

ORIGINAL ARTICLE

Health items with a novel patient-centered approach provided information for preference-based transplant outcome measure

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Abstract

Objectives: Patient-reported outcome measures (PROMs) are widely applied to assess perceived health status. To date, no transplant-specific PROM is available for generating a single, standardized score regarding the health status of transplant recipients. The objective of this study is to generate health items for a new patient-centered PROM for organ recipients: the Transplant PROM (TXP).

Study Design and Setting: A five-phase, mixed-method approach was applied to identify and select the health items: scoping literature review, expert meetings, focus-group meetings with organ recipients, a special judgmental task within an online survey, and expert meetings for final selection of health items.

Results: Based on a previously published scoping literature review, a first round of expert meetings, and a total of four focus-group meetings with kidney, lung, and liver transplant recipients ($N = 18$), a list of 83 relevant health items relating to post-transplant life was selected. In an online survey, 183 transplant recipients selected the 10 most important health items from this list. After evaluating the frequency of selected health items and combining items that assess closely related or similar concepts in the second round of expert meetings, nine health items were chosen to be included in TXP: fatigue, skin, worry/anxiety, self-reliance, activities, weight, sexuality, stooling, and memory/concentration.

Conclusion: The nine TXP health items reflect the most prominent issues transplant recipients experience. The TXP can be administered by means of a mobile phone app. © 2020 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

Keywords: Patient-reported outcome measure; Health-related quality of life; Patient-centered; Preference-based; Health item; Transplant

1. Introduction

Over the last 3 decades, the transplantation of solid organs (i.e., heart, lung, liver, kidney, and pancreas) has become the standard of care for end-stage organ failure [1]. Advances in surgical techniques and post-transplant medical therapies have improved the lifespan of all organ

recipients [2]. The lifelong immunosuppressive therapies applied in post-transplant care are nevertheless associated with complications (e.g., diabetes, arterial hypertension, osteoporosis, and psychological impairments), which can have adverse effects on the actual (or perceived) health status—often denoted by the term health-related quality of life (HRQOL)—of solid-organ transplant recipients [3,4]. Improvements in clinical outcomes and post-transplant survival time have therefore increased the urgency of gaining insight into the HRQOL of patients after transplant [5].

The multidimensional concept of HRQOL can be defined as an individual's perceived well-being within the physical, mental, and social domains of health [6]. Increasing attention is being paid to the evaluation of

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What is new?

Key findings

- We identified and selected health items for a new transplant-specific PROM (TXP) by applying a fully patient-centered approach.

What this adds to what was known?

- Health items of existing transplant-specific PROMs were identified mainly by experts, without any patient involvement. TXP's health items are derived by a fully patient-centered approach.
- The study identified the nine most prominent health issues that transplant recipients experience.

What are the implications and what should change now?

- TXP is a new transplant-specific PROM applied by means of a mobile app which provides transplant recipients, clinicians, and researchers with a convenient tool for measuring and monitoring the overall trend of HRQOL during the post-transplant period. It adds important information to the data that is traditionally collected during post-transplant care.
- Further work will entail an investigation of the practical issues that arise in the implementation of the TXP within clinical practice and in the interpretation of the results.

HRQOL in both clinical research and patient-care services [7]. The investigation of HRQOL is particularly important in the transplant setting, given that a substantial proportion of candidates and recipients are concerned about their HRQOL [8,9].

HRQOL is commonly assessed in terms of patient-reported outcomes (PROs). The National Quality Forum of the United States defined PROs as “any report of the status of a patient's (or person's) health condition, health behavior, or experience with healthcare that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else.” The term PRO encompasses a broad spectrum of outcomes that include the symptoms of a disease or the side effects of a treatment (e.g., immunosuppressant), functions (e.g., social and physical activities or cognitive functioning), and multidimensional constructs, including HRQOL. The tools to assess PROs are referred to as PRO measures (PROMs) [10]. PROMs may be taken as measurements for clinical research or program evaluation: they could be used on a one-time basis to provide a functional and psychosocial profile of individual patients; or they might be applied sequentially to

monitor patients [6,10–12]. The application of PROMs could potentially enhance care management by helping healthcare providers to understand the impact of specific treatments on the lives of patients beyond whether specific clinical values are within a given range. This could enhance patient-doctor communication and increase patient engagement in the course of treatment, thus ultimately resulting in higher patient satisfaction and better outcomes [13]. Recent reviews of the use of PROMs in studies on solid-organ transplantation have indicated that most of the PROMs in current use (e.g., the 36-item Short Form Survey [SF-36] and the EQ-5D) are generic, with only a few being specifically related to transplant [14–17]. Another issue is that the contents (i.e., items, questions, attributes) of these PROMs were derived mainly by experts, and many years ago, without any patient involvement. However, there is now a shift toward a patient-centered approach that emphasizes patient involvement and advocacy. Most of these literature reviews emphasize the necessity of developing a distinctive, patient-centered, transplant-specific PROM.

One of the most challenging tasks in the development of such a PROM is to determine which set of health items should be incorporated to capture the full range of health issues. Health items refer to single components of an individual's health state. A health item corresponds to one specific area of health functioning that usually ranges from normal to severely limited. When several health items are combined into a PROM, they describe a unique health state [18–20]. Face and content validity are crucial to the development of an HRQOL PROM, yet these are seldom evaluated. We aimed to generate health items for a short, patient-centered, preference-based, transplant-specific PROM (TXP) focusing on HRQOL. A typical feature of preference-based measurement is that all relevant characteristics of the object of study have to be evaluated together. Therefore, there is a cognitive constraint on the number of items that may be included in a description of a health status. In general, people can discriminate $7 (\pm 2)$ pieces of information at a time, and so most preference-based studies usually present no more than nine items [21]. That is probably the maximum amount of information people can process simultaneously [22].

Our aim is to develop a short, easily comprehensible preference-based PROM that can be integrated into routine care in a meaningful way while posing a minimal burden on patients and care providers. In the present study, we report on the procedure to identify and select the health items for such a PROM. We explain our novel methodology based on focus-group meetings and a special online survey conducted among transplant recipients.

2. Methods

A mixed-methods design [23] consisting of 5 sequential phases was applied to ensure the coverage of existing

PROMs and patient preferences. This mixed-methods design is characterized by an initial phase of qualitative data collection and analysis based on a scoping literature review (phase 1), followed by expert meetings (phase 2), focus-group meetings (phase 3), quantitative data collection and analysis using an online HealthFan survey (phase 4), and a second round of expert meetings for the final selection of health items to be included in the PROM (phase 5, [Figure 1](#)). The search strategy and the results of the scoping literature review (phase 1) to identify all already available PROMs that have been applied to assess quality of life, health status, or HRQOL in adult solid-organ transplant recipients have been described previously [14]. The four subsequent phases are described in the present study, the methods of which are sequentially described below.

2.1. Phase 2: first round of PROMs expert meetings

Meetings were held with four experts (E.B., S.B., P.K., K.V.) for the purpose of performing a conceptual evaluation of health items that had been collected in an earlier study (phase 1) [14]. In line with the World Health Organization's description of health as a state of complete physical, mental, and social well-being, items that were apparently not connected to one of the three major domains of health (e.g., financial matters, quality of care, adherence to medications) were excluded. As the next step, conceptually overlapping items were combined and phrased as single items. Finally, all relevant health items were selected for inclusion in the inventory.

Analytical presentations ultimately depend on the quality, relevance, and integrity of their content. In our

substantive consideration of the content of the health items, we followed a content-driven analytical design. Each of the health items that were included was categorized into one of three main health domains (physical, social, and mental functioning). The items were graphically depicted in a HealthFan [14,24]: a systematic approach that assembles related health items within subdomains. A HealthFan makes it possible to present large sets of health items to patients in a clear, informative diagram and is intended to make the cognitive task easier [25].

2.2. Phase 3: focus-group meetings

Focus-group meetings were held with transplant recipients. They were recruited at the University Medical Center Groningen (UMCG) in the Netherlands between May and June 2018. We received a waiver from the Medical Ethics Review Board of the UMCG, indicating that the study was not subject to the Dutch legislation on Medical Research Involving Human Subjects Act (METc 2017/648). Patients were invited to participate by their physicians. Exclusion criteria included inability to speak the Dutch language, impaired cognition, and unwillingness to grant informed consent. There is no guideline for the number of participants in focus-group studies [26,27]. Based on experience with previous studies, groups with the size of minimum 4 to maximum 12 people are most informative. We included a heterogeneous sample of adult solid-organ recipients to represent the post-transplant population in terms of gender and age and time since transplantation. Separate meetings were held for liver, kidney, and lung recipients. Each focus-group meeting lasted approximately 2 hours (with a short coffee break) and was held in a comfortable conversation room in the hospital [28]. The focus-group meetings were moderated by an experienced focus-group leader (K.V. or V.H.) with a background in health outcome studies. Another researcher (V.H. or C.A.) attended the meetings as an observer, in order to create an overview of the statements expressed in the meeting on a flip chart. This overview was used to stimulate discussion and generate as much feedback as possible.

Before the meetings started, signed consent forms were obtained from the participants. Each meeting started with a brief round of introductions. The audio recording was not started until after the introductions to ensure that the names of the participants were not recorded.

The moderator of the focus-group meeting followed an interview guide during the session to ensure that all of the topics were discussed ([Table 1](#)). The meetings continued until we reached saturation, which means that no new data/topics were brought into the discussion [29]. Finally, the HealthFan containing the health items that had been extracted during phase 2 were presented to the participants, who were asked to add any items that they missed in the inventory. The participants were also asked

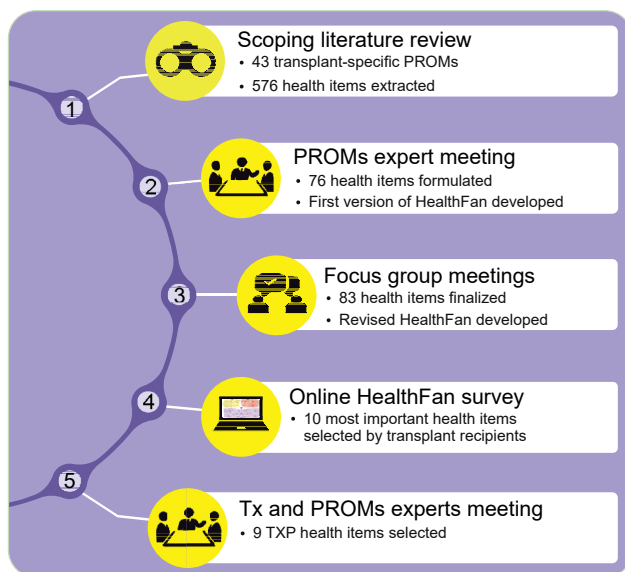


Fig. 1. Five phases of the mixed-methods design for the selection of TXP health items. The first phase has been described elsewhere [14]. The other phases, phases 2 to 5, are described in the present study. PROMs, patient-reported outcome measures; TXP, Transplant PROM.

Table 1. Focus-group meetings guiding open-ended items from the interview guide

Area	
Before transplantation	Please describe your health during the period in which you had end-stage organ disease, before you received the transplant.
Shortly after transplantation	How did your life change shortly after the transplant, as compared to the period when you were on the waiting list?
Current situation	Which health issues are important to you at this moment, including with regard to perspectives on matters relating to your health that have emerged since the transplant?
Future	Are there any other health issues that have not yet been mentioned that you expect to become important in the future?
General	Follow-up questions were formulated in each step (e.g., “What is your opinion about this?” and “Would you like to add something that has not been discussed?”).

to select the 10 health items from the HealthFan they deemed most important regarding their own health state. Based on the results of these focus-group meetings, we developed a revised version of the HealthFan for the online survey with a larger group of solid-organ recipients.

2.3. Phase 4: online HealthFan survey

Transplant recipients were invited to take part in an online survey. Data were collected from December 2018 through February 2019. The link to the survey was sent by email to 207 patients who had received transplants at the UMCG. It was also advertised on the websites of five organizations representing solid-organ transplant recipients in the Netherlands. The online survey opened with a brief introduction to the topic to familiarize respondents with the aims of research. First, they were asked to indicate their gender, age, time since transplant, and type of transplantation. Second, participants were asked to complete the Dutch version of the EQ-5D-5L instrument as a generic measure of HRQOL [30]. Third, they were asked to select the 10 health items from the second version of the HealthFan (Figure 2) that were most important to them. They were further asked to add any health items that they missed in the survey. The survey continued with two feasibility statements regarding the clarity and difficulty of the HealthFan task. At the end, respondents had the opportunity to comment on the survey.

2.4. Phase 5: second round of expert PROM meetings and final selection of health items

Meetings were held with three clinical transplant experts (S.B., H.B., W.B.) and 2 PROM experts (P.K. and K.V.) in order to select the relevant health items for the TXP. The discussions in these expert meetings were based on the results of the survey. The frequency distributions (see below) for the entire group and for the subgroups based on specific transplanted organs were analyzed separately. If several items within a similar concept (e.g., energy, fatigue, and loss of strength) from one subdomain were chosen frequently by the respondents, the overlapping items were condensed when considered appropriate and logical. To ensure a complete coverage of the range of health, items

from various subdomains were included in the final list. The final items were operationalized into questionnaire items with response categories, which were formulated in lay language.

2.5. Data analysis

Frequency distributions (proportions) were computed to determine the importance of the attributes. Data from subgroups of the transplant recipients were used to create graphs based on gender and transplanted organ. All data were analyzed using SPSS (IBM SPSS Statistics for Windows, version 23.0; IBM Corp, Armonk, NY). The graphs were created with R (ggplot2 package), working within R Studio and CorelDraw v.19 (Corel Corporation, Ottawa, Canada).

3. Results

3.1. Phase 2: first round of expert meetings

The scoping literature review performed for phase 1 of the five phases of which the development of this new patient-centered PROM for organ recipients consists was published previously [14]. Of the 287 health items identified during the scoping literature review, 40 were excluded during the expert meetings performed for phase 2, because their scope was not consistent with the World Health Organization's definition of health. After overlapping items (e.g., taste and smell) were combined and nonrelevant items were eliminated in the expert meetings, 78 distinct health items grouped in 16 subdomains were selected for the first version of the HealthFan. The items in the physical domain were subdivided into the following categories: belly, body heat, chest, eating, energy, pain, physical aspects, respiration, and skin. The items in the social domain were subdivided into activities, autonomy, and relationships. The items in the mental domain were subdivided into cognition, feelings, and worries [14].

3.2. Phase 3: focus-group meetings

Of the approximately 80 transplant recipients who were approached, 25 expressed interest in participating in the

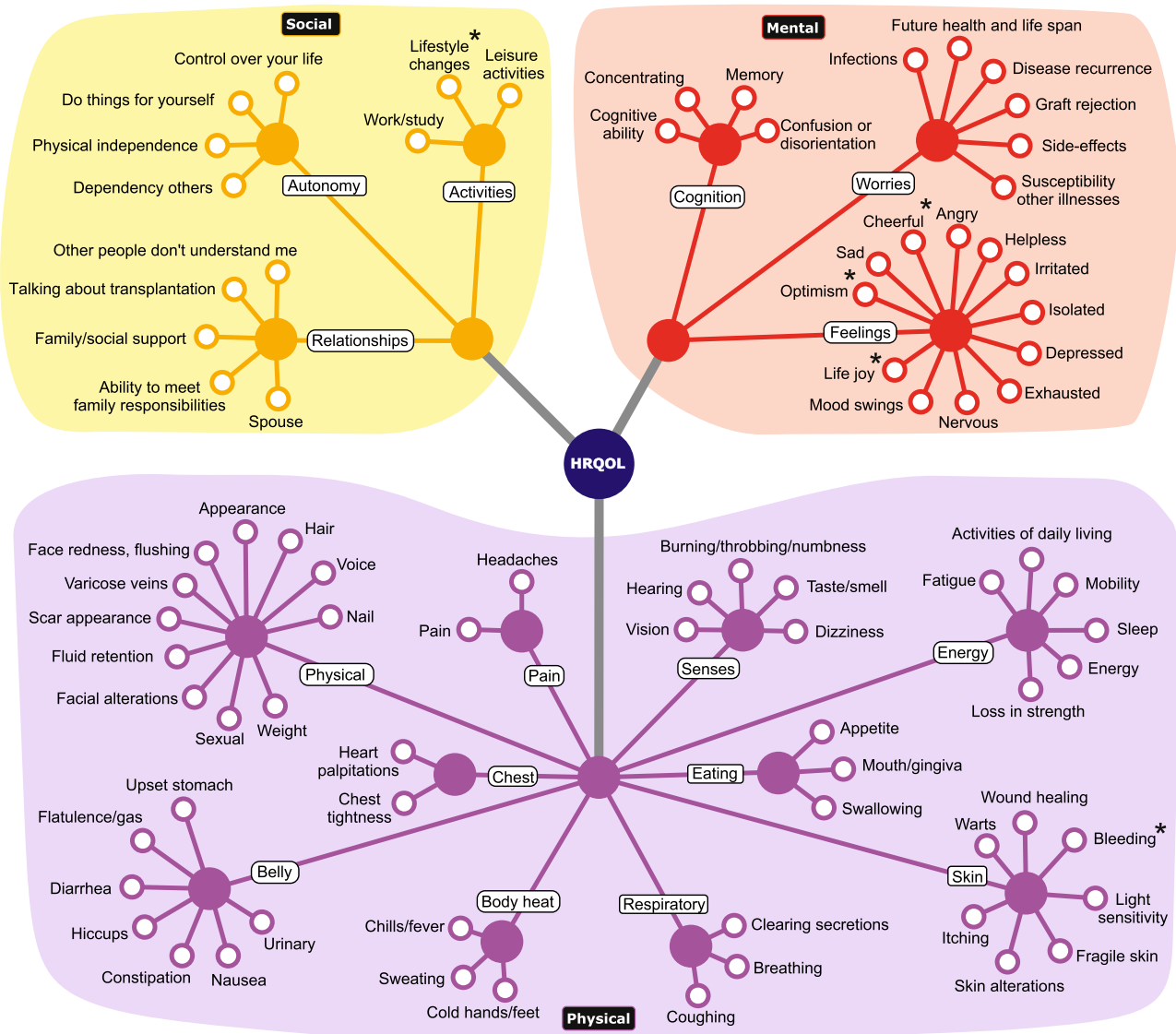


Fig. 2. Health items extracted based on the literature search, organized into physical, mental, and social domains (HealthFan), as presented to transplant recipients in the focus-group meetings and online survey. (* Items added to the HealthFan after the focus-group meetings)

focus-group meetings, and 18 were available on the planned dates and times. The meetings were organized by organ type. The study population consisted of kidney, liver, and lung recipients ranging in age from 24 to 73 years, with a history of organ transplantation ranging from 6 months to 22 years (Table 2). The health items that the transplant recipients mentioned most frequently during the focus-group meetings were lack of energy, adverse side effects of immunosuppressant drugs, and skin problems. One of the lung recipients mentioned three items that had not been identified in the literature search: joy in life, cheerfulness, and optimism. Two transplant recipients also identified lifestyle changes as an important health item. In the group of kidney recipients, excessive bleeding from surgical wounds was mentioned as an additional health item. No new health items were mentioned by the liver recipients.

3.3. Phase 4: online HealthFan survey

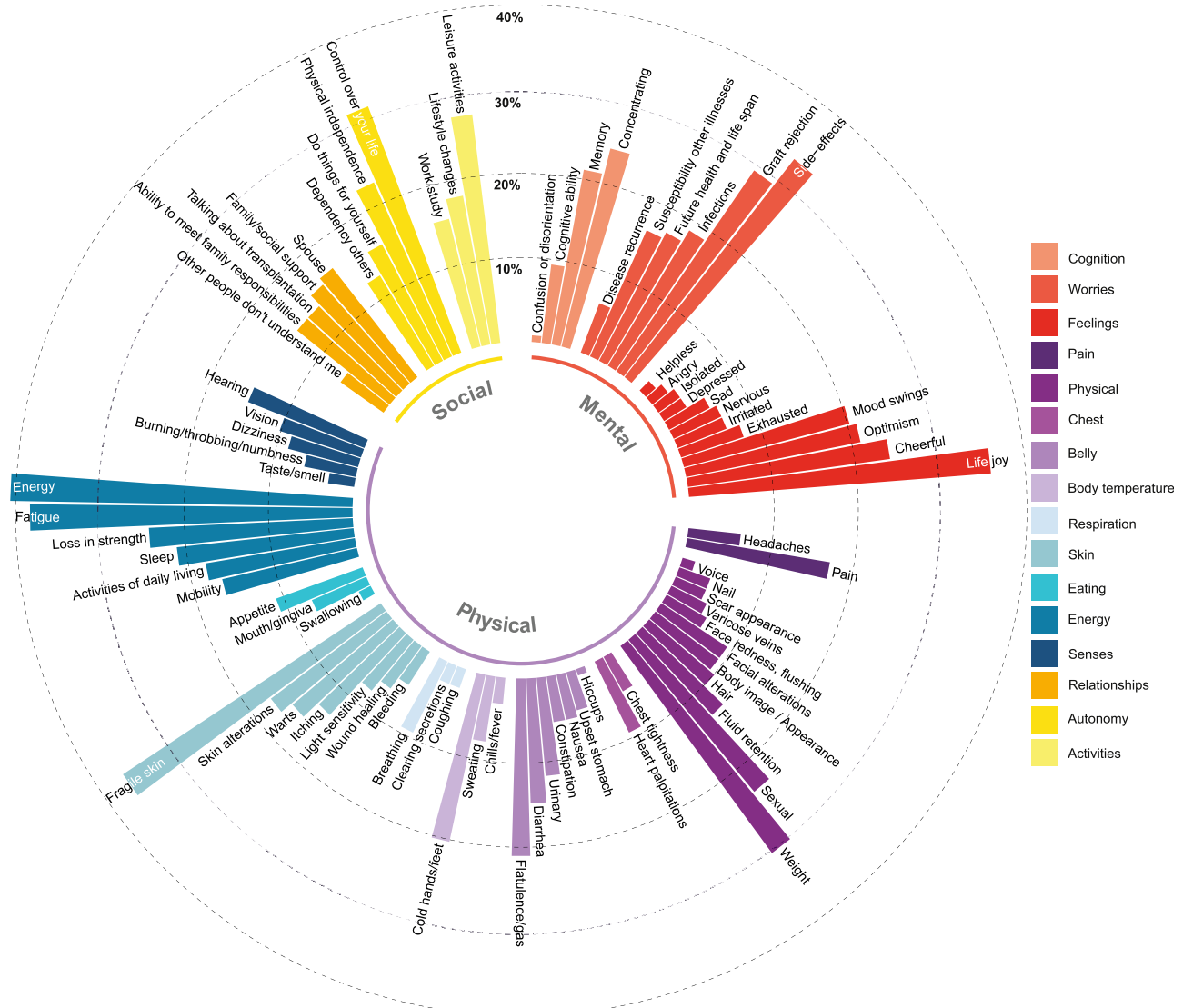
In all, 176 Dutch transplant recipients completed the online survey. Of these respondents, 26 were excluded because they had not completed any part of the survey. The respondents consisted of 97 men and 53 women (Table 2). Another 22 respondents had not selected any health items. The health items analysis was thus ultimately based on data from 128 respondents. Although 38 respondents selected more than 10 items (11–31 items) and 27 respondents selected fewer than 10 items, they were still included in the analysis.

The proportion of respondents indicating which item was important to their health was calculated (Figure 3). The 10 health items that were most frequently identified as most important were energy (41%), fatigue, fragile skin,

Table 2. Characteristics of participants in the focus-group meetings and online survey, stratified by transplanted organ

Characteristics	Liver	Lung	Kidney	Heart
Focus-group meeting (<i>N</i> = 18)				
<i>N</i>	7	4	7	N/A
Male, <i>n</i> (%)	3 (43)	2 (50)	5 (71)	N/A
Age in years, median (range)	52 (28–71)	63 (24–70)	54 (26–73)	N/A
Currently unemployed, <i>n</i> (%)	3 (43)	2 (50)	2 (29)	N/A
Time since transplant in years, median (range)	4 (0.5–17)	3.5 (0.6–12)	9 (4–22)	N/A
Online survey (<i>N</i> = 150)				
<i>N</i>	12	20	91	27
Male, <i>n</i> (%)	8 (67)	14 (70)	55 (60)	20 (74)
Age in years, median (range)	54 (18–84)	64 (25–71)	58 (18–80)	63 (26–79)
Currently unemployed, <i>n</i> (%)	5 (42)	6 (30)	21 (23)	11 (41)
Time since transplant in years, median (range)	11.5 (0.3–33)	6 (0.5–30)	8 (1–34)	11 (1–34)

N/A, not available.

**Fig. 3.** Proportion of respondents to the online survey identifying the item in question as important to their health. The three colors in the center represent the three main domains, with the bars demonstrating the percentage of patients selecting each health item. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

joy in life, side effects, control over your life, weight, graft rejection, leisure activities, and loss of strength (24%). About half of the items (39 of 83) were considered important by less than 10% of the respondents. The frequencies with which attributes were selected were also calculated separately by gender and transplanted organ (Appendix 1 and 2), but no substantial differences were identified between the various subgroups.

3.4. Phase 5: second round of expert meetings and final selection of health items

We first took into account the most frequently selected health items and included the ones that were selected by more than 20% of the respondents. Some health items with overlapping meanings were combined. Of the 20 frequently selected health items, nine were formulated for inclusion in the final set of TXP health items. The three most frequently selected health items—energy, fatigue, and loss of strength—were combined into a single item: “fatigue.” Skin-related symptoms and problems (skin alterations, fragile skin) together constituted the second most frequently selected health items and were combined into a single item: “skin.” Anxiety or worry with regard to side effects and graft rejection were also among the most frequently selected health items. During the expert meetings, however, consensus arose that these issues are container terms and abstract concepts that do not constitute generic health outcome items, but personal characteristics in response to post-transplant medical treatment. We decided to include “worry/anxiety” as a separate health item, accompanied by an explanation (in the form of a pop-up in the app) clarifying that such worries could be about side effects, the functioning of the transplanted organ, infections, future diseases, or other issues.

“Control over your life” was selected by over 30% of the transplant recipients from the subdomain of autonomy. Given the importance of this subdomain and the fact that many recipients also selected “physical independence,” the final health item covering this health outcome issue was formulated as “self-reliance.” The item “leisure activities” was frequently selected from the subdomain of activities. Because a large share (43%) of respondents to the online survey were neither students nor employed, we suspect that these two items were neglected. Both are nevertheless important health items for people who are younger or still active in the labor market. We therefore decided to include “activities” as a health item, accompanied by an explanation that the item could refer to leisure activities, work, or study.

Weight and sexuality were frequently selected from the physical subdomain, and they were included in the TXP. In the online survey, sexuality was selected more frequently by male respondents (26%) than it was by female respondents (18%). Because problems related to defecation (flatulence/gas, diarrhea, constipation) were frequently

selected by the transplant recipients responding to the online survey, “stooling” was formulated for inclusion in the TXP. Memory and concentration were the most frequently selected health items from the cognition subdomain, and they were combined into a single item: “memory/concentration.” All selected items were used to create the TXP, which is accessible through our data-collection technology HealthSnApp (Figure 4).

There were seven subdomains in the HealthFan for which all of the health items were selected by less than 20% of the respondents: relationships, senses, eating, respiratory, body heat, chest, and pain. With the exception of “relationships,” all of these subdomains belong to the physical domain of HRQOL, which is more of an issue during the pretransplant phase. During the discussions with clinical experts, we agreed that, while these items might be relevant in the lives of individual patients, these subdomains are not substantially affected by the transplantation.

4. Discussion

In this article, we report on the development of a new HRQOL-related PROM consisting of health items that are important to solid-organ transplant recipients. The opinions of patients should be included in all stages of the process of developing any patient-centered PROM for assessing the overall quality of an individual’s health condition [31,32]. We therefore involved transplant recipients throughout the entire process of determining and selecting the health items. Based on a mixed-methods approach consisting of a literature review, focus-group meetings, and an online survey, organ recipients identified and selected health items that have had the most impact on their health. The top nine health items that were selected for inclusion in the TXP were as follows: fatigue, skin, worry/anxiety, self-reliance, activities, weight, sexuality, stooling, and memory/concentration.

The absence of a patient-centered, preference-based PROM for assessing HRQOL in transplant recipients has posed a significant obstacle to the accurate measurement of the overall health condition experienced by transplant recipients after transplantation. Generic HRQOL instruments (e.g., SF-36 and EQ-5D) are the most frequently applied in studies involving transplant recipients [14]. These instruments aim to assess generic aspects of health status which make them suitable for comparisons across different health conditions and populations. The selection of health items for most current generic PROMs has predominantly relied on consensus and expert opinion, with most having been determined without any significant patient input [33,34]. Most of these instruments are profile PROMs that do not measure the impact of health conditions as they are experienced by patients. Although a few of these PROMs are preference-based (e.g., the EQ-5D), patients were not involved in assigning weights to any of the distinct items

Task 1

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

A little tired

Normal skin

Not worried

Self-reliant

Some problems with activities

No weight gain/loss

Some sexual problems/dysfunction

Stooling

Memory

NEXT

Notti red
A little tired
Quite tired
Very tired

Normal skin
Slight fragile or altered skin
Moderate fragile or altered skin
Severe fragile or altered skin

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 weight gain/loss
Some weight gain/loss
Moderate weight gain/loss
Severe weight gain/loss

No sexual problems/dysfunction
Some sexual problems/dysfunction
Moderate sexual problems/dysfunction
Severe sexual problems/dysfunction

Normal stooling
Slight stooling problems
Moderate stooling problems
Severe stooling problems

No memory/concentration problems
Some memory/concentration problems
Moderate memory/concentration problems
Severe memory/concentration problems

Fig. 4. The nine items of the TXP, each with four levels, as depicted in the HealthSnApp (mobile application).

included in them. Moreover, these generic instruments do not address many concerns that are specific to transplant recipients with regard to organ rejection and the adverse effects of immunosuppressive medications (e.g., fragile skin, stooling, weight gain, and sexual dysfunction) [35,36]. Our approach therefore involved patients throughout the entire process—from the beginning of formulating the health items to the ultimate selection of relevant items.

In the literature review, we identified 43 transplant-specific PROMs relating to HRQOL [14]. Many of these tools are modified modules of disease-specific PROMs containing health items pertaining to the context of organ transplants, although they are not necessarily driven by the perspective of transplant recipients. For example, the following items were repeated most frequently in the existing transplant-specific PROMs: hair/nails, mouth/gingiva, depression, irritation/anger, and headaches/migraines. In our study, however, none of these items was selected by more than 10% of the transplant recipients in either the focus-group meetings or the online survey. Another drawback to the existing PROMs is that almost all of them

consist of descriptive profile questionnaires, which are unable to generate a single value for HRQOL. Two transplant-specific PROMs that are frequently administered to solid-organ recipients—the Modified Transplant Symptom Occurrence and Symptom Distress Scale [37,38] and the Transplant Effects Questionnaire [39,40]—contain 59 and 23 health items, respectively. With only nine health items originating directly from transplant recipients, the TXP can facilitate the measurement of HRQOL in both clinical and research settings.

Joy in life was selected by a substantial share (36%) of the respondents to the online survey. This item had been added to the HealthFan survey based on input from a lung recipient who participated in the focus-group meetings. Although this item refers to a generic aspect of life, it is not clear whether it should be regarded as a component of health (or HRQOL). As a health item, joy in life seems to be more of an overarching concept that goes beyond the overall construct that the TXP is intended to capture (i.e., experienced health and its effect on daily life for transplant recipients). If this item is included, it could potentially dominate the other items,

thus reducing the amount of information provided about the other health items [41]. It was therefore excluded from the TXP.

Our procedure for selecting the items that transplant recipients deemed important might have been subject to some limitations. One limitation might be the low participation rate in the focus-group meetings. When we planned the focus-group meetings, we recruited organ recipients ensuring there was quite a lot of variation on a number of demographic characteristics, such as age, gender educational level, and time since transplantation. Patients were recruited in outpatient clinics and the doctors paid special attention to invite patients in such a way to generate a representative sample. Afterward, we analyzed the data and found no difference between the people who refused to participate and the people who participated in focus-group meetings. Additionally, the respondents who participated in the online HealthFan survey (phase 4) were also asked to identify missing health items. Not one missing health item was identified, which may indicate that the focus-group meetings were adequate. By inviting people from both the UMCG and from patient organizations to participate in the online survey, we aimed to have a representative selection of the transplant population. To invite the organ recipients, we addressed all patients who receive post-transplant care in our hospital, by email. Some patients could not be reached because they changed their email address. Moreover, some patients indicated that they did not feel comfortable to click on a link that was provided by email. These are possible reasons for the somewhat low participation rate. One of the limitations of our study is that we were unable to check whether respondents participated based on the invitation by email or based on the announcements done by patient organizations. This was a deliberate choice to ensure the privacy of the respondents. Of the 176 respondents who initially started the survey, 26 did not fill in any response and 22 only provided demographic information. This could indicate that the task was not what they expected or that they did not feel competent to complete it.

It appeared that most respondents were male and that the mean age was above 50 years. This might suggest a certain selection. However, this overrepresentation of males is representative for the overall population of organ recipients. We compared the employment status and the preferences in the health items selection task between male and female participants and found no significant difference between these groups.

Results seem distinctive because the results of the online survey indicated a clear difference in number of selections between the top ten frequently selected health items and all other health items. In addition, we did several bootstrapping analyses on subsamples of our data, which produced very similar results. Another potential limitation could be due to the somewhat arbitrary grouping of items in the HealthFan. For example, like previous studies, we positioned activities

of daily living within the physical domain of HRQOL, although the subdomain of activities (which consists of three other health items) is positioned within the social domain. We cannot know whether the grouping of items affected the way respondents selected the items that they considered most important to their health [22]. A limitation to this study might have to do with our application of a relatively straightforward HealthFan method, which is based largely on frequencies to select important health items. One way to extend the selection procedure could be to include ranking exercises as subsequent tasks, after the respondent has selected the most important items [42]. The frequency approach that we applied nevertheless seems adequate for our present purposes.

Health items that were collected from the, English, literature had to be translated to Dutch because the study was performed among Dutch participants. There may be a small risk of unintended changing the validity of the constructs due to this translation. However, the constructs were denoted by a single word or a short phrase, so we do not expect this to be an important issue. Nonetheless, some caution should be taken when generalizing these results.

Face validity and content validity can be investigated by establishing special methods to retrieve the relevant items, by opinion, and by special judgment procedures as presented in our article. In the next step in our research, we plan to approach transplant patients to assess their current health condition using the HealthSnApp data-collection technology. This mobile application (app) is combined with a central server (www.healthsnapp.info), which runs our newly developed measurement model according to interactive software routines that are generic and flexible. The technology is capable of generating a value based on 3–18 health items [22,43,44]. Users (i.e., transplant recipients) will first be asked to rate their current health condition by ticking nine boxes representing the nine items derived in this study, until the descriptions in all of the boxes provide the best possible description of their current health. In the second task, slightly different health states will be shown to the respondents, who will be asked to choose whether each of these health states is better or worse than their own state of health. This comparative procedure is essential for any preference-based measurement PROM [43,44]. Because the response task in this app is simply a preference (rank order) between a patient's own health state and a closely related hypothetical health state, the assessment is less likely affected by “subjective” motives and easier to accomplish. This mode of measurement largely prevents biases such as adaptation and coping. The present study is to establish the conceptual framework of the TXP and to select relevant health items. The procedure of items selection was based on patient input, not on expert opinion. Future studies are planned to use the TXP in a sample of transplant recipients. In addition, extensive exploration of the TXP's measurement properties (test–retest reliability, convergent validity) will also be done.

In conclusion, we adopted a patient-centered approach to include a total of nine health items in the novel TXP. This new PROM provides transplant recipients, clinicians, and researchers with a convenient tool for measuring and monitoring the overall trend of HRQOL during the post-transplant period.

The authors declare no conflicts of interest.

CRedit authorship contribution statement

Ahmad Shahabeddin Parizi: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Visualization, Project administration. **Paul F.M. Krabbe:** Conceptualization, Methodology, Software, Validation, Formal analysis, Resources, Data curation, Writing - original draft, Writing - review & editing, Visualization, Supervision, Project administration. **Erik Buskens:** Conceptualization, Writing - review & editing. **Wim van der Bij:** Resources, Writing - review & editing. **Hans Blokzijl:** Resources, Writing - review & editing. **Vera Hanewinkel:** Investigation, Writing - review & editing. **Coby Annema:** Investigation, Writing - review & editing. **Stephan J.L. Bakker:** Conceptualization, Resources, Writing - review & editing, Supervision, Project administration. **Karin M. Vermeulen:** Conceptualization, Methodology, Investigation, Writing - original draft, Writing - review & editing, Supervision, Project administration.

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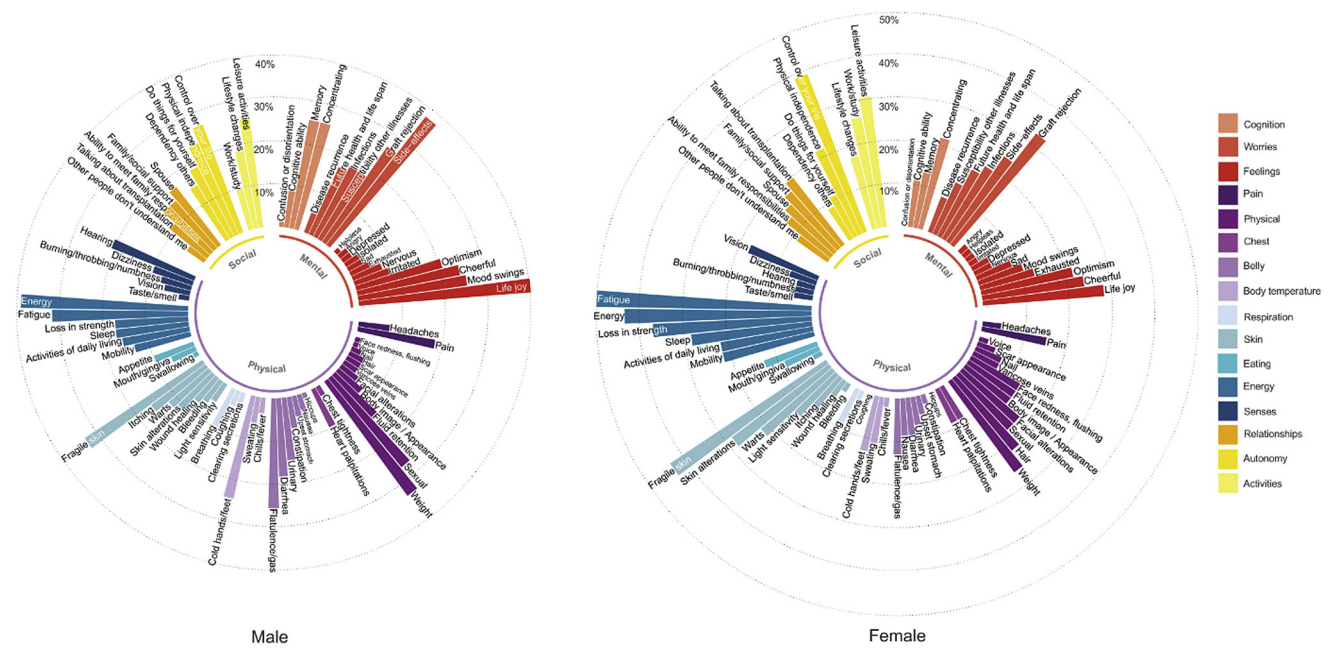
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References

- [1] Kellar CA. Solid organ transplantation overview and selection criteria. *Am J Manag Care* 2015;21:S4–11.
- [2] Lodhi SA, Lamb KE, Meier-Kriesche HU. Solid organ allograft survival improvement in the United States: the long-term does not mirror the dramatic short-term success. *Am J Transplant* 2011;11:1226–35.
- [3] Benzing C, Krezdorn N, Förster J, Hinz A, Atanasov G, Wiltberger G, et al. Impact of different immunosuppressive regimens on the health-related quality of life following orthotopic liver transplantation. *Clin Transplant* 2015;29:1081–9.
- [4] Kugler C, Geyer S, Gottlieb J, Simon A, Haverich A, Dracup K. Symptom experience after solid organ transplantation. *J Psychosom Res* 2009;66:101–10.
- [5] de Wit M, Hajos T. Health-related quality of life. In: Gellman MD, Turner JR, editors. *Encyclopedia of Behavioral Medicine*. New York, USA: Springer; 2013:929–31.
- [6] Krabbe PFM. *The Measurement of Health and Health Status: Concepts, Methods and Applications from a Multidisciplinary Perspective*. San Diego, USA: Academic Press; 2016.
- [7] Guyatt GH, Ferrans CE, Halyard MY, Revicki DA, Symonds TL, Varricchio CG, et al. Exploration of the value of health-related quality-of-life information from clinical research and into clinical practice. *Mayo Clin Proc* 2007;82:1229–39.
- [8] Howell M, Wong G, Rose J, Tong A, Craig JC, Howard K. Eliciting patient preferences, priorities and trade-offs for outcomes following kidney transplantation: a pilot best–worst scaling survey. *BMJ Open* 2016;6:e008163.
- [9] Lewis EF, Johnson PA, Johnson W, Collins C, Griffin L, Stevenson LW. Preferences for quality of life or survival expressed by patients with heart failure. *J Heart Lung Transplant* 2001;20:1016–24.
- [10] Cella D, Hahn EA, Jensen SE, Butt Z, Nowinski CJ, Rothrock N, et al. Patient-Reported Outcomes in Performance Measurement. Research Triangle Park, NC: RTI Press; 2015.
- [11] Weldring T, Smith SM. Patient-reported outcomes (PROs) and patient-reported outcome measures (PROMs). *Health Serv Insights* 2013;6:61–8.
- [12] Calvert M, Kyte D, Price G, Valderas JM, Hjollund NH. Maximising the impact of patient reported outcome assessment for patients and society. *BMJ* 2019;364:k5267.
- [13] Ridgeway JL, Beebe TJ, Chute CG, Eton DT, Hart LA, Frost MH, et al. A brief Patient-Reported Outcomes Quality of Life (PRO-QOL) instrument to improve patient care. *PLoS Med* 2013;10:e1001548.
- [14] Shahabeddin Parizi A, Krabbe PFM, Buskens E, Bakker SJL, Vermeulen KM. A scoping review of key health items in self-report instruments used among solid organ transplant recipients. *Patient* 2019;12:171–81.
- [15] Seiler A, Klaghofer R, Ture M, Komossa K, Martin-Soelch C, Jenewein J. A systematic review of health-related quality of life and psychological outcomes after lung transplantation. *J Heart Lung Transplant* 2016;35:195–202.
- [16] Wyld M, Morton RL, Hayen A, Howard K, Webster AC. A systematic review and meta-analysis of utility-based quality of life in chronic kidney disease treatments. *PLoS Med* 2012;9:e1001307.
- [17] Cleemput I, Dobbels F. Measuring patient-reported outcomes in solid organ transplant recipients. *Pharmacoeconomics* 2007;25:269–86.
- [18] Preedy VR, Watson RR. *Handbook of Disease Burdens and Quality of Life Measures*. New York, USA: Springer; 2010.
- [19] Streiner DL, Norman GR, Cairney J. *Health measurement scales: a practical guide to their development and use*. 5th ed. Oxford, UK: Oxford University Press; 2015.
- [20] DeVellis RF. *Scale development: Theory and applications*. 4th ed. Newbury Park, CA: Sage Publications Inc; 2016.
- [21] Miller GA. The magical number seven plus or minus two: some limits on our capacity for processing information. *Psychol Rev* 1956;63:81–97.
- [22] Krabbe PFM, van Asselt ADI, Selivanova A, Jabrayilov R, Vermeulen KM. Patient-centered item selection for a new preference-based generic health status instrument: CS-Base. *Value Health* 2019;22:467–73.
- [23] Creswell JW, Klassen AC, Plano Clark VL, Clegg Smith K. *Best practices for mixed methods research in the health sciences*. Bethesda, MD: National Institutes of Health; 2011.
- [24] Reneman MF, Brandsema KPD, Schrier E, Dijkstra PU, Krabbe PFM. Patients first: toward a patient-centered instrument to measure impact of chronic pain. *Phys Ther* 2018;98:616–25.
- [25] Tufte E. *Beautiful evidence*. Cheshire, Connecticut, USA: Graphics Press; 2006.
- [26] Carlsen B, Glenton C. What about N? A methodological study of sample-size reporting in focus group studies. *BMC Med Res Methodol* 2011;11:11–26.

- [27] Guest G, Namey E, McKenna K. How many focus groups are enough? Building an evidence base for nonprobability sample sizes. *Field Methods* 2016;18:59–82.
- [28] Krueger RA, Casey MA. *Focus groups: A practical guide for applied research*. 5th ed. Thousand Oaks, CA: Sage; 2015.
- [29] Saunders B, Sim J, Kingstone T, Baker S, Waterfield J, Bartlam B, et al. Saturation in qualitative research: exploring its conceptualization and operationalization. *Qual Quant* 2018;52:1893–907.
- [30] Versteegh MM, Vermeulen KM, Evers SMAA, de Wit GA, Prenger R, Stolk EA. Dutch tariff for the five-level version of EQ-5D. *Value Health* 2016;19:343–52.
- [31] Snyder CF, Jensen RE, Segal JB, Wu AW. Patient-reported outcomes (PROs): putting the patient perspective in patient-centered outcomes research. *Med Care* 2013;51:S73–9.
- [32] Deshpande PR, Rajan S, Sudeepthi BL, Abdul Nazir CP. Patient-reported outcomes: a new era in clinical research. *Perspect Clin Res* 2011;2:137–44.
- [33] Arons AMM, Schölzel-Dorenbos CJM, Olde Rikkert MGM, Krabbe PFM. Improving the measurement of QALYs in dementia: some important considerations. *Value Health* 2012;15:785–7.
- [34] Wiering B, de Boer D, Delnoij D. Patient involvement in the development of patient-reported outcome measures: a scoping review. *Health Expect* 2017;20:11–23.
- [35] Brazier J-H, Harper R, Jones N, O’Cathain A, Thomas K, Usherwood T, et al. Validating the SF-36 health survey questionnaire: new outcome measure for primary care. *BMJ* 1992;305:160–4.
- [36] EuroQol Group. EuroQol—a new facility for the measurement of health-related quality of life. *Health Policy* 1990;16:199–208.
- [37] Moons P, De Geest S, Versteven K, Abraham I, Vlamincck H, Moens G, et al. Psychometric properties of the “modified transplant symptom occurrence and symptom distress scale”. *J Nurs Meas* 2001;9:115–34.
- [38] Dobbels F, Moons P, Abraham I, Larsen CL, Dupont L, De Geest S. Measuring symptom experience of side-effects of immunosuppressive drugs: the modified transplant symptom occurrence and distress scale. *Transpl Int* 2008;21:764–73.
- [39] Ziegelmann JP, Griva K, Hankins M, Harrison M, Davenport A, Thompson D, et al. The Transplant Effects Questionnaire (TxEQ): the development of a questionnaire for assessing the multidimensional outcome of organ transplantation - example of end stage renal disease (ESRD). *Br J Health Psychol* 2002;7:393–408.
- [40] Annema C, Roodbol PF, Stewart RE, Ranchor AV. Validation of the Dutch version of the transplant effects questionnaire in liver transplant recipients. *Res Nurs Health* 2013;36:203–15.
- [41] Coast J, Al-Janabi H, Sutton EJ, Horrocks SA, Vosper AJ, Swancutt DR, et al. Using qualitative methods for attribute development for discrete choice experiments: issues and recommendations. *Health Econ* 2012;21:730–41.
- [42] Stenner PH, Cooper D, Skevington SM. Putting the Q into quality of life: the identification of subjective constructions of health-related quality of life using Q methodology. *Soc Sci Med* 2003;57:2161–72.
- [43] Groothuis-Oudshoorn CGM, van der Heuvel E, Krabbe PFM. An item response theory model to measure health: the multi-attribute preference response model. *BMC Med Res Methodol* 2018;18:62.
- [44] Krabbe PFM. A generalized measurement model to quantify health: the multi-attribute preference response model. *PLoS One* 2013;8:e79494.



Appendix 1. Proportion of respondents to the online survey identifying the item in question as important to their health, by gender.

