

What really matters: a patient-centered instrument to evaluate health-related quality of life in cardiovascular disease

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Aims

Patient-reported outcome measures (PROMs) to assess health-related quality of life (HRQoL) are increasingly used to guide decision-making in cardiovascular care. However, many of the existing PROMs are developed with limited patient involvement and overlook personal health preferences. We aim to develop a cardiovascular disease (CVD)-specific patient-centred preference-based PROM to assess and monitor HRQoL in CVD patients.

Methods and results

A mixed-methods study consisting of several phases was conducted to identify important health items: (i) a scoping literature review, (ii) first- and second-round expert group meetings, (iii) interviews with CVD patients, and (iv) an online survey asking CVD patients to indicate from a large set those health items that are considered the most important. The literature review, expert group meetings, and patient interviews resulted in a list of 55 items potentially important to CVD patients. In total, 666 CVD patients responded to the survey. The following nine items were considered the most important by CVD patients: mobility, activities, self-reliance, fatigue, shortness of breath, chest pain, palpitations, anxiety/worrying, and sexual limitations. An electronic preference-based PROM consisting of these nine items was developed within a cloud-based environment for clinical implementation.

Conclusion

Nine items considered the most important for health by CVD patients were identified and included in a new preference-based patient-centred PROM. This new CVD-specific PROM can be easily implemented using the electronic application and has the potential to improve quality of care for CVD patients.

Keywords

Health-related quality of life • Health outcome • Patient-reported outcome measure • Preference based • Cardiovascular disease • Quality of care

Introduction

Over the past decades, cardiovascular disease (CVD) mortality has declined substantially due to improved treatment strategies.¹ As a consequence, patients face the sequelae of CVD for an extended period of time.¹ Improvement of health status as perceived by patients—often referred to as ‘health-related quality of life’ (HRQoL)—has therefore become increasingly important in the treatment of CVD patients. HRQoL is a multifaceted concept, which

can be defined as an individual’s perceived well-being within the physical, mental, and social domains of health. Evaluation of HRQoL is receiving increasing attention and has the potential to support clinical care by enhancing shared medical decision-making, to evaluate the effects and appropriateness of interventions, and to improve healthcare quality assessment in both clinical research and clinical practice.² Importantly, poor HRQoL was recently reported to independently predict incident CVD events, underlining the importance of HRQoL-based monitoring and treatment.³ HRQoL is generally

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assessed by patient-reported outcomes (PROs). The National Quality Forum defines PROs as 'any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else'. A tool used to report on PROs is commonly known as a PRO measure (PROM). A multitude of PROMs are currently used in the evaluation of HRQoL in CVD, yet a broader inclusion of PROMs as a key measure of cardiovascular health profiling and monitoring in clinical practice and clinical research is needed.^{2,4}

Several systematic reviews reported that frequently used PROMS (e.g. SF-36 and EQ-5D-5L) in current clinical practice are generic; to identify and implement interventions that really have an impact on CVD patients, CVD-specific PROM development is warranted.⁴⁻⁶ One of the main challenges to the development of CVD-specific PROMs lies in the identification of items that should be included to encompass the full range of HRQoL. Most PROMs currently include items deemed important by experts or researchers in the field, and not necessarily the patients. To improve patient-centred decision-making, input from patients in early stages of the development of PROMs is necessary. In addition, each individual experiences and assesses health differently. Current PROMs do not take into account these personal preferences in generating scores used to quantify HRQoL. In this study, we aimed to provide an overview of a broad spectrum of health items potentially important to CVD patients and to identify the health items that are most important for incorporation in a new patient-centred preference-based PROM. An electronic PROM (ePROM) was developed to facilitate the use of innovative preference-based techniques while simultaneously maintaining intuitiveness and comprehensibility.

Methods

A sequential explanatory mixed-methods design was applied to distinguish health items deemed important by CVD patients to incorporate in the new ePROM, consisting of a literature review, expert group meetings, focus group meetings, and an online survey.⁷ This design is characterized by an initial phase of qualitative data collection, a phase of quantitative data collection, and a phase of ePROM development and set-up. The Medical Ethical Committee of the University Medical Center Groningen (UMCG) approved the protocol and waived the need for written informed consent because this research did not fall under the scope of the Medical Research Involving Human Subjects Act (METC 2019/538). The execution of this study complies with the Declaration of Helsinki.

Literature search

A literature search was conducted in PubMed, using the following search terms: health aspects (title) OR quality of life (title) OR health status (title) AND cardiovascular OR cardiac OR cardiology OR heart OR infarction. Articles published until November 2019 were included. Articles were included if (i) the full text was available in English or Dutch; (ii) study participants had CVD and were aged 18 years or older; and (iii) health status in terms of symptoms, functional status, psychological status, or social relationships was investigated by an instrument or questionnaire. Studies were excluded if they were systematic reviews, commentaries, letters to the editor, editorials, or meta-analyses. Each paper was screened for eligibility using the title and abstract first, and

full text second. Instruments and health items were extracted from eligible studies.

First-round expert meetings

Four cardiology experts (D.T., H.E., P.K., and PvdH.) attended the meetings, set up to perform a conceptual evaluation of health items that were collected during phase 1. Health items that were apparently not associated with one of the main domains of the World Health Organization's definition of health (physical, mental, and social well-being) were excluded (e.g. quality of care and spirituality). Next, conceptually overlapping health items were combined and rephrased into single comprehensive health items. Health items relevant for the current study were included in the final analysis. All included items were classified under the higher-order domains 'symptoms', 'emotional', 'social', and 'daily activities'. All included health items were then ordered under subdomains and graphically depicted in a HealthFan diagram (Supplementary material online, *Figure S1*). The HealthFan diagram allows for the creation of a clear and informative overview to improve the practicality of the cognitive task for patients to identify items considered important by them.⁷

Focus-group meetings

Focus-group meetings were initially planned to be held physically in two groups of 8–10 patients suffering from CVD. Unfortunately, physical group meetings could not be held due to the COVID-19 pandemic. To keep patients involved already in the early phases of the development of the instrument, CVD patients were individually interviewed during their in-hospital stay and asked to evaluate the first version of the HealthFan for missing items. The final version of the HealthFan diagram was then created and included in the online survey.

Online HealthFan survey

Patients with a CVD diagnosis were asked to participate in the online survey through telephone call or email. Patients were recruited from the UMCG clinic and from Harteraad (www.harteraad.nl), the largest Dutch patient organization for people with CVD. Data collection took place from April 2020 till November 2020. First, patients were presented a brief introduction to familiarize them with the aims of the research and to provide practical instructions. Then, patients were asked to select the 10 health items from the HealthFan diagram that they deemed most important. Third, patients were asked questions regarding age, gender, and subtype of CVD [e.g. coronary artery disease (CAD), valvular disease] they suffered from. Lastly, patients were able to comment on the survey.

Second-round expert meetings

Three cardiology experts (D.T., H.G., and PvdH.) and one PROM expert (P.K.) attended the second-round expert meetings. The results of the online survey were used as a basis for the discussion during the expert meetings. Frequencies of items considered to be important were analysed for the total population and for subgroups, overall and per health domain, to ensure full coverage of all aspects of HRQoL. Overlapping items were condensed when appropriate. Using this data-driven approach during the second-round expert meetings, nine items were finally identified to be included in the new instrument. Four response categories, ranging from no problems to severe problems, were defined for each of the nine final items. These nine items and the corresponding response categories were incorporated in the ePROM (HealthSnApp: www.chateau-sante.com).

Table 1 Baseline characteristics

Characteristics	Total population (n = 666)	Men (n = 448)	Women (n = 218)	P-value
Age (years), mean \pm SD	66.3 (9.8)	67.7 (9.1)	63.4 (10.6)	<0.001*
Age groups, n (%)				<0.001*
\leq 61	170 (25.5)	90 (20.1)	80 (36.7)	<0.001*
62–68	186 (27.9)	126 (28.1)	60 (27.5)	0.871
69–73	162 (24.3)	117 (26.1)	45 (20.6)	0.122
>73	148 (22.2)	115 (25.7)	33 (15.1)	0.002*
Gender, n (%)				
Male	448 (67.3)	—	—	—
Female	218 (32.7)	—	—	—
Cardiovascular disease, n (%)				0.080
Coronary artery disease	212 (31.8)	153 (34.2)	59 (27.1)	0.065
Heart failure	121 (18.2)	82 (18.3)	39 (17.9)	0.897
Congenital heart disease	37 (5.6)	18 (4.0)	19 (8.7)	0.013*
Cardiac arrhythmia	103 (15.5)	70 (15.6)	33 (15.1)	0.870
Valvular heart disease	35 (5.3)	20 (4.5)	15 (6.9)	0.190
Others/unknown	158 (23.7)	105 (23.4)	53 (24.3)	0.803

* P-value below the statistical significance threshold of 0.05.
SD, standard deviation.

Statistical analysis

Proportions and the 95% confidence intervals (95% CIs) of the number of participants out of all choosing an item in their top 10 were calculated and compared between subgroups of gender, age, and CVD subtype by χ^2 tests. Baseline characteristics were reported as means [\pm standard deviation (SD)] for continuous normally distributed variables, median (interquartile range) for non-normally distributed variables, and frequencies (%) for categorical variables, and compared between subgroups based on age and gender using independent t-tests, Mann–Whitney U-tests, or χ^2 tests, where appropriate. Data were analysed using STATA (version 16.1, StataCorp LCC, College Station, USA) and R (version 4.0.5, the R Foundation for Statistical Computing, Vienna, Austria).

Results

Literature search

In total, 33 PROMs were identified (Supplementary material online, Figure S2). The most used PROMs were the SF-36, Minnesota Living with Heart Failure Questionnaire (MLHFQ), and EQ-5D (Supplementary material online, Figure S3). In total, 491 health items with observable characteristics were extracted from these 33 instruments.

First-round expert meetings

First, 19 of the 491 identified items were excluded because these were not related to one of the domains of health as set out by the World Health Organization. Next, overlapping items were combined into single comprehensive items. After reaching consensus during the expert meetings, 54 items were included in further analysis. With these items, a first version of the HealthFan was created. Items were classified under the higher-order domains symptoms, emotional, social, and daily activities. Each domain was divided

into subdomains (11 subdomains in total) to improve clarity and overview in the next steps: ‘symptoms’ was subdivided into pain, change of weight, and other complaints; ‘emotional’ into feelings and control over life; ‘social’ into social relationships and sexuality; and ‘daily activities’ into personal care, mobility, hobbies, and activities.

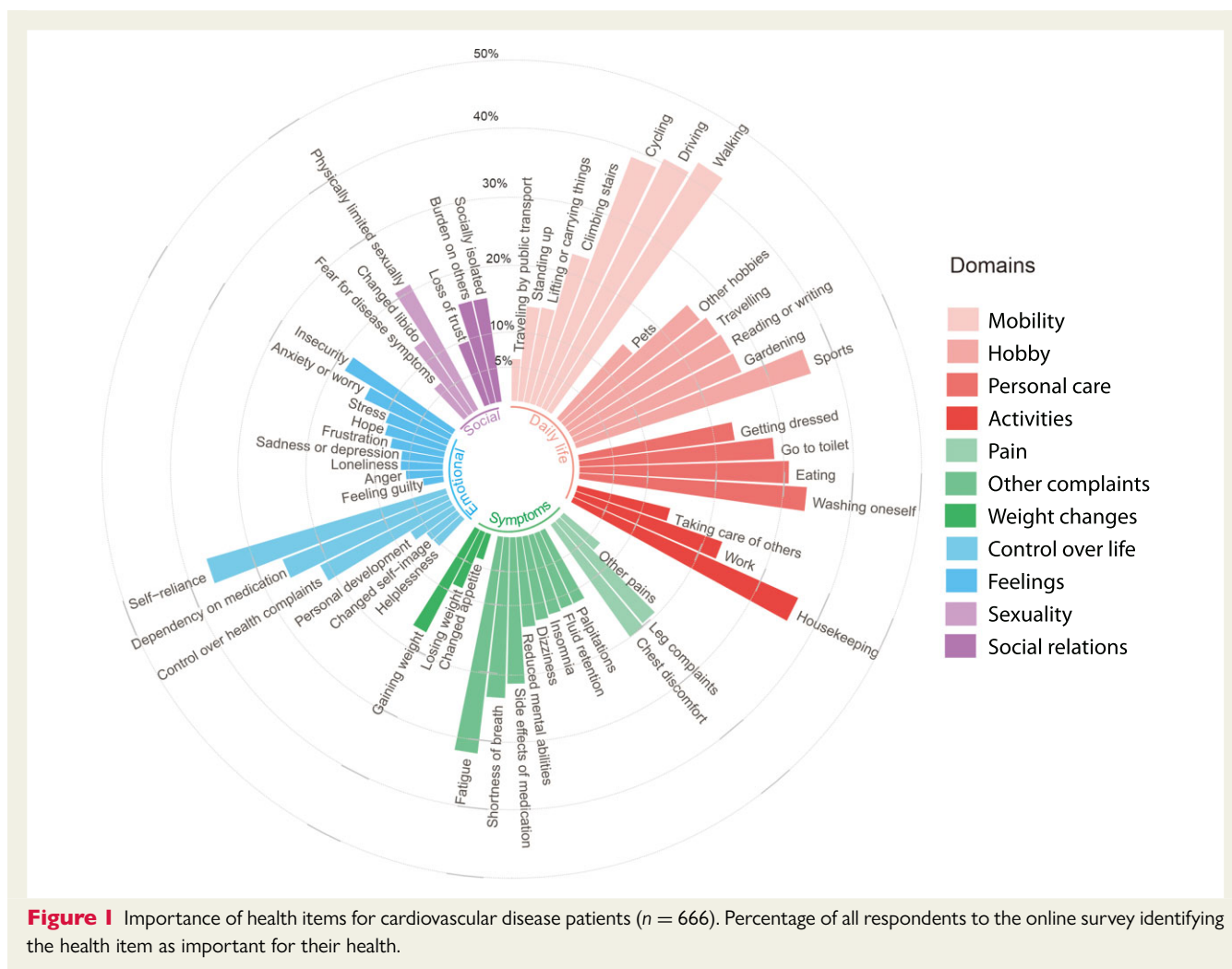
Focus-group meetings

In total, 15 random CVD patients were approached during their in-hospital stay and asked to evaluate the first version of the HealthFan for missing items. Of the 15 patients, 10 were willing to participate. One health item (‘other hobbies’) was included in the final version of the HealthFan by input from the CVD patients. The final version of the HealthFan consisted of 55 items in total (Supplementary material online, Figure S1).

Online HealthFan survey

In the Harteraad and UMCG clinic population, 419 out of 2600 individuals and 247 out of 1283 individuals responded to the invitation and completed the survey, respectively (Supplementary material online, Figure S4). In total, 666 CVD patients completed the online survey. The respondents had a mean age of 66.3 ± 9.8 years and 32.7% were female (Table 1). The most prevalent cardiovascular diagnosis was CAD (men: 34%; women: 27%).

The proportion of respondents choosing an item in their top 10 most important is presented in Figure 1. The items considered the most important overall were walking (43%, 95% CI: 39–46%), driving a car (41%, 95% CI: 37–44%), cycling (39%, 95% CI: 35–43%), independence (37%, 95% CI: 33–40%), housekeeping (36%, 95% CI: 32–40%), sports (36%, 95% CI: 32–40%), washing oneself (33%, 95% CI: 30–37%), fatigue (32%, 95% CI: 28–36%), eating (31%, 95% CI: 27–34%), and going to the toilet (29%, 95% CI: 25–32%).

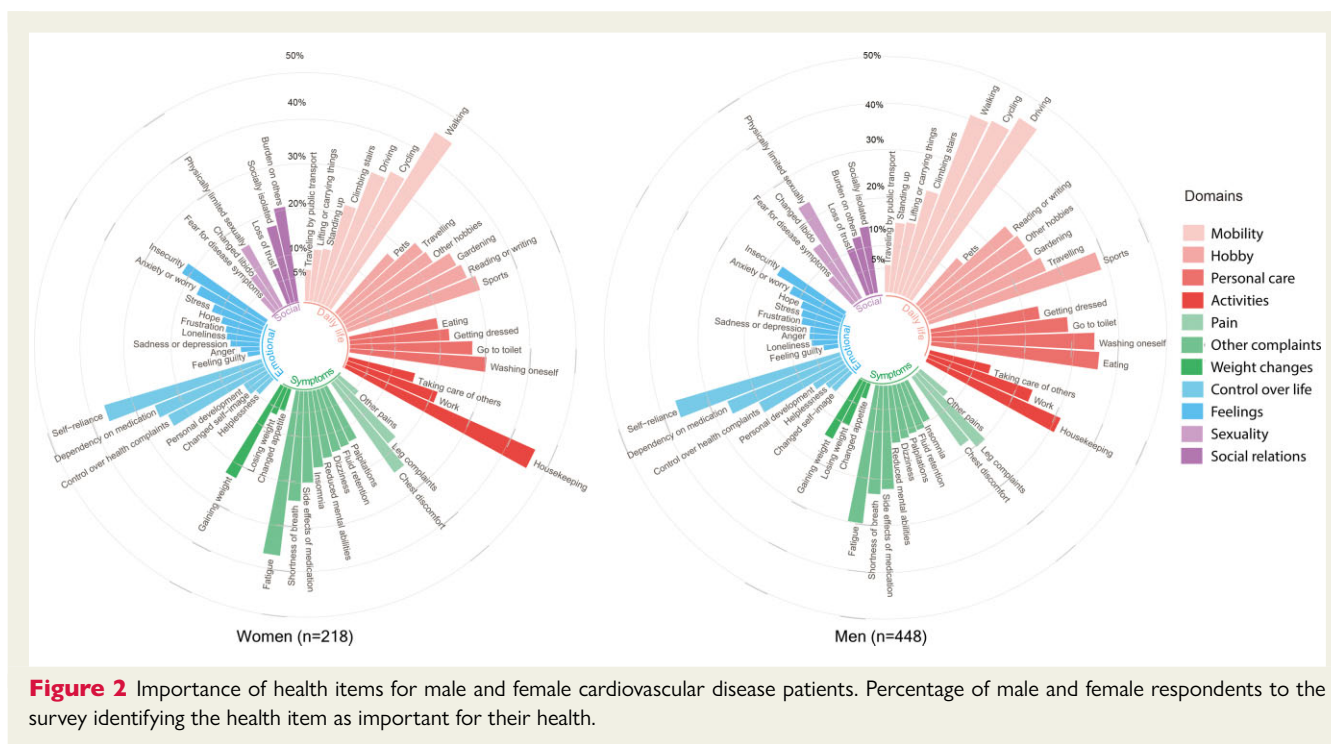


Significant differences in proportion of respondents considering an item important were observed between men and women for several items (Figure 2). Women more frequently considered housekeeping [women: 46% (95% CI: 29–53%); men: 31% (27–36%), $P < 0.001$], gaining weight [women: 23% (95% CI: 17–29%); men: 14% (95% CI: 11–17%), $P = 0.004$], burden on others [women: 21% (95% CI: 16–27%); men: 13% (95% CI: 9–17%), $P = 0.004$], and insomnia [women: 17% (95% CI: 12–22%); men: 10% (95% CI: 7–12%), $P = 0.006$] important compared with men. On the other hand, men considered driving a car [women: 31% (95% CI: 25–37%); men: 45% (95% CI: 41–50%), $P = 0.001$], cycling [women: 33% (95% CI 27–39%); men: 42% (95% CI: 37–47%), $P = 0.027$], sports [women: 31% (95% CI: 25–37%); men: 39% (95% CI: 34–43%), $P = 0.047$], eating [women: 20% (95% CI: 14–25%); men: 36% (95% CI: 32–40%), $P < 0.001$], and physical limitation in sexual activity [women: 16% (95% CI: 11–21%); men: 23% (95% CI: 20–27%), $P = 0.019$] more important compared with women.

Significant differences in the proportion of respondents considering an item important were also observed among those aged younger and older than 68 years (Supplementary material online, Figure S5) and those with different CVD subtypes for several items (Supplementary material online, Figure S6).

Second-round expert meetings

The 25 items considered most important by CVD patients and differences per subgroup of age and CVD diagnosis were evaluated during the second-round expert meeting. The three most chosen items—walking, driving, and cycling—were combined into a single item: ‘mobility’. Independence was considered very important and overlapped with several other items that were frequently chosen, such as washing oneself, going to the toilet, and dependence on medication. Therefore, an overarching single item ‘self-reliance’ covering all these aspects was included. Next, several activities—e.g. housekeeping, sports, and gardening—were frequently chosen and therefore combined in the item ‘activities’. Physical limitation in sexual activities together with changed libido was considered very important, especially by men, and were therefore condensed in a single item: ‘sexual limitations’. In the emotional domain, insecurity, anxiety/worrying, and stress were most frequently chosen and together formed a very important factor. During the expert meeting, consensus was reached that anxiety or fear for disease manifestations and worry about health are very important in treatment of CVD, e.g. relief of fear (for chest complaints or a heart attack) after revascularization of CAD. Therefore, ‘anxiety/worrying’ was included as a separate item in the instrument with a



clear explanation of the meaning of this item (anxiety or worrying in relation to CVD manifestations). In the domain of symptoms, 'fatigue' and 'shortness of breath' were considered very important and therefore included as separate items in the final instrument. Since the aim was to develop a CVD-specific PROM that could be used in all CVD patients, 'chest pain' and 'palpitations', which were among the most frequently chosen aspects by CAD and cardiac arrhythmia patients, respectively, completed the set of nine final items that were incorporated in the ePROM (Figure 3). Importantly, the individual health items on which overarching items included in the ePROM were based are mentioned in a comment available to users under the 'i-icon'. This icon clarifies the items in the ePROM to enhance full coverage of health items for all users.

Discussion

This study provides data on what CVD patients find most important for their health. In addition, it reports on the development of a novel patient-centred preference-based ePROM to quantify HRQoL in patients suffering from CVD, in which patients were involved throughout the whole process of the development. We identified nine health items deemed most important by CVD patients (i.e. mobility, activities, self-reliance, fatigue, shortness of breath, chest pain, palpitations, anxiety/worrying, and sexual limitations) and incorporated these items in a new CVD-specific ePROM that is promising to improve shared decision-making, quality monitoring, performance measurement, and policymaking in CVD care.

Generic PROMs such as EQ-5D-5L and SF-36 are frequently used to assess the HRQoL of CVD patients because they can be applied to a broad population and comparisons can be made across differ-

ent diseases. However, PROMs assessing generic items might not be accurate enough to assess modification of CVD-specific manifestations by certain treatments.⁴⁻⁶ Disease-specific PROMs such as the Seattle Angina Questionnaire assess the frequency and severity of complaints or limitations. However, each complaint or limitation has its own impact on HRQoL, depending on individual preferences. This aspect of HRQoL is neglected in the calculation of conventional summed PROM scores. Furthermore, most PROMs currently used in clinical practice and research are developed without significant patient input.⁸ PROMs developed without decent patient input may not be fitted to assess what is considered most important by CVD patients. In the setting of routine clinical care, currently the opportunity is therefore missed to improve patient monitoring and shared decision-making guided by (e)PROMs. In clinical research, HRQoL assessment by generic PROMs that do not actually measure what patients find important might result in false negative outcomes of clinical trials investigating new treatments for CVD. Clinical trials predominantly evaluate rates of composite hard endpoints with equally weighed components to report the effectiveness of interventions. Interpretation and clinical relevance of these composite endpoints could be limited and the use of other endpoints has been suggested.⁹ Importantly, patients value the importance of the outcomes of certain events differently from clinicians and researchers.^{10,11} Patient-centred endpoints truly reflect clinical relevance and could improve endpoint evaluation in clinical trials. We used a broad, data-driven approach to identify health items deemed most important for health by CVD patients themselves for incorporation in a new CVD-specific PROM, to really measure outcomes that are clinically relevant to the CVD patient.

By applying an innovative preference-based valuation model, this PROM was not only developed with patient input, but also takes

Task 1

Click on the bars to choose the description that best matches your health today.

A little tired

No problems with moving around

Not worried

Self-reliant

Some problems with activities

No shortness of breath

Some sexual limitations

Some chest pain

No palpitations

NEXT

Not tired
A little tired
Quite tired
Very tired

No problems with moving around
Some problems with moving around
Moderate problems with moving around
Severe problems with moving around

Not worried
Slightly worried
Worried
Highly worried

Self-reliant
Somewhat dependent
Largely dependent
Fully dependent

No problems with activities
Some problems with activities
Moderate problems with activities
Severe problems with activities

No shortness of breath
Some shortness of breath
Moderate shortness of breath
Severe shortness of breath

No sexual limitations
Some sexual limitations
Moderate sexual limitations
Severe sexual limitations

No chest pain
Some chest pain
Moderate chest pain
Severe chest pain

No palpitations
Some palpitations
Moderate palpitations
Severe palpitations

Figure 3 The nine items and their response categories incorporated in the novel cardiovascular-disease-specific electronic patient-reported outcome measure. A screenshot of the electronic patient-reported outcome measure (HealthSnApp), consisting of the nine items considered most important by cardiovascular disease patients.

into account personal health preferences to assess quality of life. In current PROMs, levels of impairment are often assumed to lie on a scale (e.g. from 0 to 5) with equal increments between the levels of the items and equal weights for the health domains. However, each level of impairment and each health domain affected may have a specific impact on HRQoL, determined by patient preferences. The ePROM developed here applies a novel preference-based measurement approach: the multiattribute preference response model, which is based on the Rasch model.^{12,13} Users (i.e. CVD patients) are expected to value their health on each of the nine items included in the ePROM (task 1). This is the descriptive or classification part of the assessment. Then, users are asked to indicate multiple times which item with a particular severity or level disturbs them the most (task 2). In the application, users can 'drop down' a level of an item, moving it to one level better by swiping. By repeating task 2 several times, ranked hypothetical health states are indicated by the user. Specific weights (coefficients) can then be estimated for each level of the items using a rank-ordered logistic regression model. The specific weights of each level are used to quantify HRQoL and guarantee consideration of individual health preferences of CVD patients in HRQoL quantification. Because task 2 is simply a preference ranking

within the patient's own health status, the assessment is rather easy to fulfil and can be accomplished quickly. Importantly, weights can be updated regularly due to the option to store responses in the cloud and to build a database, in order to update weights for HRQoL quantification. By taking into account the user's preferences, this method is less susceptible to various biases than the conventional methods to measure HRQoL.¹²

Comparable ePROMs based on a similar methodology have been recently applied to parents of 0–1-year-old infants, patients suffering from chronic pain, and transplant recipients.^{7,14,15} Shahabeddin Parizi *et al.* proved that this methodology reliably quantifies HRQoL.¹⁶ This CVD-specific ePROM can therefore already be used to monitor HRQoL in CVD patients and evaluate the impact interventions have on CVD patients in routine clinical care. This novel ePROM is able to improve the current suboptimal physician-centred way to assess outcomes, which is essential to allow CVD care to keep up with the more patient-centred approach promoted by patient organizations, clinicians, health policymakers, and insurance companies. To allow for further clinical testing to enhance clinical implementation, it is of the utmost importance to disseminate this novel ePROM to other researchers.

Some limitations of our study should be acknowledged. Unfortunately, focus-group meetings with CVD patients to identify missing items in the initial HealthFan could not be held due to the COVID-19 pandemic outbreak. Interviews were held to keep patients involved already in the early phases of development. Patients who independently assessed the completeness of the overview of health items did come up with an additional item to include, indicating critical appraisal by these patients. There was an over-representation of men in our study population. However, this is in line with other studies investigating the relationship between patient characteristics and HRQoL in CVD patients¹⁷ and is representative of the target population. The frequencies of items selected by CVD patients in our study are point estimates. Some uncertainty about the exact order and importance of the items remains. However, we observed same patterns among Harteraad and UMCG clinic patient populations, indicating that the findings are similar among different CVD populations and are therefore robust.

Conclusions

Nine health items considered most important by CVD patients in relationship to their health were identified by a scoping literature search, patient interviews, expert group meetings, and an online survey. A new ePROM, consisting of these nine health items and incorporating novel methods that take into account personal health preferences to assess HRQoL, was developed. This new patient-specific preference-based ePROM has the potential to improve HRQoL assessment in clinical research and routine care. Future studies should prove whether this ePROM is an improvement over current PROMs.

Supplementary material

Supplementary material is available at *European Heart Journal—Quality of Care and Clinical Outcomes* online.

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Conflict of interest: P.F.M.K. is the CEO of Château Santé. As an extension of the measurement model presented in this paper, additional measurement models, tools and instruments are developed by P.F.M.K. as part of academic/commercial activities. The other authors declare no conflict of interest relevant to this article.

Author contributions

D.T.: conceptualization; data curation; formal analysis; investigation; project administration; visualization; writing—original draft;

writing—review and editing. T.K.S.: data curation; formal analysis; investigation; project administration; visualization; writing—original draft; writing—review and editing. X.Z.: visualization; writing—review and editing. D.v.V.: writing—review and editing. I.S.: project administration; writing—review and editing. H.E.G.: conceptualization; investigation; project administration; writing—review and editing. P.F.M.K.: conceptualization; methodology; project administration; resources; software; supervision; writing—review and editing. P.vd.H.: conceptualization; funding acquisition; project administration; resources; supervision; writing—review and editing.

Data availability

Data requests should be submitted to the principal investigator (P.vd.H.) for consideration. We aim to share data to the maximum extent, but within specific boundaries relating to ethical approval, contractual and legal obligations of this study, and publication timelines. All proposals will be reviewed for their scientific merit by the trial management group. Only data relevant to the purpose of the data request will be provided.

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