Original Article

The Development of a Financial Toxicity Patient-Reported Outcome in Cancer

The COST Measure

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BACKGROUND: Considering patients' experience is essential for optimal decision-making. However, despite increasing recognition of the impact of costs on oncology care, there is no patient-reported outcome measure (PROM) that specifically describes the financial distress experienced by patients. **METHODS:** The content for a comprehensive score for financial toxicity (COST) was developed with a stepwise approach: step 1) a literature review and semistructured, qualitative interviews with patients for content generation; step 2) patients' assessment of the items for importance to their quality of life; step 3) pilot testing assessing interitem (IIC) and item–total (ITC) correlations to identify redundancy (Spearman rho, >0.7) and statistically unrelated content ($P > .05$); and step 4) exploratory factor analysis. Sociodemographic data were collected. **RESULTS:** In total, 155 patients with advanced cancer who were receiving treatment (20 patients in step 1, 35 patients in step 2, and 100 patients in steps 3 and 4) participated in the PROM development. In step 1, the literature was reviewed, and 20 patients generated 147 items, which were reduced to 58 items because of redundancy. In step 2, 35 patients rated the 58 items on importance, and 30 items were retained. In step 3, 46 patients assessed the 30 items, 14 items were excluded because of high IIC, and 3 were excluded because of nonsignificant ITC. In step 4, 2 items were discarded because of poor loadings in a factor analysis of 100 patients, resulting in an 11-item PROM. **CONCLUSIONS:** The content for a financial toxicity PROM was developed in 155 patients. The provisional COST measure demonstrated face and content validity as well as internal consistency and should be validated in larger samples. ***Cancer* 2014;000:000-000.** *© 2014 American Cancer Society.*

KEYWORDS: cost of cancer care, quality of life, comparative effectiveness, patient-reported outcome, outcomes research.

INTRODUCTION

Financial distress and cost concerns are common among patients with cancer,[1,2] because out-of-pocket costs and indirect costs, such as loss of income, negatively impact cancer patients and their families.[3-5] A recent survey of insured patients who were receiving treatment for breast, lung, or colorectal cancer demonstrated that financial distress and out-of-pocket costs have several consequences for patients[3,4]: 70% of patients reduced leisure activities, 48% withdrew savings, and 18% sold possessions. This distress also may translate into decreased compliance to treatment. For example, in a retrospective claims analysis of a large pharmacy benefits manager,[6] it was observed that higher prescription copayments were associated with both nonpersistence and nonadherence to aromatase inhibitors. Therefore, as many oncologists can attest,[7] the financial distress of cancer care can significantly affect quality of life[3,4,8] and treatment compliance.[6]

Placing financial distress in context with current policies and the Patient Protection and Affordable Care Act (PPACA), some analyses have predicted that many new insurance policies to be sold in PPACA health insurance exchanges will have deductibles greater than $1000, and these are considered high-deductible health plans.[9] It follows that many of the newly insured individuals are expected to have a higher cost share with implementation of the PPACA, and patients may be more inclined to join these high-deductible plans because of their greater upfront affordability.[9,10] Whereas patients with higher income may be more likely to focus on survival and opt for expensive treatments, putting themselves at a greater risk of bankruptcy,[11] patients of lower socioeconomic status may be more likely to avoid expensive treatments, regardless of survival or toxicity,[12] and forgo care as a result of these costs.[5] Therefore, escalating cancer care costs raise the

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concern of increasing financial distress and further disparities in cancer care, urging society, policy makers, and providers to measure this distress and identify patients at risk.

Regarding patient-reported outcome measures (PROMs), the federal government is encouraging pharmaceutical companies to include more measures of patient experience in clinical studies. In 2009, the US Food and Drug Administration released guidance to industry that outlined how PROMs will be evaluated for product labeling.[13,14] Two years later, ruxolitinib became the first cancer therapy in a decade to include symptom information on its drug label.[15] Another example is abiraterone acetate for metastatic prostate cancer, which carries label descriptions of associations with delayed time to pain progression and need for opioid pain control measured by PROMs.[15] Recognizing that there have been increasing efforts aimed at enhancing patient-centered care and incorporating patients' voices into clinical practice, in this article, we describe the content development of an instrument to quantitatively measure cancer patients' experience related to financial distress.

MATERIALS AND METHODS

The content for a comprehensive score for financial toxicity (COST)-PROM for patients with advanced cancer was developed in 4 steps. The Institutional Review Board of the University of Chicago approved this protocol, and patients were recruited from January 2012 to August 2013. Statistical analyses were performed using the Stata software package (version 13; Stata Corporation, College Station, Tex). All participants were diagnosed with advanced cancer, were receiving treatment at the time of participation, and had received treatment for at least 3 months.

Step 1: Item Generation

Item generation defines the content of the instrument and ensures that all important variables are considered for inclusion in the instrument.[16] A literature search was followed by semistructured qualitative interviews with cancer patients that was designed to elicit themes on financial issues related to their disease and treatment.[17,18] Cancer experts (medical oncologists, oncology nurses, and mental health professionals) added items judged to be important. Items were reviewed for redundancy, overlapping and tangential content, as well as problematic language. Duplicate items were eliminated, and the remaining items were classified into theoretical themes based on the qualitative interviews. A detailed description of the literature search methods is provided in the Supporting Methods (see online supporting information).

Step 2: Item Importance

Patients were approached to evaluate the importance of the items.[19] The items were presented with a 4-point Likert scale for the participants to rate importance,[20] and items were ranked according to this *importance score* from highest to lowest. Items were preserved by importance score rank, ceasing when at least 3 items per theme had been retained.

Step 3: Item Analysis

A quantitative item analysis was performed to evaluate the instrument's internal consistency. Each participant completed the preliminary instrument, which was presented in a format parallel to that of the Functional Assessment of Cancer Therapy (FACT) quality-of-life instrument, with a 7-day time window and on a 5-point Likert scale from zero ("not at all") to 5 ("a lot"). These instruments were scored according to previous FACT recommendations.[21,22] Positive items were reverse coded so that higher scores indicated greater financial distress. With the objective of minimizing redundancy, items were evaluated for their interitem correlation (IIC). Pairs of items with an IIC >0.7 were identified; and, within each correlated pair, the item with the highest importance score in step 2 was retained. Item-total correlations (ITCs) were calculated to ensure that the retained items impacted the instrument's score. Items with nonsignificant ITCs (ie, not significantly related to the instrument total score; $P > .05$) were excluded. The Spearman rank correlation coefficient (rho) was used for all tests of association, because the item scores were ordinal rather than continuous. We adopted these exclusion criteria to maintain a good level of internal consistency while retaining the breadth of the measure.[23,24] Within this sample, an interim factor analysis was also performed to estimate the sample size needed for a final analysis.[25]

Step 4: Exploratory Factor Analysis and Associations With Sociodemographic Variables

The factor structure was assessed by a principal factor analysis. The sample size for this analysis was determined based on the expected numbers of variables and factors observed in a preliminary exploratory factor analysis of the patients who participated in step 3.[25] The number of final factors underlying the data was identified using the combination of a Cattell scree plot evaluation (number of factors on scree plot just before elbow), Kaiser criterion (eigenvalues >1.0), and percentage of variance criterion. Factor loadings greater than 0.5 were considered factor-specific and of statistical and practical significance.[26,27]

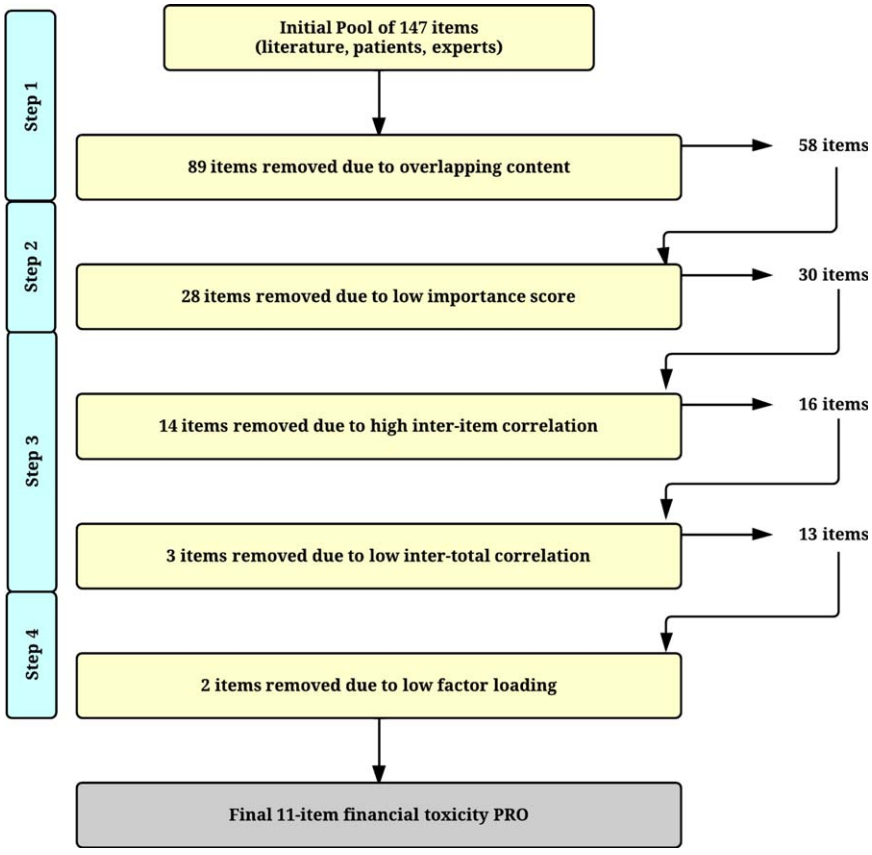

Figure 1.

The final PROM was assessed for internal consistency using the Cronbach alpha coefficient, and coefficients >0.9 were regarded as excellent. Correlations among items (IICs) and between each item and the total score (ITCs) were calculated using Spearman rank correlation coefficients, as in step 3. Associations between the provisional COST measure total score and self-reported sociodemographic variables (age, sex, race, household income, insurance type, education, and marital status) were assessed using Spearman rank correlations, *t* tests, or analyses of variance, as appropriate. A chi-square test was used when examining the association between education and the COST score dichotomized at the median. Patients who had greater than 50% missing items were excluded from the factor analysis, and a simple imputation method using means was applied to the missing data, because it previously demonstrated a strong performance.[28]

RESULTS

In step 1, a literature review yielded 80 candidate items. Then, 20 patients were interviewed, and they generated 54 candidate items. Six oncology experts then generated an additional 13 items. These 147 items were reduced to 58 by the investigators because of redundancy, overlapping content, and problematic language. The qualitative interviews with 20 patients resulted in 5 dominant themes: affect, coping, family, financial, and resources. Overall, the 58 items were classified into 8 financial items, 13 resource items, 17 affect items, 10 coping items, and 10 family items. Detailed descriptions of the qualitative interviews and the list of the preliminary 58 items are provided in the supporting materials (see online supporting information). Figure 1 summarizes the adopted stepwise approach.

In step 2, 35 patients consented to evaluate the 58 items for importance to their quality of life. With at least 3 items required per theme, in total, 30 items were retained, including 13 affect items, 7 resource items, 3 financial items, 4 family items, and 3 coping items. Their mean importance score was 1.82 (score range, 1.04-2.13). For a list of the 30 items that progressed to the third developmental step, ranked from most to least important, see

TABLE 1. Step 2: Patients Ranked Items for Importance to Their Quality of Life, and 30 Items Were Retained

Original Item	Item Content	Importance Score	Theme	Reference
26	I know that I have enough money in savings, retirement, or assets to cover the costs of my treatment	2.13	Resources	Patient
1	I am stressed about the growing amount of medical bills and debt because of my treatment	2.09	Affect	Palattiyil & Chakrabarti 2008[29]
2	My out-of-pocket medical expenses are more than I thought they would be	2.09	Financial	Palattiyil & Chakrabarti 2008[29]
24	I worry about my family's financial stability	2.06	Family	Zafar et al, 2013,[4] Patrick et al, 2011[18]
29	I worry about the financial problems I will have in the future as a result of my illness or treatment	2.03	Affect	Patient
57	I feel I have no choice about the amount of money I spend on care	2	Affect	Patient
58	I am frustrated that I cannot work or contribute as much as I usually do	1.97	Affect	Patient
17	I am optimistic about my financial future	1.94	Affect	Joo & Grable 2004[30]
19	I am satisfied with my current financial situation	1.94	Affect	Joo & Grable 2004[30]
20	I am able to meet my monthly expenses	1.91	Resources	Joo & Grable 2004[30]
54	I don't think about the costs of my health care	1.89	Affect	Patient
11	I feel financially stressed	1.88	Affect	Prawitz et al, 2006,[31] Joo & Grable 2004[30]
37	My family and loved ones are worried about how we will make ends meet because of the expense of my illness or treatment	1.87	Family	Patient; Palattiyil & Chakrabarti 2008[29]
34	I am concerned about keeping my job and income, including work at home	1.85	Affect	Patient
28	I am concerned about my ability to pay off my debts once treatment is over	1.84	Affect	Patient
31	My employer has made special arrangements with me (work schedule, advanced pay, etc) so that I can have income during my illness or treatment	1.83	Coping	Patient
44	I feel in control of my financial situation	1.83	Affect	Prawitz et al, 2006[31]
45	My insurance does not provide adequate treatment coverage for my illness and care-related expenses	1.83	Financial	Himmelstein et al, 2009[32]
46	I think that my future earnings will be limited as a result of my illness or treatment	1.83	Affect	Himmelstein et al, 2009[32]
4	My cancer or treatment has reduced my satisfaction with my present financial situation	1.79	Affect	Zafar et al, 2013[4]
42	If there was a financial emergency of $1000, I am confident that I could find the money	1.79	Resources	Prawitz et al, 2006[31]
47	The cost of my illness prevents me from supporting others/causes as I normally would	1.79	Resources	Patient
36	I worry about loss of my family's income because of the time spent on my cancer care	1.77	Family	Patient
6	I am using money set aside for my retirement to pay for my cancer care	1.75	Resources	Zafar et al, 2013[4]
12	I worry about loss of my family's income because of the cost of my cancer care	1.73	Family	Patient
33	I have taken money I was saving for another purpose (eg mortgage, appliances, vacation, etc) and used it to pay for my treatment	1.65	Resources	Patient
5	I have reduced spending on basics like food or clothing because of the costs of my cancer care	1.64	Coping	Zafar et al, 2013[4]
23	I am using money from savings to pay for my cancer care	1.6	Resources	Patient
10	I am concerned about the possibility of bankruptcy	1.29	Financial	Ramsey et al, 2013,[11] Himmelstein et al, 2009[32]
50	I rely on friends or family to help with the costs of health care	1.04	Coping	Patient

Table 1. In step 3, 46 patients completed the 30-item instrument for item analysis. Fourteen items were excluded because of high IICs (items 1, 5, 6, 10, 12, 23, 24, 28, 33, 36, 37, 42, 46, and 47), and 3 items were excluded because of nonsignificant ITCs (items 17, 31, and 54). An interim factor analysis of the 13-item instrument created in step 3 revealed 2 factors: an items/factor ratio of approximately 6 and wide communality

(communalities ranging from 0.2 to 0.8). On the basis of previous simulation studies,[25] a minimum sample size of 95 patients was considered appropriate for the final factor analysis.

In step 4, an exploratory factor analysis was performed. Two patients were excluded from the analysis because they had greater than 50% missing items. Seven patients had 1 missing item, 3 patients had 2 missing items, and 2 patients had 3 missing items. Consistent with the prior sample size estimation indicating that a minimum of 95 patients was needed for factor analysis, data from 100 patients were analyzed, including the 46 patients who participated in step 3. The median age of participants was 59.5 years (age range, 24-84 years), 55% patients were men, and all had health insurance coverage, which was mostly private or employer purchased (62%) followed by Medicare with or without supplement (32%). The median household income was $63,500, and 39% of patients had completed college or had higher education, whereas 24% had less education than college. Table 2 lists the characteristics of patients who participated in the factor analysis.

Before performing the factor analysis, the suitability of the data for factoring was assessed. The Kaiser-Meyer-Oklin value was 0.90, and the Bartlett test of sphericity reached statistical significance, supporting the factorability of the items.[33,34] One factor was clearly identified on inspection of the scree plot, with an eigenvalue of 5.68, explaining 89% of the variance. This factor was designated as *financial toxicity*. Among the 13 items, 11 had factor loadings greater than 0.5. The exceptions were item 45 ("My insurance does not provide adequate treatment coverage for my illness and care-related expenses") and item 50 ("I rely on friends or family to help with the costs of health care"), which had factor loadings of 0.44 and 0.43, respectively.

After the exclusion of items that had loadings <0.5, the 1-factor solution explained 93% of the variance in the data, with communalities between 0.3 and 0.7 (Table 3). The Cronbach α coefficient for the 11-item COST measure was .9, indicating excellent internal consistency. The mean IIC of the 11-item COST-PROM was 0.47 (range, 0.22-0.69), and the mean ITC was 0.71 (range, 0.62-0.79), demonstrating nonredundancy and good construct validity, as discussed in the supporting materials (see online supporting information). The final content included 1 financial item, 2 resources items, and 8 affect items.

The median COST score was 21 (score range, 3-44; mean $\pm$ standard deviation, 22.5 ± 11.3). When total scores on the 11-item COST were divided into low (less distress) and high (more distress) at the median, there was a statistically significant association between education and the COST score (chi-square test with 2 degrees of freedom, 7.26; $P = .03$), because 71% of those who had less than a college education scored above the median compared with 49% of those who had some college and 36% of those who had a college education or more. However, using continuous COST scores, the association with education was no longer statistically significant based on a Spearman rank correlation analysis ($P = .11$). Other analyses included Spearman correlations for age ($P = .93$) and household income ($P = .16$), t tests for sex ($P = .64$) and race ($P = .14$), and analyses of variance for marital status ($P = .43$) and insurance type ($P = .53$; all statistically nonsignificant).

DISCUSSION

The objective of this study was to develop the content for an instrument that assesses the degree of financial distress experienced by cancer patients. With extensive patient participation, the 11-item COST-PROM was developed. In the social sciences, the terms used to describe feelings about financial condition have been numerous,[31] including perceived economic well being,[35,36] personal financial wellness,[37] financial satisfaction,[30,38] perceived income adequacy,[39] financial stress,[40-42] debt stress,[43] economic strain,[44] and economic distress.[45,46] In the oncology literature, distress, burden, and toxicity[3,8] have been reported. Also, as a method to quantify the term, *financial burden* has been defined and used in some studies as the ratio of health-related spending (out-of-pocket costs) by household income.[47-50] Acknowledging that out-of-pocket costs are not the sole driver of financial distress, because other factors, such as indirect costs or loss of income,[51] also play a major role, the need for a comprehensive instrument to capture and quantitatively assess these events became evident; in that article, the term financial toxicity[3,8] was used to report the economic changes caused by treatments and disease to patients.

Currently there are no widely accepted standards for developing PROMs in comparative effectiveness research.[52] We chose a Likert scale similar to that used in the FACT instrument[22] to facilitate further validation and integration into existing quality-of-life assessments. The strength of our overall approach is the result of integrating a top-down approach that sought to include themes of financial well being using patient feedback, with a bottom-up approach to item analysis and

TABLE 2. Sociodemographic Characteristics of Patients in Steps 3 and 4

Characteristic	No. of Patients, N = 100
Age: Median (range), y	59.5 (24-84)
<65	68
>65	32
Household income by percentile: Median (range)	$63,500 ($17,000-$400,000)
10th	$37,000
25th	$46,000
50th	$63,500
75th	$84,000
90th	$111,000
Race/ethnicity	
White, non-Hispanic	74
African-American	18
Hispanic	6
Other	2
Sex	
Men	55
Women	45
Marital status	
Married	69
Divorced/separated/widowed	19
Never married	12
Education level	
<College	24
Some college	37
≥Completed college	39
Insurance type	
Private or employer-based	62
Medicare, with or without supplement	32
Medicaid	4
COBRA continuation coverage	2
Primary tumor type[a]	
Head and neck	34
Breast	11
Thyroid	10
Lung	9
Ovarian	5
Prostate	4
Esophageal	4
Pancreas	3
Colorectal	3
Cervical	3
AML, undergoing stem cell transplantation	3
Other[b]	11

Abbreviations: AML, acute myeloid leukemia; COBRA, Consolidated Omnibus Reconciliation Act.
[a] All patients had stage IV disease.
[b] These tumor types individually comprised <2%.

retention.[53] The semiqualitative interviews ensured the capture of experiences ranging from out-of-pocket costs and savings to financial concerns in the future, and each subsequent step refined the instrument by focusing on different aspects of quality improvement. The objective of the *concept-retention approach* was to retain the themes or concepts in the original theoretical framework for the instrument and select items from each theme. Further analyses were based on IIC, ITC, and item loadings. Inclusive criteria were applied, and only items with high IICs, nonsignificant ITCs, and poor loadings in factor analysis were eliminated. These item-reduction techniques have been described previously,[53] and the participation of patients and experts ensured the existence of the proposed underlying theoretical structure with enhanced face and content validity.[54,55] All participants were diagnosed with advanced cancer, were on treatment with chemotherapy, and had received treatment for at least 3 months, because most patients receive their first health care bills 1 or 2 months after treatment initiation. This also ensured the ability to capture patients' current experience of dealing with their finances.

With regard to the performed factor analysis, a sample size of 100 patients, although relatively small, would be adequate in a data set that includes 1 factor and 11 items based on simulation data from Mundfrom et al.[25] However, the ideal sample size for an exploratory factor analysis has been a theme of debate in the literature, with suggested sample sizes ranging from 3 to 20 times the number of items, with 5 to 10 times usually considered the minimum required.[27] Similarly, there is no consensus on the optimal value for item loadings, and we chose to consider 0.5 as a practically significant loading.[27] With a sample of 100 patients, as reported by Stevens,[26] the minimum value for a loading to be statistically significant is 0.512, and the last item included in the COST measure had a loading of 0.57.

Sociodemographic variables, such as age, sex, race, marital status, and insurance type, were not associated significantly with financial toxicity as measured by the COST in this cohort. However, at this developmental stage, the current study was powered for a factor analysis and was not designed or powered to detect associations with sociodemographic variables. Although not statistically significant, greater financial distress was noted in patients who were without private/employer insurance compared with those who had private/employer insurance ($P = .53$) and among nonwhite patients compared with white patients ($P = .14$). It is noteworthy that household income also was not associated significantly with financial distress in this cohort of insured patients. Although the lack of association may intuitively call into question the construct validity of the instrument, the 10th percentile of household income was $37,000, and the 90th percentile was $111,000, indicating that patients with very low income as well as those with very high income were seldom included, limiting the discriminative ability of household income in this analysis.

When the COST scores were dichotomized into low or high toxicity, less education was associated with more financial distress. Education level is related to worse

TABLE 3. Factor Analysis of the Final 11-Item Comprehensive Score for Financial Toxicity (COST) Measure With 1-Factor Solution

Item (Item No.)	Loading
Factor 1: Financial toxicity	
I feel financially stressed (11)	0.85
I am satisfied with my current financial situation (19)	0.79
I worry about the financial problems I will have in the future as a result of my illness or treatment (29)	0.77
I am frustrated that I cannot work or contribute as much as I usually do (58)	0.75
My cancer or treatment has reduced my satisfaction with my present financial situation (4)	0.73
I feel in control of my financial situation (44)	0.66
I am able to meet my monthly expenses (20)	0.62
I know that I have enough money in savings, retirement, or assets to cover the costs of my treatment (26)	0.62
I am concerned about keeping my job and income, including working at home (34)	0.61
I feel I have no choice about the amount of money I spend on care (57)	0.61
My out-of-pocket medical expenses are more than I thought they would be (2)	0.57

outcomes,[56,57] and it is expected that patients who have less education will be more vulnerable to and will have fewer mechanisms for coping with financial distress. However, the median financial distress score was arbitrarily selected as the threshold for toxicity in this specific analysis. In reality, there may be different degrees of toxicity; and, when using continuous COST scores, the association with education was no longer statistically significant, indicating that confirmation of the first association is required in adequately powered studies.

A major limitation of this study was the exclusion of uninsured patients, who typically do not receive treatment at our tertiary referral center. However, with the implementation of the PPACA, it is believed that financial burden will shift from the uninsured to the underinsured patients. Therefore, the identification of patients who, even with health insurance, still bear the financial burden of their treatments is also of paramount importance.

Finally, the COST is a provisional instrument that warrants validation, and further studies must be performed to assess the correlation between financial toxicity and quality of life or survival in cancer patients. Other construct, validity, and psychometric characteristics, including test-retest, the minimally significant difference in prospective assessments, and its use in cancer patients other than those with advanced disease, also should be determined before its widespread adoption. In addition, causality and hypothesized predictors of financial toxicity, such as length and line of therapy, receipt of oral or intravenous agents, enrollment in clinical trials, employment status, out-of-pocket costs, social support, lack of insurance, and financial literacy, should be assessed further.

In summary, by combining work from the personal finance literature (financial distress) with the health psychology and medical literature, the content for an 11-item provisional measure to assess financial toxicity was developed in 155 advanced cancer patients. The COST measure demonstrated content and face validity as well as internal consistency. This detailed developmental description of the content of this PROM is a first and major step toward measuring how financial distress impacts the lives of patients with cancer patients' lives, and it is to be followed by further validation studies assessing its construct validity and association with quality-of-life and other concurrent measures. Such patient-centered outcomes have the potential not only to provide unique data to inform shared decision-making between patients and physicians but also to guide health policy, intervention programs (such as navigation and cost-communication programs targeted for patients at higher risk of financial distress), and drug development (because cost burden may be factored into quality-of-life assessments in clinical trials).

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CONFLICT OF INTEREST DISCLOSURES

Dr. Ratain reports grants from Bristol-Myers Squibb and PharmaMar outside the submitted work; personal fees from AbbVie, Agios Pharmaceuticals, Biscayne Pharmaceuticals, Cantex Pharmaceuticals, Cerulean Pharma, Cyclacel, Daiichi Sankyo, Drais Pharmaceuticals, EMD Serono, Genentech, APP Pharmaceuticals, Teva Pharmaceuticals, MethylGene; Onconova Therapeutics, Apotex, Shionogi, Mylan Pharmaceuticals, and Xspray Microparticles outside the submitted work; and stock options in Biscayne Pharmaceuticals.

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