening CHF were eligible. Patients were informed and understood and accepted the study participation. Follow-ups were provided when needed during intervention period, which lasted between 5 – 10 days. This procedure (outside any study) is already used in patients not willing to be hospitalised through the nurse-lead HF clinic.

MAIN RESULTS

Factors related to seeking acute care (Paper I)

According to the patients, the main reason for seeking emergency attention was their symptoms while the second most common reason was that either patients were referred or relatives/caregivers had sent them in. The most frequent symptoms patients reported were dyspnoea (86%) and fatigue (53%). Only 8% of the patients reported weight gain. Many of the patients did not think their symptom warranted emergency care (57%); instead they attributed their symptoms to the external factors. Few of them (9%) were uncertain, whether they needed care at an earlier time, since they had felt feeble over a long period, and several patients attributed their symptoms to old age or to the recent hospitalisation. Thirty (34%) patients reported that although they had wanted to seek care earlier, they had simply not done so. Patient's reasons for not seeking care earlier were: (1) the problem was not serious and would go away, (2) they were unsuccessful in their attempts to make an appointment at the primary health care centre and therefore decided to wait for their scheduled follow-up visit, (3) they had no one to accompany them to the ED, (4) previous unpleasant experiences with ED care and (5) they felt that their situation was hopeless. Only 5% of the patients could relate their current symptoms to the worsening of CHF. All categories derived from interview data is presented in Figure 4.

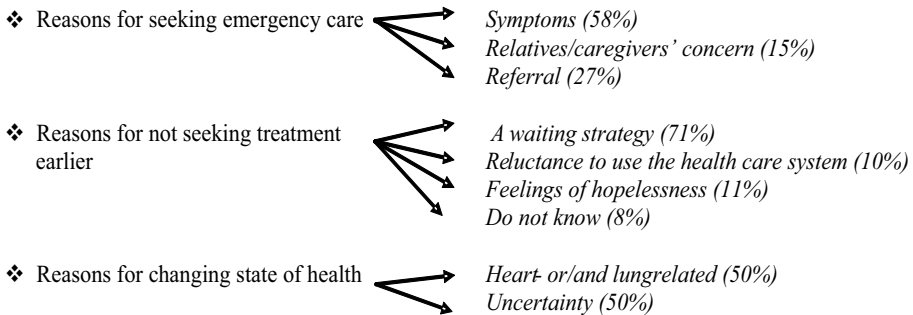


Figure 4. Illustration of the questions and categories in the Paper (I).

Associations between fatigue and anxiety, depression and symptom distress (Paper II)

The highest mean scores of fatigue were noted in General Fatigue, Physical Fatigue, and Reduced Activity, followed by Reduced Motivation and Mental Fatigue. Eleven (10 %) patients indicated a clinical significant degree of anxiety, and twenty (18 %) patients indicated a definitive degree of depression with score between 11 and 17. The most intense reported symptoms on SDS were fatigue, difficulties in breathing and insomnia.

The hierarchical multiple regression analysis showed that anxiety explained 25% of the variance in Mental Fatigue and depression explained 15% of the variance in General Fatigue, 18% in Reduced Activity and 11% in Reduced Motivation. Symptom distress explained only a small portion of the variance in General Fatigue (4%), Physical Fatigue (5%) and Mental Fatigue (3%). A stepwise multiple regression analysis identified the associations between general fatigue and nausea, pain, difficulties with breathing, and bad mood; physical fatigue was associated with bad appetite and pain; reduced activity with nausea and bad mood; reduced motivation with bad mood; and mental fatigue with concentration.

Psychometric properties of KCCQ (Paper III)

In the original article [146] two of the scales, *i.e.* Symptom Frequency (SF) and Symptom Severity (SS) were considered as two separate scales in the method section, but were analysed as a Total Symptom score (TS). In Paper III, we have followed the subsequent version of KCCQ (after contact with one of the authors, Spertus J.) and data have been analysed with a TS. Therefore, the additional analyses to test two separate scales SF and SS are presented in this section.

Scale distributions and results of the tests of internal structure are listed in Table 4. Most items had acceptable normal distributions, except question 3 and 9 (assessing oedema and paroxysmal nocturnal dyspnoea, respectively). Both of these questions had bimodal distributions on all assessments.

Table 4. Results from tests of scale properties at baseline.

	Physical limitations	Total symptom score	Self efficacy	Social interference	Quality of life
Number of items	6	7	2	4	3
% Incomplete scale / scores ^a	0	0	0	0	0
Scale score, mean (SD)	43.7 (27.2)	44.7 (22.1)	38.0 (29.2)	42.2 (33.4)	45.9 (25.8)
Theoretical range	0-100	0-100	0-100	0-100	0-100
Observed range	0-100	0-87	0-100	0-100	0-100
% at ceiling	2.7	0.0	5.4	9.8	1.8
% at floor	5.4	2.7	19.6	17.9	1.8
Skewness coefficients	0.22	0.56	0.35	0.32	0.29
Mean (R) internal consistency ^b	0.65 (0.70-0.50)	0.49 (0.59-0.20)	0.51 (0.51-0.51)	0.82 (0.85-0.79)	0.50 (0.54-0.44)
% Success rate discriminatory validity ^c	0 / 0 / 10 / 90	0 / 6 / 43 / 51	0 / 0 / 0 / 100	0 / 0 / 0 / 100	0 / 0 / 60 / 40
Cronbach's alpha	0.86	0.75	0.67	0.92	0.68

^aHalf-scale criterion. ^bCorrelations between items and hypothesised scale corrected for overlap. ^cPercent correlation that are 'significantly lower/lower/higher/significantly higher' with the hypothesised scale as compared with the other scales.

The correlation coefficients between the KCCQ and SF-36 scales followed, in part, a priori hypotheses (Table 5). NYHA class showed significant correlation with Physical Limitation, Social Interference and Total Symptom domains of KCCQ and Physical Functioning, Role physical and Vitality domains of SF-36 (data not shown). The known-groups comparison between patients differing in NYHA classification at baseline revealed significant differences in the expected KCCQ domains: Physical Limitation, Social Interference and Total Symptom scale. Tests of Cronbach’s alpha for the KCCQ scales ranged between 0.67 – 0.92 (Table 4). Test-retest reliability (intraclass correlations) for stable NYHA group was acceptable for most scales, ranging from 0.67-0.89, except for the SE scale (0.38).

Responsiveness in patients with improved NYHA, using standard response mean (SRM) showed the largest responsiveness in Total Symptom scale and the Clinical Summary Score in relation to changes in NYHA class. The mean of the SRM values for the KCCQ domains was 0.95, which can be compared with 0.29 for the SF-36.

Table 5. Correlations between the health domains in the SF-36 and the KCCQ (Spearman’s rank correlation, n=112 - 118).

SF36/KCCQ	Physical limitation	Social interference	Quality of life	Total symptom score	Symptom change	Self efficacy
Physical functioning	0.62**	0.58**	0.43**	0.61**	0.17	0.14
Role physical	0.34**	0.57**	0.37**	0.31**	0.09	-0.03
General health	0.28*	0.35**	0.50**	0.23**	0.05	0.06
Vitality	0.51**	0.51**	0.58**	0.30**	0.17	0.10
Social functioning	0.28**	0.41**	0.48**	0.39**	0.17	0.06
Role emotional	0.13	0.46**	0.27**	0.22*	0.06	0.03
Mental health	0.26**	0.41**	0.49**	0.32**	0.07	0.08
Bodily pain	0.19*	0.27**	0.36**	0.28**	0.08	0.09

*p<0.05, **p<0.01

Additional analysis of Symptom Frequency (SF) and Symptom Severity (SS) Scales

The SF scale consisted of questions 3, 5, 7 and 9 while the SS scale consisted of questions 4, 6 and 8 (Appendix). Item-scale convergent validity and discriminatory validity were found to be poor. For the SF scale, 33% of the possible item/scale correlations were significantly lower or lower with the hypothesised scale as compared with other scales; for SS, this proportion was as high as 61%. When the SF was merged with the SS scale in a Total Symptom score, it yielded 94% discriminatory validity to all other scales (Table 4). Tests of reliability with Cronbach’s alpha were 0.50 for the SF scale and 0.55 for the SS scale. The detailed examination revealed that questions (3 and 4) about leg oedema, when mixed in one multi-item scale, resulted in a Cronbach’s alpha of 0.86, and remained stable up to four months. Questions 5, 6, 7, 8 are about dyspnoea and tiredness. When merging these two symptoms, Cronbach’s alpha was 0.85. Thus, two separate scales for “symptoms” (questions 5 – 8) and “signs” (questions 3 and 4) can be recommended, at least based on these results for subjective and objective measurements.

Feasibility of home care (Paper IV)

The CC group included more men (83% vs. 46%), more highly educated persons (≥ 9 years) (44% vs. 8%) and more married individuals (44% vs. 23%) than the HC group. The mean age of the patients in the HC group was 77 years (SD, 10) and 78 years (SD, 8) for patients in the CC group.

The median time consumed for patient-care was 12 hours in the HC group vs. 120 hours in the CC group ($p < 0.001$). During the study period, the median number of visits to the HF clinic was three times in the HC group and one time in the CC group. No difference could be found either in the consumption of unplanned health-care resources or time to the first HF-related hospitalisation.

The patients in both groups improved clinically (weight, NYHA and NT-proBNP) in the similar manner. The health care cost differed significantly ($p < 0.001$) between the CC group (€1069 – 7480) and the HC group (€185 – 1796) after the initial intervention. At the end of the study, a significant difference ($p = 0.04$) was found in the health care cost between the CC (€1643 to 14783) and HC groups (€204 to 20058). Details are presented in Figure 5. Although the patients in the HC group had larger costs with respect to the HF clinic visits, the difference between groups was still significant after inclusion of these costs, which occurred after termination of home visits, for the CC (€2202 – 15502) and the HC group (€400 – 20058, $p = 0.05$). The mean QALYs generated by SG and VAS were higher (though not statistically significant) for patients in the HC group. A close association in QALYs as derived by SG and VAS ($r = 0.70$, $p < 0.001$) was found. Cost/QALY was lower in the HC group, but this difference did not reach statistical significance. The CUR (cost/QALY) for CC/HC was 2.55 (VAS) and 2.65 (SG). When missing data were replaced (LWCF), CUR for CC/HC was 1.69 (VAS) and 1.74 (SG). The ICER was €-224 for an extra QALY generated with SG and €-204 with VAS. The Cox-Regression procedure did not find an effect of individual characteristics or group regarding the hazard for serious events. No significant difference was observed in the Kaplan-Meier analysis that compared the distribution of time to the first event for the groups.

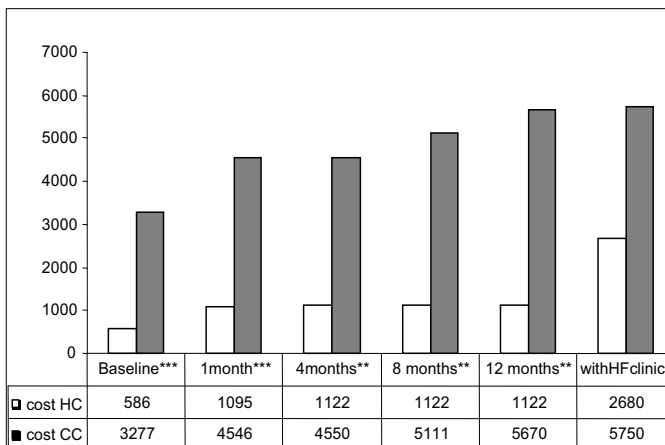


Figure 5. Median cost for the CC and HC groups in Euros. Baseline=cost for initial intervention. Included cost for blood samples, i.v. diuretics and time consumed by nurses and physicians. Cost for all events included in the total cost at the four follow-ups. With HF clinic=cost includes all cost up to 12 months and costs for HF clinic visits. *** $p < 0.001$, ** $p < 0.05$, * $p = 0.05$

DISCUSSION

This thesis enlightens several aspects on the care of patients with deteriorated CHF. The first aspect concerns factors related to seeking health care attention in exacerbation of the condition. The second is a description of the association between fatigue with depression, anxiety and symptom distress. The third aspect pertains to the validation of an instrument to measure symptoms reflecting changes in the condition. The fourth, and final aspect, deals with the evaluation of home care as an alternative to hospitalisation in worsening CHF in relation to HRQL, medical safety and cost-effectiveness.

The results of this thesis showed that only half of the patients sought emergency care because of their symptoms; the remaining patients were referred by their relatives or caregivers. The explanations given by patients for not seeking care earlier included using “a wait and see strategy”, reluctance to use the health care system and feelings of hopelessness. Fifty percent of the patients were uncertain about the reason for their current worsening status. Only 5% of the patients were able to fully grasp the relation between their symptoms and their deteriorating health. Emotional distress (defined here as emotional state of anxiety, depression and symptom distress) is associated with the experience of fatigue in patients with worsening CHF. The evaluation of the psychometric properties of a Swedish translation of the KCCQ appeared to be a reliable, valid and a responsive instrument in patients with worsening CHF. Although the sample was small, the intervention showed promising results. There was no statistically significant difference in HRQL or medical safety between the HC and CC groups; however, the cost of care was significantly lower in the HC group.

Assessment of symptom is one of the most important aspects when caring for patients with severe illness. This is because the responses to potential health problems that nursing research focuses on, is illness, with its essence in symptoms. In general, symptoms often prompt patients to seek medical attention, but this was not the case in patients with worsening CHF. Despite severe symptoms throughout the course of illness deterioration, many of the patients preferred to wait before seeking health care [162]. Symptoms are multidimensional and personal manifestation of illness is determined by frequency and severity of symptom occurrence (perception) and of symptom distress (evaluation). Health care seeking is highly influenced by how a patient perceives and evaluates her or his changing condition. Dodd [56] state that a patient perceives symptoms by recognising the sensations, whereas evaluation involves a higher cognitive process of attaching meaning to the symptom.

To be chronically ill is to live in a shifting existence between experiencing healthy periods followed by periods of illness. The ability to manage these shifts is probably related to resources in the person and the environment. The illness perspective is associated with suffering, loss and burden [163]. For example, a feeling of hopelessness associated with the illness perspective might inhibit insight into further deterioration and instead give rise to thoughts of death or cause emotional symptoms such as anxiety and depression [162]. For patients with CHF and fatigue, daily physical tasks require increased effort, which is reflected in a sense of inability to fulfil role functioning, an

observation confirmed by Ekman *et al.* [164]. Hence, feelings of burden and increasing dependency may intensify the illness experience with anxiety and depression. A depressed and anxiety-laden patient may not be able to embark on any physical or mental activity because the feelings of fatigue are so overwhelming. The symptom of fatigue is elusive for patients with worsening CHF because it can be attributed to old age or to other co-morbidities. Further, clinical symptoms of anxiety and depression are composed of a complex interplay on fatigue. The differentiation and determination of directionality are difficult. On the other hand, depression is largely related to anhedonia and in that sense is closer to the fatigue symptom. The greater the number of symptoms experienced and perceived disability, the more likely patients are to identify different contributors to their illness. Living with a healthy perspective includes the creation of consonance between self-identity and the identity that is shaped by the illness (such as CHF) [163]. This view is a revisioning of life routines and might better be related to acceptance and self-care ability.

Patient and caregivers have different ideas about disease, illness and its treatment. In contrast to caregivers, the patient's ideas about symptoms are generally formed on a broader basis. Wilson & Cleary [53] described a patient's symptom reporting as an expression of subjective experiences that summarises and integrates data from an array of different sources. On the other hand, caregivers' ideas are based on objective evidence, *i.e.* signs, which are obvious and thus unlike symptoms that are subjective. Symptoms can be viewed as subjective indicators of a disease or a change in a person's health condition as perceived by the individual. Thus, symptoms are the experiences of individual patients and reported by them as manifestations of their problem. There may be a strong psychosocial element to symptoms, which may or may not have an exact relationship to a medical problem. Many of the patients felt that their health state was worsening, but they evaluated it as being non-serious and waited either for planned follow-ups or until their caregivers noticed their deteriorated condition. Similarly, oedema and conversational dyspnoea were reported by few patients but often observed by interviewers [162]. This finding suggests in accordance to Ekman *et al.* [66] that signs and symptoms do not always have a one-to-one relationship. Symptoms might depend on several coexisting conditions and factors that could be of relevance to disease progression (*e.g.*, depression). Further, chronic illness is associated with reduced HRQL, self-esteem and meaning [165], which might affect a patient's ability to interpret changing symptoms, the significance of declining health status and handling of his or her situation. Falk *et al.* [74] noted that mental fatigue in patients with CHF was predicted by low personal disposition to manage stressful situations. Similarly, we found a strong association between anxiety and mental fatigue, which may have been mediated through the patients' inability to handle stressful situations [Paper II].

It has been suggested that the experience of uncertainty is profound in patients with chronic illness [165], and it has been found to be associated with fatigue and reduced functional status [74]. Jurgens [166] reported a high uncertainty score in patients seeking care with acute HF. Jurgens findings are similar to those of Ekman *et al.* [167] who reported higher in-hospital uncertainty in elderly patients with CHF. Uncertainty may occur because of several factors, including not knowing the reason of the symptoms, confusion with overlapping symptoms from other illnesses, lack of self-efficacy to

alleviate suffering and feeling a need to be cared for in a hospital environment [162, 168]. Although the self-efficacy beliefs need not be associated with severity of the condition [168], the threat posed by the symptoms and experienced grade of disability affect the patient's certainty and evaluation that his or her symptoms are worsening. Difficulty in determining the uncertainty and attach meaning to the symptoms prolong the illness experience. The symptoms are sometimes frightening and may lead to death thoughts and the feeling that the body is not under control. The strong feeling of uncertainty may result in denying or hiding the symptoms and hoping that they will pass away. Although many of the patients had someone to accompany them to the ED, they did not want to be a burden on relatives so they tried to hide their illness [162]. In the study of the reasons why patients with acute asthma delay treatment, 86% reported that seeking treatment would disrupt the expectations of family members [169]. In a study by Jurgens [166] participants cited several other contextual reasons for delaying care, including waiting for the family to arrive, having social plans or fear of hospitalisation. Patients in our study also conveyed different ideas in their reluctance to seek health care [162].

The way a patient attends to diverse sensations, the meaning a symptom has for the patient and the language or idiom in which distress is experienced and communicated as well as transformed into medical complaints, as well as asking for help from next of the kin are highly affected by socio-demographical or cultural factors. Dodd *et al.* [56] confirm these views that beliefs, cultural aspects, thresholds and family relations have a direct or indirect effect on the patient's current perception and on the reporting of symptoms of a changing condition. The patients' understanding of the health care structure as well as their current health status, previous experiences with health care, socio-economic circumstances and other co-morbidities (such as COPD) all play a major role in distinguishing symptoms from worsening CHF. The constant presence of physical limitations (*e.g.*, transportation problems), progressive symptoms (*e.g.*, hopelessness) and social concerns (*e.g.*, not wishing to bother relatives) were found to contribute to uncertainty in symptom interpretation [162]. Other factors (such as obesity and overweight, diabetes and anaemia) may lead to confusion in adequate symptom perception and evaluation, and consequently, come to affect the patients' response and decision regarding when to seek health care [162].

Mårtensson *et al.* [95] stated that enforced changes to their environment, frequent re-admissions and increases in financial demands may contribute to feelings of depression in patients with CHF, which might delay the process of seeking earlier attention from health care. Assessment of the illness associated with the patients' symptoms requires that nurses have a clear understanding of what the illness means to the patient. This is also necessary in order to deliver an appropriate and timely care and treatment. In this context home care would be a preferable alternative if the care can be offered at a lower cost (*i.e.* transportation cost is saved for the patient). Some of the patients in our study were concerned about reimbursement for transportation costs.

Strauss [11] found that some patients with chronic illness prefer to wait despite the fact they are very sick or even dying. According to Strauss [11], these patients do not want to be cared for and die the 'hospital style'. Being away from their home brings about separation with the familiar and their daily living practices. Hospital environ-

ment can be experienced as artificial, and thus it is reasonable to imagine that this relocation may cause the patient to experience a variety of negative feelings. The home environment for patients is commonly attached with positive emotions, such as safety, family and a place of their own. Hospital care, on the other hand, might be associated with feelings of being a stranger, one patient among several in the ward and a guest with all its implications and limitations.

Rubenstein [170] explored the meaning and function of the home for the elderly and concluded that family caregivers believed that the home environment itself had “curative” effects that other environments could not offer. His conclusions have been echoed by other researchers investigating the meaning and experience of the home [8, 167, 171]. Encountering new and unknown environments can be stressful and even dangerous because of the lack of familiarity. Ekman *et al.* [8] stressed that patients avoid exposing themselves to unpredictable hospital care no matter how medically skilful or well meaning it is. In her study the elderly with CHF experienced hospital care as unpredictable and deficient. Although their symptoms could be alleviated in hospital and the patients had confidence in the care system, the care was nevertheless experienced as incomprehensible. This may mean that the patients feel that their illness might not receive the attention necessary to fulfil their expectations of hospital care. One of the reasons might be that nurses do not feel competent to handle the anxiety, hopelessness or powerlessness that patients with CHF feel [172]. Other factors are that nurses might have limited time to perform all their duties, performing many tasks simultaneously and having the responsibility for many patients in the ward.

Although some of the patients experienced feelings of anxiety, fear and depression related to the possibility of impending death, they still chose to put off seeking care [162]. However, it is not just the symptoms themselves that are of importance but the significance given to them by the patients themselves [54]. Many of the symptoms might be frequently occurring but not necessarily bothersome for the patient. There seems to be no linear relationship between symptom frequency and symptom severity. The findings in our study [Paper II] that fatigue, dyspnoea and insomnia were the most distressing symptoms is in concordance with Zambroski *et al.* [3] and Grady *et al.* [173] who also reported that lack of energy, difficulty sleeping and dyspnoea were the most prevalent, distressing and burdensome symptoms experienced in patients with CHF. Furthermore, many symptoms are interrelated (*e.g.*, anxiety, depression, nausea, appetite and pain) with different dimensions of fatigue [Paper II]. Even though many symptoms are distressing, the major reasons for seeking health care are fatigue and dyspnoea [162], a finding also reported in previous studies. Surprisingly, after fatigue and dyspnoea, insomnia and appearance (one of the symptom in SDS questionnaire) were reported as distressing [Paper II] though the patients did not report these symptoms voluntarily. It has been reported that fragmented sleep can lead to other symptoms, including fatigue and loss of concentration [86]. This finding is confirmed in our study [Paper II] by the association between difficulties in concentration and mental fatigue. There might be some misconception about typical symptoms associated with CHF, and such issues as awareness, threshold and attribution of illness might play an important role in reporting symptoms. The potential mechanisms underlying this behaviour need further exploration.

Because of the multiple dimension of the symptoms in patients with CHF, the frequency and severity of symptoms cannot always be differentiated. The poor validity and reliability in the “symptom frequency” and the “symptom severity” sub-scales in the KCCQ validation confirms this argument [168]. In the validation of the KCCQ [168] the comparison between Physical Limitation (KCCQ) and Physical Functioning (SF-36) showed an acceptable correlation despite the generic and specific measures, reflecting similar item-contents in these sub-scales. Although, this association indicates the relationship between CHF and physical functioning, the poor responsiveness of SF-36 in physical functioning might depend on the fact that the question focuses on symptoms/problems in the context related to patients with CHF. Furthermore, the KCCQ is composed of five response alternatives, including “not applicable”, whereas SF-36 includes only three response alternatives. Another possible explanation might be that KCCQ measures a time window of 2 weeks, whereas the SF-36 measures the past 4 weeks. Although the NYHA classification system is known to differentiate between class III and IV in a more reliable way than class II and III, the poor discrimination in NYHA class III – IV in all sub-scales might be attributed to the fact that there were only a few patients in NYHA class IV. Poor discrimination between different NYHA class in the HRQL sub-scale of KCCQ might depend on the predetermined definition and response alternatives of the KCCQ. However, the HRQL measure corresponds to the emotional well-being and thus the poor discrimination mirrored by different NYHA classes in this sub-scale (HRQL) can be justified. Physical Role functioning (RP) from the SF-36 showed greater responsiveness, at the 1- and 4-month follow-up as a consequence of improvement in the patients’ condition. This can be interpreted to mean that improved NYHA class represents an increased ability to perform role functioning.

Appropriateness of intervention

The intervention in this study [Paper IV] was based on two sources: knowledge acquired from the literature and experiences from clinical nursing practice. The intervention reflects a multidisciplinary collaboration between nursing, medicine and health economics. Symptoms were assessed from patient self-reports, whereas signs were incorporated here to assess clinical status and to evaluate the effects of the intervention (HC).

This study [Paper IV] recruited patients over nearly a 2-year period and included only 3% of the screened patients. Other well-known studies evaluating nurse-led HF programmes have also included a very low percent of all screened patients (*e.g.*, the hospital-based programme by Strömberg *et al.* [5] included 5% of 1964 patients during a 30-month period and Stewart *et al.* [6] included 5% of 4055 screened patients during a period of 14 months).

The few patients included in our study [Paper IV] might be due to the restrictive inclusion criteria, co-morbidities and the need for investigation. Another reason for the small sample is that many of the patients’ relatives felt uncomfortable about returning home being discharged from the ED. This study might also explain one of the reasons for the lack of powered randomised controlled trial in clinical settings as it demands

several years and many centres in complex clinical situations. Powered studies facilitate conclusions, clinical applicability and generalisation of the results. Being in the situation with an un-powered sample, I would like to point out that what matters most is not the results per se, but the knowledge attained regarding research methods, which helps in the planning of future research.

Further, it is of immense importance that the patients' well-being can be increased without jeopardising medical safety or increasing costs by providing HC in patients with deteriorating CHF [Paper IV]. HC can be a good option in that a comprehensive understanding of each patient's clinical and psychosocial status could be obtained during a home visit. This, in turn, could optimise both treatment and encourage self-care. In examining patients' thoughts about care Falk *et al.* [174] found that continuity of care and the possibility of having the same nurse repeatedly were important and associated with a sense of comfort. HC is an alternative approach where specialist nurses can offer care that can affect patients' HRQL in a positive manner.

The effect of health care is easily assessed in monetary terms, but putting value on health improvement is much more difficult. Given that health is a multi-dimensional concept and to gauge the total impact of an intervention on a patient, both QoL and survival have to be considered. QALYs were used as indicators of effectiveness (outcome) that combined the impact of morbidity (extra QoL) and mortality (extra years of life) as a result of the intervention. The use of this outcome confirmed the underlying premise that health care is provided to improve the welfare of the patients. In our study QALYs did not differ between the groups, indicating the similar impact of care and treatment on morbidity and mortality in both the HC and CC groups [Paper IV].

Systematic analysis of the association between input of resources and output as effects on health status are usually measured in total hospitalised days, survival and health care visits. These can be considered as intermediary outputs (performance measures) and hence do not reflect the goal of the patients nor of the health care sectors. Patients strive for better health and less suffering and the final goal of the health care sector is the effects of care on health status. HRQL was selected as the outcome measure from a patient perspective; an event rate as the medical safety since experienced well-being and avoiding hospitalisation represent the ultimate success of HC. Cost-effectiveness is the primary measure of success from the perspective of the health care sector. In addition to the clinical safety parameters, these outcome measures add important information regarding the consequences of HC and CC and thus provide clinicians with useful information in their decisions concerning patient management [Paper IV].

Methodological aspects

Triangulation of methods was used to explore symptoms, elicit potential associations between symptoms, measure the change in symptoms and provide an alternative way of treating symptoms. A semi-structured short interview was chosen because an in-depth interview technique was not suitable in an emergent situation [Paper I]. To establish credibility we collected short narratives from a large number of participants in order to obtain a sufficient amount of data.

An interview technique (different questionnaires) was applied for data collection [Papers II - IV]. This approach was chosen for several reasons. First, having to respond verbally to another person reduces the number of items omitted by the respondent. Second, the interviewer can determine whether the respondent is having any difficulty understanding the items. Third, in a questionnaire such as the HAD some patients might pretend to answer the statements by haphazard underlining of response options. Fourth, the interview technique allows the interviewer to rephrase the question in terms that the person may better understand. The interviewers were trained to ask the same questions in the same manner [132]. The influence the interviewer might have on the patient was taken into consideration by ensuring that the enrolling nurse did not follow-up the same patient.

Because of having too small groups, in this thesis we did not perform separate analysis on different NYHA classes or gender. It might be possible that those in NYHA class II had recognised symptoms of deterioration earlier [Paper I] than those in NYHA classes III or IV because of an adaptation mechanism. Dahlström *et al.* [175] reported from a Swedish HF registry (representing 4% of the Swedes with CHF) that fatigue and dyspnoea two of the hallmark symptoms recognised in CHF [4, 10] were reported by 53% in NYHA class II, by 32% in NYHA class III and only by 5% in NYHA class IV. There seems to be an adaptation mechanism in patients with higher NYHA class regarding the most common symptoms because of insidious and gradual worsening, leading to difficulties in recognising that the patient's condition is worsening.

The literature has described a general lack of reliable and valid measures [119, 123] to assess symptoms and HRQL in patients with worsening CHF. Validation of the KCCQ was necessary because research evidence indicates that symptom experience of patients with CHF may be substantially more complex than initially thought [85]. Although objective measures are available, they may not accurately reflect symptom severity, which relies on the self-reports of patients. Patient self-reports about their symptoms are reliable and a better predictor of outcomes than physician reports about patient symptoms [56, 65, 66]. By focusing on symptoms that are particularly burdensome for a patient, they (symptoms) direct attention to aspects of the disease and care that are most salient to the patient [54]. In the validation of the KCCQ, SF-36 was chosen because it is comparable with other international validations. Other available CHF disease-specific measures were not used (*e.g.*, the CHQ because it showed moderate power to discriminate patients with different severities of CHF [122] and the MLHFQ because of its poor responsiveness from the original version of the KCCQ [146]). Another reason we selected not to use other measures was to reduce burden on the patients that is caused when presenting them with a battery of questionnaires.

Apart from the fact that the NYHA classification system is a crude measure and is known for interrater variability, we decided to use it in our study [168] simply because it looks at the patient's functional abilities and how they are affected by CHF. Further, there presently exists no "gold standard" to assess the true values for the measurements. Moreover, the NYHA classification system reflects the physician's perspective rather than patient's and thus was preferred here as a valid objective measure in that it correlates to the corresponding domains in the KCCQ (*e.g.*, Physical Limitation

and Symptoms), which are theoretically predicted measures in the same direction as the changes in the NYHA classes. Although the translation of the KCCQ is adequate, validation should be an ongoing process because cultural differences and a different context and setting can affect an instrument's measurement properties. To be fully confident in the instrument, a repeated validation process is required.

Several different instruments (generic, disease specific and those used in economic evaluation) were used to measure HRQL. This was done to ensure reliability and validity in the assessment of HRQL [Paper IV]. The EQ-5DVAS has its history in the social sciences and SG in the economic field, which summarises the patient's response on evaluation of the treatment. We found some difference in HRQL as measured with the VAS and SG. This difference could be explained in that values and utilities for health states differ empirically. Because risk (uncertainty) is a factor in the measurement of utilities (SG) but not in the measurement of values (VAS), the difference can be attributed to the risk attitudes of the elderly with CHF. In general, the utility score for a health state exceeds the value score for the same health state [124] and is in accordance with the score obtained in our study [Paper IV]. Dolan [176] stated that current health status has an important effect on valuations with those in poorer health, generally giving higher values. The notion behind is that people take into account any factors they consider to be relevant when expressing their preferences. Utility measures using SG are useful in determining whether patients are better off when they do not show the domains in which improvement or deterioration occurs. The simultaneous use of generic instruments (VAS and SF-36) and a disease specific instrument (KCCQ) retrieves complementary information to the utility approach.

Aspects on health care costs

In our study [Paper IV] the median cost in the CC group was 5.6 times higher than in the HC group after the initial intervention. After 12 months (*i.e.* after the end of the study) the median cost in the CC group was 5 times higher than in the HC group. The patients in the HC group were referred more frequently to the HF outpatient clinics than the patients in the CC group. This is because initially fewer patients in HC group were treated with potential medications (*e.g.*, ACE-inhibitor). While taking into consideration the cost for the HF outpatient clinic visits (occurred after the intervention was terminated) costs were found to increase in the HC group; however, these costs were still half of those in the CC group. In comparison with other chronic disease (*e.g.*, COPD), randomised to the home or hospital management [177], authors in this study found that the costs for acute care in home group was significantly lower ($p < 0.01$) than in the hospital group. This finding further suggests using home care in chronically ill patients whenever possible. Stewart *et al.* [6, 7], who presented the medical and health economic impact of a home-based intervention programme, found a reduced rate of readmissions and hospital-based costs. In a 10-year follow-up Inglis *et al.* [178] found home-based intervention to be a cost- and time-effective strategy in patients hospitalised for a short time. This finding is similar to our study with a 1-year follow-up [Paper IV].

Earlier research has shown varying costs per patient from different settings. In our study the costs were based on DRG, whereas Ryden-Bergsten and Andersson [25] estimated the average treatment cost to be 25000 SEK (€2688, 1€ = 9.30 SEK) per patient and year based on official statistics and various clinical and epidemiological studies. Agvall *et al.* [33] found the mean annual cost to be 37100 SEK (€3989) for a patient with CHF in a study setting of two health care centres. The author calculated the total annual cost for patients with CHF in Sweden to be 5.0-6.0 billion SEK, which is a higher cost than previously reported. Björck *et al.* [35] calculated that the direct health care cost for one CHF patient in a retrospective study for a 6-month period was 20000 (median) SEK (€2151). This cost was based on an official price list, where the largest part of the costs was hospitalisation, a finding similar to that in our study. In our study [Paper IV] patients in the CC group were hospitalised on a median of 5 days, whereas patients in the HC group took up only 0.5 median days of the time of nurses and physicians. Consequently, this strategy seems to be both time- and cost-effective. In a recent follow-up study [179] a specialist nurse-led telephone care system was found to be cost-effective but led to an increase in the frequency of visits to the outpatient clinic. The authors in this study concluded that the home-based care system can result in cost savings by decreasing adverse outcomes, hospitalisation and length of stay. In our study, probably because of lack of power, we did not find any significant differences between the HC and CC groups in clinical variables, HRQL, or adverse events. Although the study was conducted on a small sample, it still could reveal significant differences in health care costs, indicating that HC is useful in the care of patients with worsening CHF. In fact, to deliver HC without reducing the level of medical safety or HRQL is a hopeful ray of light in a world of limited resources. In a sense HC is an approach that makes optimal use of limited resources.

Earlier research has largely focused on various types of intervention in stable patients with CHF [5 - 7, 36, 38 - 41, 43 - 46, 178 - 180]. Bruce *et al.* [47, 48] sent patients home that required acute hospital care in a “hospital at home” model. However, the authors did not evaluate costs. In addition, the intervention was more resource consuming because of frequent home visits of nurses and physicians. Our study [Paper IV] is the first to evaluate the effects of HC with fewer resources, both in terms of time and cost as well as in terms of the composite effect of morbidity and mortality in terms of QALYs.

The comparison with earlier research has to be done with extreme caution, because of different study designs, selection of patients and settings. Further, in some of the studies the averages are presented as means instead of medians. Because the distribution of resources used is usually skewed, the median is a better way to present them. Moreover, the cost of the care given in primary health care is not completely equivalent to the cost of care given in hospital. Although our data were small, they were in agreement with other studies, *i.e.* a skewed cost distribution was present. The strength in our study was that it was a prospective randomised trial and performed in a real clinical setting. This design mirrors the actual cost based on an official DRG price list charged by the hospital to the western region in Sweden.

LIMITATIONS

The knowledge gained here may be generalisable to a similar context. A limitation, however, is that data were collected from only one hospital.

A second limitation concerns the fact that cross-sectional data [Paper II] do not permit causal inferences to be made between emotional distress and fatigue. There might be a bi-directional relationship between these two variables.

A third limitation is that a large proportion of the patients was lost to follow-up [Paper III]. Although it is not known how their responses might have altered our findings, it seems unlikely that they would significantly change our conclusions, because there were no significant differences in patient characteristics between dropouts and those who remained in the study (data not shown).

A fourth limitation has to do with the small sample size, which limits the chances of detecting differences between the HC and CC groups [Paper IV]. Because each individual is unique with his or her own needs, this could lead to problems when it comes to generalising the findings of a particular intervention from a small sample.

CONCLUSION

The findings from this thesis suggest that offering care and treatment for patients with CHF in the home and continued follow-up at HF clinics is possible without loss when it comes to HRQL or medical safety. Furthermore, home care was found to reduce patient costs. Our findings suggest that home care can play an important role in the future care and treatment of patients with CHF. The distress from symptoms such as fatigue might be relieved indirectly by the influence of other manageable symptoms. Moreover, the factors explored in this thesis should be helpful with respect to meeting individual care needs. The present study showed that responsive instruments such as the KCCQ can be helpful in measuring symptoms and in evaluating the effects of interventions in patients with CHF. Although KCCQ has proven to be a valid and acceptable instrument in patients with CHF, further studies are required with larger samples.

THE CATCH FOR NURSING PRACTICE AND FUTURE RESEARCH

It is hoped that the findings from this thesis will serve as a catalyst for the further exploration of home care. The present findings have implications for nursing and health care delivery. Now appears to be the right time to re-examine the health care structure for its efficient use of resources and change conventional policy for health care service delivery to the patients with worsening CHF. This policy should include those patients who are reluctant to be hospitalised for their condition.

The factors explored in this study serve to provide us with information about what components should be included in future education and nursing intervention, where the main goal is to enhance well-being of the patient. The KCCQ can be used in conjunction with another CHF specific measure in order to quantify specific clinical benefits from the patient's perspective. Because nurses work constantly with the cost-quality constraints of health service delivery, they are in an excellent position to provide advice on the impact of care aimed at the well-being of the patient and that is cost-effective [103].

Difficulties in navigating the health care system have been identified as a barrier in seeking care in patients with worsening CHF. Nurses should take initiative because there exists a significant need to develop a knowledge base and improve care for persons with advanced illness (*e.g.*, CHF) in primary care. Today, care for patients with asthma and diabetes is largely provided outside a hospital setting. We believe that care for patients with CHF could also be developed in the same direction. Primary care may act as a gatekeeper to the more expensive care of direct costs (hospital) and intangible costs (suffering).

Although we were able to help fill the gap in knowledge left from previous research, a similar project to ours should be conducted at several hospitals in powered studies for the purpose of improving external validity.

POPULÄRVETENSKAPLIG SAMMANFATTNING

Det övergripande syftet med denna avhandling var att öka förståelsen om olika faktorer relaterade till varför personer med kronisk hjärtsvikt söker akut vård samt vilka symptom de har. Syftet var också att utvärdera effekten av en intervention som innebar att vårdas i hemmet i stället för på sjukhus vid försämring av kronisk hjärtsvikt. Variabler som utvärderades var; medicinsk säkerhet, hälso-relaterad livskvalitet och kostnadseffektivitet.

Kronisk hjärtsvikt är en följd av andra hjärtåkommor. Tillståndet är progressivt och karaktäriseras av återkommande perioder av sjukhusvård, försämrad funktionsförmåga, påverkad livskvalitet och stort lidande. Många med kronisk hjärtsvikt har svårigheter att tolka symptom vid försämring och söker inte vård i tid, vilket leder till sjukhusinläggningar. Tidigare studier har visat att omhändertagandet av patienter med kronisk hjärtsvikt har förbättrats genom sjuksköterskebaserade hjärtsviktsmottagningar, regelbundna uppföljningar via hembesök eller via telefonkontakt efter utskrivning från sjukhuset. En svårighet i denna typ av uppföljningar är att många patienter är trötta och inte orkar åka till hjärtsviktsmottagningen på sjukhuset eller primärvården. Redan idag förekommer det att patienter med försämring i tillståndet skickas hem efter ett initialt omhändertagande på akutmottagningen eller hjärtsviktsmottagningen eftersom de inte vill stanna kvar på sjukhuset. Man vet emellertid inte om det är medicinskt säkert och mer kostnadseffektivt att patienter med försämrad hjärtsvikt åker hem direkt från akut mottagningen eller hjärtsvikt mottagningen i stället för att läggas in för fortsatt vård och behandling.

I avhandlingen studerades patienter med försämring av kronisk hjärtsvikt, vilka sökte på akutmottagningen eller hjärtsviktsmottagningen. Dessa var bedömda att läggas in på sjukhus och tillfrågades inom 72 timmar (studie I – III) och inom 48 timmar (studie IV) efter ankomst till akutmottagningen om de vill delta i studien. Patienterna bedömdes enligt speciella inklusions och exklusionskriterier.

Delstudie ett syftade till att utforska faktorer relaterade till varför man söker vård vid försämring av kronisk hjärtsvikt. Semi-strukturerade intervjuer användes. Merparten av patienterna (58%) svarade att de sökte vård huvudsakligen pga symptom, men de relaterade inte nödvändigtvis dessa till försämring av kronisk hjärtsvikt, medan 42% hade blivit inskickade antingen av anhöriga eller andra vårdgivare. En tredjedel av patienterna (34%) hade velat söka vård tidigare men gjorde inte det pga att: (1) de trodde att besvären skulle gå över, (2) de inte lyckades beställa tid hos läkare på vårdcentralen, och då bestämde att vänta till sin ordinarie tid för uppföljning och (3) de hade ingen som kunde följa med till akutmottagningen. Endast 5% av patienterna relaterade sina symptom till hjärtsvikt.

Eftersom trötthet är ett vanligt och besvärande symptom vid kronisk hjärtsvikt var syftet med den andra delstudien att undersöka samband mellan andra förekommande symptom och trötthet. Ångest visade ett samband med mental trötthet; medan depression med allmän trötthet, minskad aktivitet och minskad motivation. Svårighetsgraden av olika symptom visade endast ett begränsat samband med trötthet.

I den tredje delstudien validerades ett sjukdomsspecifikt livskvalitetsinstrument för patienter med kronisk hjärtsvikt (Kansas City Cardiomyopathy Questionnaire - KCCQ). KCCQ visade sig vara valid, tillförlitlig och mer responsiv i jämförelse med SF-36, vilket är ett generiskt livskvalitets instrument.

Syftet med den fjärde delstudien var att i en randomiserad kontrollerad studie utvärdera vård i hemmet i jämförelse med sjukhusvård. Patienter som inkluderades till "vård i hemmet" erbjöds att åka hem antingen direkt från akutmottagningen eller från vårdavdelningen inom 48 timmar. En sjuksköterska specialiserad inom hjärtsviktsvård följde upp patienten i hemmet upp till ca 5 -10 dagar, beroende på patientens tillstånd. Kliniska parametrar och patientens tillstånd bedömdes och mediciner justerades i samråd med specialistläkare. Hos varje patient genomfördes pedagogiska samtal om tillståndet, behandlingen och hur tecken på försämring kunde kännas igen. Patienter i kontroll gruppen vårdades på sjukhuset enligt gällande riktlinjer. Patienter från båda grupperna följdes upp efter 1, 4, 8 och 12 månader. Resultatet visade att båda grupperna förbättrades, det fanns inga skillnader i kvalitets justerade levnadsår (QALYs) eller i medicinsk säkerhet, men det fanns betydande skillnader i sjukvårdskostnad mellan grupperna. Vård i hemmet var billigare jämfört med sjukhus vård.

Sammanfattningsvis visar denna avhandling att trots ökad information har patienter med kronisk hjärtsvikt svårighet att relatera sina symtom till försämring av tillståndet. Ångest, depression och obehag från andra symtom visade samband med trötthet. Detta understryker vikten av en omfattande symtom-anamnes för att kunna utgå från hur patienten ser på sitt tillstånd vid fortsatt vård och behandling. Den svenska valideringen av KCCQ kan användas för att följa symtom och utvärdera effekt av given behandling. Vård i hemmet, kan spela en viktig roll i framtiden vid omhändertagandet av patienter med kronisk hjärtsvikt vid försämring. Centralt är att identifiera den enskilde patientens vårdbehov för att kunna ge adekvat vård. Studien tyder på att vård i hemmet kan erbjudas till patienter med kronisk hjärtsvikt vid försämring om uppföljning sker med hjälp av specialistsjuksköterska och i samråd med en specialistläkare.

ACKNOWLEDGMENTS

This thesis is based upon work carried out at the Department of Medicine at the Sahlgrenska University Hospital/Östra in Göteborg. I wish to thank all patients who participated in these studies, my co-authors, my colleagues at HIA & DAGA and the staff personnel and head of the departments from the Emergency Department and the Medicine clinic.

I especially want to express my sincere gratitude to my supervisors:

Professor *Inger Ekman*, my principal supervisor, for introducing me to the scientific field, her guidance, support, criticism on my writings and for sharing her great knowledge in symptoms and care with the patient perspective always in mind. In the beginning of the doctoral studies, I particularly needed and received your warm friendliness, dedication to my work and expertise.

Associate professor *Maria Schaufelberger*, for her excellent medical guidance, for her understanding and for always believing in my ability to carry out research and to complete this thesis. I appreciate you sharing some parts of your knowledge in the field of heart failure care.

Associate professor *Sören Höjgård*, who directed me into the field of health economics, which I now realise, is an important cornerstone of health care. I am very grateful to have you as my tutor and coach in matters of health economics. You have been a most valuable partner throughout this process. Few people would have been suited for this work. Your precise way of putting comments and suggestions has been very instructive.

Professor *Karl Swedberg*, head of the research department, for his immense generosity in sharing knowledge, providing a highly stimulating research setting, and encouraging support.

Associate professor *Lars-Olof Persson*, for fruitful discussions and often generating new aspects on different issues during our talks. I am particularly grateful that he took the time to share his wealth of knowledge in the field of health-related quality of life.

Professor *Dag Thelle*, who generously shared his inspiring visions under pleasant and informal conditions. I have always admired your unpretentious and encouraging attitude towards your co-workers.

Professor *Ingegerd Bergbom*, Associate professor *Charles Taft*, Associate professor *Martin Pilhall* and Dr. *Eva Jakobsson* för constructive comments at the mid-seminar and pre-disputation.

The research secretary *Eva Deutsch*, at the Institution of Health and Care Sciences, Göteborg University, for always being cheerful and for all of her assistance during these four years of my doctoral studies.

Ms *Eva Thydén*, for her enthusiastic assistance during the preparation of this thesis. Ms *Ann-Britt Johansson* for always being cheerful and for practical and moral support. My colleague, *Masoud Shafazand* for your lovely friendship.

My sincere gratitude to Professor *Inga-Lill Rahm Hallberg*, for being a “Iron lady” and a role model for all the female researchers. Your guidance, devotion, concern and encouragement throughout has been invaluable. I am profoundly grateful to Vårdal institute, the Swedish Institute for Health Sciences, for their support and providing me with genuine and favourable research conditions. I am proud to be a member of the “Vårdal” institute, with its excellent reputation.

Associate Professor *Anna-Karin Edberg*, Professor *Synneve Dahlin*, Dr. *Gunilla Hedström Gosman*, and all PhD colleagues at Vårdalinstitute, especially within the research platform for elderly care for fruitful discussions during workshops and providing me new insights into my work.

Thanks to “Anthology group”, *Kristofer Hanson*, *Anna Melke*, *Henna Hason*, *Henrik Levinson* and *Anne Wenick*, for many stimulating, constructive and multidisciplinary discussions. My deepest gratitude also goes to Professor *Björn Lindgren* for invaluable advice regarding my chapter in the bok “*Etiska Utmaningar*”. Many thanks also to *Edith Andersson*, *Marianne Gustafsson*, *Björn Carlqvist*, and *Anna Blomgren* at Vårdal Institute for providing me the administrative support during these years.

Special thanks to my beloved husband *Kirit*, my sons *Mainak*, *Keval*, *Kevin* and my daughter-in-law *Seema*, who appeared late on the scene but played a significant role for my success. You all mean to me beyond the words describe.

My loving parents, *Manubhai and Madhuben*, I am lucky to have you around and your blessings with me. My sisters, *Daksha*, *Kirti*, *Mamta* and brother, *Harshadbhai*, *Bhavnaben*, all *brother-in-laws*, *sister-in-laws*, *cousins*, *nephews*, *nieces*, *uncles & aunties* with their families. Special thanks to *P.kaka*, my role model, all my *close friends* and feed-back partner, *Harshadbhai*. I appreciate your never-ending love and faith in me and for always motivating me to do the best things in the worst times. All of you added all the other dimensions of human life, the fundament upon which even research science must rest.

Many thanks are also due the librarians *Eva-Lotte*, *Krystina* and *Maud* at the medical library Östra University Hospital for their sincere service in providing me the literature for this work.

Thank you everyone! Without you, this book would never have been written!

This thesis was financially supported by grants from the Swedish medical Research Council, the Heart/Lung Council, the Vårdal Institute, Göteborg and Southern Bohus County, The Swedish Association of Health Professionals, Working group of Swedish Cardiovascular Nurses in Heart Failure (VIC) and the Cardiology Research Foundation of the Department of Medicine, Sahlgrenska university hospital/Östra.

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Patient ID _____ Patient initialer _____ Datum/besök _____

The Kansas city Cardiomyopati frågeformulär (KCCQ)

Följande frågor handlar om din **hjärtsvikt** och hur det kan påverka ditt liv. Var vänlig läs och besvara följande frågor. Det finns inga rätt eller fel svar. Var vänlig markera det svarsalternativ som passar in bäst för dig.

1. **Hjärtsvikt** påverkar människor på många olika sätt. Somliga får svårt att andas medan andra känner trötthet. Var vänlig ange hur mycket du har känt dig begränsad p.g.a. **hjärtsvikt** (andningssvårigheter eller trötthet) vid utförandet av följande aktiviteter de senaste två veckorna.

Sätt ett X i en ruta på varje rad

Aktivitet	Mycket begränsad	Ganska begränsad	Måttligt begränsad	Lätt begränsad	Inte alls begränsad	På grund av andra orsaker eller ej utfört aktivitet
Påklädning	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Dusch/Bad	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
100meters gång på planmark	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Trädgårdsarbete, hushållsarbete eller att handla	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Gå uppför 1 trappa utan att stanna	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Gå snabbt eller springa efter en buss eller spårvagn	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

2. Jämfört med 2 veckor sedan, har dina hjärtsviktssymtom (andnöd, trötthet eller ankelsvullnad) förändrats? Mina hjärtsviktssymtom har blivit....

Mycket värre	Något värre	Oförändrat	Lite bättre	Mycket bättre	Jag har ej haft några symtom sista 2 veckorna
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

3. De sista två veckorna, hur många gånger har du haft svullna fötter, anklar eller ben när du vaknade på morgonen?

Varje Morgon	3 eller fler gånger/v, men inte varje dag	1-2 ggr/v	mindre än 1 g/v	inte alls de sista 2 v
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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4. De sista 2 veckorna, hur mycket har svullnaden i dina fötter, anklar eller ben varit besvärande för dig?
Det har varit...

Mycket besvärlig	Ganska besvärlig	Måttligt besvärlig	Lite besvärlig	Inte alls besvärlig	Jag har ej haft svullnad
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

5. De sista 2 veckorna, i genomsnitt, hur många gånger har trötthet begränsat din förmåga att göra det du ville?

Hela tiden	många ggr/dag	åtminstone 1g/dag	3 eller fler ggr/v men inte varje dag	1-2 ggr/v	mindre än 1g/v	inte alls sista 2 v
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

6. De sista 2 veckorna, hur besvärlig har din trötthet varit?
Det har varit...

Väldigt Besvärlig	Ganska besvärlig	Måttligt besvärlig	Något besvärlig	Inte alls Besvärlig	Jag har ej känt någon trötthet
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

7. De sista 2 veckorna, hur många gånger i genomsnitt, har andnöd begränsat dig från att göra det du velat göra?

Hela tiden	Många ggr/dag	Minst 1g/dag	3 el. fler ggr/v men inte dagligen	1-2ggr/v	Mindre än 1g/v	Inte alls de senaste 2 v
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

8. De sista 2 veckorna, hur mycket har andnöden besvärat dig? (hur besvärlig har andnöd varit för dig sista 2 veckorna?)

Mycket besvärlig	Ganska besvärlig	Måttligt besvärlig	Lätt besvärande	Inte alls besvärande	Jag har ej haft andnöd
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

9. I genomsnitt, hur många ggr har du varit tvungen att sova i sittande ställning i en stol eller pallat upp med minst 3 kuddar p.g.a. andnöd, de senaste 2 veckorna?

Varje natt	3 eller fler gånger/v, men inte varje dag	1-2 gånger/v	Mindre än 1gång/v	Aldrig de senaste 2 veckorna
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

10. Hjärtsviktssymtom kan förvärras av olika anledningar. Hur säker är du på att du vet vad du ska göra eller vem du ska ringa till vid försämring av din hjärtsviktstillstånd?

Inte alls säker	Inte speciellt säker	Någorlunda säker	Säker för det mesta	Helt säker
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

11. Hur mycket känner du till om hur du kan påverka själv, för att förhindra att dina hjärtsviktssymtom blir värre (T. ex. daglig vägning, äta saltfattigkost osv.)?

Förstår inte alls	Förstår inte så bra	Förstår någorlunda	Förstår i stort sett	Förstår fullständigt
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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12. Hur mycket har din hjärtsvikt begränsat dig från att njuta av livet, senaste 2 veckorna?

Mycket begränsad	Ganska begränsad	Lagom begränsad	Något begränsad	Inte alls begränsat
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

13. Om du resten av livet, skulle må som du gör just nu, vad känner du inför det?

Inte alls nöjd	För det mesta missnöjd	Någorlunda nöjd	Nöjd för det mesta	Fullständigt nöjd
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

14. Hur ofta har du känt dig ledsen eller nedstämd p.g.a. din hjärtsvikt, de senaste 2 veckorna?

Jag har känt mig så hela tiden	Jag har känt så större delen av tiden	Jag har känt så ibland	Jag har känt så sällan	Jag har aldrig känt så
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

15. Hur mycket påverkar din hjärtsvikt din livsstil? Var vänlig markera i vilken grad har din hjärtsvikt begränsat ditt deltagande i följande aktiviteter, senaste 2 veckorna?

Sätt ett X i en ruta på varje rad

Aktivitet	I mycket höggrad	Ganska mycket	Lagom begränsat	Något begränsat	Inte alls	Ej tillämpbar eller inte kunnat göra aktiviteter av andra skäl
Hobbyer, Friskvårds aktiviteter	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Hushållssysslor el. arbete	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Besöka familj eller vänner utanför hemmet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Intimrelation till dina kära	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

