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Clinical Commentary

Financial toxicity – An overlooked side effect

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HIGHLIGHTS

- Expensive novel therapeutics and underinsurance complicate the delivery of cancer care in the United States.
- "Financial toxicity" of treatment can lead to negative downstream effects (i.e., bankruptcy, non-adherence to treatment).
- Universal financial toxicity screening of cancer patients before, during, and after treatment should be standard of care.
- Identification of high-risk patients with triage to financial resources and counseling can improve cancer care delivery.

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1. The cost of gynecologic cancer therapies

The US is facing a crisis of rising health care costs. The rapid diffusion of expensive medical and pharmaceutical technologies as well as our aging population are strong contributors that are particularly relevant to the field of oncology. Once approved by the Federal Drug Administration (FDA), novel cancer therapeutics such as targeted therapy or immunotherapy, are often introduced to the market at exceptionally high prices. Using Medicare reimbursement rates (converted to 2017 dollars), estimated monthly drug acquisition costs were $5747 for bevacizumab, $12,585 for olaparib, $9567 for pembrolizumab, and $17,542 for olaratumab at the time of each drug's initial FDA approval. In the US, drug manufacturers can not only set market prices for drugs, but they are also shielded from competitive forces by regulatory and patent-related exclusivity [1]. While drug acquisition costs are important from a societal perspective, a more patient-centered measure of the anticipated magnitude and timing of out of pocket (OOP) costs is needed to help patients better manage their finances; however, these costs are complex to estimate and often not discussed with patients.

With the increasing use of maintenance therapy in certain ovarian cancer patient populations, increased attention will need to be given to patient financial considerations. In the upfront setting, bevacizumab may be utilized concurrently with platinum and taxane-based chemotherapy and then continued as maintenance therapy for up to 9–-12 months based on published studies [2,3]. In the recurrent setting, poly(ADP-ribose) polymerase (PARP) inhibitors may be prescribed as switch maintenance for patients with platinum sensitive disease or who are positive for homologous repair deficiency or germline and somatic *BRCA* mutations [4–7]. Treatment regimens that utilize maintenance strategies require a shift in our approach to discussing the potential benefits, toxicities, and associated OOP costs as treatment duration may be prolonged and disease status may be unmeasurable or asymptomatic.

While oral therapies, such as PARP inhibitors, have the benefit of more convenient administration, these drugs can place more cost-sharing pressure on patients compared to intravenous or intraperitoneal infusions that are traditionally provided in health care settings. This is because prescription benefits are separate from other health care benefits. Medicare Part D is the Medicare prescription drug benefit program and has a coverage gap (the "donut hole"). In 2018, this coverage gap begins once a patient reaches $3750 in retail prescription drug costs (retail costs are shared by the payor and the patient) and ends when an individual reaches the $5000 OOP prescription drug spending threshold (OOP costs paid by the patient only). With the passage of the Patient Protection and Affordable Care Act (ACA) in 2010, individuals receive a "donut hole" discount for generic and brand-name prescription drugs, which has increased annually so that the "donut hole" will be effectively eliminated and individuals will pay no >25% cost-sharing for covered prescription drugs by 2020. In addition, many prescription drug benefit programs utilize tiered formularies in which patient cost-sharing escalates depending on whether the drug is generic or based upon price, with expensive oral cancer therapies often falling in the highest tiers. Manufacturer-based financial assistance programs

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may offer support for these expensive therapies; however, Medicare beneficiaries are typically not eligible and this practice may actually perpetuate higher drug prices over time [8].

2. Financial strain as a side effect ("toxicity") of treatment

In this context, financial toxicity is the patient-level impact of cost and is a potential side effect just like any other "toxicity" that can result from treatment. Cancer patients are at increased risk for experiencing financial strain compared to patients without cancer due to accumulated OOP costs, which can include direct medical costs (i.e., co-pays, coinsurance, and medications) and non-medical costs (i.e., transportation, lodging, and childcare) [9]. It is estimated that low-income individuals undergoing cancer treatment spend up to 25% of their annual income on OOP medical expenditures [10]. With over 60% of bankruptcies filed due to medical reasons, cancer patients have a 2.5 times higher risk of filing for bankruptcy compared to non-cancer patients [11,12]. In addition, patients may experience indirect opportunity costs such as changes in employment, loss of wages, or strains on non-medical spending. Financial toxicity can negatively affect patients' adherence to treatment and has been found to be a risk factor in cancer patients for early mortality [13,14]. Patients may skip doses to make medications last longer, not refill medications, or delay treatments due to cost. Higher levels of financial strain have also been shown to adversely impact quality of life [15].

3. Universal screening for financial toxicity

The first step toward decreasing financial toxicity is incorporating universal screening as standard of care for cancer patients. While OOP expenditures are typically front-loaded following diagnosis, patients may not receive their bills right away and thus may be initially unaware of potential financial strain until after they have started treatment. Throughout treatment, patients may have changes in their ability to work which may be reflected in decreased income or change or loss of insurance benefits. Additionally, there is evidence that financial toxicity persists even after treatment is completed as cancer survivors ≥5 years from their diagnosis continue to experience higher medical costs and face work limitations compared to patients who have never had cancer [16]. Whether a single screening question or a brief patient reported outcome instrument such as the Comprehensive Score for Financial Toxicity (COST) is used, financial toxicity screening can be incorporated into the existing intake process (i.e., by nurses, care coordinators, or financial counselors). Screening may target patients starting or switching to a new treatment regimen and then be repeated at planned follow-up intervals to assess for both positive changes after intervention and negative changes due to fluctuating circumstances (see Table 1) [17–22].

Table 1
Financial toxicity screening instruments.

Instrument	Screening question(s)	Potential responses
National Comprehensive Cancer Network (NCCN) Distress Thermometer and Problem List [17]	Please circle the number (0—10) that best describes how much distress you have been experiencing in the past week including today.	0 (no distress) to 10 (extreme distress)
	Please indicate if any of the following has been a problem for you in the past week including today.	Under Practical Problems: Child Care, Housing, Insurance/financial, Transportation, Work/school, Treatment decisions
Behavioral Risk Factor Survey [18]	In the last 12 months, was there a time when you needed to see a doctor but could not because of cost?	Yes No
Medical Expenditure Panel Survey [19]	In the last 12 months, did you skip medications to save money?	Yes No
Aldana & Liljenquist [20]	Please indicate how often this describes you: I don't have enough money to pay my bills.	Never Rarely Sometimes Often Always
Organization for Economic Cooperation and Development (OECD) Measuring Financial Literacy [21]	Sometimes people find that their income does not quite cover their living costs. In the last 12 months, has this happened to you?	Yes No Don't know
Comprehensive Score for Financial Toxicity (COST) [22]	I know that I have enough money in savings, retirement, or assets to cover the costs of my treatment.	Not at all A little bit Somewhat
	My out-of-pocket medical expenses are more than I thought they would be.	Quite a bit Very much
	I worry about the financial problems I will have in the future as a result of my illness or treatment.	COST score > 21 proposed as threshold for severe financial toxicity
	I feel I have no choice about the amount of money I spend on care. I am frustrated that I cannot work or contribute as much as I usually do.	
	I am satisfied with my current financial situation.	
	I am able to meet my monthly expenses.	
	I feel financially stressed.	
	I am concerned about keeping my job and income, including work at home.	
	My cancer or treatment has reduced my satisfaction with my present financial situation.	
	I feel in control of my financial situation.	