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A qualitative analysis and development of a conceptual model assessing financial toxicity in cancer patients accessing the universal healthcare system

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Abstract

Purpose

This paper illustrates a conceptual model for a new Patient Reported Outcome measure (PROM) aimed at measuring financial toxicity (FT) in oncological setting in Italy, where citizens are provided universal health care coverage.

Methods

Focus groups with overall 34 patients/caregivers in three different Italian centres (from Northern, Centre and Southern Italy) and an open-ended survey with 97 medical oncologists were undertaken. Transcripts from focus groups and the open-ended survey were analyzed to identify themes and links between themes. Themes from the qualitative research were supplemented with those reported in the literature; concepts identified formed the basis for item development, that were then tested through the importance analysis (with 45 patients) and the cognitive debriefing (with other 45 patients) to test relevance and comprehension of the first draft PRO instrument.

Results

Ten domains were extracted by analyzing 156 concepts generated from focus groups and the open-ended survey. After controlling for redundancy, 55 items were generated and tested through the importance analysis. After controlling comprehension and feasibility through cognitive debriefing interviews, a first version of the questionnaire consisting of 30 items was devised.

Conclusions

This qualitative study represents the first part of a study conducted to develop a new PROM to assess FT in Italy, by using a bottom up approach that makes the most of patients' experiences and the health system analysis.

Keywords

Financial Toxicity, Qualitative research, Conceptual model, Patient experience, Cancer

Declarations

Funding. The project is supported by Fondazione AIRC (Associazione Italiana per la RicercasulCancro), a non-profit Italian charity, IG 2017 Id 20402

Conflicts of interest

SR has received personal fees from CSL-Behring and GlaxoSmithKline Foundation. MDM has received personal fees from Bristol Myers Squibb, Merck Sharp & Dohme, AstraZeneca, Janssen, Astellas, Pfizer, Eisai, Takeda. FE has received personal fees from Amgen, Bristol Myers Squibb, Incyte, Orsenix and Takeda. CJ has received personal fees from Amgen, Astra Zeneca, Biogen, Boehringer Ingelheim, Celgene, Gilead, GSK, Ipsen, Janssen-Cilag, Takeda and Sanofi. VM has received personal fees from Bristol Myers Squibb and Italfarmaco; a member of his family is employee in Bayer. CV has received personal fees from from Baxter, MSD, Novartis, Sanofi, Sanofi Genzyme. FP has received personal fees from Bayer, Ipsen, Astra Zeneca, Bristol Myers Squibb, Sandoz, Incyte, Celgene, Pierre Fabre, Janssen-Cilag. The other Authors have no conflict to disclose.

Ethics approval (include appropriate approvals or waivers) The protocol has been approved on October 10, 2017 by the Ethical Committee of the coordinating Institution and subsequently by the Ethical Committees of all participating Institutions.

Consent to participate (include appropriate statements) All caregivers and patients received detailed information on the study activities, signed the consent form and authorized to the use of their data according to European Directive n. 679/2016 and the Italian law (DL 196/2003) on the protection of personal data.

Consent for publication (include appropriate statements) No consent was seek for publication because no personal information that can be associated to a single patient is being published.

Availability of data and material (data transparency) Data are available on request to the corresponding Author.

Code availability (software application or custom code) Not applicable.

Authors' contributions

FP obtained funding. SR, JB, CG and FP planned qualitative and statistical analysis and drafted the protocol. SR led all the focus groups and performed qualitative analyses. AG did literature search and review. JB, MDM, DG, VM, AS, LS and FP allowed patients data collection. All Authors participated in writing and approved the study protocol. SR, FE, MDM, CG and FP drafted the manuscript. All authors contributed to the manuscript and approved the final version.

INTRODUCTION

Financial toxicity (FT) is increasingly being recognized as a major concern for cancer patients and their families.[5, 8, 16, 33] Cancer patients may experience working problems and work-related issues, with major consequences on income, as well as out-of-pocket costs associated with treatment, and several studies have indicated higher frequency of poverty and limited resources.[3, 9] FT is also associated with higher distress, poorer health-related quality of life (HRQoL) and reduced compliance with cancer treatment.[28, 33] Most of the research on this subject area stem from patients living in countries where all the aspects related to treatment and care are managed by private medical care. Indeed, there is paucity of data on the impact of FT for patients living in countries with public healthcare systems.[21]

The COmprehensive Score for financial Toxicity (COST) questionnaire is the first Patient- Reported Outcome Measure (PROM) to measure FT and was developed for cancer patients in the United States.[4] However, as the recent review of Rotter et al. pointed out, an in-depth description of FT cannot be separated by a careful consideration of the socio-cultural context where the care and treatment are applied.[25] Therefore, applicability of FT measures across countries with different healthcare systems may be challenging and development of such measures could best take place in the country where such tools are planned to be implemented.[20] This country-based approach could increase content validity of the measure by ensuring that the initial item generation, fully considers the socio-economic context as well as the peculiarities of the given healthcare system.

On this ground, in 2018, we launched the PROFFIT Study (Patient Reported Outcome for Fighting Financial Toxicity), a multicenter, observational study, aimed to develop a new PROM that could explain occurrence, severity, and outcomes of FT in Italian cancer patients. [24]

We herein report the results of the initial qualitative analysis aiming to illustrate a conceptual model for a new PROM measuring FT in oncological setting in Italy.

METHODS

The study protocol was registered on Clinicaltrials.gov (NCT03473379) and has been previously published.[24] The overall project is being conducted according to the methodology delineated by the International Society for Pharmacoeconomics and Outcome Research (ISPOR) Patient Reported Outcomes Content Validity Good Research Practices Task Force. [18, 19]

Results of the qualitative analysis reported in this paper refer to tasks 1 (Concept elicitation and coding) and 2 (Item generation and analysis) of the protocol. [17] The actions planned in the qualitative analysis are summarized in **Table 1** and illustrated in **Fig.1**.

Where applicable, the reporting is in line to the Standards for Reporting Qualitative Research (SRQR) in clinical setting and the Consolidated criteria for reporting qualitative research (COREQ).[15, 32]

Study Design

Theoretical framework

The study design for the qualitative development phase of the study (Task 1 and Task 2) was based on phenomenology theory using an interpretive/constructivist approach for the analysis.[22, 30] The phenomenological framework accentuates the “direct experiences” reported by patients and/or caregivers while the interpretive/constructivist approach was used with the precise intent to disentangle the FT in all its dimensions by involving a constant comparison method with open coding.[29, 31] These two methodologies permitted to interpret the descriptions of patients and translate these descriptions into a measurement approach for quantifying the occurrence, the level of severity, and consequences of FT in cancer treatment.

For Task 1 (*Concept elicitation and coding*) the following actions were planned: (a) literature review, (b) focus groups with patients and caregivers, (c) collection of experts’ opinion (oncologists associated with AIOM (Associazione Italiana Oncologia Medica) and CIPOMO (Collegio Italiano dei Primari Oncologi Medici Ospedalieri). We involved different type of participants because we

wanted to maximize the heterogeneity of sources in order to better understand the complexity of this social phenomenon.

For Task 2 (*Item generation and analysis*) the following remaining actions were developed: (d) item development, (e) importance analysis, (f) cognitive interviews for testing the level of comprehension and relevance of items developed.

Actions planned to gather quantitative and qualitative information to develop the first draft of the FT questionnaire are summarized in Table 1.

Researcher characteristics and reflexivity

Reflexivity is the capacity to reflect upon one's actions and values during the research, when producing data and writing accounts, and to view the beliefs we hold in the same way that we view the beliefs of others.[27] Reflexivity is a characteristic of the qualitative research and establishes the researchers' integrity, which is part of good practice.

In the current study, researcher's reflexivity involved a methodical approach to entering researcher notes, such as commenting on others' experiences and points of view, and asking questions to elicit additional information and provided adjunct data.

For focus groups, researcher reflections also included how they were conducted including timing, behavioral cues (e.g. body language) and any links between concepts discussed within each focus group and between all four focus groups. A local assistant was also present at all focus groups to take notes on interactions and relevant behavioral cues.

Data collection strategy

Task 1

Three sources of information were collected: literature review (action a), experts' opinion (action b), and focus groups with patients and caregivers (action c). We selected participants using a convenience sampling based on accessibility and availability. Data collection continued until saturation was achieved. To reach saturation for focus groups, the size of the group included between 6 and 12 participants (with current or past experience of cancer, and who did not know the moderator before), so that the group was small enough for all members to talk and share their thoughts, and yet large enough to create a diverse group.[10, 17]

For open-ended survey, saturation was reached when the ability to obtain additional new information was attained, and when further coding was no longer feasible. We intentionally involved a higher number of participants for the survey phase to limit a potential *shaman effect*, that occurs when someone with specialized information on a topic can overshadow the data, whether intentionally or inadvertently.[26]

Initially, Task 1 also included supplementary interviews with patients and caregivers. Because action *b* and action *c* allowed the gradual achievement of data saturation, interviews were not performed and this change represents a non-substantial protocol deviation (i.e. change in the documentation used by the research team for recording study data).

Task 2

While item development (action d) involved all the expert Steering Committee, for importance analysis (action e), and cognitive interviews (action f) consecutive patients were recruited through three hospitals located in 3 diverse regions of Italy: Napoli (Southern Italy, *Istituto Nazionale dei Tumori*, coordinator), Roma (Central Italy, *Istituto Nazionale Tumori "Regina Elena" - IFO*) and Torino (Northern Italy, *Azienda Ospedaliera Ordine Mauriziano*).

Patients were eligible if they were adult (>18 years), had a histologically or cytologically confirmed diagnosis of any type of solid or hematologic malignancy, were receiving or had terminated not later than 3 months an anticancer medical treatment (chemotherapy, target agents, immunotherapy, hormones) or radiation treatment, or a combination and had no major cognitive dysfunction or psychiatric disorders. Patients were also required to provide written informed consent.

Data analysis

Task 1

Action (a)

Literature review grounded on four databases (PubMed, Embase, Scopus, CINAHL) and on publicly available documents from Italian institutions or associations. As a conceptual framework to systematize the collected results the review of Altice et al. on FT was used where the authors identified three main categories of financial burden: material conditions, psychological responses, and coping behaviors.[1] This review had the merit to develop a typology for conceptualizing financial hardship in cancer survivors by identifying the material conditions that arise from the increased out-of-pocket expenses (material condition), the psychological reaction to the increase in personal expenses (psychological responses), and the coping behaviors that patients use to deal with their medical care while experiencing increased household expenses (coping behaviors). We used this typology to guide our investigation and to better understand our results with our participants during the focus groups and survey's phase.

Actions (b) and (c)

Collection of experts' opinion was performed by web and e-mail surveys dealing with members of four Italian Associations of health workers in oncology setting: three of which involving oncologists

(AIOM, CIPOMO). Four focus groups with patients and caregivers (two in Napoli, one in Torino and one in Roma) were performed, moderated by the same skilled psychologist (SR) with the help of an assistant moderator. Sessions were audio-recorded and transcribed verbatim.

Four distinct main stages are described in this paper: the decontextualization (by identifying meaning units and creating codes), the recontextualization (by comparing codes with original data), the categorization (by condensing meaning units and assuring triangulation of data with the involvement of some researchers of the steering group) , and the compilation (by drawing realistic conclusions). [ref vedi commento]. The software program Atlas.ti version 5.0 was used to organize coding and description of analyses.

Task 2

Action (d)

The data analysis strategy for *Action d* was content analysis (see Task 1, *point b* and *c*). The words and phrases of the study participants, recorded and synthesized, served as the pool of data to identify patterns or clusters of information and were used to inform the overall structure of the instrument, including content, questions categories, response options, and potential subscale or domain structure. This permitted to organize and elicit meaning from the data collected and to draw realistic conclusions from it.

Four team members, including the focus group moderator and the PI (SR, FP), helped to develop a coding dictionary of categories and subcategories. Disagreements were discussed with all the steering committee, internally. The final categories and subcategories were examined across gender, participant type (i.e patients, caregivers, health professionals) in order to assure a good level of heterogeneity of all contents emerged and to guarantee applicability of instrument content and structure. The initial set of items, and response options were developed based on themes and

subthemes emerged in focus groups and an open-ended survey, with the participants' words and concepts used to inform wording.

Action (e)

A quantitative data approach was used to define the final pool of items to select. All the items reaching a score of importance above the median for each category were retained for the draft of the preliminary version of the instrument.

Action (f)

Interpretation of the items was made following four main principles: 1-comprehension of the question (*what does the respondent believe the question to be asking?*), 2-retrieval from memory of relevant information (*what types of information does the respondent need to recall in order to answer the question?*), 3-decision processes (*Does the respondent devote sufficient mental effort to answer the question accurately and thoughtfully?*), and 4-response processes (*was the options scale easy to understand?*).

Cognitive interviews were analyzed by content analysis, first. Then, a quantitative statistical approach was applied in order to discriminate items with an unsatisfactory level of adequacy in one of the 4 dimensions (i.e. adequacy as low for more than 5% of participants).

All sociodemographic, clinical data and quantitative data were described using SPSS Version 23.

RESULTS

Task 1

Action (a)

Literature search produced 77 articles in English language and 3 documents in Italian language. The list of selected papers and documents is reported in **the Appendix**.

As expected, most papers were from countries without universal health service and focused on feelings of FT and their consequences on the HRQoL.

Action (b) and (c)

Overall, 34 patients and caregivers participated in four focus groups between February 2018 and March 2018 (**Table 2 - left column**). All contacted patients were able to participate.

Ninety-seven medical oncologists participated in the survey phase; 44% of them were females; 27% younger than 40 and 42% older than 55; 51% working in Northern, 28% in Central and 21% in Southern Italy.

Patients and health professionals highlighted the role of determinants of FT together with consequent behaviors. According to responses ten major themes were identified, corresponding to 156 concepts, that remained stable across all four focus groups and the open-ended survey and across age, gender, and living place. The ten identified themes were as follows:

- 1) *Bureaucracy*. Bureaucracy undermines the integrity of the medical care process. Lengthy procedures and red tape can act as deterrents for patients who, at the mercy of formalism and inefficiency, lose time, replicate medical consultations, spend additional money to speed up the diagnostic process (consulting more than one hospital, moving in a different town or even different regions causing a stretching of the timeframe in reaching the diagnosis/treatment).
- 2) *Medical access issues*. Patients often have to deal with long waiting lists, unclear information, lack of administrative personnel supporting the diagnostic process, that all cause

distress and dissatisfaction. To overcome these problems and reduce time constraints, patients can choose private treatment, resulting in high out-of-pocket costs (particularly when the cost is associated with surgery or invasive medical examinations).

3) *Domestic economy*. Cancer and its treatment can determine significant changes in family life and routines, with important repercussion on costs due to the difficulties or even the impossibility of maintaining family tasks (e.g. running a household, child care). Direct implications of that are costs related to housekeeping, babysitting/caregiving and/or loss of earnings due to the time needed for organization or direct provision of household activities

4) *Emotion*. Out-of-pocket costs lead to significant financial burden for patients and their caregivers, resulting in increased psychosocial distress, diminished patient outcomes, and poorer quality of life.

5) *Family*. The impact of costs for cancer has been identified at three different levels: (1) increase in family financial expenses as a result of travels and relocation, (2) decrease in family income produced by interruption of work or unemployment, and (3) insufficient financial support to deal with expenses and with caregivers responsibilities.

6) *Job*. Cancer changes working prospective dramatically both for patients and family members with a significant economic impact on personal/family income. Experiences can differ significantly from a number of working days lost to leaving work and from changes in functions and activities (more frequent in the public sector) to a complete loss of career opportunities (more frequent for self-employed patients).

7) *Health workers*. Poor or lacking communication among health professionals is highly associated with patients' FT. First, clarity of information is the lynchpin to reduce time and, consequently, there are costs associated with any supplementary and unnecessary consultations during the initial diagnostic journey. Second, absent or poor communication between the General Practitioners (GPs) and medical hospital staff has the potential to

increment the use of redundant medical visits and to produce repetitive examinations, with a growth of out-of-pocket costs. Patients report that medical network in and out the hospital appears often weak and disorganized.

8) *Welfare state*. Although the national public health system delivers primary, specialist and in-patients treatment, additional costs may incur as a result of the cancer treatment and outcomes (e.g. subsequent to adverse reactions or cancer stage). A number of patients reported several expenditures related to health care and social services. The first one concerns the additional services not covered by the public system such as oncological rehabilitation (physical, psychological, nutritional, cognitive and sexual), palliative care, private consultations, physiotherapy, or dental care and other expenses associated with medical and paramedical products not free of charge for cancer such as the use of supplements, or skin lotions that patients may use to reduce adverse reactions of cancer treatment. The additional social services' expenditures are due to a partial or no access to home care, migration across Italian regions and consequent accommodation and travel costs, patients and caregiver's reduced income or job loss.

9) *Free time*. The growth of out-of-pocket costs determine a significant reduction of free time and pleasure activities, both for patients and caregivers. FT can reduce the ability of people to take control of their lives, reduce social interactions and social life, causing a limitation of leisure activities, such as going out for a meal and reductions to hobbies

10) *Transportation*. Transport, parking, housing when needed, and the time spent managing the financial aspects of cancer care represent an important cost for patients

Task 2

Action (d)

Overall, 156 concepts were distributed among the 10 thematic libraries and itemized. After the Steering Committee meeting, elimination of duplicates resulted in 55 items, distributed across the ten

thematic libraries, with few changes in the attribution of items to themes decided by the Steering Committee. **Table 3** (left columns) summarizes the distribution of initial concepts and selected items within the ten thematic libraries.

Action (e)

Importance analysis was conducted in January and February 2019 with 45 patients (**Table 2**, middle column). Responses of one patient were excluded because of the high rate of missing answers (29/55). Four isolated missing responses (one each for four different patients) were substituted with the mean value of importance score given by the remaining patients. Therefore, the importance score for each item potentially ranges between 44 (not important at all) to 176 (maximum of importance). The overall median value was 111, ranging from 77 to 161. **Table 3** (right columns) summarizes the median (interquartile range) importance scores by thematic libraries. After importance analysis, 29 items scoring at or above the overall median, plus one more item (selected for decision of the Steering Committee although below the median) were retained for subsequent cognitive interviews.

Action (f)

Cognitive debriefing was conducted in April and May 2019, with 45 patients as planned (**Table 2** right column). No problem was found for retrieval from memory of relevant information, decision processes and response processes. On the contrary, the understanding rate for 10 items was problematic for more than 5% of recruited patients; therefore, the content of 9 items was slightly modified, taking into account suggestions given by the patients, mainly relating to ambiguities or lack of specificity. We decided not to include a single recall period as this approach resulted the best to describe the FT phenomenon.

DISCUSSION

This qualitative study represents the first part of the PROFFIT Study, conducted to develop a new PROM to assess FT in Italy. Although other PROMs for FT exist in literature and have been translated also in Italian language, we think that FT is a specific construct that can be conceptualized only evaluating the specific socio-economic environment and the structure of the health care system of the country of origin. This is the reason why a cross-cultural translation of other measures was considered not entirely appropriate as other measures might not be sensitive to relevant issues in health systems (e.g. as the case of a health system where co-payment for anticancer drugs and other healthcare costs is required). [23] This perspective seems to be in line with the recent four-step approach addressing the issue of FT in patients with cancer proposed by Desai and Gyawali.[5]

Nevertheless, the current research offers insights to analyze FT that are new in the literature, and provides a research model that goes beyond a specific country. It is expected, indeed, that in countries characterized by private healthcare insurance, FT is predominantly caused by the cost of private care and treatment (e.g. in US), while in countries where a more extended health coverage is assured, FT assumes different nuances in relation with the public administration, the communication with the system and the welfare service. A main merit of this research was to enucleate several dimensions of FT including both outcomes (i.e. consequences) and determinants (i.e. causes), that were given a great importance from patients by proposing a new model for FT for countries based on universal health systems. In add, results from this study highlights the need, as recently pointed out from literature, to adopt a more comprehensive model of assessment encompassing both PROM (outcome measures) and PREM (Patient-reported experience measures), with different balancing in different countries following the heterogeneity of the different health care systems.

Focus groups and survey were organized with patients and experts to explore this new concept in cancer treatment using a qualitative approach to ensure the content and structure of the new instrument was consistent with patient-reported descriptions of this personal experience. To improve

the transparency of all aspects of qualitative research actions planned, the SRQR guidelines were followed to critically appraising, and synthesizing study findings. A multiprofessional steering committee participated in the process of the research to guarantee the variety of the contents to describe from a medical, psychological and social perspective, and consistency of the methodology for instrument development, instrument structure organization, wording, and format. Importance analysis evaluated how patients interpreted the items as relevant determining a preliminary version of a new instrument. Patients' descriptions of FT and the distinctive features of this experience were consistent with literature domains of financial burden associated to out-of-pocket costs following cancer care and treatment, with distinguished domains and significant impact in every-day life of cancer patients.

Patients added clarity to this definition by characterizing FT in the context of universal health coverage (like Italy) not yet analyzed by current literature. In fact, they described FT as a result of some ineffective procedures existing in the National Health System such as excessive bureaucracy, time management with long waiting lists, lack of network between community-based medical services managed by GPs and the hospital, poor communication practices with administrative and medical operator's within hospitals. All this inefficiency may determine the use of private healthcare or multiple examinations with a substantial impact on patients' financial resources (and allocative efficiency). Patients also described the difficulty or impossibility to access to social services, such as home care, as well as the lack of social support networks. Patients have pointed out that a higher private expenditure for health care goods and services reduces resource availability for family, social and community life, with evident repercussion on HRQoL. Patients also associated FT with a reduction in work activity, consistent with previous results of National surveys in which participants described the risk of job loss and diminishment of career opportunities for cancer patient and for the caregiver, with an evident impact on general family income following a diagnosis of cancer.[6, 7]

Medical experts interviewed in the present study described the same main categories of FT using a different perspective of the phenomenon by highlighting the importance of the environmental context as significant contributing factor in the genesis and in the development of FT. Some factors described by physicians like employment status, social support networks, and close access to health care are among the most important social determinants of health and responsible for health inequities as well. In line with the perspective of WHO on social determinants of health, the context of people's lives seems to determine their health and the exposition to more or less FT.[2, 11] As reported by WHO, to a large extent, "factors such as where people live, the state of our environment, income, education level, relationships with the community" (including the knowledge of medical service) have a strong impact on access and use of health care services.[12]

Feedbacks received from medical experts together with the expert panel stimulated a reflective process on items development, language to use, dimensions to include and modality of answers helping to disentangle some intricate issues related with FT. FT, by its very nature, is oriented to investigate private life, household expenditure and other family costs, all aspects that may be often biased by *social desirability* (the tendency to answer questions in a manner that will be viewed favorably by others) or questionnaire *rosy retrospection* (the tendency to judge the past disproportionately more positively than the reality).[13, 14]

The involvement of medical expert represented an important strength for the development of a feasible measure that will be used by physicians. Physicians must assess patients for financial toxicity and have to learn how to communicate effectively about it. In the past, medical professionalism meant a focus on patient outcomes without considerations of cost. But oncologists have been reminded that the potential for "financial toxicity" exists in all clinical decisions where high costs cause treatment non-adherence, and worsening outcomes.

Importance analysis first, and then cognitive debriefing interviews, permitted prioritization of the FT categories according to Italian patients and to define the level of comprehension and clarity of the overall structure of our questionnaire.

In conclusion, the initial development of the PROFFIT questionnaire resulted in a list of 30 items, which are now being tested in a larger study, to further reduce redundancy and arrive to the final instrument, that will be the first PROM to assess FT being fully developed in Italy; hopefully, this measure will eventually be used in future clinical studies as well as in routine practice settings.

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Table 1. Summary of actions, steps and methods

Actions	Steps	Methods used
(a) literature review	<i>Type of activity</i>	Systematic search in PubMed, Embase, Scopus, CINAHL
	<i>Search criteria</i>	Original reports, national statistical data ¹⁴⁻¹⁶ and systematic or non systematic reviews that discussed FT or financial issues in Italian patients in English or Italian language and were published after 1992.
	<i>Strategy</i>	Qualitative and quantitative synthesis of paper collected by highlighting all the different determinants and outcomes related with FT
(b) collection of experts' opinion	<i>Type of activity</i>	Collection of experts' opinion about FT in oncological setting
	<i>Involvement criteria</i>	Survey with oncologists associated with the AIOM and CIPOMO Association.
	<i>Strategy</i>	Concepts elicited through responses were collected together and resulted in thematic descriptions of the FT phenomenon
(c) Focus group	<i>Type of activity:</i>	Focus groups were organized in the three different towns (located in North, Centre and South Italy) and aimed at eliciting contents associated to patients and/or caregivers' experiences on FT impact on life contexts and consequences
	<i>Involvement criteria</i>	Oncological patients and different types of caregivers (e.g. partner, parent or children) were involved.
	<i>Strategy</i>	Themes, words and phrases provided by study participants were used to inform the overall structure of the instrument, including content, questions categories, response options and potential subscale or domain structure.
(d) Item development	<i>Type of activity</i>	Identification of a pool of items for questionnaire development through an active discussion providing feedback on methodology, interpretation, and structure of the instrument.
	<i>Involvement criteria</i>	An expert Steering Committee composed by oncologists, clinical and data research experts, psychologists, nurses, patients and medical's representatives, and regulatory experts provided consultation throughout the development process
	<i>Strategy</i>	The words and phrases of all involved participants, recorded and synthesized, together with the thematic descriptions of FT (from focus groups and interviews) served as the pool of data to identify patterns and clusters of information and to develop items.
(e) Importance analysis	<i>Type of activity</i>	Patients completed the questionnaire task during one of their routine check-up visits reflecting back on their experience of FT and providing an overall rating for each of the items assessed as <i>significant</i> or <i>not significant</i> using a 5-points likert scale.
	<i>Involvement criteria</i>	45 patients from the 3 different Italian regions (North, Centre and South)

	<i>Strategy</i>	For each item a final score was calculated summing the scores given by individual patients. In addition a descriptive analysis of importance scores among thematic libraries was done. Items with a total score under the median were eliminated because of low importance
(f) Cognitive interviews	<i>Type of activity</i>	Cognitive interviewing is a specialized type of pre-test that focuses on respondents' thinking process as they hear or read questions in a survey. It actively delves into how they interpret the meaning of questions and possible responses, what they think about when they are considering how to answer, how they decide on their answers and what their answers mean.
	<i>Involvement criteria</i>	45 patients from the 3 different Italian regions (North, Centre and South)
	<i>Strategy</i>	During these interviews, participants were asked about their interpretation of the items and how they judge the relevance of the question in relation with their experience with FT.

Table 2. Characteristics of participants

	Focus groups	Importance analysis	Cognitive interviews
N. of participants	34	45	45
Gender			
Female	20 (58.8%)	22 (48.9%)	28 (62.2%)
Male	14 (41.2%)	23 (51.1%)	17 (37.8%)
Age, median (range)	54 31-82	62 (25-90)	56 (38-79)
Age category			
<=65	26 (76.5%)	29 (64.4%)	30 (66.7%)
>65	8 (23.5%)	16 (35.6%)	15 (33.3%)
Location of participating center			
North (Turin)	10 (29.4%)	15 (33.3%)	15 (33.3%)
Centre (Rome)	6 (17.6%)	15 (33.3%)	15 (33.3%)
South (Naples)	18 (52.9%)	15 (33.3%)	15 (33.3%)
Type of participant			
Patient	23 (67.6%)	45 (100.0%)	45 (100.0%)
Caregiver	11 (32.4%)	-	-
Education level			
Elementary school/Middle school	11 (32.4%)	18 (40.0%)	13 (28.9%)
High school/degree	23 (67.6%)	27 (60.0%)	32 (71.1%)
Cohabitant/married			
Yes	27 (79.4%)	37 (82.2%)	32 (71.1%)
No	7 (20.6%)	8 (17.8%)	13 (28.9%)
With dependent family members*			
No	8 (34.8%)	34 (75.6%)	27 (60.0%)
Yes	12 (52.2%)	11 (24.4%)	18 (40.0%)
Missing	3 (13.0%)	-	-
Family members with cancer or chronic invalidant disease*			
No	11 (47.8%)	23 (51.1%)	24 (53.3%)
Yes	2 (8.7%)	22 (48.9%)	21 (46.7%)
Missing	10 (43.5%)	-	-
Working status*			
Non occupied	12 (52.2%)	28 (62.2%)	24 (53.3%)
Occupied	6 (26.1%)	17 (37.8%)	21 (46.7%)
Missing	5 (21.7%)		
Distance (km) from the hospital, median (range)	15 (5-60)	15 (1-1000)	20 (1-1300)
Previously received surgery*	14 (60.9%)	35 (77.8%)	29 (64.4%)
Previously received chemotherapy*	19 (82.6%)	38 (84.4%)	36 (80.0%)
Previously received target-based drugs*	8 (34.8%)	7 (15.6%)	-
Previously received immunotherapy*	4 (17.4%)	7 (15.6%)	7 (15.6%)
Previously received hormonal therapy*	2 (8.7%)	8 (17.8%)	9 (20.0%)
Previously received radiotherapy*	4 (17.4%)	25 (55.6%)	22 (48.9%)

* for patients only

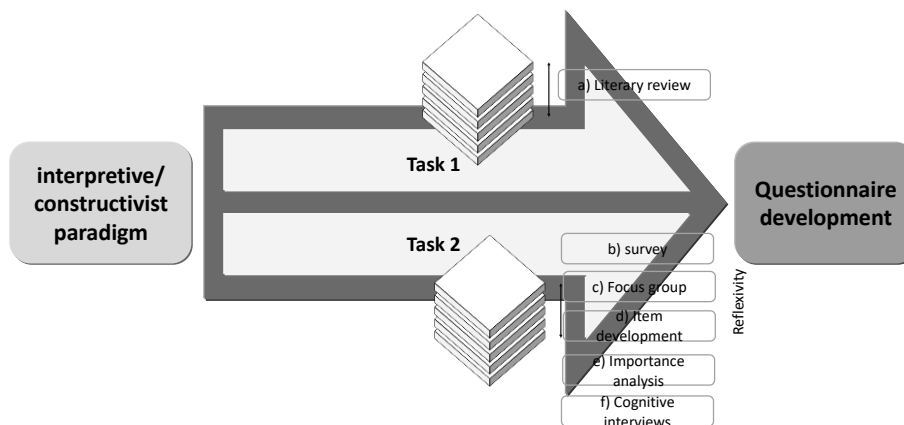
Table 3. Distribution of concepts and items and results of importance analysis by thematic libraries

Thematic library	# concepts	# items created after duplicate checking	Median importance score (IQR)	# items scoring \geq the overall median, retained after importance analysis
Medical care	49	13	108 (96-124)	6
Domestic economy	15	5	102 (99-105)	1
Emotion	18	6	119 (113-126)	5
Family	4	2	111 (110-113)	1
Job	13	6	121 (95-128)	4
Health workers	8	4	143 (140-153)	4
Welfare state	10	5	103 (97-103)	1
Free time	18	4	108 (107-111)	2*
Transportation	10	4	120 (118-122)	4
Overall	156	55	111 (99-126)	30

* one item (#122 regarding expenses for essential things like food and dresses) was maintained for subsequent phases for decision of the Steering Committee even if it scored under the median (108)

Fig. 1

Research Process



A qualitative analysis and development of a conceptual model assessing financial toxicity in cancer patients accessing the universal healthcare system

Appendix

English-language papers identified through literature search

1. **Alexander GC**, Casalino LP, Meltzer DO: Patient-physician communication about out-of-pocket costs. *JAMA* 290:953-958, 2003
2. **Altice CK. et al.** Financial Hardships Experienced by Cancer Survivors: A Systematic Review
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4. **Arozullah AM**, Calhoun EA, Wolf M, et al. The financial burden of cancer: Estimates from a study of insured women with breast cancer. *J Support Oncol.* 2004;2(3):271–278.
5. **Azzani M**, Roslani AC, Su TT. The perceived cancer-related financial hardship among patients and their families: a systematic review. *Support Care Cancer.* 2015;23(3):889-898. doi:10.1007/s00520-014-2474-y
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7. **Bernard DS**, Farr SL, Fang Z. National estimates of out-of-pocket health care expenditure burdens among nonelderly adults with cancer: 2001 to 2008. *J Clin Oncol.* 2011;29(20):2821–2826.
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9. **Bona K** et al (2013) Economic impact of advanced pediatric cancer on families. *J Pain Symptom Manag* 47(3):594–603
10. **Cagle JG**, Carr DC, Hong S, et al. Financial burden among US households affected by cancer at the end of life. *Psychooncology.* 2016;25(8):919–926.
11. **Carrera PM**, Olver I. The financial hazard of personalized medicine and supportive care. *Support Care Cancer.* 2015;23(12):3399-3401. doi:10.1007/s00520-015-2922-3
12. **Chang S**, Long SR, Kutikova L, et al. Estimating the cost of cancer: Results on the basis of claims data analyses for cancer patients diagnosed with seven types of cancer during 1999 to 2000. *J Clin Oncol.* 2004;22(17):3524–3530.
13. **Chino F**, Peppercorn J, Taylor DH Jr, et al. Self-reported financial burden and satisfaction with care among patients with cancer. *Oncologist.* 2014;19(4): 414–420.
14. **Chirikos TN**, Russell-Jacobs A, Cantor AB. Indirect economic effects of long term breast cancer survival. *Cancer Pract.* 2002;10(5):248–255.
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16. **Delgado-Guay et al.** Financial Distress and Its Associations With Physical and Emotional Symptoms and Quality of Life Among Advanced Cancer Patients_2015 *The Oncologist*
17. **Dowling EC**, Chawla N, Forsythe LP, et al. Lost productivity and burden of illness in cancer survivors with and without other chronic conditions. *Cancer.* 2013; 119(18):3393–3401.
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40. **Li C**, Li C, Forsythe L, et al. Mental health services utilization and expenditures associated with cancer survivorship in the United States. *J Cancer Surviv.* 2015;9(1):50–58.
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- implications for financial protection in health. *PLoS One*. 2013;8(11):e77549. Published 2013 Nov 11. doi:10.1371/journal.pone.0077549
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List of grey literature

- ISTAT - Report 2015: Spesa per Consumi delle famiglie in Italia:
<https://www.istat.it/it/files//2015/07/COMUNICATO-CONSUMI.pdf>
- Indagine "Ad alta voce" - FAVO/CENSIS 2011: I bisogni e le aspettative dei pazienti oncologici: https://www.perunavitacomeprima.org/public/immagini/file/censis_2011.pdf
- FAVO - 4° Rapporto sulla condizione assistenziale dei malati oncologici – 2012:
<https://www.favo.it/osservatorio/quarto-rapporto.html>

Table List of the 55 items ordered by importance score			
ID	Item text	Theme	Importance score
1*	Il personale sanitario (cioè medici, infermieri, etc.) ha agevolato il percorso di cura	Health workers	161
2*	So di avere diritto a sussidi economici (es. assegni o pensioni di invalidità) come conseguenza della mia malattia	Welfare state	149
3*	Il tempo necessario per la diagnosi è stato breve	Medical care	147
4*	C'è stata continuità nelle cure tra diversi medici e strutture sanitarie	Health workers	146
5*	Ho rapidamente trovato la struttura dove curarmi	Medical care	141
6*	Il personale ospedaliero amministrativo (cioè CUP, segreterie, etc.) ha agevolato il percorso di cura	Health workers	141
7*	Il medico di famiglia ha agevolato il percorso di cura	Health workers	140
8*	Ho perso molti giorni lavorativi a causa della mia malattia	Job	136
9*	E' stato facile ottenere sussidi economici (es. assegni o pensioni di invalidità) a causa della mia malattia	Welfare state	131
10*	Sono preoccupato di non riuscire a mantenere il mio lavoro a causa della malattia	Emotion	128
11*	Ho ridotto le ore al lavoro a causa della mia malattia	Job	128
12*	Il SSN copre solo in parte i costi associati alla mia malattia	Medical care	127
13*	Sono in grado di sostenere le mie spese mensili senza difficoltà	Domestic economy	127
14*	Sono preoccupato dei problemi economici che potrei avere in futuro a causa della mia malattia	Emotion	126
15*	Ho sostenuto spese per una o più visite private per la mia malattia	Medical care	124
16*	Ho dovuto rinunciare al lavoro a causa della mia malattia	Job	124
17*	I servizi di trasporto per raggiungere l'ospedale (mezzi pubblici, parcheggi) sono scarsi	Transportation	123
18*	Ho sentito molto il peso della burocrazia	Bureaucracy	121
19*	Ho dovuto sostenere rilevanti costi di trasporto per curarmi	Transportation	121
20*	Ho sostenuto spese per farmaci supplementari o integratori per la mia malattia	Medical care	120
21*	La mia malattia ha ridotto le mie disponibilità economiche	Emotion	120
22*	Il centro di cura è lontano dalla mia abitazione	Transportation	120
23*	I miei problemi economici mi preoccupano	Emotion	119
24*	Non riesco a guadagnare come prima per via della mia malattia	Job	119
25*	Ho dovuto sostenere i costi di trasporto, vitto e alloggio per curarmi in una città diversa da quella in cui vivo	Transportation	116
26*	Il modo in cui mi curo dipende dalla mia situazione economica	Emotion	113
27*	La mia famiglia ha dovuto sostenere i costi di trasporto, vitto e alloggio per curarmi in una città diversa da quella in cui vivo	Family	113
28*	Devo sostenere spese per cure integrative a mio carico (es. fisioterapia, psicoterapia, cure odontoiatriche)	Medical care	111

29*	Ho ridotto le spese per attività ricreative come vacanze, ristoranti o spettacoli per affrontare le spese per la mia malattia	Free time	111
30	I tempi di attesa sono stati troppo lunghi	Bureaucracy	110
31	La mia famiglia deve lavorare di più per affrontare le spese per la mia malattia	Family	110
32	Il mio stile di vita è peggiorato a causa dei costi della mia malattia	Free time	110
33	Ho difficoltà a sostenere le spese per farmaci o presidi medici non rimborsati dal SSN	Medical care	108
34	Sono tranquillo per la mia situazione economica nonostante la mia malattia	Emotion	108
35*	Ho ridotto le spese per acquisti di cibo o vestiti per affrontare le spese per la mia malattia	Free time	107
36	Ho ridotto le spese domestiche a causa della mia malattia per affrontare le spese per la mia malattia	Free time	107
37	Ho sufficienti risparmi e fonti di reddito per far fronte ai costi che devo sostenere per la mia malattia	Domestic economy	105
38	Ho dovuto sostenere spese per l'assistenza domiciliare	Welfare state	103
39	Ho dovuto sostenere il costo di badanti o infermieri a causa della mia malattia	Welfare state	103
40	Ho bisogno di aiuti economici per curarmi	Domestic economy	102
41	Ho impiegato molto tempo per capire come curarmi	Bureaucracy	99
42	Le spese mediche che devo sostenere sono maggiori di quelle previste	Medical care	99
43	Ho chiesto in prestito denaro per far fronte alla mia malattia	Domestic economy	99
44	Non sostengo spese per cure integrative se devo pagarle (es. fisioterapia, psicoterapia, cure odontoiatriche)	Medical care	99
45	Ho avuto bisogno del supporto delle associazioni di volontariato	stato sociale	97
46	Non riesco a curarmi adeguatamente per via dei costi associati al mio trattamento	Medical care	96
47	Devo sostenere il costo di baby sitter per i miei figli a causa della mia malattia	Welfare state	96
48	Sono stato discriminato al lavoro a causa della mia malattia	Job	95
49	Devo lavorare di più per affrontare le spese per la mia malattia	Job	95
50	Non eseguo accertamenti o visite specialistiche se devo pagarle	Medical care	92
51	Per motivi economici non compro tutti i prodotti prescritti	Medical care	91
52	Ho avuto bisogno di raccomandazioni per accedere ad esami o cure	Bureaucracy	90
53	Ho venduto beni o proprietà per far fronte ai costi della mia malattia	Domestic economy	90
54	Ho pagato uno o più interventi chirurgici per la mia malattia	Medical care	82
55	Possiedo una copertura assicurativa per far fronte ai costi della mia malattia	Bureaucracy	77
* selected for subsequent analysis with cognitive debriefing			

