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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

The aim of this study was to inform the development of a conceptual model for the ideation of a new Patient Reported Outcome measure (PROM) measuring financial toxicity (FT) in oncological setting in Italy, a country characterized by a free and universal health care system.

Methods

Focus groups with 34 patients/caregivers in three different Italian Institutions (from Northern, Centre and Southern Italy) and an open-ended survey with 97 medical oncologists were undertaken. Transcripts from focus groups and interviews 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

Overall, 156 concepts were generated from focus groups and interviews and were classified across 10 domains. 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 PROM 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.

[clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT03473379) NCT03473379 first posted on March 22, 2018

Keywords

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

Declarations

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Conflicts of interest/Competing interests (include appropriate disclosures)

SR has received personal fees from CSL-Behring and GlaxoSmithKline Foundation. JB has received personal fees from Novartis, AstraZeneca, Merck Sharp & Dohme. MDM has received personal fees from Bristol Myers Squibb, Merck Sharp & Dohme, AstraZeneca, Janssen, Pfizer, Eisai. FE has received personal fees from Amgen, Bristol Myers Squibb, Incyte, Orsenix and Takeda. LG has received personal fees from Bristol Myers Squibb. 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 (optional: please review the submission guidelines from the journal whether statements are mandatory)

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.[17]

We herein report the results of the initial qualitative analysis aiming to understand how patients conceive FT, including their experiences, reactions and way to cope with this burden.

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.[17, 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**.

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 and grounded theory.[22, 30] The phenomenological framework accentuates the “direct experiences” reported by patients and/or caregivers while the grounded theory framework - which is more commonly used to underpin social phenomena - can be also applied to instrument development and 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 Primari Oncologia Medica Ospedalieri).

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, researchers 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). 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), 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, 18]

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 moderate a potential *shaman effect*, that occurs when someone with specialized information on a topic (e.g. in our case we involved only specialized professionals) 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 (South region, *Istituto Nazionale dei Tumori*, coordinator), Roma (Centre region, *Istituto Nazionale Tumori "Regina Elena" - IFO*) and Torino (North region, *Azienda Ospedaliera Ordine Mauriziano*).

Patients were eligible if they were adult (>18 years), had a histologically or cytologically confirmed cancer diagnosis, were receiving or had terminated not later than 3 months anticancer medical or radiation treatment, and had no major cognitive dysfunction or psychiatric disorders.

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]

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). Three focus groups with patients (one in Napoli, one in Torino and one in Roma) and one with caregivers (in Napoli) were performed in the three participating centers and were moderated by the same skilled psychologist (SR) with the help of an assistant moderator. Sessions were audio-recorded and transcribed verbatim. 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. The software program Atlas.ti version 5.0 was used to organize coding and description of analyses.

Task 2

Action (d)

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 representability 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 interviews, with the participants' words and concepts used to inform wording.

Action (e)

All the items reaching a satisfactory level of importance (median score) were retained for the draft of the preliminary version of the instrument. Calculation was made on average scores of importance level for each category (median, IQR).

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

RESULTS

Task 1

Action (a)

Literature search produced 76 articles in English language and 5 documents in Italian language. The list of selected papers and documents is reported in **the Appendix, page xx**.

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. We selected participants using a convenience sampling based on accessibility and availability.

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 interviews 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 to additional costs for patients who, at the mercy of formalism and inefficiency, lose time, replicate medical consultations, spend additional money to reduce the diagnostic process (consulting more than one hospital, moving in a different town or even different regions).
- 2) *Medical care*. 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, determining 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 the difficulties or even the impossibility to maintain family tasks (e.g. running a household, childhood caring). Direct implications of that are housekeeping costs, babysitting/caregiving costs or, most simply, a different organizations of home tasks, with a loss of time for remuneration activities.
- 4) *Emotion*. Direct and indirect health care 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 in 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 and wages. Experiences can differ significantly from a number of days lost at job place to the renounce to work and from changes in mansions 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 to patients' FT. First, clarity of information results the lynchpin to reduce time and, consequently, costs associated to any supplementary and unnecessary consultations during the initial diagnostic journey. Second, a lack of communication between the General Practitioners (GPs) and medical hospital staff has the potential to increment the use of redundant medical accesses and to produce repetitive examinations, with a growth of out-of-pocket costs. 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 cost 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 with additional services not covered by the public system such as physiotherapy, psychotherapy 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.

9) *Free time*. The growth of out-of-pocket costs determine a significant reduction of free time and leisure 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, and disable them to live independently.

10) *Transportation*. Fees for transportation, 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)

Items were developed using a recursive process of development, revision, discussion, and forward-back process to the qualitative data to inform contents' selection. 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 and one more item for decision of the Steering Committee 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. About the recall period, 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 social, economic and welfare characteristics of the health system of the country of origin.[23] 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). 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]

Focus groups and interviews 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 representability 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 local 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. Patients also described changes in home economics that included greater use of financial resources for medications and treatment and less money 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 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 representative social determinants of health, responsible for health inequities. 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 permitted to stimulate 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]

Importance analysis first, and then cognitive debriefing interviews, permitted to prioritize 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. This is the first PROM to assess FT being fully developed in Italy, and we envisage that this measure will eventually be used in future clinical studies as well as in routine practice settings.

ACKNOWLEDGMENTS

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