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Patient-Reported Outcomes

Development and Validation of an Instrument to Measure Health-Related Out-of-Pocket Costs: The Cost for Patients Questionnaire



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ABSTRACT

Objective: The growth of healthcare spending is a major concern for insurers and governments but also for patients whose health problems may result in costs going beyond direct medical costs. To develop a comprehensive tool to measure direct and indirect costs of a health condition for patients and their families to various outpatient contexts.

Methods: We conducted a content and face validation including results of a systematic review to identify the items related to direct and indirect costs for patients or their families and an online Delphi to determine the cost items to retain. We conducted a pilot test-retest with 18 naive participants and analyzed data calculating intraclass correlation and kappa coefficients.

Results: An initial list of 34 items was established from the systematic review. Each round of the Delphi panel incorporated feedback from the previous round until a strong consensus was achieved. After 4 rounds of the Delphi to reach consensus on items to be included and wording, the questionnaire had a total of 32 cost items. For the test-retest, kappa coefficients ranged from -0.11 to 1.00 (median = 0.86), and intraclass correlation ranged from -0.02 to 0.99 (median = 0.62).

Conclusions: A rigorous process of content and face development was implemented for the Cost for Patients Questionnaire, and this study allowed to set a list of cost elements to be considered from the patient's perspective. Additional research including a test-retest with a larger sample will be part of a subsequent validation strategy.

Keywords: cost measurement, Delphi process, patient perspective, questionnaire development, questionnaire validation, test-retest.

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Introduction

In many countries, the study perspective in most economic evaluations is determined upfront by reimbursement authorities, often explicitly requiring a healthcare payer perspective or the government's and insurers' perspective.^{1,2} The patients' perspective, which is an important part of the societal perspective, is frequently omitted. Healthcare providers and insurers are often expected to report accurate and detailed information on the type and volumes of services through their administrative systems.³ With increasing healthcare costs, providers and insurers are tempted to shift costs to patients in the form of out-of-pocket costs (co-payments, co-insurance, and deductibles).^{4,5} Such cost shifting could increase patients' economic burden, which would not be measured in economic evaluations that only take the provider's or the insurer's perspective. Nevertheless, the importance of having a broader and more comprehensive perspective (eg, societal perspective) that includes the patients' perspective is increasingly being suggested in economic evaluations.^{1,2}

Integrating a patients' perspective means considering an important proportion of out-of-pocket costs and time costs incurred by patients and informal caregivers and their transportation costs.^{1,2}

In this context, using a standardized tool to measure cost for patients is relevant to have a more comprehensive measure of economic costs in economic evaluations. This tool may not provide all the information for a societal perspective, but it will contribute to the aim of many researchers to perform an economic evaluation in a societal perspective by providing a major element (ie, patients) in building up a sound picture. Several self-reported methods exist to collect data on patients' costs, such as diaries, interviews, and retrospective costs questionnaires. Diaries enable a detailed collection of data^{6,7} but they require patients to be very disciplined.⁸ Interviews are time consuming and may be not feasible with a large sample of respondents. Retrospective costs questionnaires allow to simultaneously collect several types of health information-related costs from the same person.^{6,9} Although retrospective cost questionnaires may suffer recall bias,^{10,11} they offer strong advantages such as being easily applied

to a large sample of respondents, requiring minimal effort from patients, and being less costly for researchers.³

Incorporating patients' voices into clinical practice has increased with a shift toward patient-centered care, but measuring patients' costs is still rare and available instruments to do so are rarely standardized and validated.⁷ Such instruments have been developed in the context of research on specific conditions, such as for patients with rheumatoid arthritis,¹² cancer,¹³ food allergies,¹⁴ diabetes,¹⁵ and epilepsy.¹⁶ Condition-specific instruments may miss cost items that could apply to other conditions. The diversity of measurement instruments results in a heterogeneity of cost items being collected.¹⁷ Nevertheless, incorporating the patients' perspective into the economic evaluation of healthcare interventions and the financial burden on patients and families¹⁸ warrants the development of a standardized tool following a rigorous process. The method for developing the questionnaire and the mode of administration can have serious effects on data quality.¹⁰ For this reason, generation of items during questionnaire development requires considerable pilot work to refine wording and content to ensure face and content validity.¹⁹ Items can be retrieved from a number of sources including literature and consultations with experts in the field and with target populations.

There are currently no validated tools supporting the measurement of costs outside of hospital and medical costs covered by the public insurer.²⁰ In addition, with increases in out-of-pocket costs in multiple industrialized countries, there is an increased risk that patients forgo treatments²¹ particularly for ambulatory patients with chronic conditions.^{22,23} This increase in out-of-pocket costs could affect patients' personal, social, family, and professional life and increase their financial burden. Patients' regular use of ambulatory care services involves other costs that may or may not be directly related to the use of services, and that can be recurrent as opposed to those related to an acute condition. In this context, it is relevant to focus specifically on the ambulatory care and measure patients' and their caregivers' out-of-pocket costs.^{24,25}

Thus, the purpose of this study was to develop a comprehensive tool to measure the costs (direct and indirect) of a health condition for patients and their families, the Cost for Patients Questionnaire (CoPaQ). Although it was initially conceived in French, the development was conducted with the objective that the tool would be generalizable to ambulatory care patients in different healthcare systems.

Methods

We conducted a 2-phase design. The first phase consisted of a content and face validation including a systematic review to identify relevant items and a Delphi method to determine elements to include and wording. The second phase was a study of temporal stability to evaluate the reliability of questionnaire variables.

Content and Face Validation Phase

Systematic review

We first conducted a systematic review to identify the direct and indirect cost items in patients and their families, the details of which are the object of another publication.¹⁷ Briefly, the studies were identified in 7 distinct electronic bibliographic databases and in the gray literature. The methodological quality of the included articles was evaluated using the Consensus-based Standards for the Selection of Health Measurement Instruments checklist.^{26–29} In conducting the systematic review,¹⁷ we extracted all cost

elements used in the identified studies to make a preliminary list for the Delphi panel.

Delphi method

Population (eligibility criteria and recruitment process). After the systematic review, content and face validation was completed with a Delphi method. The Delphi panel was composed of 2 categories of experts: patients and researchers. To be eligible to participate as a patient, participants had to meet the following criteria: (1) have used health services during the reference period (ie, the last 6 months), (2) have a condition that requires using healthcare services, (3) have attended a healthcare clinic, and (4) live in Quebec, Canada. Alternatively, the participant could be an informal caregiver to a person meeting those criteria. Participating researchers had to (1) have expertise in cost measurement and (2) live in Quebec. All participants had to be adults (aged 18 years or older); be able to give free and informed consent; have internet access; and own a tablet, smartphone, or computer. Patients living in institutions were excluded from participating in the Delphi.

The Delphi process involved 15 panelists: 9 patients and 6 researchers with a clinical or health economics expertise. The research coordinator identified academics and all those contacted accepted to participate. Patients were recruited through family medicine groups and medical clinics in Quebec. A generic email describing the purpose of the study was sent to the potential panelists. This email invited them to take part in a preparatory meeting before the Delphi and included a description of how the study would be conducted and a consent form to be signed. One week after the generic email sending, a reminder email was sent to those who had not responded. Completion of the first questionnaire was deemed to represent informed consent to participate. All participants were recruited on a voluntary basis from February 2019 to March 2019. The panel size was considered sufficient to reach data saturation in the Delphi.^{30–32}

Format and data collection. We used an online Delphi panel to determine the cost items to retain and then the formulation of the items. The panelists did not have access to the individual responses of other panelists. We followed an iterative multi-round approach by sending by email in each round a questionnaire to the panelists to achieve a consensus. Considering the heterogeneity of the cost items, we assumed that consensus was achieved when agreement level of panelists was 50% or more for each item.^{32,33}

Rounds. The panelists were first presented a list of cost items derived from the systematic review (Table 1) and were asked to independently determine on a dichotomic scale (yes or no) whether each item was relevant. They also identified cost items that were omitted or unnecessary or that could be broken down. In addition, following their suggestions, some items were added or grouped together. This first round of the Delphi panel also included a list of questions to collect demographic and socioeconomic information from the panelists. Although the intent was that these questions would remain in the questionnaire, they were removed from the subsequent versions submitted to the panel, for simplicity.

During the second round, each panelist was asked to independently rate on a 4-point scale (not important = 1; low importance = 2; important = 3; high importance = 4) the cost items selected in the previous round. In this round, principal investigators of the project obtained authorization to include the EQ-5D-5L, a commonly used tool developed by EuroQol to

Table 1. Initial list of items from the systematic review and result of the first round of Delphi.

Item descriptions	% Yes	% No	Decision
Costs for patients			
1) Travel costs	100.00	00.00	Accepted
2) Parking fees	92.31	7.69	Accepted
3) Accommodation expenses to go to the consultations	84.62	15.38	Accepted
4) Medical testing or examinations performed during or after the consultations	76.92	23.08	Accepted
5) Purchase of prescription drugs	92.31	7.69	Accepted
6) Purchase of drugs in pharmacies without a prescription	75.00	25.00	Accepted
7) Expenditures for the acquisition of medical devices	90.91	9.09	Accepted
8) Care services at home	91.67	8.33	Accepted
9) Other costs or medical procedures related to the use of primary care	30.00	70.00	Withdrawn
10) Other treatments or paramedical care	50.00	50.00	Accepted
11) The use of paramedical services during the period of the disease	63.64	36.36	Accepted
12) Childcare or other services for children	58.33	41.67	Accepted
13) Renovating the residence to comply with patient's needs	66.67	33.33	Accepted
14) The time spent during traveling and consultation	75.00	25.00	Accepted
15) The waiting time at the health clinic before the consultation	83.33	16.67	Accepted
Costs for informal caregivers or accompanying persons			
16) Help from an informal caregiver owing to a limited capacity with domestic tasks	66.67	33.33	Accepted
17) Help from an informal caregiver to guide the patient to the health center	91.67	8.33	Accepted
18) Informal caregiver or accompanying persons remuneration	75.00	25.00	Accepted
19) Travel costs	100.00	00.00	Accepted
20) The time spent traveling	83.33	16.67	Accepted
21) The waiting time during the patient consultation	75.00	25.00	Accepted
22) Accommodation expenses	66.67	33.33	Accepted
23) Other expenses	62.50	37.50	Accepted
Costs associated with lost productivity			
24) Loss of income owing to the diminished work capacity or working time	83.33	16.67	Accepted
25) Loss of income for short or long-term work absence	83.33	16.67	Accepted
26) Loss of income owing to the unemployment for sickness	75.00	25.00	Accepted
27) Loss of income owing to other reasons and related to health status	50.00	50.00	Accepted
28) The costs of recruiting and training of a designated alternate	30.77	69.23	Withdrawn
Intangible costs			
29) Impacts on mental health	76.92	23.08	Accepted
30) Global health-related quality of life	61.54	38.46	Accepted
31) Level of perceived stigma	46.15	53.85	Withdrawn
32) Perceived impact of the disease on the daily functioning	61.54	38.46	Accepted
33) Comorbidity (adverse effects or associated diseases)	61.54	38.46	Accepted
34) Pain felt	69.23	30.77	Accepted

measure health-related quality of life.³⁴ Although the EQ-5D-5L section of the questionnaire could not be edited, panelists commented on whether it should be included in the CoPaQ.

The objective of round 3 was to gather panelists' comments on the wording and phrasing of the questions and on the answers' choices. The comments received served as a basis for rewriting some questions after which the draft of the questionnaire was submitted for a review to a communication expert. This expert was told that the questionnaire needed to be readable and understandable by someone with a high-school education level.

Then, we conducted a fourth and last round to collect any additional comments about the questionnaire and its wording. Finally, following suggestions received during the last round to consider financial distress and cost concerns, additional questions were sent to panelists for comments. The additional questions included one about the income category and another one about the financial distress caused by the health status, which was taken from the Comprehensive Score for Financial Toxicity.³⁵

Temporal Stability Phase

To assess the reliability of the questionnaire, 18 new participants were recruited for a test-retest. This number can detect an average effect size and a value of the moderate fidelity coefficient

between 0.41 and 0.60.^{36,37} To be eligible, naive participants needed to meet the same eligibility criteria as patients from the Delphi panel. A research assistant solicited these new participants, explained to them the study, and obtained their informed consent before starting the study participation. They were recruited on August 2019. The questionnaire was administered the first time and then again 2 weeks later and specified both times that respondents should only include costs incurred during the period starting on February 1, 2019, and ending on July 31, 2019 (ie, the same period both times). It is recommended to use a longer time frame when the patients' condition does not cause regular costs. Nevertheless, for conditions that involve very frequent costs, it is best to use a shorter time frame, between 1 and 3 months to minimize recall bias.^{12,38}

Data Analysis

After each round, data were collected, synthesized, and consolidated into an Excel grid. We determined that consensus was achieved when more than 50% of panelists considered the item as relevant in the first round. We carried over those relevant items to the second round. Items from round 2 that were rated "important" or "very important" by a majority of panelists were carried over to round 3. After data from the test-retest were

collected, reliability was assessed by calculating the kappa coefficients and intraclass correlation coefficient (ICC). The ICC statistics is the most suitable and most commonly used reliability parameter for continuous measures.³⁹ ICC are reported with their 95% confidence intervals. The kappa statistics is a measure of “true” agreement for categorical variables. It indicates the proportion of agreement beyond that expected by chance, that is, the achieved beyond-chance agreement as a proportion of the possible beyond-chance agreement.⁴⁰ A sensitivity analysis was conducted by varying the level of consensus to observe the effect on the final list of items. Data analysis was performed using the software package Stata version 13 (StataCorp LLC, College Station, TX).

Ethics

The study protocol was approved by the research ethics committee of the CIUSSS de l'Estrie-CHUS (Project #2019-3102—Écosanté 2).

Results

Systematic Review

The costs elements that were identified from our systematic review are outlined in Table 1, which includes all the elements that were presented to panelists in the first round. Although there was heterogeneity in the cost elements between studies, we decided to make the list as comprehensive as possible. The costs can be categorized as direct and indirect costs to patients and to their caregivers and intangible costs. Direct costs include both direct nonmedical costs and direct medical costs, and other personal expenses were analyzed in the articles. Indirect costs include those associated with travel time or waiting time before consultations and those associated with loss of productivity. Informal caregiver costs identified were related to expenditures incurred because of the patient's limited ability to perform household tasks or as time spent supporting the patient for activities of daily living. Intangible costs were those related to comorbidities and quality of life.

The Delphi Process

Of the 15 people who agreed to participate in the Delphi, 1 patient withdrew at round 1. The baseline characteristics of panelists are presented in Table 2. Of the 34 items suggested in the first round, 31 items were judged relevant by the majority and were kept for the second round (Table 1). On the basis of comments made by some participants, 5 items were added, whereas some items were merged (items 5 and 6 and items 24, 25, and 26, respectively) (Table 1 and Fig. 1). Panelists agreed that the EQ-5D-5L (5 items) should be included in the questionnaire as a replacement for intangibles costs (items 29, 30, 31, 32, 33, and 34) (Table 1).

In the second round, a new list of 32 items (Table 3) was sent to the remaining 14 panelists. All panelists returned the completed questionnaires with their evaluation of the importance of each item. At the end of this round, 31 items (Table 3) that obtained 50% or more of scores 3 (important) or 4 (high importance) were kept for the following round. One item was deleted because fewer than 50% of participants rated it 3 or 4.

In the third round, of 14 panelists, 11 provided comments and suggestions aimed at improving understanding with better wording of the questions. A researcher did not respond to the follow-up email, and 2 patients misunderstood this step and completed the questionnaire instead of providing comments and

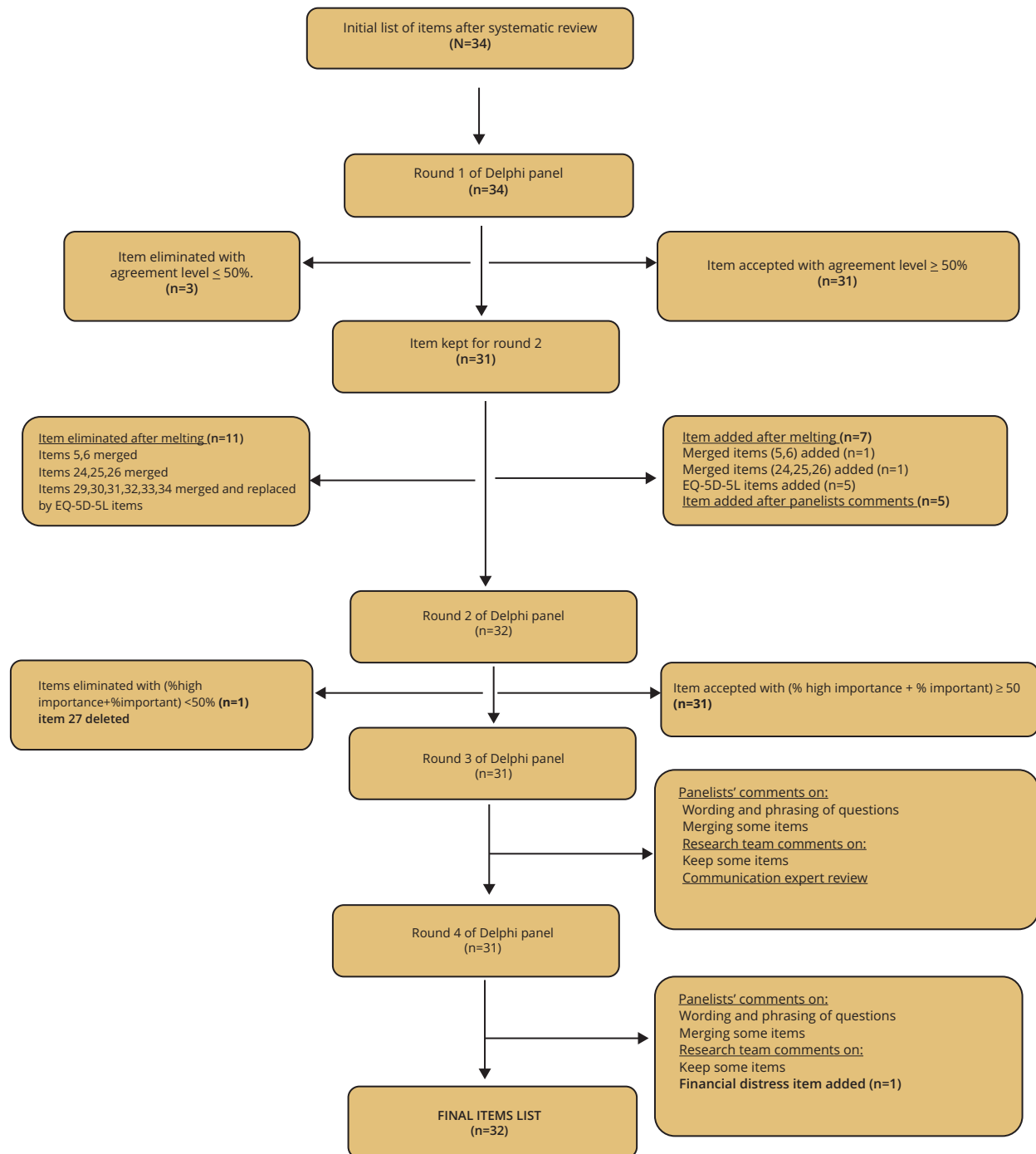
Table 2. Characteristics of participants.

Variables	Characteristics of panelists	Characteristics of test-retest participants
Stakeholder		
Researchers	6 (42.9)	
Patients	8 (57.1)	
Sex		
Women	9 (64.3)	13 (72.22)
Men	5 (35.7)	5 (27.78)
Background		
PhD	8 (57.1)	11 (61.11)
Master's degree	3 (21.4)	3 (16.67)
Bachelor's degree	1 (7.1)	4 (22.22)
High school	2 (14.2)	
Employment		
No	2 (16.7)	2 (11.11)
Yes	10 (83.3)	16 (88.89)
Marital status		
Single	2 (16.7)	4 (22.23)
Divorced	2 (16.6)	1 (5.56)
In a relationship	3 (25.0)	7 (38.88)
Married	5 (41.7)	5 (27.77)
Widowed		1 (5.56)
Geographical area		
Rural area		1 (5.56)
Urban area		17 (94.44)

Values are number (percentage).
PhD indicates Doctor of Philosophy.

suggestions. Comments from the third round led to changes in wording, adding instructions and details, and rearranging and splitting question items. In sum, 6 comprehension problems were identified. First, the term “primary care” was not understood consistently by respondents. They recommended giving a definition in the final questionnaire or replacing it with “ambulatory care.” Second, several respondents suggested distinguishing between acute and chronic care expenditures. Third, some respondents mentioned that items about additional costs, informal caregivers, and paramedical care were unclear and needed more clarifications. A fourth comment was about ensuring that time spent on travel not be counted twice if the time lost is working time already quantified by the loss of income. Finally, panelists recommended merging some items: travel costs and parking fees, using paramedical services and other treatments, and mobility and the person's autonomy (problems related to washing or dressing alone and current activities).

Given the quantity of comments received in the third round and the changes suggested by the communication expert, we decided to conduct a fourth round, for which we received additional comments from 8 panelists. Three panelists reported not having any comment and 3 panelists (3 of 14) did not respond despite the follow-up email. Revisions were mainly undertaken to overcome comprehension difficulties encountered by answering the CoPaQ. A final version of the CoPaQ was produced (the CoPaQ is available from the authors on request). CoPaQ's items were regrouped into 7 categories related to (1) patient costs, (2) average time spent on accessing medical services, (3) financial distress, (4) loss of productivity, (5) informal caregivers' or accompanying persons' costs, (6) time spent by informal caregivers or accompanying persons, and (7) EQ-5D-5L questionnaire.

Figure 1. Flowchart of items reduction.

In addition, there is a section to collect respondents' characteristics such as sex, age, education, working status, and marital status.

Results of the Test-Retest

The baseline characteristics of test-retest participants are presented in [Table 2](#). All 18 participants completed both the baseline and the follow-up 2 weeks later. Kappa coefficients varied from -0.11 to 1.00 (median = 0.86) and were poor (2 items), fair (1 item), moderate (1 item), substantial (1 item), and almost perfect

(7 items) ([Table 4](#)). ICC varied from -0.02 to 0.99 (median = 0.62) and were slight (3 items), acceptable to good (1 item), and excellent (4 items) ([Table 4](#)).

Sensitivity Analysis

With an agreement level set at 50% or more, only 3 items of 34 (8.8%) were withdrawn. If this threshold was set at 75% or more, 15 items of 34 (44.1%) would be withdrawn. Finally, if a perfect agreement was expected (ie, 100%), 32 items of 34 (94.1%) would be withdrawn.

Table 3. Results after round 2.

Items description from initial list as noted in Table 1	% Not important	% Low importance	% Important	% High importance	% Important + high importance
Costs for patients after the reimbursements received					
1) Travel costs	-	-	35.71	64.29	100.00
2) Parking fees	-	-	14.29	85.71	100.00
3) Purchase of prescription drugs-related with the illness	-	-	7.14	92.86	100.00
4) Purchase of drugs in pharmacies without a prescription	7.14	35.71	35.71	21.43	57.14
5) Care services at home	-	-	14.29	85.71	100.00
6) Expenditures for the acquisition of medical devices	-	7.14	21.43	71.43	92.86
7) Renovating the residence to comply with patient's needs	-	21.43	21.43	57.14	78.57
8) Accommodation expenses to go to the consultations	7.14	7.14	35.71	50.00	85.71
9) Time spent looking for a treatment or appointment	14.29	35.71	35.71	14.29	50.00
10) The waiting time	7.14	21.43	35.71	35.71	71.42
11) The time spent during traveling and consultation	-	7.14	35.71	57.14	92.85
12) Medical testing or examinations performed during or after the consultation(s)	-	-	21.43	78.57	100.00
13) Childcare or other services for children	-	28.57	35.71	28.57	64.28
14) The use of paramedical services during the period of the disease	7.14	-	42.86	50.00	92.86
15) Other treatments	-	7.14	28.57	64.29	92.86
16) Other expenses	-	35.71	42.86	21.43	64.29
Costs for informal caregivers or accompanying persons					
17) Training	7.14	21.43	28.57	42.46	71.03
18) Travel costs	-	-	35.71	64.29	100.00
19) Parking fees (if different from the patient's)	-	-	28.57	71.43	100.00
20) Help from an informal caregiver owing to a limited capacity with domestic tasks	7.14	14.29	21.43	50.00	71.43
21) The time spent traveling	-	7.14	14.29	78.57	92.86
22) The waiting time during the patient consultation	-	-	28.57	71.43	100.00
23) Accommodation expenses	7.14	-	50.00	42.86	82.86
24) Other expenses	7.14	28.57	35.71	28.57	64.28
Costs associated with lost productivity					
25) Loss of income	-	7.14	7.14	85.71	92.85
26) Loss of income owing to other reasons and related to health status	21.43	14.29	21.42	42.86	64.28
Intangible costs perceived or experienced (impact on health-related quality of life) from the EQ-5D-5L					
27) Mobility (problems related to walking)	7.14	7.14	50.00	35.71	85.71
28) Autonomy of the person (problems related to washing or dressing alone).	7.14	-	42.86	50.00	92.86
29) Current activities (eg, work, studies, domestic work, family, or hobbies)	14.29	14.29	14.29	57.14	71.43
30) Pain/discomfort (level of pain felt or discomfort)	7.14	-	28.57	64.29	92.86
31) Anxiety/depression (level of anxiety or depression)	14.29	-	21.43	64.29	85.72

Note. Not important = 1; low importance = 2; important = 3; high importance = 4.

Discussion

In this study, we developed a tool to measure the costs of living with a health condition for patients and their caregivers. Each round of the Delphi panel incorporated feedback from the previous round until a consensus was achieved about the most important cost items and how the questions should be formulated. Consensus on some cost items was achieved early, whereas other items were refined during the Delphi rounds. This process helped increase these items' understanding and reduced the overlap between them. The questionnaire (CoPaQ) results from the diverse expertise of the participants.

The Delphi method has been used in developing other measurement tools.^{41,42} In our study, the experts were health economists and patients. Including patients as actors in research

projects is in line with the philosophy of the Canadian Strategy for Patient-Oriented Research.⁴³ It adds a perspective that is important and that was missing in the development of other instruments.⁴⁴

One of the challenges of the Delphi process is the assessment of consensus and determining on which basis the process can be ended. Indeed, it is not required to have a perfect consensus because the concepts and items are not always clear for all panelists and that subjectivity remains. We followed the approach of Thorn et al,⁴⁴ which suggests that it is not a requirement of the Delphi process to achieve consensus for all items, but it is essential that panelists agree on a reduced number of items to be most important. As a result, we reformulated, separated, or grouped some items and retained those for which the majority agreed. The CoPaQ is a retrospective self-reported questionnaire to collect

Table 4. Reliability statistics of CoPaQ.

Kappa statistic of CoPaQ								
Question number from CoPaQ	Items (item number from Table 3)	Kappa		Kappa value (k)	Standard error	Z	Prob>Z	Kappa interpretation
		Agreement (%)	Expected agreement (%)					
1.2	Means of transportation (item 1)	44.44	29.01	0.217	0.133	1.630	0.051	Fair
1.4	Parking fees (item 2)	94.44	62.35	0.852	0.233	3.660	0.000	Almost perfect
1.7	Purchase of prescription drugs-related with the illness (item 3)	100	55.56	1.000	0.236	4.240	0.000	Almost perfect
1.8	Purchase of drugs in pharmacies without a prescription (item 4)	83.33	67.28	0.491	0.203	2.420	0.008	Moderate
1.13	Other expenses (item 16)	100	89.51	1.000	0.236	4.240	0.000	Almost perfect
1.14	Other treatments (item 15)	88.89	50	0.778	0.236	3.300	0.001	Substantial
1.15	Childcare or other services for children (item 13)	100	89.51	1.000	0.236	4.240	0.000	Almost perfect
1.16	Other expenses (item 16)	5.56	10.19	-0.052	0.030	-1.710	0.957	Poor
3.1	Loss of income (item 25)	100	52.47	1.000	0.236	4.240	0.000	Almost perfect
5.1	Costs for informal caregivers or accompanying persons (item number not defined)	94.12	56.06	0.866	0.240	3.600	0.000	Almost perfect
5.2	Training (item 17)	100	68	1.000	0.447	2.240	0.013	Almost perfect
5.6	Other expenses (item 24)	20	28	-0.111	0.199	0.560	0.712	Poor

ICC statistics of CoPaQ					
		ICC value	95% CI		ICC interpretation
1.3	Travel costs (item 1)	0.937	0.843	0.976	Excellent
1.5	The waiting time (item 10)	0.381	-0.081	0.711	Slight
2.1	The time spent during traveling and consultation (item 11)	0.415	-0.048	0.731	Acceptable to good
2.2	Time spent looking for a treatment or appointment (item 9)	-0.022	-0.486	0.451	Slight
3.2	Loss of income (item 25)	0.286	-0.478	0.822	Slight
6.1	The time spent traveling (item 21)	0.998	0.985	0.999	Excellent
6.2	Help from an informal caregiver owing to a limited capacity with domestic tasks (item 20)	0.822	0.015	0.987	Excellent
6.3	The waiting time during the patient consultation (item 22)	0.996	0.964	0.999	Excellent

CI indicates confidence interval; CoPaQ, Cost for Patient Questionnaire; ICC, intraclass correlation coefficient.

patient's costs data. Retrospective questionnaires can be administered through 4 methods face-to-face interviews, telephone interviews, postal surveys, and internet surveys.

Economic evaluations can be undertaken from a number of different perspectives. Traditionally, there are 3 perspectives the healthcare sector, the government or insurance, and the society.^{2,4} Including patients' out-of-pocket costs in the analysis is important when health economic guidelines require a societal perspective.² The societal perspective can be particularly relevant because it is the broadest and most comprehensive perspective and incorporates all costs and all effects from both the healthcare sector and patients' perspective.² It includes time costs, transportation

costs, and changes in productivity and consumption and other effects in non-healthcare sectors.^{1,2} Researchers can play a role in bringing patient costs into economic evaluations and potentially into health policy allocation decision. That may be defined by the jurisdiction of the decision maker and the applicability of the decision.¹

The indirect cost, which relates to the informal caregiver and the lost unpaid work of the patient and the companion, could be determined by using the human capital approach and on the basis of the time spent to travel, time spent in the hospital, and personal salary per hour.⁴⁵ The human capital approach involves multiplying days off work owing to illness by the individual's salary

level.⁴ The personal salary per hour will be calculated by obtaining the total salary of the patient and his or her companion per month and dividing it by the normal total number of working days per month. Then, it will be divided by normal working hours per day. Finally, the salary per hour will be multiplied by the number of hours spent to travel and at hospital during each visit.⁴⁵ The friction-cost method is an alternative to the human capital approach because it allows more realistic estimates of productivity costs to be calculated.⁴⁶

It is often unclear what is truly direct and indirect costs of illnesses and treatments because different components of costs and effects could be deemed to be “direct” depending on the perspective of the analyses.¹ According to Neumann et al,¹ with this categorization, the concepts of “direct” and “indirect” costs become obsolete because it is difficult to distinguish the differences between these kinds of costs. For these reasons, it is recommended to categorize the costs in medical or nonmedical costs.

We have also requested and received approval to use the EQ-5D-5L questionnaire during the development of the CoPaQ.³⁴ Nevertheless, to integrate the EQ-5D-5L in their projects, future users of the CoPaQ should ask for approval from the EuroQol group, which can be easily done through their website. Moreover, the issue of financial toxicity was included to the CoPaQ. In fact, financial distress and cost concerns are common among patients because the expenses and loss of income can negatively impact patients and their families.^{35,47,48} In addition, the costs of some nonmedical services are often omitted although they are related to the health condition. These costs can affect the patients' financial health. For this reason, they were also included in the CoPaQ.

A first step of temporal consistency validation was undertaken with 18 patients in CoPaQ's development process. The pilot results of the test-retest suggested that the CoPaQ had a good reliability and gives consistent results between the 2 measurement periods. Nevertheless, the small sample limits the interpretation of these preliminary results. To pursue the validation of the CoPaQ, next steps include testing various aspects of the validity (eg, cross-cultural validity) of the questionnaire to ensure that it adequately measures patients' costs for a health condition. Further validation should be subsequently conducted according to Consensus-based Standards for the Selection of Health Measurement Instruments properties.²⁶

Strengths and Limitations

The CoPaQ has multiple strengths. First, its development followed a rigorous process as described in this study. The stability of the Delphi panel was good with low attrition, and this study benefited from panelists' strong involvement. Although the Delphi process took place over the course of 4 rounds, only 1 panelist was lost at follow-up. Panelists were able to express their point of view, and the confidentiality of their comments was maintained. The Delphi process ensured the consistency of the statements, which should significantly reduce the scope effect problem. Second, our approach enabled identifying the cost elements that should be generalizable and developing a comprehensive tool which could be applied and used anywhere. Third, the CoPaQ's level of detail is quite high. A cultural adaptation of the questionnaire was foreseen.

This study and the CoPaQ also have some limitations. First, the costs were not categorized, and the CoPaQ does not yet provide an explanation of how the costs should be calculated once the data are collected. Second, the average completion time and the health condition reference period were unknown because this information was not requested from the panelists during the Delphi process. This limitation could be explained because we wanted to

obtain panelists' opinions about costs items, not to complete the questionnaire. The CoPaQ may be considered by some respondents to be too long to complete. We tested the CoPaQ with a 6-month timeframe which could lead to participants forgetting small ticket items. Nevertheless, the timeframe can easily be determined by researchers to align with their study objective.” Finally, the pilot test-retest was conducted with a small sample ($n = 18$), which limits the interpretation of the preliminary results, and the education level of respondents was higher than that of the average population. Still, results suggested that the CoPaQ has a good reliability and gives consistent results between the 2 measurement periods. Nevertheless, a new test-retest should be conducted with a larger sample and heterogeneous participants.

Study Implications and Future Research

The CoPaQ may be used by researchers who wish to capture out-of-pocket costs of a condition for patients and their caregivers, to standardize how patient costs are collected. This tool could give more information such as the costs associated with informal caregivers and could be used to cost health interventions. In addition to providing a patient perspective, the results of this study could be analyzed in relation to clinical or behavioral variables, such as adherence to treatment. The financial consequences for patients could affect not only adherence but also the choices of the treatments made by patients. The tool that we developed could be used to measure and compare the patients' costs associated with different treatment options and incorporated into decision aids for patients. The CoPaQ could be used in clinical practice to identify patients who are overwhelmed by the economic burden to begin conversations about their health-related costs.⁴⁹ The use of a reliable and validated questionnaire is a very important methodological aspect for research.⁵⁰ Future work could include the development of a CoPaQ' user guidelines. Another test-retest with a larger sample and a varied patients' groups would contribute to validate the CoPaQ's reliability.

Conclusion

A rigorous process of content and face development (systematic review and Delphi method) was implemented for the CoPaQ, and this study allowed to set a list of cost elements to be considered from the patient's perspective. This is an important tool to measure the financial consequences that health conditions may have on patients.

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