# On the origin of financial toxicity for cancer patients

Author: Addison D. McGinnis

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Shorter Title: On the Origin of Financial Toxicity

Authors: Addison D. McGinnis[1]

Corresponding author: Addison D. McGinnis

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[1]Economics Department, Boston College, 140 Commonwealth Ave, Chestnut Hill, MA
Email: amcginnis2014@gmail.com
Telephone: +15854891492

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Abbreviations: Incremental Cost-Effectiveness Ratio (ICER), Quality-Adjusted Life Year (QALY), U.S. Food and Drug Administration (FDA), Confidence Interval (CI)

Drugs mentioned: cisplatin, gemcitabine, docetaxel, enzalutamide, abiraterone, sipuleucel-T, lomustine (Gleostine®; NextSource Pharmaceuticals: Miama, Florida), nivolumab (Opdivo®; Bristol-Myers Squibb: New York City, New York), everolimus, ipilimumab (Yervoy®; Bristol-Myers Squibb: New York City, New York), bevacizumab (Avastin®; Genentech: San Francisco, California), CAR-T

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**Abstract**

The rapid growth in cancer treatment pricing has produced a new type of adverse effect for patients called "financial toxicity". Financial toxicity involves an increased likelihood that cancer patients will experience bankruptcy, relationship problems, and even mortality. Although several factors have been identified that can contribute to financial toxicity for cancer patients, this is the first study to use both logistic regression and cost-benefit analysis to evaluate those factors that contribute most to financial toxicity. Logistic regression was used to assess information on 559 cancer patients from the 2016 United States National Health Interview Survey, while incremental cost- effectiveness ratios (ICERs) were used to assess various cancer drugs. Besides previously identified factors that can contribute to financial toxicity, e.g., age, poor health status, insurance coverage, race etc., this analysis showed that younger age, inpatient care, and excessive cancer drug costs for advanced-stage cancer were the most important factors for predicting financial burden. Cost-benefit analysis showed that cancer drug cost was often not proportional to therapeutic efficacy for many advanced-stage cancers. Although financial toxicity has dire implications for patient health and societal healthcare spending, economic and therapeutic strategies are presented that could help reduce this growing problem.

## Introduction

Over 1,600 people die each day in the United States from cancer according to the American Cancer Society [1]. New cases of cancer are expected to increase by 57 percent within the next 20 years [1-2]. Due to increasing prevalence and treatment costs, national cancer expenditures totaled almost $125 billion in 2010, and are projected to reach $156 billion by 2020 [1]. The estimated yearly cost of survival for a cancer patient while undergoing traditional treatment was $54,100 (adjusted for inflation) in 1995, and was $207,000 in 2013 [3]. While the cost for those living with cancer has increased by almost 400% over the last 20 years, five-year survival rates have improved by only about 22% [1]. Indeed, cancer treatment has emerged as one of the more costly areas of healthcare [4-5].

As the cost of cancer treatment has risen, a greater burden has been placed on Medicare and Medicaid for financial reimbursement [6]. With rising cancer rates and an aging population, full reimbursement has become unmanageable [6-7]. Consequently, public and private insurance

providers have shifted parts of the treatment cost to their policyholders [8]. This shift comes in the form of higher premiums, coinsurance, and copayments [7-8]. Most cancer patients pay about $3,600-$5,500 out-of-pocket per year for treatment, while some patients pay up to $10,000 out-of-pocket for treatment [9]. Under the burden of these financial demands, many cancer patients have resorted to spending less on necessities, while others have reduced adherence to treatment [10]. The increased financial burden placed on cancer patients is now referred to as "financial toxicity" [11,12]. Financial toxicity is a new adverse effect of cancer treatments that is emerging as a widespread problem for cancer patients [8,10,11,13].

Financial toxicity has deleterious side effects. The risk of mortality is about 1.60 times greater for cancer patients with high financial stress than for cancer patients without financial stress, and is twice as high for those who have filed for bankruptcy [14]. The positive correlation between bankruptcy and mortality is particularly concerning, as cancer patients have a 2.65-times greater risk than the normal population of declaring personal bankruptcy according to a population study in Washington state [11]. Oncology patients suffering from financial toxicity are more likely to be unsatisfied with their personal relationships compared to cancer patients not suffering from financial toxicity [15]. Additionally, high out-of-pocket healthcare expenditures prior to the death of a loved are associated with prolonged poverty status and bankruptcy for family members, especially if the deceased family member was the primary wage earner [16-17]. Hence, financial toxicity has become another serious adverse effect of cancer treatment.

While all cancer patients are at risk for financial toxicity, those who had an overnight hospital stay, those < 65 years of age, and those receiving drug treatment for advanced-stage cancer are especially vulnerable [18]. The goal of this study is to highlight the significance of these three factors when considering who may be at risk for financial toxicity, and to look at the primary causes of financial burden under these factors. Possible strategies for reducing financial toxicity are also discussed.

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**Methods**

Regression Analysis

A sample of cancer patients was selected from the 2016 National Health Interview Survey (NHIS) Person File [27]. The NHIS Person File contained questions that were asked to all household members. The NHIS was given to a representative sample of households in the U.S. non-institutionalized population [27]. The publicly released data files for the 2016 NHIS contained data for 40,220 households and 97,169 persons in 40,875 families [27]. The NHIS is a voluntary survey with questions that remain mostly unchanged from year to year. The goal of the survey is to identify healthcare trends and monitor progress toward national health objectives [27].

A total of 559 cancer patients were identified in the 2016 NHIS Person File. Data obtained on sample characteristics included age, sex, race/ethnicity, education, national region, marital status, health status, cancer duration, insurance status, employment status, other physical limitations, and income levels relative to the poverty threshold. Information on missing observations for income levels was estimated using the 2016 NHIS Imputed Income File [27]. Information was also obtained on healthcare access and utilization using data on overnight medical care, the amount of times a patient received care, doctor's office visits, and reception of medical advice/results via phone. All factors were presented as independent variables in each regression in order to control for statistically significant differences between patients who gave informative answers and those who "didn't know", or refused to respond.

Financial hardship associated with cancer treatment was measured by asking patients if they, (1) had problems paying medical bills and, (2) had paid more than $3,000 out-of-pocket for medical care in the past year. Multivariate logistic regression models were used to examine patient characteristics associated with financial hardship. The first regression was on a dependent binary variable coding "1" if a patient had problems paying medical bills, or "0" if a patient had no problems paying medical bills. The second regression was on a dependent binary variable coding "1" if a patient had $3,000 or more in out-of-pocket medical expenditures over the course of the year, or "0" if a patient had less than $3,000 in out-of-pocket medical expenditures.

Bivariate odds ratio analyses were developed to verify that each categorical variable was significant to a level of $[P>|z|] < 0.1$ for at least one of the two regression measurements. Variables that were not significant for either measurement were either included or not included based upon their usage in other similar regressions in the academic literature [15,19,20]. The continuous age

variable was divided into five relevant sub-groups to account for differences in employment and insurance status (Table 1-2). Multivariate factors were found to be significant at $P < 0.05$ in each regression. All statistical analyses were performed using STATA 14.2.

Cost-benefit Analysis

This study also presented cost-benefit analysis on some common chemotherapy and immunotherapy drugs currently used to treat advanced-stage cancers. Incremental cost-effectiveness ratios (ICERs) were used to assess the relative cost and benefit of each cancer treatment. When calculating the ICER, the costs and clinical outcomes associated with one treatment were compared with an alternate strategy for treating the same diagnosis [21]. The ratio was calculated by taking the difference in cost between two treatments over the difference in their therapeutic effect [22]. An ICER was presented in terms of "dollars spent per quality-adjusted life year (QALY) gained".

QALYs consisted of a factor between the "life-years" and "utility", i.e., a quality weight that measures health-related quality of life [23]. "Life-years" refer to the number of additional years a patient might live after beginning treatment, while "utility" refers to the health-related quality of life that a patient might experience while undergoing treatment. The utility value ranged from "0" as death, to "1" as a healthy life state [23]. Each incremental increase in utility between "0" and "1" must be indicative of a small health improvement [23]. Treatments with utility values closer to "$\frac{1}{2}$" were considered treatments that caused serious side effects, while treatments with utility values closer to "1" were considered treatments that caused little or no adverse effects [23]. Each incremental increase in the utility value and life-years value would have a large impact on QALY. A lower QALY value would result in a larger ICER, reflecting a treatment that was less cost-effective. Similarly, a higher QALY value would result in a smaller ICER, reflecting a treatment that was more cost-effective.

$$ICER = \frac{(cost\ of\ treatment\ A) - (cost\ of\ treatment\ B)}{(QALY\ A - QALY\ B)}$$

To control for current drug costs, the study included only included incremental cost-effectiveness ratios reported within the last six years. The patent situations on each reported drug have not changed since the year when their ICER was reported [24, 25]. Drug prices solely within the United States were used in the study, as the prices of cancer drugs are typically lower in other countries [26].

**Ethics**

Consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the "World Medical Association Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects" adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964 and amended by the 59th WMA General Assembly, Seoul, South Korea, October 2008, as reflected in a priori approval by the appropriate institutional review committee.

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**Results**

Regression Analysis

This report uses information from the 2016 National Health Interview Survey (NHIS) and information on health care utilization for the evaluation of financial toxicity in cancer patients [27]. The final response rate for households was 67.9% for the 2016 administration of the NHIS [27]. Among the 559 patients with cancer, 100% answered the question about whether or not their family had problems paying medical bills. A total of 97% of cancer patients responded to the question about how much their family spent on medical care, while 2.5% stated they “don’t know” and 0.5% refused to answer the question. No statistically significant differences were observed for socio-demographic factors or utilization factors among informative responders, responders answering “don’t know”, or responders that refused to answer. These findings suggest the absence of a reporting bias for those cancer patients responding to how much their family spent on medical

care. In response, the regression on out-of-pocket expenditures included only those patients that gave informative responses.

Age, insurance status, income to poverty level ratio, health status, and overnight hospital stay were variables with significant coefficients when considering the effects of socio-demographic and utilization factors on the probability that a patient would have problems paying medical bills. All cancer patient sub-groups < 65 years of age were more likely to have problems paying for medical treatment than were cancer patients 65+ years of age [$P \leq .006$] (Table 1). Patients with a "poor" health status and those staying overnight in a hospital were also significantly more likely to have problems paying medical bills than patients with good health status [$P = .011$] and for those not staying overnight [$P = .017$]. Patients that were covered by Medicaid and those that were equal to or above 4.09 times the federal poverty level were less likely to have problems paying medical bills than were those not covered by Medicaid [$P = .005$] and those below 4.09 times the federal poverty level [$P < .001$]. Table 1 presents results from the logistic regression on the dependent variable "whether or not a patient had problems paying medical bills". The regression uses medical service usage and demographic characteristics as independent variables.

Age, income to poverty level ratio, race, cancer duration, and overnight hospital stay were variables that produced significant coefficients when considering the effects of socio-demographic and utilization factors on the probability that a patient or their family would spend $3,000 or more out-of-pocket. All sub-groups < 65 years of age were more likely to have $3,000 or more in out-of-pocket expenditures compared to sub-groups 65+ years of age [$P \leq .019$]. Patients who stayed overnight in a hospital and those who were equal to or above 4.09 times the federal poverty level were also more likely to have $3,000 or more in out-of-pocket expenditures compared to those who did not stay overnight in a hospital [$P = .013$] and those who were below 4.09 times the federal poverty level [$P = .009$]. Cancer patients with shorter disease duration (3 to 5 months) and those who were Asian were less likely to have $3,000 or more in out-of-pocket expenditures compared to those who had cancer for a different time span [$P = .036$] and those who were not Asian [$P = .040$]. Table 2 presents results from the logistic regression on the dependent variable "whether or not a patient had $3,000 or more in out-of-pocket expenditures". The logistic regression uses medical service usage and demographic characteristics as independent variables.

The results of this study showed that an overnight hospital stay was a significant predictor of financial duress under both measurements. Patients staying overnight in a hospital (versus those who did not stay overnight in a hospital) were 1.76 times more likely to experience problems paying medical bills (odds ratio = 1.76; 95% CI, 1.11 to 2.81) and 1.86 times more likely to have $3,000 or more in out-of-pocket expenditures (odds ratio = 1.86; 95% CI, 1.14 to 3.03) after controlling for all relevant variables. The results of this study also showed that age was a significant predictor of financial duress under both measurements. Patients < 65 years of age (versus those who were 65+ years of age) were at least 3.37 times more likely to experience problems paying medical bills (odds ratio = 3.37; 95% CI, 1.42 to 8.00) and at least 2.65 times more likely to have $3,000 or more in out-of-pocket expenditures (odds ratio = 2.65; 95% CI, 1.18 to 5.95) after controlling for all relevant variables.

Cost- Benefit Analysis of Common Chemotherapy and Immunotherapy Cancer Drugs

Cancer drug costs were also considered as a predictor of financial toxicity. Although the price of cancer drugs was not controlled for in the regression, there is reason to believe drug costs play a role in determining financial toxicity. The President's 2018 Cancer Executive Summary Panel concluded that "urgent action is needed to address the ongoing, rapid increases in cancer drug costs…" [ 28 ]. In most cancer treatments today, cancer drug expenditures account for approximately 40 % of the overall cost of care [29]**.** The cost-benefit analysis of five common chemotherapy and immunotherapy drugs was considered when used in advanced-stage or metastatic cancer. Cisplatin (Platinol®) and Docetaxel (Taxotere®) were chosen as first-line and second-line chemotherapy drugs, respectively [30,31]. Cisplatin, a platinum-based chemotherapy, is generally administered for non-small cell lung cancer (NSCLC) and for advanced biliary tract cancer among others [32,33]. Docetaxel is generally administered for locally advanced or metastatic breast and prostate cancer among others [34,35]. Both drugs are administered intravenously and have proven survival benefits.

Nivolumab (Opdivo®), ipilumumab (Yervoy®), and bevacizumab (Avastin®) are frequently used first-line or second-line immunotherapy drugs administered intravenously either alone or in

combination with other drugs for cancer treatment [36,37,38]. Nivolumab is used for treating melanoma, NSCLC, and kidney cancer among others [36,39,40]. Ipilimumab is generally administered for metastatic melanoma, while bevacizumab is generally administered for glioblastoma [37]. Bevacizumab was discontinued as a treatment for breast cancer due to a multitude of adverse effects and lack of efficacy, but remains in use for glioblastoma [38,41].

The cost-benefit analyses show that various cancer drug treatments administered for advanced-stage cancer are overpriced (Table 3). These treatments could contribute to the increased financial burden seen in cancer patients. Across studies, $100,000/QALY was commonly cited as an acceptable threshold for a cost-effective cancer drug [34,36,42]. However, the standard drug treatments that were evaluated in this study for advanced-stage cancer landed above the $100,000/QALY threshold (Table 3). Cisplatin was the only cancer drug in the study that had an ICER falling below the $100,000/QALY threshold. However, the ICER for cisplatin was higher than its quoted price of $11,000 due to high toxicity and low overall survival for patients with for advanced biliary tract cancer [33,43,44]. Table 3 presents details from 7 studies to measure the cost-effectiveness of specified chemotherapy and immunotherapy anti-cancer drugs for applicable cancers.

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**Discussion**

Although previous reports have evaluated the impact of socio-demographic factors on the likelihood that cancer patients would experience financial duress, few studies have focused on medical care utilization and treatment costs as main predictors [15,19,20]. This is the first study to use both logistic regression and cost-benefit analysis to identify the multiple factors that underlie financial toxicity for cancer patients. Age, insurance status, race, income status and health status were identified previously as predictive factors for financial duress [15,19,20,26]. In addition to these factors, overnight hospital stay was identified as another significant factor contributing to financial toxicity. This is consistent with recent evidence that cost sharing per inpatient hospitalization among nonelderly adults increased from $738 in 2009 to $1013 in 2013 [45]. This study integrated these factors with that of cancer drug costs to provide a more comprehensive analysis on the origin of financial toxicity for cancer patients.

This study focused primarily on the financial burden experienced for patients with advanced-stage cancers. An increasing number of these patients receive treatments that do not align with their subjective expectations of better long-term survival or quality of life [18,46]. Severe financial hardship has also been associated with aggressive end-of-life cancer treatments [18,47]. This last outcome increases especially when older and cheaper generic drugs are replaced with newer more expensive drugs that do not significantly improve either overall patient outcome or reduce toxicity [18]. Indeed, the cancer drugs evaluated in this study produced significant toxicity with little evidence of long-term disease management [36,43,48,49,50,51].

The President's Cancer Panel asserted in its Executive Summary that, "cancer drug prices should be aligned with their value to patients…" [28]. The cost-benefit analysis study showed this is not the case. Most standard courses of drug treatment in the study surpassed the $100,000/QALY threshold, meaning that cancer patients with advanced-stage cancer treated with these drugs paid a cost well over the benefit that the drugs actually brought. The financial burden of these "low value" drugs lands in part on the shoulders of cancer patients, and greatly increases their risk of financial toxicity [18]. There is no indication that the cost of cancer drugs will decrease in the future [18]. Although radiation therapy was not included in the study, there is also evidence to prove that radiation therapy is overpriced in treating advanced stage cancer [52,53,54].

Another cost-driver in cancer treatment is diagnostic imaging [55,56]. Magnetic resonance imaging and computed tomography have become common imaging tools used for the detection of many cancers [55, 56, 57, 58, 59, 60]. In a study conducted on the cost-effectiveness of MRI for breast cancer screening on women with an average lifetime risk of breast cancer, it was found that using MRI screening only versus mammography screening only resulted in an ICER of $18,515/QALY to $113,452/QALY depending on the cost of the MRI ($329 to $2018) [56]. In a study analyzing the cost-effectiveness of computed tomography scanning for lung cancer in current and former smokers, it was found that using a CT scan versus using no CT scan resulted in an ICER of $110,000/QALY to $169,000/QALY depending on smoking frequency and assuming normal smoking cessation rates [61]. Between the reported ICER's for MRI for breast cancer and

CT scan for lung cancer, it is apparent that diagnostic imaging results in increased cost with marginal improvements in overall survival.

The study had various limitations. The NHIS item asking whether or not a family had problems paying medical bills is a subjective measure of financial burden. As a result, patients might have had different thresholds when it came to stating whether or not they had difficulty affording medical bills. The question relating to health status is also a subjective item. An overnight stay in a hospital might include outliers for reasons other than cancer care, but there were sufficient respondents that answered "yes" to staying overnight to control for these outliers (N = 83 for medical bill regression; N = 76 for out-of-pocket expenditure regression). The NHIS provided no information regarding cancer diagnosis. Moreover, the NHIS is a cross-sectional study, so no causal relationships could be drawn between factors influencing medical bill payment and out of pocket expenditures [27]. In the cost-benefit analysis, the reported ICERs were not adjusted to 2018 drug prices. Consequently, inflation and slight price changes might have affected the data over time.

Although both docetaxel and cisplatin had high ICERs relative to their quoted prices, it was a conservative approach to use these drugs as representatives for the cost-effectiveness of chemotherapy treatment in advanced-stage cancer. Both docetaxel and cisplatin have generic options, meaning their quoted prices are competitive with other generic chemotherapy drugs. Lomustine, on the other hand, is a patented oral chemotherapy drug that is used to treat brain tumors and Hodgkin lymphoma [62,63]. The drug has risen in price by 1,400 % since 2013 [63]. Lomustine capsules (100 mg) that cost $50 in 2013 now cost $768, with no evidence of improved therapeutic effectiveness [63]. It was also a conservative approach to use Avastin, Opdivo, and Yervoy as representatives for the cost-effectiveness of immunotherapy treatment. These immunotherapy drugs have been on the market for over 5 years, and thus have lower quoted prices than more recently developed treatments such as Chimeric Antigen Receptor T cell or "CAR-T" therapy [64]. CAR-T is a complicated treatment involving the removal, genetic modification, and reintroduction of a patient's T-cells, and is limited to only a few facilities in the United States [64,65]. The treatment is currently used for acute lymphoblastic leukemia and large B cell lymphoma [64]. CART-T is a secondary line of treatment for those cancer patients who do not

respond to standard treatment [64]. While the drug has been developed only recently, it is projected to have a price of $475,000 for one full round of treatment [64]. No long-term results have been reported, but Novartis' U.S. oncology head estimates that CAR-T "could command a price of $600,000 to $750,000" [64]. These exceptionally high CAR-T prices and the appearance of price gauging for lomustine will likely contribute further to the financial toxicity of cancer patients thus raising the issue of moral responsibility [66].

**Possible Solutions**

Integration of cancer health care services and outcome-based clinical practice are current possible solutions to financial toxicity. Integrated practice units (IPU's) and bundled payments are currently used to avoid fragmentation of cancer treatment and to reduce costs, respectively [67-68]. IPU's allow for streamlined communication among members of an oncology team assigned to a particular patient. This would help reduce redundancies in treatments and procedures. Bundled payments allow for patients to pay flat rates for inpatient and outpatient care. The Affordable Care Act has addressed these initiatives and pushed for access to quality care through expanded coverage and patient-centered medical homes (PMCH's) [69]. The effect has been a reduction in unnecessary resource use, such as emergency visits and hospital admissions [69].

Global budgeting and Accountable Care Organizations (ACOs) have also been established to help reduce the overall cost of cancer care [70]. While global budgeting is a term that refers to the coordination of responsible medical spending, Accountable Care Organizations are contracts formed between physicians and physician organizations to achieve global budgeting through responsible medical spending [70]. To encourage responsible spending, ACOs reward conservative spending through shared savings, and discourage surplus spending through shared risk [70]. Through an ACO established in Massachusetts called the Alternative Quality Contract (AQC), the AQC cohort saved 6.8% on medical spending over the course of 4 years [70]. Approximately 40% of the savings were explained by decreases in medical service usage, while 60% of the savings were due to lower drug prices [70].

To address the problem of rising cancer drug prices, the President's Cancer Panel recommended a value-based framework and to facilitate outcome-based drug pricing [28]. Also

recommended was a reimbursement system that incentivized providers to use cost-effective drugs [28]. Furthermore, the Panel recommended open cost communication between caregivers and their patients so as to minimize out-of-pocket spending by patients and their families [28]. As a long-term solution to increasing cancer drug costs, the Panel urged an expansion of the cancer drug market so as to increase competition and lower prices on cancer drugs [28].

In addition to global budgeting, Accountable Care Organizations (ACOs), and Integrated Practice Units (IPUs), new biological approaches to cancer management could also help reduce cancer treatment costs. Emerging evidence indicates that cancer is primarily a metabolic disease [71]. Non-toxic metabolic therapy could therefore be used as a less costly complimentary or alternative strategy to current standards of care that primarily involve chemo-, radiation-, and immuno-therapies [71]. Hence, novel economic and biological strategies are available that can help curb financial toxicity.

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**Conclusion**

Financial toxicity has emerged as a significant adverse effect with the rising cost of cancer medical care. It is especially prevalent among cancer patients who are < 65 years of age, those who stay overnight in a hospital and those with advanced-stage cancer undergoing drug treatment. Those who stay overnight in a hospital and those with advanced-stage cancer undergoing drug treatment may suffer due to the high cost of inpatient care and the overpricing of cancer drugs, respectively. Integral Practice Units and Accountable Care Organizations are promising solutions to the high costs of inpatient care, while instituting a value-based framework and increasing cancer drug market competition are vital steps to obtaining better value for cancer drugs. Finally, metabolic therapies could be used to supplement treatment and further reduce medical costs.

**References**

1. Siegel RL, Miller K, Jemal A. Cancer statistics, 2018. CA: A Cancer Journal for Clinicians 2017; 67:7-30.

2. Stewart BW, Wild CP. World cancer report 2014. Lyon: International Agency for Research on Cancer Press, 2014.

3. Howard DH, Bach P, Berndt E, Conti R. Pricing in the Market for Anticancer Drugs. Journal of Economic Perspectives 2015; 29:139-162.

4. Elkin EB, Bach PB. Cancer's next frontier: Addressing high and increasing costs. JAMA 2010; 303:1086-1087.

5. Uber PA, Abernethy A, Zafar SY. Full Disclosure — Out-of-Pocket Costs as Side Effects. N Engl J Med 2013; 369:1484-1486.

6. Lee JA, Roehrig CS, Butto ED. Cancer care cost trends in the United States: 1998 to 2012. Cancer 2016; 122:1078-1084.

7. Ganz PA. Institute of Medicine Report on Delivery of High-Quality Cancer Care. Journal of Oncology 2014; 10:193-195.

8. Zafar SY, Abernethy A. Financial Toxicity, Part II: How Can We Help With the Burden of Treatment-Related Costs?. Oncology 2013; 27:253-254, 256.

9. McCleery J. Cancer Care Costs Pose a Huge Financial Burden on Patients. OBR green 2017; 11.

10. Zafar SY, Peppercorn JM, Schrag D, Taylor DH, Goetzinger AM, Zhong X, Abernethy AP. The Financial Toxicity of Cancer Treatment: A Pilot Study Assessing Out-of-Pocket Expenses and the Insured Cancer Patient's Experience. The Oncologist 2012; 18:381-390.

11. 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.

12. Zafar SY. Financial Toxicity in Cancer Care: It’s Time to Intervene. JNCI 2015; 5:10.1093/djv370.

13. Palmer J, Patel TT, Eldredge-Hindy H, Keith SW, Patel T, Malatesta T, et al. Patients Undergoing Radiation Therapy Are at Risk of Financial Toxicity: A Patient-based Prospective Survey Study. International Journal of Radiation Oncology 2018; 101:299-305.

14. Ramsey SD, Bansal A, Fedorenko CR, Blough DK, Overstreet KA, Shankran V, Newcomb P. Financial Insolvency as a Risk Factor for Early Mortality Among Patients With Cancer. Journal of Clinical Oncology 2016; 34:980-986.

15. Fenn KM, Evans SB, McCorkle R, DiGiovanna MP, Pusztai L, Sanft T, et al.Impact of Financial Burden of Cancer on Survivors' Quality of Life. Journal of Oncology Practice 2014; 10:332-338.

16. Community Oncology Alliance. Americans fear paying for cancer treatments as much as dying of the disease. Oncol Times 2009; 31:16-17.

17. Tucker-Seeley RD, Abel GA, Uno H, Prigerson H. Financial hardship and the intensity of medical care received near death. Psycho-Oncology 2015; 24:572–578.

18. Davis C. Drugs, cancer and end-of-life care: a case study of pharmaceuticalization?. Soc Sci Med 2015; 131:207-214.

19. Yabroff KR, Dowling EC, Guy GP Jr., Banegas MP, Davidoff A, Han X, et al. Financial Hardship Associated With Cancer in the United States: Findings From a Population-Based Sample of Adult Cancer Survivors. Journal of Clinical Oncology 2016; 34:259-267.

20. Gordon LG, Merollini K, Lowe A, Chan RJ. A Systematic Review of Financial Toxicity Among Cancer Survivors: We Can't Pay the Co-Pay. The Patient – Patient Centered Outcomes Research 2017; 10:295-309.

21. Detsky AS, Naglie IG. A Clinician's Guide to Cost-Effectiveness Analysis. Annals of Internal Medicine 1990; 113:147-154.

22. Briggs AH, Wonderling DE, Mooney CZ. Pulling cost-effectiveness analysis up by its bootstraps: A non-parametric approach to confidence interval estimation. Health Economics 2017; 6:327-340.

23. Weinstein MC, Torrance G, McGuire A. QALYs: The Basics. Value in Health 2009; 12:S5-S9.

24. Ochi N, Yamane H, Hotta K, Fujii H, Isozaki H, Honda Y, et al. Cisplatin-induced hyponatremia in malignancy: comparison between brand-name and generic formulation. Drug Design, Development and Therapy 2014; 8:2401-2408.

25. Ledford H . Melanoma drug wins US approval. Nature 2011; 471:10.1038/471561a.

26. Chhatwal J, Mathisen M, Kantarjian H. Are high drug prices for hematologic malignancies justified? A critical analysis. Cancer 2015; 121:3372-3379.

27. National Center for Health Statistics. Data from "National Health Interview Survey, 2016". Public-use data file and documentation. National Center for Health Statistics 2017; https://www.cdc.gov/nchs/nhis/data-questionnaires-documentation.htm.

28. President's Cancer Panel. Promoting Value, Affordability, and Innovation in Cancer Drug Treatment: Executive Summary of a Report to the President of the United States from the President's Cancer Panel. Bethesda: President's Cancer Panel, 2018.

29. Kumar P, Moy B. The Cost of Cancer Care—Balancing Our Duties to Patients Versus Society: Are They Mutually Exclusive?. The Oncologist 2013; 18:347-349.

30. Fennell DA, Summers Y, Cadranel J, Benepal T, Christoph DC, Lal R, et al. Cisplatin in the modern era: The backbone of first-line chemotherapy for non-small cell lung cancer. Cancer Treatment Reviews 2016; 44:42-50.

31. Bokkel Huinink WW, Prove AM, Piccart M, Alakl M. A phase II trial with Docetaxel (Taxotere™) in second line treatment with chemotherapy for advanced breast cancer: A study of the EORTC Early Clinical Trials Group. Annals of Oncology 1994; 5:527-532.

32. Lairson DR, Parikh R, Cormier J, Chan W, Du X. Cost-Utility Analysis of Treatments for Advanced Non-Small Cell Lung Cancer. The American Journal of Pharmacy Benefits 2016; 7:271-279.

33. Roth JA, Carlson J. Cost-effectiveness of gemcitabine + cisplatin vs. gemcitabine monotherapy in advanced biliary tract cancer. J Gastrointest Cancer 2012; 43:215-223.

34. Pollard ME, Moskowitz AJ, Diefenbach MA, Hall SJ. Cost-Effectiveness analysis of treatments for metastatic castration resistant prostate cancer. Asian Journal of Urology 2017; 4:37-43.

35. Jones SE, Erban J, Overmoyer B, Budd GT, Hutchins L, Lower E, et al. Randomized phase III study of docetaxel compared with paclitaxel in metastatic breast cancer. Journal of Clinical Oncology 2005; 23:5542-5551.

36. Wan XM, Peng LB, Ma JA, Li YJ. Economic evaluation of nivolumab as a second-line treatment for advanced renal cell carcinoma from US and Chinese perspectives. Cancer 2017; 123:2634-2641.

37. Fellner C. Ipilimumab (Yervoy) Prolongs Survival In Advanced Melanoma. P&T 2012; 37:503-511, 530.

38. Kovic B, Xie F. Economic Evaluation of Bevacizumab for the First-Line Treatment of Newly Diagnosed Glioblastoma Multiforme. Journal of Clinical Oncology 2015; 33:2296-2302.

39. Larkin J, Lao CD, Urba WJ, McDermott DF, Horak C, Jiang J, Wolchok JD. Efficacy and Safety of Nivolumab in Patients With BRAF V600 Mutant and BRAF Wild-Type Advanced Melanoma: A Pooled Analysis of 4 Clinical Trials. JAMA Oncol 2015; 1:433-440.

40. Brahmer J. CT077 - Five-year follow-up from the CA209-003 study of nivolumab in previously treated advanced non-small cell lung cancer (NSCLC): Clinical characteristics of long-term survivors. AACR Annual Meeting 2017; 10.1158/1538-7445.AM2017-CT077.

41. Sasich LD, Sukkari SR. The US FDAs withdrawal of the breast cancer indication for Avastin (bevacizumab). Saudi Pharmaceutical Journal 2012; 20:381-385.

42. Oh A, Tran DM, McDowell LC, Keyvani D, Barcelon JA, Merino O, Wilson L. Cost-Effectiveness of Nivolumab-Ipilimumab Combination Therapy Compared with Monotherapy for First-Line Treatment of Metastatic Melanoma in the United States. Journal of Managed Care & Specialty Pharmacy 2017; 23:653-664.

43. Blanusa M, Varnai VM, Piasek M, Kostial K. Chelators as Antidotes of Metal Toxicity: Therapeutic and Experimental Aspects. Current Medicinal Chemistry 2005; 12:2771-2794.

44. Jacobs C. A phase III randomized study comparing cisplatin and fluorouracil as single agents and in combination for advanced squamous cell carcinoma of the head and neck. Journal of Clinical Oncology 1992; 10:257-263.

45. Adrion ER, Ryan A, Seltzer A. Out-of-Pocket Spending for Hospitalizations Among Nonelderly Adults. JAMA Internal Medicine 2016; 176:1325-1332.

46. Matsuyama R, Reddy S, Smith TJ. Why do patients choose chemotherapy near the end of life? A review of the perspective of those facing death from cancer. Journal of Clinical Oncology 2006; 24:3490-3496.

47. Gyawali B, Niraula S. Cancer treatment in the last 6 months of life: when inaction can outperform action. Ecancermedicalscience 2018; 12:826.

48. Fossella F. Phase II study of docetaxel for advanced or metastatic platinum-refractory non-small-cell lung cancer. Journal of Clinical Oncology 1995; 13:645-651.

49. Andrews S, Holden R. Characteristics and management of immunerelated adverse effects associated with ipilimumab, a new immunotherapy for metastatic melanoma. Cancer Manag Res 2012; 4:299-307.

50. Tewari KS, Sill MW, Penson RT, Huang H, Ramondetta LM, Landrum LM, et al. Bevacizumab for advanced cervical cancer: final overall survival and adverse event analysis of a

randomised, controlled, open-label, phase 3 trial (Gynecologic Oncology Group 240). The Lancet 2017; 390:1654-1663.

51. Hurwitz H, Fehrenbacher L, Novotny W, Cartwright T. Bevacizumab plus Irinotecan, Fluorouracil, and Leucovorin for Metastatic Colorectal Cancer. N Engl J Med 2004; 350:2335-2342.

52. Murphy JD. Cost-effectiveness of modern radiotherapy techniques in locally advanced pancreatic cancer. Cancer 2012; 118:1119-1129.

53. Paravati AJ, Boero IJ, Triplett DP, Hwang L, Matsuno RK, Xu B, et al. Variation in the Cost of Radiation Therapy Among Medicare Patients With Cancer. Journal of Oncology Practice 2015; 11:403-409.

54. Kohler RE. Two-year and lifetime cost-effectiveness of intensity modulated radiation therapy versus 3-dimensional conformal radiation therapy for head-and-neck cancer. Int J Radiat Oncol Biol Phys 2013; 87:683-689.

55. Razek AAKA, Shamaa S, Lattif MA, Yousef HH. Inter-Observer Agreement of Whole-Body Computed Tomography in Staging and Response Assessment in Lymphoma: The Lugano Classification. Pol J Radiol 2017; 82:441-447.

56. Kimball, ML. Model of Cost-E ectiveness of MRI for Women of Average Lifetime Risk of Breast Cancer. Scholarly & Creative Works Conference 2018; 2.

57. Razek AA, Ezzat A, Azmy E, Tharwat N. Role of whole-body 64-slice multidetector computed tomography in treatment planning for multiple myeloma. Radiol Med 2013;118:799-805.

58. Ghobrial FEI, Eldin MS, Razek AAKA, Atwan NI, Shamaa SSA. Computed Tomography Assessment of Hepatic Metastases of Breast Cancer with Revised Response Evaluation Criteria in Solid Tumors (RECIST) Criteria (Version 1.1): Inter-Observer Agreement. Pol J Radiol 2017; 82:593-597.

59. Abdel Razek AA, Gaballa G, Denewer A, Tawakol I. Diffusion weighted MR imaging of the breast. Acad Radiol 2010; 17:382-6.

60. Razek AA, Tawfik AM, Elsorogy LG, Soliman NY. Perfusion CT of head and neck cancer. Eur J Radiol 2014; 83:537-44.

61. McMahon PM, Kong CY, Bouzan C, Weinstein MC, Cipriano LE, Tramontano AC, et al. Cost-effectiveness of computed tomography screening for lung cancer in the United States. J Thorac Oncol. 2011; 6:1841-1848.

62. Taal W, Oosterkamp HM, Walenkamp AM, Dubbink HJ, Beerepoot LV, Hanse MC, et al. Single-agent bevacizumab or lomustine versus a combination of bevacizumab plus lomustine in patients with recurrent glioblastoma (BELOB trial): a randomised controlled phase 2 trial. The Lancet Oncology 2014; 15:943-953.

63. Loftus P. Cancer Drug Price Rises 1,400% With No Generic to Challenge It. The Wall Street Journal 2017; Available at https://www.wsj.com/articles/cancer-drug-price-rises-1400-with-no-generic-to-challenge-it-1514203201.

64. Roland D, Loftus P. Novartis Defends Therapy's Price. The Wall Street Journal 2017; Available at http://online.wsj.com/public/resources/documents/print/WSJ_-B001-20170831.pdf.

65. Bonifant C. Toxicity and management in CAR T-cell therapy. Molecular Therapy – Oncolytics 2016; 10.1038/mto.2016.11.

66. Kushnick H. Pricing Cancer Drugs: When Does Pricing Become Profiteering?. AMA Journal of Ethics 2015; 17:750-753.

67. Teckie S, McCloskey SA, Steinberg ML. Value: A Framework for Radiation Oncology. Journal of Clinical Oncology 2014; 32:2864-2870.

68. Ali AA, Xiao H, Campbell ES, Diaby V. Improving Health Care Decision Making in the USA Through Comparative Effectiveness Research: The Role of Economic Evaluation. Pharmaceutical Medicine 2015; 29:247-253.

69. Leopold C, Park ER, Nekhlyudov L. The Impact of the Affordable Care Act on Cancer Survivorship. Cancer Journal 2017; 23:181-189.

70. Song Z, Rose S, Safran DG, Landon BE, Day MP, Chernew ME. Changes in Health Care Spending and Quality 4 Years into Global Payment. N Engl J Med 2014; 371:1704-1714.

71. Seyfried TN, Yu G, Maroon JC, D'Agostino DP. Press-pulse: a novel therapeutic strategy for the metabolic management of cancer. Nutrition and Metabolism 2017; 14:19.

65. Barzey V, Atkins MB, Garrison LP, Asukai Y, Kotapati S, Penrod JR. Ipilimumab in 2nd line treatment of patients with advanced melanoma: a cost-effectiveness analysis. J Med Econ 2013; 16:212..

66. Momekov G, Bakalova A, Karaivanova M. Novel Approaches Towards Development of Non-Classical Platinum-Based Antineoplastic Agents: Design of Platinum Complexes Characterized by an Alternative DNA-Binding Pattern and/or Tumor-Targeted Cytotoxicity. Current Medicinal Chemistry 2005; 12:2177-2191..

## Tables

**Table 1. Analysis of variables associated with medical bill payment for cancer treatment**

| Variable | Coefficient | 95% CI | P |
|---|---|---|---|
| Overnight medical service* | | | |
| No | Referent | | |
| Yes | 0.57 | (0.10 to 1.03) | **0.017** |
| Don't know | 0.00 | (empty) | (empty) |
| Poor health status | | | |
| No† | Referent | | |
| Yes | 0.61 | (0.14 to 1.08) | **0.011** |
| Refused | 0.00 | (empty) | (empty) |
| Received care 10+ times‡ | | | |
| No | Referent | | |
| Yes | 0.36 | (-0.16 to 0.87) | 0.177 |
| Visited health professional in office§ | | | |
| No | Referent | | |
| Yes | 0.37 | (-0.11 to 0.85) | 0.133 |
| Don't know | 0.00 | (empty) | (empty) |
| Received advice/test results by phone¶ | | | |
| No | Referent | | |
| Yes | 0.09 | (-0.45 to 0.62) | 0.749 |
| Sex | | | |
| Male | Referent | | |
| Female | 0.31 | (-0.14 to 0.76) | 0.173 |
| Race | | | |
| White | Referent | | |
| Black/African-American only | 0.25 | (-0.50 to 0.99) | 0.515 |
| AIAN (American Indian and Alaska Native) only | 1.02 | (-0.85 to 2.88) | 0.286 |
| Asian only | -0.58 | (-2.18 to 1.02) | 0.478 |
| Race group not releasable | 0.00 | (empty) | (empty) |
| Multiple race | 0.39 | (-0.72 to 1.49) | 0.496 |
| Ethnicity | | | |
| Not Hispanic | Referent | | |
| Hispanic | -0.35 | (-1.09 to 0.39) | 0.356 |
| Education | | | |
| No degree | Referent | | |
| High School degree | -0.25 | (-0.88 to 0.39) | 0.449 |

| | | | |
|---|---|---|---|
| Some College/Associate's degree | -0.06 | (-0.72 to 0.60) | 0.855 |
| Bachelor's degree or more[#] | -0.61 | (-1.41 to 0.19) | 0.134 |
| Refused/Don't know | 0.59 | (-1.25 to 2.42) | 0.531 |
| Region | | | |
| Northeast | Referent | | |
| Midwest | 0.07 | (-0.71 to 0.86) | 0.852 |
| South | 0.29 | (-0.41 to 0.99) | 0.420 |
| West | 0.35 | (-0.40 to 1.10) | 0.365 |
| Married | | | |
| No[‖] | Referent | | |
| Yes | -0.08 | (-0.57 to 0.40) | 0.735 |
| Duration of cancer | | | |
| Less than 3 months | Referent | | |
| 3-5 months | 0.50 | (-0.99 to 1.99) | 0.511 |
| 6-12 months | 0.61 | (-0.45 to 1.67) | 0.256 |
| More than 1 year[**] | 0.23 | (-0.75 to 1.21) | 0.647 |
| Don't know | -0.09 | (-2.82 to 2.63) | 0.946 |
| Age | | | |
| 75+[††] | Referent | | |
| 65-75 | 0.48 | (-0.19 to 1.16) | 0.161 |
| 55-64 | 1.22 | (0.35 to 2.08) | **0.006** |
| 45-54 | 1.55 | (0.63 to 2.46) | **0.001** |
| <45 | 2.86 | (1.80 to 3.92) | **<0.001** |
| Insurance status | | | |
| Uninsured | Referent | | |
| Medicaid | -1.99 | (-3.37 to -0.61) | **0.005** |
| Medicare/Medicare + Medicare Advantage | -0.60 | (-2.09 to 0.88) | 0.428 |
| Dual eligible[‡‡] | -0.86 | (-2.51 to 0.80) | 0.310 |
| Other coverage[‡‡] | -0.98 | (-2.36 to 0.40) | 0.165 |
| Private | -1.10 | (-2.41 to 0.21) | 0.100 |
| Don't know | 0.01 | (-2.83 to 2.85) | 0.994 |
| Employment | | | |
| Unemployed | Referent | | |
| Employed but cannot work | -0.24 | (-1.03 to 0.56) | 0.561 |
| Employed and able to work, but limited | 0.36 | (-0.43 to 1.15) | 0.368 |
| Employed and able to work, not limited | 1.05 | (-0.66 to 2.76) | 0.228 |
| Limited in any other way[§§] | | | |
| No | Referent | | |
| Yes | -1.41 | (-3.32 to 0.49) | 0.145 |
| Ratio: Ratio of Family Income to Poverty Threshold | | | |
| Q1: < 1.216 | Referent | | |
| Q2: 1.216 - 2.132 | -0.13 | (-0.72 to 0.46) | 0.666 |

| | | | |
|---|---|---|---|
| Q3: 2.133 - 4.080 | -0.26 | (-0.92 to 0.39) | 0.431 |
| Q4: > 4.080 | -1.64 | (-2.49 to -0.80) | **<0.001** |

N = 555, boldface type indicates statistical significance. There were four observations dropped in the regression.
Abbreviations: NHIS, National Health Information Survey; Q, quartile (Q1 is the lowest family income as a ratio of federal poverty line quartile, and Q4 is the highest family income quartile); CI, Confidence Interval.
[*]Hospitalized overnight within the past 12 months, including all infants born in a hospital. Does not include an overnight stay in the emergency room. Number of nights not reported.
[†]Possible responses were "fair", "good", "very good", and "excellent". Response could be given by patient or their alias.
[‡]Received care from doctors or other health care professionals. Does not include telephone calls.
[§]Only includes visits during the last 2 weeks. Includes visits to a doctor's office, a clinic, an emergency room, or another medical facility. Does not include an overnight hospital stay.
[¶]Only includes phone calls with a doctor, nurse, or other health care professional during the last 2 weeks. Does not include phone calls for scheduling appointments, billing questions, or prescription refills.
[#]Education top-coded doctoral degree by the NHIS.
[‖]Not married includes separated, divorced, single/never married, and widowed.
[**]Duration of cancer top-coded $> 1$ year by the NHIS.
[††]Age top-coded $\geq 85$ by the NHIS.
[‡‡]Dual eligible includes patient's age $\geq 65$ eligible for both Medicare and Medicare Advantage. Other coverage includes State Children's Health Insurance Program (SCHIP), a State-sponsored health plan, other government programs, or military health plan (includes TRICARE, VA, CHAMP-VA).
[§§]Limited in any other way in any activities because of physical, mental or emotional problems.
**Pseudo $R^2$: 0.1979**

**Table 2. Analysis of variables associated with out-of pocket expenditures for cancer treatment.**

| Variable | Coefficient | 95% CI | P |
|---|---|---|---|
| Overnight medical service[*] | | | |
| No | Referent | | |
| Yes | 0.62 | (0.13 to 1.11) | **0.013** |
| Don't know | 0.00 | (empty) | (empty) |
| Poor health status | | | |
| No[†] | Referent | | |
| Yes | 0.30 | (-0.22 to 0.82) | 0.259 |
| Refused | 0.00 | (empty) | (empty) |
| Received care 10+ times[‡] | | | |

| | | | |
|---|---|---|---|
| No | Referent | | |
| Yes | 0.19 | (-0.36 to 0.74) | 0.495 |
| Visited health professional in office[§] | | | |
| No | Referent | | |
| Yes | 0.28 | (-0.21 to 0.78) | 0.264 |
| Received advice/test results by phone[¶] | | | |
| No | Referent | | |
| Yes | 0.13 | (-0.42 to 0.68) | 0.648 |
| Sex | | | |
| Male | Referent | | |
| Female | -0.02 | (-0.50 to 0.45) | 0.920 |
| Race | | | |
| White | Referent | | |
| Black/African-American only | 0.03 | (-0.86 to 0.93) | 0.943 |
| AIAN (American Indian and Alaska Native) only | -1.25 | (-3.65 to 1.16) | 0.310 |
| Asian only | -2.29 | (-4.48 to -0.11) | **0.040** |
| Race group not releasable | 0.00 | (empty) | (empty) |
| Multiple race | 0.25 | (-0.96 to 1.46) | 0.686 |
| Ethnicity | | | |
| Not Hispanic | Referent | | |
| Hispanic | -0.08 | (-0.91 to 0.74) | 0.847 |
| Education | | | |
| No degree | Referent | | |
| High School degree | -0.32 | (-1.09 to 0.44) | 0.406 |
| Some College/Associate's degree | -0.08 | (-0.84 to 0.68) | 0.843 |
| Bachelor's degree or more[#] | 0.56 | (-0.24 to 1.35) | 0.171 |
| Refused/Don't know | -0.63 | (-3.25 to 1.99) | 0.638 |
| Region | | | |
| Northeast | Referent | | |
| Midwest | 0.20 | (-0.59 to 0.99) | 0.616 |
| South | 0.23 | (-0.49 to 0.95) | 0.529 |
| West | 0.42 | (-0.34 to 1.18) | 0.278 |
| Married | | | |
| No[‖] | Referent | | |
| Yes | 0.40 | (-0.12 to 0.91) | 0.131 |
| Duration of cancer | | | |
| Less than 3 months | Referent | | |
| 3-5 months | -2.49 | (-4.82 to -0.16) | **0.036** |
| 6-12 months | -0.24 | (-1.33 to 0.85) | 0.668 |
| More than 1 year[**] | -0.28 | (-1.29 to 0.74) | 0.593 |
| Don't know | 0.00 | (empty) | (empty) |
| Age | | | |

| | | | |
|---|---|---|---|
| 75+[††] | Referent | | |
| 65-75 | 0.28 | (-0.38 to 0.95) | 0.403 |
| 55-64 | 0.97 | (0.16 to 1.78) | **0.019** |
| 45-54 | 1.19 | (0.31 to 2.07) | **0.008** |
| <45 | 1.79 | (0.71 to 2.86) | **0.001** |
| Insurance status | | | |
| Uninsured | Referent | | |
| Medicaid | -0.97 | (-2.48 to 0.54) | 0.206 |
| Medicare/Medicare + Medicare Advantage | 0.92 | (-0.55 to 2.40) | 0.219 |
| Dual eligible[‡‡] | -0.86 | (-3.33 to 1.61) | 0.495 |
| Other coverage[‡‡] | -0.11 | (-1.54 to 1.31) | 0.876 |
| Private | 0.50 | (-0.81 to 1.81) | 0.453 |
| Don't know | 0.61 | (-2.21 to 3.44) | 0.671 |
| Employment | | | |
| Unemployed | Referent | | |
| Employed but cannot work | -0.52 | (-1.32 to 0.28) | 0.206 |
| Employed and able to work, but limited | 0.19 | (-0.58 to 0.95) | 0.632 |
| Employed and able to work, not limited | 0.78 | (-0.78 to 2.33) | 0.327 |
| Limited in any other way[§§] | | | |
| No | Referent | | |
| Yes | -1.34 | (-2.82 to 0.13) | 0.074 |
| Ratio: Ratio of Family Income to Poverty Threshold | | | |
| Q1: < 1.216 | Referent | | |
| Q2: 1.216 - 2.132 | 0.22 | (-0.56 to 0.99) | 0.585 |
| Q3: 2.133 - 4.08 | 0.74 | (-0.05 to 1.52) | 0.066 |
| Q4: > 4.08 | 1.13 | (0.29 to 1.97) | **0.009** |

N = 533, boldface type indicates statistical significance. Nine observations dropped.
Abbreviations: NHIS, National Health Information Survey; Q, quartile (Q1 is the lowest family income as a ratio of federal poverty line quartile, and Q4 is the highest family income quartile); CI, Confidence Interval.
[*]Hospitalized overnight within the past 12 months, including all infants born in a hospital. Does not include an overnight stay in the emergency room. Number of nights not reported.
[†]Possible responses were “fair”, “good”, “very good”, and “excellent”. Response could be given by patient or their alias.
[‡]Received care from doctors or other health care professionals. Does not include telephone calls.
[§]Only includes visits during the last 2 weeks. Includes visits to a doctor’s office, a clinic, an emergency room, or another medical facility. Does not include an overnight hospital stay.
[¶]Only includes phone calls with a doctor, nurse, or other health care professional during the last 2 weeks. Does not include phone calls for scheduling appointments, billing questions, or prescription refills.
[#]Education top-coded doctoral degree by the NHIS.
[‖]Not married includes separated, divorced, single/never married, and widowed.

[**]Duration of cancer top-coded $> 1$ year by the NHIS.
[††]Age top-coded $\geq 85$ by the NHIS.
[‡‡]Dual eligible includes patients age $\geq 65$ eligible for both Medicare and Medicare Advantage. Other coverage includes State Children's Health Insurance Program (SCHIP), a State-sponsored health plan, other government programs, or military health plan (includes TRICARE, VA, CHAMP-VA).
[§§]Limited in any other way in any activities because of physical, mental or emotional problems.
**Pseudo $R^2$: 0.1949**

**Table 3. Cost-benefit analysis of common chemotherapy and immunotherapy cancer drugs**

| ICER Source | Drug Name | ICER Indication | Comparing Interventions | Reported ICER |
|---|---|---|---|---|
| Pollard 2017 (34) | Docetaxel (Taxotere®) | mCRPC | **docetaxel** + enzalutamide + abiraterone + sipuleucel-T vs enzalutamide + abiraterone + sipuleucel-T[¶¶] | 207,714 |
| Pollard 2017 (34) | Docetaxel (Taxotere®) | mCRPC | **docetaxel** + enzalutamide + abiraterone vs enzalutamide + abiraterone[¶¶] | 165,460 |
| Roth 2012 (33) | Cisplatin (Platinol®) | aBTC | **cisplatin** + gemcitabine vs gemcitabine | 59,480 |
| Lairson 2016 (32) | Platinum-based chemotherapy[##] | aNSCLC | **platinum-based chemotherapy** vs placebo | 124,645 |
| Wan 2017 (36) | Nivolumab (Opdivo®) | RCC | **nivolumab** vs everolimus | 151,676 |
| Barzey 2013 (65) | Ipilimumab (YERVOY®) | MM | **ipilimumab** vs BSC (best supportive care) | 146,000 |
| Oh 2017 (42) | Nivolumab + Ipilimumab | MM | **nivolumab + ipilumumab** vs nivolumab | 454,092 |
| Kovic 2015 (38) | Bevacizumab (Avastin®) | GBM | **bevacizumab** + radiotherapy + temozolomide vs radiotherapy + temozolomide | 787,519 |

This table was adapted from *Cancer* (26).
Abbreviations: ICER, incremental cost-effectiveness ratio; mCRPC, metastatic castration-resitant prostate cancer; aBTC, advanced biliary tract cancer; aNSCLC, advanced non-small cell lung cancer; RCC, renal cell carcinoma; MM, metastatic melanoma; GBM, glioblastoma; BSC, best supportive care.
¶¶ Study looking at differences in cost-effectiveness resulting from the inclusion or non-inclusion of sipuleucel-T.
## Platinum-based chemotherapy drugs are platinum complexes primarily stemming from the structural analogues of cisplatin (66).