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Challenges and gaps delivering palliative care to patients with heart failure

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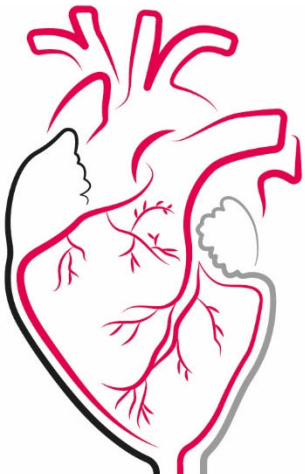

Challenges and gaps delivering palliative care to patients with heart failure

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Abstract

Background: People living with heart failure (HF) have a wide range of physical and psychological symptoms and comorbidities. These affect their quality of life throughout the HF trajectory. Therefore, patients with HF, especially in advanced stages of this disease, may benefit from palliative care (PC). However, despite PC being widely recommended, few hospitals and HF clinics offer concurrent PC along with life-prolonging therapies. Due to the unpredictability of the HF disease trajectory, prognostication is challenging, as well as identifying patients who might benefit from PC or have unmet needs. Additionally, patients with HF and implantable cardioverter defibrillators (ICD) have specific end-of-life (EoL) device management needs.

Aims: In this thesis, I contribute knowledge about the challenges and gaps in the delivery of PC to patients with HF. Through the 4 articles that form my thesis, I provide knowledge about the challenges of identifying patients who might benefit from PC or those who have unmet PC needs. I evaluate the performance of the surprise question (SQ) predicting 1-year mortality in ambulatory HF clinics, in article 1. In article 2, I assess the prevalence of patients with PC needs in outpatient HF clinics with the *NECesidades PALiativas* (NECPAL) or Palliative Needs tool. Additionally, I use the NECPAL tool to identify patients with HF who might benefit from PC. For article 3, I evaluated the psychometric characteristics of the German Needs Assessment Tool: Progressive Disease – Heart Failure (NAT: PD-HF). Finally, I quantify gaps from anticipatory care planning and EoL care of patients with ICD in article 4.

Methods: I used a cohort of 178 patients from 2 ambulatory HF clinics in Colombia for articles 1 and 2. To assess the performance of the SQ to predict 1-year mortality (article 1), I consulted Colombia's national mortality register for participants' 1-year vital status. To assess the NECPAL tool's identification of patients with HF who might benefit from PC (article 2), I conducted a cross-sectional analysis that compared health-related quality of life and physical and psychosocial problems, between patients needing (+NECPAL group) and not needing (-NECPAL group) PC. To validate the German NAT: PD-HF, I used a single-center study at Inselspital's Heart Failure Clinic in Bern, Switzerland (article 3). The tool was translated from English into German using a forward–backward translation. I assessed the German NAT: PD-HF's psychometric characteristics, including internal consistency, inter-rater reliability, test-retest reliability, and face validity. I conducted a systematic review and meta-analysis for article 4.

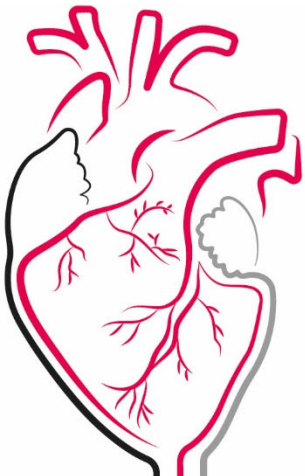
Results: These studies' results are presented in 4 articles. Article 1 shows the SQ's sensitivity to predict 1-year mortality is 85% and its specificity is 57%. The SQ's positive and negative likelihood ratios were 1.98 and 0.26, respectively. Its performance was similar among women and men, yet performed better in patients younger than 70 years, in patients with reduced or mildly reduced ejection fraction, and in patients at the New York Heart Association class III or IV. Article 2 shows that among patients under optimal medical

treatment in outpatient HF clinics, 44% met the NECPAL tool criteria to receive concurrent PC (+NECPAL). Compared to –NECPAL patients, +NECPAL patients had worse quality of life; more severe shortness of breath, tiredness, drowsiness, and pain; and greater psychosocial problems. Article 3 shows that the German NAT: PD-HF validation had good internal consistency, substantial inter-rater agreement for most of the items, and an almost perfect test-retest reliability. Moreover, patients thought well of the tool, and they agreed that it could help to improve their quality of care. Article 4 shows that nearly 3 out of 4 patients (pooled estimate 28%, 95% CI 22-36%) died with their ICD's shock function active, despite guidelines recommending deactivation of this function at the EoL. For those with advance directives, few directives mentioned what to do with ICD devices at the EoL; the pooled prevalence estimate was only 1% (95% CI 1-3%).

Conclusion: In this thesis, I contribute knowledge about gaps and challenges delivering palliative care to patients with heart failure. I show gaps regarding anticipatory care planning and end-of-life care for patients with implantable cardioverter defibrillators and offer strategies to address these gaps. Additionally, I provide knowledge and suggestions to overcome identifying patients' palliative care needs. I assessed 3 tools to support the identification of palliative care needs; 2 of them, to support the identification of the needs due to limited life expectancy (the SQ and the NECPAL), and 1 to identify palliative care needs regardless of prognosis (the NAT: PD-HF). The best screening tool depends on the situation, and whatever tool we use, it is better to screen and think about the palliative care needs of the patients using any tool than no screening at all.

Abbreviations

COPD	Chronic obstructive pulmonary disease
CRT	Cardiac resynchronization therapy
EoL	End-of-life
ESAS	Edmonton Symptom Assessment System
HF	Heart failure
HFmrEF	Heart failure with mildly reduced ejection fraction
HFpEF	Heart failure with preserved ejection fraction
HFrEF	Heart failure with reduced ejection fraction
ICD	Implantable-cardioverter defibrillator
IHD	Ischemic heart disease
IPOS	Integrated Palliative Care Outcome Scale
KCCQ	Kansas City Cardiomyopathy Questionnaire
LVEF	Left ventricular ejection fraction
MLHFQ	Minnesota Living with Heart Failure Questionnaire
NAT: PD-HF	Needs Assessment Tool: Progressive Disease – Heart Failure
NECPAL	*NECesidades PALiativas* (Palliative Needs)
–NECPAL	Negative NECPAL tool
+NECPAL	Positive NECPAL tool
NYHA	New York Heart Association
PC	Palliative care
SF-12	12-Item Short Form Survey
SF-36	36-Item Short Form Survey
SQ	Surprise Question



1. Introduction

"Nothing in life is to be feared, it is only to be understood. Now is the time to understand more, so that we may fear less."

- **Marie Skłodowska-Curie** (November 7, 1867 – July 4, 1934)

Support
Communication
Autonomy

1.1 Heart failure

Heart failure (HF) is a complex clinical syndrome that results from structural or functional abnormalities of the heart [1]. A clinical syndrome is a set of signs and symptoms that are correlated with each other [2]. Typical signs of HF include peripheral edema, pulmonary crackles, and elevated jugular venous pressure [3]. A typical presentation of HF includes symptoms such as shortness of breath (dyspnea), difficulty breathing when lying down (orthopnea), fatigue, and ankle swelling [3]. Structural causes of these signs and symptoms are abnormal cardiac chamber enlargement, ventricular hypertrophy, valvular lesion, and myocardial tissue abnormalities such as fibrosis [1]. Functional abnormalities include abnormal diastolic dysfunction (reduced filling) and reduced ventricular systolic function (reduced blood ejection) [1]. There are different ways to assess cardiac function but none of them makes a diagnosis of HF, as it is largely a clinical diagnosis based on the clinical history and a careful physical examination [4].

People with advanced HF have more severe symptoms and more comorbidities, making the HF a higher burden for patients and their caregivers [5]. Patients with advanced HF also have social and spiritual needs; therefore, interdisciplinary management is necessary. Additionally, patients at advanced stages have a higher risk of frequent emergency visits, hospital admissions, and death. Thus, discussions about end-of-life (EoL) matters are required [6].

1.1.1 Classification

HF can be acute or chronic. Acute HF refers to the first episode of HF (*de novo)* or episodes of decompensation of chronic HF. After the first episode of HF and in between decompensations, patients are diagnosed with chronic HF.

There are several ways to classify HF. The most common is to classify HF according to its etiology, to the patient's left ventricular ejection fraction, or to the patient´s New York Heart Association (NYHA) functional class. These classifications are used to communicate between health care professionals and with the patient, and they are used for research purposes.

HF classification by etiology

Treatment response and prognosis depend on identifying the underlying cause(s) of HF [7]. However, multiple causes tend to be interrelated and often coexist so that identifying the primary etiology of the HF is either not possible or complex [8].

Myocardial abnormalities can cause systolic and/or diastolic ventricular dysfunction leading to HF; however, the causes of HF may also lie in abnormalities of the valves, pericardium, endocardium, heart rhythm, or electric conduction. Myocardial abnormalities can be due to ischemia or infarction; genetic factors; infections, such as Chagas disease, rheumatic fever, human immunodeficiency virus, or COVID-19. These abnormalities can

also be the result of toxic exposure from a variety of agents, including cocaine, alcohol, or chemotherapeutic drugs; or they can be developed in the period close to giving birth (peripartum cardiomyopathy) [9, 10]. Non-myocardial causes of HF include congenital heart disease, arrhythmias, and valvular heart disease [9]. In some cases, the cause cannot be found and is called idiopathic cardiopathy.

Due to sex differences, the pathophysiological mechanisms leading to HF are different between women and men. The most common underlying cause of HF in women is hypertension; in men, it is coronary artery disease (a macrovascular disease) [11]. Some HF etiologies are singular to women, such as peripartum or Takotsubo cardiomyopathies. Peripartum cardiomyopathy occurs in the last months of pregnancy or within the first 6 months after delivery; however, its exact cause is unknown. Takotsubo cardiomyopathy is a stressed-induced cardiomyopathy; however, its cause is unclear. Both entities are thought to be related to microvascular coronary diseases, which are more common in women [12, 13].

HF classification by left ventricular ejection fraction (LVEF)

HF can also be classified based on how much blood is pumped out of the left ventricle with each contraction, that is, the left ventricular ejection fraction (LVEF); it can be assessed using echocardiography and calculated with the formula [14]:

$$\text{LVEF (\%)} = \frac{\text{end-diastolic volume} - \text{end-systolic volume}}{\text{end-diastolic volume}} \times 100$$

Patients with LVEF ≤40% are classified as having HF with reduced ejection fraction (HFrEF); patients with LVEF between 41% and 49% are classified as having HF with mildly reduced (also called mid-range) ejection fraction (HFmrEF); and patients with LVEF ≥50% are classified as having HF with preserved ejection fraction (HFpEF) [1].

Most patients diagnosed with HFrEF are men; whereas HFpEF is twice as common in women than men. Coronary artery disease—a macrovascular disease leading to myocardial infarction—is more common in men, and it is the highest risk factor for HFrEF. Conversely, coronary microvascular disease, which is more common in women, appears to play a key role in HFpEF [12, 13].

HF classification by New York Heart Association (NYHA) functional class

The New York Heart Association (NYHA) classification is based on symptom severity and exercise tolerance (as reported by patients); and it is related to prognosis. Worsening NYHA classification is associated with a worse prognosis [15, 16] (**Table 1**). A patient can be NYHA class II, III, or IV, and then reclassified lower after treatment adjustment.

NYHA class	Symptoms
I	No limitations on physical activity.
II	Slight limitations on physical activity. Comfortable at rest, but **ordinary** physical activity results in undue shortness of breath, fatigue, or palpitations.
III	Marked limitations on physical activity. Comfortable at rest, but **less than ordinary** physical activity results in undue shortness of breath, fatigue, or palpitations.
IV	Unable to carry out **any physical activity** without discomfort. Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increased.

Table 1. NYHA functional classification based on severity of symptoms and physical activity tolerance. Adapted from Ponikowski et al. [4]

LVEF and NYHA classifications have been widely used as part of the inclusion criteria for participants in clinical trials. Therefore, they are considered in clinical recommendations for treatments such as drugs or cardiac devices [1].

1.1.2 Prevalence and incidence of heart failure in the general population

Prevalence of HF

In high-income countries, the prevalence of diagnosed HF is 1%-2%; women account for half of those living with HF [17]. In high-income countries, prevalence varies widely; values range from 1.2% in Spain and 1.3% in the Netherlands to 4% in Germany [18]. HF data from low- and middle-income countries are scarce [17].

The variability of HF prevalence across countries may be due to underdiagnosis, which occurs in countries with limited diagnostic capabilities [19]. Underdiagnosis may also be due to misclassifications, such as obesity, deconditioning, or aging [20]. Generally, cases that go undiagnosed correspond to HFpEF [19]. Conversely, higher HF prevalence observed in some countries may be due to overreporting. For example, the use of administrative data and diagnostic billing codes may not be accurate and lead to overreporting, depending on a country's reimbursement incentive policies [17, 21].

Beyond reported prevalence differences due to diagnostic and reporting problems, another possible explanation is that there are indeed differences in HF prevalence. These differences may be due to age distribution, predisposition, management of the most important risk factors (hypertension, diabetes, obesity, and smoking), or socioeconomic factors [18].

Over time, HF prevalence has increased due to an aging population and an increase in survival after HF diagnosis [22]. In addition, part of this increase is due to improved diagnostic methods that allow identifying more cases of HFpEF. Currently, about half of all patients with HF have HFpEF [17].

Furthermore, countries that have conducted echocardiographic and biomarker screenings in general populations, have found higher HF prevalence than previously reported in those same countries. This shows that precise HF prevalence in general populations remains unknown [19, 23].

Incidence of HF

As with prevalence, the incidence of HF varies greatly even among high-income countries with similar age distributions within populations. These incidences range from 1.99 new cases of HF per 1000 person-years in Italy or Denmark to 6.55 new cases of HF per 1000 person-years in Germany [18]. Although data from low- and middle-income countries are scarce, evidence suggests that the incidence of HF in these countries is increasing due to the burden of communicable diseases and risk factors related to lifestyle, especially in low-income countries [17].

Strategies to prevent HF have reduced its incidence, while improvements in the treatment of patients with established HF have reduced mortality, leading to an increase in the prevalence of HF. Given that the most common cause of HF is ischemic heart disease (IHD), the marked reduction of myocardial infarction rates would have led to a lower incidence of HF cases [24]. However, among those who have a myocardial infarction, it is now less severe and less fatal thanks to improvements in early diagnostic methods and therapies, which have led to an increase in the number of survivors susceptible to develop post-myocardial infarction HF [17]. Even so, the incidence in high-income countries remains stable and is even trending downwards lately, mainly because of a decrease in cases of HFrEF [17, 22].

1.1.3 Frequent comorbidities

Most patients with HF have at least 1 and often multiple comorbidities. These multiple comorbidities contribute to accelerated disease progression, reduced treatment response, diminished quality of life, and increased mortality. The most prevalent comorbidities with the most clinical and prognostic implications in patients with HF are chronic kidney disease, iron deficiency, anemia, diabetes mellitus, depression, anxiety, obstructive sleep apnea, and chronic obstructive pulmonary disease (COPD). All these comorbidities are highly prevalent in patients with HF and are much more common in these patients than in the general population. There are complex interactions between comorbidities and HF. These comorbidities predispose people to develop HF, and if they do, they also make their HF more severe. Therefore, patients with HF usually have diverse

sources of their symptoms, which makes it difficult to identify and understand them [25, 26].

Chronic kidney disease

Around 55% of patients with HF have chronic kidney disease [27] . The heart and the kidneys contribute to conserving hemodynamic stability and organ perfusion through a network in which they communicate with each other. Acute or chronic dysfunction of 1 organ may induce cardiorenal syndrome—the acute or chronic dysfunction of the other [27, 28].

Chronic kidney disease is one of the most frequent reasons for hospitalization in patients with HF, and it is independently associated with all-cause mortality [29]. Although chronic kidney disease's influence on HF patient's quality of life has not been studied extensively, the available evidence suggests a negative impact on quality of life [29]. In addition to chronic kidney disease, deteriorating renal function has been associated with worse prognoses [30].

Iron deficiency and anemia

Iron deficiency is present in up to half of all patients with chronic HF, and it is the most common cause of anemia. Other major anemia etiological factors are hemodilution because of fluid retention in decompensated patients with HF and decreased erythropoietin synthesis because of renal dysfunction [31]. Due to differences defining anemia, prevalence indices vary between 4% and 61% [27]. Independent of anemia, left ventricular function, and HF severity, iron deficiency is a strong predictor of all-cause mortality in chronic patients with HF [32]. Anemia is also associated with impaired cardiac function, diminished clinical status, and increased mortality [27]. A recent review reported the significant and negative impact of anemia or iron deficiency on the quality of life for patients with HF [29].

Diabetes mellitus

Around 30-40% of patients with HF have diabetes mellitus. Compared to people without diabetes mellitus, the risk of developing HF is twice as high for men and 5 times higher for women with diabetes mellitus [13]. Even without diabetes mellitus, high glucose levels predispose people to HF and increase the risk of HF hospitalizations for patients with HF diagnoses [33]. Additionally, diabetes mellitus increases the length of hospitalizations and the risk of death. Along with iron deficiency, diabetes mellitus is one of the comorbidities with the greatest negative impact on the quality of life of patients with HF [29].

Depression and anxiety

Partly explained by behavioral mechanisms, depressive and anxiety disorders are associated with the HF progression and risk of death [34]. Approximately 20% of patients with HF have depressive disorders, which is 2 to 3 times higher than the prevalence found in the general population [34, 35]. Depressive symptoms and depressive disorders

contribute, among other things, to decreased medication adherence and undesirable lifestyle habits, resulting in poor prognoses [6, 34].

Anxiety disorders, and mainly generalized anxiety disorder, are present in 13% of patients with HF, which is four times higher than the prevalence for the general population [34, 36]. The presence of anxiety disorders is associated with poor prognoses for patients with HF, although the association is not clear for anxiety symptoms [34]. Women with HF present higher rates of anxiety and depression than men with HF [13].

Obstructive sleep apnea

For patients with HF, obstructive sleep apnea is an emerging interest. However, its prevalence in patients with HF is still unknown due to its overlapping symptoms with HF. Without screening for obstructive sleep apnea, its symptoms (struggling to breathe at night, tiredness, and difficulty concentrating) can be considered HF-related [27].

Patients with obstructive sleep apnea tend to have multiple comorbidities such as obesity, diabetes mellitus, asthma, and IHD, as well as greater risks of arrhythmias [37-39]. Obstructive sleep apnea is an independent predictor for all-cause and cardiovascular mortality [40]. All-cause mortality seems to be twice as high for patients with HF with untreated obstructive sleep apnea when compared to those with treated or no obstructive sleep apnea [27].

Chronic obstructive pulmonary disease (COPD)

The prevalence of chronic obstructive pulmonary disease (COPD) is 7 times higher in patients with HF than for the general population. Studies in both North America and Europe estimate prevalence to be as high as 50% in patients with HF [27, 41]. Patients with HF and COPD have worse overall health-related quality of life than those with HF without COPD [29].

1.1.4 Symptoms and quality of life

Patients with HF have a wide range of physical and psychological symptoms that reduce their quality of life [42]. Patients in advanced stages of HF also tend to have more symptoms that negatively impact patient's quality of life [42]. Therefore, HF symptoms require similar therapeutic effort and attention as improving heart function and increasing survival do [6]. Since the main symptoms patients with HF report are part of the Edmonton Symptom Assessment System (ESAS) [43] scale (Supplementary material 1), it has been commonly used to evaluate symptoms in patients with HF [44-46].

The symptoms typically associated with HF are shortness of breath, fatigue, and ankle swelling [3]. Affecting more than half of patients, the most prevalent ones are shortness of breath, fatigue, drowsiness, and pain. Difficulty sleeping, worrying, and sadness are also common [42]. As these symptoms are non-specific and may be caused by other entities, it is essential for symptomatic management to look for other, potentially reversible causes.

For example, fatigue or drowsiness may be caused by iron deficiency or by interrupted sleep because of diuretics. However, even in patients with compensated HF, who are under optimal medical treatment, these symptoms may be still present and difficult to improve [42].

To assess the health-related quality of life of patients with HF, generic or HF-specific tools can be used. Among the generic tools, the most commonly used for HF are the 36-Item Short Form Survey (SF-36); the EuroQol-5 Dimension; the World Health Organization Quality of Life: Brief Version; and the 12-item Short Form Survey (SF-12) (Supplementary material 2) [47]. The most commonly used HF-specific tools to assess health-related quality of life are the Minnesota Living with Heart Failure Questionnaire (MLHFQ) and the Kansas City Cardiomyopathy Questionnaire (KCCQ) (Supplementary material 3) [47]. Overall, the most used is the MLHFQ, followed by the SF-36, and the KCCQ [47]. The KCCQ and the MLHFQ are the most highly rated by experts [48].

The application of these tools has shown that people with HF have a lower quality of life than the general population or people with other chronic diseases, such as chronic kidney disease [49], hepatitis C [49], or IHD [50]. Additionally, among people with HF, women have a lower quality of life than men [13, 47]. This difference may be because women report more physical and mental symptoms than men [13] and receive less physical and social support from their informal caregiver, which is usually the partner [51, 52].

1.1.5 Social and spiritual aspects

Symptoms either from HF or comorbidities, plus HF-related disabilities, cause patients with HF and their informal caregivers to progressively reduce their social circles, leading to social isolation [42, 53]. Social isolation and restrictions due to HF disabilities make it difficult for patients with HF to maintain a sense of a meaningful life [42, 53]. Compared to patients with cancer, patients with HF complain more about daily activities and social problems [54].

For some patients with HF, spiritual distress is confused with a depressed mood when they find it difficult to maintain hope because they feel useless and a burden to the caregiver and the family [54]. Patients with HF-related disabilities and their caregivers report spiritual needs related to feeling hopeless and isolated and distorted self-images [54].

1.1.6 Treatment

Pharmacological therapy

Due to pathophysiologic differences between HFrEF and HFpEF, treatment is different for these HF classifications. Most therapeutic evidence comes from clinical trials conducted among patients with HFrEF [27]. Drug therapy commonly includes diuretics, beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor-neprilysin inhibitors, sodium-glucose cotransporter-2 inhibitors, and mineralocorticoid receptor antagonists [4]. Drug therapy has proven to decrease morbidity and mortality in HFrEF; however, there

is no or inconsistent evidence for HFpEF. Because HFmrEF is a recent categorization, there is not much evidence about drug effectiveness for this group either. Patients diagnosed with HFmrEF have generally been included in HFpEF trials [4, 27].

Non-pharmacological therapy

Non-pharmacological management of patients with HF includes exercising regularly, moderating alcohol consumption, and avoiding tobacco. Other non-pharmacological strategies include educating and self-monitoring (eg, daily weighing to detect fluid retention) [4].

Some patients also have indications for implanting intracardiac devices, such as pacemakers, implantable cardioverter-defibrillators (ICD) or cardiac resynchronization therapy (CRT). Because of its antitachycardia functions, the ICD is of specific interest. Depending on the type of tachycardia, it can either use high-voltage shocks (usually painful) or low-voltage shocks (usually imperceptible) [55].

Additionally, some patients with HF have indications for ventricular assist devices, which are a mechanical circulatory support. The ventricular assist device can be used as a bridge therapy for those on cardiac transplantation waiting lists and as a destination therapy alternative for patients with end-stage HF for whom cardiac transplantation is not an option [4].

To comprehensively manage patients with HF, other services, such as cardiac rehabilitation and palliative care (PC), should be integrated to form multidisciplinary teams. On these multidisciplinary teams, close collaboration is required between staff directly managing a patient's HF (eg, cardiologists, HF nurses, and general practitioners) and other experts, such as nutritionists, physiotherapists, social workers, psychologists, and PC providers [4].

1.1.7 Survival and prognosis

Survival

After HF diagnosis, survival rates are 76% after 1 year, 45% after 5 years, 25% after 10 years, and 13% after 15 years (**Table 2**). Among those who develop post-myocardial infarction HF, the highest mortality risk is 3 months after the event [56].

When analyzing age-specific survival rates by sex, there is no significant difference between men and women; however, there are slightly better survival rates for women [60], except when the cause of HF is ischemic. In that case, women have shorter survival rates [12].

Subgroup	Survival rates			
	At 1 year	At 5 years	At 10 years	At 15 years
Overall	75.9%	45.5%	24.5%	12.7%
Age group (years)				
45-54	90.3%	78.5%	64.7%	54.4%
55-64	87.9%	70.6%	52.8%	38.4%
65-74	83.5%	59.1%	35.4%	17.2%
75-84	76.5%	43.2%	18.4%	5.8%
85-94	63.2%	22.3%	4.4%	0.2%
≥95	43.9%	6.0%	---	---

Table 2. Survival rates at 1, 5, 10, and 15 years after HF diagnosis, overall and by 10-year age groups. Data from a primary care UK database, including 55 959 patients aged 45 and over with a new HF diagnosis between January 1, 2000 and December 31, 2017. Adapted from Taylor et al. [56].

In clinical trials, survival for patients with HF categorized as NYHA class II and NYHA class III varies significantly; however, the 20-month survival rates between these 2 groups overlap [57]. Observational studies have shown a trend of increasing mortality rates as NYHA stage increases [16]. The same trend has been described for patients with ICD [58].

Most deaths of patients with HF are due to cardiovascular causes; the most common are sudden cardiac death and HF death [29, 56, 59, 60]. Sudden cardiac death is defined as an unexpected, non-traumatic death occurring within 1 hour of the onset of new or worsening symptoms [61]. In adult men and women, the most common cause is an ischemic event in the heart muscle (ie, ischemic heart disease), which leads to cardiac electrical dysfunction, such as ventricular fibrillation or ventricular tachycardia. In a small number of cases, the rhythm disturbance is asystole (ie, the absence of electrical activity) or pulseless electrical activity. In the case of asystole or pulseless electrical activity, the origin may be noncardiac [62]. Most sudden deaths occur outside hospitals, whereas most deaths from progressive organ failure (due to progressive HF) occur within hospitals [42].

The second most common cause of death of patients with HF is pulmonary disease followed by cancer. Other non-cardiovascular causes of death are neurological, gastrointestinal, genitourinary, or endocrine diseases [29, 56, 59].

Prognosis

HF disease trajectory is hard to predict and, therefore, prognostication is difficult (**Figure 2**). However, there are some indicators of poor prognosis, such as persistent NYHA class IV despite optimal treatment, recurrent hospital admissions, and cardiac cachexia (unintentional severe weight loss caused by HF) [42]. Hospitalizations can be seen as a turning point during HF disease trajectory. Evidence from observational studies suggests that the risk of death after the first hospitalization is 3 times higher than that of patients who have never been hospitalized. This risk increases progressively after each subsequent hospitalization [63].

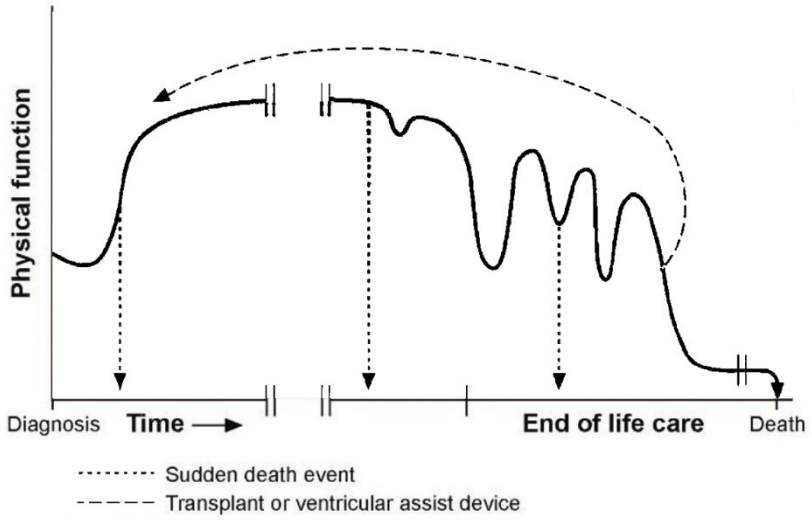


Figure 2. HF trajectory. Adapted from Connolly et al., 2014 [64]

1.2 Palliative care for patients with heart failure

1.2.1 What is palliative care?

The World Health Organization defines PC as a team approach to improve the quality of life for patients living with chronic conditions and their families [65]. PC focuses on providing relief from symptoms and stress that accompany serious illnesses, including cancer, chronic HF, COPD, Parkinson's disease, Amyotrophic Lateral Sclerosis, and many others [66]. However, although PC is widely used for patients with cancer, its use is infrequent for patients with other conditions, such as HF [67, 68]. PC can be appropriate at any age and any stage of serious illness and can be provided in combination with curative treatment [69].

PC aims to prevent and relieve suffering through early identification and treatment of physical, psychological, social, or spiritual problems [65]. To identify these needs as early

as possible, it is recommended to incorporate PC when HF is diagnosed. PC providers assess physical and psychological symptoms and their impact on daily life activities. Additionally, they assess social problems for patients and informal caregivers, such as social isolation due to disability [53]. Spiritual needs, such as the needs to love and feel loved, to have a sense of belonging, and to feel peace and forgiveness, are also assessed [70]. PC providers discuss the patient's care preferences and treatment expectations to make clinical decisions that align with these.

The process of discussing and defining current and future treatment goals and preferences with patients and their family is an essential component of PC called *anticipatory care planning* [71]. Anticipatory care planning uses open communication to promote patient autonomy concerning medical decisions. The decisions from anticipatory care planning conversations should be recorded in case a patient later becomes unable to make decisions. The written record can be in the form of an advance directive or designating a legal decision maker if a patient becomes incapacitated. Although anticipatory care planning can be initiated at any stage of the HF disease trajectory, due to its unpredictability and the risk of cognitive impairment for patients with HF, it is better to start the discussions at the early stages of the trajectory [5, 6]. A recent systematic review and meta-analysis of randomized controlled trials showed that for patients with HF, anticipatory care planning improves patients' quality of life, patients' satisfaction with EoL care, and the quality of communication at the EoL [71]. Finally, the physical, social, and emotional needs of patients' caregivers are also assessed [5].

When patients with a serious illness approach the EoL, EoL care helps them live as comfortably as possible during this last stage of life. This kind of EoL care is also offered through PC. PC includes but is not limited to EoL care [72]. PC continues after a patient's death, offering support to the family or informal caregivers throughout the grieving process.

1.2.2 General and specialized palliative care

Evidence has shown that for patients with HF, specialized PC improves patient-centered outcomes such as quality of life and symptom burden in inpatient and outpatient settings [73-76]. However, an aging population poses multiple challenges for health care systems [77]. One of the challenges is an increase in the number of patients with chronic conditions. These patients might benefit from a PC approach, but the number of PC specialists is insufficient to meet the needs of these patients [78]. Yet not all patients have the same levels of need. For example, primary care physicians or nurses with PC training can deliver general PC, whereas patients with complex needs may require additional support from PC specialists [79].

In Switzerland, indications for specialized PC include needs for training caregivers to manage symptomatic crises, such as respiratory distress or hemorrhage; developing living wills; managing vulnerabilities for patients with mental disorders; facilitating decision

making around assisted suicide; aligning patient and family goals; and monitoring caregiver workload and support [80].

1.2.3 Concurrent palliative care: a palliative gaze throughout the HF trajectory

Since patients with HF have a higher burden of physical and psychological symptoms that negatively impact their quality of life, guidelines and experts position statements recommend a concurrent PC approach [81] with life-prolonging therapies in patients with HF [4-6]. Therefore, health care personnel on a multidisciplinary team can use a *palliative gaze* to treat patients throughout the HF disease trajectory (**Figure 1**). The palliative gaze uses an integrated, problem-centered approach. A multidisciplinary team might include cardiologists, HF nurses, general practitioners, nutritionists, physiotherapists, psychologists, and social workers [5].

If a member of the multidisciplinary team cannot provide a palliative service the patient needs, a referral to general or specialized PC is necessary. Possible triggers for involving general or specialized PC for patients with HF are persistent symptoms despite optimal HF therapy; declining functional status; recurring hospital admission for HF; qualifying for heart transplantation or mechanic circulatory support with ventricular assist devices; or advising before cardiac device implantation [5, 6]. Referrals to general or specialized PC do not mean that all efforts to look at patients and their needs in a comprehensive manner are relegated to the person providing PC. All other members of the multidisciplinary team should continue treating patients with the palliative gaze.

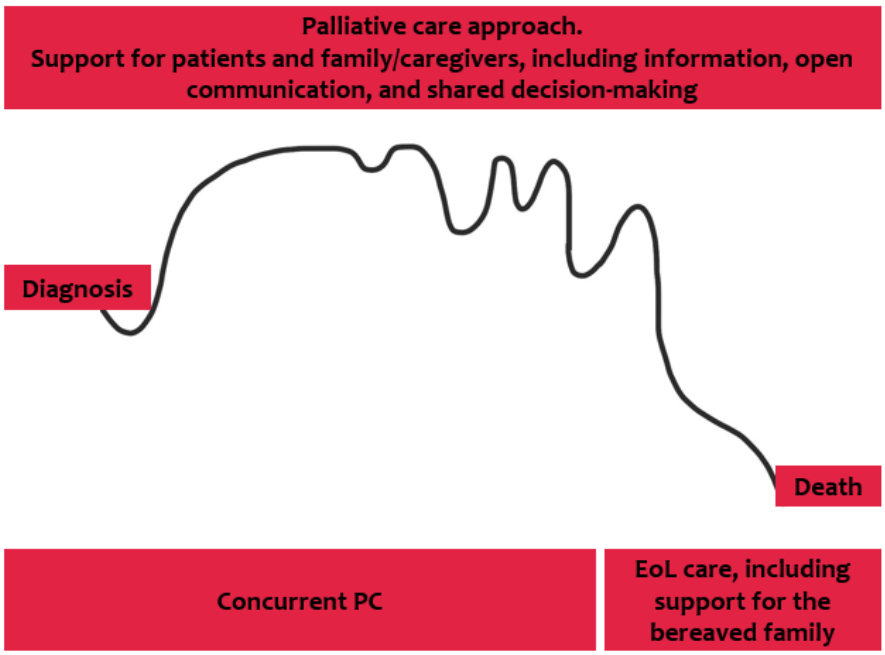


Figure 1. Integration of a PC approach throughout the HF trajectory.

1.2.4 End-of-life care for patients with heart failure

The EoL is a period when the possibility of dying in the upcoming months increases, either due to the progression of advanced disease, general frailty, or an acute life-threatening situation. Although there is no internationally accepted agreement on when the EoL period starts, the UK´s General Medical Council and the Australian Institute for Health and Welfare refer to patients approaching the EoL when they are likely to die within the next 12 months [82, 83]. At this stage, it is common to find progressive physical and mental deterioration and worsening symptoms in patients with HF [42, 64]. The active dying phase is a short period (usually just days) immediately before death in which symptoms worsen further or new symptoms appear [6, 42, 84].

Recognizing the EoL period is important because it prompts a gradual transition of care toward improving comfort, supporting the family, and inquiring about what is a good death for the patient. Patients with HF have reported that having a good death includes care focused on comfort with symptom relief, reducing the physical and emotional burdens on family, communicating honestly, and avoiding unnecessary interventions. In addition, a good death would be sudden [42]. However, death from sudden cardiac events have been reduced with therapies such as ICD, CRT, and beta-blockers [42, 55, 85]. Therefore, the proportion of progressive deaths, whether due to cardiovascular or non-cardiovascular causes, has increased in patients with HF; thus, the number of patients needing support in the EoL and active dying phases has also increased [42, 55].

Although preparation for the EoL can start when a life-threatening illness is diagnosed, when patients are identified as being at their EoL, discussions about the dying process should be discussed further. Discussions should include patient and family preferences about the places of care and death, roles of current cardiac therapies, and resuscitation attempts. Most people with HF prefer to die at home [86]. However, some patients require a higher level of care than informal caregivers and ambulant care can provide. Therefore, arranging for patients to die at home is more difficult to achieve and can lead to more distress for patients and their families [5, 42]. In cases when patients and families prefer an at-home death, health care providers must work closely with the family to offer guidance for managing symptoms and other patient needs. For example, a useful strategy for at-home or nursing home deaths is called *anticipatory prescribing*, or prescribing medications in advance that may be urgently needed in the immediate future.

Recognizing the active dying phase is important to initiate actions that are defined in the care plans for dying patients, including preparing families for death. Additionally, as patients approach the active dying phase, both cardiac and noncardiac medications should be reviewed to assess the need for deprescription if they are not aligned with the newly established management goals. Other reasons for deprescribing include treatment burdens that exceed benefits, adverse reaction risks that increase with polypharmacy, and poor patient medication tolerance or adherence [5, 42]. Besides deprescribing, the care of

patients include prescribing medication for frequent symptoms in the dying phase, such as shortness of breath, pain, delirium, nausea/vomiting, congestion, and anxiety [5].

In the active dying phase, cardiac device management needs special attention. For example, since they fail to control arrhythmias, high-voltage shocks from ICDs are useless and repetitive, causing further distress to patients and their families. Therefore, deactivating the shock function, commonly and inaccurately called ICD deactivation, should be discussed with patients and their families to avoid possible painful shocks [6, 55]. A temporary option for "acute" deactivation is to place a magnet over the chest to prevent or stop shocks. However, software reprogramming is necessary for long-term control of the device [6, 55]. The ICD's antitachycardia pacing and low voltage function can be left active in the dying phase because it does not cause discomfort to patients [55].

Pacemakers remain active since their antibradycardia pacing function improves the quality of life even for dying patients by preventing bradycardia symptoms, such as dizziness and shortness of breath [6]. The CRT, another implantable electrical device, does not need to be modified, as it helps to control symptoms related to HF [6, 55].

1.2.5 Gaps and challenges delivering palliative care to patients with heart failure

This thesis covers issues related to gaps and challenges delivering PC to patients with HF. Specifically, it provides knowledge to overcome the challenges of identifying patients with unmet needs who might benefit from PC, and it quantifies gaps in anticipatory care planning and EoL care in patients with ICDs.

Gaps

For several decades, evidence has shown that patients with HF have similar PC needs as patients with cancer and often for longer time periods [42, 67]. However, in most countries, access to PC for patients with HF is suboptimal, showing gaps between PC needs and its delivery for patients with HF [67, 68]. Since the first position statement about PC and HF was published by the European Society of Cardiology in 2009 [87], consensus statements have been published, guidelines have recommended PC for patients with HF, and PC for HF has been discussed at conferences [3-6]. In the latest European atlas of PC services, it showed that only 8 European countries have cardiology services that provide PC: the Czech Republic, Denmark, Ireland, the Netherlands, Portugal, Spain, Sweden, and the United Kingdom. The atlas also showed that collaboration between cardiology services and PC specialists occurs only occasionally [78]. In the United Kingdom, only a minority of patients with HF receive PC (offered either by family physicians and their teams or by specialized PC services); 7% of those dying from HF compared with 48% of those dying from cancer. [67, 68]. Moreover, those patients with HF who receive specialized PC receive it for a shorter time compared to patients with cancer; since the average referral time for patients with HF is 2 weeks prior to death [67].

Although it is widely known that EoL discussions are an integral part of anticipatory care planning, they rarely happen for patients with HF [6]. Physicians have expressed that anticipatory care planning is infrequent for patients with HF because patients and families are reluctant to accept poor prognoses [6]. In addition, physicians reported that patients' and families' do not know about the advantages of discontinuing life-sustaining treatments, which is another barrier to anticipatory care planning. Furthermore, health care personnel need more training to conduct such care planning [88].

Anticipatory care planning is essential for patients with ICDs to avoid EoL shocks that may be misaligned with a patient's wishes. However, a recent qualitative study showed that in the subgroup of patients with ICDs, infrequent discussions do not inform patients about device and EoL issues. Some patients were unaware that disabling shocks was an option or that they could die with the device turned on [89]. Due to uninformed patients regarding EoL device management and the infrequency with which this topic is discussed with health care personnel, it is logical to think that device reprogramming at the EoL rarely occurs. Several studies have investigated the prevalence of deactivation and shocks at the EoL [90-93]. However, most of them were limited by small sample sizes and the evidence was inconclusive. For this reason, I synthesized study results that reported the proportion of patients in whom the ICD shock function was deactivated before death.

Decisions from anticipatory care planning discussions are recorded in advance directive forms. An advance directive is a document where patients record their wishes regarding medical care if they become unable to make or express medical decisions [6]. ICD management should be explicitly addressed in advance directives; however, evidence suggests that ICD management decisions are rarely included in advance directives [91, 94, 95]. For this reason, I synthesized study results that reported the proportion of patients with advance directives explicitly mentioning ICD management.

Challenges

There are several challenges for which the integration of PC into evidence-based HF management is suboptimal. Recurrent challenges are difficulties recognizing the EoL phase, the negative connotation of the term "palliative care," and the identification of PC needs [6, 90].

Identifying the EoL or active dying phases is a challenge [42] because disease trajectory for HF is unpredictable (**Figure 2**) and HF decompensations are potentially reversible. Therefore, prognostication is difficult. For example, even in advanced stages, phases of decompensation and remission alternate. PC has been commonly associated with death, discontinuation of treatment, and loss of hope; further, patients and physicians often equivocate PC to hospice care [96, 97]. When offered PC, these kinds of misunderstanding cause patients and their families anxiety and discomfort, and also pose barriers for health care providers when considering referrals to PC. Therefore, some PC programs have been renamed supportive care, a strategy supported by results from a randomized trial that

showed better impressions and understandings of PC services using "supportive" rather than "palliative" [97].

One of the main challenges delivering PC to patients with HF are difficulties identifying patients with PC needs in the first place. These difficulties persist when identifying patients with and without limited life expectancies [5].

1.2.6 Identifying palliative care needs for patients with heart failure

Different tools are available to assist identifying palliative needs for patients with limited life expectancy (prognostic tools) and patients without limited life expectancy (needs assessment tools); the tools are either often generic or specifically created for patients with HF.

Prognostic tools

Because the HF trajectory is unpredictable, generic prognostic tools may not perform well for this population. Therefore, it is necessary to evaluate their performance in patients with HF. Initially conceived for cancer patients, the "Surprise Question" (SQ) is one of the most common prognostic tools [98]. It consists of a reflective question that health care providers ask themselves: would I be surprised if the patient died within the next year? If the answer is "no, I would not be surprised," that response means the patient might be at EoL and might require PC services and support. There are also versions of the SQ that ask the same question within a context of 3 or 6 months; however, 1 year is the most used version of the SQ. Performance of the SQ has been evaluated among patients with HF in emergency [99] and inpatient settings [100]. It has not been evaluated in outpatient setting, which is essential as most encounters between health care personnel and patients occur in this setting.

The Spanish language *NECesidades PALiativas* (NECPAL; Palliative Needs) is a prognostic tool that begins with the SQ [101]. A positive SQ (ie, the health care provider would not be surprised if the patient dies within a year) is the precondition to use the tool. The tool's following questions are then answered based on medical records data, such as nutritional information, functional and disease severity markers, comorbidities, and emotional distress. The NECPAL tool has been used to assess PC needs for patients with HF in clinical practice in different countries [102-104], and it is currently available in several languages. However, its performance identifying patients with PC needs had not been assessed. Later I present results the SQ's performance predicting 1-year mortality in outpatients with HF and the NECPAL tool's performance identifying palliative needs for outpatients with HF.

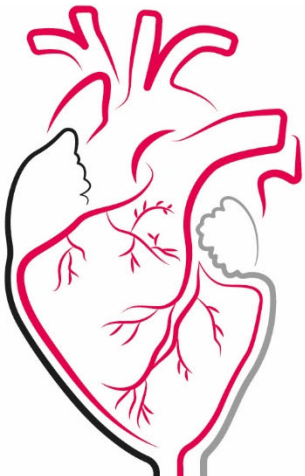
Needs assessment tools

Since patients with life expectancies of more than 1 year may also have palliative needs, regardless of their prognosis, tools assessing their needs are also necessary. Several generic tools are available to assess palliative needs in patients with HF: the Integrated Palliative Care Outcome Scale (IPOS) [105], the Radboud Indicators for Palliative Care

Needs [106], and the Supportive and Palliative Care Indicators Tool [107]. Among these, IPOS stands out since it is the only one that assesses all PC domains: physical, psychological, social, and spiritual. The Needs Assessment Tool: Progressive Disease – Heart Failure (NAT: PD-HF) is a HF-specific tool and it also covers all PC domains (Supplementary material 4) [108]. The NAT: PD-HF was created in Australia. In addition to English, it is also available in Dutch [109]. To make the tool available for German-speaking populations, this tool was translated as part of this thesis, which is later described.

The NAT: PD-HF contains more items than the other tools, which can be a disadvantage as it takes longer to complete, but it provides a more comprehensive assessment of the patient's and informal caregivers' needs. The NAT: PD-HF was designed to provide support during consultations, and it is based on classifying concerns and matching those with actions. Psychometric properties have been evaluated for this tool: acceptability (although not by patients), feasibility, validity (face, content, and construct), and reliability (although only inter-rated, not test-retest) [110, 111]. I later present the acceptability of the tool by patients and the test-retest reliability.

Two systematic reviews about tools assessing PC needs for patients with HF were published recently [110, 111]. Among the studies that have assessed palliative needs in patients with HF, they found that the most used screening tools were the NAT: PD-HF and the NECPAL tools. Based on the tools development, content, contexts of use, and psychometrics, the systematic reviews concluded that the NAT: PD-HF is the most appropriate tool to assess PC needs in patients with HF [110, 111].



2. Aims

"To cure sometimes, to relieve often, and to comfort always."

- **folk saying**

2.1 General aims

In this PhD thesis, I contribute knowledge about the challenges and gaps delivering PC to patients with HF. In the first 3 articles, I provide information about how to overcome challenges through identifying patients who might benefit from PC or have unmet needs. To do this, in article 1 my aim was to evaluate the SQ as a predictor of 1-year mortality for patients with HF. The SQ can be used to identify patients with PC needs due to limited life expectancy. Similarly, for article 2 I aimed to assess the performance of the NECPAL tool identifying PC needs in the HF population. Additionally, in article 3, I aimed to provide a German version of the NAT: PD-HF and assess its psychometric characteristics and patient and health care personnel acceptability. Finally, in article 4 I aimed to quantify gaps anticipatory care planning and EoL patient care for those with ICDs.

2.2 Specific aims

2.2.1 Article 1. The 'Surprise question' in heart failure: a prospective cohort study

The SQ's performance had not been evaluated for patients with HF in outpatient settings. Its performance according to patients' demographic and clinical characteristics had also not been evaluated. Therefore, I aimed to:

1) assess the performance of the SQ predicting 1-year mortality among patients in ambulatory HF clinics; and
2) assess whether the SQ's performance changes according to demographic (age groups, sex) or clinical (NYHA functional class and LVEF classification) characteristics.

2.2.2 Article 2. Prevalence and characteristics of patients with heart failure needing palliative care

Since there is no standard measure for comparing tools that identify PC needs, the NECPAL's performance had not been studied. This tool is available in several languages, and it is used in several countries. Hence, I considered it important to know its performance identifying patients with HF with PC needs (ie, those with lower quality of life, more physical symptoms, and psychosocial problems). Therefore, I aimed to

1) assess the prevalence of PC needs for outpatients at HF clinics with the NECPAL tool;
2) assess the prevalence of PC needs for age groups, sex, NYHA functional class, and LVEF classification; and
3) assess the NECPAL tool's performance identifying PC needs based on patients' health-related quality of life and symptom burden.

2.2.3 Article 3. Validation of the German version of the Needs Assessment Tool: Progressive Disease – Heart Failure

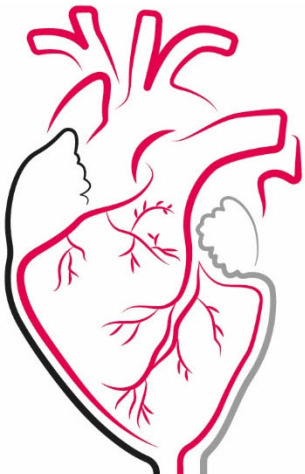
Until our translation, the NAT: PD-HF had been available in only English and Dutch. Thus, I aimed to

1) translate the tool into German and culturally adapted it;
2) assess psychometric characteristics of the German NAT: PD-HF, including internal consistency, inter-rater reliability, and test-retest reliability;
3) evaluate patients and health care personnel's understandings of the tool and its use; and
4) assess the face validity, applicability, relevance, and acceptability of the German NAT: PD-HF among health care personnel.

2.2.4 Article 4. Unmet device reprogramming needs at the end of life among patients with implantable cardioverter defibrillator: A systematic review and meta-analysis

I conducted a systematic appraisal of the literature about managing ICDs at the EoL. In our review, I aimed to

1) assess the prevalence of ICD reprogramming to deactivate shock function at the EoL;
2) assess the prevalence of advance directives among patients with ICDs and the prevalence of advance directives explicitly mentioning the device;
3) assess the role advance directives play in ICD reprogramming at the EoL.



3. Results

"To know the patient that has the disease is more important than to know the disease that the patient has."

- **William Osler** (July 12, 1849 – December 29, 1919)

Support
Communication
Autonomy

3.1. Article 1.

The 'Surprise question' in heart failure: a prospective cohort study

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Clara Saldarriaga
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Contribution: I participated in the conceptualization of study. I consulted the national mortality records to assess vital status of participants. I performed the analysis, made the figures and wrote the first draft of the manuscript. After that, I incorporated coauthors and reviewers' comments.

OPEN ACCESS

The 'Surprise question' in heart failure: a prospective cohort study

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ABSTRACT

Objective The Surprise Question (SQ) is a prognostic screening tool used to identify patients with limited life expectancy. We assessed the SQ's performance predicting 1-year mortality among patients in ambulatory heart failure (HF) clinics. We determined that the SQ's performance changes according to sex and other demographic (age) and clinical characteristics, mainly left ventricular ejection fraction (LVEF) and the New York Heart Association (NYHA) functional classifications.

Methods We conducted a prospective cohort study in two HF clinics. To assess the performance of the SQ in predicting 1-year mortality, we calculated the sensitivity, specificity, positive and negative likelihood ratios, and the positive and negative predictive values. To illustrate if the results of the SQ changes the probability that a patient dies within 1 year, we created Fagan's nomograms. We report the results from the overall sample and for subgroups according to sex, age, LVEF and NYHA functional class.

Results We observed that the SQ showed a sensitivity of 85% identifying ambulatory patients with HF who are in the last year of life. We determined that the SQ's performance predicting 1-year mortality was similar among women and men. The SQ performed better for patients aged under 70 years, for patients with reduced or mildly reduced ejection fraction, and for patients NYHA class III/IV.

Conclusions We consider the tool an easy and fast first step to identify patients with HF who might benefit from an advance care planning discussion or a referral to palliative care due to limited life expectancy.

Key messages

What was already known?

- The performance of the Surprise Question (SQ) screening tool to predict 1-year mortality had been assessed among inpatient populations with heart failure (HF) and populations with HF in an emergency setting.

What are the new findings?

- The SQ's performance predicting 1-year mortality in an ambulatory setting, a HF clinic, where patients with HF are more stable.
- The SQ's performance predicting 1-year mortality for a population with HF according to patients' sex, age, New York Heart Association functional class and left ventricular ejection fraction.

What is their significance?

Clinical:

- The SQ's new psychometric profile allows for determining the appropriateness of its use in clinical practice at HF clinics and its predictive value for subgroup populations.

Research:

- This study contributes to filling gaps in the knowledge of the SQ's performance in patients with HF in the ambulatory setting.

INTRODUCTION

People living with heart failure (HF), especially those in advanced stages of the disease, might present with uncontrolled symptoms such as shortness of breath, pain, sleep disorders and fatigue[1] ; they also often suffer from comorbidities, such as depression and anxiety.[2] Advance care planning (ACP) has proven to improve the quality of life and patient satisfaction with end-of-life care for patients with HF by promoting their autonomy concerning medical decisions.[3] Identifying those with HF who are in the last year of their life is paramount to guide discussions and determine other strategies that are part of ACP, including possible referrals to specialised palliative care (PC).

The Surprise Question (SQ) is a prognostic screening tool used to identify patients with limited life expectancy. The

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SQ is a reflective question a physician or other healthcare providers ask themselves about a patient's prognosis: 'would I be surprised if this patient dies within the next 12 months?' An SQ is positive (+SQ) if the healthcare provider's answer is 'no, I would not be surprised'. There are also versions of the SQ within the context of 3 or 6 months. However, 1 year is the most common version.

The SQ's performance has been evaluated for patients with both oncological[4–7] and non-oncological diseases, including chronic kidney disease[8] and chronic obstructive pulmonary disease.[9] For patients with oncological diseases, the sensitivity of the 1-year SQ has varied from 58% to 85%.[4–7] For patients with non-oncological diseases, the performance also varies even within the same disease.[8–10] Despite the heterogeneity among performance measures, two systematic reviews suggest that, in general, the performance of the SQ predicting 1-year mortality is better for patients with oncological disease than for patients with non-oncological disease.[10 11] Recently, the SQ's performance was assessed for an inpatient population with HF[12] and for a population with HF in an emergency setting.[13] The results were promising with a sensitivity of 85% for hospitalised patients and 79% for the emergency setting. However, the SQ's performance in ambulatory settings, such as HF clinics where patients are more stable, is unknown. Furthermore, understanding the SQ's performance for men and women is important to ensure equity in the delivery of ACP and PC. To our knowledge, the SQ's performance for patients with HF, stratified according to the patient's sex, has not yet been reported. Finally, given that HF clinic admission criteria and samples vary, it is important to understand the SQ's performance according to other demographic and clinical characteristics to increase the generalisability of the results. Performance of the SQ is likely to differ across subgroups due to previous knowledge of the staff answering the question. For example, evidence has shown a trend of increasing mortality rates with increasing New York Heart Association (NYHA) stage,[14] increasing age[15] and decreasing left ventricular ejection fraction (LVEF).[16 17]

Therefore, our objectives included (1) assessing the performance of the SQ predicting 1-year mortality among patients in ambulatory HF clinics, and (2) assessing whether performance changes according to sex, age, NYHA classification and LVEF category.

METHODS

This study was conducted and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[18]

Study design and setting

The prospective cohort included 174 ambulatory patients with HF who were recruited from two HF clinics in Medellín, Colombia between November 2017 and November 2018. One-year vital status was determined by consulting the national mortality register in Colombia. Both clinics are part of tertiary care institutions that are referral centres for patients with cardiovascular disease. They offer comprehensive, multidisciplinary care that includes clinical follow-up by HF cardiologists, nursing education and telephone follow-up, cardiac rehabilitation, and a psychoeducational programme for patients and their families.

Participants

Patients were potentially eligible for the study if they were 18 years or older and existing patients at the HF clinic who had at least two prior consultations. Since the first two consultations provide the cardiologist an opportunity to optimise treatment if necessary and to get to know patients under optimal treatment circumstances according to clinical guidelines, we did not enrol newer HF clinic patients. We enrolled consecutive eligible patients in the study. There were no exclusion criteria.

Ethical aspects

We conducted the study in accordance with the ethical guidelines from the Declaration of Helsinki[19]; our study was approved by the research ethics committees of the institutions involved in the study. Informed consent was collected before participants enrolled in the study.

Data sources and measurements

We obtained sociodemographic characteristics (age, sex and marital status) from electronic medical records, along with values of the clinical variables: LVEF, number of hospitalisations in the last year, presence of cardiac implantable devices, NYHA functional class, comorbidities and current medications. Comorbidities included clinical depression, atrial fibrillation, type 2 diabetes mellitus, kidney disease, lung disease, coronary artery disease, obstructive sleep apnoea and hypothyroidism. Current medications included ACE inhibitors, beta-blockers and angiotensin receptor blockers.

When a patient met the eligibility requirements for study inclusion, the treating cardiologist answered the SQ for that patient. For patients that the cardiologist would not be surprised if they died within the next year, we coded as +SQ. For patients that the cardiologist would be surprised if they died within the next year, we coded as a negative SQ (−SQ).

Statistical methods

To describe the study sample, we used mean and SD to summarise continuous variables in case of normal distribution. In cases of skewed distribution, we used median and IQR. We assessed normality using Q–Q plots. We summarised categorical variables as frequencies and percentages.

To assess the SQ's performance predicting 1-year mortality, we calculated the sensitivity and specificity, as well as the SQ's positive (+LR) and negative (–LR) likelihood ratios and the positive (PPV) and negative (NPV) predictive values (online supplemental tables 1 and 2). We interpreted the effect of the +LR on the likelihood of dying within 1 year based on the following classifications: no change if +LR=1; minimal increase if +LR between 1 and 2; small increase if +LR between 2 and 5; moderate increase if +LR between 5 and 10; and substantial increase if +LR >10.[20]

To illustrate how the result of the SQ changes the probability that a patient dies within 1 year, we created Fagan's nomograms.[21] We also conducted a univariable regression to assess the relation between a +SQ and 1-year mortality.

We performed subgroup analysis, comparing groups according to sex, age, LVEF and NYHA functional class. We created a categorical variable for median age (70 years) and another for LVEF (reduced LVEF ≤40%; mildly reduced LVEF 41%–49%; and preserved LVEF ≥50%).[22]

We performed all analyses with STATA V.15 (Stata Corp, College Station, Texas, USA).

RESULTS

Participants

Of the 184 patients who met the inclusion criteria and were potentially eligible, 178 consented to participate in the study. Among these 178 participants, 4 were excluded because their 1-year vital status was unknown (figure 1).

Table 1 shows baseline demographic and clinical characteristics of the study's 174 participants. The sample had a median age of 70 (58–77), was predominantly male, had reduced LVEF and NYHA class II. The prevalence of a +SQ was 48%. After 1 year, 20 patients had died, giving an overall mortality rate of 12%.

Performance of the SQ predicting 1-year mortality

After 1 year, mortality among those with a +SQ was 21%; mortality among those with a –SQ was 3% (p<0.001). Participants with a +SQ had 7.5 times higher odds of death at 1 year compared with those with a –SQ (OR 7.6, 95% CI 2.1 to 26.9).

The +LR is the probability that patients with +SQ will die within 1 year divided by the probability that patients with +SQ will be alive in 1 year.[20] The +LR of the SQ was 1.98. The +SQ was nearly twice as likely for patients who died within 1 year than it was for patients who were alive in 1 year (figure 2). According to the classification of the +LR's effect on the likelihood of dying within 1 year, it is a minor increase. The 1-year mortality rate for our study was 12%. With the pretest probability of a patient dying within 1 year at 12% and a +LR of 1.98, the post-test probability of dying within 1 year is 20% (figure 3). A +SQ increased the probability that an ambulant patient with HF died within 1 year by 8 percentage points. The –LR was 0.26. The –SQ was nearly four times more likely assigned to participants who were alive in 1 year than it was for patients who died within 1 year.

For our sample, the probability that the SQ correctly identified an individual who would die in the course of a year, the sensitivity was 85% (95% CI 69% to 100%). The probability that the SQ would correctly identify an individual who would survive over a year, the specificity was 57% (95% CI 49% to 65%) (figure 2).

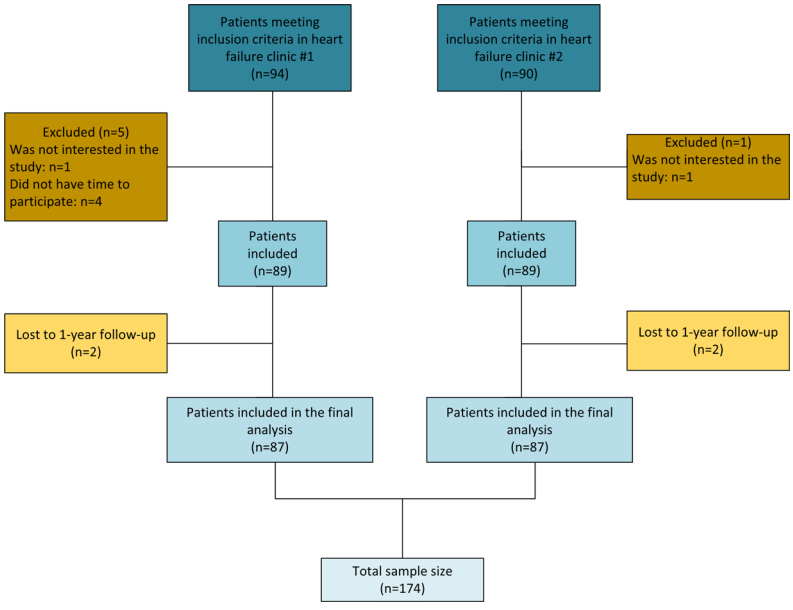

Figure 1 Flow chart of the patients included in the study.

Table 1 Clinical and demographic characteristics of study participants

	Patients included (n=174)
Age	70 (58–77)
Sex	
Women	78 (44.8%)
Men	96 (55.2%)
Marital status	
Single	25 (14.4%)
Married	91 (52.3%)
Divorced/separated	11 (6.3%)
Widow/widower	47 (27.0%)
Aetiology	
Ischaemic	62 (35.6%)
Hypertensive	15 (8.6%)
Idiopathic	69 (39.7%)
Valvular	22 (12.6%)
Toxic	6 (3.5%)
LVEF (%)	32 (25–44)
Classification according to LVEF	
HFrEF	116 (66.7%)
HFmrEF	28 (16.1%)
HFpEF	30 (17.2%)
NYHA functional class	
I	57 (32.8%)
II	82 (47.1%)
III	34 (19.5%)
IV	1 (0.6%)
Comorbidities	
Type 2 diabetes mellitus	55 (31.6%)
Chronic kidney disease	84 (48.3%)
Lung disease	25 (14.4%)
Coronary artery disease	64 (36.8%)
Atrial fibrillation	51 (29.3%
Depression	18 (10.3%)
Anxiety	7 (4.0%)
Obstructive sleep apnoea	13 (7.5%)
Obesity	20 (11.5%)
Hospitalisations in the last year	2 (1–2)
Implantable cardioverter defibrillator	42 (24.1%)
+SQ	83 (47.7%)
Mortality	20 (11.5%)
Medication	
Beta-blockers	164 (94.3%)
ACE inhibitors	136 (78.2%)
ARBs	130 (74.7%)

Data presented as number of patients (%) for categorical data or as median (IQR) for continuous data.

Those patients for whom the cardiologist would not be surprised if the patient died within the next year were coded as a +SQ.

ARBs, angiotensin receptor blockers; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; SQ, Surprise Question.

Subgroup analyses

We compared the SQ's performance between women and men. Whereas other parameters were similar, the SQ's sensitivity was 5 percentage points higher for women. With higher sensitivity, higher specificity and higher +LR, the SQ performed better for participants younger than 70 years (figure 2). Regarding LVEF's classification, sensitivity, NPV and –LR were better for patients with reduced LVEF. Specificity, PPV and +LR were better for patients with mildly reduced LVEF. We observed the SQ's worst performance for patients with preserved LVEF (figure 2). Among patients classified as NYHA III/IV, the SQ's sensitivity was perfect (100%). This subgroup also had the best values of PPV and NPV. However, the SQ's specificity was very low (31%) for patients at NYHA III/IV classification (figure 2).

Based on Fagan's nomograms, we accounted for the clinical application of the +LR. We observed the biggest probability changes for patients with +SQ dying within 1 year for those aged under 70 years and for patients with mildly reduced LVEF. Having a +SQ increased the probability of dying within 1 year by 12 and 14 percentage points, respectively (online supplemental figures 1–8). According to the +LR's effect on the likelihood of dying within 1 year, the +LRs showed a small increase in the likelihood among women; those aged under 70 years and patients with mildly reduced LVEF. In the remaining subgroups, +LR showed a minimal increase in the likelihood of dying within 1 year.

DISCUSSION

Key results

Our primary objective was to assess the SQ's performance predicting 1-year mortality among patients in ambulatory HF clinics. With a sensitivity of 85%, the SQ is a good tool to screen ambulatory HF clinic patients who might be in the last year of life. The SQ's performance predicting 1-year mortality was similar among women and men. We also assessed the SQ's performance according to sex and other demographic (age) and clinical characteristics. The SQ performed better for patients aged under 70 years; for those with reduced or mildly reduced ejection fraction; and for patients at NYHA III/IV classification. For the whole sample and the different subgroups, +LRs showed a minor or a small increase in the likelihood of a patient dying within 1 year, which is not good enough to consider that a patient has a life expectancy limited to 1 year.

Performance of the SQ by subgroup

The risk factors for developing HF differ between men and women, as do responses to treatment, symptom burden, and comorbidities due to both biological and cultural factors.[23] Because of this, sex-specific results should be presented in research.[24] Accounting for sex, determining survival rates for patients with HF has been inconclusive. Initially, the Framingham study showed better survival rates after HF diagnosis for women than for men.[25] Later, other studies suggested worse survival rates for women,[15] which was supported

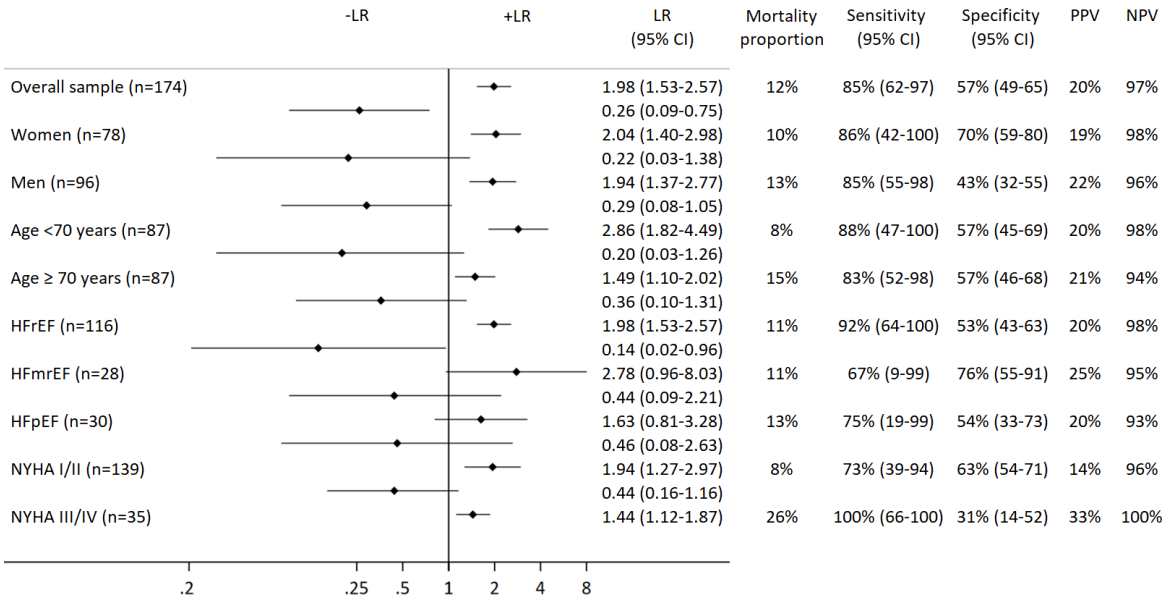

Figure 2 Performance of the SQ in predicting 1-year mortality among patients in ambulatory HF clinics. HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LR, likelihood ratio; NPV, negative predictive value; NYHA, New York Heart Association; PPV, positive predictive value; SQ, Surprise Question.

by women presenting with HF when they are older and have more comorbidities.[23] However, the most recent evidence suggests that age-adjusted mortality is similar between sexes.[26]

Among the subgroups, the SQ's best performance was for those aged under 70 years. The main difference between its performance for those older and younger than 70 years was specificity. An age over 70 years likely contributes to a +SQ response from cardiologists, leading to an increase in the proportion of false positives; thus, a reduction in specificity.

The best sensitivity was for the group of patients with reduced LVEF. With more evidence of effective therapies to reduce morbidity and mortality, this type of HF is the most studied and best understood.[27] In addition, evidence has shown that for patients with LVEF regardless of age, the lower the LVEF, the higher the mortality.[28] This might explain why the performance of an intuitive prognostic tool is better for this type of HF. The worst performance was among patients with preserved LVEF. This type of HF is not well understood, and there is no evidence of pharmacological therapy that decreases mortality for patients with preserved LVEF.[27 29] An intuitive prediction of mortality for this group of patients is especially complex because the relationship between LVEF and mortality is U shaped.[16 28] Above certain LVEF values, age-adjusted mortality increases, which is comparable with patients with LVEF between 30% and 35%.[16 28]

As for NYHA classifications, all patients classified at NYHA III/IV who died had a +SQ, which led to a sensitivity of 100%. However, for patients at NYHA III/IV functional class who survived 1 year, the majority also had a +SQ. Perhaps due to previous knowledge that mortality increases with increasing NYHA functional class, cardiologists are more likely to assign +SQ to patients with HF in more advanced stages of NYHA,[14] which is similar to what happens with older patients with HF.

Comparison with previous studies

Previously, the SQ's performance predicting 1-year mortality had been evaluated for patients with HF in emergency[13] and inpatient settings.[12] In the emergency department, the SQ has a sensitivity of 79% and a specificity of 57% when answered by emergency physicians.[13] For hospitalised patients, the SQ has a sensitivity of 85% and a specificity of 59% when answered by cardiologists.[12] We found that the SQ's sensitivity (85%) and specificity (57%) for outpatient settings are equal to inpatient settings. Since the SQ's sensitivity and specificity were the same for decompensated (inpatients) and stable patients (outpatients), it suggests that the SQ's performance predicting 1-year mortality for patients with HF does not vary significantly. However, to compare the SQ's performance across settings and its interpretation in clinical practice for individual patients, we would have to compare LRs. No studies assessing the SQ's performance for populations with HF reported LRs. However, since LRs are calculated using sensitivity and specificity, we estimated them using other studies' reported test sensitivities and specificities. The +LR and –LR were similar across settings and represent minimal increases in the likelihood of dying within 1 year.

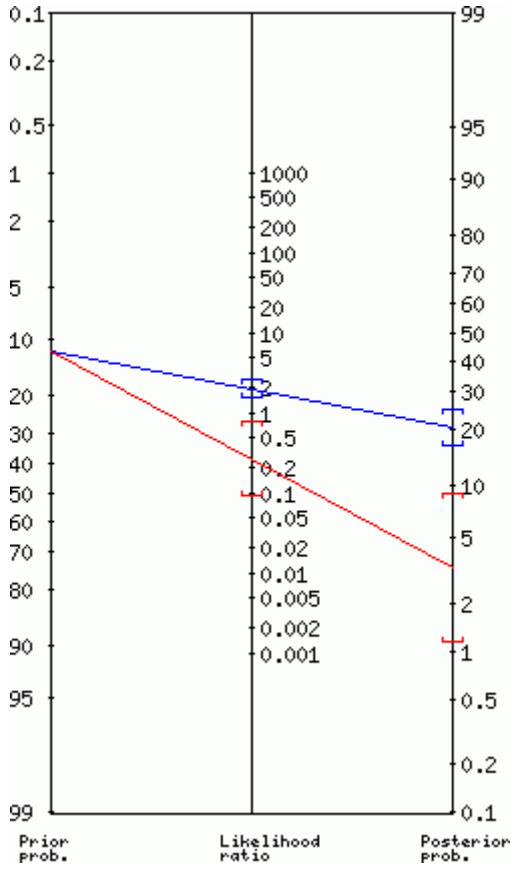

Figure 3 Fagan's nomogram for the overall sample. Based on a pretest probability of dying within 1 year of 12%, the blue line shows a post-test probability of a patient with a positive Surprise Question (+SQ) dying within a year of 20% (95% CI 17% to 25%) according to the positive likelihood ratio (+LR) of 1.98. A +SQ increases the probability of a patient dying within 1 year by 8 percentage points. The red line shows a post-test probability of a patient with a negative SQ (–SQ) dying within a year of 3% (95% CI 1% to 9%) according to the negative LR (–LR) of 0.22. A –SQ decreases the probability of a patient dying within 1 year by 9 percentage points.

Interpretations for clinical practice

When there is high test sensitivity, fewer false negatives occur, which increases the chance that patients with HF in need of ACP or PC will receive these services. Since determining sensitivity was the main criterion to evaluate the SQ's performance, we consider it is an acceptable prognostic screening tool for patients with HF. Yet, there remains a significant percentage of patients with HF within the last year of their life who might be left out (15% of the whole sample) and might benefit from ACP or PC. Both in this population and in the literature, the SQ predicts 1-year mortality well among patients with HF.[12 13] However, there are several aspects of the tool that users should be aware of before applying it in clinical practice.

First, the SQ's performance depends on the clinical expertise and experience of the staff using it, as well as their knowledge of the patient with HF. For example, Straw *et al* conducted a study that evaluated the SQ's performance among an inpatient population with HF.[12] They showed that the SQ's sensitivity decreased from 85% when cardiologists used the tool to 75% when physicians in training used it; and from 90% when HF nurses used the SQ to 66% among non-specialist nurses. Second, screening strategies such as the SQ do not afford assessment of the complexity of patients' needs or the level of training that professionals should have to address ACP discussions or provide PC .

Finally, a major limitation of this screening tool is that it potentially excludes patients who will survive longer than 1 year but still would benefit from ACP or PC. Even in scenarios when the SQ predicts mortality well, using life expectancy as the sole criterion for assessing the need for ACP or PC is limiting. We consider the SQ can be used as a screening tool to initiate ACP or refer to PC for patients with a life expectancy of less than 1 year. However, we also consider the parallel use of needs assessment tools for patients with life expectancy of more than 1 year. For example, two recent systematic reviews of available tools to assess PC needs in patients with HF concluded that the Needs Assessment Tool: Progressive Disease-Heart Failure (NAT: PD-HF) was the most appropriate tool to determine the unmet needs of patients with HF.[30 31]

The NAT: PD-HF offers an alternative solution to several previously discussed points: it is not based on survival prognosis or severity factors, but it comprehensively evaluates different spheres.

The NAT: PD-HF is made of questions to determine a patient's physical and psychological symptoms, daily life activity limitations, spiritual concerns, financial or legal concerns, and health-related information needs. Although the NAT: PD-HF does not focus on PC needs or referrals for specialised PC services, it does assess patients' unmet needs and matches those needs with appropriate services, including specialised PC and other services. Finally, the NAT: PD-HF assesses the patients' and the caregivers' needs, including the caregiver's ability to take care of the patient.[32] However, in clinical situations where there is not enough time to gather answers to the NAT: PD-HF's comprehensive question sets, there is enough time for the clinician to ask themselves the singular SQ, which is better than no needs screening at all.

Strengths and limitations of this study

The low proportion of patients classified as NYHA III/IV might be a limit of the generalisability of our results. The risk of mortality increases with a higher NYHA classification.[33] Among our population, 80% of the patients were classified as NYHA I or II. As expected, the mortality rate was low compared with what has been reported in other HF clinics where mortality is around 30%.[12 13] However, as we conducted different subgroup analyses, including analysis according to NYHA functional class, we provide different analyses

that can be assessed according to each HF clinic population.

As most encounters between healthcare personnel and patients occur in ambulatory settings, a strength of this study is the contribution of the SQ's psychometric profile for ambulatory patients with HF. In addition, when screening for limited life expectancy and the need to initiate ACP, since the outpatient population are more stable patients, ACP needs may be overlooked. The systematic use of a tool such as the SQ could help identify patients with HF eligible for end-of-life care without being limited by having ACP discussion or making decisions within unstable medical contexts. Furthermore, to support better generalisation, this study provides substantial data regarding subcategories.

CONCLUSION

The SQ showed a good sensitivity predicting 1-year mortality for patients in ambulatory HF clinics. However, the likelihood of dying within 1 year increases little when having a +SQ. We suggest that the SQ can be used as a starting point to identify patients who might benefit from having an ACP discussion or a referral to PC due to limited life expectancy toward a patient's end of life.

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Contributors LFAO designed the study and collected the data. VG-J performed the analysis, drafted the manuscript and designed the figures. NG-J designed the figures and contributed to the analysis of results. LFAO, CS, AK, JJV, NG-J, SE and MM did a critical revision of the manuscript. All authors discussed the results and commented on the manuscript. VG-J and MM are responsible for the overall content of the manuscript.

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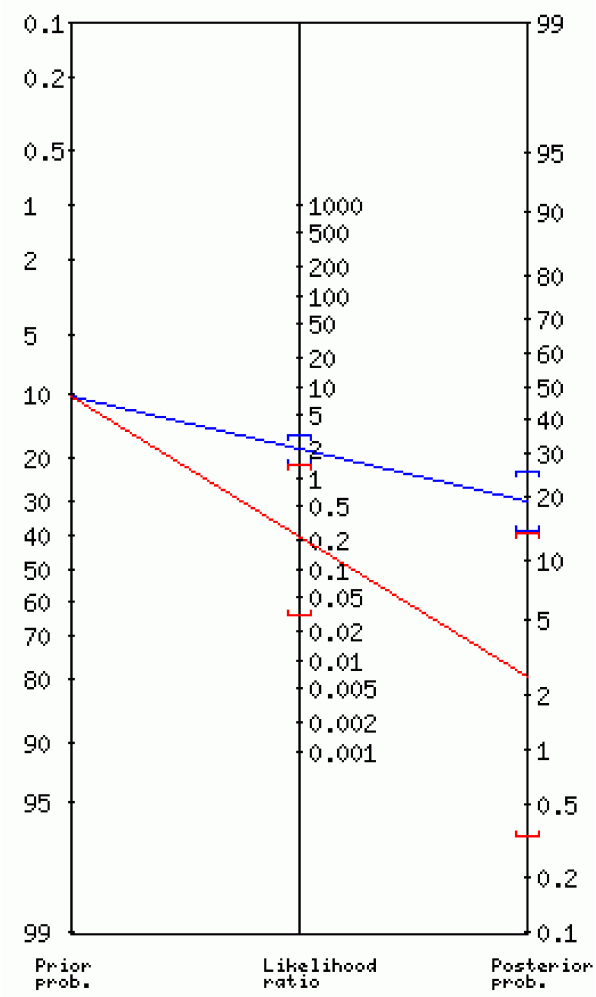
Supplementary Table 1. Two by two table

		1-year mortality		**Total**
Surprise question		+	-	
	+	17 **a**	66 **b**	83 **a+b**
	-	3 **c**	88 **d**	91 **c+d**
Total		20 **a+c**	154 **b+d**	174

Supplementary Table 2. Performance of the SQ to predict 1-year mortality among ambulatory patients with HF

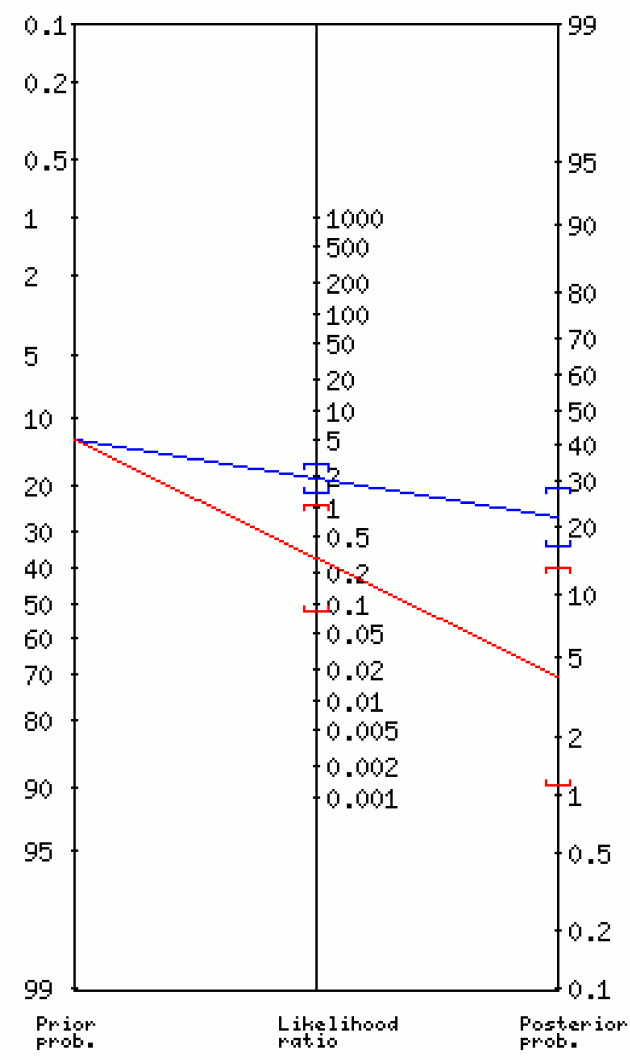
Sensitivity	0.85 **a/(a+c)**	Specificity	0.57 **d/(d+b)**
Positive Likelihood Ratio (+LR)	1.98 **Sensitivity/1-Specificity**	Negative Likelihood Ratio (-LR)	0.26 **1-Sensitivity/Specificity**
Positive Predictive Value (PPV)	0.20 **a/(a+b)**	Negative Predictive Value (NPV)	0.97 **d/(c+d)**

Supplementary Figure 1. Fagan´s nomogram for women



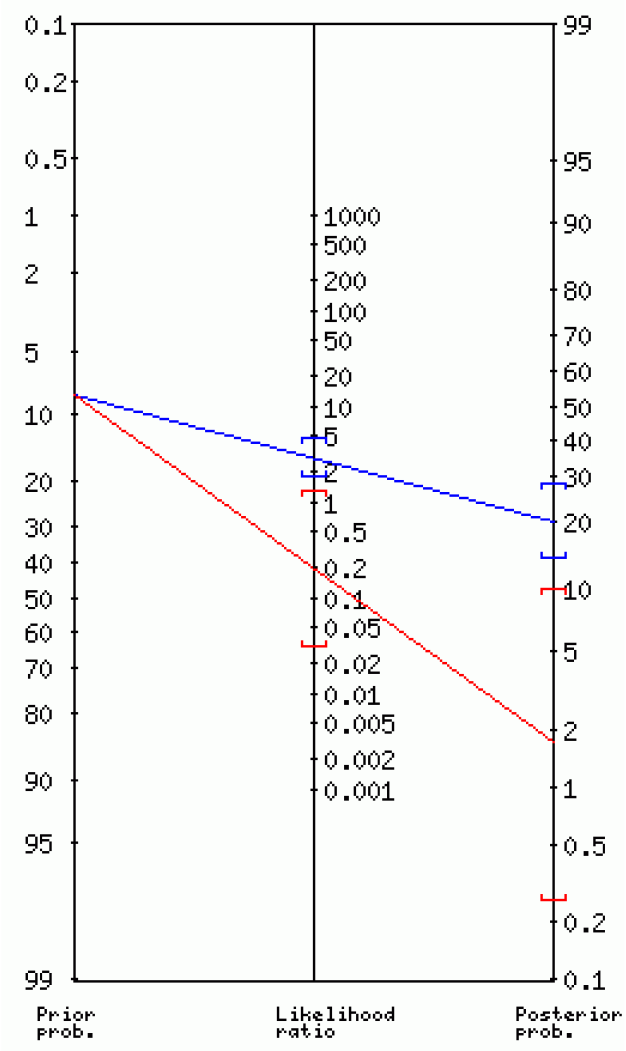
Based on a pre-test probability of dying within 1 year of 10%, the blue line shows a post-test probability of a patient with a positive Surprise Question (+SQ) dying within 1 year of 19% (95% CI, 14%-25%) according to the +LR of 2.04. A +SQ increases the probability of a patient dying within 1 year by 9 percentage points.
The red line shows a post-test probability of a patient with a negative SQ (–SQ) dying within one year of 2% (95% CI, 0%-14%) according to the negative likelihood ratio (–LR) of 0.22. A -SQ decreases the probability of a patient dying within 1 year by 8 percentage points.

Supplementary Figure 2. Fagan´s nomogram for men



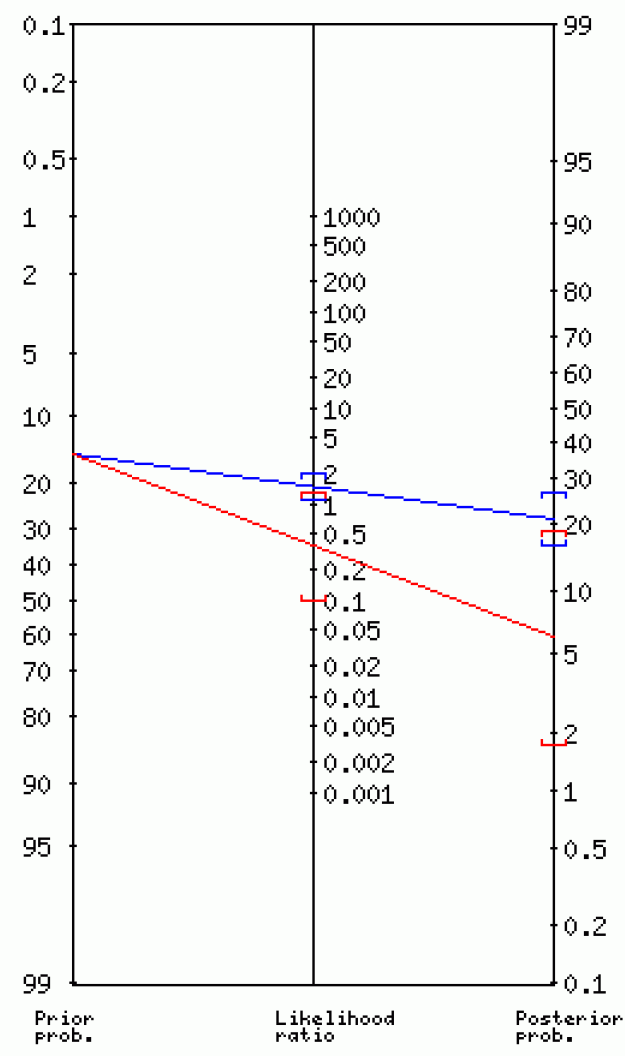
Based on a pre-test probability of dying within 1 year of 13%, the blue line shows a post-test probability of a patient with a positive Surprise Question (+SQ) dying within a year of 22% (95% CI, 16%-28%) according to a positive likelihood ratio (+LR) of 1.94. A +SQ increases the probability of a patient dying within 1 year by 9 percentage points. The red line shows a post-test probability of a patient with a negative SQ (–SQ) dying within a year of 4% (95% CI, 1%-13%) according to the negative LR (–LR) of 0.29. A -SQ decreases the probability of a patient dying within 1 year by 9 percentage points.

Supplementary Figure 3. Fagan´s nomogram for those aged under 70



Based on a pre-test probability of dying within 1 year of 8%, the blue line shows a post-test probability of a patient with a positive Surprise Question (+SQ) dying within 1 year of 20% (95% CI, 14%-28%) according to the positive likelihood ratio (+LR) of 2.86. A +SQ increases the probability of a patient dying within 1 year by 12 percentage points. The red line shows a post-test probability of a patient with a negative SQ (–SQ) dying within a year of 2% (95% CI, 0%-10%) according to the negative LR (–LR) of 0.20. A -SQ decreases the probability of a patient dying within 1 year by 6 percentage points.

Supplementary Figure 4. Fagan´s nomogram for those aged 70 or older



Based on a pre-test probability of dying within 1 year of 15%, the blue line shows a post-test probability of a patient with a positive Surprise Question (+SQ) dying within 1 year of 21% (95% CI, 16%-26%) according to the positive likelihood ratio (+LR) of 1.49. A +SQ increases the probability of a patient dying within 1 year by 6 percentage points. The red line shows a post-test probability of a patient with a negative SQ (–SQ) dying within a year of 6% (95% CI, 2%-19%) according to the negative LR (–LR) of 0.36. A -SQ decreases the probability of a patient dying within 1 year by 9 percentage points.

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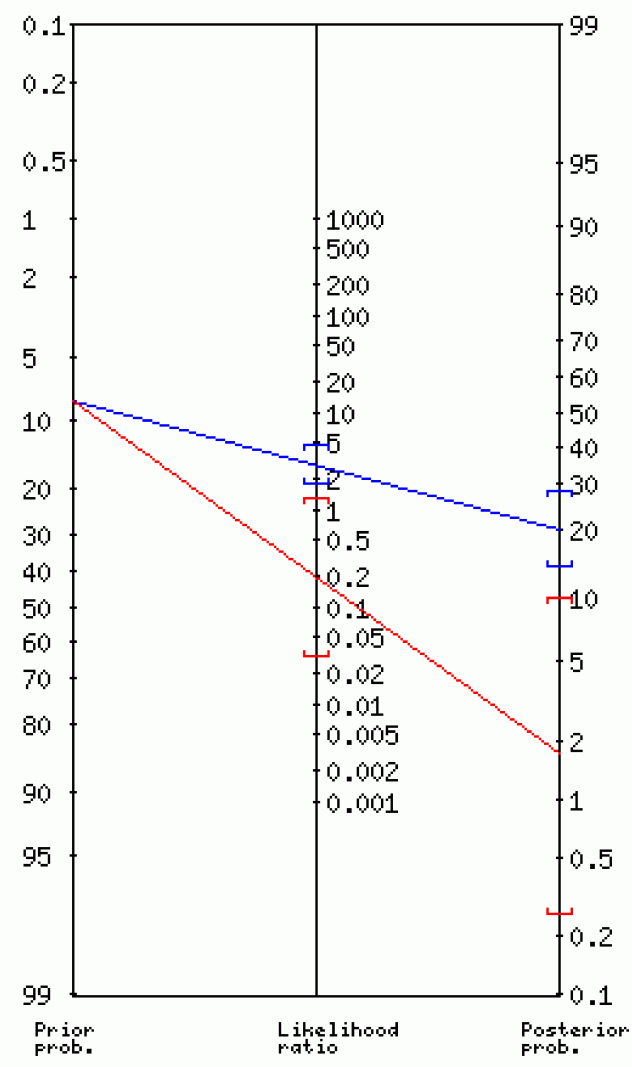
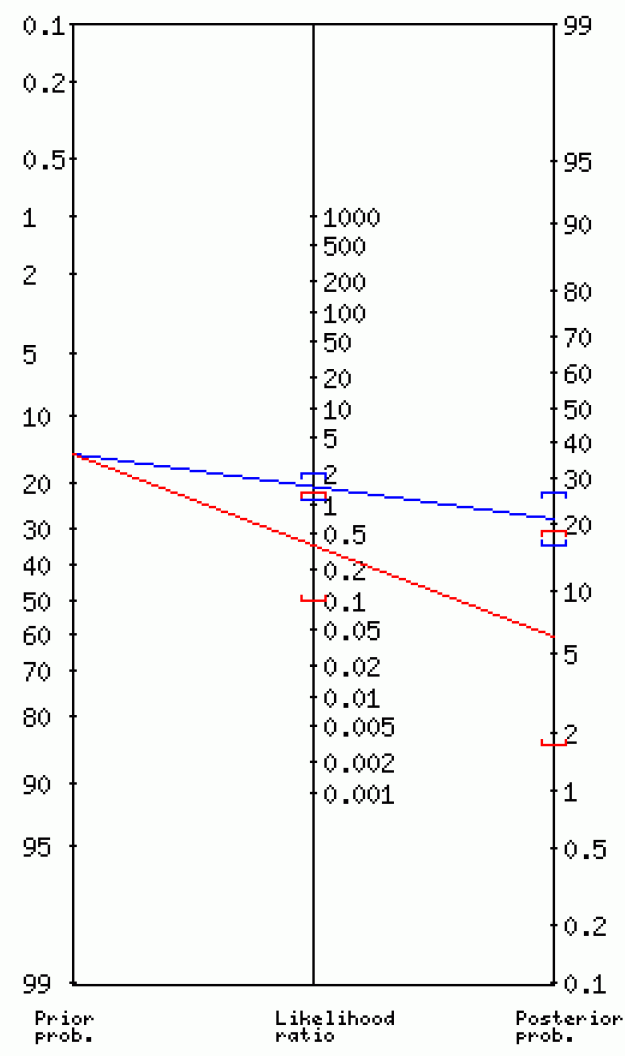
Supplementary Figure 5. Fagan´s nomogram for those with reduced ejection fraction (HFrEF)



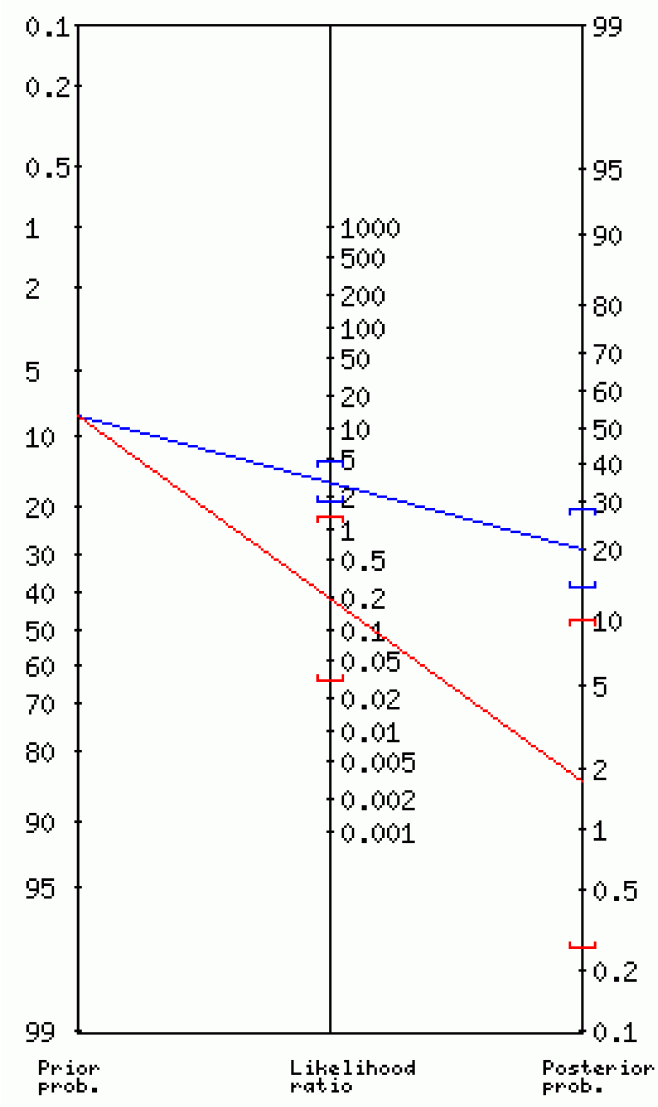
Based on a pre-test probability of dying within 1 year of 11%, the blue line shows a post-test probability of a patient with a positive Surprise Question (+SQ) dying within 1 year of 20% (95% CI, 16%-24%) according to the positive likelihood ratio (+LR) of 1.98. A +SQ increases the probability of a patient dying within 1 year by 9 percentage points. The red line shows a post-test probability of a patient with a negative SQ (–SQ) dying within a year of 2% (95% CI, 0%-11%) according to the negative LR (–LR) of 0.14. A -SQ decreases the probability of a patient dying within 1 year by 9 percentage points.

Supplementary Figure 6. Fagan´s nomogram for those with mildly reduced ejection fraction (HFmrEF)



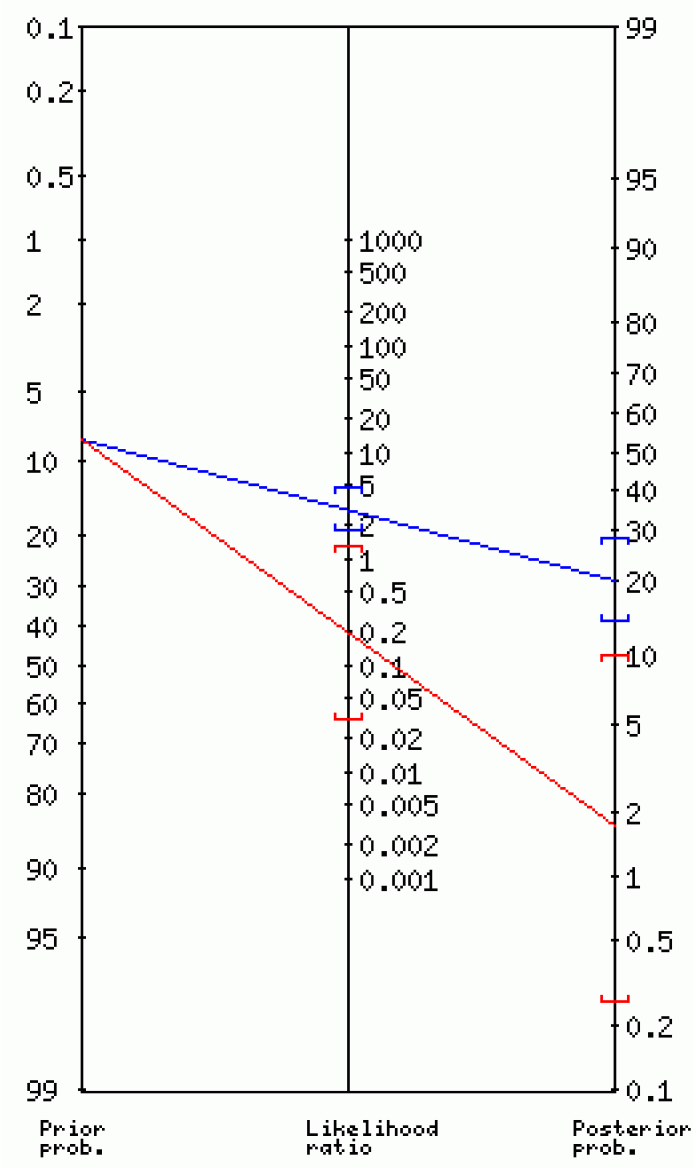
Based on a pre-test probability of dying within 1 year of 11%, the blue line shows a post-test probability of a patient with a positive Surprise Question (+SQ) dying within 1 year of 25% (95% CI, 10%-49%) according to the positive likelihood ratio (+LR) of 2.78. A +SQ increases the probability of a patient dying within 1 year by 14 percentage points. The red line shows a post-test probability of a patient with a negative SQ (–SQ) dying within a year of 5% (95% CI, 1%-21%) according to the negative LR (–LR) of 0.44. A -SQ decreases the probability of a patient dying within 1 year by 6 percentage points.

Supplementary Figure 7. Fagan´s nomogram for those with preserved ejection fraction (HFpEF)



Based on a pre-test probability of dying within 1 year of 13%, the blue line shows a post-test probability of a patient with a positive Surprise Question (+SQ) dying within 1 year of 20% (95% CI, 11%-34%) according to the positive likelihood ratio (+LR) of 1.63. A +SQ increases the probability of a patient dying within 1 year by 7 percentage points. The red line shows a post-test probability of a patient with a negative SQ (–SQ) dying within a year of 7% (95% CI, 1%-29%) according to the negative LR (–LR) of 0.46. A -SQ decreases the probability of a patient dying within 1 year by 6 percentage points.

Supplementary Figure 8. Fagan´s nomogram for those at NYHA class I/II



Based on a pre-test probability of dying within 1 year of 8%, the blue line shows a post-test probability of a patient with a positive Surprise Question (+SQ) dying within 1 year of 14% (95% CI, 10%-20%) according to the positive likelihood ratio (+LR) of 1.94. A +SQ increases the probability of a patient dying within 1 year by 6 percentage points. The red line shows a post-test probability of a patient with a negative SQ (–SQ) dying within a year of 4% (95% CI, 1%-9%) according to the negative LR (–LR) of 0.44. A -SQ decreases the probability of a patient dying within 1 year by 4 percentage points.

3.2. Article 2.

Prevalence and characteristics of patients with heart failure needing palliative care

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Contribution: I participated in the conceptualization of study. I performed the analysis, made the figures and wrote the first draft of the manuscript. After that, I incorporated coauthors and reviewers' comments.

Prevalence and characteristics of patients with heart failure needing palliative care

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Tables: 2

Figure: 1

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Abstract

Background: Few hospitals and heart failure (HF) clinics offer concurrent palliative care (PC) together with life-prolonging therapies. To know the prevalence of patients in HF clinics needing PC and useful tools to recognize them are the first steps to extending PC in those settings. However, it is still unknown whether tools commonly used to identify patients with HF needing PC can correctly distinguish them. Two systematic reviews found that the NECesidades PALiativas (NECPAL) tool was one of the two most commonly used tools to asses PC needs in HF patients. Therefore, we assessed 1) the prevalence of PC needs in HF clinics according to the NECPAL tool, and 2) the characteristics of the patients identified as having PC; mainly, their quality of life (QoL), symptom burden, and psychosocial problems.

Methods: This cross-sectional study was conducted at two HF clinics. We assessed the prevalence of PC in the overall sample and in subgroups according to clinical and demographic variables. We assessed QoL, symptom burden, and psychosocial problems using the 12-Item Short-Form Health Survey (SF-12), the Kansas City Cardiomyopathy Questionnaire (KCCQ) and the Edmonton Symptom Assessment Survey (ESAS). We compared the results of these tools between patients identified as having PC needs (+NECPAL) and patients identified as not having PC needs (–NECPAL).

Results: Among the 178 patients, 78 (44%) had PC needs. The prevalence of PC needs was twice as nigh in patients NYHA III/IV as in patients NYHA I/II and almost twice as high in patients older than 70 years as in patients younger than 70 years. Compared to –NECPAL patients, +NECPAL patients had worse QoL, more severe shortness of breath, tiredness, drowsiness, and pain, and more psychosocial problems.

Conclusion: The prevalence of PC needs in outpatient HF clinics is high and is even higher in older patients and in patients at more advanced NYHA stages. Compared to patients identified as not having PC needs, patients identified as having PC needs have worse QoL, more severe symptoms, and greater psychosocial problems. Including a PC provider in the multidisciplinary team of HF clinics may help to assess and cover these needs.

Key words

Heart failure, palliative care, needs assessment, prognosis, patient-centered care, health services needs and demands

Background

Through the heart failure (HF) trajectory, patients have a wide range of physical and psychological symptoms that affects their quality of life (QoL) (1). According to the World Health Organization (WHO), palliative care (PC) is an approach that aims to improve the QoL of patients and families facing challenges associated with a chronic condition, whether physical, psychological, social, or spiritual (2). Despite current recommendations to incorporate a PC approach into the standard care of patients in advanced stages of HF (1, 3-6), important gaps have been identified in its delivery (7). Although widely used for oncological patients, few hospitals and HF clinics offer concurrent PC together with life-prolonging therapies. To know the prevalence of patients in HF clinics needing PC and useful tools to recognize them are the first steps to extending PC in those settings. However, it is still unknown whether tools commonly used to identify patients with HF needing PC can correctly distinguish them. The NECesidades PALiativas (NECPAL) tool was created to identify in clinical practice patients with chronic disease and a limited life expectancy who might benefit from PC (8). The tool has been widely used in clinical practice in different countries and is currently available in several languages (8-11). Two recent systematic reviews found that, among the studies assessing PC needs in patients with HF, the NECPAL tool was one of the two most commonly used screening tools (12, 13).

Methods

This study was conducted and reported in accordance with the STROBE guidelines (14).

Aim

In this study, we assessed 1) the prevalence of PC needs in outpatient HF clinics according to the NECPAL tool, and 2) the characteristics of the patients identified as having PC needs; mainly, their health-related QoL, symptom burden, and psychosocial problems, assessed using the 12-Item Short-Form (version 2) Health Survey (SF-12) (15), the Kansas City Cardiomyopathy Questionnaire (KCCQ) (16), and the Edmonton Symptom Assessment Survey (ESAS) (17).

Study design and setting

This cross-sectional study was conducted at two HF clinics. Both clinics are part of tertiary care institutions in Medellin (Colombia) that are referral centers for patients with cardiovascular disease. They offer comprehensive, multidisciplinary care that includes clinical follow-up by HF cardiologists, nursing education and telephone follow-up, cardiac rehabilitation, and a psychoeducational program for both patients and their families.

Participant selection

We invited consecutive eligible patients to participate in the study. Patients were eligible to participate if they were ≥ 18 years old and were already enrolled in the HF clinic. New patients in HF clinics may not be receiving optimal treatment according to clinical guidelines; therefore, the first consultations are fundamental for adjusting the treatment if necessary. An inclusion criterion was to have attended at least two appointments at the HF clinic before enrolling in the study so that the cardiologist could evaluate the patient under optimal treatment and rule out inadequate management as a cause of symptoms. There were no exclusion criteria.

Ethical aspects

All the participants provided informed consent before the enrolment. The study was carried out according to the guidelines of the Declaration of Helsinki (18) and was granted ethical approval.

Data collection

Enrollment occurred between October 2017 and November 2018. Participants were asked to fill out three instruments: the SF-12 (15), the KCCQ (16), and the ESAS (17). A research assistant was available to support patients in case of queries when answering the instruments. A researcher scored the answers from the SF-12 and the KCCQ instruments. The attending cardiologist filled out the NECPAL tool (8).

Sociodemographic and clinical characteristics

To describe the population included in the study, we obtained patient sociodemographic characteristics and clinical variables from electronic medical records. Sociodemographic characteristics included age, sex, marital status, and religious affiliation. Clinical variables included left ventricular ejection fraction (LVEF), number of hospitalizations in the last year, presence of an implantable cardiac device, functional class according to the New York Heart Association (NYHA), comorbidities, and medications. Comorbidities included atrial fibrillation, type 2 diabetes mellitus, kidney disease, lung disease, coronary artery disease, obstructive sleep apnea, and hypothyroidism. Medications included angiotensin-converting enzyme inhibitors, beta-blockers, and angiotensin receptor blockers.

The NECPAL CCOMS-ICO (NECPAL) tool

The NECPAL CCOMS-ICO© tool (in Spanish, NECesidades PALiativas; in English, Palliative Needs) (8) consists of four blocks of questions 1) The surprise question, which is a reflexive question the doctor or another health care provider asks about the patient´s prognosis: would I be surprised if this patient dies within the next 12 months? A surprise question is positive if the health care provider's answer is no, I would not be surprised. In this event, the health care provider continues assessing the other three blocks. 2) Request for PC care by health professionals or the patient/family, 3) clinical markers of health status and frailty that mainly focus upon nutrition, functional status, emotional distress, and comorbidities, and 4) disease-specific clinical prognostic markers. Patients with a positive NECPAL (+NECPAL) are those in need of PC. A patient is considered to have a +NECPAL if block 1, the surprise question, is positive and at

least one of the other three blocks is positive. Otherwise, patients have a negative NECPAL (–NECPAL) and, according to the tool, do not need PC.

The 12-Item Short-Form Health Survey

This 12-item SF-12 is a subset of the SF-36 Survey, which is one of the most widely used instruments to evaluate health-related QoL. We used a Spanish version of the survey that had been validated previously and shown good internal consistency with a Cronbach´s alpha of 0.7 at its validation (15). The survey score ranges from 0 to 100, with higher scores indicating better QoL. It assesses subjects´ perception of their health and their limitations in activities of daily life. The 12 items are grouped in eight subscales from which two summary measures derive. The physical summary is derived from the subscales physical function, physical role, body pain, and general health, and the mental summary results from the subscales vitality, social function, emotional role, and mental health.

The Edmonton Symptom Assessment System (ESAS)

This tool evaluates the presence and severity of common symptoms in the PC context. We used a previously validated Spanish version of the survey that assess 10 symptoms: pain, tiredness, drowsiness, nausea, lack of appetite, shortness of breath, depression, anxiety, sleep disturbances, and wellbeing, and an additional symptom that the patient is free to name (17). The scores range from 0 to 10, with higher scores indicating worse severity of the item assessed and 0 indicating its absence.

The Kansas City Cardiomyopathy Questionnaire (KCCQ)

This questionnaire was designed to quantify the health status of patients with heart failure and its impact on their QoL. We used a previously validated Spanish version of the questionnaire that consists of 23 items that are grouped in seven dimensions: physical limitations; stability, frequency, and severity of symptoms; self-efficacy; QoL; and social limitations. In addition, two summary scores are calculated: the clinical summary and the general summary (16). The score ranges from 0 to 100, with higher scores indicating better QoL.

Data analysis

Categorical data were summarized as count (%). Continuous variables were summarized as mean (SD) if they had a normal distribution or as median (interquartile ranges [IQR]) if they had a non-normal distribution. We assessed normality using Q-Q plots.

Sample size calculation

For the sample size calculation, we assumed a prevalence of PC needs in HF programs of 50% due to the lack of information in the literature. With an expected proportion of PC need of 50%, a 95% confidence level, and a precision of 5%, the required sample size was 178 patients.

Prevalence of palliative care needs according to NECPAL tool

The prevalence of patients with PC needs was calculated using the proportion of patients with +NECPAL (numerator) out of the total number of patients included in the study (denominator). We assessed the prevalence within age groups, sex, NYHA functional class, and LVEF classification. To do this, we created a categorical variable for age according to the median, and another for LVEF as follows: reduced if LVEF was ≤40%, mildly reduced if LVEF was between 41% and 49%, and preserved with LVEF ≥50% (19). We compared prevalence between categories with a chi-square test.

Characteristics of the patients with heart failure identified as having palliative care needs

Palliative care aims to improve QoL by assessing and treating pain and other physical and psychosocial problems(20). Therefore, we compared NECPAL groups (–NECPAL and +NECPAL) according to health-related QoL, pain, other physical problems, and psychosocial problems. We evaluated these characteristics using the F-12, the KCCQ, and the ESAS.

We used the Mann-Whitney U test to compare scores between groups. All analyses were performed using STATA release 15 (Stata Corp, College Station, Texas).

Health-related quality of life

We used physical and mental summaries of the SF-12, and the QoL dimension from the KCCQ to assess health-related QoL.

Pain

We used the subscale body pain of the SF-12 and extracted the pain score from the ESAS.

Other physical problems

Other physical problems included tiredness, drowsiness, nausea, lack of appetite, shortness of breath, and sleep disturbances. These were extracted from the ESAS.

Psychological problems

To assess psychological problems, we used the emotional role and mental health subscales of the SF-12 and the depression and anxiety scores from the ESAS.

Social problems

The subscale social function was extracted from the SF-12 and the dimension social limitation from the KCCQ.

Results

General characteristics of the participants included in the study

Of the 184 patients who met the inclusion criteria, 178 accepted participation, 89 from each HF clinic (**Figure 1**).

Table 1 shows the baseline demographic and clinical characteristics of the 178 participants. The population had a median age of 70 (58-77) and 99 (56%) were male. The majority (86, 48%) were classified as NYHA class II, followed by NYHA I (57, 32%), and NYHA III (34, 19%). Only one patient was classified as NYHA IV. The majority of the patients (118, 66%) had a reduced LVEF. Among the remainder, 29 (16%)

had a mildly reduced LVEF, and 31 (18%) a preserved LVEF. Among the 73 patients with an implantable cardiac device, 45 (62%) had an implantable cardioverter defibrillator.

Patients from the two HF clinics had similar characteristics; they were mainly patients with reduced ejection fraction, male, and at NYHA II. The prevalence of hypertension, coronary disease, diabetes mellitus, COPD, and chronic kidney disease, and use of implantable cardioverter-defibrillator was also similar (**Supplementary Table 1**).

Prevalence of palliative care needs according to NECPAL tool

Among the 178 patients, 78 (44%) had PC needs (+NECPAL). According to question number two of the tool, cardiologists considered almost half of them (40 patients) to need PC. Cardiologists also considered four other patients to need PC despite those patients having a –NECPAL due to a negative surprise question (yes, the physician would be surprised by patient death). The median age of patients with +NECPAL was 74 (IQR 64-82), and the median age of patients with –NECPAL was 65 (IQR 54-72).

The prevalence of PC needs in patients at NYHA III/IV was two times fold the prevalence in patients at NYHA I/II (77% vs 36%). The prevalence of PC among patients older than 70 years was almost two times fold the prevalence in patients under or equal to 70 years (57% vs 30%). There was no difference between PC needs of men and women, nor across LVEF categories (**Table 2**).

Characteristics of the patients with heart failure identified as having palliative care needs

Patients classified as +NECPAL had lower scores on the physical and mental summaries of the SF-12, and on the QoL dimension of the KCCQ, with a difference of at least 15 points for each score compared to those classified as –NECPAL (**Table 3**). A lower score on the SF-12 body pain subscale and a higher score on the ESAS pain item in the +NECPAL group indicate more severe pain in this group. Other physical problems extracted from the ESAS, mainly tiredness, drowsiness, and shortness of breath, were more severe among those in the +NECPAL group, while there was no difference between groups for nausea, lack of appetite, and sleep disturbances. As indicated by its lower SF-12 mental health and emotional role

subscale scores, psychological problems were higher in the +NECPAL than the –NECPAL group. Furthermore, the depression item of the ESAS also showed greater severity in the +NECPAL group, though the ESAS anxiety item showed no difference between the groups. Social problems were worse in the +NECPAL group as shown by the lower scores on the social function subscale from SF-12 and the social limitation dimension from the KCCQ compared to the –NECPAL group (**Table 3**).

Discussion

Key results

To our knowledge, this is the first time the characteristics of patients with HF needing PC are evaluated. We found that among patients under optimal medical treatment in outpatient HF clinics, 44% met the NECPAL tool criteria to receive concurrent PC. Those with a +NEPCAL were mostly classified as NYHA III/IV and were older than those with a -NEPCAL. Compared to –NECPAL patients, +NECPAL patients had worse QoL according to the SF-12 and the KCCQ, more severe shortness of breath, tiredness, drowsiness, and pain, and more psychosocial problems.

Patients identified as needing palliative care

Given that patients may have PC needs regardless of life expectancy and disease severity, PC concurrent with life-prolonging therapies has gained importance in recent years (21, 22). In addition to the early identification of PC needs, it is advised to assess them in a comprehensive manner, taking into account physical symptoms, psychosocial factors, and health-related QoL (20). Despite the NECPAL tool is based on life expectancy and disease severity, we found that patients in need of PC were also those with more symptoms, more psychosocial problems, and lower disease-related QoL. This could be explained by the fact that patients with a more severe disease tend to be more symptomatic, which, in turn, impairs their QoL. As supported by previous evidence, patients and their informal caregivers considered the presence

of physical symptoms and their negative impact on psychosocial wellbeing as a sufficient reason to receive early concomitant PC (23).

Several studies have been described the complex interactions among symptoms, QoL, and prognosis. Pain is associated with disease severity and has been correlated with worse QoL, more frequent hospital admissions due to HF, and increased risk of mortality (24-26). Pain is also correlated with a higher prevalence of depression(24), which in turn contributes to decreased medication adherence and worse lifestyle habits, and thus poor prognoses (3, 27).

Our findings support a recent position statement by the PC task force of the European Society of Cardiology, highlighting that persistent symptom despite optimal treatment according to clinical guidelines should trigger a PC approach. Importantly, HF symptoms require equal therapeutic effort and attention as improving heart function and increasing survival (3).

Comparison with previous estimates of prevalence of PC needs in HF using NECPAL

We identified two previous studies utilizing the NECPAL tool to assess the prevalence of PC needs in populations with HF. The first study was of an inpatient population, classified as NYHA III or IV, and found a prevalence of PC of 55% (28). Compared to ours, this higher proportion of patients with PC needs can be explained by the setting since an inpatient population is decompensated or in worse condition than an outpatient population. The second study included patients from outpatient HF clinics and found a prevalence of PC of 32% (29). In that study, researchers assessed only HF-specific criteria of the NECPAL tool. Therefore, patients with HF needing PC due to comorbidities' severity may not have been captured in that study.

Strengths and limitations of this study

A strength of our study is the comprehensive evaluation of needs in patients with HF using multiple instruments. We provided consistent results supporting the utilization of NECPAL as an important tool to identify PC needs in patients with HF. Additionally, we assessed all the items in the NECPAL tool beyond

disease-specific clinical prognostic markers, as multiple comorbidities might be the source of or contribute to the need for PC.

Our study had virtually no representation of patients with NYHA functional class IV. As this study shows, PC needs increase with increasing NYHA classification. Therefore, the prevalence of PC needs among outpatient HF populations is probably higher than ours. However, the profile of patients from each of the two HF clinics included in this study was similar to each other. In both clinics, the majority of the patients were classified as NYHA II, followed by NYHA I, and NYHA III (**Supplementary Table 1**). Besides similarities between the two clinics, they are also similar to outpatient HF clinics from other studies (30-32), suggesting that the results of this study are generalizable to other ambulatory HF clinics.

Implications for clinical practice

HF clinics usually consist of a multidisciplinary team that includes cardiologists, HF-trained nurses, internists, nutritionists, psychologists, physical therapy, and social workers (33-35). According to evidence from observational studies and clinical trials, HF clinics are effective in reducing HF hospitalizations and all-cause mortality when compared to usual care (36-38). These clinics are widely available in countries such as Norway and Italy. However, given the increasing burden and complexity of HF treatment, the current number of HF centers in other countries may not be sufficient to ensure a comprehensive evaluation according to current standards and recommendations (39). Likely, more HF clinics or multidisciplinary HF programs will be created soon, so now is a proper time to consider including PC specialists or PC-trained staff as part of the team.

The tool we used to assess the PC needs (the NECPAL tool) starts with the Surprise Question. An advantage of the Surprise Question is that it integrates clinical knowledge and experience of the staff answering it, as well as their perception of the patient. However, this also can be a disadvantage for inexperienced staff. In accord with the tool's instructions, patients who were believed by the cardiologists to have a life expectancy greater than one year were judged as not in need of PC. Although we found that the patients

identified by the tool have more indication for PC in terms of symptoms and their related QoL, we consider important to highlight that some patients who might need PC were not identified by the tool because of the cardiologist's negative answer to the Surprise Question. Yet according to the cardiologist, four out of the 100 patients excluded by the tool needed PC. The NECPAL tool was created to identify people with PC needs and limited life expectancy. However, we consider its use could be extended to patients with a life expectancy greater than one year if the Surprise Question is used to help inform a PC referral decision rather than serve as a yes/no gateway to an additional assessment of PC needs in patients with HF.

Conclusion

A wide range of physical and psychological symptoms affects the QoL of people living with HF. The prevalence of PC needs in outpatient HF clinics is high and is even higher in older patients and in patients at more advanced NYHA stages. Compared to patients identified as not having PC needs, patients identified as having PC needs have worse QoL, more severe symptoms, and more psychosocial problems. Including a PC provider in the multidisciplinary team of HF clinics may help to assess and cover unmet needs in patients with HF, improving their QoL and that of their caregivers and families.

List of abbreviations

ESAS	Edmonton Symptom Assessment Survey
HF	Heart failure
KCCQ	Kansas City Cardiomyopathy Questionnaire
LVEF	Left ventricular ejection fraction
NECPAL	NECesidades PALiativas (Palliative needs)
NYHA	New York Heart Association
PC	Palliative care
QoL	Quality of life
SF-12	12-Item Short-Form (version 2) Health Survey
WHO	World health organization

Declarations

Ethics

The study was carried out according to the guidelines of the Declaration of Helsinki (18) and was approved by the Ethics Committees of the institutions involved in the study. All the participants provided informed consent before the enrolment including consent to publish using anonymized data.

Availability of data

The datasets used and/or analysed during the current study are available from the corresponding author upon request.

Competing interest

The authors have no conflicts of interest to declare that are relevant to the content of this article.

Funding

None

Authors contributions

LA, AK, and NGJ participated designing the study and co-supervising the study procedure. AK, JV supervised LA who was a residency student at the time the study was conducted. LA contributed to the acquisition of data and drafting of the manuscript. ML contributed with the data analysis. VGJ performed the statistical analyses and drafted the manuscript. CS, XGB, and SE contributed to the study design or results discussion with their clinical input. All authors participated in reviewing the manuscript. All authors read and approved the final manuscript.

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Figure 1. Flowchart of the participants included in the study

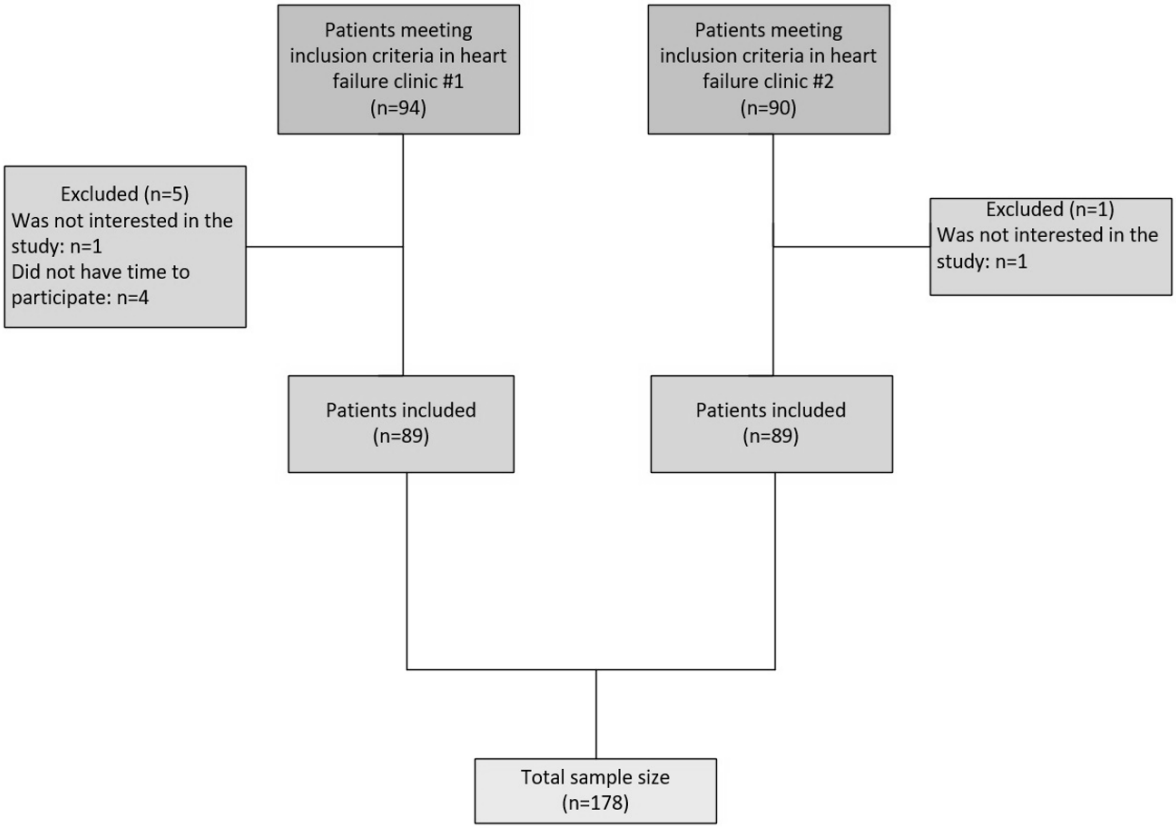

Table 1. Clinical and demographic characteristics of patients included in the study

	Patients included in the study (n=178)
Sociodemographic characteristics	
Age in years	70 (58-77)
Sex	
Men	99 (55.6)
Women	79 (44.4)
Marital status	
Single	25 (14.0%)
Married	94 (52.8%)
Separated or divorced	11 (6.2%)
Widow(er)	48 (27.0%)
Religious affiliation	
Yes	177 (99.4%)
No	1 (0.6%)
Clinical variables	
LVEF (%)	32 (25-45)
Classification according to the LVEF	
HFrEF	118 (66%)
HFmrEF	29 (16%)
HFpEF	31 (18%)
Hospitalizations in the last year	
0	1 (0.6%)
1	46 (25.8%
2	109 (61.2%)
>2	22 (12.4%)
Presence of implantable cardiac device	
Yes	73 (41.0%)
No	105 (59.0%)
NYHA functional class	
I	57 (32.0%)
II	86 (48.3%)
III	34 (19.1%)
IV	1 (0.6%)
Comorbidities	
Atrial fibrillation	53 (29.8%)
Type 2 diabetes mellitus	56 (31.5%)
Chronic kidney disease	86 (48.3%)
Chronic obstructive pulmonary disease	25 (14.0%)
Coronary artery disease	66 (37.1)
Obstructive sleep apnea	13 (7.3%)
Medication	
Beta-blockers	168 (94.4%)
ACE inhibitors	140 (78.7%)
ARBs	134 (75.3%)

Data presented as amount of patients and (%) for categorical data, or as median and (IQR) for continuous data.
LVEF: left ventricular ejection fraction; HFrEF: heart failure with reduced ejection fraction; HFmrEF: heart failure with mildly reduced ejection fraction; HFpEF: heart failure with preserved ejection fraction; ACE: angiotensin-converting-enzyme; ARBs: angiotensin receptor blockers.

Table 2. Prevalence of palliative care needs by subgroups

Variable	**-NECPAL (n=100)**	**+NECPAL (n=78)**	**p-value [a]**
Age (years)			<0.001
<70 (n=89)	62 (69.7%)	27 (30.3%)	
≥70 (n=89)	38 (42.7%)	51 (57.3%)	
Sex			0.674
Men (n=99)	57 (57.6%)	42 (42.4%)	
Women (n=79)	43 (54.4%)	36 (45.6%)	
LVEF classification			0.058
HFrEF (n=118)	63 (53.4%)	55 (46.6%)	
HFmrEF (n=29)	22 (75.9%)	7 (24.1%)	
HFpEF (n=31)	15 (48.4%)	16 (51.6%)	
NYHA functional class			
I/II (n=143)	92 (64.3%)	51 (35.7%)	<0.001
III/IV (n=35)	8 (22.9%)	27 (77.1%)	

[a] Chi-square test

LVEF: left ventricular ejection fraction; HFrEF: heart failure with reduced ejection fraction; HFmrEF: heart failure with mildly reduced ejection fraction; HFpEF: heart failure with preserved ejection fraction

Table 3. Performance of the NECPAL tool to identify palliative care needs in patients with HF

	Total (n=178)	–NECPAL (n=100)	+NECPAL (n=78)	p-value
Quality of life				
SF-12				
Physical summary	43.75 (31.25-75.00)	62.50 (37.50-78.13)	37.50 (18.75-56.25)	<0.001
Mental summary	66.87 (37.50-85.25)	74.38 (45.63-88.13)	53.13 (27.50-82.50)	0.002
KCCQ				
Quality of life dimension	66.66 (41.66-91.66)	75 (50-91.66)	58.33 (33.33-75.00)	0.002
Pain				
SF-12				
Body pain subscale	100 (50-100)	100 (75-100)	75 (50-100)	0.009
ESAS				
Pain	0 (0-5)	0 (0-2)	0 (0-6)	0.004
Other physical problems				
ESAS				
Tiredness	3.5 (0-7)	2 (0-5.5)	5 (0-8)	0.009
Drowsiness	0 (0-6)	0 (0-5)	2.5 (0-7)	0.019
Nausea	0 (0-0)	0 (0-0)	0 (0-0)	0.692
Lack of appetite	0 (0-5)	0 (0-3.5)	0 (0-5)	0.692
Shortness of breath	0 (0-5)	0 (0-3)	0 (0-6)	0.002
Sleep disturbances	3 (0-6)	2 (0-6)	4 (0-6)	0.321
Psychological problems				
SF-12				
Emotional role subscale	100 (0-100)	100 (50-100)	50 (0-100)	0.003
Mental health subscale	70 (50-90)	80 (50-95)	65 (40-90)	0.045
ESAS				
Depression	0 (0-5)	0 (0-4.5)	3 (0-8)	0.003
Anxiety	0 (0-5)	0 (0-5)	0 (0-6)	0.092
Social problems				
SF-12				
Social function subscale	50 (25-75)	75 (50-75)	50 (0-75)	<0.001
KCCQ				
Social limitation dimension	66.66 (41.66-100.00)	87.50(58.33-100.00)	43.75 (25.00-75.00)	<0.001

SF-12: 12-Item Short Form Survey; KCCQ: Kansas City Cardiomyopathy Questionnaire; ESAS: Edmonton Symptom Assessment System.

Supplementary Table 1. Clinical and demographic characteristics of patients included in the study

	HF clinic 1 (n=89)	HF clinic 2 (n=89)
Age	67 (56-76)	72 (62-77)
Sex		
Women	35 (39%)	44 (49%)
Men	54 (61%)	45 (51%)
LVEF (%)	35 (25-45)	31 (22-42)
LVEF classification		
HFrEF	52 (59%)	66 (74%)
HFmrEF	18 (20%)	11 (12%)
HFpEF	19 (21%)	12 (14%)
NYHA classification		
NYHA I	24 (27%)	33 (37%)
NYHA II	49 (55%)	37 (42%)
NYHA III	15 (17%)	19 (21%)
NYHA IV	1 (1%)	0
ICD	23 (26%)	22 (25%)
Diabetes mellitus	27 (30%)	29 (33%)
CAD	33 (37%)	33 (37%)
COPD	14 (16%)	11 (12%)
CKD	48 (54%)	38 (43%)
Hypertension	69 (78%)	58 (65%)

LVEF: left ventricular ejection fraction; HFrEF: heart failure with reduced ejection fraction; HFmrEF: heart failure with mildly reduced ejection fraction; HFpEF: heart failure with preserved ejection fraction; NYHA: New York Heart Association; ICD: implantable cardioverter defibrillator; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; CKD: chronic kidney disease

3.3. Article 3.

Validation of the German version of the Needs Assessment Tool: Progressive Disease – Heart Failure

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Contribution: I participated designing the study and co-supervising the study procedure. I did the analyses, made the figures and wrote the first draft of the manuscript. After that, I incorporated coauthors and reviewers' comments.

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Validation of the German version of the needs assessment tool: progressive disease-heart failure

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Abstract

Background: The Needs Assessment Tool: Progressive Disease-Heart Failure (NAT: PD-HF) is a tool created to assess the needs of people living with heart failure and their informal caregivers to assist delivering care in a more comprehensive way that addresses actual needs that are unmet, and to improve quality of life. In this study, we aimed to (1) Translate the tool into German and culturally adapt it. (2) Assess internal consistency, inter-rater reliability, and test–retest reliability of the German NAT: PD-HF. (3) Evaluate whether and how patients and health care personnel understand the tool and its utility. (4) Assess the tool's face validity, applicability, relevance, and acceptability among health care personnel.

Methods: Single-center validation study. The tool was translated from English into German using a forward–backward translation. To assess internal consistency, we used Cronbach´s alpha. To assess inter-rater reliability and test–retest reliability, we used Cohen´s kappa, and to assess validity we used face validity.

Results: The translated tool showed good internal consistency. Raters were in substantial agreement on a majority of the questions, and agreement was almost perfect for all the questions in the test–retest analysis. Face validity was rated high by health care personnel.

Conclusion: The German NAT: PD-HF is a reliable, valid, and internally consistent tool that is well accepted by both patients and health care personnel. However, it is important to keep in mind that effective use of the tool requires training of health care personnel.

Keywords: Needs assessment, Heart failure, Palliative care, Patient-centered care, NAT: PD-HF

Introduction

Heart failure (HF) is a global pandemic currently affecting at least 26 million people worldwide. Its prevalence is growing as the population ages and other risk factors increase [1]. Despite optimal recommended therapies, and apart from uncontrolled disease-related symptoms such as shortness of breath, pain, sleep disorders, and fatigue [2], people living with HF often suffer from other conditions such as depression and anxiety [3]. Moreover, taking care of or living with a person suffering from chronic HF can be stressful and burdensome [4]. Both patients with HF and their families are at increased risk of experiencing physical, emotional, and financial burdens that may impair their quality of life [5]. Failure to assess such burdens routinely and systematically in daily medical practice contributes to undertreatment and unnecessary suffering.

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Needs assessment tools are clinical decision aids, facilitating the detection of patient needs and the assignment of actions to address them according to the available care options. These tools used as a support and a starting point for delivering patient-centered care [6]. Two recent systematic reviews found six needs measurement tools that can be used with patients with HF [6, 7]. Both systematic reviews found that the most comprehensive of these tools and the only one created specifically for patients with HF is the "Needs Assessment Tool: Progressive Disease-Heart Failure" (NAT: PD-HF) [8].

The NAT: PD-HF was developed in 2013 by Australian researchers to help health care personnel identify the needs of patients with HF and their informal caregivers, and match them with the most appropriate services regardless of whether they may be psychology, social work, cardiology, specialized palliative care, or general medicine [8]. The NAT: PD-HF, more than a questionnaire, is a direct, face-to-face interaction guide aimed to increase the attention dedicated to patients and their narratives in a highly efficient and effective way. Clinical environments that optimize this attention, will not only improve the quality of care and patient and staff satisfaction, but also reduce care costs [9, 10]. The implementation of the NAT: PD-HF in the clinical practice could be a fundamental basis for strategies focusing on optimizing attention.

To date the NAT: PD-HF has been available in only English [8] and Dutch [11]. We therefore (1) translated the tool into German and culturally adapted it, (2) assessed psychometric characteristics of the translated NAT: PD-HF that include internal consistency, inter-rater reliability, and test–retest reliability, (3) evaluated whether and how patients and health care personnel understood the tool and its utility, and (4) assessed the face validity, applicability, relevance, and acceptability of the German NAT: PD-HF among health care personnel.

Methods

Study design

We conducted this work at Inselspital, the University Hospital of Bern, Switzerland, a tertiary academic hospital with a dedicated HF clinic and a specialized palliative care service. Translation and validation of the original tool was performed in accordance with the guidelines of the European Organisation for Research and Treatment of Cancer [12]. We performed separate forward and backward translations (Additional file 1), and evaluated internal consistency, inter-rater reliability, and test–retest reliability.

We surveyed patients (Additional file 2) and health care personnel (Additional file 3) to gauge their level of understanding of the NAT: PD-HF and perception of its utility. Face validity, applicability, relevance, and acceptability of the tool by health care personnel were assessed with interviews of personnel specializing in cardiology and palliative care (PC) at our institution (Additional file 4). Sociodemographic and basic clinical information of the participants was extracted from electronic medical records.

The original NAT: PD-HF tool

The NAT: PD-HF is a comprehensive tool designed for health care personnel to assess both a patient's and a main informal caregiver's physical, psychological, social, and spiritual needs [8]. It consists of three parts: the first one is a user guide explaining the purpose of the tool and how to complete it, the second is a questionnaire comprised of 20 items, and the third section has examples of what to address within each item of the questionnaire (Additional file 5). The questionnaire is subdivided into sections addressing four topics: (1) priority referral for further assessment, (2) patient well-being, (3) ability of the informal caregiver or family to care for the patient, and (4) caregiver well-being. For each question, health care personnel selects the level of concern together with the patient: (1) none, (2) some/potential, (3) significant. If there is some/potential or significant concern in one of the questions, the patient has unmet needs. The health care worker proceeds to choose an appropriate action: (1) directly manage it, (2) management by another care team member, or (3) refer. If the last option is chosen, the yellow box at the end of the questionnaire (under the heading: referral required for further assessment of care) should be filled in. In this section, there is the option to refer to other providers such as the patient's general practitioner, social worker, psychologist, specialist PC service, cardiologist, or other.

Translation and cultural adaptation

The NAT: PD-HF was translated from English to German using a forward–backward translation procedure and cultural adaptation by four translators, one of which was a professional medical text translator (Additional file 1). Cultural adaptation required minimal change to the third part of the NAT: PD-HF, which includes examples of what to address within each of the questionnaire items (Additional file 6). The second part of the NAT: PD-HF, the questionnaire itself, did not require any cultural adaptation. Therefore, we did not consider it necessary to validate the content of the culturally adapted version.

After pilot testing the translated tool with 19 patients, we made small adjustments to the translation, and in the recruitment process. The pilot test also revealed the need to train health care personnel who will use the

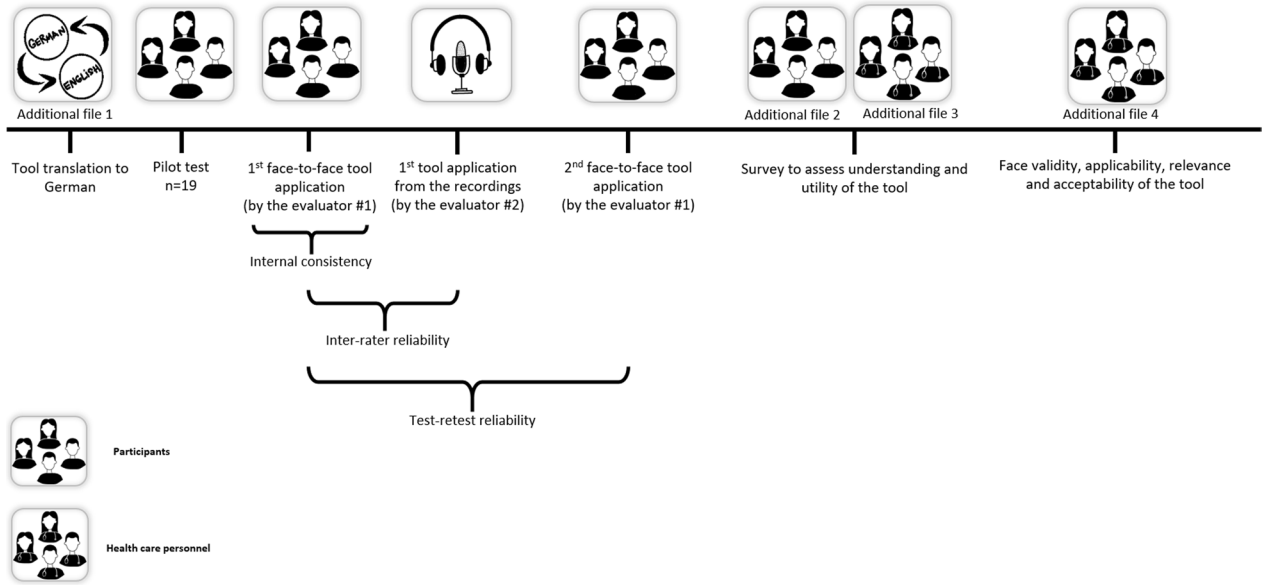

Fig. 1 Study procedure. Adobe Illustrator Draw was used to create the artwork

tool. Because of the adjustments after the pilot test, we excluded pilot participants from the final analysis.

Participants and recruitment

Eligible participants were adult patients (≥ 18 years of age) with an appointment at the Heart Failure Clinic at Inselspital Bern who had had at least one consultation in the clinic and who could fluently communicate in German. No specific stage or severity of HF was selected to ensure a representative, full spectrum of the disease.

Patients meeting the inclusion criteria received a study invitation package containing an invitation letter and study description, a participant information sheet and consent form, and a removable response card that patients could send back to the research team stating whether they were interested in taking part of the study or not. For those who were interested, we arranged an appointment with a study member immediately before or after their scheduled consultation at the HF clinic.

We evaluated patients' cognitive capacity by asking them three questions about the study after having explained its purpose and the content from the consent form. The questions were (1) what is the aim of the study? (2) In which patients will the study be performed? (3) As part of this study, will you have blood tests or ultrasounds? In case of satisfactory answers to the three questions, the interviewer proceeded with the signing of the consent form and the interview.

Study procedure

Using the tool with HF patients

Using the German version of the NAT: PD-HF a general practitioner trained in administering the tool directly queried the patient and, if present, an informal caregiver. From these data we estimated internal consistency (Fig. 1). The encounter was recorded to allow a second evaluator to provide data for gauging inter-rater reliability using the audio recording (Fig. 1). After 10 to 20 days, a second appointment was scheduled with the patient and the NAT: PD-HF was repeated face-to-face by the same evaluator who used the tool during the first assessment to provide data for gauging test–retest reliability (Fig. 1).

Assessing understanding of the German NAT: PD-HF and its utility

At the end of the study, we asked patients to tell us whether they thought the NAT: PD-HF questions were easy to understand and answer, and whether the questions might lead to better care. We obtained their answers via a five-point Likert scale ranging from "strongly agree" to "strongly disagree" (Additional file 2). We also asked about whether such questions are addressed in the course of their regular clinical consultations, and asked them what other questions they thought should be included in the tool.

We asked health care personnel representing all potential patient referral services to complete the same survey that patients completed (Additional file 3).

Face validity, applicability, relevance and acceptability

Interviews were conducted with the group of health care personnel to assess face validity, applicability, relevance, and acceptability of the German NAT: PD-HF (Additional file 4).

Data analysis

Internal consistency and sample size

We used Cronbach's alpha to assess internal consistency. Sample size calculations were based on Feldt´s formula [13]. To have 80% power at an alpha error of 5%, a lowest acceptable Cronbach´s alpha value of 0.75, and an expected value of 0.85, the sample size calculated was 66. Estimating a dropout rate of 10% we aimed to recruit 75 patients.

Inter-rater reliability and test–retest reliability

To assess the agreement between the results obtained from the physician using the NAT: PD-HF the first time and the results when the second evaluator filled out the tool listening the recordings, it is the inter-rater reliability, we used Cohen`s kappa. Since our data were ordinal, we used Cohen's weighted kappa. According to Cohen, 1968, the investigators choose the weights based on their own judgment [14]. Weights should be defined so that a weight of 1 (a full weight) is assigned to diagonal agreements, whereas decreasing weights are assigned to partial agreements depending on the problem under investigation [15]. We defined weight in such a way that the difference between "No concern" and "Some/potential concern" is less than the difference between "No concern" and "Significant concern." We similarly regarded the difference between "No concern" and "Some/potential concern" as greater than the difference between "Some/potential concern" and "Significant concern" since, in the second case, at least, the professionals agreed that some additional action should be taken. (The NAT: PD-HF instructions state that the professional using the tool should act on each identified need). We weighted the agreement of the two evaluators acknowledging these differences as presented in Additional file 7: Table 1.

The frequency of some/potential and significant concerns were low for some of the NAT: PD-HF items (Additional file 8: Table 2). We therefore decided to additionally report the results of the prevalence-adjusted and bias-adjusted kappa (PABAK) to avoid obtaining inflated agreements due to bias introduced by those low frequencies [16].

To assess the agreement between the results of the physician using the tool the first time and the results of the same physician using the tool the second time, it is the test–retest reliability, we estimated Cohen`s. For this calculation, we used the same weights presented in the Additional file 7: Table 1, as well as PABAK.

We interpreted inter-rater and test–retest reliabilities as near-perfect agreement if the kappa was greater than 0.81, as substantial if the kappa was between 0.61 and 0.80, moderate if it was between 0.41 and 0.60, and poor if it was less than 0.40 [17].

Unlike the first evaluator, the second evaluator was not always the same. Therefore, we did a sensitivity analysis to assess the inter-rater reliability for each one of the two second evaluators and define whether the data could be analyzed as a whole or if we needed to account for second evaluator differences.

Survey of patients and health care personnel

To summarize surveys results, "Strongly agree" and "Agree," were pooled with each other and "Disagree" and "Strongly disagree" were pooled with each other. The original five-point Likert scale was thus converted into a three-point scale for the analysis. All analyses were performed using STATA release 15 (Stata Corp, College Station, Texas).

Results

Participants

Between December 2019 and March 2020, 200 patients meeting the inclusion criteria were invited to participate. Among those invited, 70 patients consented to participate, giving a recruitment rate of 35% (Fig. 2). Though men predominated among the invitees, women (12/30, 40%) were slightly more willing to participate than men (58/170, 34%) (Fig. 2). There was no loss to follow-up.

A large majority of the patients included in the study were men (58/70, 83%); the mean age of all participants was 62.0 years (SD 13.7) (Table 1). The majority of the patients (45/70, 64%) had a reduced ($\leq$40%) left ventricular ejection fraction (LVEF). Among the remaining 25 patients, three had a borderline (41–49%) LVEF, and the LVEF was preserved ($\geq$50%) in 22. Half of the patients were classified as NYHA II, while none was classified as NYHA IV.

The interviews took an average of 24.1 min (SD 9.7) and the frequency of answers for each question is presented in Additional file 8: Table 2. Almost all the patients (67/70) reported the availability of an informal caregiver in case of need, the majority of whom are their partners (49/67, 73%). Patients were also asked about their need for more information about the course and prognosis of the disease and about treatment. Twenty-six reported a need for more information about one or more of seven aspects of living with HF; the largest need reported was that for information on legal and financial issues (Additional file 8: Table 2).

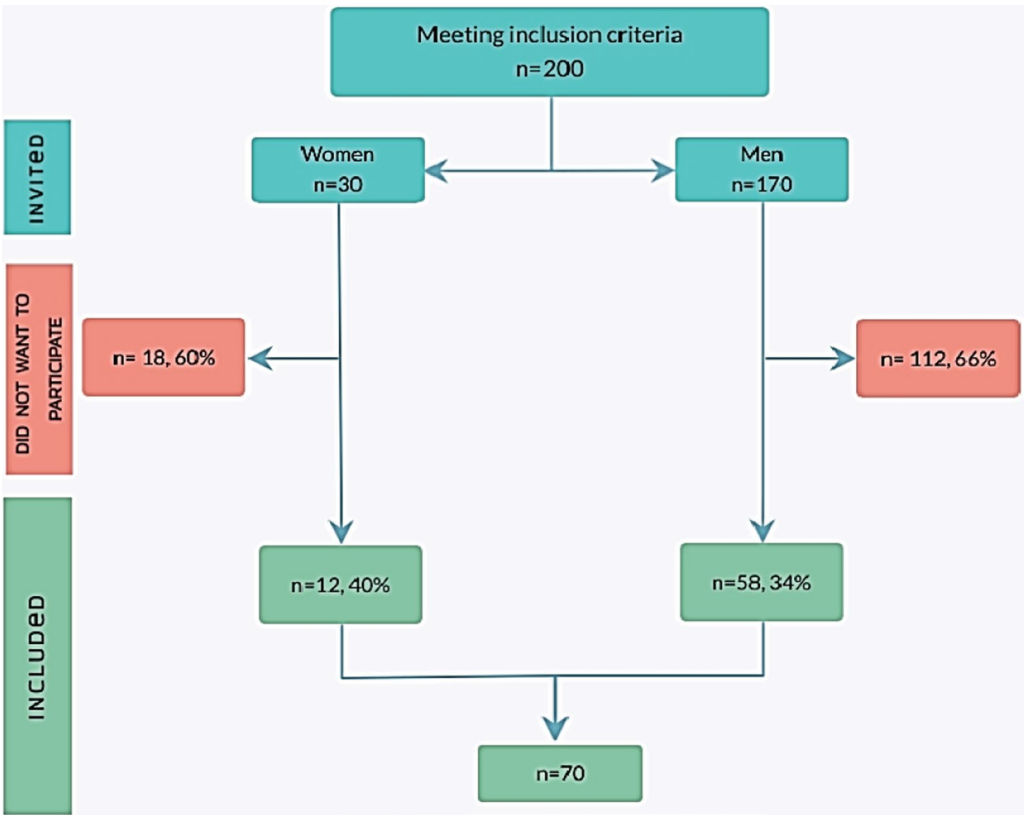

Fig. 2 Flowchart of the participants included in the study

Tool translation

The culturally adapted German translation of the NAT: PD-HF is presented in Additional file 1.

Psychometric characteristics of the German NAT: PD-HF

Internal consistency

With a Cronbach's alpha of 0.83, the internal consistency was high. Furthermore, when removing each question to evaluate how the alpha changed without each item Cronbach's alpha ranged from 0.80 and 0.84. Details of the psychometric characteristics are presented in Table 2.

Inter-rater reliability

Overall, based on Cohen´s kappa 13 out of the 14 questions reached at least moderate agreement (defined as a kappa value ≥ 0.41). Three questions about patient´s wellbeing in section "2" had an almost perfect, three had substantial and only one had poor agreement. This last question, that is the last one of the section, aims to identify the health beliefs of patients and cultural or social factors that might be barriers to health delivery. Among the six questions assessing the ability of the caregiver to take care of the patient in section "3", three questions were in almost perfect agreement, two had substantial agreement, and the remaining one moderate agreement. The question from section "4" about the caregiver´s wellbeing had substantial agreement (Table 2).

We observed no differences in the performance of the different first and second evaluators (Additional file 9: Table 3). Therefore, there was no need to account for second evaluators' differences in the analyses.

Test–retest reliability

The median time between the two appointments was 15 days (IQR 14–20) and none of the patients reported any significant change in his or her condition between the two appointments. Test–retest reliability of the German NAT: PD-HF was very high and all questions had almost perfect agreement, with Cohen`s kappa ranging from 0.82 to 1.00 (Table 2).

Survey of patients

All of the 70 participants agreed that the tool questions were easy to understand and answer. Sixty-one patients (87%) thought that discussing the issues raised in the questions may improve quality of care. Only three

Table 1 General characteristics of the population included in the study

Sociodemographic characteristics	n (%) or median (IQR)
Women	12 (17%)
Age	62 (54–72)
Marital status	
Single	12 (17%)
Widowed	2 (3%)
Divorced	13 (19%)
Married/partnership	43 (61%)
Religion	
Protestant	37 (55%)
Roman catholic	19 (28%)
Non-denominational	11 (17%)
Clinical characteristics	
NYHA functional class	
I	22 (31%)
II	35 (50%)
III	13 (19%)
LVEF (%)	35 (20–50)
Classification according to LVEF	
HFrEF	45 (64%)
HFmrEF	3 (4%)
HFpEF	22 (32%)
ICD	38 (54%)
VAD	12 (17%)
Transplant list	9 (13%)
COPD	11 (16%)
CAD	30 (43%)
CKD	32 (46%)
Palliative care-related characteristics	
Presence of caregiver	67 (95%)
Caregiver	
Couple	49 (73%)
Son or daughter	6 (9%)
Sibling	4 (6%)
Parent	3 (4%)
Other	5 (8%)
Have requested referral to palliative care	0 (0.0%)
Have an advance directive	25 (36%)

IQR interquartile rate, *LVEF* left ventricular ejection fraction, *HFrEF* heart failure with reduced ejection fraction, *HFmrEF* heart failure with mildly reduced ejection fraction, *HFpEF* heart failure with preserved ejection fraction, *ICD* implantable cardioverter defibrillator, *VAD* ventricular assist device, *COPD* chronic obstructive pulmonary disease, *CAD* coronary artery disease, *CKD* chronic kidney disease

patients reported these questions being routinely asked or discussed during clinical consultations (Table 3).

Regarding other questions that should be included in the tool, the most frequently mentioned topics were lifestyle habits and sexuality. More specifically, patients suggested inquiry about exercise and nutrition habits, and whether there have been changes in a couple's sex life and there are side effects of medication that interfere with it.

Survey of health care personnel

We interviewed 27 health care professionals. These included eight cardiologists, five cardiology nurses, four PC specialists, three PC nurses, three psychologists from the HF clinic, two general practitioners, and two social workers. Among the 27 interviewees, 21 were women, and 14 of the interviewees have worked in the profession for more than 10 years.

In general, the health care personnel rated the questions easy for patients to understand, but not to answer. Most (23 of the 27 professionals) considered the tool helpful for improving the quality of patient care. Eleven of the health care personnel reported that the questions in the tool are usually asked during a clinical consultation, while the remaining 16 responded in a neutral manner, neither agreeing nor disagreeing. The four PC specialists agreed that topics from the tool are discussed during a routine consultation with a PC specialist. In contrast to that, only two of the cardiologists said topics from the tool are discussed in consultations, while the remaining six said that most "are not addressed," and that "psychosocial aspects are not discussed" (Table 3).

Face validity, applicability, relevance and acceptability

Face validity

Face validity was rated high, with most of the health care personnel (23 of 27) agreeing that the tool appears to measure unmet needs of both patients with HF and their caregivers. The remaining four interviewees partially agreed, but thought that to properly assess caregiver needs the caregiver needs to be present in the interview (Table 4).

Applicability

Among the 27 health care personnel, 17 (63%) consider the tool easy to use, and all but two consider the written instructions on use the tool helpful. However, some thought the tool and its instructions were too long and too detailed.

PC specialists, psychologists, and social workers think that doctors (general practitioners, cardiologists, PC specialists) as well as nurses can use the tool, while cardiology staff think that mainly nurses should use it (Table 4).

Relevance

Two PC specialists, one general practitioner and a psychologist, each questioned the relevance of some elements of the tool. One of the PC specialist was not sure what question 2.5 should cover. The other PC specialist said that question 2.7 is not very useful since it collapses

Table 2 Inter-rater and test–retest reliability

	Inter-rater reliability		Test–retest reliability	
	Cohen´s kappa	PABAK	Cohen´s kappa	PABAK
Section 2: Patient wellbeing				
1. Is the patient experiencing unresolved physical symptoms (including problems with breathlessness, pain, fatigue, nausea, edema, insomnia, or cough)?	0.43	0.49	0.94	0.94
2. Does the patient have problems with daily living activities?	0.59	0.79	0.99	0.98
3. Does the patient have psychological symptoms that are interfering with well-being or relationships?	0.69	0.76	0.94	0.94
4. Does the patient have concerns about how to manage his/her medication and treatment regimens?	0.48	0.94	1.00	1.00
5. Does the patient have concerns about spiritual or existential issues?	0.88	0.96	0.90	0.97
6. Does the patient have financial or legal concerns that are causing distress or require assistance?	0.85	0.89	0.93	0.94
7. From the health delivery point of view, are there health beliefs, cultural, or social factors involving the patient or family that are making care more complex?	0.17	0.80	0.90	0.97
Section 3: Ability of caregiver or family to care for patient				
1. Is the caregiver or family distressed about the patient's physical symptoms?	0.83	0.98	0.83	0.98
2. Is the caregiver or family having difficulty providing physical care?	0.78	0.84	0.82	0.87
3. Is the caregiver or family having difficulty coping?	0.82	0.88	0.97	0.98
4. Is the caregiver having difficulty managing the patient's medication and treatment regimens?	1.00	1.00	1.00	1.00
5. Does the caregiver or family have financial or legal concerns that are causing distress or require assistance?	0.66	0.87	1.00	1.00
6. Is the family currently experiencing problems that are interfering with their functioning or interpersonal relationships or is there a history of such problems?	0.57	0.79	0.96	0.97
Section 4: Caregiver wellbeing				
1. Is the caregiver or family experiencing physical, practical, spiritual, existential, or psychological problems that are interfering with their well-being or functioning?	0.73	0.89	0.85	0.93

PABAK prevalence-adjusted and bias-adjusted kappa

Table 3 Results of the survey applied to patients and health care personnel

	Agree	Neither agree nor disagree	Disagree
Survey to patients (n = 70)			
1.The questions were, generally, easy to understand (n = 69)	69 (100%)		
2.The questions were, generally, easy to answer (n = 69)	69 (100%)		
3.If my doctor asks me these questions, it may help to improve the quality of my care (n = 68)	61 (90%)	6 (9%)	1 (1%)
4.The questions asked in the questionnaire are usually dealt with during the clinical consultation (n = 70)	3 (4%)	38 (54%)	29 (42%)
Survey to health care personnel (n = 27)			
1.In general, the questions were easy to understand for the patient (n = 27)	13 (48%)	14 (52%)	
2.In general, the questions were easy to answer for the patient (n = 27)	10 (37%)	16 (59%)	1 (4%)
3.The quality of the care is improved by applying this tool (n = 27)	23 (85%)	4 (15%)	
4.The questions asked in the questionnaire are usually dealt with during the clinical consultation (n = 25)	11 (44%)	14 (56%)	

different factors into a single question, and suggested that section three, which is about the ability of caregiver to care for the patient, and section four, about caregiver well-being, should be merged. The GP thought question 3.6 is not very clear and should be rephrased, and the psychologist thought that questions 2.3 and 2.5 have similar content (Table 4).

Acceptability

There was no consensus on either when or how often the NAT: PD-HF should be employed in clinical practice. Some believe that it should be used early, at the first or second consultation, while others believe that it is better not to use it early, but only after a basis of trust has been built with the interviewer and the patient has already

Table 4 Results of the interview to assess tool´s face validity, applicability, relevance and acceptability among health care personnel

	Agree	Neutral	Disagree	Comments to highlight
Face validity (n = 27)				
1) The tool measures unmet needs of patients with heart failure and their caregivers	23 (85%)	4 (15%)		"to properly assess caregiver needs, the caregiver should be present in the interview", "the tool is more useful for younger patients as they may have a higher disease burden than older patients"
Applicability (n = 27)				
1) The tool is easy to use	17 (63%)	7 (26%)	3 (11%)	"very complex and detailed", "difficult to differentiate between *Some/Potential* and *Significant* in the level of concern"
2) Different professional groups can fill out the tool	23 (85%)	4 (15%)		
2. a) Which professional group should fill out the tool?				Palliative care staff (nurses and physicians) replied: physicians and nurses; General practitioners and social workers replied: physicians, nurses, social worker; Psychologists replied: physicians and nurses Cardiology staff (nurses and physicians) replied: mainly nurses;
3) The tool instructions are was easy to understand	27 (100%)			
4) The tool instructions are helpful	25 (93%)	2 (7%)		"instructions are useful but too long"
5) A special training is necessary to fill out the tool	16 (59%)	1 (4%)	10 (37%)	"for certain items, explanations are required", "maybe not a training, but an introduction to explain the purpose of the tool to increase motivation", "online training is an option", "training is required for non-specialized nurses", "the first and the last page of the tool have a lot of information that can be explained during a training session"
6) There are some difficulties in using the tool	18 (67%)	4 (15%)	5 (18%)	"many questions involve several aspects", "regarding the field *action taken*, there are situations you cannot act", "patients' needs sufficient linguistic and cognitive skills", "an entire clinic needs to be willing to use the tool", " time consuming, especially with patients who have a lot to say", "needs a lot of time and empathy", "if filled out by nurses, they are not allowed to refer patients"
Relevance (n = 27)				
2) Some questions are irrelevant and can be left out	1 (4%)	3 (11%)	23 (85%)	"3.6: it is not clear what the question intends to assess", "2.7: not very useful", "2.7: formulated very complicated and too long", "section 3" and "4" are repeated and should be merged", "questions 2.5 and 2.3 have a similar content", "2.5: not sure what it should capture"
Acceptability (n = 27)				
1) Filling out the tool does not take too much time and can be integrated into daily routine clinical practice	13 (48%)	5 (19%)	9 (33%)	"it is too long and takes too much time", "it requires training or a very complete introduction", "not possible in the cardiology consultation, maybe the palliative care has time"
a) When should the tool be applied?				"early, in the first or second consultation", "not too early, it needs a basis of trust", "not too early, when the patient has dealt with the disease", "if the patient becomes more symptomatic or consultations become more frequent"
b) How often should the tool be applied?				"when something has change", "at rehospitalisation", "regularly, every 6 months", "during annual controls", "in patients who are deteriorating faster", "after regular intervals of 6 -12 months ask those questions where there were needs", "ask in every consultation if something has changed"
2) I feel uncomfortable asking some of the questions	4 (15%)	9 (33%)	14 (52%)	"questions 2.3, 2.5, 2.6, 3.6 and 4.2 are about topics hard to discuss (emotional, spiritual concerns, family or financial issues)", "patient may not like to talk about financial issues (question 2.6)", "2.5 and 2.6 need to be asked carefully (spiritual concerns or financial issues)", "2.3 is very personal (psychological issues)"

dealt with the disease. Some respondents think it should be used at regular intervals such as every six months or at annual check-ups, while others think it should be used again after major changes in health status or after hospitalization (Table 4).

The main concerns about accepting the NAT: PD-HF are lack of time to use it, and that being able to use it requires some training or at least a very thorough introduction to using it and its value (Table 4).

Another reservation about using the NAT: PD-HF reported by cardiologists and cardiology nurses was that some staff members do not feel comfortable discussing emotional, spiritual, or financial issues with their patients (Table 4).

Discussion

Key results

We translated the NAT: PD-HF into German, culturally adapted, and validated it. The validation showed good internal consistency and substantial inter-rater agreement for the majority of the items. Additionally, we were able to assess the test–retest reliability and we found almost perfect agreement between the first and second assessments. Moreover, patients thought well of the tool, and they agreed that it could help to improve their quality of care and that it covered relevant topics that are not normally addressed in clinical consultations. Similarly, face validity and user-friendliness were rated highly by health care professionals. However, like the participating health care personnel we also believe training is necessary to ensure correct use of the tool.

NAT: PD-HF strengths

Other such tools based on patient prognosis ignore the needs that patients with longer prognoses may have, and how difficult it is to predict disease trajectory in HF [18–20]. The NAT: PD-HF evaluates patient needs in a more integrated and profound way. It assesses not only patient well-being and information needs, but also the needs and well-being of family members and informal caregivers. Two recently published systematic reviews of tools to assess PC needs in patients with HF concluded that the NAT: PD-HF was the most appropriate tool to assess the needs of patients with HF [6, 7]. The English version of the tool had already demonstrated a good correlation between evaluators [8] and good acceptability by health professionals [8, 11]. Our study supports the previous findings and additionally shows that the NAT: PD-HF is stable over time and that patients regard it as useful.

NAT: PD-HF limitations

We observed no consensus across medical staff on when to use the tool for the first time, nor on how often to use it. However, a recently published position statement from the European Association of Palliative Care proposed an algorithm for when to employ the NAT: PD-HF. The association also recommended assessing PC needs in patients in less advanced stages of HF at annual reviews or after any significant health-related event for those in more advanced stages [21].

Although the tool was designed to be used without training, experience with the staff in this study showed that prior training is necessary. Training was mainly on how to discuss the needs of the patients and the informal caregiver in an empathic, respectful and efficient way by applying situation-specific adaptations of the example sentences of the instruction manual and on how to decide on cut-off points of the scoring system. In a similar study assessing the NAT: PD-HF in the Netherlands, nurses trained in using the tool still requested they referred that more training to assess PC needs [11]. A qualitative study that evaluated barriers in the implementation of the Needs Assessment Tool: Progressive Disease-Interstitial Lung Disease (NAT: PD-ILD), also found the need for training for the correct application of that tool [22].

The majority of the questions had a substantial inter-rater agreement. In section "2", question number seven had a Cohen´s kappa of 0.17, which is a poor correlation. This finding is consistent with the validation of the English version of the NAT: PD-HF and the NAT: PD-Cancer [8, 23]. The poor correlation might be the result of aiming to assess multiple factors in one question. The question, aiming to identify barriers for the health care delivery, tries to assess social factors, health beliefs, and cultural beliefs from both the patient and the family. One rater may focus more on one factor than on others, leading to obtaining different answers from patients. In section "3", question number six had the lowest kappa of the section. The difficulties discussing delicate topics such as interpersonal problems in the family might explain the low kappa. Additionally, this question also aims to assess multiple issues within the same question.

Implications for future research

Its high face validity suggests that the translated tool appears to measure unmet needs of patients with HF and their informal caregivers, and both medical staff and patients think the tool could help to improve quality of care. However, its effectiveness in reducing unmet needs and consequently even improving quality of life has not yet been studied. It would be interesting to prospectively study the effectiveness of this tool in reducing unmet needs and increasing quality of life in clinical practice.

Additionally, this study aimed to assess the psychometric characteristics of the German NAT: PD-HF in a representative full-spectrum of HF patients. However, the

psychometric profile of the tool might differ according to characteristics such as NYHA functional class, patient gender, or the availability of a caregiver. A study assessing these differences should take into account the sample size needed to make such subgroup analyses.

Implications for clinical practice

Although we tried to include patients from across the disease spectrum, most patients were male and had reduced ejection fraction. Patients with preserved ejection fraction are more often women, are older, and have more comorbidities (and therefore more symptoms) such as diabetes, hypertension, and renal dysfunction [24, 25]. In addition, drugs that have shown to improve symptoms in patients with reduced ejection fraction have shown little or no effectiveness in patients with preserved ejection fraction [26]. Therefore, the latter patients might have different types of needs than patients with reduced ejection fraction. However, this study did not seek to assess the needs in patients with HF but rather to evaluate the psychometric characteristics of the tool. Hence, we believe that the low proportion of patients with preserved ejection fraction and women does not limit the generalizability of our results to clinical practice. However, we acknowledge that, due to the low proportion of women in our study (17%), we do not know the acceptability and women´s opinion of the German NAT: PD-HF. Similarly, due to the lack of participation of patients at NYHA IV, we do not know their acceptance of the tool, which could be low due to the cognitive challenge that answering this questionnaire could pose for these patients.

More than one-third of the patients cited a need for further information. During interviews some staff also mentioned that they did not feel comfortable discussing certain topics. These reports from patients and staff together suggest that improving doctor-patient communication may assist using the NAT: PD-HF more effectively in clinical practice to recognize unmet needs and improve daily life for people living with HF. As attention is linked to higher-quality communication, one way to improve communication would be to adjust the conditions of clinical practice so that patients and their narratives receive sufficient attention for the physician to fully understand their situation or need [9].

Conclusion

The German NAT: PD-HF is a reliable, valid, and internally consistent tool that is well accepted by both patients and health care personnel. However, it is important to keep in mind that effective use of the tool requires training of health care personnel.

Abbreviations

HF: Heart failure; NAT: PD-HF: Needs assessment tool: progressive disease-heart failure; PC: Palliative care.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12955-021-01817-6.

Additional file 1. German version of the "Needs Assessment Tool: Progressive Disease-Heart Failure (NAT: PD-HF)". Instrument zur Erfassung der Bedürfnisse: progressive Erkrankung - Herzinsuffizienz (IEB: PE-HI).

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Additional file 6. Changes made for the cultural adaptation.

Additional file 7. **Table 1.** Matrix of the weights used to assess inter-rater reliability and test-retest reliability.

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Additional file 9. **Table 3.** Sensitivity analysis to assess the inter-rater reliability for each one of second evaluators.

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Authors' contributions

PZ made substantial contributions to the conception of the study and revised the manuscript. MM, NL, and VGJ participated designing the study and co-supervising the study procedure. RZ and JG recruited the participants and conducted the interviews. NL and ER were the second evaluators of the interviews. MM and SE supervised PZ who was a medical student at the time the interviews were conducted. LH contributed to the acquisition of data and the revision of the manuscript. VGJ performed the statistical analyses and drafted the manuscript. All authors participated in reviewing the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Code availability

Do file with coding for statistical analyses performed in STATA release 15 (Stata Corp, College Station, Texas), will be available upon request to the corresponding author.

Declarations

Ethics approval
The study was carried out according to the guidelines of the Declaration of Helsinki [27], and was approved by the Cantonal Ethics Committee of Bern (KEK Nr. 2018-02175).

Consent to participate
We obtained written consent from all the patients.

Competing interests
The authors declare that they have no competing interests.

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Publisher's Note

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Instrument zur Erfassung der Bedürfnisse: progressive Erkrankung - Herzinsuffizienz (IEB:PE-HI)

Benutzerleitfaden

Zweck des IEB:PE-HI

- Das Instrument zur Erfassung der Bedürfnisse: Progressive Erkrankung - Herzinsuffizienz (IEB:PE-HI) wird sowohl im allgemeinmedizinischen als auch im spezialisierten Bereich verwendet. Es kann dazu beitragen, die Art und den Umfang der Bedürfnisse von Menschen mit Herzinsuffizienz und ihren Betreuungspersonen mit den geeigneten Personen oder Diensten abzustimmen, um auf diese Bedürfnisse einzugehen.
- Im allgemeinmedizinischen Bereich (z. B. Hausarztpraxis und Kardiologie) kann das IEB:PE-HI verwendet werden, um zu eruieren, welcher Bedarf in diesem Umfeld gedeckt werden kann und welche Bedürfnisse komplexer sind und eher in die Hände anderer Fachpersonen gehören.
- Im spezialisierten Bereich (z. B. spezialisierte Palliativdienste) kann das IEB:PE-HI bei der Feststellung komplexer Bedürfnisse helfen und als Instrument zur Koordination der Betreuung nach einer Hospitalisierung oder zur Ermittlung des Bedarfs nach weiterer Unterstützung dienen.
- Das IEB:PE-HI ist ein wichtiges Instrument zur Erleichterung der Kommunikation zwischen Leistungserbringern der Grundversorgung und der spezialisierten Versorgung über Patientenbedürfnisse und zu deren Deckung ergriffene Massnahmen.

Ausfüllen des IEB:PE-HI

Das IEB:PE-HI ist ein Instrument zur Erfassung der Bedürfnisse, das von Gesundheitsfachpersonen auf zahlreichen Fachgebieten verwendet werden kann. Beim Ausfüllen des IEB:PE-HI sollte wie folgt vorgegangen werden:

1. BEWERTEN Sie FÜR JEDEN PUNKT die Besorgnis des Patienten bzw. der Betreuungsperson, und zwar mithilfe der Optionen: «Keine», «Mittel/potenziell» und «Erheblich».
2. BEDENKEN Sie bei jedem Thema die diversen Fragen, die für die Person in der aktuellen Krankheitsphase relevant sind. Als Grundlage können Sie die separate Anleitung verwenden.
3. HANDELN Sie bei jedem Bedürfnis, das besorgniserregend ist («Mittel/potenziell» und «Erheblich»). Ihre Massnahmen können umfassen: direkt von Ihnen zu erledigen, von einem anderen Mitglied des professionellen Behandlungsteams zu erledigen oder Überweisung an eine Person ausserhalb des Behandlungsteams. Halten Sie Ihre Massnahmen auf dem IEB:PE-HI fest.
4. ÜBERWEISEN Sie die Person im Bedarfsfall, indem Sie den diesbezüglichen Abschnitt am Ende des Fragebogens ausfüllen. Stellen Sie dabei sicher, dass die Angaben über die Stelle, an die überwiesen wird, die Priorität der Überweisung und den Kenntnisstand des Betroffenen über die Überweisung vollständig sind.
5. INFORMIEREN Sie die anderen Mitglieder des Behandlungsteams über die Ergebnisse der Bedürfniserfassung durch:
    a. Einfügen einer Kopie des IEB:PE-HI in die Patientenakte.
    b. Übermitteln einer Kopie an den Hausarzt, Kardiologen bzw. einen anderen Facharzt, der die betroffene Person betreut.
    c. Weiterleiten einer Kopie an die Überweisungsstelle (falls Überweisung erforderlich).
6. BEWERTEN Sie die Bedürfnisse ERNEUT, indem Sie das IEB:PE-HI ungefähr im Monatsabstand oder bei einer Änderung des funktionellen Status des Patienten bzw. der Betreuungsperson ausfüllen.

Anmerkung: Zur besseren Lesbarkeit wird jeweils nur die männliche Form verwendet; gemeint sind jedoch immer beide Geschlechter.

Instrument zur Erfassung der Bedürfnisse: progressive Erkrankung-herzinsuffizienz (IEB:PE-HI)
Bitte alle abschnitte ausfüllen
Name des Patienten/der Patientin:_____ Datum:_____

PATIENTEN-/ADRESSEN-ETTIKETTE

Abschnitt 1. Prioritäre Überweisung zur weiteren Abklärung

	Ja	Nein	Falls Felder mit Punkt angekreuzt wurden: Ziehen Sie eine Abklärung durch einen spezialisierten Palliativdienst in Betracht.
1. Steht dem Patienten im Bedarfsfall eine Betreuungsperson zur Verfügung?		*	
2. Hat der Patient oder die Betreuungsperson um die Überweisung an einen spezialisierten Palliativdienst gebeten?	*		
3. Benötigen Sie Unterstützung bei der Organisation der Betreuung des Patienten und/oder seiner Betreuungsperson?	*		

Abschnitt 2. Wohlbefinden des Patienten (weitere Hinweise: siehe Anleitung auf der nächsten Seite)

	Grad der Besorgnis			Zu ergreifende Massnahmen		
	Keine	Potenziell / Mittel	Erheblich	Direkt zu erledigen	Von anderem Mitglied des Behandlungsteams zu erledigen	Überweisung erforderlich
1. Hat der Patient unkontrollierten körperliche Symptome (z.B. Atemnot, Schmerzen, Müdigkeit, Übelkeit, Ödeme, Schlaflosigkeit, oder Husten)?						
2. Hat der Patient Probleme bei alltäglichen Tätigkeiten?						
3. Hat der Patient psychologische Symptome, die das Wohlbefinden oder die Beziehungen beeinträchtigen?						
4. Hat der Patient Schwierigkeiten beim Umgang mit seinen Medikamenten und dem Behandlungsplan?						
5. Ist der Patient über spirituelle oder existenzielle Fragen besorgt?						
6. Beschäftigen den Patienten finanzielle oder juristische Fragen, die ihn belasten oder bei denen er Unterstützung benötigt?						
7. Gibt es vom Standpunkt der Gesundheitsversorgung gesehen vonseiten des Patienten und/oder der Angehörigen Vorstellungen über Gesundheit oder kulturelle oder soziale Faktoren, durch die die Betreuung komplexer wird?						
8. Benötigt der Patient Informationen über: (Zutreffendes ankreuzen)	☐ Die Prognose	☐Behandlungsmöglichkeiten	☐ Herzkrankheit	☐ Patientenverfügung / lebensverlängernde Massnahmen	☐ Medizin- / Gesundheits- / Unterstützungsdienste	☐ Finanzielle / juristische Fragen ☐ Beziehungsfragen/ psychologische Fragen

ANMERKUNGEN:_____

Abschnitt 3. Fähigkeit der Betreuungsperson, für den Patienten zu sorgen (weitere Hinweise: siehe Anleitung auf der nächsten Seite)

Von wem stammen diese Angaben? (Zutreffendes ankreuzen) ☐ Patient ☐ Betreuungsperson ☐ Beide	Grad der Besorgnis			Zu ergreifende Massnahmen		
	Keine	Potenziell / Mittel	Erheblich	Direkt zu erledigen	Von anderem Mitglied des Behandlungsteams zu erledigen	Überweisung erforderlich
1. Wird die Betreuungsperson durch die körperlichen Symptome des Patienten belastet??						
2. Hat die Betreuungsperson Schwierigkeiten bei der alltäglichen körperlichen Versorgung des Patienten?						
3. Wird die Betreuungsperson durch die psychologischen Symptome des Patienten belastet?						
4. Hat die Betreuungsperson Schwierigkeiten beim Umgang mit den						

verordneten Medikamenten und dem Behandlungsplan des Patienten?							
5. Beschäftigen die Betreuungsperson finanzielle oder juristische Fragen, die sie belasten oder bei denen sie Unterstützung benötigt?							
6. Haben die Angehörigen derzeit Probleme, die Konflikte verursachen oder die zwischenmenschlichen Beziehungen beeinträchtigen, oder bestanden solche Probleme in der Vergangenheit?							

7. Benötigt die Betreuungsperson Informationen über: (Zutreffendes ankreuzen)	☐ Die Prognose	☐Behandlungsmöglichkeiten	☐ Patientenverfügung / lebensverlängernde Massnahmen	☐ Finanzielle / juristische Fragen
	☐ Verhalten im Falle des Ablebens des Patienten	☐ Herzkrankheit	☐ Medizin- / Gesundheits- / Unterstützungsdienste	☐ Beziehungsfragen/ psychologische Fragen

ANMERKUNGEN: _____

Abschnitt 4. Wohlbefinden der Betreuungsperson (weitere Hinweise: siehe Anleitung auf der nächsten Seite)

Von wem stammen diese Angaben? (Zutreffendes ankreuzen) ☐ Patient ☐ Betreuungsperson ☐ Beide	Grad der Besorgnis			Zu ergreifende Massnahmen		
	Keine	Potenziell / Mittel	Erheblich	Direkt zu erledigen	Von anderem Mitglied des Behandlungsteams zu erledigen	Überweisung erforderlich
1. Hat die Betreuungsperson körperliche, praktische, spirituelle, existenzielle oder psychologische Probleme, die ihr Wohlbefinden beeinträchtigen oder die Alltagsbewältigung erschweren?						
2. Empfindet die Betreuungsperson Trauer aufgrund des bevorstehenden oder kürzlich geschehenen Ablebens des Patienten, sodass ihr Wohlbefinden oder ihre Alltagsbewältigung darunter leidet?						

ANMERKUNGEN: _____

Falls zur weiteren Abklärung oder Behandlung Überweisung nötig: bitte diesen Abschnitt ausfüllen

1. Überweisung an: (Name) _____
2. Überweisung an: (Fachgebiet) ☐ Allgemeinmedizin
   ☐ Sozialarbeit
   ☐ Psychologie
   ☐ Kardiologie
   ☐ Spezialisierten Palliativdienst
   ☐ Andere: _____
3. Priorität der Abklärung: ☐ Dringend (innert 24 h) ☐ Halb dringlich (2–7 Tage) ☐ Nicht dringend (sobald möglich)
4. Überweisung mit dem/der Betroffenen besprochen: ☐ Ja ☐ Nein
5. Betroffene(r) stimmt Überweisung zu: ☐ Ja ☐ Nein
6. Überweisung von: Name: _____

Funktion: _____ Unterschrift: _____

Anleitung: wichtige Fragen bei der Bewertung des Besorgnis Grads

Abschnitt 2. Wohlbefinden des Patienten

1. Körperliche Symptome
- Präsentiert sich der Patient mit unkontrollierten körperlichen Symptome, etwa Schläfrigkeit, Müdigkeit, Atembeschwerden, Übelkeit, Erbrechen, andauernder Husten, Schmerzen, Ödeme, Verstopfung, Schlafstörungen, Appetitverlust oder reduzierter Leistungsfähigkeit?

2. Alltagstätigkeiten
- Hat der Patient Schwierigkeiten beim Toilettengang, Duschen, Baden oder der Essenszubereitung?
- Gibt es eine Betreuungsperson, die ihm dabei hilft?

3. Psychologische Aspekte
- Leidet der Patient an anhaltenden Stimmungstiefs, Traurigkeit, Schuldgefühlen, Reizbarkeit, Verlust der Freude oder des Interesses an bisher üblichen Tätigkeiten?
- Empfindet der Patient Besorgnis, Anspannung, Wut, Angst, Nervosität, Hoffnungslosigkeit oder Isolation?
- Äussert der Patient den Wunsch nach einem raschen Tod?

4. Medikamente und Behandlung
- Ist der Patient in der Lage, mit komplexen Medikationen und Behandlungen umzugehen?

5. Spirituelles und Existentielles
- Fühlt sich der Patient isoliert oder hoffnungslos?
- Empfindet der Patient, dass das Leben sinnlos ist oder dass er das Leben vergeudet hat?
- Benötigt der Patient Unterstützung, um geeignete spirituelle Ressourcen oder Dienste zu finden?

6. Finanzielles und Juristisches
- Gibt es finanzielle Fragen im Zusammenhang mit Einkommensverlust, Behandlungskosten, Reiseausgaben oder Materialbedarf?
- Ist die Familie sozioökonomisch benachteiligt?
- Gibt es Meinungsverschiedenheiten zwischen dem Patienten und der Betreuungsperson über juristische Fragen wie Behandlungsmöglichkeiten am Lebensende (end-of-life decisions) und vorausschauende Behandlungsplanung (advance care planning)?
- Kennt der Patient die verfügbaren Finanzierungsmöglichkeiten und benötigt er Unterstützung, diese in Anspruch zu nehmen?

7. Überzeugungen über Gesundheit, kulturelle oder soziale Faktoren
- Haben der Patient bzw. die Betreuungsperson Überzeugungen oder Haltungen, die die Gesundheitsversorgung erschweren (z.B. ein Verbot für bestimmte Behandlungen)?
- Gibt es Sprachschwierigkeiten? Ist ein Dolmetscher nötig?
- Fühlt sich der Patient bzw. die Betreuungsperson gesellschaftlich isoliert?
- Hat der Patient Schwierigkeiten, die medizinische Grundversorgung zu erreichen und in Anspruch zu nehmen? (z.B. Organisation des Transports, kein Hausarzt, kein Vertrauen zum Hausarzt)
- Hat der Patient Migrationshintergrund und fühlt sich schlecht integriert?
- Ist der Patient über 75 Jahre alt? (Anmerkung: Ältere Patienten sind bei spezialisierten Palliativdiensten unterrepräsentiert.)

8. Information
- Möchte der Patient mehr Informationen über den Verlauf und die Prognose der Krankheit und die Behandlungsmöglichkeiten?

Kennt der Patient die verschiedenen (Pflege-)Dienste, die ihm als Unterstützung zur Verfügung stehen, oder benötigt er Hilfe, um sie in Anspruch zu nehmen (z. B. finanzielle und juristische Unterstützung, psychologische Dienste, Selbsthilfegruppen, Seelsorge)?

Abschnitt 3. Fähigkeit der Betreuungsperson, für den Patienten zu sorgen

Mit Betreuungsperson ist diejenige Person gemeint, die den Patienten im Alltag am meisten unterstützt. (z.B. Partner/in, Angehörige, Nachbar/in, Pflegeperson, Haushälter/in). Bei einigen Fragen können damit auch mehrere Personen gemeint sein (z.B. alle nahen Angehörigen).

1. Körperliche Betreuung
- Hat die Betreuungsperson Schwierigkeiten mit alltäglichen Tätigkeiten oder praktischen Fragen wie medizinische Ausrüstung, Mobilität und Transport?

2. Körperliche Symptome
- Belasten die körperlichen Symptome des Patienten die Betreuungsperson?

3. Psychologische Aspekte
- Hat die Betreuungsperson Schwierigkeiten, mit den psychologischen Symptomen des Patienten umzugehen?
- Äussert die Betreuungsperson den Wunsch nach einem raschen Tod des Patienten?

4. Medikamente und Behandlung
- Hat die Betreuungsperson Schwierigkeiten beim Umgang mit komplexen Medikationen und dem Behandlungsplan?

5. Finanzielles und Juristisches
- Gibt es finanzielle Fragen im Zusammenhang mit Einkommensverlust, Behandlungskosten, Reiseausgaben oder Materialbedarf?
- Ist die Familie sozioökonomisch benachteiligt?
- Gibt es Meinungsverschiedenheiten zwischen dem Patienten und der Betreuungsperson über juristische Fragen wie die Verweigerung lebensverlängernder Massnahmen und die Patientenverfügung?
- Kennt die Betreuungsperson die verfügbaren Finanzierungsmöglichkeiten und benötigt Sie Unterstützung, diese in Anspruch zu nehmen?

6. Angehörige und Beziehungen
- Gibt es zwischen dem Patienten und den Angehörigen Kommunikationsprobleme oder Konflikte wegen der Prognose, der Behandlungsmöglichkeiten oder der Verteilung der Rollen bei der Pflege?
- Ist der Patient insbesondere über die Folgen der Krankheit für die Betreuungsperson bzw. die Angehörigen besorgt?

7. Information
- Möchte die Betreuungsperson mehr Informationen, etwa über den Verlauf und die Prognose der Krankheit und die Behandlungsmöglichkeiten?
- Kennt die Betreuungsperson die verschiedenen (Pflege-)Dienste, die ihr als Unterstützung zur Verfügung stehen, oder benötigt sie Hilfe, um sie in Anspruch zu nehmen (z. B. Kurzzeitpflege, finanzielle und juristische Unterstützung, psychologische Dienste, Selbsthilfegruppen, Seelsorge)?

Abschnitt 4. Wohlbefinden der Betreuungsperson

1. Körperliches und Psychosoziales
- Hat die Betreuungsperson körperliche Symptome, etwa Müdigkeit, körperliche Belastung, Blutdruck- und Herz-Kreislauf-Störungen, eine stressbedingte Krankheit oder Schlafstörungen?
- Fühlt sich die Betreuungsperson deprimiert, verzweifelt, verängstigt, nervös, angespannt, wütend, reizbar oder verärgert gegenüber Dritten oder von der Situation überfordert?
- Hat die Betreuungsperson relevante spirituelle oder existenzielle Probleme?

2. Verlust und Trauer (vor und nach Todesfall)
- Erlebt die Betreuungsperson intrusive Bilder, plötzliche Emotionen? Bestreiten sie, dass sich der Verlust auf sie auswirkt, und vernachlässigen sie nötige Anpassungen zu Hause oder im Beruf?

Additional file 2. Template of the survey to patients

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
The questions were, generally, easy to understand.					
The questions were, generally, easy to answer.					
If my doctor asks me these questions, it may help to improve the quality of my care.					
The questions asked in the questionnaire are usually dealt with during the clinical consultation.					
Bearing in mind that the purpose of the questionnaire is to identify unmet needs: Do you think are there other questions we should include in the questionnaire?					

Additional file 3. Template of the survey to health care personnel

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
In general, the questions were easy to understand for the patient.					
In general, the questions were easy to answer for the patient.					
The quality of the care is improved by applying this tool.					
The questions asked in the questionnaire are usually dealt with during the clinical consultation.					

Additional file 4. Template of the interview to assess face validity, applicability, relevance and acceptability of the tool among health care personnel

Face validity: Needs Assessment Tool: Progressive disease – Heart failure (NAT: PD-HF)

Interview code_____

Date_____ Time_____

General characteristics of the staff	
Professional category	sex
☐ physician cardiology ☐ physician palliative care ☐ nurse cardiology ☐ nurse palliative care ☐ psychologist ☐ social worker ☐ general practitioner ☐ others (e.g. medical student)	☐ female ☐ male professional experience ☐ < 5 ☐ 5-10 ☐ > 10

Interview			
Face validity	Agree	Neutral	Disagree
1) The tool measures unmet needs of patients with heart failure and their caregivers ➔ comment:	☐	☐	☐
Applicability	Agree	Neutral	Disagree
1) The tool is easy to use ➔ comment:	☐	☐	☐
2) Different professional groups can fill out the tool ➔ comment: 2.a Which professional group should fill out the tool?	☐	☐	☐
3) The tool instructions are easy to understand	☐	☐	☐
4) The tool instructions are helpful	☐	☐	☐
5) A special training is necessary to fill out the tool	☐	☐	☐
6) There are some difficulties in using the tool ➔ If yes, which:	☐	☐	☐
Relevance	Agree	Neutral	Disagree

1) Some questions are irrelevant and can be left out ➔ If yes, which ones	☐	☐	☐
Acceptability	Agree	Neutral	Disagree
1) Filling out the tool does not take too much time and can be integrated into daily routine clinical practice 1.a) When should the tool be applied? 1.b) How often should the tool be applied?	☐	☐	☐
2) I feel uncomfortable asking some of the questions ➔ If yes, which and why:	☐	☐	☐

Additional file 5. Original version (English) of the "Needs Assessment Tool: Progressive Disease-Heart Failure (NAT: PD-HF)".

NEEDS ASSESSMENT TOOL: PROGRESSIVE DISEASE – HEART FAILURE (NAT: PD-HF) USER GUIDE

Purpose of the NAT: PD-HF

- Used in both generalist and specialist settings, the Needs Assessment Tool: Progressive Disease – Heart Failure (NAT: PD-HF) can assist in matching the types and levels of need experienced by people with heart failure and their caregivers with the most appropriate people or services to address those needs.
- In generalist settings (eg general practice and cardiology), the NAT: PD-HF can be used to determine which needs may be met in that setting and which needs are be more complex and may be better managed by specialists.
- In specialist settings (eg specialist palliative care services), the NAT: PD-HF can assist in determining when complex needs have been met and act as a discharge planning tool, or to identify the need for ongoing support.
- The NAT: PD-C is an important tool for facilitating communication between primary and specialist care providers about patient needs and actions taken to address these.

Completing the NAT: PD-HF

The NAT: PD-HF is a one-page assessment tool that can be completed by health professionals across a range of disciplines. When completing the NAT: PD-HF, the following steps should be followed:

1. ASSESS patient/caregiver level of concern FOR EVERY ITEM, using the response options: "none", "some/potential for" or "significant".
2. CONSIDER the range of issues within each domain that apply to a person at this stage of their illness. Prompts are provided on a separate page to help you.
3. ACT on each need where you identified some concern ("some/potential for" or "significant"). Your actions may include: directly managed by you, managed by another member of your care team, or referral to someone outside your care team. Record your action on the NAT: PD-HF.
4. REFER if required by completing the referral section at the bottom of the tool, ensuring that information regarding the type of referral, the priority of the referral and client knowledge of the referral is included.
5. INFORM other members of the care team of the outcomes of the needs assessment by:
   a. Filing one copy of the NAT: PD-HF in the patient's medical file.
   b. Sending a copy to the person's GP/cardiologist/other specialist.
   c. If a referral is required, forwarding a copy to the referee.
6. REASSESS needs by completing the NAT: PD-HF approximately monthly or when the patient's or family's situation, or functional status changes.

NEEDS ASSESSMENT TOOL : PROGRESSIVE DISEASE HEART FAILURE (NAT: PD-HF)

COMPLETE ALL SECTIONS

PATIENT NAME: _____

DATE: _____ DIAGNOSIS: _____

PATIENT/ADDRESS LABEL

SECTION 1: PRIORITY REFERRAL FOR FURTHER ASSESSMENT

	Yes	No	If yellow boxes are ticked, consider assessment by SPCS
1. Does the patient have a caregiver readily available if required?			
2. Has the patient or caregiver requested a referral to a specialist palliative care service (SPCS)?			
3. Do you require assistance in managing the care of this patient and/or family?			

SECTION 2: PATIENT WELLBEING (Refer to the back page for assistance)

	Level of Concern			Action Taken		
	None	Some/ Potential	Significant	Directly managed	Managed by other care team member	Referral required
1. Is the patient experiencing unresolved physical symptoms (including problems with breathlessness, pain, fatigue, nausea, oedema, insomnia or cough)?						
2. Does the patient have problems with daily living activities?						
3. Does the patient have psychological symptoms that are interfering with wellbeing or relationships?						
4. Does the patient have concerns about how to manage his/her medication and treatment regimes?						
5. Does the patient have concerns about spiritual or existential issues?						
6. Does the patient have financial or legal concerns that are causing distress or require assistance?						
7. From the health delivery point of view, are there health beliefs, cultural or social factors involving the patient or family that are making care more complex?						

8. Does the patient require information about: (tick any options that are relevant)
☐ The prognosis ☐ Treatment options ☐ Advance directive/resuscitation preferences ☐ Financial/legal issues
☐ Heart disease ☐ Medical/health/support services ☐ Social/emotional issues

COMMENTS: _____

SECTION 3: ABILITY OF CAREGIVER OR FAMILY TO CARE FOR PATIENT (Refer to the back page for assistance)

Who provided this information? (please tick one)
☐ Patient ☐ Caregiver ☐ Both

	Level of Concern			Action Taken		
	None	Some/ Potential	Significant	Directly managed	Managed by other care team member	Referral required
1. Is the caregiver or family distressed about the patient's physical symptoms?						
2. Is the caregiver or family having difficulty providing physical care?						
3. Is the caregiver or family having difficulty coping?						
4. Is the caregiver have difficulty managing the patient's medication and treatment regimes?						
5. Does the caregiver or family have financial or legal concerns that are causing distress or require assistance?						
6. Is the family currently experiencing problems that are interfering with their functioning or inter-personal relationships, or is there a history of such problems?						

7. Does the caregiver require information: (tick any options that are relevant)
☐ The prognosis ☐ Advance directive/resuscitation preferences ☐ Medical/health/support services ☐ Heart disease
☐ Treatment options ☐ What to do in event of patient's death ☐ Social/emotional issues ☐ Financial /legal issues

COMMENTS: _____

SECTION 4: CAREGIVER WELLBEING (Refer to the back page for assistance)

Who provided this information? (please tick one)
☐ Patient ☐ Caregiver ☐ Both

	Level of Concern			Action Taken		
	None	Some/ Potential	Significant	Directly managed	Managed by other care team member	Referral required
1. Is the caregiver or family experiencing physical, practical, spiritual, existential or psychological problems that are interfering with their wellbeing or functioning?						
2. Is the caregiver or family experiencing grief over the impending or recent death of the patient that is interfering with their wellbeing or functioning?						

COMMENTS: _____

IF REFERRAL REQUIRED FOR FURTHER ASSESSMENT OR CARE, PLEASE COMPLETE THIS SECTION

1. Referral to: (Name) _____
2. Referral to: (Specialty) ☐ General practitioner ☐ Social worker ☐ Psychologist ☐ Specialist palliative care service
☐ Cardiologist ☐ Other _____
3. Priority of assessment needed: ☐ Urgent (within 24 hours) ☐ Semi-Urgent (2-7 days) ☐ Non-Urgent (next available)
4. Discussed the referral with the client. ☐ Yes ☐ No
5. Client consented to the referral. ☐ Yes ☐ No
6. Referral from: Name: _____ Position: _____ Signature: _____

ISSUES TO CONSIDER WHEN RATING THE LEVEL OF CONCERN

PATIENT WELLBEING

Physical symptoms

- Does the patient present with unresolved physical symptoms such as drowsiness, fatigue, dyspnoea, vomiting/nausea, persistent cough, pain, oedema, constipation, sleep problems or loss appetite?

Activities of daily living

- Is the patient having difficulty with toileting, showering, bathing, or food preparation?
- Is there a caregiver to assist the patient?

Psychological

- Is the patient experiencing sustained lowering of mood, tearfulness, guilt or irritability, loss of pleasure or interest in usual activities?
- Is the patient experiencing feelings of apprehension, tension, anger, fearfulness or nervousness, hopelessness or a sense of isolation?
- Is the patient requesting a hastened death?

Medication and treatment

- Is the patient able to manage complex medication and treatment regimes?

Spiritual/Existential

- Is the patient feeling isolated or hopeless?
- Does the patient feel that life has no meaning or that his/her life has been wasted?
- Does the patient require assistance in finding appropriate spiritual resources or services?

Financial/Legal

- Are there financial concerns relating to loss of income or costs of treatment, travel expenses, or equipment?
- Is the family socio-economically disadvantaged?
- Are there conflicting opinions between patient and family relating to legal issues such as end-of-life care options and advance care plans?
- Is the patient or family aware of the various financial schemes available and do they need assistance in accessing these?

Health Beliefs, Social and Cultural

- Does the patient or family have beliefs or attitudes that make health care provision difficult?
- Are there any language difficulties? Does the patient or family require a translator?
- Is the family preventing information about prognosis from being disclosed to the patient?
- Does the information have to be passed on to a particular member of the family or cultural group?
- Is the patient or family feeling socially isolated?
- Does the family live more than 50km from the primary service provider?
- Is the patient of Aboriginal or Torres Strait Islander descent?
- Is the patient over 75 years of age? (NB: older patients are under-represented in SPCSs.)

Information

- Does the patient want more information about the course and prognosis of the disease and treatment options?
- Is the patient aware of the various care services available to assist them and do they need assistance in accessing these? (eg financial and legal assistance, psychological services, support groups, pastoral care.)

ABILITY OF CAREGIVER OR FAMILY TO CARE FOR PATIENT

Physical symptoms

- Are the patient's physical symptoms causing the caregiver and family distress?

Providing physical care

- Is the caregiver having difficulty coping with activities of daily living or practical issues such as equipment and transport?

Psychological

- Is the caregiver having difficulty coping with the patient's psychological symptoms?
- Is the caregiver requesting a hastened death for the patient?

Medication and treatment

- Is the caregiver having difficulty managing complex medication and treatment regimes?

Family and Relationships

- Is there any communication breakdown or conflict between patient and family over prognosis, treatment options or care giving roles?
- Is the patient particularly concerned about the impact of the illness on the caregiver or family?

Information

- Does the caregiver or family want more information about the course and prognosis of the disease and treatment?
- Is the caregiver or family aware of the care services available to assist them and do they need assistance in accessing these? (eg respite, financial and legal services, psychological services, support groups, pastoral care.)

CAREGIVER WELLBEING

Physical and psychosocial

- Is the caregiver experiencing physical symptoms eg fatigue, physical strain, blood pressure/heart problems, stress related illness, or sleep disturbances?
- Is the caregiver feeling depressed, hopeless, fearful, nervous, tense, angry, irritable or critical of others, or overwhelmed?
- Does the caregiver have spiritual/existential issues that are of concern?

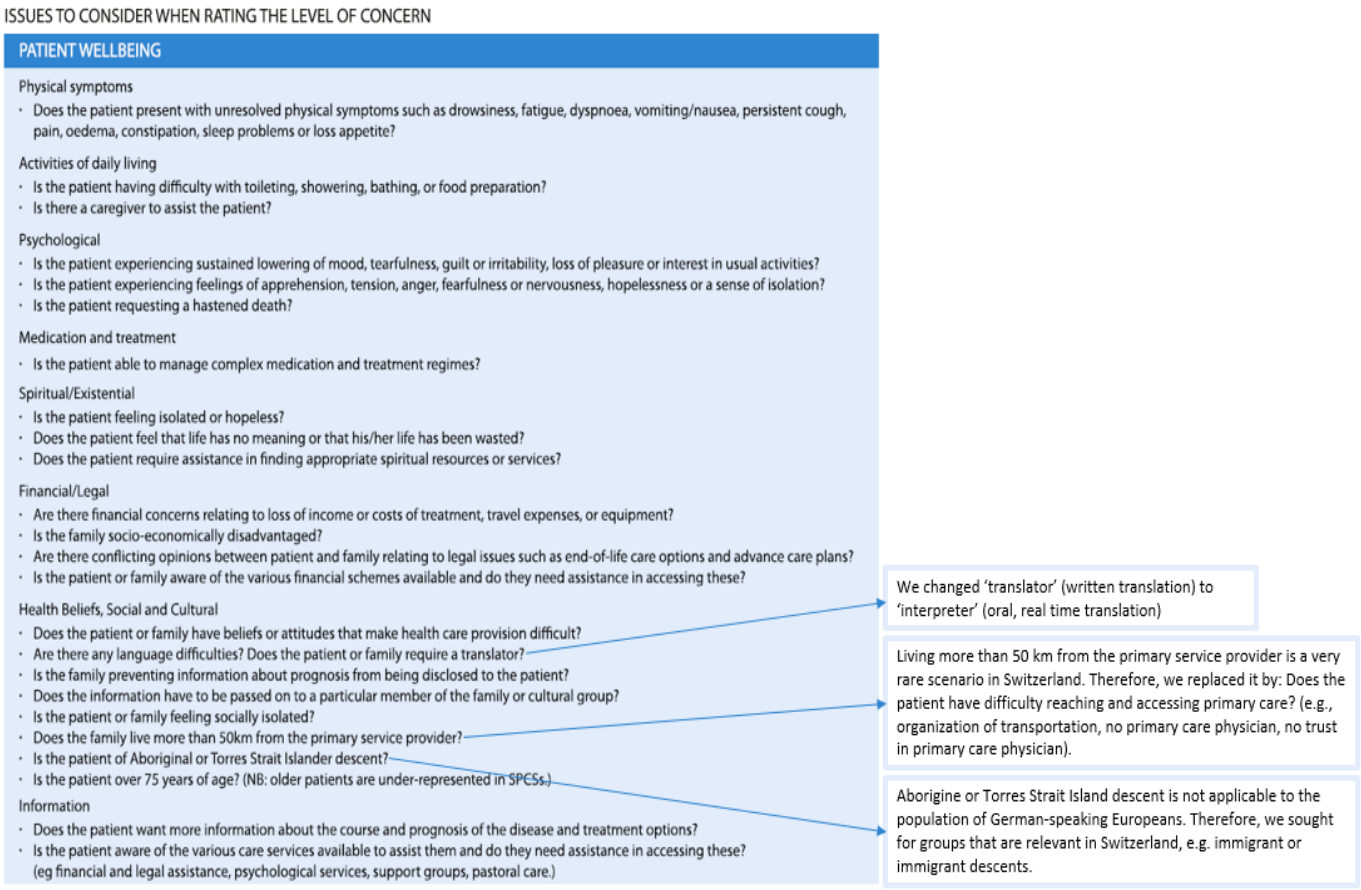
Bereavement Grief (pre and post death)

- Is the caregiver or family experiencing intrusive images, severe pangs of emotion, denial of implications of loss to self and neglect of necessary adaptive activities at home or work?

Funded by the Australian Government Department of Health and Ageing and Cancer Council NSW

Further copies are available at: http://www.newcastle.edu.au/research-centre/cherp/professional-resources

Additional file 6. Changes made for the cultural adaptation



Additional file 7. Table 1. Matrix of the weights used to assess inter-rater reliability and test-retest reliability

	No concern	Some/potential concern	Significant concern
No concern	1	0.2	0
Some/potential concern	0.2	1	0.8
Significant concern	0	0.8	1

Additional file 8. Table 2. Frequency of answers from the first application of the tool

	None	Some/potential	Significant
Section 2. Patient wellbeing (n=70)			
1. Is the patient experiencing unresolved physical symptoms (including problems with breathlessness, pain, fatigue, nausea, edema, insomnia, or cough)?	28 (40%)	38 (54%)	4 (6%)
2. Does the patient have problems with daily living activities?	60 (86%)	9 (13%)	1 (1%)
3. Does the patient have psychological symptoms that are interfering with well-being or relationships?	40 (57%)	30 (43%)	0 (0%)
4. Does the patient have concerns about how to manage his/her medication and treatment regimens?	67 (96%)	3 (4%)	0 (0%)
5. Does the patient have concerns about spiritual or existential issues?	64 (91%)	6 (9%)	0 (0%)
6. Does the patient have financial or legal concerns that are causing distress or require assistance?	51 (73%)	19 (27%)	0 (0%)
7. From the health delivery point of view, are there health beliefs, cultural, or social factors involving the patient or family that are making care more complex?	64 (91%)	6 (9%)	0 (0%)
Section 3. Ability of caregiver or family to care for patient (n=67)			
1. Is the caregiver or family distressed about the patient's physical symptoms?	66 (99%)	1 (1%)	0 (0%)
2. Is the caregiver or family having difficulty providing physical care?	43 (64%)	24 (36%)	0 (0%)
3. Is the caregiver or family having difficulty coping?	49 (73%)	18 (27%)	0 (0%)
4. Is the caregiver having difficulty managing the patient's medication and treatment regimens?	67 (100%)	0 (0%)	0 (0%)
5. Does the caregiver or family have financial or legal concerns that are causing distress or require assistance?	58 (87%)	9 (13%)	0 (0%)
6. Is the family currently experiencing problems that are interfering with their functioning or interpersonal relationships or is there a history of such problems? (n=70)	55 (79%)	15 (21%)	0 (0%)
Section 4. Caregiver wellbeing (n=67)			
1. Is the caregiver or family experiencing physical, practical, spiritual, existential, or psychological problems that are interfering with their well-being or functioning?	59 (88%)	8 (12%)	0 (0%)

	Yes	**No**
Does the patient require information about: (n=70)		
Heart disease	3 (4%)	67 (96%)
Treatment options	4 (6%)	66 (94%)
Financial/legal issues	16 (23%)	54 (77%)
Living will, life-extending measures	6 (9%)	64 (91%)
Prognosis	3 (4%)	67 (96%)
Medical/health/support services	5 (7%)	65 (93%)
Social/emotional issues	2 (3%)	68 (97%)

Additional file 9. Table 3. Sensitivity analysis to assess the inter-rater reliability for each one of second evaluators.

	Cohen´s kappa for second evaluator #1	Cohen´s kappa for second evaluator #2	higher kappa obtained by:
Section 2. Patient wellbeing			
1. Is the patient experiencing unresolved physical symptoms (including problems with breathlessness, pain, fatigue, nausea, edema, insomnia, or cough)?	0.38	0.46	evaluator #2
2. Does the patient have problems with daily living activities?	0.58	0.58	equal
3. Does the patient have psychological symptoms that are interfering with well-being or relationships?	0.66	0.68	
4. Does the patient have concerns about how to manage his/her medication and treatment regimens?	1.00	0.48	evaluator #1
5. Does the patient have concerns about spiritual or existential issues?	0.88	0.88	equal
6. Does the patient have financial or legal concerns that are causing distress or require assistance?	0.83	0.85	evaluator #2
7. From the health delivery point of view, are there health beliefs, cultural, or social factors involving the patient or family that are making care more complex?	0.00	0.20	evaluator #2
Section 3. Ability of caregiver or family to care for patient			
1. Is the caregiver or family distressed about the patient's physical symptoms?	1.00	0.70	evaluator #1
2. Is the caregiver or family having difficulty providing physical care?	0.77	0.77	equal
3. Is the caregiver or family having difficulty coping?	1.00	0.72	evaluator #1
4. Is the caregiver having difficulty managing the patient's medication and treatment regimens?	1.00	1.00	equal
5. Does the caregiver or family have financial or legal concerns that are causing distress or require assistance?	1.00	0.51	evaluator #1
6. Is the family currently experiencing problems that are interfering with their functioning or interpersonal relationships or is there a history of such problems?	0.86	0.44	evaluator #1
Section 4. Caregiver wellbeing			
1. Is the caregiver or family experiencing physical, practical, spiritual, existential, or psychological problems that are interfering with their well-being or functioning?	0.71	0.80	evaluator #2

3.4. Article 4.

Unmet device reprogramming needs at the end of life among patients with implantable cardioverter defibrillator: A systematic review and meta-analysis

Valentina González-Jaramillo
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Maud Maessen

Systematic review and meta-analysis. Published in *Palliative Medicine*, 2020

Contribution: I participated in the conceptualization of study, did abstract and full-text screening of hints, and extracted the data. I performed the analysis, made the figures and wrote the first draft of the manuscript. After that, I incorporated coauthors and reviewers' comments.

Review Article

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Unmet device reprogramming needs at the end of life among patients with implantable cardioverter defibrillator: A systematic review and meta-analysis

Valentina Gonzalez-Jaramillo[1], Piotr Sobanski[2*], Jose A Calvache[3,4*], Luisa F Arenas-Ochoa[5], Oscar H Franco[1], Lukas Hunziker[6], Steffen Eychmüller[7] and Maud Maessen[1,7]

Abstract

Background: Use of implantable cardioverter defibrillators is increasingly common. As patients approach the end of life, it is appropriate to deactivate the shock function.

Aim: To assess the prevalence of implantable cardioverter defibrillator reprogramming to deactivate the shock function at the end of life and the prevalence of advance directives among this population.

Design: Following a previously established protocol available in PROSPERO, we performed a narrative synthesis of our findings and used the logit transformation method to perform our quantitative synthesis.

Data sources: We searched seven bibliographic databases (Embase, Cochrane Central register of controlled Trials, Medline-Ovid, Web-of-Science, Scopus, PsychInfo, and CINAHL) and additional sources until April 2019.

Results: Of the references we identified, 14 were included. We found a pooled prevalence of implantable cardioverter defibrillator reprogramming at the end of life of 28% (95% confidence interval, 22%–36%) with higher reprogramming rates after the recommendations for managing the device at the end of life were published. Among patients with advance directives, the pooled prevalence of advance directives that explicitly mentioned the device was 1% (95% confidence interval, 1%–3%).

Conclusions: The prevalence of implantable cardioverter defibrillator reprogramming and advance directives that explicitly mentioned the device was very low. Study data suggested reprogramming decisions were made very late, after the patient experienced multiple shocks. Patient suffering could be ameliorated if physicians and other healthcare professionals adhere to clinical guidelines for the good management of the device at the end of life and include deactivating the shock function in the discussion that leads to the advance directive.

Keywords

Defibrillators, implantable, advance directive, terminal care, palliative care, advanced care planning, heart failure, meta-analysis, systematic review

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What is already known about the topic?

- Although implantable cardioverter defibrillator is a successful therapy, all patients eventually progress to the end-of-life phase.
- In patients with a progressive and marked decline, the shock function of the implantable cardioverter defibrillator no longer prolongs life and may instead cause them and their families unnecessary distress.
- Expert consensus statements and several guidelines recommend discussing deactivating the implantable cardioverter defibrillator shock function with patients who are nearing the end of their lives.

What this paper adds?

- In these meta-analyses, including data from six different developed countries, we found a low device-reprogramming rate and a very low rate of advance directives explicitly mentioning the device.
- This study shows an improvement in the rates of implantable cardioverter defibrillator reprogramming at the end of life, after the publication of a consensus statement as the ones from the Heart Rhythm Society and the European Heart Rhythm Association.

Implications for practice and policy

- We highlight the importance of more physicians and other health professionals adhering to clinical guidelines in discussing with the patient their preferences regarding the management of the implantable cardioverter defibrillator at the end of life and in documenting them.
- Healthcare directors could facilitate the compliance with the guidelines by organizing training for physicians to initiate discussions on device reprogramming, as well as by organizing informative talks for patients and their families to inform them about end-of-life device management options and encourage them to take the initiative to discuss this with their treating physicians.

Introduction

Both the incidence and prevalence of heart failure are growing as the population ages and risk factors increase.[1] Implantable cardioverter defibrillator has become the standard of care for both primary and secondary prevention of sudden cardiac death in selected patients.[2,3] With the expansion of the indications for its use, the number of patients with prolonged survival increased.[4–6]

Although implantable cardioverter defibrillator is a successful therapy, all patients eventually progress to the end-of-life phase. If the health of a patient with an irreversible condition is deteriorating, the device's shock function no longer prolongs life and may instead cause them and their families unnecessary distress.[7] Patients who have a recognizable end-of-life phase, with marked progressive decline, may need to reappraise their treatment goals. A discussion should be initiated with these patients so that they and their health providers can decide on the treatments that best meet the patient's goals of alleviating symptoms and preventing suffering. The discussion should cover the reprogramming of the implantable cardioverter defibrillator to deactivate the shock function, as mentioned in the Heart Rhythm Society (HRS) and the European Heart Rhythm Association (EHRA) recommendations for managing implantable cardioverter defibrillator at the end of life, published in 2010.[8,9] Note that the term implantable cardioverter defibrillator "deactivation" is a misnomer since besides shocks, the device has other functions such as pacemaker capacity and antitachycardia pacing should be kept active and helps controlling symptoms.[10] Therefore, the term implantable cardioverter defibrillation reprogramming will be used thorough the manuscript.

Discussing implantable cardioverter defibrillator reprogramming during a patient's end-of-life phase is a Class I recommendation in the 2017 AHA/ACC/HRS guideline for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death.[2] The result of these discussions is often indicated in a written document called an advance directive, which specifies the procedures and actions required or allowable when a patient is incapacitated or no longer able to communicate. Although implantable cardioverter defibrillator management should be discussed and explicitly mentioned in the advance directive, we do not yet know if advance directives change end-of-life outcomes for patients with the device.

We thus conducted a comprehensive and systematic appraisal of the literature on managing implantable cardioverter defibrillator at the end of life, with the goals of (1) assessing the prevalence of implantable cardioverter

defibrillator reprogramming to deactivate its shock function at the end of a patient's life, (2) determining the prevalence of advance directives among patients with implantable cardioverter defibrillator, and (3) evaluating the role advance directive plays in implantable cardioverter defibrillator reprogramming at the end of a patient's life. Finally, we set out to critically appraise limitations and gaps in the literature.

Methods

Literature search

Our systematic review followed the Joanna Briggs Institute Guide for conducting a systematic review of incidence and prevalence and was reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline;[11,12] the protocol was registered in PROSPERO (code CRD42019131219).

We searched for formal, peer-reviewed scientific literature on studies published before April 20, 2019 (date of last search), in seven electronic databases (Embase, Cochrane Central register of controlled Trials, Medline (Ovid) Web of Science, Scopus, PsychInfo, and CINAHL). We built our search construct for each database in consultation with an experienced medical information specialist. We combined terms related to the exposure (implantable defibrillators, intracardiac defibrillator, implantable cardioverter defibrillator) and the outcomes (deactivation, withholding treatment, turnoff, advance directive). We did not apply language or date restrictions.

To identify informal sources and gray literature, we searched Google Scholar and screened the first 200 hits. To identify more sources, we inspected the reference lists of studies that qualified for a full-text evaluation (backward searching). We performed a forward search by searching these titles in Google Scholar with the "cited by" function. We continued this procedure until it returned no new results.

Study selection and inclusion criteria

A pair of persons screened all titles and abstracts and then conducted full-text reviews to evaluate potentially relevant articles. Reviewers resolved disagreements through discussion. In the case of no consensus between the reviewers, a third reviewer was available to solve any disagreement.

We included prospective and retrospective observational studies (cross-sectional, case-control, or cohort) and randomized and nonrandomized interventional studies of adults ($\geqslant$ 18 years old), if the studies assessed the prevalence of implantable cardioverter defibrillator reprogramming at the end of life or assessed prevalence of advance directives among patients with the device.

Data extraction

We used a predesigned data collection form to extract data on study design, characteristics of the study population, and sample size. We extracted each outcome assessed, and the corresponding measure of associations (e.g. prevalence of implantable cardioverter defibrillator reprogramming, prevalence of advance directives, prevalence of shocks at the end of life, and place of death).

Assessing the risk of bias

Two reviewers independently rated the quality of studies, based on the Joanna Briggs Institute Critical Appraisal tools used for the JBI Systematic Reviews Checklist for Prevalence Studies.[13]

Data synthesis

We performed a narrative synthesis of findings of included studies and a quantitative synthesis using random-effects models to minimize the effect of between-study heterogeneity. We used STATA release 15 (Stata Corp, College Station, Texas) for all statistical analyses. We used the logit transformation method to combine proportions, using the command *metaprop_one* to fit the generalized linear mixed model (GLMM) with the option *logit*,[14] and we assessed heterogeneity using tau-square and the estimated prediction intervals as proposed by Higgins 2009, adding the *rfdist* option.[15] Prediction intervals help, as the name says, to predict the true effect in a new study. The narrower these intervals are, the more homogeneous the results. Therefore, the prediction intervals relate the true estimate, in this case, the true prevalence, with the heterogeneity, in this case, measured by tau-square. To deal with high heterogeneity, we performed subgroup analysis based on variables that could have caused the heterogeneity, such as publication year when the outcome was prevalence of device reprogramming or information source when the outcome was prevalence of advance directives. To assess if those variables were indeed a source of heterogeneity, we compared how the prediction intervals changed, expecting them to become narrower in the case of source of heterogeneity.

Results

Relevant studies

After deduplication, we identified 2422 potentially relevant citations. We screened titles and abstracts and selected the full texts of 34 articles to evaluate in detail. After full-text assessment, we excluded 20 papers (see Figure 1). We included 14 articles in the systematic review, 11 of which were included in the meta-analysis.

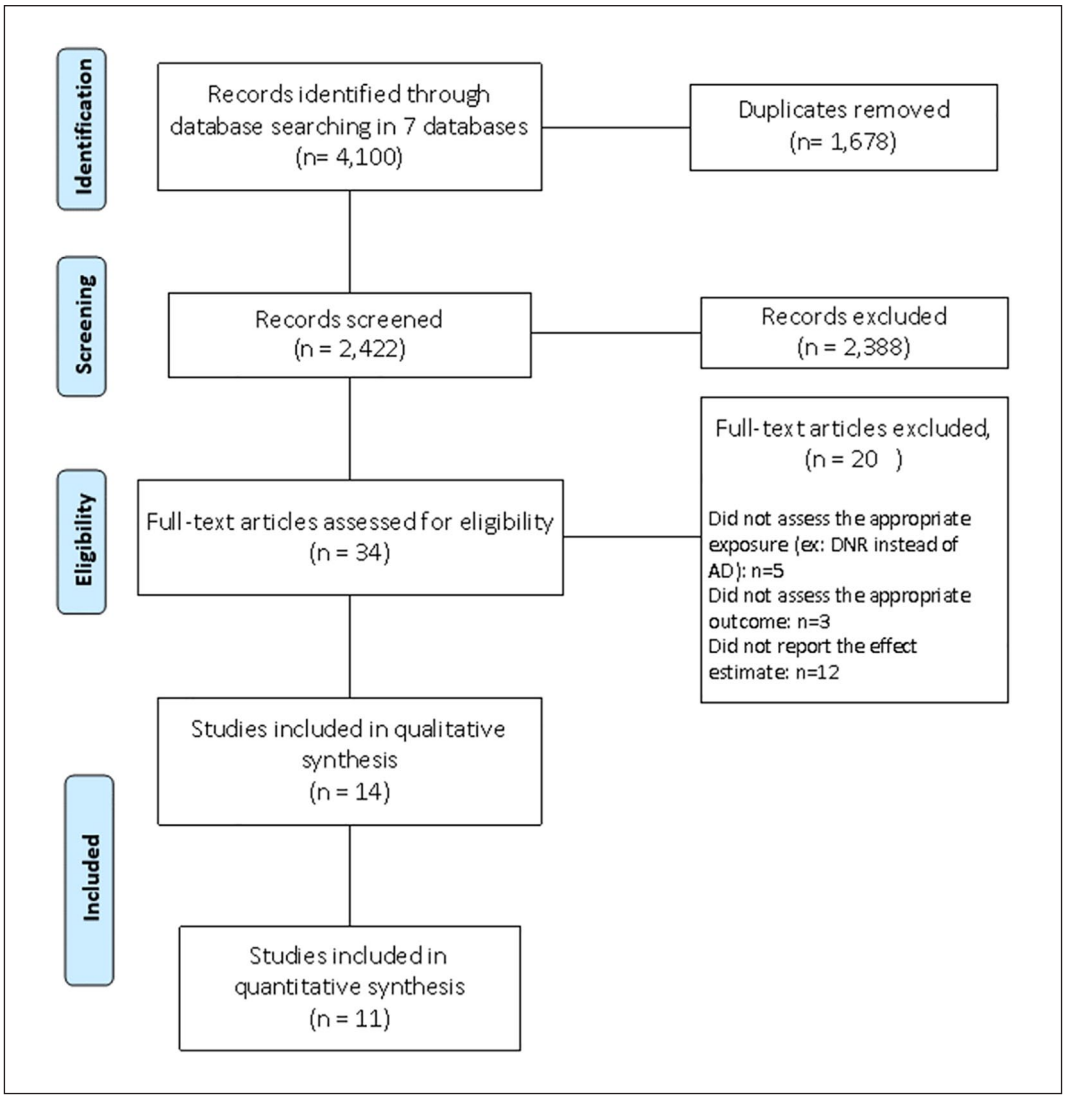

Figure 1. PRISMA 2009 flow diagram.
DNR: do-not-resuscitate; AD: advance directive.

General characteristics of the included studies

Detailed characteristics of the 14 included studies are summarized in Table 1, eight of which were retrospective cohorts, two were prospective cohorts, two had a cross-sectional design, one was a case-control study, and one was a noncontrolled intervention study. Participants totaled 2745 (range 26–701), 21% of whom were women. Eight studies included participants from the United States, two from Sweden, one from Canada, one from Ireland, one from England, and one from the Netherlands. Two studies included only patients who died in a hospital setting; the others did not distinguish between patients by place of death.

Of the 14 included studies, two assessed both prevalence of implantable cardioverter defibrillator reprogramming and prevalence of advance directives, eight assessed only prevalence of implantable cardioverter defibrillator reprogramming, and four assessed only prevalence of advance directives.

Supplemental Table 1 shows the risk-of-bias assessment for each study.

Main outcomes

Prevalence of implantable cardioverter defibrillator reprogramming (shock function deactivation). Ten studies reported prevalence of implantable cardioverter defibrillator reprogramming at the end of life; we included seven in the quantitative synthesis of the results (Figure 2). We explain why we excluded three studies in **Supplemental** Table 2.

Studies included in the quantitative synthesis. The pooled prevalence of implantable cardioverter defibrillator reprogramming at end of life was 28% (95% CI:

Table 1. Demographic characteristics and results of the studies included in the systematic review.

Author, year of publication	Study design	% of women, age*	Sample size	Main outcome			Proportion, (prevalence in percentage)	Results
				Prevalence of ICD reprogramming	Prevalence of AD among patients with ICD	Prevalence of AD explicitly addressing the ICD		
Goldstein et al.[16]	Retrospective cohort	17, 76 (49–91)	n = 100	X			21/100, (21%)	The 100 next of kin who were included in the survey reported that discussions about reprogramming the ICD occurred in 27 cases. Of these, the patient or relative decided to reprogram the ICD in 21 cases.
Berger et al.[17]	Cross-sectional	18, 72 (40–86)	n = 57		X	X	AD: 35/57, (61%) AD addressing the ICD: 0/35 (0%)	An AD was completed by 35 subjects. None of them addressed the use of ICD. Yet, 15 of the 35 subjects, when asked by the researchers, indicated preferences for disabling the ICD.
Lewis et al.[18]	Case control	19, 71 ± 10	n = 63	X			20/63, (32%)	Out of the 63 patients, 20 had the device reprogrammed before dead (Group 1) and 43 did not (Group 2). Both groups were compared in terms of age, sex, indication for ICD, and cause of death. Causes of death in Group 1 were more commonly due to a chronic condition, whereas in the Group 2 it was acute.
Kirkpatrick et al.[19]	Cross-sectional	30, 61 (19–90)	n = 278		X	X	AD: 140/278, (50%) AD addressing the ICD: 3/140, (2%)	One-half of the subjects had some form of AD, either a living will (n = 71, 26%), a power of attorney for healthcare (n = 7, 3%), or both (n = 62, 22%). Only three of the subjects had included a plan for their ICD.
Tajouri et al.[20]	Retrospective cohort	29, 63 ± 17	n = 420	X			7/44	By the moment of the data collection, 44 patients had died. The researchers were unable to determine end-of-life ICD management for most of those patients (n = 30, 68%). Among the remaining 14, seven had the device reprogrammed.
					X	X	AD: 127/420, (30%) AD addressing the ICD: 2/127, (1.6%)	Out of the 420 patients, 127 had an AD. Among these, 83 ADs (65%) were completed more than 12 months before ICD implantation, 44 (35%), within 12 months before implantation, 39 (31%), within 6 months before implantation, and 10 (8%), after implantation. Only two ADs mentioned the ICD or ICD reprogramming at the patient's end of life.
Sherazi et al.[21]	Retrospective cohort	17, 69 ± 9	n = 98	X			15/98, (15%)	Among the 98 patients who died during the study, ICD reprogramming was performed in 15 (15%).Of these, the ICD was reprogrammed in the last week for 11 patients. In the remaining four patients, the ICD was reprogrammed the day of death.
Buchhalter et al.[22]	Retrospective cohort	33, 79 (31–95)	n = 150		X	X	AD: 85/150, (57%), AD addressing the ICD: 1/85, (1%)	Eighty-five patients (57%) had ADs in their medical records, of which 41 (48%) executed ADs before implantation. Only one patient specifically mentioned the ICD in the AD.
Westerdahl et al.[23]	Retrospective cohort	11, 74 ± 9	n = 125	X			25/125, (20%)	Among the 125 patients with ICD, 25 had the device reprogrammed 24 h before the patient died. More than half (52%) of the patients had a DNR order. Despite this, 51% of the patients with a DNR order still had shock therapy programmed "on" at 1 h before death.

(Continude)

Table 1. (Continude)

Author, year of publication	Study design	% of women, age*	Sample size	Main outcome			Proportion, (prevalence in percentage)	Results
				Prevalence of ICD reprogramming	Prevalence of AD among patients with ICD	Prevalence of AD explicitly addressing the ICD		
Hill et al.[24]	Retrospective cohort	14, 73 ± 10	n = 44	X			16/44, (36%)	Out of the 44 patients, 16 had their ICD reprogrammed, all of them following an end-of-life discussion.
Kramer et al.[25]	Prospective cohort	25, 71 ± 8	n = 51	X			5/7	During study follow-up, nine patients died. Two patients' circumstances were entirely unknown, and five received ICD shocks in the days immediately prior to death. Four patients died of progressive heart failure and all had their ICDs reprogrammed, but only after having received multiple shocks.
					X			At baseline, 62.7% of patients had completed a living will and 84% had identified a healthcare proxy. Over the course of the 18 month follow-up period, these cumulative outcomes increased to 88% and 98%, respectively.
Merchant et al.[26]	Prospective cohort	44, 61 ± 15	n = 701		X	X	AD: 243/701, (35%) AD addressing the ICD: 1/164	701 patients were followed for at least 1 year after device implantation. Of those, 164 had an AD at any point up to 1 year after ICD implant. In only one case out of the 164, the AD specifically addressed the ICD. 79 additional patients had ADs documented more than 1 year after ICD implant, resulting in 243 patients with ICDs who had an AD documented at any time point.
Javaid et al.[27]	Nonrandomized intervention study	Not described	n = 26	X				At baseline, in 2015, 13 patients died without premortem reprogramming (0% of reprogramming). In January 2016, educational campaigns were conducted for health personnel of the hospital to remind them of the importance of discussing the management of ICD at the end of life and a local guide was published on how to do this. Between February and July 2016, out of 13 patients who died in the hospital, 7 had the device reprogrammed (reprogramming in 54% of patients).
Stoevelaar et al.[28]	Retrospective cohort	12, 67 (58–73)	n = 380	X			Before 2010: 15/96, (16%). After 2010: 97/284, (34%)	Between 2007 and 2009, 15 of 96 patients (16%) had the device reprogrammed; between 2010 and 2012, 24 of 108 (22%); and between 2013 and 2016, 73 of 176 patients (42%). On average, 30% of the patients had the device reprogrammed.
Kinch Westerdahl et al.[29]	Retrospective cohort	17, 73 ± 9	n = 341	X			Before 2010: 30/89, (34%); In 2014: 130/252, (52%)	Consensus statements to address and highlight the management of the ICD in patients nearing end of life were published in 2010. The authors investigated the prevalence of ICD reprogramming before and after the statements. After the publication in 2010, the reprogramming increased by 53%.

AD: advance directive; ICD: implantable cardioverter defibrillator.
*Presented as mean ± standard deviation or as median (IQR).

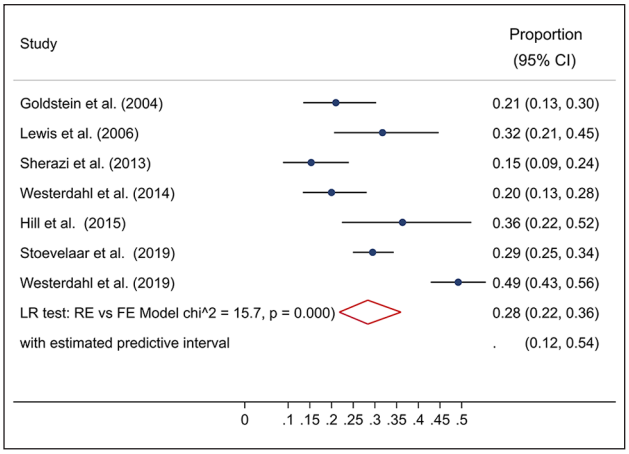

Figure 2. Prevalence of implantable cardioverter defibrillator reprogramming (shocking function deactivation) at the end of life. Forest plot of the studies examining the prevalence of implantable cardioverter defibrillator reprogramming using random-effects meta-analysis. Data presented as proportion and 95% confidence interval (CI, %).

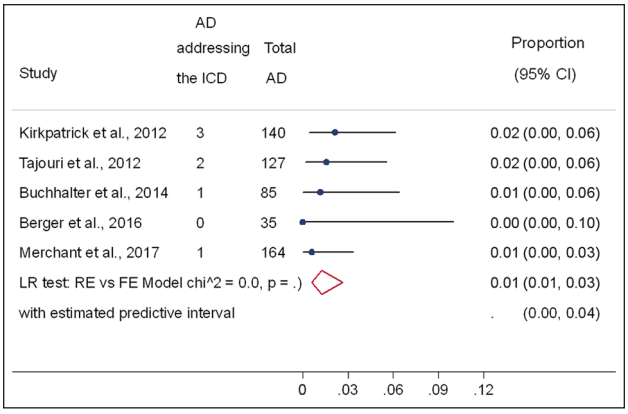

Figure 3. Prevalence of advance directives (AD) explicitly addressing the implantable cardioverter defibrillator. Forest plot of the studies examining the prevalence of advance directives that addressed the implantable cardioverter defibrillator using random-effects meta-analysis. Data presented as proportions and 95% confidence interval (CI, %).

22%–36%), with a tau-square of 0.14 and an estimated predictive interval of 12%–54%. Publication of the EHRA and HRA recommendations explained some of this heterogeneity; when we stratified by outcome assessment date, the estimated predictive interval among studies conducted before the statement publication narrowed to 13%–29% (**Supplemental** Figure 1).

Five studies included patients treated before the recommendations were published in 2010.[16,18,21,23,28] They reported lower reprogramming prevalence (pooled proportion prevalence of 20%, 95% CI: 16%–25%) than articles evaluating the outcome after 2010 (pooled proportion prevalence of 40%, 95% CI: 32%–49%).[24,28,29] Two studies included patients treated both before and after 2010 and presented the results separately. Kinch Westerdahl et al.[29] conducted a study in 2019 that included 341 patients from more than 60 hospitals in Sweden and reported the prevalence of implantable cardioverter defibrillator reprogramming at the end of life among patients who died between 2003 and 2010 (34%) and the prevalence of reprogramming among patients who died in 2014 (52%). Stoevelaar et al. conducted a study that included 380 deceased patients from Dutch hospitals; the prevalence of reprogramming among patients who died between 2007 and 2009 was 16% and the prevalence among those who died between 2010 and 2016 was 34%.[28] In both studies, there was a difference in prevalence of 18% over the time, with higher rates after the statements publication.

Studies not included in the quantitative synthesis. Among the three studies that could not be included in the meta-analysis, one assessed the effectiveness of an institutional education campaign about device reprogramming at the end of life and showed that, after the campaign, out of the 13 patients who died, seven had the device reprogrammed.[27] The remaining two studies had a sample size of less than 15 patients for the analysis, due to missing data or because, being a prospective study, most of the patients were still alive.[20,25]

Prevalence of advance directives among patients with implantable cardioverter defibrillator. Six studies assessed prevalence of advance directives in patients with implantable cardioverter defibrillator. Advance directives included living wills and personal representatives for medical decision-making.

The pooled prevalence was 53% (95% CI: 37%–68%), with a tau-square of 0.58 and an estimated predictive interval of 10%–92% (Supplemental Figure 2).

The presence or absence of advance directives across the studies was assessed in two ways: studies used interviews/self-assessment questionnaires or extracted the information from clinical charts. Due to this difference in the information source, the prevalence of advance directives ranged from 30% to 84%, which explains the broad predictive interval of the pooled estimate. Studies that relied on interviews or self-assessment questionnaires (n = 3) reported higher rates of advance directives than studies that extracted this information from clinical charts (n = 3) (Supplemental Figure 3).

The minimum prevalence of advance directives across the studies was 30%, but the prevalence of advance directives that specifically addressed the implantable cardioverter defibrillator was much lower. Five studies reported that implantable cardioverter defibrillator was rarely explicitly discussed; pooled prevalence was 1% (95% CI: 1%–3%), with a tau-square < 0.001 and an estimated predictive interval from 0% to 4% (Figure 3).[20,17,19,22,26] The

study by Kirkpatrick et al. had the highest prevalence of advance directives that directly addressed the implantable cardioverter defibrillator: advance directives prevalence was 50.4% (140/278 patients had one), but only 2.1% (3/140) of advance directives addressed the implantable cardioverter defibrillator.[19]

Influence of the presence of advance directives on implantable cardioverter defibrillator reprogramming. Just one study reported an association between advance directives and implantable cardioverter defibrillator reprogramming at the end of life, concluding that patients who had advance directives were no more likely to have had their devices reprogrammed.[20] In this study, data about implantable cardioverter defibrillator reprogramming were missing in 68% of patients (30/44) who died. Since the finding of no association was derived from the remaining 14 patients, there was not enough evidence on the role of advance directives on implantable cardioverter defibrillator reprogramming at the end of life.

Additional outcomes

Prevalence of delivered shocks at the end of life. Five of the studies we included reported prevalence of shocks at the end of life in addition to the main outcomes we defined. Because "end of life" is not a well-defined period, reports on outcomes were so heterogeneous that we could not quantitatively pool prevalence of shocks. Some studies reported prevalence in the last 3 months,[18,21] others in the last month,[16,18,21,28] last week,[21] last days/day,[23,28] or last minutes.[16] Prevalence of shocks in the last months of life ranged from 7% to 27%.

Discussion

Main findings

We found that nearly three out of four patients died with a fully active device, half of the patients with an implantable cardioverter had an advance directive, and few of them had an advance directive that specifically addressed device activity at the end of life; the pooled prevalence estimate was only 1%.

Since the 2010 publication of the EHRA and the HRA statements, others have also recommended discussing implantable cardioverter defibrillator reprogramming in patients nearing the end of life.[2,30] Although protocols now guide physicians and healthcare providers through the deactivation process step by step,[31,32] our review found only a 28% pooled prevalence of implantable cardioverter defibrillator reprogramming at the end of life. Across studies, prevalence ranged from 15% to 52%, and almost all of the device reprogramming happened in a hospital setting, with fewer in hospices and nursing homes, and very few in patients at home. Our pool estimate is low, given the results of studies that have assessed patients' desire for reprogramming.[17,33,34] In one of these studies, the authors included patients who were not yet at the end of life and told them about the potential benefits and burdens of an active shock function. Then, the authors presented to them hypothetical common scenarios such as incurable disease and permanent inability to get out of bed; 71% of participants wanted the implantable cardioverter defibrillator reprogrammed in at least one of these scenarios.[33]

Between 0% and 0.01% of patients with implantable cardioverter defibrillator had an advance directive that explicitly addressed the device. In the subgroup of implantable cardioverter defibrillator patients that had any form of advance directive, the pooled prevalence of advance directives that explicitly addressed device activity at the end of life was 1%. This is very low for any cut-off of percentage indicating a satisfactory use of advance directive and indicates that the advance directive, which was created to increase patients' autonomy and ensure medical management that aligns with their preferences, is an underused legal document. Berger et al. showed that only 35/57 patients with implantable cardioverter defibrillator had an advance directive and none of them addressed or discussed modifying the activity of the device. However, when they interviewed the patients, 15 of that 35 reported that they wanted the device reprogrammed at the end of life.[17] In this small sample, 15 patients could have suffered shocks against their will at the end of their life; an unwanted outcome that could have been prevented through discussion.

Strengths and limitations

The quality of studies included in this review, assessed by the risk of bias, was compromised mainly by the lack of confidence intervals when reporting prevalence (in all the studies) and insufficient sample size (in 9 out of the 14 studies), suggesting they were underpowered to correctly estimate prevalence. However, since the meta-analysis allowed us to increase power by increasing the sample size, we think our study is not similarly limited. Regarding the statistical analysis, although all studies failed to report confidence intervals, the statistical methods employed were adequate.

As a limitation for the external validity of our study, the hospitals most likely to investigate the prevalence of advance directive and the prevalence of implantable cardioverter defibrillator reprogramming may be those most likely to have implemented them in everyday practice. However, many hospitals and care settings do not implement this proceeding into their routine. Even among the institutions that care for people near death, such as hospices, a few have clear policies on implantable cardioverter defibrillator management. A study of

100 randomly selected hospices among the 3750 in the United States found that only 10% had a reprogramming policy.[35] Thus, the real prevalence of advance directives that specifically addresses implantable cardioverter defibrillator, and the prevalence of implantable cardioverter defibrillator reprogramming at the end of life, might be much lower than our results suggest.

Finally, certain study designs may not be the most appropriate to assess the outcomes included in this review. For our first aim, to assess the prevalence of implantable cardioverter defibrillator reprogramming at the end of life, a prospective design could be appropriate as long as it includes only patients with short life expectancy or in whom a progressive decline has been detected. Otherwise, the follow-up needed to evaluate the outcome would be too long, with the risk of high loss of follow-ups or not obtaining the expected number of events. Such was the case in the study conducted by Kramer et al.,[25] in which, at the end of the follow-up, only nine patients had died. Similarly, institutional studies assessing the effectiveness of an intervention in a short period are not adequate as the sample size tends to be very small and the reported estimate would correspond to a specific intervention rather than a prevalence derived from routine clinical practice.[27]

The main strength of our study is that ours was the first to summarize and critically assess the prevalence of the implantable cardioverter defibrillator reprogramming at the end of life. On the other hand, without claiming to demonstrate or infer causality, the study showed an improvement in the prevalence of the device reprogramming at the end of life after the publication of the HRS and the EHRA statements in 2010. In addition, we both qualitatively and quantitatively summarized the prevalence of advance directives among patients with implantable cardioverter defibrillator, and the prevalence of advance directives that explicitly addressed the device.

Implications and recommendations

This study shows the underuse of implantable cardioverter defibrillator reprogramming and the underuse of documents that record patients' preferences for end-of-life device management as are the advance directives. Although the rates of deactivation have been higher following the publication of the statements, they continue to be low. Thus, guidelines alone are not sufficient to bring about a change in practice. It is therefore important to design institutional strategies involving both health personnel and patients with their families. These strategies should focus on informing patients with implantable cardioverter defibrillator and their families about the consequences of dying with an active shock function and encouraging them to discuss this with their treating physician. In addition, healthcare personnel should be trained to discuss this with patients and to know how to proceed if the patients desire the device reprogramming.

Furthermore, clinicians must also consider the timing to reprogram the cardioverter defibrillator, as some evidence suggest that the decision to reprogram the device may have been triggered by the patients' experience of multiple shocks over the preceding weeks.[21]

As a gap, women were underrepresented in these studies (21% of included patients). National registries show that women are less likely to receive implantable cardioverter defibrillator than men (e.g. 15% in France and 21% in Australia).[3,36] Registry data from 11 European countries found women made up only 23% of the patients with implantable cardioverter defibrillator.[37] Women are also underrepresented in trials for prevention of sudden cardiac death with the device, including MADIT II (15%) and SCD-HeFT (23%).[38,39] It is necessary to increase the participation rate of women in both clinical trials and cardiovascular interventions in order to achieve gender balance in outcome assessment and medical care.[40]

Conclusion

Although expert consensus statements and several guidelines recommend discussing deactivating the device shock function with patients who are nearing the end of their lives, and studies that have assessed patients' preferences have shown that most patients would prefer the shock function deactivation,[33,34] we found that nearly 75% of patients die with a fully active device. This reveals a gap both between guidelines and clinical practice and between patients' preferences and the reality of their last days of life.

If more physicians and other healthcare professionals adhered to the clinical guidelines for discussing with the patient their preferences for managing the device, including recommending and establishing advance directives, fewer patients and families would suffer the stress and distress of repeated and futile shocks in the last weeks of their lives.[7] Healthcare directors could facilitate the compliance with the guidelines by organizing training for physicians to initiate discussions on device reprogramming, as well as by organizing informative talks for patients and their families to inform them about end-of-life device management options and encourage them to take the initiative to discuss this with their treating physicians.

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Author contributions

VG, JC, and LA screened titles and abstracts. VG obtained full text, determined eligibility of articles, and participated in data extraction. VG, JL, and LA assessed the quality of the included studies. VG conducted the data synthesis and analysis. PS, MM, and SE contributed in the interpretation of the data. VG, PS, SE, and MM drafted the final paper. All authors contributed to the critical revision of the paper and approved the final version.

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Supplemental material

Supplemental material for this article is available online.

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Supplemental Figure 1. Prevalence of implantable cardioverter defibrillator reprogramming (shocking function deactivation) at the end of life, stratified by the date of outcome assessment (before or after statements publication in 2010).

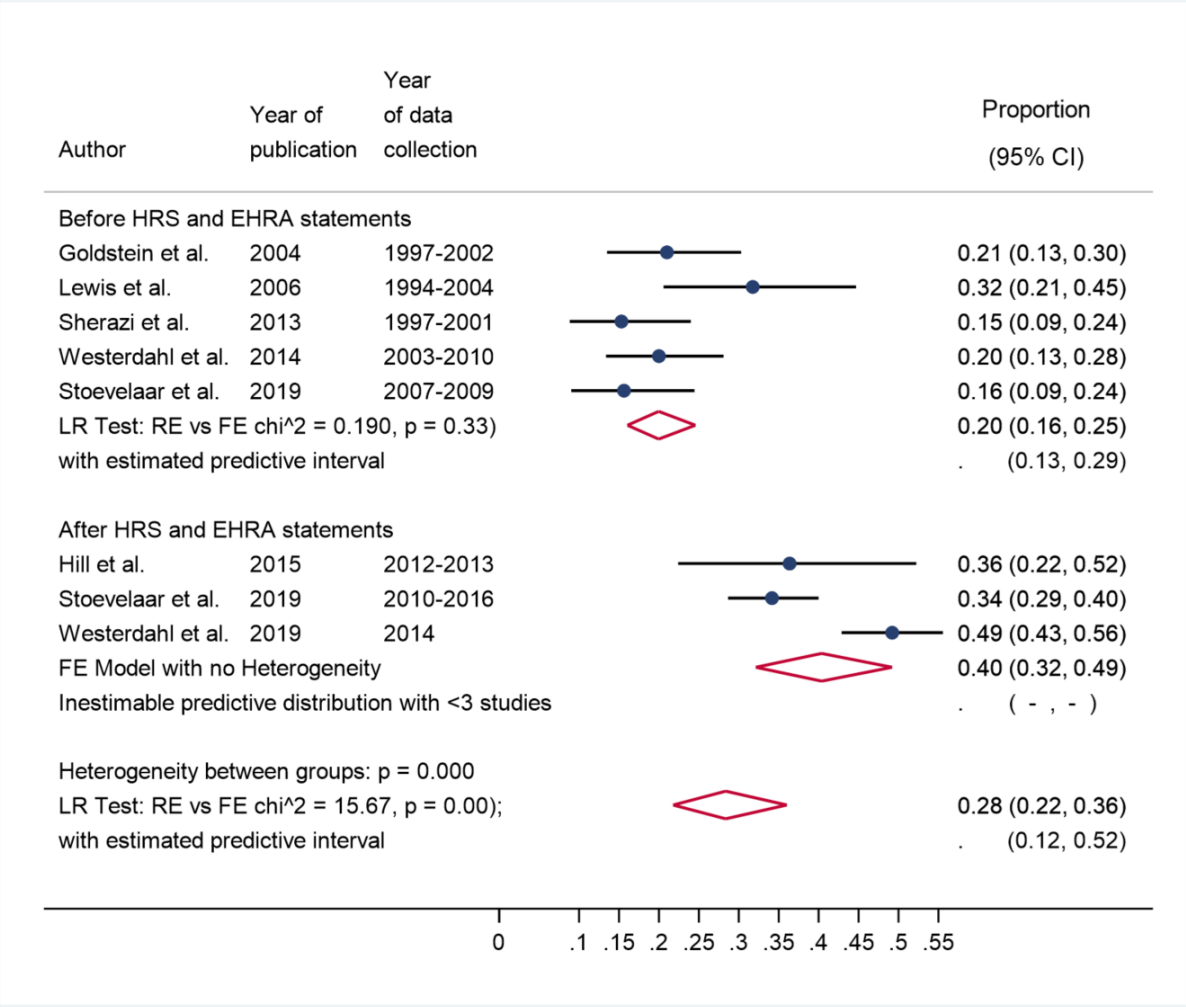
Supplemental Figure 2. Prevalence of advance directives among patients with implantable cardioverter defibrillator.

Supplemental Figure 3. Prevalence of advance directives among patients with implantable cardioverter defibrillator, stratified by information source (interviews or self-report questionnaires vs clinical chart).

Supplemental Table 1. Risk of bias assessment

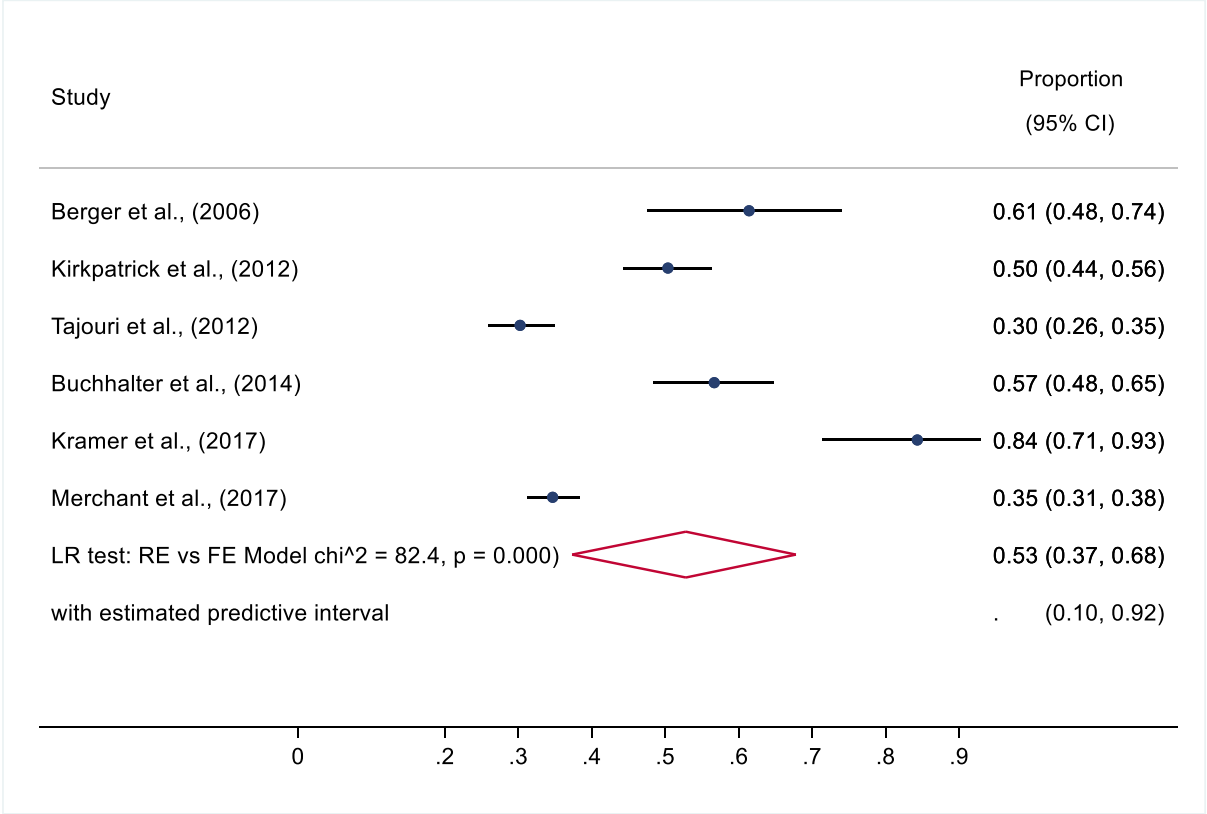
Supplemental Table 2. Reasons to exclude studies from the meta-analysis

Supplemental Figure 1. Prevalence of implantable cardioverter defibrillator reprogramming (shocking function deactivation) at the end of life, stratified by the date of outcome assessment (before or after statements publication in 2010).



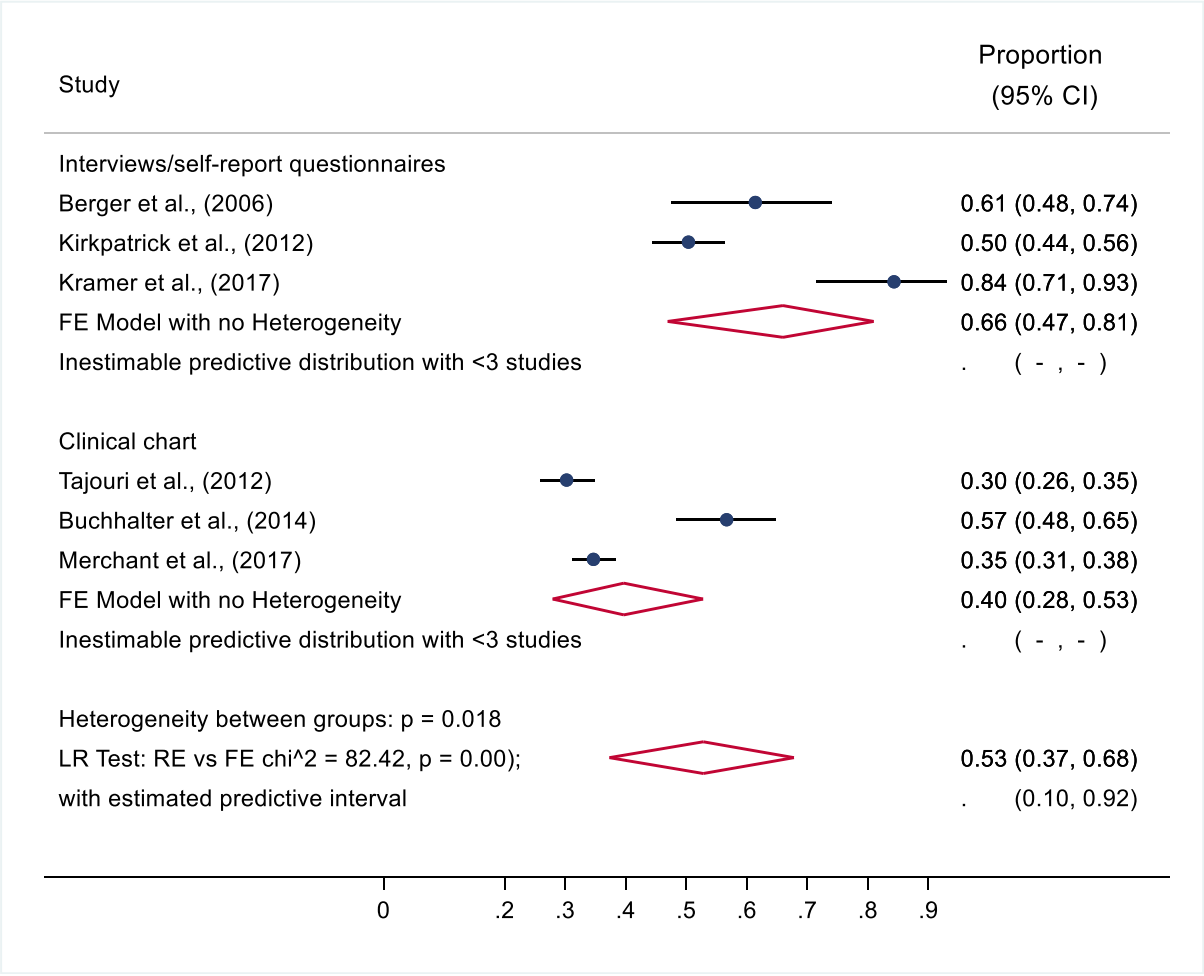
Forest plot of the studies examining the prevalence of implantable cardioverter defibrillator reprogramming using random effects meta-analysis, stratified by date of outcome assessment. Data presented as proportions and 95% confidence intervals (CI; %).

Supplemental Figure 2. Prevalence of advance directives among patients with implantable cardioverter defibrillator.



Forest plot of the studies examining the prevalence of advance directives among patients with implantable cardioverter defibrillator using random effects meta-analysis. Data presented as proportions and 95% confidence intervals (CI; %).

Supplemental Figure 3. Prevalence of advance directives among patients with implantable cardioverter defibrillator, stratified by information source (interviews or self-report questionnaires vs clinical chart).



Forest plot of the studies examining the prevalence of advance directives among patients with implantable cardioverter defibrillator reprogramming using random effects meta-analysis, stratified by information source. Data presented as proportions and 95% confidence intervals (CI; %).

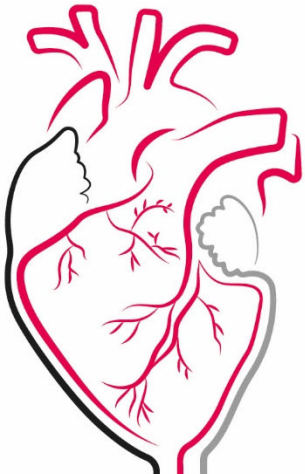
Supplemental Table 1. Risk of bias assessment

Study	1. Was the sample frame appropriate to address the target population?	2. Were study participants sampled in an appropriate way?	3. Was the sample size adequate?	4. Were the study subjects and the setting described in detail?	5. Was the data analysis conducted with sufficient coverage of the identified sample?	6. Were valid methods used for the identification of the condition?	7. Was the condition measured in a standard, reliable way for all participants?	8. Was there appropriate statistical analysis?	9. Was the response rate adequate, and if not, was the low response rate managed appropriately?
Goldstein et al., 2004	✓	✓	✓	✓	✓	✗	✗	✗	✓
Berger et al., 2006	✓	✓	✗	✓	✓	?	?	✗	✓
Lewis et al., 2006	?	?	✗	✓	?	✓	✓	✗	?
Kirkpatrick et al., 2012	✓	✓	✓	✓	✗	✗	✗	✗	✗
Tajouri et al., 2012	✓	✓	✓	✓	?	✓	✓	✗	✗
Sherazi et al., 2013	✓	✓	✓	✓	✓	✓	✓	✗	–
Buchhalter et al., 2014	✗	✓	✓	✓	✓	✓	✓	✗	–
Westerdahl et al., 2014	✓	✓	✓	✓	✓	✓	✓	✗	–
Hill et al., 2015	✓	✓	✗	✓	✓	✓	?	✗	–
Wkramer et al., 2017	✗	✓	✗	✓	✓	✓	✓	✗	–
Merchant et al., 2017	✓	✓	✓	✓	✓	✓	✓	✗	?
Javaid et al., 2018	?	✓	✗	✗	✓	✓	✓	✗	–
Stoevelaar et al., 2015	✓	✓	✓	✓	✓	✓	✓	✗	–
Westerdahl et al., 2019	✓	✓	✓	✓	✓	✓	✓	✗	–

Risk of bias summary: review authors' judgements about each risk of bias item for each included study (✓ = low risk of bias; ✗ = high risk of bias; ? = unclear risk of bias, – = not applicable).

Supplemental Table 2. Reasons to exclude studies from the meta-analysis

Author, year of publication	Sample size of the study	Sample size of the outcome for the meta-analysis	Reason for exclusion from the quantitative analysis
Tajouri et al., 2012	n=420	n=14	Among 420 participants, 44 had died. Of them, information about end-of-life ICD management was missing for 30 patients (68% of missing data).
Kramer et al., 2017	n=51	n=9	This prospective study included 51 patients. During the follow-up, only nine died. Therefore, the sample size is too small to be included in the meta-analysis.
Javaid et al., 2018	n=26	n=13	This is a non-randomized, single-centre pilot study, assessing the utility of educational campaigns for health personnel of the hospital to remind them the importance of discussing the management of ICD at the end of life. This was motivated after realizing that in the last year, out of the 13 patients who had died in the hospital, none had the device reprogrammed. During the pilot study, 13 patients were included.



4. Overall discussion

"As for the future, your task is not to foresee it, but to enable it."

- **Antoine de Saint-Exupéry** (June 23, 1900 – July 31, 1944)

4.1. Summary of the findings

Article 1. Using the Surprise Question in ambulatory populations with heart failure: a prospective cohort study (Chapter 3.1)

Two of the challenges delivering PC for patients with HF are prognostication and the identification of PC needs. In this prospective cohort study, I evaluated the performance of the SQ, a generic tool used to predict 1-year mortality in the HF population. Treating cardiologists answered the SQ for 174 ambulatory patients who were recruited from 2 outpatient HF clinics between 2017 and 2018. After 1 year, mortality among those with a positive SQ was 21%, and 3% among those with a negative SQ ($p<0.001$). Patients with a positive SQ had 7.5 times higher odds of death at 1 year compared to those with a negative SQ (OR 7.6, 95% CI 2.1-26.9). Sensitivity was 85% (95% CI 69%-100%), and specificity 57% (95% CI 49%-65%). The positive and the likelihood ratios of the SQ were 1.98 and 0.26, respectively. The SQ's performance predicting 1-year mortality was similar among women and men. The SQ performed better in patients younger than 70 years; in patients with reduced or mildly reduced ejection fractions; and in patients at NYHA class III or IV.

Article 2. Performance of the NECPAL tool to identify palliative needs in patients with heart failure (Chapter 3.2)

The NECPAL tool is another prognostic tool, and it begins with the SQ. Using the same cohort as in article 1, I conducted a cross-sectional analysis to assess the prevalence of PC needs for outpatients at HF clinics with the NECPAL tool. Additionally, I assessed its performance identifying PC needs based on patients' health-related quality of life and symptom burden. Health-related quality of life was evaluated using the SF-12 and the KCCQ, and the ESAS was used to assess symptom burden. Among patients under optimal medical treatment in outpatient HF clinics, 44% met the NECPAL tool criteria to receive concurrent PC (+NECPAL). Those with a +NEPCAL were mostly classified as NYHA III/IV and were older than those with a -NEPCAL. There was no difference between the prevalence of PC needs between men and women, nor across LVEF categories. Compared to -NECPAL patients, +NECPAL patients had worse quality of life according to the SF-12 and KCCQ. In addition, they had more severe shortness of breath, tiredness, drowsiness, and pain, as well as more psychosocial problems.

Article 3. Validation of the German version of the Needs Assessment Tool: Progressive Disease – Heart Failure (Chapter 3.3)

As PC needs or other types of needs can be present across the spectrum of HF, there are tools used to assess needs regardless of prognosis. These tools are called need assessment tools, such as the NAT: PD-HF. We translated the NAT: PD-HF tool from English into German and culturally adapted it. Then, we assessed its psychometric characteristics, including internal consistency, inter-rater reliability, and test-retest reliability. Additionally, we evaluated whether and how patients and health care personnel understood the tool and

its utility, and we assessed the face validity, applicability, relevance, and acceptability of the German NAT: PD-HF among health care personnel. The validation showed good internal consistency and substantial inter-rater agreement for most of the items. Regarding the test-retest reliability, we found almost perfect agreement between the first and second assessments. Patients thought well of the tool, and they agreed that it could help to improve their quality of care and that it covered relevant topics that are not normally addressed during clinical consultations. Similarly, health care professionals rated face validity and user-friendliness highly. However, like the participating health care personnel, we also believe training is necessary to ensure the correct use of the tool.

Article 4. Unmet device reprogramming needs at the end of life among patients with implantable cardioverter defibrillator: A systematic review and meta-analysis (Chapter 3.4)

In a systematic review and meta-analysis that included 14 studies from North America and Europe, I assessed gaps in EoL care for patients with ICDs. Specifically, I evaluated the proportion of patients who died with an ICD and whose ICD shock function was deactivated before death (to avoid painful shocks in the last stage of life). I found that nearly 3 out of 4 patients (pooled estimate 28%, 95% CI 22-36%) died with a fully active device (ie, an activated shock function). Additionally, I assessed the proportion of patients who died with an ICD who had an advance directive. Among those who had this document, few mentioned what to do with the device at the EoL; the pooled prevalence estimate was only 1% (95% CI 1-3%).

4.2. Strengths and limitations

Strengths

Since low participation rates or significant losses at follow-up are a threat to the internal validity of results in prospective studies because of the risk of selection bias [112], high participation rates and low rates of loss in follow-up studies are strengths of our collective studies. For the NAT: PD-HF translation and validation, the participation rate was 30% and there were no losses to follow-up. In the other 2 studies, participation rates were high (95% and 99% in each HF clinic) and follow-up losses were 2% for each HF clinic. Furthermore, to keep inclusion criteria broad, we invited eligible patients to participate in the study who were at least 18 years and understood 1 of the questionnaire languages. Regardless of severity or clinical profile, we included participants from across the entire HF spectrum.

We also consider women's representation in our studies a strength. Although sex and gender bias in data are present in medicine and other fields of science, sex and gender bias in cardiology are frequently mentioned when talking about data bias in medicine [113]. To address this, we followed recommendations from organizations such as the National Institutes of Health, academia, industry, as well as physicians and advocacy groups. Our studies present results stratified by sex and discuss issues related to the underrepresentation of women, if applicable. Although the proportion of women who

participated in the study conducted in a HF clinic in Switzerland was low (17%), which limits the conclusions about the acceptability of the NAT: PD-HF tool among women, this does not limit our evaluation of the psychometric characteristics of the tool. The proportions of women in the HF clinics in Colombia were good (39% and 49%). Therefore, this strength aligns with our approach to account for sex throughout our studies.

According to clinical and demographic characteristics, patients have similar profiles across the 3 clinics, which is another strength of our collective studies. Mainly patients were males, had reduced ejection fractions, and were classified as NYHA class II. The prevalence of hypertension, coronary disease, diabetes mellitus, COPD, and chronic kidney disease was also quite similar (Supplementary material 5). Besides these clinical and demographic similarities among participants, they are also similar to outpatient HF clinics from other studies [114-116], suggesting that the results of the studies that are part of this thesis are generalizable to other ambulatory HF clinics.

Limitations

Of the 3 original studies that are part of this thesis (Chapters 3.1, 3.2, and 3.3), there are several underrepresented patient characteristics. For example, patients classified as NYHA class IV were underrepresented. Even though the participation rate for 2 of the 3 original research studies was 97%, the mental fatigue that patients at NYHA class IV may experience might mean they are less likely to agree to participate, especially since all 3 studies involved 1 or more questionnaires. In these 2 studies, however, 6 patients declined to participate, stating that they were either not interested in participating (2) or did not have time (4). Therefore, the reason we had minimal participation from patients at NYHA class IV (no patients from 1 clinic and 1 patient from the other clinic) does not seem to be related to selection bias or study design. For article 3, the NAT: PD-HF translation and validation, participation rate was 30%. We did not document the reasons for patients declining participation in the study. The lack of representation of patients classified as NYHA IV in this study may impact the NAT: PD-HF's comprehension and acceptability results for these patients.

The low proportion of patients with HFpEF is also a limitation because these patients may have more PC needs as they usually have more comorbidities and are older than patients with HFrEF [4, 29]. In addition, in this group of patients therapies are less effective, leading to more frequent decompensations and more uncontrolled symptoms [4, 29]. In the 3 HF clinics (2 in Colombia and 1 in Switzerland) where we recruited participants, patients with preserved LVEF were underrepresented. Because preserved LVEFs rates have fluctuated from more than 40% to more than 50%, it is difficult to estimate the proportion of patients in the general population with HF who have preserved ejection fractions because of the heterogeneity of the cut-off points. However, it is estimated 10%-20% of patients have LVEFs between 40%-50%; and for the rest, half have reduced and half have preserved ejection fractions, which suggests a 1:1 ratio of patients with reduced and preserved

ejection fractions [117-119]. For the HF clinics included in the studies, the ratio was at least double for patients with HFrEF (Supplementary material 5). In addition, in this group of patients therapies are less effective, leading to more frequent decompensations and more uncontrolled symptoms.

There are other limitations. In addition to the limitations I described in the systematic review and meta-analysis (Chapter 3.4), another limitation is that the evidence only comes from high-income countries in North America and Europe. Other limitations are described within Chapter 3.4's discussion section.

4.3. Implications and interpretation

Our systematic review and meta-analysis revealed low adherence to clinical recommendations and inconsistencies between patients' preferences and their care during their last days of life. By gathering examples of EoL ICD device reprogramming within advance directives, I noted inconsistencies between recommendations and care. For example, despite multiple recommendations, ICD reprogramming is only occasionally performed. I suggest that other measures beyond giving recommendations are necessary.

Even though the SQ is a simple and quick tool that has been widely used in clinical practice and research [99, 120-123], its performance has not been evaluated in outpatient settings. Outpatient is an important setting because most encounters with health personnel occur there, and it is harder to predict mortality for stable patients. Additionally, despite its limited contribution predicting mortality based on likelihood ratios (LRs), I argue that it can be used as a starting point to identify patients who might benefit from having PC referrals because of limited life expectancy.

Although its performance predicting 1-year mortality has been evaluated for patients with HF in emergency and inpatient settings [99, 123], no studies that assessed the SQ's performance for HF population reported LRs, which are useful in clinical practice as they allow interpretation of the SQ results for individual patients. When answered by physicians in emergency departments, the SQ has a sensitivity of 79% and a specificity of 57% [99]. When answered by cardiologists about hospitalized patients, the SQ has a sensitivity of 85% and a specificity of 59% [123]. In one of the studies in this thesis, I found that the sensitivity (85%) and specificity (57%) were equal to those for inpatient settings.

Since there was no standard tool to compare with the NECPAL tool, its performance identifying PC needs was unknown. We were unsure whether it would accurately identify patients with palliative needs (ie, those with lower quality of life, more physical symptoms, and psychosocial problems). However, the NECPAL tool did correctly identify PC patients, and therefore, it could be used. Since this prognostic tool is available in several languages and used in several countries, it was important to investigate if it correctly identified PC needs.

Although prognostic tools can identify palliative needs at the EoL, we wanted a more expansive tool to identify patients' needs independent of prognosis. We sought a tool that includes patients within the full spectrum of disease, not just those with limited life expectancies. No such tool was available for patients with HF in German-speaking territories. The NAT: PD-HF, available in English [108] and Dutch [109], was found to be the most recommended need-assessment tool for patients with HF, according to recent systematic reviews [110, 111]. However, its stability over time and acceptance by patients had not been evaluated. In article #3 (Chapter 3.3), we show that patients' results are consistent over time and the tool was accepted by patients.

The duration to administer the German NAT: PD-HF tool was not ideal and training for those who administer the tool is recommended. The Dutch NAT: PD-HF study found that its use in clinical practice was not feasible because on average, it took 26 (±12) minutes to apply the questionnaire [109]. Our study also showed a similar duration (24 minutes ±10). Based on the organization of current health care systems, I agree that it takes too long to apply the NAT: PD-HF as part of a follow-up visit. I suggest that the NAT: PD-HF tool is initially used during a special HF program entry consultation, a consultation longer than follow-ups. After that, it could be applied in annual or biannual check-ups, according to HF stages. Although there was no agreement among the multidisciplinary staff about who should apply the tool and how often, our study revealed it necessary to train personnel who administer the NAT: PD-HF. These results align with the Dutch NAT: PD-HF study. Furthermore, I propose that the same health care personnel trained to administer the tool always perform these HF special consultations (during program entry and annual and/or biannual check-ups).

Finally, to identify palliative needs in patients with HF, I suggest complementary use of prognostic and needs assessment tools. For example, the SQ can be used to quickly identify a limited or 1-year prognosis; then, for those not identified by the SQ and to assess patients' needs more thoroughly, the NAT: PD-HF can be administered during hospital admission, HF program consultations, and annual and/or biannual follow-up appointments.

4.4. Outlook and perspective

Despite multiple recommendations that health care personnel discuss EoL management regarding ICDs with patients and their families, this rarely happens, which suggests it is time to develop more patient-centered strategies. Since the goal of anticipatory care planning is respecting patients' autonomy by empowering them to make medical decisions, patients should be included as active participants from the start, not just when the physician decides to invite them to have an active role. Although ICD guidelines recommend that EoL issues be discussed before device implantation, it is unlikely that most electrophysiologists or cardiologists do so. First, they might not have the necessary training to facilitate these conversations. Second, they might fear that such conversations

are uncomfortable or confuse patients, which might result in decisions to reject the device. Third, even if they are informed and comfortable talking about the device, there is generally not enough time to discuss this during a typical consultation [5, 110]. These are all valid reasons. However, accounting for the previous considerations, patient-centered strategies to increase discussions about EoL management of the ICD might include organizing informative group talks. Ideally, these talks pave the way for EoL ICD discussions with the physician at the patient's convenience. Further, in parallel with informative group talks, other strategies such as training staff to communicate about EoL ICD management should be implemented. In addition, it is important to have administrative support by allocating staff time for these kinds of EoL discussions.

We recommend further study of the NECPAL tool and its usefulness in determining how it contributes when compared to the SQ alone. Although the NECPAL tool showed good differentiation between impaired quality-of-life and symptomatic patients, perhaps it was not because of the additional questions that are part of the NECPAL, but mainly because of the SQ.

Although I provide knowledge and tools to meet the challenge of identifying the needs of patients with HF (Chapters 3.1, 3.2, and 3.3), there is no point in translating and validating tools or evaluating their performance if they are not going to be used. There are still challenges to the widespread use of tools identifying PC needs. One of the main barriers is stigma about the term PC. To overcome this barrier, informational work that PC is not equivalent to discontinuing treatment, losing hope, or moving to hospice has been undertaken with unsatisfactory results [97]. The process of unlearning is complex, and some even argue that it is not possible since knowledge cannot be discarded or eliminated [124, 125]. Hence, getting rid of stigmas is a difficult task. Perhaps instead of trying to correct misunderstandings that PC is equivalent to EoL care, supportive care or integrated patient management should be used instead of PC [97]. However, if patients continue to receive PC only at the EoL, even if the name of the care is changed, it will likely become incorrectly associated with EoL care again. Therefore, changes in clinical practice are needed, such as concurrently offering PC early in the HF disease trajectory.

Other challenges delivering PC to patients with HF include insufficient knowledge and training about PC in HF; the shortage of EoL communication between patients, physicians, and caregivers; and the burden on cardiologists and other health care personnel [5, 110]. One solution could be a person trained in PC at every HF clinic periodically screening patients' needs and, if necessary, treating or referring them as appropriate. HF clinics usually consist of multidisciplinary teams of cardiologists, HF-trained nurses, internists, nutritionists, psychologists, physical therapists, and social workers [126-129]. According to evidence from observational studies and clinical trials, HF clinics are effective in reducing HF hospitalizations and all-cause mortality when compared to usual care [114, 130, 131]. These HF clinics are widely available in countries such as Norway and Italy. However, given the increasing burden and complexity of HF treatments, the current number of HF clinics

in other countries are insufficient to offer comprehensive evaluations according to current standards and recommendations [18]. It is likely that more HF clinics and multidisciplinary HF programs will be created soon, so now is an ideal time to consider including PC specialists or PC-trained staff as part of multidisciplinary HF teams.

Including PC specialists in HF clinics does not mean that comprehensive PC needs assessment efforts are relegated to PC specialists. All multidisciplinary team members should use a palliative gaze when treating patients with HF throughout the HF trajectory. PC specialists provide additional support if unmet PC needs remain or other team members feel unable to discuss sensitive topics with patients, such as EoL ICD management or advance directive decisions.

4.5. Conclusion

In this thesis, I contribute knowledge about gaps and challenges delivering palliative care to patients with heart failure. I show gaps regarding anticipatory care planning and end-of-life care for patients with implantable cardioverter defibrillator and offer strategies to address these gaps. Additionally, I provide knowledge and suggestions to overcome identifying patients' palliative care needs. I assessed 3 tools to support the identification of palliative care needs: two of them, to support the identification of the needs due to limited life expectancy (the SQ and the NECPAL) and 1 to identify palliative care needs regardless of prognosis (the NAT: PD-HF). The best screening tool depends on the situation, and whatever tool we use, it is better to screen and think about the palliative care needs of the patients using any tool than no screening at all.

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6. Supplementary material

6.1. Supplementary material 1. The Edmonton Symptom Assessment System (ESAS)

Date:_____ Time: _____

Please circle the number that best describes your average symptom over the past 24 hours:

No Pain	0 1 2 3 4 5 6 7 8 9 10	Worst Pain
No Fatigue	0 1 2 3 4 5 6 7 8 9 10	Worst Fatigue
No Nausea	0 1 2 3 4 5 6 7 8 9 10	Worst Nausea
No Depressed	0 1 2 3 4 5 6 7 8 9 10	Worst Depression
Not Anxiety	0 1 2 3 4 5 6 7 8 9 10	Worst Anxiety
No Drowsiness	0 1 2 3 4 5 6 7 8 9 10	Worst Drowsiness
No Shortness of Breath	0 1 2 3 4 5 6 7 8 9 10	Worst Shortness of Breath
Best Appetite	0 1 2 3 4 5 6 7 8 9 10	Worst Possible
Best Feeling or Well Being	0 1 2 3 4 5 6 7 8 9 10	Worst Feeling of Well Being
Best Sleep	0 1 2 3 4 5 6 7 8 9 10	Worst Sleep

Completed by: ☐ Patient ☐ Family

Assessed by (Signature/Credentials/ID#/ Date/ Time)_____

Print / Stamp Name: _____

6.2. Supplementary material 2. The 12-item Short Form Survey (SF-12)

SF-12 Health Survey

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. **Answer each question by choosing just one answer**. If you are unsure how to answer a question, please give the best answer you can.

1. **In general, would you say your health is**:

□1 Excellent □2 Very good □3 Good □4 Fair □5 Poor

The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	YES, limited a lot	YES, limited a little	NO, not limited at all
2. **Moderate activities** such as moving a table, pushing a vacuum cleaner, bowling, or playing golf.	□1	□2	□3
3. Climbing **several** flights of stairs.	□1	□2	□3

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	YES	NO
4. **Accomplished less** than you would like.	□1	□2
5. Were limited in the **kind** of work or other activities.	□1	□2

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	YES	NO
6. **Accomplished less** than you would like.	□1	□2
7. Did work or activities **less carefully than usual**.	□1	□2

8. **During the past 4 weeks, how much did pain interfere with your normal work (including work outside the home and housework)?**

□1 Not at all □2 A little bit □3 Moderately □4 Quite a bit □5 Extremely

These questions are about how you have been feeling during the past 4 weeks.
For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the past 4 weeks…

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
9. Have you felt calm & peaceful?	□1	□2	□3	□4	□5	□6
10. Did you have a lot of energy?	□1	□2	□3	□4	□5	□6
11. Have you felt down-hearted and blue?	□1	□2	□3	□4	□5	□6

12. **During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?**

□1 All of the time □2 Most of the time □3 Some of the time □4 A little of the time □5 None of the time

6.3. Supplementary material 3. The Kansas City Cardiomyopathy Questionnaire (KCCQ)

The following questions refer to your **heart failure** and how it may affect your life. Please read and complete the following questions. There are no right or wrong answers. Please mark the answer that best applies to you.

1. **Heart failure** affects different people in different ways. Some feel shortness of breath while others feel fatigue. Please indicate how much you are limited by **heart failure** (shortness of breath or fatigue) in your ability to do the following activities over the past 2 weeks.

Place an X in one box on each line

Activity	Extremely Limited	Quite a bit Limited	Moderately Limited	Slightly Limited	Not at all Limited	Limited for other reasons or did not do the activity
Dressing yourself	❑	❑	❑	❑	❑	❑
Showering/Bathing	❑	❑	❑	❑	❑	❑
Walking 1 block on level ground	❑	❑	❑	❑	❑	❑
Doing yardwork, housework or carrying groceries	❑	❑	❑	❑	❑	❑
Climbing a flight of stairs without stopping	❑	❑	❑	❑	❑	❑
Hurrying or jogging (as if to catch a bus)	❑	❑	❑	❑	❑	❑

2. Compared with 2 weeks ago, have your symptoms of **heart failure** (shortness of breath, fatigue or ankle swelling) changed?
My symptoms of **heart failure** have become . . .

Much worse	Slightly worse	Not changed	Slightly better	Much better	I've had no symptoms over the last 2 weeks
❑	❑	❑	❑	❑	❑

3. Over the past 2 weeks, how many times did you have **swelling** in your feet, ankles or legs when you woke up in the morning?

Every morning	3 or more times a week, but not every day	1–2 times a week	Less than once a week	Never over the past 2 weeks
❑	❑	❑	❑	❑

4. Over the past 2 weeks, how much has **swelling** in your feet, ankles or legs bothered you?
It has been . . .

Extremely bothersome	**Quite a bit** bothersome	**Moderately** bothersome	**Slightly** bothersome	**Not at all** bothersome	I've had **no swelling**
❑	❑	❑	❑	❑	❑

5. Over the past 2 weeks, on average, how many times has **fatigue** limited your ability to do what you want?

All of the time	Several times per day	At least once a day	3 or more times per week but not every day	1–2 times per week	Less than once a week	Never over the past 2 weeks
❑	❑	❑	❑	❑	❑	❑

6. Over the past 2 weeks, how much has your **fatigue** bothered you?
It has been . . .

Extremely bothersome	**Quite a bit** bothersome	**Moderately** bothersome	**Slightly** bothersome	**Not at all** bothersome	I've had **no fatigue**
❑	❑	❑	❑	❑	❑

7. Over the past 2 weeks, on average, how many times has **shortness of breath** limited your ability to do what you wanted?

All of the time	Several times per day	At least once a day	3 or more times per week but not every day	1–2 times per week	Less than once a week	Never over the past 2 weeks
❑	❑	❑	❑	❑	❑	❑

8. Over the past 2 weeks, how much has your **shortness of breath** bothered you?

It has been . . .

Extremely bothersome	**Quite a bit** bothersome	**Moderately** bothersome	**Slightly** bothersome	**Not at all** bothersome	I've had **no shortness of breath**
❑	❑	❑	❑	❑	❑

9. Over the past 2 weeks, on average, how many times have you been forced to sleep sitting up in a chair or with at least 3 pillows to prop you up because of **shortness of breath**?

Every night	3 or more times a week, but not every day	1–2 times a week	Less than once a week	Never over the past 2 weeks
❑	❑	❑	❑	❑

10. **Heart failure** symptoms can worsen for a number of reasons. How sure are you that you know what to do, or whom to call, if your **heart failure** gets worse?

Not at all sure	**Not very** sure	**Somewhat** sure	**Mostly** sure	**Completely** sure
❑	❑	❑	❑	❑

11. How well do you understand what things you are able to do to keep your **heart failure** symptoms from getting worse? (for example, weighing yourself, eating a low salt diet, etc.)

Do not understand at all	Do not understand very well	Somewhat understand	Mostly understand	Completely understand
❑	❑	❑	❑	❑

12. Over the past 2 weeks, how much has your **heart failure** limited your enjoyment of life?

It has **extremely** limited my enjoyment of life	It has limited my enjoyment of life **quite a bit**	It has **moderately** limited my enjoyment of life	It has **slightly** limited my enjoyment of life	It has **not limited** my enjoyment of life at all
❑	❑	❑	❑	❑

13. If you had to spend the rest of your life with your **heart failure** the way it is right now, how would you feel about this?

Not at all satisfied	Mostly dissatisfied	Somewhat satisfied	Mostly satisfied	Completely satisfied
❑	❑	❑	❑	❑

14. Over the past 2 weeks, how often have you felt discouraged or down in the dumps because of your **heart failure**?

I felt that way **all of the time**	I felt that way **most of the time**	I **occasionally** felt that way	I **rarely** felt that way	I **never** felt that way
❑	❑	❑	❑	❑

15. How much does your **heart failure** affect your lifestyle? Please indicate how your **heart failure** may have limited your participation in the following activities over the past 2 weeks.

Please place an X in one box on each line

Activity	**Severely** limited	Limited **quite a bit**	**Moderately** limited	**Slightly** limited	**Did not** limit at all	Does not apply or did not do for other reasons
Hobbies, recreational activities	❑	❑	❑	❑	❑	❑
Working or doing household chores	❑	❑	❑	❑	❑	❑
Visiting family or friends out of your home	❑	❑	❑	❑	❑	❑
Intimate relationships with loved ones	❑	❑	❑	❑	❑	❑

6.4. Supplementary material 4. Original version (English) of the "Needs Assessment Tool: Progressive Disease-Heart Failure (NAT: PD-HF)"

NEEDS ASSESSMENT TOOL: PROGRESSIVE DISEASE – HEART FAILURE (NAT: PD-HF) USER GUIDE

Purpose of the NAT: PD-HF

- Used in both generalist and specialist settings, the Needs Assessment Tool: Progressive Disease – Heart Failure (NAT: PD-HF) can assist in matching the types and levels of need experienced by people with heart failure and their caregivers with the most appropriate people or services to address those needs.
- In generalist settings (eg general practice and cardiology), the NAT: PD-HF can be used to determine which needs may be met in that setting and which needs are be more complex and may be better managed by specialists.
- In specialist settings (eg specialist palliative care services), the NAT: PD-HF can assist in determining when complex needs have been met and act as a discharge planning tool, or to identify the need for ongoing support.
- The NAT: PD-C is an important tool for facilitating communication between primary and specialist care providers about patient needs and actions taken to address these.

Completing the NAT: PD-HF

The NAT: PD-HF is a one-page assessment tool that can be completed by health professionals across a range of disciplines. When completing the NAT: PD-HF, the following steps should be followed:

1. ASSESS patient/caregiver level of concern FOR EVERY ITEM, using the response options: "none", "some/potential for" or "significant".
2. CONSIDER the range of issues within each domain that apply to a person at this stage of their illness. Prompts are provided on a separate page to help you.
3. ACT on each need where you identified some concern ("some/potential for" or "significant"). Your actions may include: directly managed by you, managed by another member of your care team, or referral to someone outside your care team. Record your action on the NAT: PD-HF.
4. REFER if required by completing the referral section at the bottom of the tool, ensuring that information regarding the type of referral, the priority of the referral and client knowledge of the referral is included.
5. INFORM other members of the care team of the outcomes of the needs assessment by:
   a. Filing one copy of the NAT: PD-HF in the patient's medical file.
   b. Sending a copy to the person's GP/cardiologist/other specialist.
   c. If a referral is required, forwarding a copy to the referee.
6. REASSESS needs by completing the NAT: PD-HF approximately monthly or when the patient's or family's situation, or functional status changes.

NEEDS ASSESSMENT TOOL : PROGRESSIVE DISEASE HEART FAILURE (NAT: PD-HF)

COMPLETE ALL SECTIONS

PATIENT NAME: _____

DATE: _____ DIAGNOSIS: _____

PATIENT/ADDRESS LABEL

SECTION 1: PRIORITY REFERRAL FOR FURTHER ASSESSMENT

	Yes	No	If yellow boxes are ticked, consider assessment by SPCS
1. Does the patient have a caregiver readily available if required?			
2. Has the patient or caregiver requested a referral to a specialist palliative care service (SPCS)?			
3. Do you require assistance in managing the care of this patient and/or family?			

SECTION 2: PATIENT WELLBEING (Refer to the back page for assistance)

	Level of Concern			Action Taken		
	None	Some/ Potential	Significant	Directly managed	Managed by other care team member	Referral required
1. Is the patient experiencing unresolved physical symptoms (including problems with breathlessness, pain, fatigue, nausea, oedema, insomnia or cough)?						
2. Does the patient have problems with daily living activities?						
3. Does the patient have psychological symptoms that are interfering with wellbeing or relationships?						
4. Does the patient have concerns about how to manage his/her medication and treatment regimes?						
5. Does the patient have concerns about spiritual or existential issues?						
6. Does the patient have financial or legal concerns that are causing distress or require assistance?						
7. From the health delivery point of view, are there health beliefs, cultural or social factors involving the patient or family that are making care more complex?						

8. Does the patient require information about: (tick any options that are relevant)
☐ The prognosis ☐ Treatment options ☐ Heart disease ☐ Advance directive/resuscitation preferences ☐ Medical/health/support services ☐ Financial/legal issues ☐ Social/emotional issues

COMMENTS: _____

SECTION 3: ABILITY OF CAREGIVER OR FAMILY TO CARE FOR PATIENT (Refer to the back page for assistance)

Who provided this information? (please tick one)
☐ Patient ☐ Caregiver ☐ Both

	Level of Concern			Action Taken		
	None	Some/ Potential	Significant	Directly managed	Managed by other care team member	Referral required
1. Is the caregiver or family distressed about the patient's physical symptoms?						
2. Is the caregiver or family having difficulty providing physical care?						
3. Is the caregiver or family having difficulty coping?						
4. Is the caregiver have difficulty managing the patient's medication and treatment regimes?						
5. Does the caregiver or family have financial or legal concerns that are causing distress or require assistance?						
6. Is the family currently experiencing problems that are interfering with their functioning or inter-personal relationships, or is there a history of such problems?						

7. Does the caregiver require information: (tick any options that are relevant)
☐ The prognosis ☐ Treatment options ☐ Advance directive/resuscitation preferences ☐ What to do in event of patient's death ☐ Medical/health/support services ☐ Social/emotional issues ☐ Heart disease ☐ Financial /legal issues

COMMENTS: _____

SECTION 4: CAREGIVER WELLBEING (Refer to the back page for assistance)

Who provided this information? (please tick one)
☐ Patient ☐ Caregiver ☐ Both

	Level of Concern			Action Taken		
	None	Some/ Potential	Significant	Directly managed	Managed by other care team member	Referral required
1. Is the caregiver or family experiencing physical, practical, spiritual, existential or psychological problems that are interfering with their wellbeing or functioning?						
2. Is the caregiver or family experiencing grief over the impending or recent death of the patient that is interfering with their wellbeing or functioning?						

COMMENTS: _____

IF REFERRAL REQUIRED FOR FURTHER ASSESSMENT OR CARE, PLEASE COMPLETE THIS SECTION

1. Referral to: (Name) _____
2. Referral to: (Specialty) ☐ General practitioner ☐ Social worker ☐ Psychologist ☐ Specialist palliative care service ☐ Cardiologist ☐ Other _____
3. Priority of assessment needed: ☐ Urgent (within 24 hours) ☐ Semi-Urgent (2-7 days) ☐ Non-Urgent (next available)
4. Discussed the referral with the client. ☐ Yes ☐ No
5. Client consented to the referral. ☐ Yes ☐ No
6. Referral from: Name: _____ Position: _____ Signature: _____

ISSUES TO CONSIDER WHEN RATING THE LEVEL OF CONCERN

PATIENT WELLBEING

Physical symptoms

- Does the patient present with unresolved physical symptoms such as drowsiness, fatigue, dyspnoea, vomiting/nausea, persistent cough, pain, oedema, constipation, sleep problems or loss appetite?

Activities of daily living

- Is the patient having difficulty with toileting, showering, bathing, or food preparation?
- Is there a caregiver to assist the patient?

Psychological

- Is the patient experiencing sustained lowering of mood, tearfulness, guilt or irritability, loss of pleasure or interest in usual activities?
- Is the patient experiencing feelings of apprehension, tension, anger, fearfulness or nervousness, hopelessness or a sense of isolation?
- Is the patient requesting a hastened death?

Medication and treatment

- Is the patient able to manage complex medication and treatment regimes?

Spiritual/Existential

- Is the patient feeling isolated or hopeless?
- Does the patient feel that life has no meaning or that his/her life has been wasted?
- Does the patient require assistance in finding appropriate spiritual resources or services?

Financial/Legal

- Are there financial concerns relating to loss of income or costs of treatment, travel expenses, or equipment?
- Is the family socio-economically disadvantaged?
- Are there conflicting opinions between patient and family relating to legal issues such as end-of-life care options and advance care plans?
- Is the patient or family aware of the various financial schemes available and do they need assistance in accessing these?

Health Beliefs, Social and Cultural

- Does the patient or family have beliefs or attitudes that make health care provision difficult?
- Are there any language difficulties? Does the patient or family require a translator?
- Is the family preventing information about prognosis from being disclosed to the patient?
- Does the information have to be passed on to a particular member of the family or cultural group?
- Is the patient or family feeling socially isolated?
- Does the family live more than 50km from the primary service provider?
- Is the patient of Aboriginal or Torres Strait Islander descent?
- Is the patient over 75 years of age? (NB: older patients are under-represented in SPCSs.)

Information

- Does the patient want more information about the course and prognosis of the disease and treatment options?
- Is the patient aware of the various care services available to assist them and do they need assistance in accessing these? (eg financial and legal assistance, psychological services, support groups, pastoral care.)

ABILITY OF CAREGIVER OR FAMILY TO CARE FOR PATIENT

Physical symptoms

- Are the patient's physical symptoms causing the caregiver and family distress?

Providing physical care

- Is the caregiver having difficulty coping with activities of daily living or practical issues such as equipment and transport?

Psychological

- Is the caregiver having difficulty coping with the patient's psychological symptoms?
- Is the caregiver requesting a hastened death for the patient?

Medication and treatment

- Is the caregiver having difficulty managing complex medication and treatment regimes?

Family and Relationships

- Is there any communication breakdown or conflict between patient and family over prognosis, treatment options or care giving roles?
- Is the patient particularly concerned about the impact of the illness on the caregiver or family?

Information

- Does the caregiver or family want more information about the course and prognosis of the disease and treatment?
- Is the caregiver or family aware of the care services available to assist them and do they need assistance in accessing these? (eg respite, financial and legal services, psychological services, support groups, pastoral care.)

CAREGIVER WELLBEING

Physical and psychosocial

- Is the caregiver experiencing physical symptoms eg fatigue, physical strain, blood pressure/heart problems, stress related illness, or sleep disturbances?
- Is the caregiver feeling depressed, hopeless, fearful, nervous, tense, angry, irritable or critical of others, or overwhelmed?
- Does the caregiver have spiritual/existential issues that are of concern?

Bereavement Grief (pre and post death)

- Is the caregiver or family experiencing intrusive images, severe pangs of emotion, denial of implications of loss to self and neglect of necessary adaptive activities at home or work?

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Further copies are available at: http://www.newcastle.edu.au/research-centre/cherp/professional-resources

6.5. Supplementary material 5. Comparison of clinical and demographic characteristics of patients included in publications #1, #2 and #3.

	HF clinic 1 (Colombia, n=89)	HF clinic 2 (Colombia, n=89)	HF clinic 3 (Switzerland, n=70)
Age	67 (56-76)	72 (62-77)	62 (54-72)
Sex			
Women	35 (39%)	44 (49%)	12 (17%)
Men	54 (61%)	45 (51%)	58 (83%)
LVEF (%)	35 (25-45)	31 (22-42)	35 (20-50)
Classification according to LVEF			
HFrEF	52 (59%)	66 (74%)	45 (64%)
HFmrEF	18 (20%)	11 (12%)	3 (4%)
HFpEF	19 (21%)	12 (14%)	22 (31%)
NYHA functional classification			
NYHA I	24 (27%9	33 (37%)	22 (31%)
NYHA II	49 (55%)	37 (42%)	35 (50%)
NYHA III	15 (17%)	19 (21%)	13 (19%)
NYHA IV	1 (1%)	0	0
ICD	23 (26%)	22 (25%)	38 (54%)
Diabetes mellitus	27 (30%)	29 (33%)	21 (29%)
CAD	33 (37%)	33 (37%)	30 (43%)
COPD	14 (16%)	11 (12%)	11 (16%)
CKD	48 (54%)	38 (43%)	32 (46%)
Hypertension	69 (78%)	58 (65%)	37 (53%)

LVEF: left ventricular ejection fraction; HFrEF: heart failure with reduced ejection fraction; HFmrEF: heart failure with mildly reduced ejection fraction; HFpEF: heart failure with preserved ejection fraction; NYHA: New York Heart Association; ICD: implantable cardioverter defibrillator; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; CKD: chronic kidney disease

7. Related publications as first author

7.1. Related publication 1.

Impact of home-based palliative care on health care costs and hospital use: A systematic review

Valentina Gonzalez-Jaramillo
Valérie Fuhrer
Nathalia Gonzalez-Jaramillo
Doris Kopp-Heim
Steffen Eychmüller
Maud Maessen

Systematic review. Published in *Palliative and Supportive Care*, 2020

Contribution: I participated in abstract and full-text screening of hints, and in the data extraction. I made the figures and wrote the first draft of the manuscript. After that, I incorporated coauthors and reviewers' comments.

Palliative and Supportive Care

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Impact of home-based palliative care on health care costs and hospital use: A systematic review

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Review Article

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Abstract

Objective. To assess the effectiveness of home-based palliative care (HBPC) on reducing hospital visits and whether HBPC lowered health care cost.

Method. We searched six bibliographic databases (Embase (Ovid); Cochrane Central Register of Controlled Trials; Medline (Ovid); PubMed; Web of Science Core Collection; and, CINAHL) until February 2019 and performed a narrative synthesis of our findings.

Results. Of the 1,426 identified references, 21 articles based on 19 unique studies met our inclusion criteria, which involved 92,000 participants. In both oncological and non-oncological patients, HBPC consistently reduced the number of hospital visits and their length, as well as hospitalization costs and overall health care costs. Even though home-treated patients consumed more outpatient resources, a higher saving in the hospital costs counterbalanced this. The reduction in overall health care costs was most noticeable for study periods closer to death, with greater reductions in the last 2 months, last month, and last two weeks of life.

Significance of results. Stakeholders should recognize HBPC as an intervention that decreases patient care costs at end of life and therefore health care providers should assess the preferences of patients nearing the end-of-life to identify those who will benefit most from HBPC.

Introduction

As the population of the world ages (He et al., 2016), demand for health and social care is increasing, raising costs, and placing ever greater burdens on national health care systems (Guzman-Castillo et al., 2017).

In this context, a careful evaluation of healthcare resources is crucial to deliver the most appropriate treatments to patients with severe chronic illnesses. Besides treatments focused on curing, patients with prevalent non-curative chronic conditions have a great need of care-oriented treatments, including palliative care (PC). Such a treatment is an approach that seeks to improve the quality of life of patients and their families by the prevention and alleviation of suffering through early identification, evaluation, and treatment of pain and other physical, psychosocial, and spiritual problems ("World Health Organization. WHO definition of palliative care," 2019). Inpatient PC effectively improves patients' quality of life and satisfaction with their care (Gade et al., 2008) and a recent meta-analysis showed that PC lowers hospital costs for patients (May et al., 2018). However, inpatient PC is not for everyone; patients with a terminal illness benefit even more when PC and other types of care are delivered to them at home. Home care reduces hospital visits and hospital deaths, which is associated with a better quality of life for patients at the end of life (Zhang et al., 2012).

Effectiveness and cost-effectiveness of home-based general care have already been shown (Maru et al., 2015; Winkler et al., 2018). A 2013 Cochrane systematic review determined the effectiveness of home-based palliative care (HBPC) in reducing symptom burden for patients and also pointed out that there was not enough literature to assess cost-effectiveness. It also found that most of the literature focused on oncological patients (Gomes et al., 2013). Several more recent studies have assessed the economic impact of HBPC. To date, a comprehensive and systematic appraisal of the existing literature on this impact is missing. Therefore, we conducted a systematic review to (1) assess the effectiveness of HBPC on reducing hospital visits and (2) assess whether HBPC lowered health care costs.

Methods

Literature search

We conducted a systematic review that follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline and registered the protocol in PROSPERO (Moher et al., 2009).

With the aid of an experienced medical information specialist (DK), we searched six electronic databases for peer-reviewed scientific literature related to cost of HBPC, with the goal of identifying studies published between 2013 and 11 February 2019 (date of last search). The search was done in Embase (Ovid); Cochrane Central Register of Controlled Trials; Medline (Ovid); PubMed; Web of Science Core Collection; and, CINAHL. We combined terms related to the exposure (PC, end-of-life care, ambulatory care, domiciliary care) and our outcomes (health expenditures, health care costs, hospitalization rate). We did not apply a language restriction. The full search strategies are available in the appendix (Supplementary material 1). To identify additional sources, we added a Google Scholar search and inspected the references of studies that qualified for full-text review (backward searching).

Study selection and inclusion criteria

Two independent reviewers (VG and VF) screened all titles and abstracts and then reviewed potentially relevant articles based on full text. They resolved differences through discussion before coming to consensus. If no consensus was reached, a third independent reviewer solved discrepancies between the two reviewers.

We included prospective and retrospective observational studies (case–control or cohort) cross-sectional studies, and interventional studies (randomized and non-randomized) that studied an adult palliative population (≥18 years old), at the end of life, with severe illness or with a disease end-stage and compared hospital visits or health care costs of those who received PC at home to those who received usual care. Usual care might include PC in the hospital, but not at home. We defined HBPC as PC that includes home visits.

Data extraction

We used a predesigned data collection form to extract relevant information from the selected studies including study design, sample size, characteristics of the study population, intervention, and type of controls. We also extracted the outcomes each study assessed, and the correspondent measure of associations (e.g., hospitalization rate, mean length of stay, overall cost, inpatient cost, prevalence of death at home).

Assessing the risk of bias

Three reviewers (VG, VF, and NG) independently rated study quality based on the Joanna Briggs Institute Critical Appraisal Tools Checklists for use in systematic reviews. The checklist has 11 items for cohort studies, nine items for quasi-experimental studies, and 13 items for RCTs.

Data synthesis

We conducted a narrative synthesis of the findings of the included studies. For each study, we determined if cost or utilization differed between groups, and whether the difference favored the intervention or the control. Initially, we sought to pool their results using a random effects meta-analysis model. Because studies varied in duration and type of exposure, the time points of outcome assessment, and were conducted in different health systems, we could not pool these results. However, we could make a summary estimate of cost savings by calculating the percentage of costs reduced by the HBPC intervention for those studies that reported the difference between overall costs for patients with and without HBPC. Because several studies reported total costs at different time periods (e.g., from 6, 3, or 1 month until death), we performed two calculations: one included data from the period furthest from death and the other included data from the period closest to death. For studies that stratified cost by groups (e.g., disease), we calculated the average cost in savings across the groups.

Results

We identified 1,426 unique references (Figure 1). Based on the title and abstract, we selected the full text of 30 articles for detailed evaluation; 21 of these articles, based on 19 studies, met our eligibility criteria and were included in this review. Figure 1 explains the reasons why the remaining nine articles were excluded.

General characteristics of the included studies

Table 1 details the characteristics of the 19 included studies, which together included data on 92,871 people. Most of the studies (n = 12) assessed health care cost and use, six assessed only health care use, and one assessed only health care cost. Ten studies assessed the place of death. The majority of the studies (n = 9) included participants from the U.S., two from Italy, and the rest included participants from Belgium, Denmark, England, Israel, Singapore, Spain, Sweden, and Taiwan. Twelve were retrospective cohort studies, five were quasi-experimental studies (before–after studies), and two were randomized controlled trials (RCTs).

Most of the studies included both oncological and non-oncological patients (n = 10) (Chitnis et al., 2013; Lukas et al., 2013; Murphy et al., 2013; Kerr et al., 2014; Hopp et al., 2015; Brian Cassel et al., 2016; Lustbader et al., 2017; Pouliot et al., 2017; Sudat et al., 2018; Maetens et al., 2019); six studies (reported in seven publications) included only oncological patients (Alonso-Babarro et al., 2013; Bentur et al., 2014; Riolfi et al., 2014; Blackhall et al., 2016; Chiang and Kao, 2016; de Miguel et al., 2018; Skov Benthien et al., 2018), two studies (reported in three publications) included only patients with heart failure (Wong et al., 2013; Brannstrom and Boman, 2014; Sahlen et al., 2016), and one study included non-oncological patients (Ferroni et al., 2016). Non-oncological conditions included in the studies were dementia, senility, respiratory disease, liver disease, kidney disease, coronary artery disease, neurodegenerative disease, and diabetes.

Supplementary Tables 1–3 show the risk of bias assessment for each study. Although RCTs are rare within PC research, we found three. These studies were the studies at lower risk of bias. The risk within those studies mainly consisted out of non-concealment of the HBPC intervention. The five quasi-experimental studies also had low risks of bias scores. The biggest problem with quasi-experimental studies was the lack of an independent control group as those studies were before-after studies. The 13 retrospective cohort studies were at higher risk of bias due to unclear or non-existing handling of confounding (Chiang and Kao, 2016; Lustbader et al., 2017; de Miguel et al., 2018).

HBPC intervention

Out of the 19 studies, 18 clearly described the intervention. The remaining one used claim data to search for care codes and those patients with home hospice codes were included in the

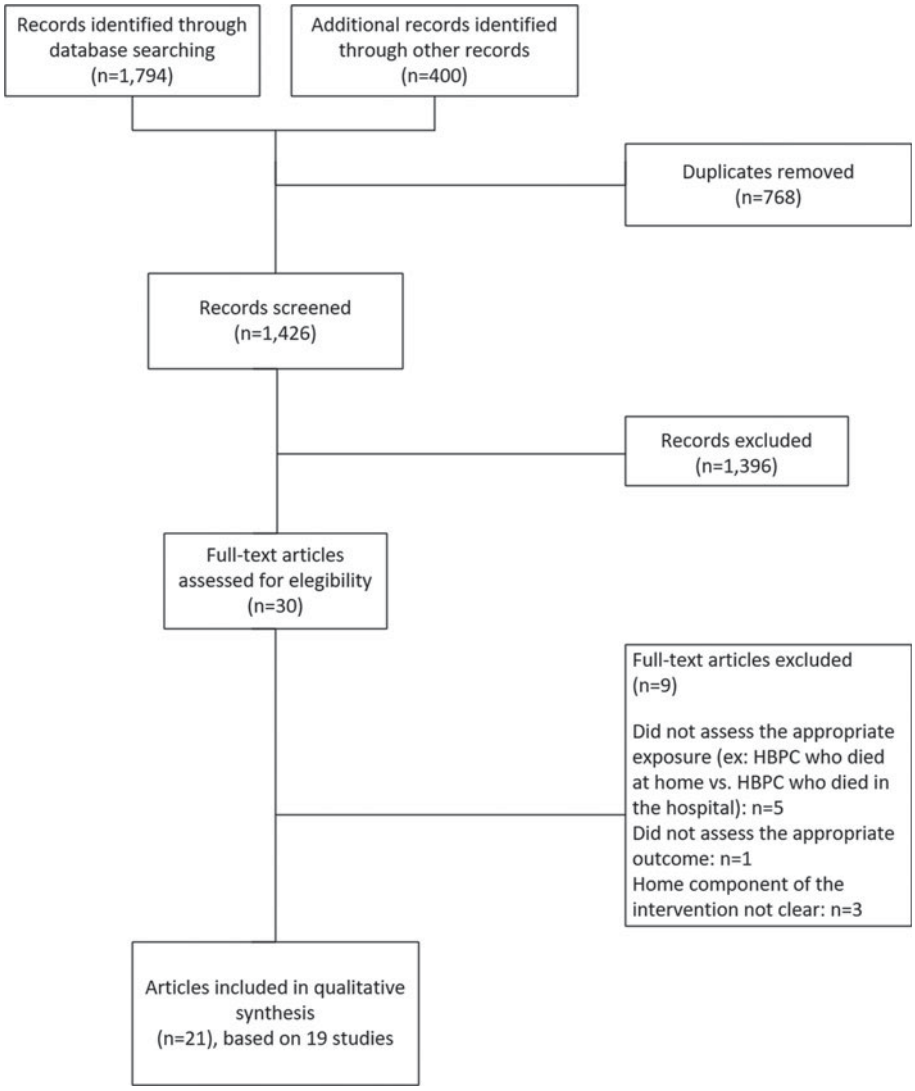

Fig. 1. Flowchart of the studies included in the systematic review.

intervention group (Chiang and Kao, 2016). The majority of the studies ($n = 11$) consisted of a multidisciplinary team that involved nurses, PC specialists, social workers, psychologists, physiotherapists, chaplains, or other spiritual care providers. In five studies, the care in the intervention group was only provided by physicians and nurses, in one by PC specialist and heart failure specialist and in one by nurses and assistants (Table 1). At least six of the studies stated the availability of the assistance was 24 h per day, seven days of the week, whether face-to-face or by telemedicine.

Main outcomes

Hospital use

Hospital admission. Fourteen studies assessed hospital admission rates; two of these evaluated admissions to an intensive care unit (ICU) (Brian Cassel et al., 2016; Maetens et al., 2019). Most studies ($n = 9$) compared groups of patients who had and did not have access to HBPC (Table 1). These studies found that the group of patients with HBPC had a smaller percentage of patients being hospitalized or admitted at least once to the ICU compared to the group without HBPC. Additionally, the group with HBPC showed a lower average number of hospitalizations per patient or per intervention group and lower risk of hospital admission. Only one study, a secondary analysis of an RCT, noted more hospital admissions in the intervention group, but the difference was not significant. This study's results were derived from an intention-to-treat analysis in which two thirds of the patients in the control group also received the intervention (Skov Benthien et al., 2018).

These results aligned with the results of the five quasi-experimental studies in which the control was the patient before HBPC intervention. These five studies found hospital admissions dropped after the HBPC service was introduced regardless when the mark before/after was chosen. Four of them compared the hospital admissions in a symmetric way, for example, 18 months before intervention vs. 18 months after intervention (Lukas et al., 2013), or 6 months before vs. 6 months after the intervention (Hopp et al., 2015). They found the reduction in hospital admission to be significant (Lukas et al., 2013; Wong et al., 2013; Hopp et al., 2015; Pouliot et al., 2017). The remaining study, which was the only one not assessing the outcome in a symmetric way, did not reach the established significance level (Murphy et al., 2013).

Hospitalization length. The length of hospital stay was assessed by nine studies. All of them found that significantly shorter

Table 1. General characteristics of the studies included

Author, publication year	Population	Sample size	Study design	Confounder control	Exposed group	Exposition/Intervention	Comparison group
Alonso-Babarro et al., 2013[a]	Oncological	*n* = 549	Retrospective cohort	Age, sex, marital status, SES, cancer type	Patients living in an area with access to HBPC who received HBPC	The HBPC team was composed of two physicians, two nurses, an assistant nurse, and an administrative clerk. The team conducted a regular follow-up of patients referred by acute care hospitals, medical oncologists, or family physicians when these patients were perceived as having a progressive incurable disease and high symptom distress.	Patients without HBPC
Chitnis et al., 2013	Oncological and non-oncological	*n* = 59,076	Retrospective cohort	Matched analysis	Patients who received home-based end-of-life nursing care delivered by the Marie Curie Nursing Service	The intervention, provided by registered nurses and healthcare assistants, gives hands-on care and emotional support for people in their own homes, day and night at the end of life. It aims to provide care that makes it possible for people to spend their last days of life at home rather than in hospital.	Controls individually matched on variables including age, socioeconomic deprivation, prior hospital use, number of chronic conditions, and prior diagnostic history.
Lukas et al., 2013	Oncological and non-oncological	*n* = 369	Quasi-experimental	Adjusted (no specifications)	Patients with advanced complex illness referred for home-based palliative consultation	Patient care was provided by three nurse practitioners who were supported by a collaborating physician (20% effort). Follow-up visits varied by need for symptom management and advanced care planning. Psychospiritual needs that exceeded the nurses' scope of practice were addressed by referral to a psychiatric homecare nurse, network chaplain, or behavioral health physician.	Controls were the same patients before the intervention.
Murphy et al., 2013	Oncological and non-oncological	*n* = 146	Quasi-experimental		Patients receiving care from the Primary Palliative and Supportive Care Clinic	The clinic provides 24-h access to a PC specialist. The mission is to provide both primary care and PC to patients with life-limiting illness and no primary provider. Patients also have weekday access to a PC nurses who address and coordinate needs.	Controls were the same patients before the intervention.
Wong et al., 2013	Heart failure	*n* = 44	Quasi-experimental	Follow-up duration	End-stage heart failure patients recruited into the PC program	The HBPC program consisted of a multidisciplinary team of a doctor, a nurse, and/or a counselor. Telephonic consults were made available 24/7 to facilitate updates of clinical conditions and delivery of advice/educations.	Controls were the same patients before the intervention.
Bentur et al., 2014	Oncological	*n* = 193	Retrospective cohort	Adjusted (no specifications)	Deceased patients that lived in an area with community care, who received community care and were referred to home hospice	The home hospice unit is a 24-h service provided by a multidisciplinary PC team that includes physicians, nurses, and social workers who visit the patient's home once a week or more, as needed.	Deceased patients that lived in an area with community care, who received regular community care
Brannstrom and Boman, 2014[b]	Heart failure	*n* = 72	RCT	Randomization	Patients randomly assigned to the PREFER intervention	PREFER is a multidisciplinary approach involving collaboration between specialists in palliative and heart failure care. The patients also get person-centered care at home. The home care unit provides services Monday–Friday during the day. The home visits and the phone calls use ranges from several times per day to every other week.	Patients randomly assigned to the control arm: usual care provided mainly by GPs or doctors and/or the nurse-led heart failure clinic at the Medicine-Geriatrics department.

Kerr et al., 2014	Oncological and non-oncological	*n* = 686	Retrospective cohort	Matched analysis	Expired patients that were under the Home Connections program	The program includes a PC-trained registered nurse, social worker, volunteers, and PC physician. Service includes 24/7 on-call PC nurse support. Nurses and social workers visit participants a minimum of once per month and a biweekly interdisciplinary group meeting is held to discuss each patient case with the PC physician.	Controls were patients matched with propensity score using age, gender, insurance product, median household income, neighborhood percentage minority, prospective risk score, and diagnoses historically associated with PC.
Riolfi et al., 2014	Oncological	*n* = 402	Retrospective cohort	Age, sex, and type of cancer	Patients living in an area with Palliative Home care Team who received this care.	The team consists of 2 PC physicians and 30 non-specialist nurses, who cooperate with GPs. GPs have to guarantee their on-call availability. The services are assured from Monday to Friday (8.00 a.m. to 20.00 p.m.). During the night and weekends, PC physicians are available by phone.	Patients living in an area with Palliative Home Care Team who did not receive this care.
Hopp et al., 2015	Oncological and non-oncological		Quasi-experimental		Older population (mean age 69 ± 15) with both oncological and non-oncological diagnosis in the @HOMe Support program	The @HOMe program is an interdisciplinary home-based program for patients and caregivers facing advanced illness. Services of the program were delivered by health care clinicians (physicians, nurses, social workers, and aides).	Controls were the same patients before the intervention.
	Primarily advance-stage cancer		Quasi-experimental		Younger population (mean age 53 ± 9.4) with advanced cancer in the @HOMe Support program	The @HOMe program is an interdisciplinary home-based program for patients and caregivers facing advanced illness. Services of the program were delivered by health care clinicians (physicians, nurses, social workers, and aides).	Controls were the same patients before the intervention.
Blackhall et al., 2016	Oncological	*n* = 376	Retrospective cohort	Demographics and malignancy characteristics	Patients in the CARE track program	The program provides outpatient PC including home hospice. The staff includes registered nurses, physicians, and nurse practitioners. The same physicians and nurse practitioners staff all of the settings. PC providers often serve as the hospice attending once a patient is referred to that service.	Patients who died without any contact with PC or had contact with PC only while hospitalized (inpatient PC)
Brian Cassel et al., 2016	Oncological and non-oncological	*n* = 1,443	Retrospective cohort	Matched analysis	Patients with home-and clinic-based PC	The team includes doctors, nurses, spiritual care providers, and social workers. They provide in-home medical consultation, ongoing evidence-based prognostication of further survival, caregiver support, advance health planning, pain management, education, and psychosocial and spiritual support.	A comparison patient was chosen based on propensity score matching based on age, race, sex, and hospital and nonhospital charges in the first 6 months of the 2-year period. For comparison participants, an index date was created that was the same number of days before death as the matching intervention participant.

(*Continued*)

Table 1. (*Continued.*)

Author, publication year	Population	Sample size	Study design	Confounder control	Exposed group	Exposition/Intervention	Comparison group
Chiang and Kao, 2016	Oncological	*n* = 568	Retrospective cohort		Patients under home hospice care.	Home hospice care.	Patients under inpatient hospice care.
Ferroni et al., 2016	Non-oncological	*n* = 2,087	Retrospective cohort	Diagnosis, age, sex, marital status, Charlson score	Patients under HBPC for Chronic Diseases	HBPCe for Chronic Diseases plan of care: GPs, nurses, out-of-hours physicians, and PC physicians. The GPs are generally readily available on call 12 h/5 days with on-call physicians providing coverage for the rest of time. For more complex patients, PC nurses and PC specialist readily available on call 24 h/7 days and 12 h/days, respectively.	Patients that were never seen by HBPC for Chronic Diseases
Sahlen et al., 2016[b]	Heart failure	*n* = 72	RCT	Randomization	Patients randomly assigned to the PREFER intervention	PREFER is a multidisciplinary approach involving collaboration between specialists in palliative and heart failure care. The patients also get person-centered care at home. The home care unit provides services Monday–Friday during the day. The home visits and the phone calls use ranges from several times per day to every other week.	Patients randomly assigned to the control arm: usual care provided mainly by GPs or doctors and/or the nurse-led heart failure clinic at the Medicine-Geriatrics department.
Lustbader et al, 2017	Oncological and non-oncological	*n* = 651	Retrospective cohort		Decedents enrolled in the HBPC program	The HBPC team comprised six registered nurses, two social workers, two doctors, one data analyst, three administrative staff, and volunteers. Most patients get at least one house call and two telephone calls per month (additional as needed). Telepalliative care is available for a virtual visit for patients and their caregivers using their own smart phone or computer. The nurses may also receive physician support via telemedicine while in the patient's home. Patients have access to coverage 24/7 by telephone or telemedicine to one of the program physicians.	Patients who died under usual care
Pouliot et al., 2017	Oncological and non-oncological	*n* = 123	Quasi-experimental		Patients seen by Care Choices, an in-home PC program provided by the Visiting Nurse Services of Northeastern New York and Ellis Medicine's community hospital serving New York's Capital District.	The program offers interdisciplinary in-home care by a team (medical director, nurse, social worker, chaplain, and home health aides) exclusively dedicated to palliative home care to meet the patient's physical, emotional, and spiritual needs. Additionally, home visits offer education, advance directive planning, and psychosocial and spiritual support.	Controls were the same patients before the intervention.
de Miguel et al., 2018[a]	Oncological	*n* = 226	Retrospective cohort		Patients living in an area with access to HBPC who received HBPC	The HBPC team was composed of two physicians, two nurses, an assistant nurse, and an administrative clerk. The team conducted regular follow-up of patients referred by acute care hospitals, medical oncologists, or family physicians when these patients were perceived as having a progressive incurable disease and high symptom distress.	Patients without HBPC

Skov Benthien et al., 2018	Oncological	*n* = 322	RCT (Secondary analysis)	Randomization	Patients randomly assigned to specialized PC at home	Specialized PC at home: Basic PC at home by district nurses, psychological sessions, home conference with specialist PC team, district nurses, and (if possible) GP.	Patients randomly assigned to usual care that includes referral to specialized PC at home on demand.
Sudat et al., 2018	Oncological and non-oncological	*n* = 7,938	Retrospective cohort	Matched analysis	Patients enrolled in the home-based support program called Advanced Illness Management	The program is part of the PC service and includes physician- and call-center-based telephonic support, hospital-based care liaisons, and nursing and social work home visits.	At least four controls were matched with each intervention patient using "genetic matching", a matching that takes into account age, sex, race, co-morbidity, nurse utilization, and death date.
Maetens et al., 2019	Oncological and non-oncological	*n* = 17,674	Retrospective cohort	Matched analysis	People who used at least one type of palliative home care support in the last 2 years of life.	The intervention included 1.The use of a multidisciplinary palliative home care team, which includes at least one GP, two nurses and an administrative assistant; 2. Palliative home care nursing or physiotherapy, or 3. Allowance for palliative home patients.	People who did not use palliative home care support in the last two years of life.

SES: socioeconomic status; HBPC: home-based palliative care; PC: palliative care; RCT: randomized controlled trial; GP: general practitioner.
[a]Population of the study published in 2018 is a sub-sample of the one published in 2013.
[b]Data derived from the same RCT (same population).

hospital stays were significantly shorter among patients with HBPC than among controls. One study of more than 7,900 oncological and non-oncological patients compared the length of hospital stay over the last 3 months of life in patients receiving HBPC compared to their matched controls. They found a significant reduction in length of hospital stay in the patient group receiving HBPC. They found that the number of days in the hospital during the last 3, 2, and 1 months of life was significantly reduced; the difference was greater than 30% (Sudat et al., 2018). Another study of more than 2,000 non-oncological participants assessed the risk of prolonged hospitalization at the end of life, defined as a stay that exceeds the 75th percentile of the stay that occurred during the last month of life. The authors found that there was a dose–response relationship: risk decreased with an increase in the number of HBPC visits per week (Ferroni et al., 2016) (Table 2).

Emergency department admission. Seven studies assessed emergency department (ED) admission; five found that patients with HBPC used significantly less ED, measured as the percentage of patients admitted at least once to ED or as risk of an ED admission. One large study of over 59,000 oncological patients found that only 12% of the patients with HBPC had at least one ED admission vs. 35% of the matched controls (Chitnis et al., 2013). Another large study of more than 17,000 oncological and non-oncological patients found that the risk of ED admission during the last two weeks of life was twice as high for those without HBPC than those with HBPC (Maetens et al., 2019). The remaining two studies found no difference or an insignificantly lower difference in ED use (Murphy et al., 2013; Bentur et al., 2014) (Table 2).

Health care cost

Average overall cost. There were 11 studies assessing this outcome. Of them, the majority of the studies ($n = 10$) compared a group of patients who had access to HBPC to patients without access. The remaining study used the same patients as controls (before the introduction of HBPC) and as the intervention group (Hopp et al., 2015) (Table 1). The studies assessed the outcome over different periods, ranging from the last month to the last year of life (Table 3). Seven studies included both oncological and non-oncological patients (Chitnis et al., 2013; Kerr et al., 2014; Hopp et al., 2015; Brian Cassel et al., 2016; Lustbader et al., 2017; Sudat et al., 2018; Maetens et al., 2019), three only oncological patients (Bentur et al., 2014; Blackhall et al., 2016; Chiang and Kao, 2016), and one only patients with heart failure (Sahlen et al., 2016).

Of the 11 studies that assessed overall cost in health, six studies specified that they had taken into account the costs of the intervention itself while the other five did not specify whether they had included these costs or not. When taking into account all the articles that evaluated overall cost in health, regardless of whether or not they included the costs of the intervention itself, the average total health care cost per patient was lower for those with access to HBPC than for controls.

Studies that assessed the outcome at different points in time found that the cost reduction was most noticeable closer to death, with the greatest reductions in the last 2 months, 1 month, and two weeks of life (Kerr et al., 2014; Blackhall et al., 2016; Lustbader et al., 2017). Including all 11 studies assessing average overall cost, the intervention saved 36.3% (IQR: 28.8–51.8%) when taking into account the costs reported at the period closest to death. Similar results were obtained when taking into

Table 2. Results of the studies assessing health care utilization

Author, publication year	Population	Sample size	Study design	Outcome period	Outcome	Result
Alonso-Babarro et al., 2013[a]	Oncological	$n = 549$	Retrospective cohort	Last 2 months of life	Hospital admission	The patients from the area with HBPC used inpatient services less frequently than those in the area without HBPC (66% vs. 76%, $p = 0.012$).
					Emergency department admission	The patients from the area with HBPC used emergency services less frequently than those in the area without HBPC (68% vs. 79%, $p = 0.004$).
Chitnis et al., 2013	Oncological and non-oncological	$n =$ 59,076	Retrospective cohort	From start with the program to death	Emergency department admission	Only 12% of the patients with HBPC had an emergency hospital admission compared with 35% of controls ($p < 0.001$).
Lukas et al., 2013	Oncological and non-oncological	$n = 369$	Quasi-experimental	18 months before vs. 18 mothers after intervention	Hospital admission	The average number of hospitalizations was 2.23 before intervention, compared to 1.25 post-intervention ($p < 0.001$).
					Hospitalization length	The average lengths of stay were 11.2 pre-intervention and 4.5 days after the intervention ($p < 0.001$).
Murphy et al., 2013	Oncological and non-oncological	$n = 146$	Quasi-experimental	12 months before enrollment vs. date of data extraction	Hospital admission	The average number of hospital admissions decreased post-enrollment (pre: mean = 1.28 ± 1.99; post: mean = 1.02 ± 1.44). This represents a 20.2% reduction in hospital admissions ($p = 0.057$).
					Emergency department admission	The mean number of ED visits per week decreased significantly after enrollment, from mean = 2.46 ± 4.74 to 1.76 ± 3.13. This represents a 28.6% reduction in ED utilization.
Wong et al., 2013	Heart failure	$n = 44$	Quasi-experimental	1 year before vs. 1 year after intervention or death	Hospital admission	After adjustment for follow-up duration, mean all-cause hospitalisations were 3.6 and 1.2 episodes per patient ($p < 0.001$) before and after enrollment, respectively; mean HF hospitalisations were 2 and 0.5 episodes per patient ($p < 0.001$) before and after enrollment, respectively.
Bentur et al., 2014	Oncological	$n = 193$	Retrospective cohort	Last 6 months of life	Hospital admission	About 89% of those under home hospice had been hospitalized at least once during the last 6 months of their life, compared to 83% in the control group.
					Emergency department admission	53% of those receiving HBPC care had visited ED at least once during the last 6 months of their life, compared to 52% in the control group.
Brannstrom and Boman, 2014	Heart failure	$n = 72$	RCT	Last 6 months of life	Hospital admission	The mean number of hospitalizations was significantly lower in the group with HBPC than in the control group (0.42 ± 0.60 vs. 1.47 ± 1.81, $p = 0.009$), as well as the total number of hospitalizations (15 in the HBPC group and 53 in the control).
					Hospitalization length	The mean number of days was significantly lower in the HBPC group (2.9 ± 8.3 vs. 8.5 ± 12.4, $p = 0.011$) compared with the control group. The total number of days spent in hospital was 103 (range 1–45 days) in the HBPC group and 305 (range 2–46 days) in the control group.
					Hospitalization length	Mean hospital days declined from 7.65 in the 6 months pre entry to 5.77 in the period following entry into the program ($p = 0.027$).

(*Continued*)

Table 2. (*Continued.*)

Author, publication year	Population	Sample size	Study design	Outcome period	Outcome	Result
Riolfi et al., 2014	Oncological	$n = 402$	Retrospective cohort	Last 2 months of life	Hospital admission	HBPC patients had fewer hospital stays compared with patients without HBPC (0.4 ± 0.7 vs. 1.3 ± 1.0 admissions), respectively, $p < 0.001$.
					Hospitalization length	HBPC patients had shorter hospital stays (4.4 vs. 19.6 days, $p < 0.001$) than patients without HBPC.
Hopp et al., 2015	Oncological and non-oncological		Quasi-experimental	6 months before vs. 6 months after intervention	Hospital admission	The percentage of participants who experienced at least 1 hospitalization decreased from 83% in the 6 months pre entry to 54% in the period following entry ($p = 0.001$).
Blackhall et al., 2016	Oncological	$n = 376$	Retrospective cohort	Last 3 months of life	Hospital admission	Of the patients with access to HBPC, 37.6% were hospitalized in the last month of life, compared to 80.6% of patients who received PC only in the hospital. The difference remains significant after adjustment.
Brian Cassel et al., 2016	Oncological and non-oncological	$n =$ 1,443	Retrospective cohort	From start with the program to death	Hospital admission	For each disease, the percentage of participants hospitalized during the evaluation period, as well as in the last month of life, was lower for HBPC than for controls (all $p \leq 0.001$). The percentage using the intensive care unit in the final month of life was also lower for HBPC than controls ($p < 0.001$).
					Hospitalization length	For each disease, the number of hospital days was lower for HBPC than for controls (all $p \leq 0.001$).
Chiang and Kao, 2016	Oncological	$n = 568$	Retrospective cohort	Last month of life	Hospitalization length	The median days of hospital stay in the last month of life were fewer in the home hospice group than in the control (10.5 vs. 22.0, $p < 0.001$).
					Home deaths	Compared with patients in the inpatient group, the home group had a significantly larger proportion of death at home (55.5% vs. 22.1%, $p < 0.001$).
Ferroni et al., 2016	Non-oncological	$n =$ 2,087	Retrospective cohort	Last month of life	Hospitalization length	The relative risk of prolonged EOL hospital stay decreased significantly, with a dose–response relationship, according to the number of homecare visits/week performed during the last 90–31 days before death.
Lustbader et al, 2017	Oncological and non-oncological	$n = 651$	Retrospective cohort	Last year of life	Hospital admission	Hospital admissions were reduced by 34% in the final month of life for patients enrolled in HBPC ($p = 0.022$).
					Emergency department admission	ED visits were reduced by 20% in the final month of life for patients enrolled in HBPC ($p < 0.001$).
Pouliot et al., 2017	Oncological and non-oncological	$n = 123$	Quasi-experimental	Entire duration in the program. If a patient had been enrolled in the program for 2 months, hospitalization records 2 months before enrollment were used for comparison.	Hospital admission	There was a significant decline in the average number of inpatient admissions after enrollment in the home care program (mean 1.21 ± 1.01, before vs. mean 0.38 ± 0.70, after) $p < 0.001$.
					Emergency department admission	There was a significant decline in the average number of ED visits after enrollment in the home care program (mean 1.79 ± 1.46, before vs. mean 1.00 ± 1.08, after) $p < 0.001$.

(*Continued*)

Table 2. (*Continued.*)

Author, publication year	Population	Sample size	Study design	Outcome period	Outcome	Result
de Miguel et al., 2018[a]	Oncological	$n = 226$	Retrospective cohort	Last 2 months of life	Hospital admission	The percentage of patients who had at least one hospital admissions was significantly lower in the group with access to HBPC (41%) compared to those without it (71%). The number of hospital admissions per patient was also lower in the group with HBPC.
					Hospitalization length	The average number of inpatient days was 7.5 vs. 16.5, depending on whether they had HBPC or not, respectively, $p < 0.001$.
					Emergency department admission	The percentage of patients who had at least one ED visit was lower in the group with HBPC (57% vs. 70%). The number of ED visits was also lower in the group with access to HBPC, borderline in statistical significance.
Skov Benthien et al., 2018	Oncological	$n = 322$	RCT (Secondary analysis)	6 months	Hospital admission	Mean number of admissions per patient was 2.02 (Control) vs. 2.14 (Intervention) ($p = 0.6304$).
Maetens et al., 2019	Oncological and non-oncological	$n = 17,674$	Retrospective cohort	Last two weeks of life	Hospital admission	Those using HBPC had, compared with those who did not, lower risk of hospital admission (27.4% vs. 60.8%; RR = 0.45, 95% CI 0.43 to 0.46), and lower risk of ICU admission (18.3% vs. 40.4%; RR = 0.45, 95% CI 0.43 to 0.48).
					Emergency department admission	Patients with HBPC had a lower risk of ED admission (15.2% vs. 28.1%; RR = 0.54, 95% CI 0.51 to 0.57).

HBPC: home-based palliative care; ED: emergency department; RCT: randomized controlled trial; COPD: chronic obstructive pulmonary disease; HF: heart failure.
[a]Population of the study published in 2018 is a sub-sample of the one published in 2013.

account for the analysis the cost reported at the period most distant to death, with a saving in the overall health cost of 35.7% (IQR: 26.2–36.8%) in favor of the HBPC group.

The largest study, a retrospective cohort that included more than 29,500 oncological and non-oncological patients who had been under HBPC and had died matched them 1:1 to patients without HBPC who died during the same period, had similar demographic and clinical characteristics, and similar prior hospital use; average overall cost per person for those under HBPC was significantly lower than the cost for the controls (Chitnis et al., 2013).

Those six studies that took into account the cost of the intervention program (Kerr et al., 2014; Brian Cassel et al., 2016; Sahlen et al., 2016; Lustbader et al., 2017; Sudat et al., 2018; Maetens et al., 2019) also found a reduction in average total health care. Of them, three large studies summing up more than 27,000 found costs to be lower among patients with HBPC in the last 3, 2, and 1 months of life (Brian Cassel et al., 2016; Sudat et al., 2018; Maetens et al., 2019). One of these studies presented results by patient diagnosis and found that cost reductions were significant across all conditions they included (cancer, COPD, heart failure, and dementia) (Brian Cassel et al., 2016). Another study taking into account the cost of the intervention program analyzed the average overall cost in different periods (Kerr et al., 2014). This study showed that patients with HBPC had significantly lower average overall costs compared to patients without HBPC during the last 3 months, last month, and last two weeks of life. When they analyzed these same costs during the last 6 months and last 2 years of life, the costs were equal between both groups. Another study found HBPC lowered cost over the last year of life and significantly lowered cost over the last 6 months, last 3 months, and last month of life (Lustbader et al., 2017). Outpatient cost and staff cost were generally equal or higher for patients with HBPC than for patients without HBPC (Kerr et al., 2014; Sahlen et al., 2016; Maetens et al., 2019), so the drop in overall health care costs was a result of significantly lower inpatient cost among patients with HBPC.

Hospitalization cost. Seven studies assessed costs generated by hospitalizations, and all found that inpatient costs were lower in patients who received palliative home care. One RCT conducted among patients with heart failure with 6 months follow-up found that inpatient cost in the group with access to HBPC was at least three times less than the cost in the control arm (Sahlen et al., 2016). Two large retrospective cohorts with a combined total of over 25,000 participants used matched analysis to adjust for confounders and found significantly lower hospitalization cost among patients with HBPC during the last 3 months, 2 months, 1 month, and two weeks of patients' life (Sudat et al., 2018; Maetens et al., 2019) (Table 2).

Other costs. Two studies assessed outpatient cost. Of them, one included the home care cost in the outpatient cost and found higher values for those with access to HBPC (Maetens et al., 2019). The other one reported no difference in cost at 6 months before death and lower cost in the lasts 3 months, 2 months, and two weeks of life among patient with access to HBPC. This last study additionally reported costs derived from visits to the ED and found no difference in none of the time periods (Kerr et al., 2014) (Table 2).

Table 3. Results of the studies assessing health care cost

Author, publication year	Population	Sample size	Study design	Outcome period	Outcome	Result
Chitnis et al., 2013	Oncological and non-oncological	*n* = 59,076	Retrospective cohort	From start with the program to death	Average overall cost in health	The costs of care were lower for intervention patients than matched controls (average overall costs £610 per person vs. £1,750, $p < 0.001$).
Lukas et al., 2013	Oncological and non-oncological	*n* = 369	Quasi-experimental	18 months before vs. 18 mothers after intervention	Hospitalization cost	The average hospitalization costs were $23,386 and $16,467 before and after the intervention, respectively.
Bentur et al., 2014	Oncological	*n* = 193	Retrospective cohort	Last 6 months of life	Average overall cost in health	The average cost of care for the last 6 months of life, for patients with home hospice care, was US$13,648 compared to US $18,503 for patients without home hospice care.
Kerr et al., 2014	Oncological and non-oncological	*n* = 686	Retrospective cohort	2 years, 1 year, 6 months, 3 months, 1 month, and two weeks before death	Average overall cost in health	There were statistically significant differences from the last 3 months to the last two weeks of life, in which HBPC patients incurred lower costs, even with program fees included. There were statistically significant differences from the last 3 months to the last two weeks of life, in which HBPC patients incurred lower costs, even with program fees included. At 3 months prior to death the average total cost per member per month was $6,804 for those with HBPC, compared to $10,712 for those not enrolled. At 1 month prior death $7,170 vs. $13,440 for controls and in the last two weeks $6,674 compared to $13,846 for controls.
					Hospitalization cost	HBPC participants had significantly lower inpatient costs than controls at all time points, with the greatest differences at the last one month and two weeks of life.
					Outpatient cost	No difference was observed at 6 months. At 3 months, 1 month, and two weeks, outpatient costs were significantly lower for HBPC members.
					Emergency department cost	There were no significant differences in ED costs or utilization between HBPC members and controls at any time point analyzed.
Hopp et al., 2015	Oncological and non-oncological		Quasi-experimental	6 months before vs. 6 months after intervention	Average overall cost in health	Total monthly costs declined US$3,416, from an average of US$9,294 per month at baseline to US $5,878 at 6 months ($p < 0.001$).
	Primarily advance-stage cancer		Quasi-experimental	6 months before vs. 6 months after intervention	Average overall cost in health	1. Participants where all monthly costs post entry < US$70,000: Although non-significant, the average total costs decreased from US$18,787 to US$13,781.
					Average overall cost in health	2. Participants where at least 1 monthly cost > US $70,000: Although significant reductions in outpatient costs, there was a dramatic increase in inpatient costs, leading to an overall increase in average total costs pre- and post entry from US $20,845 to US$51,435 ($p = 0.004$).
					Hospitalization cost	For each disease, hospital costs per month were lower for HBPC participants (all $p \leq 0.002$).
Chiang and Kao, 2016	Oncological	*n* = 568	Retrospective cohort	Last month of life	Average overall cost in health	The mean health care costs in the last month of life were significantly less for patients in the home hospice group than for those in the inpatient hospice group (US $1,385 versus US $2,155, $p < 0.001$).
Sahlen et al., 2016	Heart failure	*n* = 72	RCT	6 months	Average overall cost in health	Average costs per participant were €4,078 and €5,727 for patients with and without HBPC, respectively. Including program cost, during 6 months, the intervention saved €61,000.

(*Continued*)

Table 3. (*Continued.*)

Author, publication year	Population	Sample size	Study design	Outcome period	Outcome	Result
					Hospitalization cost	During the 6 months, the total cost of hospital care was 58,793 in the home care group compared to 176,357 in the control.
Lustbader et al, 2017	Oncological and non-oncological	*n* = 651	Retrospective cohort	Last year of life	Average overall cost in health	Including home health services, the average cost per patient was significantly lower in the HBPC group than in the control during the last 6 months ($32,869 vs. $44,291, respectively), last 3 months ($20,420 vs. $32,420, respectively), and last month of life ($6,423 vs. $10,712, respectively). There was no difference in the last year.
Sudat et al., 2018	Oncological and non-oncological	*n* = 7,938	Retrospective cohort	Last 3 months, 2 months, and 1 month of life	Average overall cost in health	Incorporating the estimated cost of home-based program, in the final month of life, those enrolled in the HBPC program generated on average US$4,824 (23%) less in overall health cost (CI = US$3,379, US $6,268). In the last three and last 2 months of life, there was no significant difference.
					Hospitalization cost	Inpatient cost was significantly lower in the home-based program during the last 3 months, 2 months, and 1 month of life.
de Miguel et al., 2018	Oncological	*n* = 226	Retrospective cohort	Last 2 months of life	Hospital cost (hospitalization + ED)	The average cost per patient was significantly lower in the HBPC (€3,363) group than in the group without access to HBPC (€7,324).
Maetens et al., 2019	Oncological and non-oncological	*n* = 17,674	Retrospective cohort	Last two weeks of life	Average overall cost in health	After matching, mean total costs of care were lower for those using HBPC (€3,081 [95% CI €3,025 to €3,136] vs. €4,698 [95% CI €4,610 to €4,787]). Including home care cost, outpatient cost was higher in the HBPC group compared to the controls but this was counterbalanced by lower inpatient cost in the HBPC group (difference in cost: −€1,617 [$p < 0.001$]).
					Hospitalization cost	Mean total inpatient costs were lower for people using HBPC (€1,766; 95% CI €1,706 to €1,826) compared with those who did not use HBPC (€4,222; 95% CI €4,133 to €4,311) ($p < 0.001$)
					Outpatient cost	Mean total outpatient costs were higher for people using HBPC (€1,314; 95% CI €1,291 to €1,337) compared with those without HBPC (€476; 95% CI €461 to €492) ($p < 0.001$).

HBPC: home-based palliative care; ED: emergency department; RCT: randomized controlled trial; COPD: chronic obstructive pulmonary disease; HF: heart failure.

Additional outcomes

Place of death

Among the 10 studies reporting this outcome, 6 reported percentage of deaths at home. Among these studies, the percentage of patients who died at home was at least twice as high among those who had access to HBPC compared to those who did not, with a ratio ranging from 2.2 to 6.8 (Chitnis et al., 2013; Bentur et al., 2014; Riolfi et al., 2014; Chiang and Kao, 2016; de Miguel et al., 2018; Maetens et al., 2019). Three studies reported the percentage of patients who died outside the hospital, including home and health care facilities such as hospices (Blackhall et al., 2016; Brian Cassel et al., 2016; Sudat et al., 2018). Their results were consistent, with a higher amount of patients dying outside hospitals in the HBPC group. Finally, the remaining study reported the risk of hospital in each group and found that the relative risk of hospital death decreased with a dose–response relationship, according to the number of homecare visits per week performed in the last months of life (Ferroni et al., 2016).

Discussion

Main findings

We found HBPC was consistently effective in reducing the number and length of hospital visits, regardless of a patient's oncological status. The number of ED visits was lower or equal to the number in the control group. HBPC consistently reduced health care costs by reducing costly hospital stays, even though home-treated patients consumed more outpatient resources.

Since the studies designed their interventions differently and were implemented in widely different health systems, they were too heterogeneous to allow us to conduct a meta-analysis so we could not generate a pooled estimate cost saving. Despite their heterogeneity, their results consistently demonstrate that HBPC reduced costs.

This review found cost reductions were highest in studies that assessed the outcome closer to death possibly because the number of hospitalizations increases as patients near death and with it the number of hospital deaths (Alonso-Babarro et al., 2013; Bentur

et al., 2014; Blackhall et al., 2016; Chiang and Kao, 2016; Chitnis et al., 2013; de Miguel et al., 2018; Maetens et al., 2019; Riolfi et al., 2014). The average number of hospitalizations increases when the patients near death, because chronic diseases progress, symptoms worsen, and standard (home) care is overburdened. Additionally, when a patient is hospitalized in a period close to death, the chances of dying in the hospital increase which can be showed to be much more expensive than dying in another setting. Using data from Medicaid, data analysts reported that dying in hospital is seven times more expensive than dying at home (Solutions, 2016).

Applicability of evidence

All the studies we included were carried out in high-income countries where the cost of hospitalization is higher than it is in middle- and low-income countries ("World Health Organization. Public Spending on Health: A Closer Look at Global Trend," 2018), so our results may not be generalizable to those countries. To improve the applicability of our evidence, we provided the results of the savings in the average overall health costs as percentages, instead of the net decrease in costs. However, the results from our systematic review should be taken with caution before generalization.

Limitations

The studies we included did not aggregate the total cost of health care. They did not include out-of-pocket expenses or other informal costs of care like the drop in household income when family members reduce their working hours to help care for a patient at home. These costs are difficult to measure but informal care has shown to account for a high proportion of costs during the last year of life, highlighting the important role of informal caregivers in PC (Brick et al., 2017). There is a risk that HPBC reduced overall health care costs less than they appeared to, since they may have shifted costs from the system to patients and their caregivers, and thus rendered those costs invisible.

As others also report (Brereton et al., 2017), we were limited by the fact that study authors did not clearly describe their interventions, which meant we could draw only general conclusions. For example, most authors did not clearly define the precise content of HBPC or describe patient diagnosis and any associated need for intensive and specialist care in hospitals, although these influence the hospital admission rate. We could only focus on cost and easily measurable effect outcomes like hospital utilization but did not have enough comparable information to include important effectiveness outcomes like quality of death and the burden imposed on family caregivers.

Studies were generally of good quality but because few clearly reported the exposure there is a risk of non-differential misclassification, which could have led us to underestimate the effect. Additionally, given that most studies were observational, despite having used different strategies to control for confounders, there may still be residual confounding introducing bias into the results.

Despite the heterogeneity of interventions and study design (Table 1), results were consistent across studies, especially for health care cost outcome, but there was some inconsistency in findings about the use of health care. Skov et al.'s study, a secondary analysis of an RCT that assessed hospital admissions as outcome, found no difference between those randomized to specialized PC at home and those in the control arm (usual care including referral to specialized PC at home on demand); 66% of patients assigned to the control group received specialized PC at home (Skov Benthien et al., 2018). Bentur et al.'s study was also problematic, since patients in the reference group also received home-based care as part of usual community care (Bentur et al., 2014).

Implications

The ethical argument for HBPC is strong for patients with a marked prognosis decline who want to remain at home. Our study bolsters that ethical argument with evidence that HBPC reduces health care system costs.

When analyzing the cost-effectiveness of a new intervention, results are divided into four quadrants. If a new intervention is less effective and more expensive (upper left quadrant), it ought to be discarded. If it is more effective but also more expensive (upper right quadrant) or less effective and cheaper (lower left quadrant), it warrants discussion. If it is cheaper and more effective (lower right quadrant), it is dominant and should be implemented. Therefore, from an economic perspective, our finding that HBPC decreases hospital visits while decreases costs suggests that, when properly analyzed in a cost-effectiveness analysis, the home-based approach may be a dominant technology when compared to the traditional care (Petrou and Gray, 2011). However, the studies identified did not report classic cost-effectiveness metrics such as the incremental cost-effectiveness ratio. Therefore, we could not perform the cost-effectiveness analysis.

HBPC should be available to all patients in a recognizable end-of-life phase, e.g., with a marked progressive decline, who desire to remain at home and die there. Further research would be necessary to determine which specific type of patient benefits the most from HBPC and has the highest impact on reducing health care cost. Our findings apply at the population level, but patients must be managed individually, taking into account the complexity of their underlying pathology to determine if patients with complex conditions (e.g., polymorbid patients) will benefit most from HBPC or in-hospital management. We thus recommend linking HBPC programs to a hospital PC program in case referral is necessary. In addition, reducing hospital utilization at the end of life should be a goal for health care planners only if access to quality home care at the end of life is guaranteed. The main objective should not be where to die, but how.

Conclusion

Our systematic review provides clear and homogenous evidence that HBPC reduces overall end-of-life health care costs by reducing the number of hospitalizations in the last months of life, and thus the number of in-hospital deaths. Therefore, stakeholders should recognize HBPC as an intervention that decreases patient care costs at end of life and health care providers should assess the preferences of patients nearing the end-of-life to identify those who will benefit most from HBPC.

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Conflict of interest. There are no conflicts of interest.

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Supplementary Table 1. Risk of bias assessment of retrospective cohort studies

Study	Were the two groups similar and recruited from the same population?	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	Was the exposure measured in a valid and reliable way?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	Were the outcomes measured in a valid and reliable way?	Was the follow up time reported and sufficient to be long enough for outcomes to occur?	Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	Were strategies to address incomplete follow up utilized?	Was appropriate statistical analysis used?
Alonso-Barbarro et al., 2013	✓	✓	?	✓	✓	–	✓	✓	–	–	✓
Chitnis et al., 2013	✓	✓	?	✓	✓	–	✓	✓	–	–	✓
Bentur et al., 2014	✓	✓	?	✓	?	–	✓	✓	–	–	✓
Kerr et al., 2014	✓	✓	?	✓	✓	–	✓	✓	–	–	✓
Riolfi et al., 2014	✓	✓	?	✓	✓	–	✓	✓	–	–	✓
Blackhall et al., 2016	✓	✓	?	✓	?	–	✓	✓	–	–	✗
Cassel et al., 2016	✓	✓	?	✓	✓	–	✓	✓	–	–	✓
Chiang et al., 2016	✓	✓	✓	✗	✗	–	✓	✓	–	–	?
Ferroni et al., 2016	✓	✓	?	✓	✓	–	✓	✓	–	–	✓
Lustbader et al, 2017	✓	✓	?	✗	✗	–	✓	✓	–	–	?
Sudat et al., 2017	✓	✓	?	✓	✓	–	✓	✓	–	–	✓
de Miguel et al., 2018	✓	✓	?	✗	✗	–	✓	✓	–	–	?
Maetens et al., 2019	✓	✓	✓	✓	✓	–	✓	✓	–	–	✓

Risk of bias summary: review authors' judgements about each risk of bias item for each included study (✓ = low risk of bias; ✗ = high risk of bias; ? = unclear risk of bias, – = not applicable).

Supplementary Table 2. Risk of bias assessment of quasi-experimental studies

Study	Is it clear in the study what is the 'cause' and what is the 'effect' (i.e. there is no confusion about which variable comes first)?	Were the participants included in any comparisons similar?	Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Was there an independent control group?	Were there multiple measurements of the outcome both pre and post the intervention/exposure?	Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	Were the outcomes of participants included in any comparisons measured in the same way?	Were outcomes measured in a reliable way?	Was appropriate statistical analysis used?
Lukas et al., 2013	✓	✓	✓	✗	✗	✓	✓	✓	✓
Murphy et al., 2013	✓	✓	✓	✗	✓	✓	✓	✓	✓
Wong et al., 2013	✓	✓	✓	✗	✗	✓	✓	✓	✓
Hopp et al., 2014	✓	✓	✓	✗	✗	✓	✓	✓	✓
Pouliot et al., 2016	✓	✓	✓	✗	✓	✓	✓	✓	✓

Risk of bias summary: review authors' judgements about each risk of bias item for each included study (✓ = low risk of bias; ✗ = high risk of bias; ? = unclear risk of bias, – = not applicable).

Supplementary Table 3. Risk of bias assessment of randomized controlled trials.

Study	Was true randomization used for assignment of participants to treatment groups?	Was allocation to treatment groups concealed?	Were treatment groups similar at the baseline?	Were participants blind to treatment assignment?	Were those delivering treatment blind to treatment assignment?	Were outcomes assessors blind to treatment assignment?	Were treatment groups treated identically other than the intervention of interest?	Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	Were participants analyzed in the groups to which they were randomized?	Were outcomes measured in the same way for treatment groups?	Were outcomes measured in a reliable way?	Was appropriate statistical analysis used?	Was the trial design appropriate, and any deviations from the standard RCT design accounted for in the conduct and analysis of the trial?
Brännström et al., 2014	✓	✓	✓	–	–	✗	✓	✓	✓	✓	?	✓	✓
Sahlen et al., 2016	✓	✓	✓	–	–	✗	✓	✓	✓	✓	✓	✓	✓
Skov et al., 2018	✓	✓	✓	–	–	✓	✓	✓	✓	✓	✓	✓	✓

Risk of bias summary: review authors' judgements about each risk of bias item for each included study (✓ = low risk of bias; ✗ = high risk of bias; ? = unclear risk of bias, – = not applicable).

Supplementary Material 1. Search strategy

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R)

1 exp Palliative Care/ (50078)

2 exp Palliative Medicine/ (248)

3 palliativ*.ti,ab,kw. (58107)

4 palliativ*.ot. (1647)

5 exp Terminal Care/ (48300)

6 ("end of life" or "last month* of life" or "last year of life" or "last day of life" or end-of-life care or incurable* or "last stage of disease" or "die at home" or "life care end").ti,ab,kw. (30930)

7 or/1-6 (131555)

8 exp Health Expenditures/ (20303)

9 exp "Costs and Cost Analysis"/ (221857)

10 exp Cost-Benefit Analysis/ (75379)

11 exp Cost Savings/ or "Health Care costs"/ (45813)

12 (cost*1 or cost-effectiv* or savings or cost-saving*).ti,ab,kw. (500575)

13 exp Patient Readmission/ or exp "Length of Stay"/ or exp Health Services Research/ (243112)

14 ("hospital readmission*" or "hospital admission*" or rehospitali#ation or "length of stay" or "hospital utili#ation*" or "days in hospital").ti,ab,kw. (90523)

15 or/8-14 (856901)

16 exp Ambulatory Care/ or exp Outpatients/ or Primary Health Care/ (132558)

17 (ambulant* or outpatient* or domiciliary).ti,ab,kw. (158036)

18 (home adj2 care).ti,ab,kw. (24041)

19 (primary adj2 care).ti,ab,kw. (120914)

20 or/16-19 (351499)

21 7 and 15 and 20 (1556)

22 limit 21 to yr="2013 -Current" (587)

23 (editorial or letter or case reports or comment).pt. or case report*.ti. (3473781)

24 22 not 23 (575)

25 (child not adult).mp. (1268435)

26 24 not 25 (563)

Ovid Embase

1 exp palliative therapy/ (98809)

2 palliativ*.ti,ab,kw. (91847)

3 palliativ*.ot. (2182)

4 exp terminal care/ (62833)

5 ("end of life" or "last month* of life" or "last year of life" or "last day of life" or end-of-life care or incurable* or "last stage of disease" or "die at home" or "life care end").ti,ab,kw. (46522)

6 or/1-5 (197909)

7 exp "health care cost"/ (272767)

8 exp "cost"/ (328021)

9 exp "cost benefit analysis"/ (80168)

10 exp "cost control"/ (64354)

11 (cost*1 or cost-effectiv* or savings or cost-saving*).ti,ab,kw. (670112)

12 exp hospital readmission/ (50191)

13 exp "length of stay"/ (160656)

14 exp health services research/ (32269)

15 ("hospital readmission*" or "hospital admission*" or rehospitali#ation or "length of stay" or "hospital utili#ation*" or "days in hospital").ti,ab,kw. (156035)

16 or/7-15 (1119094)

17 exp ambulatory care/ (44996)

18 exp outpatient/ (106036)

19 primary health care/ (60662)

20 (ambulant* or spitex or outpatient* or domiciliary).ti,ab,kw. (249728)

21 (home adj2 care).ti,ab,kw. (30038)

22 (primary adj2 care).ti,ab,kw. (164870)

23 or/17-22 (504475)

24 6 and 16 and 23 (2283)

25 limit 24 to yr="2013 -Current" (1284)

26 limit 25 to embase (491)

27 (editorial or letter or case reports or comment).pt. or case report*.ti. (1930873)

28 26 not 27 (481)

29 (child not adult).mp. (1421536)

30 28 not 29 (467)

CINAHL

((((MH "Palliative Care") OR (TI palliativ* OR AB palliativ*) OR (MH "Terminal Care+") OR (TI "end of life" OR AB "end of life" OR TI "last month* of life" OR AB "last month* of life" OR TI "last year of life" OR AB "last year of life" OR TI "last day of life" OR AB "last day of life" OR TI "end-of-life care" OR AB "end-of-life care" OR TI incurable* OR AB incurable* OR TI "last stage of disease" OR AB "last stage of disease" OR TI "die at home" OR AB "die at home" OR TI "life care end" OR AB "life care end")))

AND ((MH "Costs and Cost Analysis+") OR (MH "Cost Benefit Analysis") OR (MH "Cost Savings") OR (MH "Health Care costs") OR (TI cost* OR AB cost* OR TI cost-effectiv* OR AB cost-effectiv* OR TI savings OR AB savings OR TI cost-saving* OR AB cost-saving*) OR (MH "Readmission") OR (MH "Length of Stay") OR (MH "Health Services Research+") OR (TI "hospital readmission*" OR AB "hospital readmission*" OR TI "hospital admission*" OR AB "hospital admission*" OR TI rehospitalization* OR AB rehospitalization* OR TI rehospitalisation* OR AB rehospitalisation* OR TI "length of stay" OR AB "length of stay" OR TI "hospital utilization*" OR AB "hospital utilization*" OR TI "hospital utilisation*" OR AB "hospital utilisation*" OR TI "days in hospital" OR AB "days in hospital")) AND (((MH "Ambulatory Care") OR (MH "Outpatients") OR (MH "Outpatient Service") OR (MH "Primary Health Care") OR (TI ambulant* OR AB ambulant* OR TI outpatient* OR AB outpatient* OR TI domiciliary OR AB domiciliary) OR ((TI home OR AB home) N2 (TI care OR AB care)) OR ((TI primary OR AB primary) N2 (TI care OR AB care)))))

Cochrane Central Register of Controlled Trials (CENTRAL)

98 Trials matching on '("end of life" OR "last month* of life" OR "last year of life" OR "last day of life" OR end-of-life care OR incurable* OR "last stage of disease" OR "die at home" OR "life care end" OR palliative) in Title Abstract Keyword AND (cost OR cost-effective OR savings OR cost-saving OR "hospital readmission*" OR "hospital admission*" OR rehospitalization OR "length of stay" OR "hospital utilization" OR "days in hospital") in Title Abstract Keyword AND (ambulant OR outpatient OR domiciliary OR "home care" OR "home based care" OR "primary care" OR "primary health care") in Title Abstract Keyword - with Publication Year from 2013 to 2019, with Cochrane Library publication date Between Jan 2013 and Feb 2019, in Trials (Word variations have been searched)'

Web of Science Core Collection

TS=(("end of life" OR "last month* of life" OR "last year of life" OR "last day* of life" OR end-of-life care OR incurable* OR "last stage of disease" OR "die at home" OR "life care end" OR palliative) AND (cost OR cost-effectiv* OR savings OR cost-saving OR "hospital readmission*" OR "hospital admission*" OR rehospitalisation OR "length of stay" OR "hospital utilization" OR "days in hospital") AND (ambulant OR outpatient OR domiciliary OR "home care" OR "home based care" OR "primary care" OR "primary health care"))

Refined by: PUBLICATION YEARS: (2019 OR 2018 OR 2017 OR 2016 OR 2015 OR 2014 OR 2013)

PubMed Subsets for status publisher and pubmednotmedline

Search ((((Palliative Care OR Palliative Medicine[MeSH Terms]) OR (palliativ*[Title/Abstract]) OR (palliativ*[Transliterated Title]) OR (Terminal Care[MeSH Terms]) OR ("end of life"[Title/Abstract] OR "last month* of life"[Title/Abstract] OR "last year of life"[Title/Abstract] OR "last day of life"[Title/Abstract] OR end-of-life care[Title/Abstract] OR incurable*[Title/Abstract] OR "last stage of disease"[Title/Abstract] OR "die at home"[Title/Abstract] OR "life care end"[Title/Abstract])) AND ((((((("Health Expenditures"[Mesh]) OR "Costs and Cost Analysis"[Mesh]) OR "Cost-Benefit Analysis"[Mesh]) OR "Cost Savings"[Mesh]) OR "Health Care Costs"[Mesh]) OR (cost[Title/Abstract] OR costs[Title/Abstract] OR cost-effectiv*[Title/Abstract] OR savings[Title/Abstract] OR cost-

saving*[Title/Abstract]) OR ((("Patient Readmission"[Mesh]) OR "Length of Stay"[Mesh]) OR "Health Services Research"[Mesh]) OR ("hospital readmission*"[Title/Abstract] OR "hospital admission*"[Title/Abstract] OR rehospitalisation[Title/Abstract] OR rehospitalization[Title/Abstract] OR "length of stay"[Title/Abstract] OR "hospital utilisation*"[Title/Abstract] OR "hospital utilization*"[Title/Abstract] OR "days in hospital"[Title/Abstract])) AND ((Ambulatory Care OR Outpatients OR Primary Health Care[MeSH Terms]) OR (ambulant*[Title/Abstract] OR outpatient*[Title/Abstract] OR domiciliary[Title/Abstract]) OR (home-based care[Title/Abstract] OR primary care[Title/Abstract] OR primary health care[Title/Abstract]))) AND pubmednotmedline[sb]) OR ((((Palliative Care OR Palliative Medicine[MeSH Terms]) OR (palliativ*[Title/Abstract]) OR (palliativ*[Transliterated Title]) OR (Terminal Care[MeSH Terms]) OR ("end of life"[Title/Abstract] OR "last month* of life"[Title/Abstract] OR "last year of life"[Title/Abstract] OR "last day of life"[Title/Abstract] OR end-of-life care[Title/Abstract] OR incurable*[Title/Abstract] OR "last stage of disease"[Title/Abstract] OR "die at home"[Title/Abstract] OR "life care end"[Title/Abstract])) AND ((((((("Health Expenditures"[Mesh]) OR "Costs and Cost Analysis"[Mesh]) OR "Cost-Benefit Analysis"[Mesh]) OR "Cost Savings"[Mesh]) OR "Health Care Costs"[Mesh]) OR (cost[Title/Abstract] OR costs[Title/Abstract] OR cost-effectiv*[Title/Abstract] OR savings[Title/Abstract] OR cost-saving*[Title/Abstract]) OR ((("Patient Readmission"[Mesh]) OR "Length of Stay"[Mesh]) OR "Health Services Research"[Mesh]) OR ("hospital readmission*"[Title/Abstract] OR "hospital admission*"[Title/Abstract] OR rehospitalisation[Title/Abstract] OR rehospitalization[Title/Abstract] OR "length of stay"[Title/Abstract] OR "hospital utilisation*"[Title/Abstract] OR "hospital utilization*"[Title/Abstract] OR "days in hospital"[Title/Abstract])) AND ((Ambulatory Care OR Outpatients OR Primary Health Care[MeSH Terms]) OR (ambulant*[Title/Abstract] OR outpatient*[Title/Abstract] OR domiciliary[Title/Abstract]) OR (home-based care[Title/Abstract] OR primary care[Title/Abstract] OR primary health care[Title/Abstract]))) AND publisher[sb])

Filters: Publication date from 2013/01/01 to 2019/12/31

Google Scholar

"end of life"|"last months of life"|"last year of life"|"last days of life"|end-of-life care|incurable|"last stage of disease"|"die at home"|"life care end"|palliative cost|cost-effective|savings|cost-saving|"hospital readmission"|"hospital admission"|rehospitalisation|"length of stay"|"hospital utilization"|"days in hospital" ambulant|outpatient|domiciliary|"home care"|"home based care"|"primary care"|"primary health care"

8. Other activities

8.1. Swiss Dapagliflozin Study

In 2014, the Food and Drug Administration (FDA) approved the sodium-glucose cotransporter 2 (SGLT2) inhibitor dapagliflozin to control hyperglycemia for type 2 diabetic patients. In 2019, a phase 3 placebo-controlled trial (DAPA-HF) found that for patients with HF and a reduced ejection fraction, dapagliflozin was associated with a lower risk of worsening HF or death from cardiovascular causes, even for patients without diabetes. Therefore, dapagliflozin received FDA and European Medicine Agency approvals in 2020 with indications for reducing risks of cardiovascular death and hospitalization for HF.

In Switzerland, there are no prevalence or incidence of HF data regarding dapagliflozin. There are also no national data on the prevalence of diabetes in patients with HF or the frequency of dapagliflozin to treat HF. For Swissmedic approval of dapagliflozin for patients with HF, Taulant Muka (head of Cardiometabolic Research at ISPM) and Lukas Hunziker (head of the Inselspital's Heart Failure Center) led a study describing the HF population from a tertiary hospital in Switzerland (Inselspital). For this study, I participated through accessing Insel's data and running a feasibility analysis. Additionally, as part of a multicenter study across Europe funded by AstraZeneca, I analyzed patient data for clinical characteristics and mortality. The study described the epidemiology and health care utilization of the Cardiovascular-Renal-Metabolism (CaReMe) comorbidity.

8.2. Nurses' Health Study

Established in 1976, the Nurses' Health Study (NHS) is a prospective cohort for 11 of the most populous states in the United States. Since its establishment, cohort members receive follow-up questionnaires every 2 years. Since 2012, study investigators have collected responses related to questions about anticipatory and EoL care planning. The study investigators are affiliated to the Channing Division of Network Medicine at Brigham and Women's Hospital, Harvard Medical School, and Harvard T.H. Chan School of Public Health.

Upon submission of a research proposal and after an institutional collaboration training with Brigham and Women's Hospital, data from the NHS cohort may be used by third parties. Together with Taulant Muka and Monica Fliedner (co-director of Inselspital's Palliative Care Center), I sent a research proposal and requested NHS data. My proposed study aims to assess barriers and facilitators of anticipatory care planning among female nurses. The proposal was approved, and I will proceed with the project after my doctoral defense.

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10. Curriculum vitae and publication list

PERSONAL INFORMATION Valentina González Jaramillo

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Sex Female | Date of birth 15.03.1990 | Nationality Colombian

EDUCATION

July 2018 - Present	PhD in Health Sciences Institute of Social and Preventive Medicine, University of Bern, Switzerland
August 2016 – August 2018	Research Master (MSc) in Health Sciences: Clinical Epidemiology Erasmus University of Rotterdam, The Netherlands
June 2016 – June 2017	Global Clinical Scholars Research Training Programme Certificate Harvard Medical School, Boston, United States
January 2008 – July 2014	Medical Doctor (MD) Diploma in General Medicine, Universidad de Antioquia, Medellín, Colombia

WORK EXPERIENCE

Appointments

October 2021 - now — Postdoctoral researcher

University Center for Palliative Care, Inselspital, Bern, Switzerland
Research group: Palliative Care

July 2018- September 2021 — Researcher

University Center for Palliative Care, Inselspital, Bern, Switzerland
Research group: Palliative Care

Institute of Social and Preventive Medicine, University of Bern, Switzerland
Research group: Cardiometabolic Health

- Reference: Prof. Dr. med. Steffen Eychmüller, Head of Palliative Care research group
  Phone number: +41 31 632 63 20
- Reference: Dr. Taulant Muka, Head of Cardiometabolic Health research group
  Phone number: +41 78 740 31 11

Researcher

August 2017- June 2018

Erasmus MC, Rotterdam, The Netherlands.
Research groups: Erasmus AGE and Cardiovascular Disease

- Reference: Dr. Taulant Muka, supervisor.
  Phone number: +41 78 740 31 11

May 2015 – January 2015

Attending Physician and Health Promotion and Disease Prevention program Coordinator

Hospital Santa Teresita, Pácora, Colombia.

- Reference: Dra. Catalina Sánchez, former medical coordinator.
  Phone number: +57 301 5994782

October 2014 - April 2015

Rural Emergency Physician

Hospital La Inmaculada, Guatapé, Colombia.

- Reference: Dr. Tomás Martínez, former health promotion program coordinator.
  Phone number: +57 311 7969648

RESEARCH ACTIVITY

Publications

First author

Gonzalez-Jaramillo, V, Guyer, J, Luethi, N. et al. Validation of the German version of the needs assessment tool: progressive disease-heart failure. Health Qual Life Outcomes 19, 214 (2021). https://doi.org/10.1186/s12955-021-01817-6

Gonzalez-Jaramillo V, Arenas Ochoa LF, Saldarriaga C, Krikorian A, Vargas JJ, Gonzalez-Jaramillo N, Eychmüller S, Maessen M. The 'Surprise question' in heart failure: a prospective cohort study. BMJ Support Palliat Care. 2021 Aug 17:bmjspcare-2021-003143. doi: 10.1136/bmjspcare-2021-003143. Epub ahead of print. PMID: 34404746.

Gonzalez-Jaramillo V, Fuhrer V, Gonzalez-Jaramillo N, Kopp-Heim D, Eychmüller S, Maessen M. Impact of home-based palliative care on health care costs and hospital use: A systematic review. *Palliat Support Care*. 2020 Dec 9:1-14. doi: 10.1017/S1478951520001315. Epub ahead of print. PMID: 33295269.

Gonzalez-Jaramillo V, Sobanski P, Calvache JA, Arenas-Ochoa LF, Franco OH, Hunziker L, Eychmüller S, Maessen M. Unmet device reprogramming needs at the end of life among patients with implantable cardioverter defibrillator: A systematic review and meta-analysis. *Palliat Med*. 2020 Sep;34(8):1019-1029. doi: 10.1177/0269216320929548. Epub 2020 Jun 26. PMID: 32588755; PMCID: PMC7388150.

Gonzalez-Jaramillo V, Portilla-Fernandez E, Glisic M, Voortman T, Bramer W, Chowdhury R, Roks AJM, Jan Danser AH, Muka T, Nano J, Franco OH. The role of DNA methylation and histone modifications in blood pressure: a systematic review. *J Hum Hypertens*. 2019 Oct;33(10):703-715. doi: 10.1038/s41371-019-0218-7. Epub 2019 Jul 25. Erratum in: J Hum Hypertens. 2019 Aug 27;: PMID: 31346255.

Gonzalez-Jaramillo V, Portilla-Fernandez E, Glisic M, Voortman T, Ghanbari M, Bramer W, Chowdhury R, Nijsten T, Dehghan A, Franco OH, Nano J. Epigenetics and Inflammatory Markers: A Systematic Review of the Current Evidence. *Int J Inflam*. 2019 May 8;2019:6273680. doi: 10.1155/2019/6273680. PMID: 31205673; PMCID: PMC6530203.

Coauthor

Chowdhury R, Heng K, Shawon MSR, Goh G, Okonofua D, Ochoa-Rosales C, **Gonzalez-Jaramillo V**, Bhuiya A, Reidpath D, Prathapan S, Shahzad S, Althaus CL, Gonzalez-Jaramillo N, Franco OH; Global Dynamic Interventions Strategies for COVID-19 Collaborative Group. Dynamic interventions to control COVID-19 pandemic: a multivariate prediction modelling study comparing 16 worldwide countries. *Eur J Epidemiol*. 2020 May;35(5):389-399. doi: 10.1007/s10654-020-00649-w. Epub 2020 May 19. PMID: 32430840; PMCID: PMC7237242.

Chen Z, Glisic M, Song M, Aliahmad HA, Zhang X, Moumdjian AC, **Gonzalez-Jaramillo V**, van der Schaft N, Bramer WM, Ikram MA, Voortman T. Dietary protein intake and all-cause and cause-specific mortality: results from the Rotterdam Study and a meta-analysis of prospective cohort studies. *Eur J Epidemiol*. 2020 May;35(5):411-429. doi: 10.1007/s10654-020-00607-6. Epub 2020 Feb 19. PMID: 32076944; PMCID: PMC7250948.

Asllanaj E, Zhang X, Ochoa Rosales C, Nano J, Bramer WM, Portilla-Fernandez E, Braun KVE, **Gonzalez-Jaramillo V**, Ahrens W, Ikram A, Ghanbari M, Voortman T, Franco OH, Muka T, Glisic M. Sexually dimorphic DNA-methylation in cardiometabolic health: A systematic review. *Maturitas*. 2020 May;135:6-26. doi: 10.1016/j.maturitas.2020.02.005. Epub 2020 Feb 13. PMID: 32252966.

Glisic M, Kastrati N, **Gonzalez-Jaramillo V**, Bramer WM, Ahmadizar F, Chowdhury R, Danser AJ, Roks AJ, Voortman T, Franco OH, Muka T. Associations between Phytoestrogens, Glucose Homeostasis, and Risk of Diabetes in Women: A Systematic Review and Meta-Analysis. *Adv Nutr*. 2018 Nov 1;9(6):726-740. doi: 10.1093/advances/nmy048. PMID: 30462180; PMCID: PMC6247339.

Honors and scholarships

GlobalP3HS scholarship: The SSPH+ Global PhD Fellowship Program in Public Health Sciences funded by Marie Skłodowska-Curie Actions (Horizon 2020 - COFUND).

Harvard Medical School Scholarship for Global Clinical Scholars Research Training Program (GCSRT). Harvard University, Boston, United States (June 2016- June 2017)

COLFUTURO: Scholarship-loan offered by the Government of Colombia for Master of Health Sciences studies (August 2016- August 2018).

Congress activity

European Association of Palliative Care

2021 Online. Poster presentation: "Using the surprise question to assess palliative care needs in ambulatory population with heart failure: a prospective cohort study" and "Validation of the German version of the Needs Assessment Tool: Progressive Disease – Heart Failure"

	2020 Palermo, Italy. Poster presentation: "Unmet device reprogramming needs at the end of life among patients with ICD: a systematic review and meta-analysis" *
	2019 Berlin, Germany. Poster presentation: "Advance directives: expectation vs reality. How is Switzerland doing?"
European Society of Cardiology	2019 Paris, France.
	2021 Online
European Society of Cardiology -Heart Failure	2020 Barcelona, Spain. Poster presentation: "Screening Palliative care needs in heart failure population" *
	* Cancelled due to COVID-19 pandemic.

Teaching activity

Berner Fachhochschule	Internship leader for a Swiss master's in nursing student, Marina Maier.
University of Bern	Assisted Steffen Eychmüller's supervision of a medical dissertation by Jelena Anna Guyer.
	Assisted Steffen Eychmüller's supervision of a master's in medicine student, Rut Zbinden.
SSPH+	Teaching assistant for Fundamental Concepts in Epidemiology.

Review activity

Palliative Medicine
International Journal of Epidemiology
Journal of the European Academy of Dermatology and Venerology
European Journal of Preventive Cardiology
JAMA

OTHER SKILLS

Languages

Spanish	Native speaker
English	For professional use
German	Basic command

Digital competence

Stata, SPSS
Microsoft Word, Excel, Outlook
EndNote
Adobe Illustrator Draw, Procreate

11. Declaration of originality

Last name, first name: González Jaramillo, Valentina

Matriculation number: 17-126-244

I hereby declare that this thesis represents my original work and that I have used no other sources except as noted by citations.
All data, tables, figures and text citations, which have been reproduced from any other source, including the internet, have been explicitly acknowledged as such.
I am aware that in case of non-compliance, the Senate is entitled to withdraw the doctorate degree awarded to me on the basis of the present thesis, in accordance with the "Statut der Universität Bern (Universitätsstatut; UniSt)", Art. 69, of 7 June 2011.

Place, date

Wallisellen, 06.09.2021

Signature