Review Article

Relationships Between Financial Toxicity and Symptom Burden in Cancer Survivors: A Systematic Review

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Abstract

Context. Financial toxicity (FT) is used to describe the financial distress/hardship associated with cancer and its treatment.

Objectives. The aim of this review was to explore the relationship between FT and symptom burden.

Method. A systematic review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. We searched MEDLINE, EMBASE, and CINAHL (from January 2000 to January 2018) and accepted quantitative, mixed-methods and qualitative studies. Data were extracted and appraised by two reviewers. Owing to significant heterogeneity in the included studies, a narrative synthesis was performed.

Results. Nine studies involving 11,544 cancer survivors were included. Of these nine studies, eight were of high quality. The relationships between FT and psychological symptoms and physical symptoms were examined in eight and three studies, respectively. Six studies reported a positive relationship between FT and depression. Three studies found a positive association between FT and anxiety. Limited evidence was found for an association between FT and stress, fear of recurrence, spiritual suffering, pain, and overall symptom burden.

Conclusions. A relatively clear association exists between FT and psychological symptoms. Clinicians should regularly screen for, assess, and manage emotional distress that may be attributed to FT. Although the causal pathway is not known, future intervention studies aimed at minimizing or preventing FT should evaluate psychological symptoms as secondary outcomes. Little is known about the relationships between FT and physical symptoms. Future research should overcome methodological limitations by incorporating longitudinal data collection, use of mixed-methods approaches, and homogeneity of samples. J Pain Symptom Manage 2019;57:646–660. *Crown Copyright © 2018 Published by Elsevier Inc. on behalf of American Academy of Hospice and Palliative Medicine. All rights reserved.*

Key Words
Cancer survivors, financial toxicity, financial burden, symptom distress, symptom burden, systematic review

Introduction

Cancer care is one of the fastest growing components of global health care costs. In the U.S. alone, approximately $87.8 billion was spent on cancer care in 2014.[1] Although advances in science, technology, and consumers' expectations have improved patient outcomes, they are associated with significant costs to the health care system and to patients.[2–4] Cancer

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treatments have direct and indirect impacts on the finances of patients and their family caregivers.[5,6] The term financial toxicity (FT) is used to describe the financial distress or hardship associated with cancer and its treatment.[5,6]

A recent systematic review reported that FT occurred in 28% to 48% of cancer survivors using monetary measures such as "percentage of household income" (spent on medical services) and in 16% to 73% of cancer survivors using self-report measures such as impact on everyday living expenses.[4] In another systematic review of 45 studies,[6] 12% to 62% of cancer survivors reported being in debt due to their treatment and 47% to 49% of survivors experienced some form of financial distress.[6] Common outcomes associated with FT included reduced treatment compliance, medication nonadherence, and treatment refusal.[4,6,7] Although several studies found that higher financial burden was associated with reductions in health-related quality of life, especially with emotional well-being,[8–12] little is known about the relationship between FT and symptom burden, especially the occurrence and severity of symptoms.[13]

Undoubtedly, the relationships between FT and symptom burden are complex.[13] Therefore, investigations that evaluate how FT and symptom burden may interact with each other are warranted. Currently, it is unclear whether the relationships between FT and symptom burden are causal, bidirectional, or modifying. For example, it is reasonable to postulate that patients with a higher symptom burden (e.g., fatigue, pain, cognitive dysfunction, depression, peripheral neuropathy) may reduce hours at work or not be able to return to work,[14] which may exacerbate financial pressures. On the other hand, FT can contribute to depression and anxiety,[15] which may in turn influence physical symptoms such as sleep disturbance and fatigue. Increased knowledge of the associations between FT and symptom burden will inform the development and testing of interventions to alleviate symptom burden associated with FT.[13] Therefore, the primary aim of this review was to explore the relationships between FT and symptom burden in cancer survivors.

Methods

This systematic review was prepared in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and was registered prospectively in PROSPERO (ID 42016036924).

Identification of Studies and Inclusion Criteria

The following databases were searched: Medical Literature Analysis and Retrieval System Online (MEDLINE), Excerpta Medica Database (EMBASE), and Cumulative Index to Nursing and Allied Health Literature (CINAHL) for articles published from January 2000 to January 2018. In addition, we searched the reference lists of any relevant studies and reviews, as well as Google Scholar. The limits on the years of publication were set due to the rapidly evolving cancer treatment and care experiences of cancer survivors. We defined "cancer survivors" as people living with cancer from the time of diagnosis until the end of life.[16,17] The search strategies were guided by the following four groups of search terms: 1) cancer, 2) patients, 3) cost, and 4) symptom burden. Synonyms and related terms are detailed in Table 1. For each of the terms in the four groups, we used Boolean operators "OR" and between the groups we used "AND." We used medical subject headings (MeSH) when available. To be included in this current review, studies were required to meet following prespecified criteria: published in English; published or were in press in a peer reviewed journal; and examined and reported the relationships between FT and symptom burden in cancer survivors. Symptom burden could be 1) assessed using the following dimensions: symptom occurrence, severity, frequency and/or distress; 2) measured using valid and reliable measures or investigator-constructed instruments; and 3) reported by patients, proxy, or health care professionals. Where symptom burden was reported as part of a quality-of-life measure, symptom burden had to be explicitly evaluated and reported. Definitions and measures of FT used in this review were informed by our previous systematic review.[4] These measures were categorized as 1) monetary: currency values of out-of-pocket expenses and percentage of out-of-pocket spending to income ratios; 2) objective: question sets on tangible solutions to ease financial burden such as to increase debt levels, borrow money from family or friends, sell assets, withdraw money from retirement or savings funds, file for bankruptcy; and 3) subjective: question sets on perceptions of cancer-related financial burden. No limitations were placed on cancer stage or time since diagnosis. We accepted quantitative, mixed-methods, and qualitative research studies.

Study Screening and Data Extraction

The Endnote X8.2 referencing management software (Clarivate Analytics, Philadelphia) was used for the screening and inclusion of studies. One author (O. A. A.) prescreened all search results (i.e., titles and abstracts) for possible inclusion and selected articles for full-text assessment. Two authors (R. J. C. and O. A. A.) independently assessed the full-text articles for inclusion. All articles that met the prespecified inclusion criteria were included in this review. Data extraction was conducted by one author (R. J. C.)

Table 1
Search Terms

1. Cancer: cancer care, oncology, treatment, management, p(a)ediatric, breast, prostate, colorectal, cervical, thyroid, brain, lung, lymphoma, stomach, liver, MeSH cancer
2. Patients: patient, survivor, sufferer, family, MeSH patient care
3. Costs: cost, productivity loss, expense, treatment cost, out-of-pocket, economic burden, financial toxicity, financial hardship, financial burden, financial effect, financial stress, co-payment, MeSH cost analysis
4. Symptom burden: symptom management, symptom burden, symptom occurrence, symptom distress, symptom severity, symptom experience, symptom frequency, pain, fatigue, depression, anxiety, psychological stress

and checked by another author (C. M.). Data extracted included study methods, authors, publication year, country, study design, setting, demographic characteristics (i.e., age, income levels, educational levels, health insurance, and employment status), clinical characteristics (i.e., disease, disease stage, time since diagnosis), outcome measures, and key findings.

Study Quality Assessment and Data Synthesis

Quality assessment was conducted independently by two authors (R. J. C. and O. A. A.) using predefined criteria adapted from Mols et al.'s standardized checklist (see Supplementary Data 1).[18,19] The checklist included criteria for the quality indicators concerning methodology, reporting, and interpretation of results. Across the 12 items that were evaluated, if the study met the quality indicator, it received one point. If the study did not fulfill the specific criterion, did not sufficiently describe whether the criterion was fulfilled, or did not mention the criterion at all, a score of zero was assigned. Studies that scored ≥75% of the maximum attainable score (i.e., ≥9 points) were considered "high quality." Studies that scored between 50% and 75% were considered "moderate quality." Studies scoring <50% were considered "low quality" (i.e., ≤6 points).

We did not exclude studies based on study quality. For the included studies, we expected significant heterogeneity in terms of methods and populations. Although we initially planned to conduct a narrative synthesis,[20] because of the board range of cancer survivors who were evaluated in the included studies, we summarized our study findings using two board groups, namely cancer survivors with mixed stages of disease or cancer type and those with advanced disease. For studies that provided measures of strength of association, the strength of association for correlation coefficients is described as weak if <0.3, moderate if 0.3 to 0.5, strong if 0.5 to 0.7, and very strong if >0.7, and for odds ratios as weak if < 2.5, moderate if 2.5 to 4.0, strong if 4.0 to 10.0, and very strong if >10.0.[21]

Results

The database searches resulted in 7162 titles. After the addition of records identified through reference lists and other sources ($n = 7$) and the removal of duplicates ($n = 1396$), a total of 5773 were screened and 24 full-text articles were retrieved for full assessment. Of these 24 articles, a total of nine were included. The PRISMA flowchart is shown in Figure 1. The study characteristics and key findings are reported in Table 2.

Study Characteristics and Quality Assessment

Of the nine included studies, eight[3,8,12,15,22–25] examined the relationships between FT and psychological symptoms. Three studies examined the relationships between FT and physical symptoms.[15,22,26] Eight studies[3,8,12,15,22–25] adopted a cross-sectional design, and one longitudinal study[26] collected data over two time points. Six were conducted in the U.S.,[3,8,12,15,24,26] with the remainder in Australia,[23] France,[22] and Ireland.[25] The sample sizes ranged from 100 to 500,[3,15,22,24] 501 to 1000,[25] 1001 to 5,000,[8,12,23] and >5000.[26] All the studies used a quantitative observational design. Six studies[8,12,23–26] included cancer survivors at various time points after diagnosis, with the remainder including patients with advanced cancer.[3,15,22] Five studies recruited patients from population-level registries,[8,12,23,25,26] and four recruited from local cancer centers.[3,15,22,24] A range of self-report measures of FT and symptom burden were used across the nine studies. Only one study[25] measured FT using monetary measures in addition to subjective measures. However, this study only assessed and reported the relationships between the subjective measures of FT and symptom burden.[25] These measures are described in detail in Table 2. Most studies were of high quality (≥9).[3,8,15,22–26] One study was judged as low quality (≤6),[12] mainly due to lack of use of validated measures, insufficient reporting of cancer treatment types and informed consent, and a relatively low response rate. Supplementary Data 1 summarizes the quality assessment criteria and results for each study.

Relationships Between Financial Toxicity and Symptom Burden

Table 3 summarizes the findings on the relationships between FT and symptom burden reported across the nine studies. A number of studies reported weak-to-moderate, positive relationships between FT

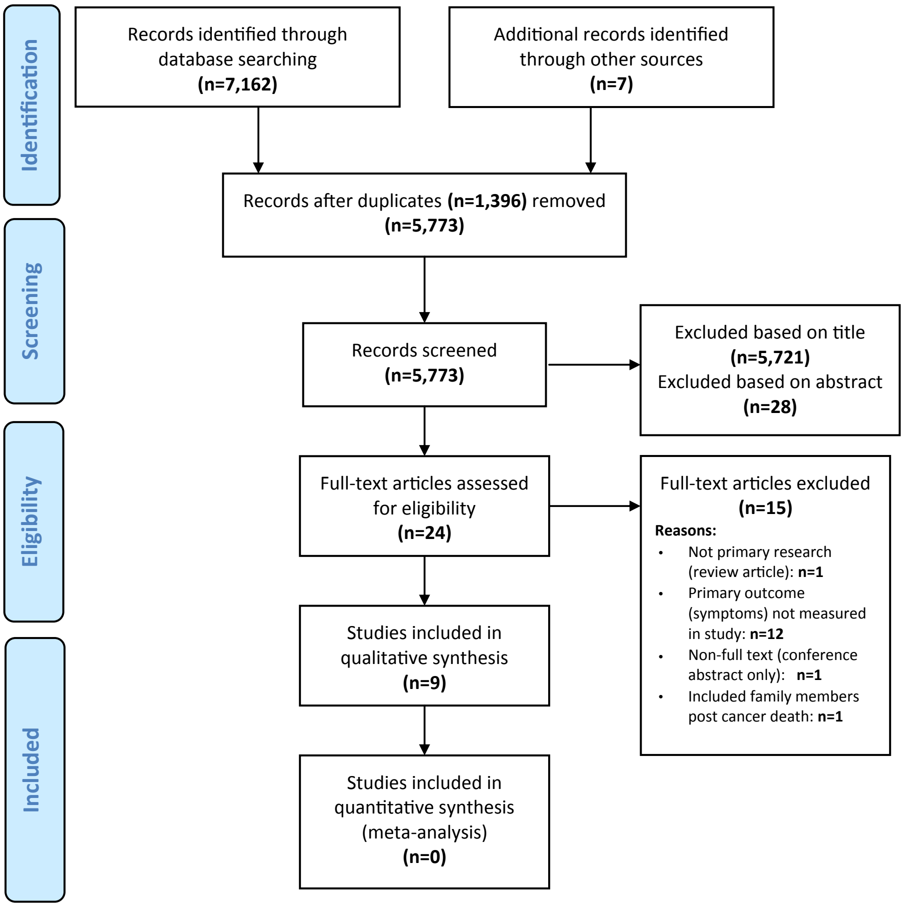

Fig. 1. PRISMA flowchart.

and depression,[8,15,22,23,25,26] anxiety,[15,22,25] overall psychological distress,[3,22,24] stress, fear of recurrence,[8,12] spiritual suffering,[22] pain,[26] and overall symptom burden.[22,26] In terms of the relationships between FT and symptom burden, seven studies[3,8,12,23–26] reported results from their multivariable analyses controlling for a number of demographic and clinical characteristics, whereas the remaining two[15,22] were limited to univariate and bivariate analyses.

Cancer Survivors (Mixed Stage of Disease and Cancer Diagnosis). In an Irish study of 654 breast, prostate, and lung cancer survivors (who were less than 6 months after diagnosis), the multivariable analyses suggested that the risks of depression and anxiety increased almost threefold among those with increased cancer-related financial stress and strain.[25] In this study, depression risk increased by threefold in survivors who reported increased cancer-related financial stress (OR = 2.79, 95% CI 1.8-4.17) and increased cancer-related financial strain (OR = 3.56, 95% CI 2.23-5.67). Risk estimates were higher for those survivors with severe or worse depression, and who reported increased financial stress (OR = 4.36, 95% CI 2.35-8.10), and increased financial strain (OR = 8.21, 95% CI 3.79-17.77).[25] Similar associations were found for anxiety and distress.[25] Similar effect sizes were reported in the multivariable analysis from another cross-sectional study of 1380 cancer survivors (mixed cancer diagnoses) who were at various time points after diagnosis.[8] Specifically, higher levels of depression, psychological distress, and fear of recurrence were associated with a higher number of financial problems (i.e., borrowed money or declared bankruptcy, worried about paying large medical bills, unable to cover costs of medical care visits, other financial sacrifices).[8] In a multivariable analysis, compared with those who did not report financial problems, the odds for depression and being worried about cancer recurrence were 3.4 and 3.5 times more likely, respectively, for people with three or more financial problems.[8] In terms of worry about cancer recurrence, in a U.S. study of 2108 cancer survivors, those who reported a higher level of cancer-related financial problems were more likely to worry "all the time" that the cancer would return (43%) than those who did not worry about cancer recurrence (28%; $P < 0.001$).[12]

Table 2

Summary of Characteristics and Findings From Included Studies

Author, Year, Country, Sample Size, Study Purpose	Patient Characteristics	Measures, Analyses, and Key Findings	Quality Scores, Strengths, and Weaknesses
Sharp, Carsin & Timmons, 2013 Ireland $N = 654$ Purpose: Investigate associations between cancer-related financial stress and strain and psychological outcomes among cancer survivors	Setting: a population-based sample from the National Cancer Registry Ireland (patients less than six months after diagnosis) Time frame: June to October 2008 Cancer type: breast (69.3%), prostate (28.1%), and lung (2.6%) Disease stage: NR Treatment: Surgery (78.6%), CTX (43%), XRT (65.6%), and HRT (39.8%) Time since diagnosis (yrs): NR Age range: 26–88 yrs Male: 30.7% Income level: Q1: lowest quartile (20.2%), Q2 (21.9%), Q3 (23.6%), and Q4: highest quartile (22.2%) Education level: primary (19.2%), secondary (51.2%), and tertiary (29.6%) Health insurance at diagnosis: 66% Health insurance at the time of study: NR Employment status: employed (40.6%), self-employed (12.3%), not working (24.5%), and retired (22.6%)	Financial toxicity measures: - Direct medical and nonmedical costs and indirect costs as a result of cancer - Objective Family Financial Stress Index - Subjective financial strain—assessed by one question on how the respondents had felt about the household's financial situation since their cancer diagnosis - Cancer-related financial stress—assessed by one question on the impact of the cancer diagnosis on the household's ability to make ends meet Symptom burden and other relevant measures: - DASS-21 Analysis: - Logistic regression Key findings: - Depression risk increased by threefold in participants reporting increased cancer-related financial stress (OR = 2.79, 95% CI 1.8-4.17) and increased cancer-related financial strain (OR = 3.56, 95% CI 2.23-5.67). - Risk estimates were higher for severe or worse depression, increased financial stress (OR = 4.36, 95 CI% 2.35-8.10), and increased financial strain (OR = 8.21, 95% CI 3.79-17.77). - Similar associations were reported for anxiety and distress.	Quality score: 9 Strengths: - Relatively large sample size ($n = 654$) Weaknesses: - Participants had varying time since diagnosis - 97% were cancer types associated with higher socioeconomic status (i.e., breast and prostate)
Delgado-Guay et al., 2015 U.S. $N = 149$ Purpose: Examine the frequency of financial distress and its correlates in patients with advanced cancer	Setting: CCC and GPH Time frame: NR Cancer type: breast (26%), colorectal (24%), lung (26%), and prostate (24%) Disease stage: advanced stage Treatment: CTX (77.2%), targeted therapy (20.1%), and XRT (24.8%) Time since diagnosis (yrs): NR Median age: 60 yrs (95% CI 58.6-61.5) Male: 50% Income level: CCC patients—median monthly income of $3000 USD (IQR $1400-7000); GPH patients—median monthly income of $940 USD (IQR: $350-$1300)	Financial toxicity measures: - Participants were asked to rate the impact of financial distress using a "strongly agree" to strongly disagree" statement - Four self-rated items on "subjective financial burden," "financial concerns," "financial difficulties," "financial worries," and using a numeric rating scale (0 = absent, 10 = worst) Symptom burden and other relevant measures: - ESAS, HADS, FACT-G, and MSPSS Analysis: - Pearson and Spearman correlation Key findings:	Quality score: 9 Strengths: - This study examined and compared financial distress in two cohorts with different income levels. This design provides insights that FT does not only affect people with lower income levels. - This study measured symptom burden including physical symptoms (ESAS) Weaknesses: - Use of nonvalidated scale to assess financial toxicity - Relatively small sample size, limited to bivariate analyses

	Education level: college (32.6%), advanced degree (9.6%), and high school or less (57.8%) Health insurance at diagnosis: NR Health insurance at the time of study: NR Employment status: NR	- Financial distress was reported as more severe than physical distress, distress about physical functioning, social/family distress, and emotional distress by 45 (30%), 46 (31%), 64 (43%), and 55 (37%) of patients, respectively (was significantly worse in patients at GPH as than patients at the CCC). - Patients reported that financial distress was affecting their well-being (0 = not at all, 10 = very much) with a median score of 5 (IQR: 1−8). FD correlated (Spearman correlation) with FACT-G ($r = -0.23$, $P = 0.057$), HADS-anxiety ($r = 0.27$, $P = 0.0014$), ESAS-anxiety ($r = 0.2$, $P = 0.0151$), and ESAS-depression ($r = 0.18$, $P = 0.0336$). - Financial distress was not significantly correlated with other items on the ESAS other than anxiety and depression including pain, fatigue, nausea, drowsiness, shortness of breath, appetite, sleep, feeling of well-being, and spiritual pain	
Barbaret et al., 2017 France $N = 143$ Purpose: Examine frequency and severity of financial distress and its association with quality of life and symptoms among patients with advanced cancer	Setting: teaching hospital, CCC Time frame: March 2013−June 2014 Cancer type: lung (25%), breast (25%), colorectal (25%), and prostate (25%) Disease stage: metastatic (85%), relapse (4%), locally advanced (8%), and other (2%) Treatment: surgery (52%), CTX (92%), XRT (56%), and targeted (6%) Time since diagnosis (days): had financial distress: 1979 (4997), had no financial distress: 1619 (1814) Mean Age: 58 yrs Male: 49% Income level (annual): <$15,000 Euro (38%), >$15,000 Euro (62%) Education level: college (27%), completed high school (15%), and did not complete high school (59%) Health insurance at diagnosis: NR Health insurance at the time of study: 91% Employment status: NR	Financial toxicity measures: - Financial distress was assessed using a self-rated numeric scale from 0 to 10 (0 = absent, 10 = worst). Patients were considered to have FD if they rated 1 or above on the 0−10 scale. High FD was defined as rating 4 or above—four self-rated items on "subjective financial burden," "financial concerns," "financial difficulties," "financial worries," and using a numeric rating scale (0 = absent, 10 = worst). Symptom burden and other relevant measures: - ESAS, HADS, FACT-G Analysis: - Student t-test, Chi-square (Mann-Whitney or Fisher test), Pearson or Spearman correlation ANOVA/Wilcoxon Key findings: - Patients with FD had higher HADS-D (8 versus 6 $P = 0.007$) and HADS-A (9 versus 7, $P = 0.009$) scores. - FD was linked to increased total ESAS score ($P = 0.005$) and spiritual suffering ($P = 0.045$).	Quality score: 10 Strengths: - This study measured symptom burden including physical symptoms (ESAS). Weaknesses: - Use of nonvalidated scale to assess financial toxicity - Small sample size, limited to bivariate analyses
de Souza et al., 2017 U.S. $N = 233$ Purpose: Examine the COST measure with	Setting: Cancer centers at the University of Chicago Medicine and the NorthShore University Health System. Time frame: May 2013 to February 2015.	Financial toxicity measures: - COST Symptom burden and other relevant measures:	Quality score: 9 Strengths: - This study is the first to validate an instrument to measure FT as a construct.

(*Continued*)

Table 2
Continued

Author, Year, Country, Sample Size, Study Purpose	Patient Characteristics	Measures, Analyses, and Key Findings	Quality Scores, Strengths, and Weaknesses
respect to its psychometric properties and to evaluate if patient-reported financial toxicity correlated with HRQOL.	Cancer type: NR Disease Stage: Stage IV solid tumors Treatment: NR Time since diagnosis (y): <1 (39%), >1 (61%) Median age (range): 59 (27–88) Male: 41.6% Income level: Median household income (range) of poverty level = 376.6% (0–7964%) Education level: < college (15.5%), some college or technical training (37.3%), completed college and above (47.2%) Health insurance at diagnosis: NR Health insurance at the time of study: Private or employer-based (61.8%), Medicare (31.3%), Medicaid (5.6%), COBRA coverage (1.3%) Employment status: Working (33.5%), Unemployed (9%), Retired (32.6%), On short-term/long-term disability (19.3%), other (5.1%)	- Brief POMS, FACT-G, EORTC-C30 Analysis: - Multivariable linear regression analyses Key findings: - FT (as measured by COST) was correlated with income (correlation coefficient [r] = 0.28, $P < 0.001$), psychosocial distress ($r = -0.26$, $P < 0.001$), and HRQOL, as measured by the FACT-G ($r = 0.42$, $P < 0.001$) and by the EORTC QOL instruments ($r = 0.33$, $P < 0.001$). - Independent factors significantly associated with FT were: race ($P = 0.4$), employment status ($P < 0.001$), income ($P = 0.003$), number of inpatient admissions ($P = 0.01$), and psychological distress ($P = 0.49$).	Weaknesses: - Sample was drawn from tertiary referral centers where all participants had some form of insurance coverage - The sample was only limited to those with ECOG performance status of <3
Hall et al., 2016 Australia $N = 1414$ Purpose: Explore outcomes of psychological distress (including anxiety, depression, and stress) in adult hematological cancer survivors, with a specific focus on potential differences between rural and urban survivors.	Setting: five Australian state population-based cancer registries Cancer type: Hematological 100%: NHL (55%–60%), leukemia (17%–18%), myeloma (14%–16%), other lymphoma (9%–11%) Disease stage: NR Treatment: CTX, XRT, BMT, and HRT (21%–24%) (did not provide breakdown) Time since diagnosis (months): 1–12 (6.7%–9.3%), 13–24 (13%), 25–36 (21%–24%), 37–60 (43%–51%), >60 (2.7%–17%) Age range: 15 to >70 yrs Male: 57% Income level: 41%–43% Education level: high school and below (49%–45%), vocational training (32%–36%), university (19%–30%) Health insurance at diagnosis: NR Health insurance at the time of study: NR Employment status: 41%–43%	Financial toxicity measures: - Self-reported questionnaire (researcher developed): financial difficulties as a result of cancer (including a range of indicators with varying impact) Symptom burden and other relevant measures: - DASS-21 Analysis: - Logistic regression Key findings: Factors associated with above normal levels of anxiety: 40–49 yrs (vs. >70 yrs), single (vs. partnered), less income, not taking time off work. Factors associated with above normal levels of depression: 40–49 yrs (vs. >70 yrs), lymphoma diagnoses (vs. myeloma), currently receiving active treatment of curative or palliative intent, other types of care (vs. receiving follow-up appointment only), had used up their savings due to cancer, and did not have or were unsure of their private health insurance. Factors associated with above normal levels of stress: 50–59 yrs (vs. >70 yrs), reported	Quality score: 11 Strengths: - This study focused only on hematological cancer. Weaknesses: - Use of nonvalidated measures of FT - Relatively low response rate (35%), which creates a potential for response bias

		difficulties in paying their bills due to cancer, having used up their savings due to cancer.	
Kale and Carroll, 2016 U.S. $N = 1380$ Purpose: Determine the prevalence and assess predictors of cancer-related financial burden and examine the association between financial burden and HRQOL and psychological health	Setting: 2011 Medical Expenditure Panel Survey (MEPS) data Time frame: 2011 Cancer type: breast (17%), prostate (12%), colorectal (4%), melanoma (6%), and other (61%) Disease stage: NR Treatment: NR Time since diagnosis (yrs): ≥5 (65%), <1 (6%), 1 to <3 (15%), 3–5 (14%) Age: <65 (72%), ≥65 (28%) Male: 44% Income/poverty level: high (46%), medium (29), low (12%), poor (13%) – (did not define) Education level: <high school (11%), high school (28%), college (45%), and >college (16%) Health insurance at diagnosis: 92% Health insurance at the time of study: 96% Employment status: NR	Financial toxicity measures: - The Cancer Self-Administered Questionnaire (CSAQ): 1. You or anyone in family had to borrow money or go into debt. a. How much money was borrowed or how much debt was incurred? b. Have you or a family member ever filed for bankruptcy? 2. Have you or a family member made any other financial sacrifices? 3. Ever worried about paying large medical bills? 4. Unable to cover cost of medical care visits? - Participants were judged to have a financial burden if they answered “Yes” to one of the above questions - Authors also examined the number of financial problems (range, 0–4) as a proxy for the extent of financial burden: 1) borrowed money, 2) declare bankruptcy, 3) worried about paying large medical bills, and 4) unable to cover cost of medical care visits Symptom burden and other relevant measures: - Depressed mood: Patient Health Questionnaire-2 - Psychological distress: Index of Kessler - Worries related to cancer recurrence, three-question survey: 1) how often survivors worry about cancer getting worse or coming back, 2) how often they worry about cancer recurrence affecting their responsibilities at home or work, and 3) what they believe about their changes of cancer recurrence or the disease getting worse within the next 10 years? Analysis: - Chi-square, Student t-tests, binary logistic regression, and multivariable linear regression Key findings: - Multivariable level: Compared with those without financial burden, survivors with financial burden (yes/no): 1) had increased odds of depressed mood (odds ratio, 1.95). [The odds for depressed mood were 3.41 times higher for survivors	Quality score: 9 Strengths: - Relatively large sample size (>1000) Weaknesses: - The data set did not include cancer stage and treatment type and did not control for these factors. - Recall bias could be present because most participants were diagnosed over five years ago.

(*Continued*)

Table 2
Continued

Author, Year, Country, Sample Size, Study Purpose	Patient Characteristics	Measures, Analyses, and Key Findings	Quality Scores, Strengths, and Weaknesses
		reporting ≥3 financial problems]; and 2) were more likely to worry about cancer recurrence (odds ratio, 3.54). - Survivors reporting ≥3 financial problems had 2.56 times higher odds of psychological distress than those without.	
Meeker et al., 2016 U.S. $N = 120$ Purpose: Assess and characterize the relationships among financial distress, emotional symptoms, and overall distress in insured patients with cancer	Setting: Insured patients within a CCC Time frame: September 2013 to April 2014 Cancer type: genitourinary (38%), gastrointestinal (24%), gynecologic (13%), sarcoma (8%), and other (17%) Median age (range): 62 (22−87) yrs Disease stage: NR Treatment: Surgery (68%), CTX (67%), XRT (39%), targeted therapy (16%), and HRT (1%) Time since diagnosis (yrs): <1 (37%), 1−3 (22%), 3−5 (17%), and >5 (25%) Male: 48% Income level: >100K (23%), 75−100K (13%), 50K−≤75K (20%), 25K−≤50K (20%), <25K (16%), and missing (8%) Education level: <high school (7), high school (33%), trade school/some college (27%), degree (21%), advanced degree (11%), and missing (1%) Health insurance at diagnosis: 100% Health insurance at the time of study: 100% Employment status: retired (41%), used for wages (26%), unable to walk (19%), out of work (5%), other (6%), and missing (3%)	Financial toxicity measures: - The InCharge Financial Distress/Financial Well-being Scale Symptom burden and other relevant measures: - Overall distress was measured using the National Comprehensive Cancer Network Distress Thermometer. - Emotional distress was measured using the self-reported six-item questionnaire (part of the problems list). Analysis: - Structural equation modeling Key findings: - A 1-unit increase in the financial distress scale (which indicates improved financial well-being) leads to a 0.3-unit decrease in the emotional distress scale (which indicates less emotional distress) ($P = 0.008$). - A 1-unit increase in the emotional distress scale leads to a 0.58-unit increase in overall distress (which indicates increased overall distress) ($P < 0.001$). - A 1-unit increase in the financial distress scale (which indicates improved financial well-being) leads to a 0.553-unit decrease in overall distress ($P < 0.001$). - After controlling for demographic variables, the total effect was that a 1-unit increase in the financial distress scale (which indicates improved financial well-being) leads to a 0.727-unit decrease in overall distress. - *Conclusion:* The total effect can be divided into two routes: pathways A and B (emotional distress mediates the association between financial distress and overall distress) and pathway C (financial distress directly increases overall distress.	Quality score: 11 Strengths: - This is the only one study that investigated the mediating effects of emotional distress between financial distress and overall distress. Weaknesses: - The instrument used to measure both overall and emotional distress is a screening tool (i.e., the distress thermometer problem checklist), which is not a validated measure of emotional and overall distress. - This study only included insured patients receiving care at a CCC.
Lathan et al., 2016 U.S.	Setting: Cancer Care Outcomes Research and Surveillance (CanCORS) Consortium.	Financial toxicity measures:	Quality score: 9 Strengths:

$N = 5343$ Purpose: Measure the association between patient financial strain and symptom burden, and quality of life for patients newly diagnosed with lung or colorectal cancer	Time frame: cancer diagnosis between 2003 and 2005. Cancer type: Colorectal (54%) and lung (46%) Treatment: NR Male: 56% Health insurance at diagnosis: NR Health insurance at the time of study: 94% Employment status: NR **Lung cancer (*n* = 2434)** Disease stage: I (30%), II (9%), III (28%), and IV (28%) Time since diagnosis (months): baseline (median): 4.2, follow-up interview (median) 12.4 Age: <59 (27%), 60−69 (32%), 70−79 (30%), and ≥80 (10%) Income level: <20K (34%), 20 to <40K (31%), 40 to <50K (16%), and ≥60K (18%) Education level: <high school (21%), high school (62%), and college degree or higher (18%) **Colorectal cancer (*n* = 2909)** Disease stage: I (30%), II (9%), III (28%), and IV (28%) Time since diagnosis (months): baseline (median): 4.2, follow-up interview (median) 12.4 Age: <59 (27%), 60−69 (32%), 70−79 (30%), and ≥80 (10%) Income level: <20K (34%), 20 to <40K (31%), 40 to <50K (16%), and ≥60K (18%) Education level: <high school (21%), high school (62%), college degree or higher (18%)	- Patients (or their surrogates) asked an interview question, “If you lost all of your current sources of income (for example, your pay check, Social Security or pension, public assistance) and had to live off of your savings, how long could you continue to live at your current address and standard of living?” Response options were less than one month, one to two months, three to six months, 7− 12 months, more than one year, and do not know Symptom burden and other relevant measures: - BPI, EORTC-C30, and EQ5D Analysis: - Univariable and multivariable linear regression and univariable and multivariable ordinal logistic regression (Spearman’s rank correlation coefficient was used to examine the potential for collinearity Key findings: - At four months after diagnosis: relative to patients with more than 12 months of financial reserves, those with limited financial reserves reported significantly increased pain (adjusted mean difference, 5.03 [95% CI 3.29 to 7.22] and 3.45 [95% CI 1.25 to 5.66], respectively, for lung and colorectal), greater symptom burden (5.25 [95% CI 3.29 to .22] and 5.31 [95% CI 3.58 to 7.04]), and poorer QOL (4.70 [95% CI 2.82 to 6.58] and 5.22 [95% CI 3.61 to 6.82]). - At 12 months (since diagnosis), financial strain was an independent predictor of pain and depression (results not reported).	- Large sample size: >5000, this is the only included study that measured financial reserves Weaknesses: - N/A
Fenn et al., 2014 U.S. $N = 2108$ Purpose: Examine the relationship between the financial problems caused by cancer and quality of life	Setting: 2010 National Health Interview (NHIS) Survey Time frame: 2010 Cancer type: Multiple cancer type Disease stage: NR Treatment: NR Time since diagnosis (yrs): NR Age: NR Male: NR Income level: NR Education level: NR Health insurance at diagnosis: NR Health insurance at the time of study: NR Employment status: NR	Financial toxicity measures: - The following question from the Cancer Control Supplement, “To what degree has cancer caused financial problems for you and your family?” The question was answered using a four-point scale ranging from 0 = not at all to 4 = a lot. Symptom burden and other relevant measures: - Worry of cancer recurrence: “what do you think the chances that your cancer will come back or get worse within the next 10 years?”/and their worry regarding the same “how often do you worry that your cancer may come back or get worse?	Quality score: 6 Strengths: - Relatively larger sample size >2000 - This study is the only longitudinal study that provides insights about changes in outcome measures over 12 months. Weaknesses: - This study did collect participant characteristics, but did not report them.

(*Continued*)

Table 2
Continued

Author, Year, Country, Sample Size, Study Purpose	Patient Characteristics	Measures, Analyses, and Key Findings	Quality Scores, Strengths, and Weaknesses
		[unclear how patients' responses were categorized] Analysis: - Bivariate analysis and binary logistic regression model Key findings: - Patients who had a higher level of cancer-related financial problems were more likely to worry that the cancer may return all the time (43%) when compared with patients with lower financial burden (28.1%) ($P < 0.001$).	

ANOVA = analysis of variance; BMT = bone marrow transplantation; BPI = Brief Pain Inventory; CCC = Comprehensive Cancer Center; COST = COmprehensive Score for financial Toxicity; CTX = chemotherapy; DASS = Depression Anxiety Stress Scale; ECOG = Eastern Cooperative Oncology Group Performance Status; EORTC = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; EQ5D = EuroQoL-5 Dimension scale; ESAS = Edmonton Symptom Assessment System; FACT-G = Functional Assessment of Cancer Therapy—General; FD = financial distress, GPH = General Public Hospital; HADS = Hospital Anxiety and Depression Scale; HRQOL = Health-Related Quality of Life; HRT = hormonal therapy; IQR = interquartile range; MSPSS = Multidimensional Scale of Perceived Social Support; NHL = non-Hodgkin lymphoma; NR = not reported; POMS = Profile of Mood States; Q = quartile; QoL = Quality of Life; SF12 = Short-Form Health Survey; USD = U.S. dollars; XRT = radiotherapy.

In an Australian study of 1414 hematological cancer survivors, *trouble meeting day-to-day expenses, difficulty paying bills, stopped work, travel time to treatment,* and *using home services in the last month* were not associated with anxiety and depression.[23] However, *not having private health insurance* was an independent predictor of depression. Difficulty paying bills (OR: 1.94, 95% CI 1.03-3.67) was an independent predictor of stress. *Using up savings* was an independent predictor of depression (OR: 1.79, 95% CI 1.10-2.92) and stress (OR: 1.81, 95% CI 1.07-3.05).

To allow for a greater understanding of the direct and indirect relationships between FT, emotional distress, and overall distress, in a small U.S. study ($n = 120$) that examined the relationships between these constructs in insured cancer survivors,[24] financial distress was associated with overall distress both directly (accounting for 76% of the effect) and indirectly (accounting for 24% of the effect) via mediation by emotional distress. Within this structural equation model, a one-unit increase on the financial distress scale (which indicates improved financial well-being) led to a 0.3-unit decrease on the emotional distress scale (which indicates less emotional distress; $P = 0.008$).[24]

Of the six studies that involved cancer survivors at various time points after diagnosis, only one study assessed physical symptoms.[26] In a longitudinal study of 5343 lung and colorectal survivors, those individuals with greater financial strain (defined as less financial reserves—the length of time patients could continue to live at their current address and standard of living if they lost all their current sources of income and had to live off their savings) had significantly higher levels of pain (adjusted mean difference [MD] = 5.03 [95% CI 3.29 to 7.22] and MD = 3.45 [95% CI 1.25 to 5.66], respectively, for lung and colorectal) and greater (overall) symptom burden (MD = 5.25 [95% CI 3.29 to .22] and MD = 5.31 [95% CI 3.58 to 7.04]). At 12 months after diagnosis, financial strain was an independent predictor of pain and depression (results not reported).[26]

Cancer Survivors with Advanced Cancer

Three studies of patients with advanced cancer (mixed cancer diagnoses) reported positive relationships between FT and depression,[15,22] anxiety,[15,22] and psychological distress[3] (all $P < 0.05$). In a French study of 143 patients with advanced cancer, a significant difference in spiritual suffering was found between those with financial distress and those without ($P = 0.045$)[22]. In addition, patients with FT had higher levels of depression ($P = 0.007$), anxiety ($P = 0.009$), and total symptom burden ($P = 0.005$). In a research instrument validation study ($n = 233$),[3] higher psychological distress was independently

Table 3

Findings of Relationships Between Symptom Burden and Financial Toxicity (by Types of Measures)

	Physical			Psychological and Spiritual						Overall
Measures of FT	Pain	Dyspnea	Physical Symptoms Other Than Pain	Depression	Anxiety	Stress	Fear of Recurrence	Spiritual Suffering	Overall Psychological Distress	Overall Symptom Burden
1. Monetary measures										
Sharp et al. 2013[a]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
2. Objective measures										
De Souza et al. 2017[b]	NA	NA	NA	NA	NA	NA	NA	NA	+ (weak)	NA
Hall et al. 2016[c]	NA	NA	NA	+ (weak)	+/−[d] (weak)	+ (weak)	NA	NA	NA	NA
Kale et al. 2016	NA	NA	NA	+ (weak)	NA	NA	+ (moderate)	NA	N	NA
3. Subjective measures										
Sharp et al. 2013[e]	NA	NA	NA	+/−[f] (moderate)	+/−[f] (moderate)	+/−[f] (moderate)	NA	NA	NA	NA
Delgado-Guay et al. 2015	N	N	N	+ (weak)[g]	+ (weak)[g]	NA	NA	N	NA	NA
Barbaret et al. 2017[h]	Measured, but not reported	Measured, but not reported	Measured, but not reported	+	+	NA	NA	+	+	+
De Souza et al. 2017[i]	NA	NA	NA	NA	NA	NA	NA	NA	+ (weak)	NA
Meeker et al. 2016[h]	NA	NA	NA	NA	NA	NA	NA	NA	+	NA
Lathan et al. 2016[j]	+ (weak)	+ (weak)	NA	+ (weak)	NA	NA	NA	NA	NA	+ (weak)
Fenn et al. 2014[h]	NA	NA	NA	NA	NA	NA	+	NA	NA	NA

"+" = findings indicate a positive correlation; "−" = findings indicate a negative correlation; "N" = findings indicate no correlation; "NA" = did not assess; ESAS = Edmonton Symptom Assessment System; HADS = Hospital Anxiety and Depression Scale; FT = financial toxicity.

[a] Monetary measures were used but only descriptive analysis was conducted.

[b] Measure of FT used has both objective and subjective components.

[c] Used multiple (7) measures to indicate FT.

[d] Inconsistent direction of correlation for different indicators of FT: positive correlation with decreased income, but negative correlation with taking time off work.

[e] Used two indicators of FT.

[f] Findings showed higher odds of anxiety, depression, and distress in both patients who have more and less concerns of their financial situation after being diagnosed with cancer, than those who report unchanged levels of concern.

[g] Both depression and anxiety were measured with two tools: ESAS and HADS.

[h] Did not report measures of strength of association.

[i] Measure of FT used has both objective and subjective components.

[j] Findings for two separate disease cohorts (lung and colorectal cancer) were reported; however, findings were generally consistent.

associated with worse self-perceived FT ($P = 0.003$).[3] Of the three studies that included patients with advanced cancer, only one study ($n = 149$) evaluated psychological and physical symptoms.[15] This study reported positive correlations between FT (defined as financial distress) and anxiety ($r = 0.2$, $P = 0.015$) and depression ($r = 0.18$, $P = 0.034$). However, no associations were found between FT and a range of physical symptoms including pain, fatigue, nausea, drowsiness, dyspnea, appetite, sleep, feeling of well-being, and spiritual pain.[15]

Discussion

Although the literature on FT has grown exponentially over recent years,[4] the relationships between FT and symptom burden are not well understood. To our knowledge, this systematic review is the first to evaluate the literature that explored these relationships. In this review, six studies found positive relationships between increases in FT and higher levels of psychological symptoms (i.e., depression and anxiety). This finding has an immediate implication for practice. Clinicians should regularly screen for, assess, and manage emotional distress related to FT when it occurs.[13,27] The distress thermometer and problem checklist[28] could be considered as a screening tool for distress potentially attributed to FT. The checklist items relevant to FT included those within the "practical problems" domain, which include childcare, housing, insurance/financial, transportation, work/school, and treatment decisions. Future intervention studies that aim to minimize or prevent FT should evaluate psychological symptoms as secondary outcomes. A limited amount of emerging evidence suggests that positive relationships exist between FT and psychological (or existential) symptoms other than depression and anxiety (e.g., fear of recurrence,[12,24] spiritual suffering,[22] stress).[23] Measuring these variables in future investigations of FT may increase our understanding of the mechanisms that underlie the associations between FT and symptom burden.

In this review, only two of the nine studies evaluated and reported physical symptoms.[15,26] In the two studies that examined the association between pain and FT, the findings were inconsistent.[15,26] Given the high occurrence rates for fatigue, cognitive dysfunction, pain, and sleep disturbance in cancer survivors, additional research is warranted to examine the relationships between these symptoms and FT. In addition, it is important to consider symptoms that may potentially affect work productivity (e.g., cognitive dysfunction, fatigue) and in turn lead to financial distress. In future studies, symptom inventories that are more comprehensive in nature and tailored for the appropriate populations (e.g., patients undergoing active treatment, long-term cancer survivors) should be considered. Besides evaluating self-perceived symptoms using patient-reported outcome tools, objective measures to quantify symptom burden (e.g., neuropsychological tests, biomarkers) should be included in future investigations. Furthermore, it is important to determine if the relationships between symptom burden and FT depend on which measure of FT is used. The three types of FT measures (i.e., monetary, objective, and subjective measures) could capture different dimensions of financial burden experienced by cancer survivors. The findings from this review highlight that no study has assessed the relationship between symptom burden and FT using monetary measures. Although the use of validated subjective FT measures (i.e., FACIT-COST) has increased, well-recognized, monetary, and objective measures are yet to be developed and validated. This gap should be addressed in future studies.

The relationships between FT and symptom burden are undoubtedly complex and warrant more in-depth investigations. Below, we highlight a number of gaps that should be addressed in future studies. Most of the studies in this review involved a heterogeneous sample of cancer survivors with various cancer diagnoses, time points since diagnosis, and stage of disease. These studies mainly focused on the long-term impact of FT and symptom burden after treatment ends. Because FT may occur at the time of or even before diagnosis,[29] the studies cited in this review do not provide a comprehensive understanding of *when* FT occurs and *how* FT is associated with and/or interacts with symptom burden at an early stage of the cancer trajectory. The lack of longitudinal studies with multiple measures of both FT and symptoms limit our ability to develop predictive models. Future research should use a longitudinal design and examine which phenotypic and symptom characteristics are associated with a worse FT trajectory and the direction of these relationships. As financial distress can emerge from causes unrelated to cancer, the use of control groups is important to determine the proportion of financial distress attributable to cancer, especially since a significant portion of FT outcomes are subjectively reported by patients. Interestingly, we were unable to locate any mixed-methods or qualitative studies in our search. A mixed-methods approach will likely offer insights into these complex relationships. Qualitative approaches will allow investigators to explore and understand aspects of FT not adequately described by outcomes defined in quantitative studies. This approach will provide a more comprehensive picture of FT and can further assess if FT outcomes evaluated in existing studies are sufficiently sensitive to describe the financial distress experienced by cancer survivors. In addition to investigating the relationships between FT and individual symptoms, there might be value in understanding the relationships between FT and symptom burden (as a collective measure).[22,26]

Several limitations warrant consideration. First, we did not do an exhaustive search including the "gray literature" and databases that are suitable for publications in South America and China. In addition to key medical literature databases (i.e., MEDLINE, CINAHL, and EMBASE), we hand-searched the reference lists of all relevant articles and reviewers, as well as Google Scholar. It is unlikely that any English articles were missed. Second, the included studies involved samples from high-income, developed countries including the U.S., Australia, France, and Ireland. It is likely that people in different health systems have different experiences of FT. With the limited studies conducted with high variations in the study samples across a small number of countries, it makes comparisons across multiple countries or health systems impossible. Therefore, the findings from this review cannot be generalized to other parts of the world. Third, publication bias could potentially exist where negative findings were not published at all or were not published in the English language. However, given the small number of included studies, we were not able to assess publication bias. Despite these limitations, this review is the first to explore the relationships between FT and symptom burden and provided recommendations for future research.

Conclusions

Based on the findings from this review, relatively clear evidence supports an association between FT and psychological symptoms. Clinicians should regularly screen for, assess, and manage emotional distress that is attributable to FT. Although the causal pathway is not yet clear, future intervention studies aimed at minimizing or preventing FT may incorporate psychological symptoms as secondary outcomes. Little is known about the relationships between FT and physical symptoms. Future research should overcome the methodological limitations of the current literature including the lack of longitudinal data collection, use of mixed-methods approaches, inclusion of validated monetary, subjective, and objective FT measures, and homogeneity of samples. This review did not evaluate workability and work productivity, which is closely related to FT, an evaluation of the association between symptom burden, financial hardship, and workability and productivity outcomes might provide insights to support the development of future interventions.

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Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jpainsymman.2018.12.003.

References

1. Singleterry J. The Cost of Cancer: Addressing Patient Costs (American Cancer Society Cancer Action Network). Washington, DC: The Cost of Cancer, 2017.

2. Burstein HJ, Krilov L, Aragon-Ching JB, et al. Clinical cancer advances 2017: Annual report on Progress against cancer from the American Society of clinical Oncology. J Clin Oncol 2017;35:1341–1367.

3. de Souza JA, Wong Y-N. Financial distress in cancer patients. J Med Person 2013;11:73–77.

4. Gordon LG, Merollini KMD, Lowe A, Chan RJ. A systematic review of financial toxicity among cancer survivors: we Can't Pay the Co-Pay. Patient 2017;10:295–309.

5. Yabroff KR, Lawrence WF, Clauser S, Davis WW, Brown ML. Burden of illness in cancer survivors: findings from a population-based national sample. J Natl Cancer Inst 2004;96:1322–1330.

6. Altice CK, Banegas MP, Tucker-Seeley RD, Yabroff KR. Financial hardships experienced by cancer survivors: a systematic review. J Natl Cancer Inst 2016;109:1–17.

7. Kent EE, Forsythe LP, Yabroff KR, et al. Are survivors who report cancer-related financial problems more likely to Forgo or Delay medical care? Cancer 2013;119:3710–3717.

8. Kale HP, Carroll NV. Self-reported financial burden of cancer care and its effect on physical and mental health-related quality of life among US cancer survivors. Cancer 2016;122:283–289.

9. Khera N, Chang YH, Hashmi S, et al. Financial burden in recipients of allogeneic hematopoietic cell transplantation. Biol Blood Marrow Transplant 2014;20:1375–1381.

10. Sharp L, Timmons A. Pre-diagnosis employment status and financial circumstances predict cancer-related financial stress and strain among breast and prostate cancer survivors. Support Care Cancer 2016;24:699–709.

11. Catalano PJ, Ayanian JZ, Weeks JC, et al. Representativeness of participants in the cancer care outcomes research and surveillance consortium relative to the surveillance, epidemiology, and end results program. Med Care 2013;51:e9–e15.

12. Fenn KM, Evans SB, McCorkle R, et al. Impact of financial burden of cancer on survivors' quality of life. J Oncol Pract 2014;10:332—338.

13. Chan RJ, Gordon L, Zafar SY, Miaskowski C. Financial toxicity and symptom burden: what is the big deal? Support Care Cancer 2018;26:1357—1359.

14. Islam T, Dahlui M, Majid HA, et al. Factors associated with return to work of breast cancer survivors: a systematic review. BMC Public Health 2014;14(Suppl 3):S8.

15. Delgado-Guay M, Ferrer J, Rieber AG, et al. Financial distress and its associations with physical and emotional symptoms and quality of life among advanced cancer patients. Oncologist 2015;20:1092—1098.

16. National Cancer Institute. Survivor defintion (NCI Dictionary), 2018. Available at https://www.cancer.gov/publications/dictionaries/cancer-terms/def/survivorship.

17. National Coalition for Cancer Survivorship. Our Mission. NCCS, 2018. Available at https://www.canceradvocacy.org/about-us/our-mission/.

18. Mols F, Vingerhoets AJ, Coebergh JW, van de Poll-Franse LV. Quality of life among long-term breast cancer survivors: a systematic review. Eur J Cancer 2005;41:2613—2619.

19. So WK, Chan RJ, Chan DN, et al. Quality-of-life among head and neck cancer survivors at one year after treatment–a systematic review. Eur J Cancer 2012;48:2391—2408.

20. The Cochrane Collaboration. Cochrane Handbook for Systematic Reviews of Interventions. Chichester, West Sussex: Wiley, 2011.

21. Rosenthal J. Qualitative Descriptors of strength of association and effect size. J Social Serv Res 1996;21:37—59.

22. Barbaret C, Brosse C, Rhondali W, et al. Financial distress in patients with advanced cancer. PLoS One 2017;12:e0176470.

23. Hall AE, Sanson-Fisher RW, Carey ML, et al. Prevalence and associates of psychological distress in haematological cancer survivors. Support Care Cancer 2016;24:4413—4422.

24. Meeker CR, Geynisman DM, Egleston BL, et al. Relationships among financial distress, emotional distress, and overall distress in insured patients with cancer. J Oncol Pract 2016;12:e755—e764.

25. Sharp L, Carsin AE, Timmons A. Associations between cancer-related financial stress and strain and psychological well-being among individuals living with cancer. Psychooncology 2013;22:745—755.

26. Lathan CS, Cronin A, Tucker-Seeley R, Zafar SY, Ayanian JZ, Schrag D. Association of financial strain with symptom burden and quality of life for patients with lung or colorectal cancer. J Clin Oncol 2016;34:1732—1740.

27. Gordon LG, Chan RJ. Financial toxicity among patients with cancer-where to from Here? Cancer Nurs 2017;40:257—258.

28. Donovan KA, Grassi L, McGinty HL, Jacobsen PB. Validation of the distress thermometer worldwide: state of the science. Psychooncology 2014;23:241—250.

29. Carrera PM, Kantarjian HM, Blinder VS. The financial burden and distress of patients with cancer: understanding and stepping-up action on the financial toxicity of cancer treatment. CA Cancer J Clin 2018;68:153—165.

Appendix

Supplementary Data

Quality Assessments of the Included Studies

Assessment criteria	Sharp, Carsin & Timmons, 2013	Delgado-Guay et al., 2015	Barbaret et al., 2017	de Souza et al., 2017	Hall et al., 2016	Kale and Carroll, 2016	Meeker et al., 2016	Lathan et al., 2016	Fenn et al., 2014
Did the study explain **how the patient sample was selected**?	1	1	1	1	1	1	1	1	1
Was the inclusion/exclusion criteria clearly formulated?	1	1	1	1	1	1	1	1	1
Was the **sociodemographic and medical data** described (age, race, employment status, educational status, tumor stage, diagnosis etc.) in the study?	1	1	1	1	1	1	1	1	1
Is the type of (cancer) treatment described?	1	1	1	0	1	0	1	0	0
Are the results of study **compared between two or more groups** (healthy population, groups with different cancer treatment or age, comparison with time at diagnosis etc.)?	0	1	0	0	1	0	0	0	0
Was the mean/median or standard deviation/range **of time since diagnosis and treatment** given?	1	0	1	1	1	1	1	1	0
Were the **participation and response rates of the participants** described and if so were they **more than 75%?**	0	0	1	0	0	1	1	0	0
Was information about patient/**disease characteristics** presented?	1	1	1	1	1	1	1	1	1
Was a **standardized or valid quality of life/symptom measure** (i.e., questionnaire, scale) used?	1	1	1	1	1	1	1	1	0
Are **mean, median, standard deviations, or percentages** reported for the most important **outcome measures**?	1	1	1	1	1	1	1	1	1
Was an attempt made to find a set of **determinants with the highest prognostic value?**	1	0	0	1	1	1	1	1	1
Did the patient **sign an informed consent form** before study participation?	0	1	1	1	1	0	1	1	0
Total	9	9	10	9	11	9	11	9	6

Note. 1 = yes; 0 = no; each yes score is assessed 1 point: studies with ≥10 points = high quality, studies with 7 to 9 points = moderate quality, and studies with ≤6 points = low quality.