Financial toxicity in cancer care: origins, impact, and solutions

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Abstract
Financial toxicity describes the financial burden and distress that can arise for patients, and their family members, as a result of cancer treatment. It includes direct out-of-pocket costs for treatment and indirect costs such as travel, time, and changes to employment that can increase the burden of cancer. While high costs of cancer care have threatened the sustainability of access to care for decades, it is only in the past 10 years that the term “financial toxicity” has been popularized to recognize that the financial burdens of care can be just as important as the physical toxicities traditionally associated with cancer therapy. The past decade has seen a rapid growth in research identifying the prevalence and impact of financial toxicity. Research is now beginning to focus on innovations in screening and care delivery that can mitigate this risk. There is a need to determine the optimal strategy for clinicians and cancer centers to address costs of care in order to minimize financial toxicity, promote access to high value care, and reduce health disparities. We review the evolution of concerns over costs of cancer care, the impact of financial burdens on patients, methods to screen for financial toxicity, proposed solutions, and priorities for future research to identify and address costs that threaten the health and quality of life for many patients with cancer.

Keywords
Cancer, Cost, Financial toxicity, Access, Health policy

INTRODUCTION
Cancer care has always involved tradeoffs between the benefits of interventions designed to remove, treat, or prevent the recurrence of potentially life-threatening disease, and the inherent toxicity of these interventions. Considering the risks of an intervention, informing patients of these risks, and managing them is central to the practice of oncology. Relatively recently it has become clear that one aspect of “risk” from cancer care is often overlooked with potentially serious consequences for patients. This is the risk of “financial toxicity.”

Financial toxicity describes the financial burden and distress that can arise for patients, and their family members, as a result of cancer treatment [1]. The degree to which financial toxicity is an inherent risk of an intervention, as opposed to a byproduct of our healthcare and health insurance system, can be debated. Yet there is little question that cancer care can result in severe financial consequences for patients that may subsequently translate into diminished quality of life, reduced adherence and limited access to care [2–5]. These impacts of costs of care for patients are related to, although distinct from, the increasing costs of cancer care for all in need, while reducing utilization of low value care that can bring financial burdens without clinical benefit.

Implications
Practice: Clinicians should consider the direct and indirect financial consequences of cancer treatment decisions that can impact patient distress, access and adherence to treatment, and clinical outcomes. There is a need to consider potential for financial toxicity at the time of clinical decision making and to screen for financial burdens, distress and limitations on access throughout the course of cancer treatment.

Policy: Policymakers, payers, industry and health systems need to consider the impact of costs of care on patients and their families and seek policy solutions that can promote equitable access to high quality cancer care for all in need, while reducing utilization of low value care that can bring financial burdens without clinical benefit.

Research: There is a need to identify effective and optimal strategies to screen for and address financial burdens and distress among patients with cancer in order to minimize financial toxicity, promote access to high value care, and reduce health disparities.
Total oncology costs, including costs of physician services, hospitalization and hospital services, and medication are estimated to reach $246 billion in the United States by 2030 [8]. While financial toxicity may be particularly acute in the USA due to gaps in insurance coverage and higher costs of care, financial toxicity is recognized as a global issue affecting countries across health system structures and income levels [9–12].

Concerns over the financial impact of cancer on patient distress date at least as far back as the 1970s, but came to broader attention in the 1990s, perhaps due to wider consideration of health insurance reform during this period [13, 14]. With progress in cancer therapeutics in the 2000s came rising costs resulting in growing discussion of the sustainability of the U.S. health care system [15]. Following the 2008 election, with health care reform again on the national agenda, oncologists demonstrated increased concern about costs, contributing to a policy statement from the American Society of Clinical Oncology (ASCO) that recognized cancer costs as burdensome to patients and calling for discussions of cost in the clinic as a component of high-quality cancer care [16]. This growing concern over costs was provocatively captured in 2013 with the description of “out-of-pocket costs as side effects” and the coining of the term “financial toxicity [1,17,18].” Concerns over cost were amplified by the development of increasingly expensive oral drugs, exemplified by the alarm raised publicly by oncologists over the cost of tyrosine kinase inhibitors [19]. This period also saw major academic centers balk at providing approved cancer drugs due to high cost and marginal benefit [20]. Concern about the impact of high costs on patients was not confined to the U.S. and the European Society for Medical Oncology (ESMO) released their own position statement in 2014 [21].

Today, financial toxicity is estimated to affect approximately half of cancer survivors [22]. Thus, identifying solutions to ensure access to care and reduce financial burdens is a priority for cancer care delivery and research [7,23].

Financial toxicity affects patients across types and spectrums of cancer care. These include medical and radiation oncology, through high-cost interventions, frequent outpatient encounters, employment disruption, and long-term physical and financial effects [24-26]; surgical oncology, marked by high-cost single episodes of care and subsequent recovery needs [27]; pediatric oncology, impacted by high caregiver costs as well as immense long-term survivorship needs [28]; and palliative or end-of-life care, conveying particularly high costs in the last days or weeks of a patient’s life [29]. Across the care continuum, financial toxicity has also emerged as a key mediator of disparities in care and clinical trial access, exacerbating already-critical inequities in cancer treatment [25,30].

In this review, we will characterize the high costs of care and mechanisms of cost shifting to patients that are driving financial toxicity, describe current screening tools for financial toxicity and expand on frameworks for understanding types of financial hardship caused by cancer care. Additionally, we will describe the impacts of financial toxicity on access, distress, adherence, and outcomes. Finally, we discuss potential solutions to financial toxicity and priorities for future research.
DOCUMENTATION AND IMPACT OF THE HIGH COSTS OF CANCER CARE

High costs of care and key trends in cost shifting

The costs of cancer care can be broadly grouped into direct and indirect costs (Fig. 1). Direct costs include drugs, diagnostics, imaging, hospital services, and physician and ancillary service fees while indirect costs include time costs to patients and caregivers as well as long-term opportunity costs (such as changes in employment) caused by cancer treatment [24, 31].

Drivers of cost growth can similarly be divided amongst these direct and indirect costs. Three key trends contributing to the rise in direct costs are the growing costs of cancer medications, including shifts to oral medications; progressive rise in patient contributions to insurance coverage; and intensifying usage of other medical services as a part of standard care. As noted by Bach and colleagues, the costs of new cancer drugs seem more closely tied to what the market will bear than the marginal value of the new drug [32]. This is not a surprising outcome in a system with no price controls or negotiation, and a for-profit drug development industry with a fiduciary responsibility to shareholders. A key driver of the indirect costs is the large “time cost” of cancer treatment, which can have far-reaching effects on quality of life. Over time, the impact of changes in employment due to cancer and other opportunity costs are magnified for patients diagnosed during their working years [33]. These issues are compounded for adolescents and young adults with cancer. As more patients do well and survive a cancer diagnosis, the downstream economic impacts are magnified raising a novel challenge that must be recognized as a by-product of our growing success in treatment.

Similarly, the increase in development of oral therapies for cancer is a welcome advance for patient convenience, but it brings new challenges. Growth of oral medications and combination regimens for cancer contribute not only to the national cost of cancer therapy, but also to the proportion of those costs that are borne by patients [34]. Because intravenous therapies are covered by Medicare Part B and oral therapies by Medicare Part D, changes in standard of care to include oral therapies in earlier treatment lines can raise patient costs by over 100-fold in some cancers [24, 35]. As catastrophic coverage thresholds continue to rise, annual front-loading of costs may further the risk of acute financial toxicity for patients who do not have adequate savings, despite reduction of the coverage gap in 2020 [36, 37]. Similarly, the increasing use of combination regimens and addition of biologics to standard regimens in earlier lines may increase costs to patients [38, 39]. In particular, the rapid emergence of effective immunotherapeutic agents brings remarkable promise for treatment in many settings, but adds both drug costs and costly toxicity-associated hospital stays and monitoring [40].

In addition to rising drug costs, increasing complexity of care such as increased imaging and adjunctive visits also contributes to out-of-pocket costs for patients, and to the immense indirect “time cost” of oncology care [41]. For example, Yabroff and colleagues calculated “time costs” by applying national estimates of time-per-medical service type from the National Ambulatory Medical Care Survey to the documented number of visits and visit types (including emergency care and hospital stays) in the 2008–2011 national Medical Expenditure Panel Survey. They then used the median U.S. wage rate to convert this time into estimated costs. They found that in the first two years after diagnosis, medical time costs were estimated to be up to nine times higher than those of age matched controls without cancer, depending on cancer type. The cost of this lost time alone was estimated to be an average of $1,188 per year for survivors 18–64 years old and $1,542 for survivors >65 years old [42, 43]. Further, while indirect time cost is highest in the initial diagnostic period, in longer-term survivors the severity of financial distress often remains high throughout the treatment period, and the risk of bankruptcy and employment disruption persists for years beyond diagnosis [44–46]. Perhaps not surprisingly, the cost of time required for cancer care is particularly marked at the end of life. Estimates of in-hospital days in the last year of life for patients with prostate cancer, for example, range from 16 to 24 days, and total time spent on cancer care is estimated to reach up to 30 days for ovarian cancer, 31 days for lung cancer, and 32 days for gastric cancer [42, 43, 47]. The average patient with these cancers spends close to 1 month of time in the hospital in the last year of life.

Beyond the cost of time spent in the hospital and undergoing treatment, the financial costs of care at the end of life for patients with cancer can be exorbitant [48, 49]. Palliative care, focused on symptom management as opposed to disease directed therapy, can reduce costs and improve quality of life for patients with advanced care, but is inconsistently engaged in end of life care [50–52].

Measuring financial toxicity

Financial toxicity describes the impact of cancer care on both objective financial burden and subsequent financial distress of patients [6,24]. It is not purely a function of the cost of care, but includes the impact of that cost on a patient based on financial and other patient characteristics. Co-payments that may be insignificant for some patients may lead to distress or absolute barriers to care for others. In order to identify, manage, and, ideally, prevent financial toxicity, we need to be able to measure it. Multiple assessment tools for financial toxicity have
emerged, several of which are specific to oncology. The most widely used is the Comprehensive Score for Financial Toxicity (COST), while other tools include the Breast Cancer Finances Survey Inventory (BCFS), the Consumer Financial Protection Bureau scale of financial well-being, and the Personal Financial Wellness scale (PFW scale) [53]. The COST measure is an 11-item survey that covers financial spending, financial resources, and psychosocial response; it has been found to be correlated to income, psychosocial distress, and health-related quality of life [54]. The BCFS, by contrast, is an early and longer instrument designed to detail individual components of financial and emotional coping behaviors, while the PFW scale is a noncancer-specific scale designed primarily to focus on subjective distress related to finances [53,55]. Key themes that emerge from these scoring systems are the measurement of both objective financial burden and also its mediation by behavioral and financial coping strategies and emotional impact [53].

In a comprehensive review of measures used to evaluate financial burdens of cancer care, ranging from single questions within broader quality of life scales to financial toxicity specific tools, Witte and colleagues identify several distinct domains that may be addressed: total spending, use of financial resources, psychological impact, seeking financial support, adjustments in care to control costs, and lifestyle adjustments [53]. While single questions may serve to flag financial hardship as an issue, there is a need to better understand the association between the economic impact of cancer care and the psychological impact associated with this burden for patients that can only be captured in scales addressing both domains [53,56].

One domain that is not well captured by current scales is a measurement of access to various types of social support or “social capital,” which may mediate racial disparities in how cost translates to material and psychosocial burden [57–59]. These aspects of financial toxicity are pivotal because while direct and indirect costs are themselves mediated by an individual patient’s circumstances, the experienced psychological and material toxicity of these costs is magnified by poverty and structural barriers to care and social support [58,60]. A growing body of literature documents the disparate effects of financial toxicity on the basis of patient characteristics including: lower income [61-64], younger age [62,65], lower financial literacy [66,67], membership in a group facing structural racism [65,68], rural residence [69,70], or membership in sexual and gender minority groups [71]. While these disparities have been identified, mediating factors such as geographic variation in insurance and transportation costs as well as effective mitigation strategies remain understudied [72].

Impact on financial outcomes
Perhaps the most obvious impact of financial toxicity is on the patient’s finances. The cumulative financial toll of direct and indirect costs can have devastating long-term effects on the financial health of people with cancer and their families. In a pivotal retrospective study of 197,840 people diagnosed with cancer in Washington State, Ramsey and colleagues found that those with cancer were 2.65 times more likely to declare bankruptcy than age- and location-matched controls. Those with lung cancer were 3.8 times more likely to file for bankruptcy [73]. This may be mediated by diminished ability to save: cancer patients not only lose assets during the treatment period, but must increasingly liquidate assets in order to be able to finance catastrophic costs [74]. In addition, employment disruption during the cancer treatment period has long-term career effects for both patients and families [75,76]. Consistent with these findings, cancer survivorship in adults under age 55 is associated with lower asset ownership and lower net worth compared to adults of the same age without cancer [33].

Fig 2 | Conceptual model of financial toxicity. The cancer treatment plan can lead to out-of-pocket expenses for imaging, drugs, and medical visits, in addition to other direct and indirect costs. This leads to financial toxicity which is mediated by the magnitude of cost and the patients individual characteristics such as household income, social support, employment status. Financial toxicity then leads to downstream financial impact (such as forgoing other priorities such as housing, recreation, other healthcare, and potential bankruptcy), emotional distress, and lower adherence with medication or avoidance of visits or other medical expenses. These impacts in turn can lead to inferior quality of life or disease specific outcomes, including survival.
Impact of financial toxicity: patient and caregiver distress

Beyond defining and measuring the purely economic impact of financial toxicity, there are important questions about how this form of “toxicity” impacts the quality of life (QOL) and other outcomes for patients with cancer and their families. Figure 2 provides a conceptual model of how cancer treatment decisions translate into direct out-of-pocket costs, which can lead to financial toxicity which then brings downstream effects. One of the best measured impacts to date is on the correlation between financial toxicity and psychological distress. Large surveys of cancer patients have found that between 19% and 29% report severe financial distress, with strong correlations to emotional distress, mental health problems, fear of recurrence, and poor physical and social functioning [77–79]. Measurement of psychological distress, as noted above, is an evolving area for standardization and study in financial toxicity. However, a growing body of both qualitative and quantitative literature identifies recurrent themes in the psychological response to financial toxicity, including changes in affect and coping behaviors [53]. Additionally, financial toxicity creates strain on patients’ caregivers and their support networks [80–82]. Even relatively smaller cost items, such as parking costs, which are prevalent nationally and rarely reimbursed, can cause disproportionate emotional duress and require burdensome cost coping behaviors [80,83].

Impacts of cost on access, adherence, and outcomes

Beyond adding to the emotional burden and financial hardship of a cancer diagnosis is the question of how financial toxicity impacts access to care and cancer outcomes. Financial toxicity has the potential to exacerbate existing health disparities by raising additional barriers to access to care. Financial toxicity touches on each of five dimensions of access: availability, accessibility, affordability, acceptability, and accommodation [84,85]. Affordability directly mediates care decisions among patients and physicians. Out-of-pocket costs are associated with delayed initiation of prescribed chemotherapy [86], early discontinuation of medications, particularly oral medications [4,87,88], and may even prompt patients and clinicians to adjust their choice of treatment [89,90]. For example, when faced with higher copayments, patients with chronic myelogenous leukemia were almost twice as likely to discontinue potentially life-saving imatinib [4]. The impact of financial toxicity is greatest among younger, non-white, and rural patients who are more likely to forgo medical care and follow-up of their cancer as a result [91]. Overall, financial toxicity is associated with reduced treatment adherence, inferior health-related quality of life, and increased cancer-related fatigue [1,91–93]. Rural patients with cancer also face higher financial burden due to lack of local care options [70,94]. Closure and mergers of rural hospitals in the USA has exacerbated this problem [95].

Direct evidence on the effect of financial toxicity on disease outcomes is limited; however, in one study of patients with head and neck cancers, those with financial toxicity were more likely to miss clinic visits and had lower use of supplements and medications to manage side effects. These patients were also more likely to require feeding tubes, possibly as result of inadequately managed side effects [96]. Ramsey and colleagues compared mortality among patients in a Washington-based cancer registry who did and did not file for bankruptcy and found that this severe financial outcome was associated with worse survival after controlling for patient and disease characteristics [97].

Access to clinical trials is an important component of access to cancer care, and it is also heavily influenced by financial toxicity despite the fact that many of the direct costs in clinical trials are provided for patients. Financial concerns regarding geographic accessibility and acceptability are large driving factors in the decision to decline clinical trials and once in trials, participants face higher indirect costs from increased clinical visits, travel to clinical trial sites, and uncertainty regarding potential adverse effects and supportive care needs of investigational agents [30,98]. In one study, Phase I clinical trial participants averaged $1,550 in monthly medical costs, with greater costs for those living >100 miles from the hospital or with incomes of <$60,000/year [99]. Inability to bear these costs and gamble on these uncertainties likely contributes to large disparities in enrollment across age, racial, and urban/rural groups [100]. Even the specter of these costs can impact willingness to participate in research: in one survey of 1,256 patients, perceived risk of financial burden was one of the largest deterrents keeping patients from pursuing or asking about clinical trials [98]. Of course, the financial toxicity associated with standard care also raises ethical concerns about undue inducement to participate in research because drug costs will be covered. This potential threat to voluntary informed consent is another downstream consequence to high costs of cancer care.

SOLUTIONS TO FINANCIAL TOXICITY

In the face of these massive and varied aspects of financial toxicity, a growing field of research is investigating strategies to mitigate cost and distress to patients. We review several key initiatives regarding patient-centered discussions of cost in clinic, financial navigation programs, and policy initiatives.

Cost conversations: patient perspective

As noted above, in 2009 ASCO embraced discussions of cost at the time of decision making as a
means to reduce financial burdens and as a component of quality cancer care [16]. Evidence suggests that most, but not all, patients are interested in discussing costs of cancer care. In survey data, the proportion of patients with cancer interested in discussing costs of care with a provider has ranged from 59% to as high as 94% depending on the patient population and context [101,102]. However, costs are often not addressed unless patients raise the issue. One study analyzing the initial clinic visit of outpatients at two urban cancer hospitals found that among 45% of visits with cost conversations, 63% of discussions were started by the patient [103]. Similarly, in an analysis of outpatient encounters at three large hospitals, although financial concerns were discussed in only 28% of visits, patients or caregivers were the ones who raised cost concerns 70% of the time [104]. Interestingly, the financial topics discussed differed depending on the initiating party. When patients raised concerns, they often concerned non-pharmacologic interventions, such as restaging scans, and opportunity costs such as time off work. Physicians largely focused on the direct costs of expensive therapies, which have been a major driver of the push for financial toxicity management [103,105].

Although many cancer patients are amenable to discussing costs with their oncologists, some are not. In one study, only 20% of those surveyed saw it as the oncologist’s job to discuss costs [106]. A similar survey found that nearly one-third of patients preferred to discuss finances with someone other than the treating physician [101]. This hesitancy may stem from a fear that discussion of costs could adversely impact delivery of care. The majority of patients prefer that direct costs, such as out-of-pocket expenses, remain separate from treatment decisions, including both decisions made by the patient themselves and decisions made by the treating oncologist [101,102,106]. Patients feel even more strongly that societal costs, such as those incurred by insurance companies and the government, should not factor into treatment decisions [102,106]. Those undergoing therapy for advanced disease may be particularly adverse to discussing costs compared to cancer survivors, further suggesting that some patients may fear substandard treatment if financial concerns are discussed or a more affordable option is proposed [101]. Those with lower baseline financial wellness are more likely to fear treatment plan alteration if financial toxicity is discussed, indicating that those who may most benefit from cost conversations are also those who may be the most hesitant to raise concerns [106]. Additionally, some patients may believe that higher costs actually lead to better outcomes. In one survey, just 28% of patients reported they would want a lower cost treatment regimen, even if it was proven to be just as effective as the more expensive option [106].

Collectively, this literature on patient preferences and experiences with discussions of cost suggest that many patients do wish to discuss costs, but primarily to understand the out-of-pocket expenses they will encounter and not to discuss the total costs of care. Further, the variation in preferences suggests a need to screen for financial hardship and interest in discussing cost, but not to assume that every patient wishes to have these discussions, particularly with their oncologist. Consideration should be given to how and when to approach cost in clinic, the goals of such discussions, and how screening for financial toxicity that may impact access and the other outcomes noted above can be normalized without adding distress for some patients or paradoxically exacerbating disparities. Clinicians should be careful to clarify what expenses are most concerning to their patients and to separate discussions regarding cost from treatment recommendations.

Cost conversations: clinician perspective
If financial toxicity can be addressed by discussing costs in clinic, oncologists need to be educated and willing participants in these discussions. An early survey of oncologist views on costs of care found that 80% felt the impact of treatment decisions on patient finances was important, but 20% felt that cost discussions had no role in practice and 31% felt uncomfortable discussing costs [15]. More recent surveys of oncologists demonstrate ongoing concerns over potential misunderstanding or harm to patient relationships with cost conversations, but substantial interest in discussing costs in clinic. A 2016 survey of ASCO members (medical, radiation, and surgical oncologists) found that a majority (75%) of oncologists agree it was their responsibility to consider out-of-pocket costs to patients [107]. Sixty percent of oncologists in this survey reported that they often or frequently discussed costs of cancer care with patients (though the remainder stated they rarely or never discuss costs). In addition, 80% reported that their patients are often surprised by out-of-pocket costs for care [107]. In a recent survey of breast surgeons, 87% of surgeons agreed that patients should have access to the costs of their cancer treatment prior to making oncologic treatment decisions and 53% of surgeons agreed that doctors should consider patient costs when considering cancer treatment [108]. Despite this, just 20% felt prepared to discuss treatment costs with their patients and few (6%) identified out-of-pocket costs of surgery as one of the top 3 priorities for women facing a surgical decision.

While these surveys demonstrate that oncologists strongly favor price transparency and have an interest and willingness to discuss costs of cancer care, they also identify structural and normative barriers to effective cost discussions. By far the largest and most consistent barrier identified by physicians across surveys is simply lack of knowledge.
and resources to discuss costs [90, 107, 109]. Another structural barrier commonly identified is a perception of inadequate time during the visit. Normative barriers, as reflected by patients’ misperceptions as well, included the avoidance of cost discussion due to perceived inability to help with the costs and discomfort/embarrassment discussing costs with patients [90, 107]. Discussions of cost may also be limited due to variation and lack of transparency in insurance coverage at the time of the clinical encounter and lack of transparency regarding costs of care even within the physician’s own healthcare organizations [110, 111]. It is also notable that one in five oncologists consistently report that it is not their place to discuss cost or reported that they felt cost discussions harmed care [15, 107]. While these are minority views among oncologists this still represents a significant portion of the field and highlights the need to address cultural barriers if physicians are to lead in protecting patients from financial toxicity.

Financial navigation
Another approach that does not directly affect the physician-patient relationship is to offer financial navigation services within the clinic or cancer center. While the services and target patient populations for these programs vary widely, they exist to identify and assist patients with financial distress. For example, some cancer centers primarily provide financial assistance for those who are uninsured or underinsured, whereas others meet with all new patients to proactively identify those at risk for financial hardship [112]. Moreover, some centers primarily provide assistance with high medication costs, while others also address non-medical costs (e.g., transportation, housing, etc.). Recent surveys have highlighted some of these variations. A 2017 survey of members of the National Comprehensive Cancer Network (NCCN) found that 75% of centers screened all patients for financial distress, while the other 25% screened only targeted groups deemed to be at higher risk of financial toxicity [113]. A 2019 survey of the 62 National Cancer Institute Comprehensive Cancer Care Centers found a range of financial services available: over 95% of respondents provided assistance in applying for pharmaceutical industry programs and medication discounts, assistance with non-medical costs, and assistance with health insurance optimization [114]. In addition, roughly half of responding centers included counseling on medical debt management and/or costs when discussing treatment options as part of their financial navigation services. Over 70% of centers agreed that lack of price transparency was a barrier to effective financial navigation [114]. Notably, these programs are not limited to large academic centers: 72% of community oncology practice groups indicated having a financial screening process, primarily through patient intake forms [115].

Whether these programs work and how they impact financial toxicity and access to care is an ongoing area of research. Thus far, small case studies and case series have highlighted large financial savings for both patients and hospital systems. A case series of four hospitals that each implemented a financial navigation program found that financial navigators helped patients save, on average, $33,265 per year from free medications, $35,293 from premium assistance, $12,256 through insurance optimization, and $900 on non-medical costs (e.g., transportation) [116]. Hospitals, in turn, were estimated to save on average $2.1 million per year, thought to be from avoiding unpaid costs that the hospital would have otherwise absorbed. Other case studies of individual cancer centers have found similar results, albeit in non-controlled settings [112].

Less is known, however, about whether these savings translate into meaningful differences in patients’ experiences and outcomes. Shankaran and colleagues evaluated the impact of a financial navigation course coupled with regular contact with financial advisors, finding that while there was high patient satisfaction with the program, there were no differences in patients’ self-reported financial burden and inconsistent changes in patients’ cost-related anxiety [117]. Another solution under investigation is mobile-application based financial navigation, which in an early randomized trial was associated with improved awareness and financial application assistance [118]. Further work should continue to characterize specific services provided, as well as the impact of these programs on financial and patient-centered clinical outcomes.

Ultimately, whether financial navigation services will be a sustainable long-term solution remains controversial. Some argue that these programs reduce financial barriers to accessing high-quality cancer care. In contrast, others argue that these programs fail to address the root causes of financial toxicity, such as rapidly rising costs of various cancer treatments that may or may not reflect their value added [119].

Defining value
Beyond these direct patient-facing interventions, one way to try to mitigate financial toxicity and promote access to cancer care is to characterize the value of care and develop policies or guidelines that promote high value care, while limiting low value care. In this framework, financial barriers to high value care should be eliminated. The challenge is in defining value.

In general, value is a relative evaluation of the benefit (e.g., overall survival, disease free progression, palliation of symptoms, etc.) versus the cost (e.g., financial cost, toxicity, etc.) of an intervention.
However, the appreciation of the benefits and costs depends on how it is measured and from whose perspective. A patient’s perspective of value could be quite different from an insurer or a policymaker. Drugs A and B could be determined to be equally effective in the potential to extend life by months with limited toxicities, but insurers might prefer Drug A because it is cheaper, while a patient may prefer Drug B because they are less troubled by its particular side-effects, frequency of infusions, or route of administration. Alternatively, Drug B could be more effective but because the co-pay is less for Drug A, the patient may prefer the cheaper drug, even if they lose some clinical benefit. Additionally, just because a drug is of high value, its cost may be unsustainable for society or unaffordable to an individual patient, particularly given that 40% of Americans cannot easily pay $400 for an unexpected cost without borrowing money [120].

Therefore, when determining value, it is essential to take a multi-stakeholder approach that is inclusive of the patient perspective and that includes an assessment of affordability [121–123].

Several frameworks for assessing value in oncology have been created including the ASCO Value Framework, the ESMO Magnitude of Clinical Benefit Scale (ESMO-MCBS), Memorial Sloan Kettering Drug Abacus, NCCN Evidence Blocks, and Institute for Clinical and Economic Review (ICER) Value Framework [124]. Initially, ASCO defined clinically meaningful outcomes (e.g., an increase in overall survival of 4–5 months for pancreatic cancer) to help guide clinical trial development, and then created the Value Framework that calculates a Net Health Benefit score to help physicians and patients engage in shared decision-making to determine optimal treatment regimens [125,126]. The ESMO-MCBS has a greater focus on policymakers and allows for a ranking of cancer therapeutics in terms of effectiveness [127]. The two frameworks have shown moderate levels of concordance as each continue to be revised and improved [128].

**FUTURE DIRECTIONS**

There is a critical need for increased research both characterizing the extent and nature of financial toxicity among cancer patients, as well as interventions that successfully mitigate these harms. One area of notable concern is the current limited data describing how the combined sequelae of financial toxicity (bankruptcy, decreased treatment adherence, changes in health-seeking behavior, etc.) directly translates to long-term health outcomes. Of note, financial instability associated with oncologic care may detrimentally impact both cancer-related health outcomes, as well as routine care for other health conditions and patients’ health-seeking behaviors. Further, there is a need to evaluate the broader impact of costs of cancer care on the burden, health, and health care decisions of caregivers [129].

The identification of detrimental health outcomes related to financial toxicity may further inform the evaluation of interventions seeking to mitigate financial toxicity.

The extent to which individual providers and health centers may play a role in mitigating financial toxicity remains unclear. While existing data suggests a proportion of patients do hold negative views towards costs of care conversations with providers, it is imperative to more fully understand if these are static beliefs inherent to individual patients, or a reflection of unfixed social norms and patients’ prior experiences in the healthcare system. In one study, patients with lower financial wellness were significantly more likely to cite concerns regarding fear of judgment and consequent altering of their treatment regimen as reasons for not wanting to discuss costs of care with their oncologist [97]. Fears such as these serve as barriers to optimal care and represent potential areas for quality improvement. Costs of care conversations may often be sensitive in nature similar to goals-of-care conversations or the delivery of distressing test results that have benefitted significantly from the development of evidence-based approaches. Efforts should be taken to develop similar best practices for engaging patients in conversations regarding financial toxicity and identifying optimal roles for members in multidisciplinary care teams. It should be noted that the optimal role of physicians in financial navigation may take various forms, from leading conversations to simply normalizing financial concerns in an empathetic and nonjudgmental manner and coordinating connections to other members of the care team. Novel approaches of incorporating curricula related to cost-of-care conversations and financial toxicity (didactics, simulation models, etc.) for medical trainees may increase the number of providers who feel prepared to discuss treatment costs with their patients.

Increased efforts should be made to understand existent disparities in financial toxicity and their interplay with disparities in health outcomes. Recent policy statements by ASCO and American Association for Cancer Research (AACR) have served as powerful reminders of the extent to which social determinants of health influence cancer outcomes [130,131]. The consequences of catastrophic financial instability involve various systems outside of healthcare — housing and lending, employment, legal system (medical debt); a robust body of literature exists demonstrating the discriminatory treatment historically marginalized populations receive in these systems. Future research characterizing financial toxicity, as well as proposed interventions, should ensure participation of robustly diverse patient populations (including those with limited English proficiency) with a focus on how different demographic factors may influence outcomes. Considerable care should be taken to not categorize patient groups as monolithic entities, but to instead...
perform nuanced assessments of how factors such as race/ethnicity, immigration status, limited-English proficiency, age, sexual orientation, and gender identity, etc. are associated with financial toxicity, patient perceptions, and the broad applicability of interventions.

One novel solution to the costs of cancer care is research aimed at doing more with less. The field of “pharmaco-economics” is relatively new, but aims to develop clinical trials that test the efficacy of lower dose medications, dose adjustments based on diet, and other mechanisms of achieving similar disease outcomes at lower cost [132]. One of the pioneering studies in this field has shown that the biological efficacy of an expensive novel leukemia drug, ibrutinib, can be maintained with dose reduction (and associated cost savings) after the first cycle of therapy [133]. Whether this approach can reduce costs for patients or society, or if it will simply trigger changes in price from manufacturers remains to be seen.

In the realm of policy interventions, increasing scrutiny of value for new cancer therapeutics is critical. Health Technology Assessments (HTA) are a method of determining the cost-effectiveness of new therapeutics, used widely in the United Kingdom and internationally but not required by Medicare for coverage of FDA-approved anticancer chemotherapeutic regimens. In situations in which regimens have been proven to have equal therapeutically benefit, increased use of both HTA and patient-reported outcome measures for determining which chemotherapies are covered and used are important [134]. Between 2002 and 2014 only 42% of drugs approved by the FDA for solid malignancies met ASCO benchmarks for meaningful improvements, and thus some clinically interchangeable drugs may be raising prices without improving outcomes [135]. High costs for emerging therapies such as immunotherapy and CAR-T which do typically offer considerable clinical value make these analyses particularly pressing. As targeted or even tissue-specific advances continue in the diagnosis and treatment of cancer, mitigating financial toxicity for patients and their families will be a critical factor in ensuring that the benefits of innovation are shared by all.

**Conclusion**

Financial toxicity is not inherent in a drug or intervention in the same way that a physical risk or side effect may be, but in the context of our health care system, it is a real consequence of care and treatment decisions for many patients with cancer and it has real consequences. Both direct and indirect costs of care can have devastating effects on patients’ quality of life and long-term financial health, and the best ways to measure and mitigate this distress are under active investigation. Key areas for further research are cost conversations and financial navigation, policy initiatives to promote access to the high value of care, and work aimed at understanding the mediators of inequity in financial toxicity. As advances continue in the diagnosis and treatment of cancer, mitigating financial toxicity for patients and their families will be a critical factor in ensuring that the benefits of innovation are shared by all.

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**Compliance with Ethical Standards**

**Conflicts of Interest:** J.P. has an employment relationship (spouse) with GlaxoSmithKline, and has consulted for Abbott Labs. S.F.J. consults for Venn Therapeutics.

**Ethics:** This is a review, not original research. This article does not contain any studies with human participants performed by any of the authors. This study does not involve human participants and informed consent was therefore not required. This article does not contain any studies with animals performed by any of the authors.

**Transparency Statement**

Financial Toxicity in Cancer Care: Origins, Impact, and Solutions.

**References**


