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RESEARCH ARTICLE

Preferences for Monitoring Chronic Heart Failure Patients: A Multi-Profile Best–Worst Scaling Analysis

[Préférences des patients pour la surveillance de l'insuffisance cardiaque chronique : une analyse multi-profils de l'échelle de différence maximale]

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Abstract: Heart failure patients are facing trade-offs when deciding on medical devices to use to monitor changes in pulmonary artery pressure, indicating worsening. To assess patient preferences for benefits and risks of chronic heart failure monitoring a literature search and pre-test interviews were conducted to determine patient-relevant endpoints. A multi-profile best-worst scaling (BWS) was applied. Treatment profiles comprised the attributes mobility, mortality risk, risk of hospitalization, type/frequency of monitoring, and risk of medical device and system relevant complications. Each respondent answered 14 choice tasks, including dominance test and assessment of test-retest stability. Data was analyzed using random parameter logit models. A market simulator was used to examine what share of respondents would prefer a specific therapy alternative. A total of 278 patients were included. Mortality risk, hospitalization risk, and mobility attributes highly impacted choice decisions. The change from the best to the worst level of mortality risk had the greatest negative impact (level difference: 3.999). Type/frequency of monitoring was less important (level difference: 0.919), with 56 doctor visits per year being least preferred (coeff. -0.531). Risk of medical device complications seemed to be of less (relative) importance for the respondents. A significant preference variation for all attributes could be observed. Market simulation showed that therapies with low mortality, low hospitalization, and high improvement in mobility would be preferred with increasing monitoring. These results indicated that patients value low risks of death and hospitalization. An increase in risk would significantly impact respondents' choices. Type/frequency of monitoring does not strongly influence patients' value. Standard deviations in the logit model indicate heterogeneity in the preference structure.

Keywords: Heart failure Treatment; Monitoring pulmonary artery pressure; Health Preference Study; Best–Worst Scaling Case 3.

Résumé : Les patients souffrant d'insuffisance cardiaque sont confrontés à des compromis lorsqu'ils décident des dispositifs médicaux à utiliser pour surveiller les changements de pression artérielle pulmonaire, indiquant une aggravation. Pour évaluer les préférences des patients concernant les bénéfices et les risques de la surveillance de l'insuffisance cardiaque chronique, une recherche documentaire et des entretiens préalables ont été menés pour déterminer les critères d'évaluation pertinents pour le patient. Une analyse multi-profils de l'échelle de différence maximale a été appliquée. Les profils de traitement comprenaient les attributs de mobilité, risque de mortalité, risque d'hospitalisation, type/fréquence de surveillance et risque de complications liées au dispositif médical et au système. Chaque répondant a répondu à 14 tâches de choix, y compris un test de dominance et une évaluation de la stabilité test-retest. Les données ont été analysées à l'aide de modèles logit à paramètres aléatoires. Un simulateur de marché a été utilisé pour examiner quelle proportion de personnes interrogées préférerait une alternative thérapeutique spécifique. Au total, 278 patients ont été inclus. Les attributs de risque de mortalité, risque d'hospitalisation et mobilité ont eu un impact important sur les décisions de choix. Le passage du meilleur au pire niveau de risque de mortalité a eu l'impact négatif le plus important (différence de niveau : 3,999). Le type/fréquence de surveillance était moins important (différence de niveau : 0,919), avec 56 visites médicales par an étant la moins préférée (coeff. -0,531). Le risque de complications liées aux dispositifs médicaux semblait avoir une importance (relative) moindre pour les personnes interrogées. Une variation significative des préférences pour tous les attributs a pu être observée. La simulation de marché a montré que les thérapies à faible mortalité, faible hospitalisation et forte amélioration de la mobilité étaient préférées avec une surveillance accrue. Ces résultats indiquent que les patients apprécient les faibles risques de décès et d'hospitalisation. Une augmentation du risque aurait un impact significatif sur les choix des répondants. Le type/fréquence de surveillance n'influence pas fortement la valeur des patients. Les écarts types dans le modèle logit indiquent une hétérogénéité dans la structure des préférences.

Mots clés : Traitement de l'insuffisance cardiaque; Surveillance de la pression de l'artère pulmonaire; Étude de préférence en santé; Échelle de différence maximale de type 3.

Introduction

Heart failure is a syndrome caused by cardiac dysfunction leading to water and salt retention that, left unchecked, will cause increasing breathlessness and peripheral oedema [1]. It is common and predominantly affects older people. It is the final common pathway of many cardiovascular diseases and may be associated with debilitating symptoms, a poor quality of life and an adverse prognosis, both in terms of hospitalization and death. However, good management can control symptoms, maintain wellbeing, and delay death for many years [1-3].

Chronic Heart Failure (CHF) affects approximately 64.3 million people worldwide [4]. The prevalence is 3–20 cases/1000 population in the western world [5]. An estimate of the prevalence of the total European population is between 0.4 and 2 %. The number of heart failure cases in Germany has been rising steadily for years. In 2015, heart failure was the most frequent individual diagnosis treated in hospitals, with around 450,000 patients. Most patients are over 65 years old [4]. The incidence of heart failure increases with age. Men have a higher incidence than women [6]. The incidence of heart failure in the USA is between 2 and 5 per 1,000 person-years, depending on the cohort studied. At higher age, the heart chambers and atria become increasingly rigid, diastolic dysfunction can occur, blood pressure fluctuations increase and the ability to increase cardiac output decreases [7]. The most common causes of heart failure are arterial hypertension and coronary heart disease. Other causes may include arrhythmias or heart valve defects [8, 9].

The diagnosis of CHF can be difficult as many of the symptoms of CHF are non-specific and do not help discriminate between CHF and other problems. The symptoms of heart failure can range from physical weakness to edema or even organ failure. Chronic heart failure is clinically present when the typical symptoms such as dyspnea, breathlessness, fatigue or rather performance reduction occur [3, 7].

Heart failure is usually diagnosed based on clinical symptoms. If the symptoms indicate a heart failure, a thorough anamnesis and physical examination should follow [10]. The anamnesis provides information on possible causes, the severity of heart failure and a prognosis. The anamnesis can be used to determine risk factors that can lead to coronary heart disease and, later on, to chronic heart failure [9]. Risk factors include smoking, hypertension, diabetes mellitus, familial predisposition or obesity [11]. During the physical examination, the patient's body is auscultated to detect changes in cardiac sounds. Further diagnostic procedures include a 12-channel ECG, basic laboratory diagnostics and echocardiography, which is the core of the diagnostic procedure. Echocardiography can be used to differentiate between systolic and diastolic heart failure and in most cases to determine the causes of heart failure [9].

A common classification of chronic heart failure is determined by the severity of the stress at which symptoms of heart failure occur. There is the New York Heart Association (NYHA) classification, which includes four stages. In the first stage the heart disease is present, however, there are no complaints with everyday physical burdens. In the second stage, complaints occur like exhaustion, rhythm disturbances, shortness of breath or angina pectoris by increased physical exercise. Stronger physical strains are, for example, going uphill or climbing stairs. In the third stage, complaints develop by low physical activity like walking in the plain and in the fourth stage, complaints already occur in a resting phase [7]. The percentage distribution of NYHA Classes I-IV in Germany is 50% in NYHA Class I. NYHA Class II has a frequency of 35%, NYHA Class III has a frequency of 10% and NYHA Class IV has a frequency of 5%.

Therapy goals include reducing heart failure symptoms, increasing exercise tolerance, reducing mortality and hospitalization rates, and improving quality of life [12]. If heart failure is in NYHA stages I-III, moderate physical exercise should be practiced [13]. In addition, 1.5-2 liters of fluid should be taken per day [14]. Furthermore, the intake of salt during meals should be reduced, alcohol should be consumed in small amounts and smoking should be stopped [9, 14]. Even traveling to high altitudes, in very humid or hot climates should be avoided [15]. Long flights should also be avoided [16]. If underlying diseases that are the cause of heart failure can be treated, interventional or surgical treatments should be made [17]. In chronic heart failure, drugs such as ACE inhibitors, AT1 receptor antagonists or ß-blockers can be taken [18].

Innovative heart failure monitoring technologies exist that allow electronic transmission of physiological data using remote access technology via wireless implantable electronic devices. This enables continuous monitoring of physiological parameters associated with heart failure [19]. However, there are few well-conducted studies investigating the views of patients.

Only a few studies analyze the perspective of patients with heart failure on benefit-risk trade-offs [20]. This study analyzes treatment preferences of chronic heart failure patients facing trade-offs when confronted with the decision on implanting a monitoring system. The study identifies, ranks, and weights patient-relevant endpoints of monitoring options for heart failure. A multi-profile best-worst scaling (BWS case 3) was performed to evaluate patients' value and how treatment effects impact choice decisions. Patient preference information (PPI) can improve treatment decisions and thus treatment outcomes to make heart failure treatments more patient-centered in the future.

Methods

Multi-profile Best–Worst Scaling

Stated preferences methods are widely used in healthcare and increasingly discussed by regulatory bodies [21-23]. The methods are based on the assumption that products or services can be described in terms of their characteristics (attributes and levels). Participants are repeatedly asked to choose between two or more alternatives, such as healthcare products, drugs or services. Each choice alternative differs in the arrangement of the presented attribute levels. The choice scenarios are systematically varied by means of an experimental design [24-27]. As a result, it can be shown how patients are willing to trade between attribute levels, which is useful in deciding on the most appropriate way to provide a treatment or service when resources are limited. Additionally, the relative importance of attributes and levels can be analyzed. This allows to identify which attribute was most important for the respondents and which attribute level had a statistically significant influence on the choice decisions [28].

BWS is a development of the classical Discrete Choice Experiment (DCE). In contrast to DCE, where respondents choose only the best from a set of options, BWS requires respondents to identify the best and worst options in a choice scenario. The main principle of the approach is that respondents define the extremes of a latent, subjective continuum. Essentially, they are asked to choose the pair that maximizes the value difference (on the scale of latent utility) between them [29]. The BWS method distinguishes three different cases: the objective case (Case 1), the profile case (Case 2), and the multiprofile case (Case 3). Case 1 is used when the relative values of a set of objects or items (mostly called attributes) are of main interest. A Case 2 scenario shows a single choice alternative, e.g., treatment, defined by different attribute levels. The respondents are asked to choose the best (most attractive) and the worst (least attractive) attribute level of the given alternative. BWS Case 3 is similar to a classical DCE which provides multiple alternatives. However, next to the most preferred alternative respondents also must choose the least preferred alternative. Supposing that there are only three choice alternatives in a choice scenario, a full preference ranking of the given alternatives can be determined. For a complete ranking of more than three alternatives in a choice scenario, a follow-up question regarding the remaining alternatives must be answered [30]. BWS has been shown to be a valuable tool for analyzing patients' preferences [31, 32] and it has already been used successfully in the healthcare sector [33-35].

Attributes and levels

Hence, the "treatment" in this case encompasses rather a monitoring than actual therapy. Consequently, the attributes used refer to place and frequency of monitoring in terms of comparing an implantable (home-based) device to a standard regular check at the physician office. To determine patient-relevant attributes and levels for the BWS survey, a literature review and qualitative pre-test interviews were conducted to describe the benefits and risks of an innovative implantable monitoring system. Development of the questionnaire and identification of attributes and levels for the BWS was based qualitative pre-test interviews conducted with patients in June 2018 in Germany. The purpose of the interviews was to use the information provided by the patients in an open dialogue to identify and evaluate their wishes and needs for heart failure treatment. In a semi-structured interview and pretest, all relevant attributes of a therapy for chronic heart failure were identified. In the further course of the interviews, it was asked to what an impact these characteristics have on the decision to monitor hemodynamics/ changes in pulmonary artery (PA) pressure. In subsequent interviews, the developed questionnaire was tested for comprehensibility and meaningfulness. Based on the preliminary investigations, five attributes with different levels were determined as critical for patient diagnosed with chronic heart failure: mobility, mortality risk (over one year), risk of hospitalization (over one year), type and frequency of monitoring, and risk of medical device and system relevant complications. The attributes mobility and type and frequency of monitoring included six levels; the remaining attributes included three levels each. 'Type and frequency of monitoring' attribute was used as one compound attribute resulting in its own experimental design providing a more detailed insight into the importance of its components of "time" and "frequency" of the monitoring.

Experimental design

Combining all possible attribute levels would result in a total of 972 possible treatment alternatives ($L^A = 6^2 * 3^3 = 972$). A full factorial experimental design that includes the full set of possible variations of all attribute levels, that is each possible choice situation, would result in an impractically large combination of three alternative choice scenarios. In a BWS, a full-choice design that includes the full set of all possible level variations over three-alternative choice scenarios would result in an impractically large combination. A more practical fractional factorial design in which each respondent was only shown a subset of choice scenarios from the total number of choice scenarios was used for the questionnaire.

Survey design

In the questionnaire, respondents first completed an adaptive choice-based conjoint [36] and then a BWS. The use of both methods was intended to optimize data collection and allow comparison of methods. However, this is not the subject of the manuscript. Within the BWS, each respondent had to complete 12 choice tasks. The respondents were asked to choose between three different therapy options. There was no status quo alternative. At the beginning an illustrated example was shown to explain the choice tasks. The respondents were informed that the presented therapies might not be currently offered in this particular form. The respondents were asked to choose the best and the worst therapy. An additional fix-choice task was included as a dominance test (the attribute levels of one therapy option were significantly worse than those of the other alternatives). This dominance test was identical for all respondents and was used to assess the validity with respect to the rationality of the choice decisions and the respondents' understanding of the task. In addition, a stability test was performed with a duplicated choice task. To avoid order effects, the order of the attributes in the BWS was randomized once per respondent and then shown in this given order in all choice tasks of the respondent.

The survey also included socioeconomic questions and questions about the patients' experiences and perceptions in the context of their therapy and diagnosis. The patients were surveyed by interviewers in a computer-assisted personal interview.

Data collection

The study population included German patients with NYHA class 3 heart failure aged 18 years and older, recruited in cooperation with an external market research company. The referral was made via the treating physicians. Due to these specific characteristics of the recruitment, the calculation of refusal or acceptance rates is impossible.

The respondents needed to have sufficient German language skills. Patients who did not meet all inclusion criteria were not eligible to participate and were excluded from the survey. The survey was conducted between October 2019 and August 2020. All individual participants included in the study provided online consent to participate. Recruiting such severely ill patients for a study in sufficient numbers is extremely difficult. Therefore, no quotas were used to fulfill representativeness or similar.

Statistical model and data analysis

The statistical analysis and interpretation were mainly focused on the Random Parameter Logit (RPL), also known as Mixed Logit (ML) model. The use of BWS data allows the application of different models with more or less flexible specifications. Additional models were calculated where only the best choices were considered instead of the best and worst choices. Also models with reduced sample compared to models with full sample were calculated. Details of additional model analysis are given in supplementary file.

Results

Sociodemographic data, attitudes, and experiences

Overall, 278 respondents completed the survey in 2020. The sociodemographic data of the sample is shown in Table 1. The majority of the participants were male (56%). Most of the respondents were in the age group 61-70 (34%) followed by the age group 51-60 (30%). Regarding marital status, the largest group of respondents were married (47%). Most respondents were retired or pensioner (42%); 28% stated that they were employed full-time; 19% were employed part-time and only 6% were self-employed/freelance. Regarding the highest level of education, a small group of respondents (5%) stated that they had a junior/middle-school certificate, another 5% had a technical college degree, and 6% had a Vocational school or advanced technical certificate. 19% owned a high school diploma or university entrance qualification. While 30% had a university degree, the largest group of the sample had an intermediate school leaving certificate or a secondary school leaving certificate (35%).

Table 1. Sociodemographic data

Variable	N	%
Age		
18-40 years	15	5
41-50 years	48	17
51-60 years	82	30
61-70 years	94	34
>70 years	39	14
Gender		
Male	156	56
Female	122	44
Marital status		
Married	131	47
Widowed	19	7
Divorced or separated	37	13
Single	47	17
In a committed relationship, but not married	44	16
Highest educational level		
Junior or middle school certificate (8 classes)	14	5
Intermediate high school certificate, secondary school certificate (10 classes)	97	35
Vocational school or advanced technical certificate	16	6
Abitur, high school diploma, university entrance qualification	53	19
Technical college degree	14	5
University degree	82	30
Other	2	1
Employment status		
Employed, full-time	77	28
Employed, part-time	53	19
Self-employed/freelance	16	6
Retired or pensioner	118	42
Other	14	5

The questionnaire contained questions on general health, previous illnesses, experiences and attitudes towards the illness and therapy, as well as opinions regarding the critical attributes for monitoring heart failure that are at the primary focus of the survey. Most of the sample stated to have a very good (4%), good (27%) or satisfactory state of health (48%). Few respondents described their state of health as less good (19%) or bad (1%).

About 25% of the respondents have been diagnosed with a heart failure within the last 2 years. A further 26% of the respondents received the diagnosis 2 to 5 years ago. For 19% the diagnosis was given 5 to 10 years ago and for about 29% it was more than 10 years ago.

Almost half of the respondents are currently treated predominantly through a cardiology or specialist practice (46%). Almost as many respondents (26.6%) are treated in the cardiological main/specialist and general practice as by a general practitioner only (28%). Only 9% are treated predominantly in the clinic (outpatient clinic). Regarding the New York Heart Association (NYHA) classification, the majority of the respondents reported that their degree of heart failure was equivalent to NYHA Class 3 (84%). A smaller percentage of respondents were diagnosed with NYHA Class 2 (12%), NYHA Class 1 (2.5%) or NYHA Class 4 (0.36%).

In a 6-minute walking test, 22% of respondents stated that they were able to walk 300 meters within 6 minutes. Further 37% said they could walk more than 300 meters but less than 500 meters in 6 minutes, and about 38% of the respondents were able to walk more than 500 meters in this time.

A majority of 53% of respondents (cumulative) estimated their own mortality risk to be 15% or less. About 31% of the sample (cum.) estimated their own mortality risk to be 20% or higher, and 16% of the respondents (cum.) did not know or did not state their own mortality risk.

About 41% of the respondents estimated their individual risk of hospitalization to be less than 10% and almost 39% of the respondents estimated their risk of hospitalization due to heart failure to be 10-25% within the next year. About 15% of respondents estimated their individual risk of hospitalization to be above 25-40%, and a few respondents even believed their risk of hospitalization to be above 40%.

One-third of respondents required up to 10 minutes to get to their doctor, and almost 50% reported that it took them between 11 and 30 minutes to get there. About 18% of respondents needed more than 30 minutes to travel to their doctor.

Most respondents measured their blood pressure regularly at home (70%).

Half of the sample (cum.) estimated the risk of complications to be up to 2%. Almost 23% of respondents (cum.) estimated the risk of complications to be 3% to 4%, and 27% (cum.) estimated the risk of complications to be 5% or above 5%.

A majority of the sample with about 65% would prefer to make the decision about treatment together with their doctor. A smaller part of the sample of 19% would prefer to make the decision on treatment themselves, taking the doctor's opinion seriously into account. About 10% would prefer the doctor to make the final decision about the treatment, taking the opinions of the respondent seriously into account. Only a small part of 4% would prefer to make the decision on the treatment entirely on their own.

A complete tabular overview of all questions can be found in the supplementary file.

Patients' preferences

Table 2 shows the estimation results for the RPL model. The model output includes mean coefficients which represent the relative utility of an attribute level, and standard deviations which shows the variation about the corresponding mean estimate, indicating preference heterogeneity among the respondents. All variables were effects-code. All random parameters were assumed to be normally distributed. All coefficients are shown with their corresponding standard errors, t-values, significance levels, and confidence intervals at the 95% confidence level.

Positive signs of mean coefficients indicate a higher benefit, that is, respondents more preferred this respective attribute-level, and negative signs indicate a lower benefit. The larger the coefficient, the greater was the influence on choice decisions of the respondents. Negative coefficients indicate a negative influence on choice decisions. The sign of the estimated standard deviations is irrelevant. When confidence intervals do not overlap for adjacent levels within an attribute, the coefficients for the respective levels are statistically different from each other. And when the confidence intervals do not cross the zero line, they are statistically different from zero.

Table 2. Estimates of the random parameter logit model

Attribute	Level	*Mean* Coef.	Std. Err.	z	p	[95% Conf.	Interval]
Mobility	500m	0.543	0.074	7.340	0.000	0.398	0.689
	400m	0.485	0.067	7.270	0.000	0.354	0.615
	300m	0.140	0.056	2.510	0.012	0.031	0.249
	200m	0.065	0.055	1.190	0.235	-0.042	0.173
	100m	-0.406	0.053	-7.640	0.000	-0.510	-0.302
	50m	-0.827	0.085	-9.770	0.000	-0.992	-0.661
Risk of death	Low (3%)	1.947	0.113	17.160	0.000	1.725	2.170
	Medium (13%)	0.105	0.034	3.060	0.002	0.038	0.171
	High (23%)	-2.052	0.113	-18.140	0.000	-2.273	-1.830
Risk of hospitalization	Low (10%)	0.818	0.057	14.450	0.000	0.707	0.929
	Medium (25%)	0.108	0.034	3.170	0.002	0.041	0.175
	High (40%)	-0.926	0.062	-14.890	0.000	-1.048	-0.805
Type and frequency of monitoring	At home 9x per year	0.322	0.067	4.820	0.000	0.191	0.453
	At home 32x per year	0.078	0.056	1.380	0.168	-0.033	0.188
	At home 56x per year	-0.303	0.055	-5.550	0.000	-0.411	-0.196
	At the doctor 9x per year	0.388	0.061	6.350	0.000	0.268	0.507
	At the doctor 32x per year	0.046	0.053	0.880	0.378	-0.057	0.149
	At the doctor 56x per year	-0.531	0.077	-6.930	0.000	-0.680	-0.381
Risk of complications	No risk (0%)	0.107	0.034	3.110	0.002	0.039	0.174
	Mild (1%)	0.080	0.032	2.470	0.014	0.016	0.143
	High (2%)	-0.186	0.035	-5.300	0.000	-0.255	-0.117
Attribute	**Level**	***SD* Coef.**	**Std. Err.**	**z**	**p**	**[95% Conf.**	**Interval]**
Mobility	500m	0.959	0.078	12.350	0.000	0.807	1.111
	400m	0.646	0.073	8.790	0.000	0.502	0.790
	300m	0.393	0.094	4.180	0.000	0.209	0.578
	200m	0.336	0.085	3.970	0.000	0.170	0.502
	100m	-0.177	0.102	-1.740	0.082	-0.376	0.022
	50m	-2.157	0.181	-11.910	0.000	-2.512	-1.802
Risk of death	Low (3%)	1.537	0.092	16.770	0.000	1.358	1.717
	Medium (13%)	-0.289	0.049	-5.840	0.000	-0.386	-0.192
	High (23%)	-1.249	0.099	-12.630	0.000	-1.442	-1.055
Risk of hospitalization	Low (10%)	0.764	0.051	15.060	0.000	0.665	0.864
	Medium (25%)	-0.058	0.109	-0.540	0.592	-0.271	0.155
	High (40%)	-0.706	0.127	-5.560	0.000	-0.955	-0.457
Type and frequency of monitoring	At home 9x per year	0.664	0.067	9.920	0.000	0.533	0.795
	At home 32x per year	0.349	0.082	4.260	0.000	0.189	0.510
	At home 56x per year	-0.325	0.066	-4.950	0.000	-0.454	-0.196
	At the doctor 9x per year	0.386	0.078	4.970	0.000	0.234	0.539
	At the doctor 32x per year	-0.192	0.086	-2.240	0.025	-0.361	-0.024
	At the doctor 56x per year	-0.882	0.155	-5.710	0.000	-1.185	-0.579
Risk of complications	No risk (0%)	0.195	0.050	3.860	0.000	0.096	0.294
	Mild (1%)	-0.086	0.059	-1.480	0.140	-0.201	0.028
	High (2%)	-0.109	0.073	-1.480	0.139	-0.252	0.035

Obs: 20016; N: 278; ll(null): -5311.61; ll(model): -4231.05; df: 32: AIC: 8526.10; BIC: 8779.03; SD: Standard Deviation.

Figure 1 clearly shows that an objectively better attribute level (e.g., low risk) was preferred to any other objectively worse level of this attribute. The type and frequency of monitoring is an exception, because there is objectively no better or worse level of this attribute. More frequent monitoring can also be individually perceived as better than less frequent monitoring.

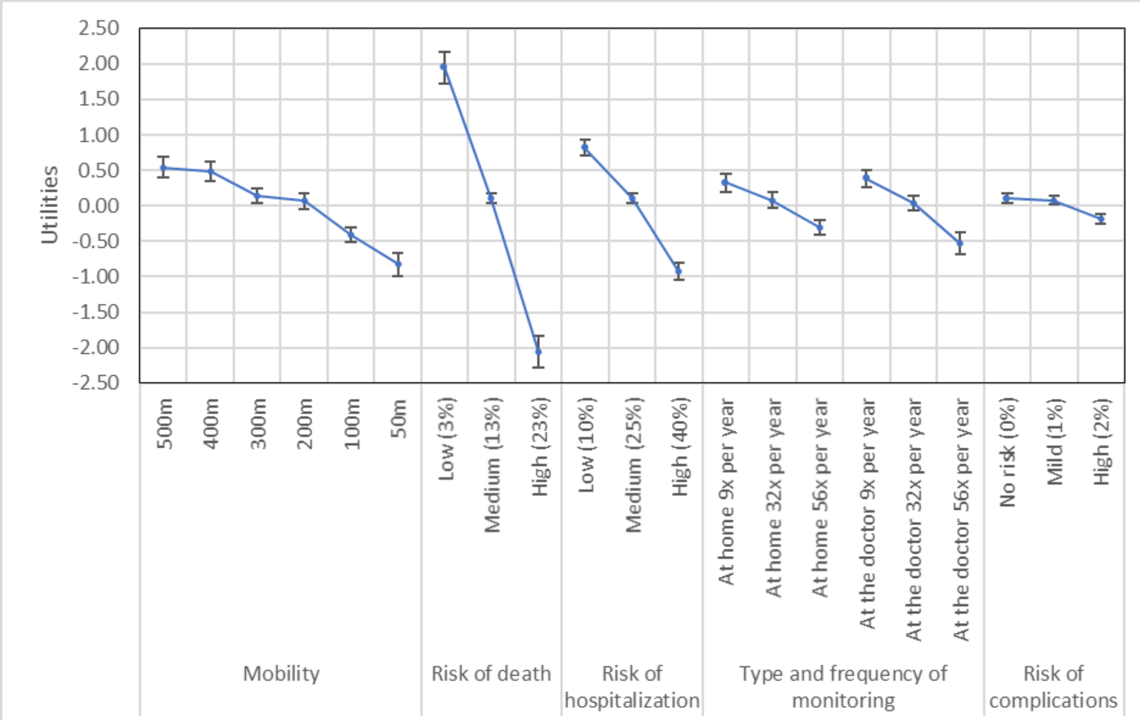

Figure 1. Part-worth utilities and standard errors in the mixed logit model (95% confidence interval)

Mobility

For the attribute mobility all signs are as expected. A longer distance is more preferred by the respondents than a shorter distance. Regarding the attribute it is noticeable that the two attribute levels 500 and 400 meters are on the same plateau. The confidence intervals overlap indicating that the respondents seem to be indifferent between the two levels. This also applies to the next two levels 300 and 200 meters. Both are on the same level, but less important than the first two levels. A change from 400 to 500 meters has the same meaning as a change from 200 to 300 meters. However, the change from 300 to 400 meters is associated with a greater benefit for the respondents. At the levels 100 and 50 meters the slope decreases more. Both levels have a negative sign and are therefore disliked by the respondents.

Risk of death

The attribute risk of death has the largest level difference between the most preferred and the least preferred attribute level, and thus the greatest impact on choice decision. The attribute level low (3%) risk of death was most important. In contrast, the level high (23%) risk of death has a large adverse effect on respondent`s choice decision. The three attribute levels of low (3%), medium (13%) and high (23%) risk of death show an approximately linear curve, with the distance from low risk of death to medium risk of death slightly smaller than the distance from medium risk to high risk of death. Even though the increase from medium risk of death to high risk of death seems to be steeper compared to low risk of death, an approximate linearity in the benefit for attribute levels can be assumed. A flattening of the curve is not apparent in this range.

Risk of hospitalization

The attribute risk of hospitalization has an almost linear preference order similar to the attribute risk of death. The last level high risk (40%) seems to fall off steeply. The benefit from high (40%) to medium risk (25%) seems to be slightly larger than the benefit gain from medium (25%) to low (10%). The low risk (10%) had the greatest influence on the choice decisions, in contrast, the high risk (40%) had a strong negative influence on the respondents' choices.

Type and frequency of monitoring

The attribute type and frequency of monitoring distinguishes between monitoring at home and monitoring at the doctor's office. The monitoring can take place 9, 32 or 56 times per year. Regarding the attribute, it is noticeable that the two levels "at home 9x per year" and "at the doctor 9x per year" are on the same plateau. The confidence intervals overlap, indicating that respondents seem to be indifferent between the two levels. This also applies to the next two levels "at home 32x per year" and "at the doctor 32x per year". Both are on the same plateau but are less important than the first two levels. Since the confidence intervals cross the zero line, a non-significant benefit, not different from zero, can be assumed. A change from 32 to 9 times per year at home has the same significance as a change from 32 to 9 times per year at the doctor's office. However, a change from 56 times per year at the doctor to 32 or to 9 times per year is associated with a greater benefit for the respondents than the same change in monitoring at home. The respondents clearly prefer a lower monitoring frequency. They seem to be indifferent between monitoring at home and monitoring at the doctor's office when monitoring is done 9 times or 32 times per year. However, when the frequency of monitoring increases to 56 times per year, respondents prefer monitoring at home to monitoring at the doctor. For both types, a monitoring of 9 times per year is preferred. In contrast, monitoring 56 times per year is the least preferred for both types, with monitoring at home being preferred to monitoring at the doctor's office.

Risk of medical device and system relevant complications

Alongside the type and frequency of monitoring, respondents rated the risk of complications as the least important attribute in the treatment of heart failure. Accordingly, the impact on choice decisions was minimal. The vertical distance from risk-free (0%) to mild (1%) is smaller than from mild (1%) to high (2%). The latter falls somewhat steeper in the graphical representation. Respondents attach more importance to the transition from high to mild than from mild to no risk.

The relative importance of the attribute was calculated based on the vertical distance between the most and least preferred level within an attribute. The greater the difference, the more important the change from the most and least preferred level. The importance weights can be compared across different attributes. The calculated level differences were normalized on a scale of 10. The figure shows the mean relative importance for each attribute.

To interpret the significance of relative importance, it is important to note that the scores represent the increase in benefit from the lowest to the highest level within an attribute.

For the attribute " Risk of death ", the change from one level to the next represents a 10% change in risk. The relative importance is calculated based on an overall change of 20%. The value for the attribute "Risk of hospitalization" represents the 15% increase in benefit for each level. However, the relative importance represents a change of 30%. The same procedure is used for the remaining attributes.

Main findings

In general, the benefits of treatment are higher for respondents when the risks are lower, and mobility is better. Less frequent monitoring also seems to contribute to an attractive treatment. This corresponds to the a priori expectations.

It is obvious that the risk of death in its importance strongly dominates the other attributes. The risk of hospitalization is also of great importance. On the other hand, there is no concern about the risk of complications among the respondents.

With the same frequency of monitoring, respondents appear to be indifferent between monitoring at home or at the doctor's office. However, with a 56 times per year monitoring, the respondents rather prefer the monitoring at home.

In the regression model, all signs of the coefficients are as expected. Except for the middle attribute levels 200 meters mobility, 32 times monitoring at home and at the doctor's office, all mean coefficients are statistically significantly different from zero with p-values of less than 0.01, most even less than 0.001, and therefore, have a significant influence on the choice decisions of the respondents.

Significant standard deviations at all attribute levels indicate high variability in the effects. This is particularly the case for the high and low levels of the attributes mobility, risk of death, risk of hospitalization, as well as for the levels monitoring at home 9 times a year and at the doctor 56 times a year. These standard deviations have a p-value of less than 0.001.

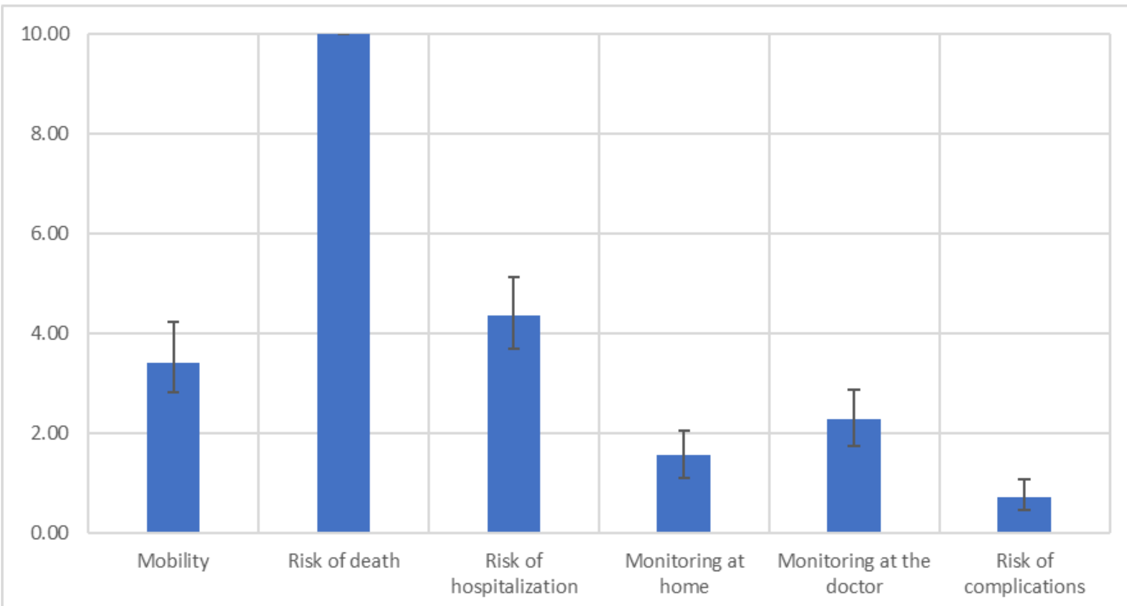

Figure 2. Relative attribute importance in 95% confidence interval

Choice simulation

Choice simulators (also market or what-if simulators) use coefficients to predict choices among a set of competing alternatives [37]. The alternatives are introduced within a simulated market scenario, and the simulator reports the percentage of respondents expected to choose each alternative.

Smart devices and other devices of modern telemedicine enable healthcare providers to continuously monitor the patient. To demonstrate the realistic application of the preference data, an alternative was developed in this case based on actual clinical data (therapy 3) and contrasted with hypothetical alternatives (therapies 1 and 2) [38].

Assuming that the choice action reflects individuals' utility evaluations, the choice simulator can be used to compare alternatives based on study participants' utility expectations.

For the specific case of this study, we performed a simulation with various therapy alternatives including a base case therapy that mimics the outcomes of competing monitoring devices for chronic heart failure patients. The alternatives differ in detail in their characteristics. The calculation of the choice probabilities is based on the calculated overall benefits of the individual alternatives. The first scenario is the base case, which reflects a moderate frequency of doctor visits. We used the coefficients of the mixed logit model and designed a competitive scenario with a base case as control and three alternative comparator therapies. Each therapy alternative is defined using the attribute levels in the DCE. First, a base case was defined. Using the base case as a starting point, three modified comparator therapies were defined. Compared to the base case, the therapy alternatives show improvement in mobility (therapy 3), mortality (therapy 2, and 3), and hospitalization (therapy 1, 2, and 3). As these improvements are expected to require continuous monitoring of the patient, the frequency of monitoring is correspondingly higher for the alternative therapies than for the base case. Table 3 shows all therapy alternatives considered in the market simulation.

Table 3. Competing therapy alternatives in the simulated market scenario

Alternatives	Mobility	Mortality	Hospitalization	Monitoring	Complications	Share of choice
Base Case	200m	Medium (13%)	Medium (25%)	At the doctor 32x per year	Mild (1%)	4%
Therapy 1	200m	Medium (13%)	Low (10%)	At home 56x per year	Mild (1%)	5%
Therapy 2	200m	Low (3%)	Low (10%)	At home 56x per year	Mild (1%)	35%
Therapy 3	500m	Low (3%)	Low (10%)	At home 56x per year	Mild (1%)	56%

When respondents are presented with these alternatives and it is assumed that they all choose one therapy alternative, given the competitive environment outlined above, 4% would likely choose the base case. Therapy 1, which has a lower risk of hospitalization compared with the base case, would probably be chosen by 5% of respondents. Therapy 2 also improves mortality compared with the base case, in addition to hospitalization. The probability of this therapy being chosen by the respondents is 35%. Therapy 3 represents a further improvement or increase in benefit compared to the comparative therapies. The additional improvement in mobility indicates that 56% of respondents, representing the majority of the study population, would likely choose therapy 3. The simulation shows that a reduction in hospitalization risk, a reduction in mortality, and an improvement in mobility would increase participants' probabilities of choosing an alternative. The higher frequency of doctor visits, which was perceived negatively by the study participants, would be compensated.

As a reminder, a what-if simulation gives the possibility to compare new product alternatives that do not exist today. Besides the difficulty that simulations based on aggregate preference models are subject to the IIA problem (independence of irrelevant alternatives), the preference shares resulting from these predictions do not have to correspond to the actual market shares [37]. These predictions are built on the aggregated model results, the decision model, and the study sample used. In the real world, additional factors such as awareness may shape market shares and play a role in the choice decision for or against a therapy alternative.

Discussion

Chronic heart failure is a severe condition that places high demands on patient compliance and adherence. To better involve patients in the decision-making process of a therapy, which is also the preferred approach of respondents in this study, it is necessary to analyze patients' preferences and wishes. Decisions on the therapy of heart failure are very complex and require a trade-off between possible outcomes such as improved mobility and at the same time more or less serious risks.

To the best of our knowledge, this is the first study to analyze patient preferences for benefit-risk trade-offs in heart failure care using the best-worst scaling approach. There has been one preference study in heart failure (e.g., a conjoint analysis study of individual preferences for heart failure outcomes [39]), but no study has been published in the context of heart failure device implantation. This study aims to help analyze and better understand the preferences of heart failure patients. This should contribute to improved decision making in heart failure treatment, to make treatment more patient-centered in the future.

Limitations

A larger sample size could have improved the precision of the results with respect to smaller standard errors. An attribute level can be statistically significant even with a larger standard error, but with less precision. Moreover, it must be stated that this is a rather young, well-educated, well-managed group of patients who are doing well with treatment. They might not be completely representative of the majority of patients with heart failure nor the sicker end of the spectrum that might benefit most from intensive monitoring.

The BWS included two additional selection tasks, which were designed as a dominance test to identify irrational decision makers and as a consistency test. The dominance test was not passed if the respondent chose the worst alternative with the highest risks and poorest mobility. A total of 255 respondents passed the test. The consistency test, in which a choice task was duplicated and repeated during the course of the BWS, was passed by 166 respondents. Both tests in combination passed 154 respondents. Various models are shown in the supplementary file with the full and reduced sample.

In addition to the BWS, where the best and worst choice was analyzed, models were also calculated where only the choice of the best alternative was analyzed.

When comparing the models with the full sample, it is noticeable that in the models with best choices only, the coefficients of the attribute mobility between adjacent levels are further apart than in the models with best and worst choices, and thus seem to be somewhat more distinct from each other. This is particularly noticeable for the first levels of the attribute. The course of the level attributes is thus slightly straightened overall. Nevertheless, the confidence intervals of adjacent levels for 500 and 400 meters and 300 and 200 meters overlap in the best choice only model as well as in the best and worst choice models, which indicates an indifference in the choice between the levels.

Furthermore, the BWS models benefit from the full available choice information, especially with a relatively small sample. This is reflected in smaller standard errors and thus greater significance.

With decreasing sample size, the standard errors of the coefficients increase and thus the precision of the estimation. However, the exclusion of irrational decision-makers can lead to more consistent choices for the analysis and thus to larger coefficients, which can somewhat compensate for the negative effect of smaller standard errors on significance.

The model that excluded those respondents who failed both tests had on average the largest standard errors, but sometimes also larger coefficients compared to the full sample model (e.g., for mobility and risk of death). In this model there is also a rank reversal with relative attribute weighting for mobility and risk of hospitalization. Whereas in the full model the risk of hospitalization is ranked second behind the risk of death, in the reduced model mobility is ranked second, just ahead of the risk of hospitalization. However, both attributes are far behind risk of death in both models. Likewise, the confidence intervals in the full and reduced model overlap, indicating an indifference between second and third place in the ranking.

For the main analysis of this study, the model with all respondents was chosen also due to the small sample size. And even with small statistical differences in the models, there are no significant changes in the overall statement and interpretation. For the purposes of this study, it is assumed that the location of monitoring (at home or at doctor's office) does not impact other attributes (i.e., monitoring location has no impact on mobility, risk of death or risk of complication). While this approach was necessary to evaluate the importance of each individual attribute, some studies do suggest that home monitoring may reduce risk of heart failure hospitalization, reduce risk of death, improve quality of life [40-43]. These simultaneous outcomes have been observed in patients being remotely managed with the knowledge of their pulmonary artery pressures.

Monitoring technologies can be of great benefit to disease management. Patients in the study were asked about monitoring without explicitly providing the value of it. It is possible that patients did not see or understand the benefits of monitoring. And it remains unclear whether respondents perceive it as a burden to be constantly monitored. Sicker patients may place greater value on wellbeing and less on prognosis. Well patients are likely to place greater value on longevity (because life is worth living). A subgroup analysis by severity, sex and age could is done to answer this question.

Additionally, the survey was conducted before the Covid-19 pandemic outbreak. It is also quite possible that the results would have been different had the survey been conducted after the pandemic outbreak and that patient preferences for home monitoring would be significantly greater than monitoring at a doctor's office. With the increase in telemedicine, digital consultation and care following the coronavirus outbreak, a differentiated view and choice of affected individuals is conceivable or even assumed. Avoiding the risk of infection through contact in waiting rooms, doctors' offices, or public transportation could be critical in this regard. However, healthcare also depends on the personal doctor-patient relationship. And the discussion about data protection could also be perceived negatively and reinforce an unpleasant feeling of being constantly monitored. A further study under different circumstances may provide insight here.

After all, the corona pandemic could act as a digital health accelerator for a change in perception and uptake of digital health solutions.

Further research

In the best only model, the order of the level coefficients for the attribute mobility seemed to be more rational. This could indicate that the classic DCE with only one choice per task works better, especially for older people. The respondents in this study are 59 years old on average. 34% of the respondents belong to the age category 61-70 years and 14% are older than 70 years. It is possible that BWS was cognitively too demanding at the end of the questionnaire, which required a lot of attention from the patients. It would have to be investigated what the different curve of the levels in the attribute mobility is due to. It is possible that the need to walk greater distances is overestimated, i.e., there is a threshold value that if exceeded will no longer bring any substantial additional benefit to the patients.

Data analysis revealed a significant variation in preferences within the sample. Further investigation should address the identification of patient groups with regard to the identification of different preferences and the causes of these preferences. Identifying heterogeneous patient preferences could help health care decision makers to distinguish one group from another and thus focus on the treatment design of homogeneous groups and their needs.

The analysis of interaction effects between feature levels may be further analyzed. Mobility might interact with other attributes such as the type and frequency of monitoring. With improved mobility, frequent visits to the doctor may be acceptable. Or with the possibility of monitoring at home, low mobility is perhaps not perceived as a disadvantage. Similarly, there may be interaction effects between the type and frequency of monitoring and risk attributes. Furthermore, in the case of a choice task in BWS, the presentation of frequent monitoring together with a higher risk could be perceived by the respondents as illogical, even if an existing risk requires frequent monitoring. A therapy accepted by patients may depend not only on the type and frequency of monitoring, but also on the expected risks and benefits. Frequent monitoring several times a week with reduced risks could be more acceptable. However, the consideration of interaction effects would require a larger sample.

Conclusion

The study results show that heart failure patients attach the highest importance to the risk of death. Second and third place are the risk of hospitalization and mobility. Patients rate low risk of death and low risk of hospitalization higher than the other attribute levels in the decision context of this study. Higher risks of death and hospitalization would have a significant impact on patients' decisions to choose a treatment alternative. The type and frequency of monitoring is less important.

In a choice simulation, we predicted the demand for therapy alternatives in a given market scenario. The prediction results showed a high market share for a therapy with a low risk of mortality and hospitalization. In addition, therapy benefits from a high improvement in mobility, which ensures a high probability of therapy uptake. BWS offers a practical approach to improving communication between patients and healthcare professionals. Clinical and allocative decision making can be supported, the quality of interpretation of clinical data can be improved over time and therapies can be made more patient-oriented based on the findings.

This will enable more effective and efficient patient care and increase patient benefits. Further analyses are required to detect patient heterogeneity. In addition, it should be analyzed whether and under which circumstances the method of BWS is too burdensome for older heart failure patients and another method such as the classical DCE might be more practicable.

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Conflict of interest

Axel Mühlbacher, Andrew Sadler, Christin Juhnke were employed by GEB mbH and Hochschule Neubrandenburg. GEB mbH received funding from Abbott Medical to conduct the research.

Consent

All individual participants included in the study provided online consent to participate.

Availability of data and material

The datasets generated during and/or analyzed during the current study are not publicly available as no consent was sought from participants to allow sharing of data with third parties

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