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ORIGINAL ARTICLE

Using a novel concept to measure outcomes in solid organ recipients provided promising results

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Abstract

Objectives: Efforts to evaluate the health of solid organ transplant recipients are hampered by the lack of adequate patient-reported outcome measures (PROMs) targeting this group. We developed the Transplant ePROM (TXP), which is based on a novel measurement model and administered through a mobile application to fill this gap. The main objective of this article is to elucidate how we derived the weights for different items, and to report initial empirical results.

Study design and setting: The nine health items in the TXP were fatigue, skin, worry, self-reliance, activities, weight, sexuality, stooling, and memory. Via an online survey solid organ recipient participating in the TransplantLines Biobank and Cohort study (NCT03272841) were asked to describe and then compare their own health state with six other health states. Coefficients for item levels were obtained using a conditional logit model.

Results: A total of 232 solid organ transplant recipients (mean age: 54 years) participated. The majority (106) were kidney recipients, followed by lung, liver, and heart recipients. Fatigue was the most frequent complaint (54%). The strongest negative coefficients were found for activities and worry, followed by self-reliance and memory.

Conclusion: A set of coefficients and values were developed for TXP. The TXP score approximated an optimal health state for the majority of respondents and recipients of different organs reported comparable health states.

Keywords: Health-related quality of life; Health outcome; Patient-reported outcome measure; Preference based; Transplantation; TXP

What is new?

Key findings

- We estimated coefficients and values for a new transplant-specific ePROM (TXP).

What this adds to what was known?

- TXP is the first transplant-specific ePROM for which health items are derived by a fully novel patient-centered approach. We estimated coefficients to put a single value to health states of solid-organ recipients.

What are the implications and what should change now?

- The development of the TXP marks an important advancement in the process of valuing health states. Further work will entail applying the TXP within a larger population of solid organ recipients, and investigating the sensitivity of the TXP values in comparison with existing PROMs.

Abbreviations: HRQOL, health-related quality of life; PROM, Patient-reported outcome measure; TXP, Transplant PROM.

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1. Introduction

Assessments and comparisons of the outcomes of different medical interventions and treatment modalities, such as solid organ transplantation, from patients' perspectives are essential [1]. In recent decades, with advances in surgical techniques and post-transplant care, the outcomes of traditional treatments (e.g., the survival of patients and grafts) have improved considerably. As for other therapeutic interventions, the maintenance or enhancement of (perceived) health status or health-related quality of life (HRQoL) has emerged as a key objective within the medical field of transplantation [2–5].

The term HRQoL is generally considered to reflect the physical, psychosocial, and social impacts of diseases and treatments on a patient's disability and daily functioning [6,7]. Previous studies have shown that for a large proportion of patients, HRQoL may be more relevant than length of life, and many patients are more concerned about their general health and infirmity than they are about their survival [8,9]. This is especially the case for solid organ recipients for whom presently the goal of post-transplant interventions is focused on maintaining graft function and keep the patients symptom free [10]. Therefore, adequate measurement and follow-up of HRQoL in transplant recipients is pertinent for clinicians and researchers.

Patient-reported outcome measures (PROMs), which encompass any direct reporting by patients on how they function or feel without any interpretation or filtering by physicians or others, can be used to assess HRQoL [6]. PROMs can be used as measures within clinical practice, research, or program evaluation, serving multiple functions. Some examples of their use include monitoring patients' clinical status, assessing the extent to which the objectives of a health intervention are being achieved, and comparing or assessing the cost-effectiveness of interventions. It is determined in a recent review of the use of PROMs in studies on solid-organ transplantation that most of the PROMs in current use are generic, with only a few being specifically related to transplant. Among the all 418 instruments applied, only 43 were transplant-specific[11]. These PROMs are designed conventionally, entailing sections yielding separate measures for different health domains rather than providing a single score that expresses the overall quality of a patient's state of health. Measuring the overall health condition of a patient expressed in a single number requires preference-based methods. PROMs developed using such methods explicitly incorporate weights that reflect the importance attached to a set of health items. Rather than measuring the levels of reported complaints (i.e., their frequency and intensity), these preference-based PROMs generate a single number that reflects the patient's health state as a whole. Consequently, such a single number can be more easily understood and used to compare different populations or groups within a population over time.

The source of health items is another important aspect of HRQoL PROMs. There is now consensus that patients' views should have a central place in the development of the entire PROM trajectory [12,13]. Reneman et al. recently generated the content of a PROM for chronic pain and surprisingly, the item that patients considered most important was "fatigue," which is not included in the PROMs that are generally used for reporting on chronic pain [14]. This indicates that content validity of a PROM may be reduced if not constructed on profound input from patients. In our review relating to solid organ transplantation, we found out that most of the recent HRoQL instruments currently in use are not specifically designed for transplant recipients and/or their content was obtained by experts without the patients' involvement [11]. Our review, as well as some previously published reviews [15–17], revealed the necessity of developing a HRQoL PROM specifically for transplant recipients that is patient-centered throughout its development and assessment process and entails a preference-based methodology. Accordingly, we sought to develop a patient-centered PROM for measuring HRQoL in solid organ recipients.

We applied a novel measurement model [18,19] that requires interactive routines within an electronic environment to derive the weights of the items in this new Transplant PROM (TXP). In this paper, we report on the empirical results of administering the recently developed TXP within a group of solid organ recipients. Our primary aim was to elucidate how weights for different items were derived using a novel measuring method. Our secondary aim was to report initial empirical results for the HRQoL of solid organ recipients obtained by TXP.

2. Methods

2.1. Framework of the study

The core of a preference-based measurement framework consists of a response task comparing at least two objects with the objective of expressing which object is preferred (is better) [6]. A health state is often described as a small set of health items, whereby each health item entails a limited number of levels of severity. The respondents score the set of health items as a whole, and not the individual health items separately. In comparing complete health item sets, which differ according to levels of severity (i.e., the health state), a preference for one health states is evoked.

It has been posited that the immediate memory span limits the amount of information that individuals are able to receive, process, and recall. In general, individuals can discriminate 7 ($\pm$2) information items at a time. Consequently, most preference-based studies usually include no more than nine items [20,21]. This figure likely represents the maximum amount of information that can be simultaneously processed by an individual. Therefore, the TXP comprised nine health items.

In a previous study, we conducted focus group discussions with solid organ recipients to select health items for the TXP [22]. Some of these participants also volunteered to contribute to the current study. The prototype version of the 9-item TXP was evaluated by eight of these participants. Subsequently the TXP was finalized based on their feedback.

2.2. Sample

Participants were recruited via emails sent to listed participants in the TransplantLines Biobank and Cohort Study (NCT03272841) conducted at the University Medical Center Groningen. TransplantLines is a single-center, prospective cohort study and including all different types of solid organ transplant recipients as well as living organ donors [23]. Inclusion criteria for this study were being a solid-organ recipient, age $\geq$18, and sufficient

Dutch language skills. Our study was approved by the institutional review board (METc 2017/648) and in accordance with the Declarations of Helsinki and Istanbul. A link to the survey was sent to the participants by email along with clear instructions in the Dutch language.

2.3. Instrument

Electronic PROMs (ePROMs) have been proposed as an improved data collection method compared with paper-based data collection. We applied a mixed method step-by-step model, entailing an extensive search of the current HRQoL literature along with surveys and focus group discussions with transplant recipients and experts that enabled us to identify the most important health items to be incorporated in the Transplant ePROM [22]. The following nine health items were included in the TXP: fatigue, skin, worry, self-reliance, activities, weight, sexuality, stooling, and memory. Each item comprised four levels, most of which were ranked according to severity. For example, the four levels for "worry" were "not worried," "slightly worried," "worried," and "highly worried." We administered the TXP using a mobile application, HealthSnApp, which we developed and improved after testing it on a group of patients (Fig. 1A). When the interactive box for a specific health item is clicked on in this app, the box rotates, displaying the response options. For instance, when the box labeled "worry" is clicked on, it rotates, displaying the first response option for worry. If it is clicked on again, the second response option is displayed and so forth. The transplant recipients were asked to identify their current health status by rotating the boxes until the best-fitting descriptions were obtained in all the boxes (Fig. 1B). The TXP app thus generated a description of a patient's overall state of health expressed as nine digits (e.g., 321131224). There is also an information click point beside each health item in the app that provides explanation regarding each item, once a respondent clicks on it (Appendix 1).

2.4. Ranking task

We applied a multi-attribute preference response (MAPR) model to obtain weights for the levels of the nine health items. This novel preference-based framework for conducting measurements is based on the Rasch model, which draws on item-response theory [18,19]. The MAPR mechanism for obtaining preference-related information is based on a simple assessment made by patients regarding their own health status, as classified in the first task, which serves as a reference state in relation to other states in a second ranking task. Because the response task in the MAPR model simply entails a preference ranking of the patients' own health status with one or more slightly different hypothetical health states, the assessment is relatively easy to accomplish.

During the online survey administered using the HealthSnApp, each respondent was first asked to specify his or her current health state regarding each of the nine TXP items. In the second task, the respondent's health state, as defined in the first task (the reference state), was compared with some slightly different hypothetical health states. Based on our previous experience in other studies, we concluded that six is the optimal number for the hypothetical health states in the second task [24]. The respondents were informed that the health states presented in the second task were those of another patient with the same health status, with the exception of two alternating health items. If a respondent reported having perfect health (111111111) or the worst possible condition (444444444) in the first task, then any other hypothetical health-related state in the second task would by definition be worse or better, respectively, than the reference state. Therefore, individuals who reported perfect health or the worst possible condition in the first task did not complete the second task.

A total of 4^9 health-related states (262,144; nine items with four levels) can be generated using the TXP classification system. The hypothetical health states portrayed in the second task differed from the actual health states described by the respondents for only two health items. One of these items depicted an improvement by one level compared with the respondent's health state. This item was marked with a green contrast. In addition, one item showed a reduction by one level compared with the respondent's health state and was marked with a red contrast (Fig. 1C). For example, a patient with a self-constructed health state of 321131224 could compare his or her health state with other health states, such as $3\underline{1}11\underline{4}1224$ and $3211\underline{2}12\underline{3}4$. The underlined digits indicate the items that have changed compared to the self constructed health state. The items to become red and green were randomly selected. Respondents were asked to indicate whether the reference health state (their own health state identified in the first task) was better or worse than each of the six hypothetical health states. Thus, they made trade-offs between two different health aspects, which is the central element of

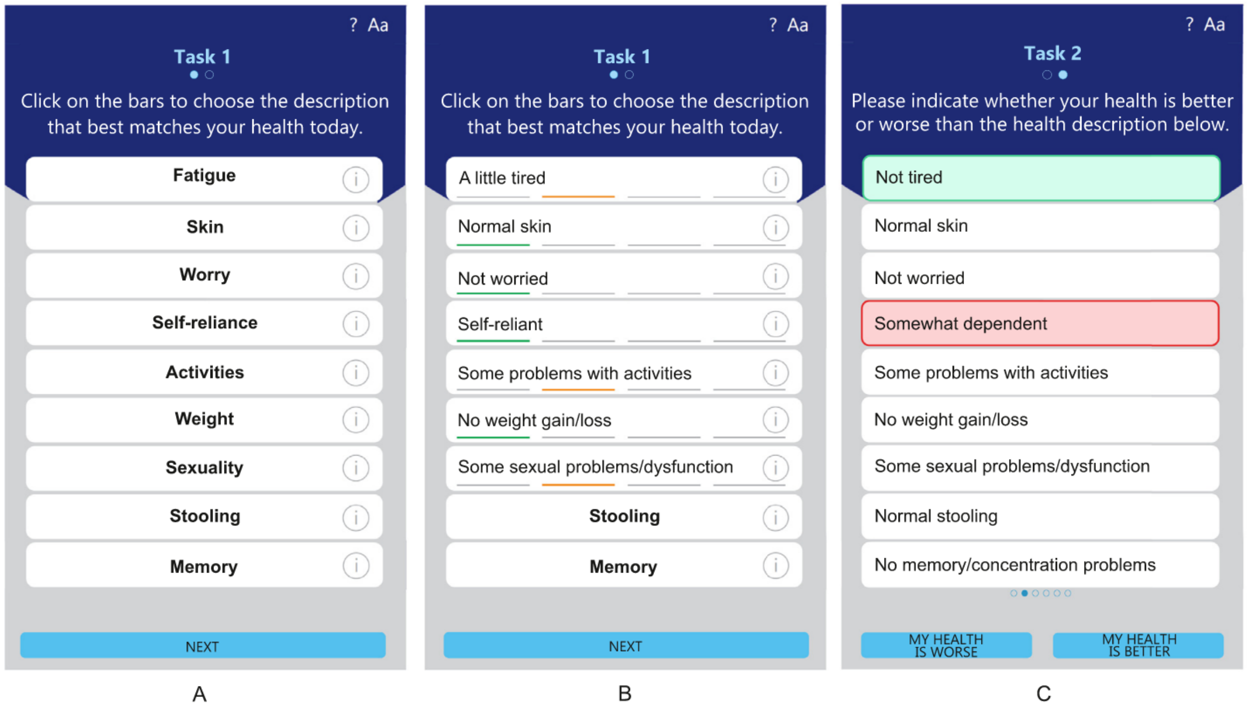

Fig. 1. The mobile app comprised two tasks. (A) Task 1 was a descriptive task in which all health items were listed in interactive boxes presented on a single screen. (B) When the interactive box for a specific item was selected, the box display response options. For instance, when the box labeled "fatigue" was selected, it changed, displaying the following response options: "not tired," "a little tired," "quite tired," and "very tired." (C) The information collected from the first task was used to determine the states in the second task. In this second task, the respondents compared their own health states, identified in the first task, with other health states. The aim of this task was to derive preferences that were subsequently used to estimate weights for the levels of each item.

preference-based measurement, enabling the weights for the nine items and their levels to be obtained.

After the respondents had completed the preference-based task, they were questioned to provide information on their sex, age, and the type of transplanted organ(s). Respondents who were not willing to share their personal information could have left one or more questions blank.

2.5. Analyses

The frequencies of levels for each of the nine TXP health items were calculated. The coefficients for the item levels were estimated using a conditional logit model (Stata, asmprobit). The first level of each item (no problems or an optimal condition) was considered the reference category. The coefficients for the remaining three levels were estimated using 27 dummy variables (9 × 3). V_{ij} denoted the value of health state j for individual i. We assumed that V_{ij} was a linear combination of the levels of the health items and included an error term ε_{ij} for an individual. The model specifications were as follows:

$$V_{ij} = \sum_{j=1}^{n} \beta x_{ij} + \varepsilon_{ij}$$

where β represents a vector of 27 regression coefficients and x_{ij} is a vector of 27 binary dummy explanatory variables ($x^{\delta\lambda}$). $\lambda = 2, 3,$ and 4 indicates levels 2, 3 and 4 for each of the nine items ($\delta = 1, 2, \ldots, 9$) of a health state. For example, x^{43} represents the third level (moderate problems) of the fourth health item (self-reliance).

Descriptive statistics were used to summarize the patients' demographic characteristics. Three independent variables (age, sex, organ) were entered in the analysis as determinants of TXP values. Chi-square tests performed to determine possible differences in TXP scores among different organ recipients. The patients were divided into three groups with almost equal members according to age: <45 years old, 45–55 years old, and >55 years old. The following software packages were used: SPSS, Stata, R, R Studio and CorelDraw.

3. Results

3.1. Sample

Invitation emails with the link of the TXP app were sent to 1220 persons. A total of 232 respondents were recruited for this study. The mean age of the respondents was 54 years (SD: 13.68), with women comprising 34% of the total sample. Most of the respondents were kidney recipients (106), followed by lung, liver, and heart recipients. Five respondents, considered as "combined" re-

Table 1. Demographic data on the respondents in the study

	All tasks completed (n = 189)	Only task 1 completed (n = 43)
Sex, N (%)		
Male	84 (44)	24 (56)
Female	64 (34)	19 (44)
Not known	41 (22)	0 (0)
Age		
Median (Range)	57 (20-80)	57 (23-78)
Organ N (%)		
Kidney	81 (43)	25 (58)
Lung	24 (13)	10 (23)
Liver	28 (15)	5 (12)
Heart	10 (5)	3 (7)
Combined	5 (3)	0 (0)
Not known	41 (22)	0 (0)

cipients, each received two organs (one received heart and lung, one received lung and kidney, and three each received liver and kidney). In case of privacy concerns, there was an option for respondents to skip the demographic section. About 30% of respondents did not specify one or several background characteristics (Table 1).

3.2. Respondents' states

In the first task, the current self-identified health states of 43 respondents matched the best possible TXP health state (111111111) and were therefore excluded from the analysis of the second task. None of the respondents reported the worst possible health state (44444444).

The majority of the respondents in this study reported experiencing fatigue (46% of the respondents selected the option for no fatigue in the first task). However, worry was more commonly reported than fatigue by heart recipients. Lack of self-reliance was the least reported complaint, with 84% experiencing no problem relating to this item. Chi-square tests showed no significant differences among recipients of different organs regarding the health issues reported (Table 2).

3.3. Coefficients

A total of 169 unique health states were identified by 232 respondents in the first task. Because the optimal health state (111111111) was excluded from the second task, 168 reference states were used for the analysis of the coefficients. Accordingly, ((232 - 43) x 6 = 1,134) hypothetical states, including 854 unique health states, were generated and accessible in the second task. An analysis of all respondents' comparisons revealed that for 845 (74.5%) of the comparisons between a hypothetical health state and their own health state were favoring of the latter.

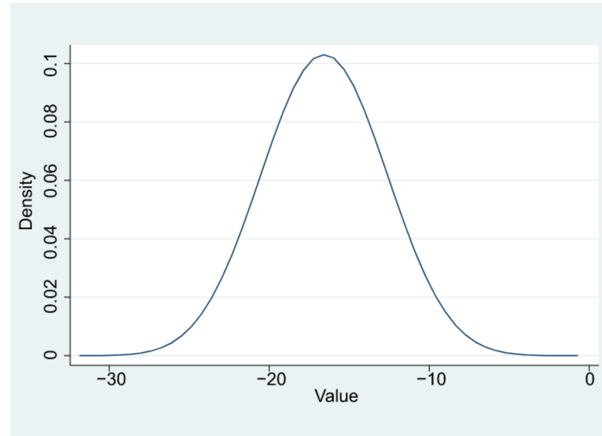

Fig. 2. Kernel density plot of computed values for all health states of the Transplant ePROM (TXP).

The coefficients were negative for all levels of TXP health items, which is a common finding in this type of logit regression analysis. Moreover, they followed a logical order (slight problems < moderate problems < severe problems). A negative coefficient indicated that a particular level was worse than the optimal reference level, which in our study was the first level of each item. Moreover, a lower level of preference for an item corresponded to a more negative coefficient for this item. The items evidencing the highest negative coefficients were activities and worry (Table 3). Standard errors for the coefficients were larger for higher levels of the items, probably because fewer recipients categorized themselves at the third and fourth levels of items in the first task.

3.4. Values

The values calculated for all possible TXP health states (n = 262,144) ranged between -31.55 and -1.03 (Fig. 2). The observed values among the respondents in the TXP ranged from -27.30 to -1.03. Values for male respondents were almost equal to those for female respondents (-6.40 ± 0.5 and -6.55 ± 0.4, respectively). Values for young, middle age, and elderly were -5.53 ± 0.5, -6.30 ± 0.8, and -6.74 ± 0.4 respectively. Over 90% of the respondents specified a health state with a value above -15 in the first task. The worst reported health state was 333444434 with a value of -27.30 (Fig. 3).

4. Discussion

In a previous study, we described how we selected health items for inclusion in the TXP to assess HRQoL in solid organ transplant recipients [22]. In the current study, we have built on this earlier work, showing how weights for the different levels of the nine health items were derived using an adapted type of preference-based methodology. Our study showed that the majority of solid

Table 2. The frequency distributions of solid organ recipients' self-classifications of their health statuses based on the nine selected health items in the TXP (each with four levels) and the calculated values for each transplanted organ

TXP attributes and levels	All (n = 232)	Kidney (n = 106)	Lung (n = 34)	Liver (n = 33)	Heart (n = 13)	Combined (n = 5)	Unspecified (n = 41)
Fatigue N, (%)							
Not tired (1)	107 (46)	52 (49)	14 (41)	15 (45)	6 (46)	2 (40)	18 (44)
A little tired (2)	73 (31)	29 (27)	15 (44)	8 (24)	4 (31)	1 (20)	16 (39)
Quite tired (3)	41 (18)	18 (17)	4 (12)	8 (24)	3 (23)	2 (40)	6 (15)
Very tired (4)	11 (5)	7 (7)	1 (3)	2 (6)	0 (0)	0 (0)	1 (2)
Skin N, (%)							
Normal skin (1)	134 (58)	59 (56)	20 (59)	21 (64)	9 (69)	2 (40)	23 (56)
Slight fragile or altered skin (2)	64 (28)	30 (28)	10 (29)	7 (21)	3 (23)	3 (60)	11 (27)
Moderate fragile or altered skin (3)	28 (12)	13 (12)	4 (12)	5 (15)	1 (8)	0 (0)	5 (12)
Severe fragile or altered skin (4)	6 (2)	4 (4)	0 (0)	0 (0)	0 (0)	0 (0)	2 (5)
Worry N, (%)							
Not worried (1)	133 (57)	61 (57)	22 (65)	16 (48)	5 (38)	5 (100)	24 (58)
Slightly worried (2)	68 (29)	30 (28)	9 (26)	10 (30)	6 (46)	0 (0)	13 (32)
Worried (3)	28 (12)	15 (14)	3 (9)	4 (12)	2 (15)	0 (0)	4 (10)
Highly worried (4)	3 (1)	0 (0)	0 (0)	3 (9)	0 (0)	0 (0)	0 (0)
Self-reliance N, (%)							
Self-reliant (1)	195 (84)	93 (88)	26 (76)	24 (72)	10 (77)	5 (100)	37 (90)
Somewhat dependent (2)	33 (14)	11 (10)	8 (24)	7 (21)	3 (23)	0 (0)	4 (10)
Largely dependent (3)	3 (1)	2 (2)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
Fully dependent (4)	1 (1)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
Activities N, (%)							
No problems with activities (1)	139 (60)	66 (62)	20 (59)	18 (54)	9 (69)	3 (60)	23 (56)
Some problems with activities (2)	67 (29)	29 (27)	12 (35)	11 (33)	2 (15)	1 (20)	12 (29)
Moderate problems with activities (3)	21 (9)	9 (9)	2 (6)	2 (6)	1 (8)	1 (20)	6 (15)
Severe problems with activities (4)	5 (2)	2 (2)	0 (0)	2 (6)	1 (8)	0 (0)	0 (0)
Weight N, (%)							
No weight gain/loss (1)	140 (60)	63 (59)	21 (62)	19 (58)	9 (69)	2 (40)	26 (63)
Some weight gain/loss (2)	70 (30)	33 (31)	9 (26)	10 (30)	3 (23)	3 (60)	12 (29)
Moderate weight gain/loss (3)	14 (6)	8 (8)	2 (6)	1 (3)	1 (8)	0 (0)	2 (5)
Severe weight gain/loss (4)	8 (3)	2 (2)	2 (6)	3 (9)	0 (0)	0 (0)	1 (2)
Sexuality N, (%)							
No sexual problems/dysfunction (1)	142 (61)	69 (65)	23 (68)	20 (61)	9 (69)	1 (20)	20 (49)
Some sexual problems/dysfunction (2)	50 (22)	18 (17)	5 (15)	9 (27)	2 (15)	4 (80)	12 (29)
Moderate sexual problems/dysfunction (3)	24 (10)	12 (11)	4 (12)	2 (6)	2 (15)	0 (0)	4 (10)
Severe sexual problems/dysfunction (4)	16 (7)	7 (7)	2 (6)	2 (6)	0 (0)	0 (0)	5 (12)
Stooling N, (%)							
Normal stooling (1)	151 (65)	78 (73)	21 (62)	22 (67)	6 (46)	4 (80)	20 (49)
Slight stooling problems (2)	51 (22)	20 (19)	8 (23)	7 (21)	4 (31)	1 (20)	11 (27)
Moderate stooling problems (3)	29 (12)	8 (8)	5 (15)	3 (9)	3 (23)	0 (0)	10 (24)
Severe stooling problems (4)	1 (1)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)

(continued on next page)

Table 2 (*continued*)

TXP attributes and levels	All (n = 232)	Kidney (n = 106)	Lung (n = 34)	Liver (n = 33)	Heart (n = 13)	Combined (n = 5)	Unspecified (n = 41)
Memory N, (%)							
No memory/concentration problems (1)	140 (60)	71 (67)	21 (62)	21 (64)	8 (62)	2 (40)	17 (41)
Some memory/concentration problems (2)	75 (32)	29 (27)	8 (23)	10 (30)	5 (38)	3 (60)	20 (49)
Moderate memory/concentration problems (3)	13 (6)	4 (4)	5 (15)	2 (6)	0 (0)	0 (0)	2 (5)
Severe memory/concentration problems (4)	4 (2)	2 (2)	0 (0)	0 (0)	0 (0)	0 (0)	2 (5)
TXP value (mean, SD)	-6.87 (5.06)	-6.49 (5.05)	-6.64 (4.77)	-7.64 (6.24)	-6.72 (5.12)	-6.59 (3.26)	-6.91 (4.85)

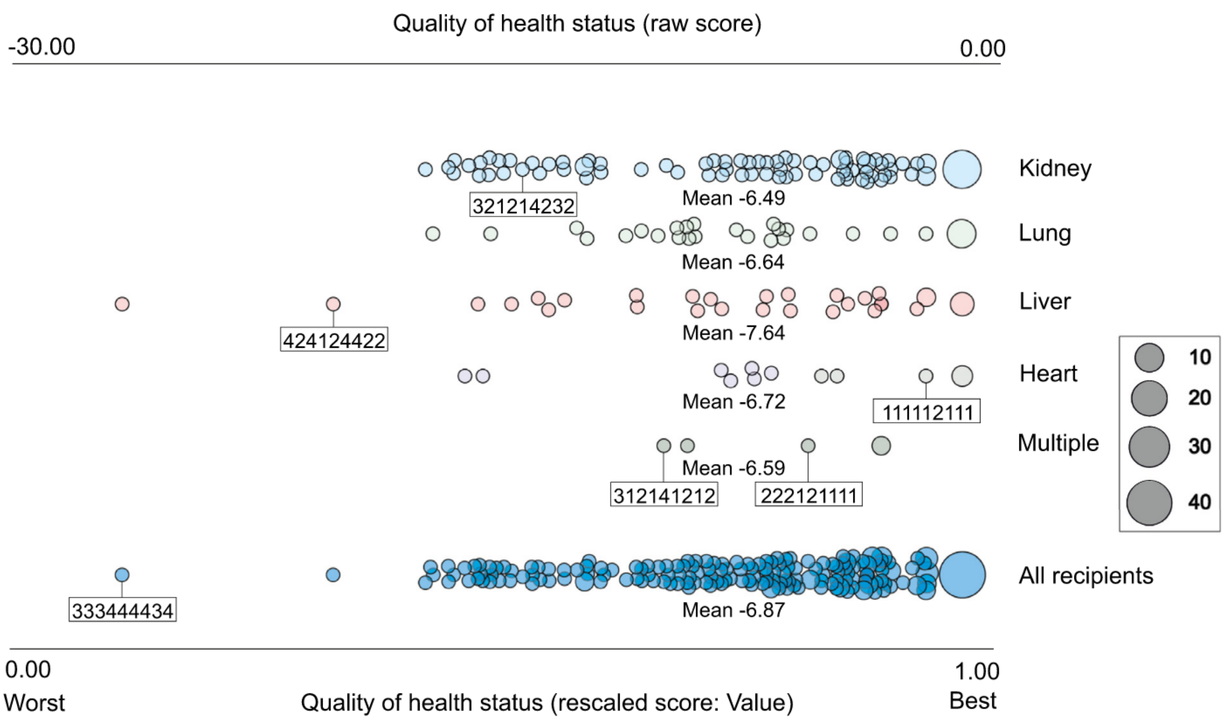

Fig. 3. The distribution of computed TXP values obtained for respondents in the HealthSnApp.

organ recipients reported a high level of HRQoL. We also found out that there is no substantial difference between the overall health states of different solid organ recipients.

The most common problem reported by transplant recipients in this study was fatigue. Previous studies have also shown that although HRQoL increases dramatically after transplantation, fatigue is still a prominent issue for many organ recipients [25–28]. Among the nine TXP health items, activities and worry were found to have the largest absolute coefficients, followed by self-reliance and memory. This means that changes in these four items would have the highest impact on the overall health state values of transplant recipients. The majority of the solid organ recipients had an overall value approximating an optimal health state. Several previous studies [29–33] reported comparable findings, which may indicate that the self-reported quality of life of organ recipients is comparable to those of the general population.

The results of our study indicate that the tasks in the HealthSnApp (entailing respondents' determination of their current health states and their comparison of these states with hypothetical ones) are appropriate for organ recipients. The coefficients for the different levels of each of the nine items followed a logical order in this study. However, the degree of precision for these coefficients was modest, as the confidence intervals, and therefore the standard errors of the coefficients, were wide. The sample size of the pairs that were compared in our study (n = 1,134) could account for this lack of precision. The number

Table 3. Coefficients for all levels of the nine items of the Transplant ePROM (TXP)

Item level	Coefficient	SE	Significance
Fatigue (2)	-1.117	1.10	0.311
Fatigue (3)	-2.422	2.20	0.271
Fatigue (4)	-3.121	3.30	0.344
Skin (2)	-1.399	1.10	0.203
Skin (3)	-2.458	2.20	0.264
Skin (4)	-2.695	3.31	0.415
Worry (2)	-1.140	1.09	0.297
Worry (3)	-2.534	2.19	0.247
Worry (4)	-4.070	3.31	0.219
Self-reliance (2)	-1.622	1.11	0.144
Self-reliance (3)	-2.292	2.22	0.303
Self-reliance (4)	-3.960	3.45	0.252
Activities (2)	-1.860	1.11	0.093
Activities (3)	-2.523	2.20	0.251
Activities (4)	-4.206	3.31	0.204
Weight (2)	-1.106	1.10	0.315
Weight (3)	-1.569	2.20	0.476
Weight (4)	-2.898	3.31	0.382
Sexuality (2)	-1.126	1.09	0.302
Sexuality (3)	-1.970	2.19	0.369
Sexuality (4)	-3.171	3.30	0.336
Stooling (2)	-1.185	1.10	0.283
Stooling (3)	-1.813	2.21	0.411
Stooling (4)	-2.541	3.32	0.445
Memory (2)	-1.420	1.09	0.195
Memory (3)	-2.088	2.20	0.342
Memory (4)	-3.865	3.32	0.245

of responses for robust estimations tend to be relatively small.

Another explanation could be that the recipients in our study tended to consider their own health state to be better than the hypothetical health states in the second task. The levels of the nine health items for these states were identical to the respondents' own health states, with the exception of those of two randomly selected items, one of which was raised by one level while the other health item was lowered by one level. Accordingly, on average, 50% of the respondents' selections in favor of their own current health states or of the hypothetical states should have been based on logical grounds. However, we found that 74.5% of respondents chose their own health state over any hypothetical one. This could be partially attributed to a general resistance to change and adaptation. Many individuals may resist trading off their current health state with other almost equivalent health states after undergoing a long period of chronic illnesses because of their personality traits, childhood experiences, or social backgrounds [34,35]. Human Individuals, often prefer to select a known alternative with certain outcomes (their own experienced health status) rather than an uncertain outcome [36].

Prospect theory, which was developed by Kahneman and Tversky [37], offers a more reasonable explanation for clear tendency that respondents prefer their own health state over the hypothetical ones. According to this theory, most individuals react differently to potential losses and gains, with many people being averse to risk [38]. In our study, the six hypothetical health states for each respondent differed from their own states only in the case of two health items. According to prospect theory, individuals tend to avoid losses and neglect gains. Many respondents considered an improvement for one health item to be nonequivalent to an equivalent decline of another health item. It appears that many solid organ recipients are reluctant to any decline on a health item, even if this goes together with an improvement on another health item. They might fear any decline of health aspects, as the impact is unknown, whereas they might be used to cope with their declined health aspects.

Conventional methods used to obtain preference-based measures (e.g., standard gamble and time trade-off) are mostly derived from health economics. These econometric methods entail the use of hypothetical health states that are assessed by a sample of mostly healthy members of the general population. It is reasonable to assume that because they lack adequate information and an ability to imagine others' health situations, healthy individuals are not appropriate choices for assessing the impacts of patients' health conditions [39]. Moreover, these methods are susceptible to various documented biases [40]. The MAPR model applied in our study was developed to overcome most of these limitations. Additionally, this is the first HRQoL preference-based ePROM that is fully based on patients' perceptions and reports.

An innovative aspect of the TXP is that it is an ePROM that can be operated as an app on personal computers or mobile phones. Therefore, the coefficients can be updated after each new respondent uses the app. The information generated from new respondents is used to obtain a more precise value function. This is the first methodological approach to enable simultaneous measurement of respondents' current health states.

Our study had some limitations. The online app is designed to store data only when respondents proceed to the last step and finish the survey. Therefore, we do not know the number of incomplete responses. Information on sex, age, or transplanted organ(s) was not provided by approximately 30% of the respondents. However, these information gaps did not affect the coefficients. Furthermore, the data that we used to calculate the values for health states were derived solely from a single center. Thus, we had a representative sample of solid organ recipients from the entire country in terms of sex, age, and organ types. Nevertheless, cultural differences might exist, and these differences may have affected the generalizability of our results.

Another issue was the large standard error of the calculated coefficients in this study. This issue can be attributed partly to the sample size and partly to the tendency of the respondents to prefer their own health states (in 74.5% of the pair comparisons in the second task). This study marked the first attempt to generate values for the TXP. Further applications of TXP will generate more precise estimates. One limitation of this study was that due to technical restrictions of the mobile application, individual background variables such as time since transplantation, function of the graft, or comorbidities could not be included in the survey. Because this study was done via email invitation and an online app, we only had participants who are familiar with electronic technologies.

The TXP is the first patient-centered ePROM to be developed specifically for measuring HRQoL in transplant recipients using a preference-based methodology. The strength of this methodology is that through the inclusion of more patients over time (even from different studies), the accuracy of the values for health states will continuously improve. Thus, we will be able to generate increasingly precise coefficients. The next step will be to exam the TXP within a larger population of solid organ recipients, and investigate the sensitivity of the TXP values in comparison with existing PROMs (e.g., EQ-5D). We are currently investigating an alternative method to overcome the reluctance of respondents to consider a preference for a health state that is different from their own state we observed in this study. Eventually, if the values are normalized to a dead = 0 scale, utilities for cost-effectiveness analyses can be produced.

In conclusion, the preliminary results of the TXP indicate that the instrument can be applied in regular monitoring of organ recipients. The development of the TXP marks an important advancement valuing health states that are relevant from a patient's perspective during the post-transplant period. The various steps taken in the development of the TXP make it fully patient centered. The TXP constitutes an alternative to conventional PROMs as it can put a single value to health states of solid-organ recipients in the post-transplant phase.

Author contribution

Research design: Shahabeddin Parizi A, Krabbe PFM, Buskens E, Bakker SJL, Vermeulen KM. Writing of the paper: Shahabeddin Parizi A, Krabbe PFM, Vermeulen KM. Performance of the research: Shahabeddin Parizi A, Krabbe PFM, Vermeulen KM. Contributed new reagents or analytic tools: Krabbe PFM. Participated in data analysis: Shahabeddin Parizi A; Vermeulen KM; Gomes-Neto AW; van der Bij W; Blokzijl H; Buskens E; Bakker SJL; Krabbe PFM. Revising the manuscript critically and final approval: Shahabeddin Parizi A; Vermeulen KM; Gomes-Neto AW; van der Bij W; Blokzijl H; Buskens E; Bakker SJL; Krabbe PFM.

Conflict of interest

The authors declare no conflicts of interest. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jclinepi.2021.07.005.

Appendix 1. Information regarding each health item provided for the respondents

Health item	Information
Fatigue	Fatigue refers to tiredness, loss of energy and strength when performing daily activities.
	Levels for fatigue are:
	- Not tired
	- A little tired
	- Quite tired
	- Very tired
Skin	Deals with skin related issues. These can be a fragile, irritated skin, or unpleasant skin alteration, itchiness or bleeding.
	Levels for skin are:
	- Normal skin
	- Slightly fragile or altered skin
	- Moderately fragile or altered skin
	- Severe fragile or altered skin
Worry	Worries are related to the side-effects of treatments after transplantation, functioning of the transplanted organ, future health and being prone to other diseases or infections.
	Levels for worry are:
	- Not worried
	- Slightly worried
	- Worried
	- Highly worried
Self-reliance	Self-reliance is related to the having control over your life, autonomy and being physically independent.
	Levels for self-reliance are:
	- Self-reliant
	- Somewhat dependent
	- Largely dependent
	- Fully dependent

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Activities	Activities are related to leisure activities and being active in work or study.
	Levels for activities are:
	- No problems with activities
	- Some problems with activities
	- Moderate problems with activities
	- Severe problems with activities
Weight	Deals with unwanted weight gain or loss.
	Levels for weight are:
	- No weight gain/loss
	- Some weight gain/loss
	- Moderate weight gain/loss
	- Severe weight gain/loss
Sexuality	Deals with problems such as sexual dysfunction, and intercourse problems.
	Levels for sexuality are:
	- No sexual problems/dysfunction
	- Some sexual problems/dysfunction
	- Moderate sexual problems/dysfunction
	- Severe sexual problems/dysfunction
Stooling	Deals with symptoms such as flatulence/gas, diarrhea or constipation.
	Levels for stooling are:
	- Normal stooling
	- Slight stooling problems
	- Moderate stooling problems
	- Severe stooling problems
Memory	Deals with your memory and ability to concentrate.
	Levels for memory/concentration are:
	- No memory problems
	- Some memory problems
	- Moderate memory problems
	- Severe memory problems

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