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For Working-Age Cancer Survivors, Medical Debt And Bankruptcy Create Financial Hardships

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Abstract

The rising medical costs associated with cancer have led to considerable financial hardship for patients and their families in the United States. Using data from the LIVESTRONG 2012 survey of 4,719 cancer survivors ages 18–64, we examined the proportions of survivors who reported going into debt or filing for bankruptcy as a result of cancer, as well as the amount of debt

Some of the preliminary results from this study were presented at the Seventh Annual American Association for Cancer Research Conference on the Science of Cancer Health Disparities, San Antonio, Texas, November 9–12, 2014, and at the Twenty-First Annual HMO Research Network Conference, Long Beach, California, March 11–13, 2015. This work was completed while Matthew Banegas was a fellow in the Healthcare Delivery Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute (NCI), as part of the NCI's Cancer Prevention Fellowship Program.

incurred. Approximately one-third of the survivors had gone into debt, and 3 percent had filed for bankruptcy. Of those who had gone into debt, 55 percent incurred obligations of \$10,000 or more. Cancer survivors who were younger, had lower incomes, and had public health insurance were more likely to go into debt or file for bankruptcy, compared to those who were older, had higher incomes, and had private insurance, respectively. Future longitudinal population-based studies are needed to improve understanding of financial hardship among US working-age cancer survivors throughout the cancer care trajectory and, ultimately, to help stakeholders develop evidence-based interventions and policies to reduce the financial hardship of cancer.

The cost of cancer care in the United States has become a significant social and public health issue. Cancer care costs are rising at two to three times the rate of other health care costs¹ and are projected to continue increasing over the next decade.² Novel cancer therapy agents can cost more than \$60,000 for a month of treatment,³ and the average monthly cost per agent has more than doubled over the past decade, to \$10,000.¹ Health insurers have been adopting strategies to control their costs—for example, by increasing patient cost sharing through higher premiums, deductibles, copayments, coinsurance, and other out-of-pocket expenses.⁴

Average out-of-pocket expenses for an individual are \$1,107 in the first year after a cancer diagnosis and \$747 annually thereafter.⁵ Some cancer patients must pay \$10,000 in out-of-pocket expenses before comprehensive insurance coverage begins, while other patients reach their annual out-of-pocket maximum in just the first month of treatment.¹ Consequently, an increasing number of patients experience financial hardship following a cancer diagnosis, including accruing large medical debts, exhausting assets and savings to pay for treatment, and filing for bankruptcy.^{6–9}

Previous research has shown that approximately 30 percent of cancer survivors report experiencing financial hardship,^{9–11} as well as bankruptcy rates that are 2.5 times higher than those of people without a history of cancer.⁷ The risk of financial hardship and bankruptcy associated with cancer is higher among the working-age population (ages 18–64) than among the elderly.^{6,7,9,12–14}

Working-age cancer survivors may face unique challenges, given that the majority of them rely on employment as the primary source of health insurance. A cancer diagnosis and subsequent treatment may prevent them from working or lead to disabilities that limit their ability to perform work-related tasks.^{15–25} Additionally, financial hardship resulting from cancer has been associated with forgoing or delaying the receipt of medical care, both care related to cancer and unrelated care.^{6,26} Treatment nonadherence^{6,10,27} and difficulties paying for basic necessities such as utilities and mortgages^{28–30} may have a negative effect on health outcomes.

Other studies have compared overall medical and out-of-pocket expenses of working-age cancer survivors with those of people without a history of cancer to control for the potential impact of other medical conditions, instead of having directly assessed financial hardship due to cancer.^{5,31,32} In this study we used data on financial hardship reported in a web-based survey of working-age cancer survivors conducted by the LIVE-STRONG Foundation in

2012. We assessed the proportion of working-age cancer survivors who reported that they or their families had gone into debt (respondents also gave the amount of debt incurred) and the proportion who reported having filed for bankruptcy because of cancer, its treatment, or the lasting effects of that treatment.

By estimating the prevalence of debt and bankruptcy among working-age cancer survivors, our study may lead to a better understanding of the extent to which financial hardship from cancer disproportionately affects working-age people, highlighting the potential need for financial protection assistance (such as financial counseling, payment assistance, or medication assistance programs). Importantly, while our findings address a significant gap in evidence, longitudinal population-based studies are warranted to improve the understanding of the magnitude and extent of financial hardship among cancer survivors and their families.

Study Data And Methods

Data Source And Study Population

This study used data from the 2012 LIVESTRONG Survey. The online survey was designed to elucidate the needs of individuals diagnosed with cancer, both during and after their cancer treatment. Survey respondents were recruited through several channels, including the LIVESTRONG Foundation constituency (donors, participants in events or programs, advocates, and others), Facebook, Twitter, and partnerships with national and community-based organizations.

We excluded respondents who did not have a personal history of cancer (caregivers, family members, and other respondents who had not survived cancer themselves), those who resided outside the United States or a US territory, and those who were age sixty-five or older. Our study sample consisted of 4,719 working-age adults with a previous diagnosis of cancer. Respondents came from all fifty states, the District of Columbia, Puerto Rico, and the US Virgin Islands.

Measures

The 2012 LIVESTRONG Survey used the same measures to assess financial hardship among cancer survivors as did the 2011 Medical Expenditure Panel Survey (MEPS) Experiences with Cancer Survivorship Supplement.³³ All questions in the MEPS supplement were developed using cognitive testing of a representative group of cancer survivors. More details about the survey design, developmental cognitive testing, and content are available elsewhere.^{33,34}

The primary outcomes in our analysis were participants' responses to the following questions: "Have you or has anyone in your family had to borrow money or go into debt because of your cancer, its treatment, or the lasting effects of that treatment?" and "Did you or anyone in your family ever file for bankruptcy because of your cancer, its treatment, or the lasting effects of that treatment?" We also analyzed participants' responses to other measures of financial hardship, including the amount of money borrowed and the size of the debt incurred; worry about paying large medical bills; having to make other financial

sacrifices; and types of out-of-pocket expenses (for the LIVESTRONG survey items used in our analysis, see the online Appendix).³⁵

Demographic information included age, sex, race/ethnicity, educational attainment, marital status, annual household income, and employment and insurance status. Insurance status was coded into four categories: private (private, employer-sponsored, or military insurance), public (coverage through a federal program such as Medicare or Medicaid), uninsured, and other (including respondents who said they preferred not to answer or did not know and those who did not answer). Cancer-related information included cancer type, time since first cancer diagnosis, and time since last cancer treatment.

Statistical Analysis

Descriptive statistics were calculated for all demographic characteristics, cancer-related characteristics, and outcome measures. For each of the outcomes—going into debt and bankruptcy—demographic and cancer-related characteristics with an alpha value of 0.20 in bivariate logistic regression analysis were retained in the final multivariable logistic regression models. In the final multivariable models, a two-sided *p* value less than 0.05 was considered significant. Separate logistic regression models were used for each outcome. Analyses of the amount of debt incurred and sources of out-of-pocket spending were limited to participants who reported going into debt. All analyses were performed using Stata, version 13.1.

Limitations

This study provides valuable information about financial hardship among working-age cancer survivors. However, several limitations should be noted. First, cancer survivors were recruited from multiple sources, and thus our study was not population based. Compared to a nationally representative sample of cancer survivors from MEPS,^{14,33} survey participants were more likely to be privately insured and had higher income levels and educational attainment. In addition, all participants needed to have access to the Internet to complete the survey. Because many of these factors are associated with a reduced risk of financial hardship,^{5–7,15,25} our results may underestimate the level of financial hardship among US working-age cancer survivors. Nonetheless, a high proportion of our sample population was young and recently diagnosed with their first cancer, factors associated with increased risk of financial hardship.³⁶

Second, our study data were self-reported and subject to recall bias and misclassification. Third, we did not have information on specific clinical characteristics, including stage of cancer at diagnosis, presence of comorbid conditions, and whether subsequent cancers actually represented a recurrence for survivors reporting two or more cancers.

Fourth, small sample sizes of survivors with specific cancers (such as breast, lung, and prostate cancer) precluded us from reporting results for each cancer type. Accordingly, ongoing evaluation of financial hardship by cancer type will be important for future research. Fifth, given the cross-sectional study design, we were not able to determine the underlying cause of the financial hardship of cancer attributable to specific characteristics

(for example, whether the costs of care or loss of employment caused the financial hardship).

Sixth, our analysis was limited to US cancer survivors. The paucity of evidence on the financial hardship of cancer among survivors in other countries suggests the need for future research in this area to assess access to affordable health care. Lastly, we did not have detailed information on the type of bankruptcy filed—involuntary (filed under Chapter 7 of the US Bankruptcy Code) or voluntary (filed under Chapter 13).

Study Results

The majority of cancer survivors in our study were non-Hispanic white (88 percent), female (67 percent), married (69 percent), employed full time (54 percent), and privately insured (85 percent) (Exhibit 1). Sixty-two percent had a bachelor's or advanced degree, and 42 percent had an annual household income of at least \$81,000. Seventy-five percent reported having been diagnosed with only one cancer. Sixty percent had received their first cancer diagnosis within the past five years, and 56 percent had had their last treatment within the past five years.

Sixty-four percent reported worrying about having to pay large bills related to their cancer, its treatment, or the treatment's lasting effects (Exhibit 2). Thirty-four percent reported that they or someone in the family had gone into debt because of cancer, and 3 percent said that they or their families had filed for bankruptcy as a result of cancer. Forty percent reported making other financial sacrifices.

Among the subset of survivors who reported that they or someone in their family had gone into debt, 87 percent said that they had worried about paying large bills related to cancer, and 9 percent reported that they or someone in their family had filed for bankruptcy as a result of their cancer. Sixty-eight percent made other financial sacrifices. Ninety-four percent had out-of-pocket spending on medical expenses, and 60 percent had such spending for transportation (Exhibit 3).

Of the 1,583 cancer survivors who reported that they or someone in their family had gone into debt, 1,558 reported the amount of debt incurred. Among this sample, 45 percent incurred less than \$10,000, 30 percent incurred \$10,000–\$24,999, 12 percent incurred \$25,000–\$49,999, and 13 percent incurred \$50,000 or more (for more details on the amounts of debt, see the Appendix).³⁵

Survivors ages 18–44 or 45–54 were significantly more likely to go into debt than those ages 55–64 (Exhibit 4). Also significantly more likely to go into debt were people who had lower annual incomes, compared to those in the highest annual income category (\$81,000 or more); survivors who were unemployed, compared to those employed full time; people who reported two or more cancer diagnoses, compared to those with only one cancer diagnosis; and survivors who had public insurance such as Medicaid or who were uninsured, compared to those with private insurance.

Filing for bankruptcy because of cancer was also significantly associated with younger age, lower annual household income, being unemployed, having public insurance, and having two or more cancer diagnoses (Exhibit 4). In addition, time since last cancer treatment was associated with bankruptcy: People whose last cancer treatment was more than two years in the past were significantly more likely to file for bankruptcy, compared to survivors in their first year of treatment.

Discussion

Using data from the LIVESTRONG 2012 survey, we found evidence of both material and psychological financial hardship among working-age cancer survivors, manifested as debt, bankruptcy, and worry about paying large medical bills. The extent of financial hardship was more pronounced for survivors who reported that they or their families had gone into debt because of cancer: Nine percent of these survivors reported filing bankruptcy, and 55 percent incurred debt of \$10,000 or more. Working-age survivors (and their families) at greater risk for debt and bankruptcy included those who were younger, unemployed, and uninsured or publicly insured, compared to those who were older, employed full time, and those with private insurance; and those who had a lower annual household income and two or more cancer diagnoses, compared to those with a higher income and only one cancer diagnosis.

The results of this study underscore the potential financial implications of cancer and the need for population-based surveys to further evaluate the financial hardship of cancer, its treatment, and the lasting effects of that treatment.

Affordability Of Care

Given that the costs of health care are increasing faster than household incomes in the United States,³⁷ there is growing concern among patients, providers, and other stakeholders about the affordability of care.³⁸ This is particularly so in the case of the working-age cancer survivor population, whose mean annual health care expenditures (\$17,170 for cancer survivors within one year of diagnosis and \$9,369 for cancer survivors after the first year) far exceed those of the working-age population with no history of cancer (\$3,611).⁵

Furthermore, studies indicate that the proportion of working-age US households facing financial hardship as a result of health care expenses remains high, regardless of insurance status.^{37,39,40} In 2011 nearly one in five working-age Americans lived in families whose combined out-of-pocket spending on medical expenses and insurance premiums was 10 percent or more of the family income.⁴¹ If this trend continues, such high out-of-pocket spending may become the primary driver of financial hardship for working-age cancer survivors and may lead to higher levels of debt and bankruptcy than this study found.

Our estimates of bankruptcy filing among working-age cancer survivors are consistent with the work of Scott Ramsey and colleagues,⁷ who reported that 2.2 percent of people with a cancer diagnosis in western Washington State filed for bankruptcy following the diagnosis, and the work of Karen Meneses and colleagues,¹² who found that 3.1 percent of breast cancer patients declared bankruptcy within six months after treatment. Although the proportion of cancer survivors filing for bankruptcy across studies is relatively low, it is

important to recognize that bankruptcy caused by medical expenses is an indication of extreme financial hardship.

To help prevent bankruptcy, people should receive help identifying sources of financial assistance and information that can be used in decision making about the costs of care shortly after diagnosis instead of long after treatment, when fewer medical debt assistance options exist. Given that illness or medical bills contribute to approximately 62 percent of all bankruptcies,^{13,42} our findings help highlight the issue of medical debt in the United States and the importance of helping patients understand the costs of care at each stage of their disease experience.

A recent population-based study of US cancer survivors using MEPS data showed that approximately 13 percent of working-age survivors reported ever borrowing money or going into debt, 2.3 percent said that they had ever filed for bankruptcy, and 32 percent reported having worried about medical bills related to their cancer.¹⁴ In contrast, we found higher prevalence of debt, bankruptcy, and worry about paying large medical bills because of cancer.

Our sample was larger than that in the previous study, which allowed us to evaluate patient factors associated with medical debt. Although our study population had high educational attainment and high income levels—factors associated with reduced risk of financial hardship—we found that other characteristics of the population (such as more recent cancer diagnosis and younger age) were associated with greater risk of financial hardship, compared to survivors who had been diagnosed less recently or who were older.^{9,10,28} Together, these studies add valuable information to a growing body of evidence that highlights specific components of both the material (debt, bankruptcy, and inability to cover medical costs) and psychological (worry about paying medical bills) aspects of financial hardship among cancer survivors.

While documenting the financial hardship that working-age survivors experience is a critical step, the current level of evidence is insufficient to guide the development of specific interventions. Future longitudinal population-based studies will be important in providing a clear picture of the multiple aspects of financial hardship and its impact on health outcomes among working-age cancer survivors. For instance, there is a need for more information about the occurrence and progression of financial hardship and about the relationship among survivors' financial, employment, and insurance status from the time of cancer diagnosis through the completion of treatment and beyond.⁷

Studies that follow working-age cancer patients over time will provide insights into what kinds of assistance are needed most, when, and by whom. Additionally, studies on the financial hardship that arises from specific cancer types or recurrent disease are warranted to improve understanding of the variation across populations of survivors. The findings from these studies will help focus efforts to prevent financial hardship resulting from cancer on the level—for example, the patient, provider, payer, or system level—at which interventions and policies may be most effective.

IMPACT OF THE AFFORDABLE CARE ACT

The Affordable Care Act (ACA) was designed to increase access to health insurance and protect people from high or unexpected medical care expenses.^{37,41} Furthermore, the ACA contains provisions that may assist working-age people diagnosed with cancer, such as the elimination of annual and lifetime limits on coverage for essential health benefits, caps on out-of-pocket spending for in-network medical services, and insurance premium tax credits and cost-sharing subsidies for individuals and families who meet eligibility requirements.

There is evidence of significant out-of-pocket burden for cancer survivors prior to the ACA,^{6,43,44} even among survivors who were insured. Thus, these ACA provisions may help reduce the likelihood of financial hardship by limiting out-of-pocket expenses. Additionally, for those populations that our study found to be at greatest risk of financial hardship from cancer, including survivors with low household incomes and without insurance, the ACA may improve insurance availability through both expanded eligibility for Medicaid in selected states and premium tax credits in the health insurance Marketplaces.⁴⁵

However, states' decisions about whether or not to expand eligibility for Medicaid may affect the number of cancer survivors who could benefit.⁴⁵ Moreover, most working-age US adults obtain health insurance through their employers and often do not meet eligibility requirements for benefiting from the ACA cost-containing provisions.⁴¹ Consequently, it will be important for future researchers to assess the impact of the ACA on barriers to access to care, costs of care for cancer survivors, and the associated financial hardship of cancer.

Identifying the extent to which the rising costs of care lead to financial hardship is essential for evaluating their impact on care quality. Efforts such as those related to the American Society of Clinical Oncology's Value in Cancer Care initiative have been made to help patients, providers, payers, and other stakeholders understand the importance of recognizing the implications of cost, understand the various costs associated with care, and integrate information about cost into treatment discussions to optimize medical decision making.⁴⁶

Studies indicate that financial hardship may have a negative impact on individuals' access to care, quality of care, and health outcomes³⁸ and that there are associations between financial hardship and decreased initiation of cancer therapy, delays in therapy initiation, and discontinuation of recommended therapy regimens.⁴⁷⁻⁵⁰ Furthermore, treatment delays and nonadherence can lead to the progression of disease or increased disease severity, adverse events, premature death, and increased overall health care expenditures (such as those caused by increased use of hospitals, particularly emergency departments).^{49,51} Thus, it is imperative that the costs of cancer care be balanced with the ability to access care that is high quality and clinically beneficial, particularly because patients must make decisions about care that could lead to substantial financial hardship for themselves and their families.

Conclusion

Our study provides evidence of the financial hardship that working-age cancer survivors and their families may experience. We identified characteristics of those who may be at greatest financial risk. The substantial proportion of cancer survivors who reported going into debt

and the high amount of debt incurred raise important questions about the financial well-being of working-age individuals diagnosed with cancer.

Essential to reducing the financial hardship caused by cancer is early education of patients— at the time of diagnosis—so that they can engage in conversations with their families and clinicians to optimally manage the physical, emotional, and financial impacts of cancer. Improving our understanding of financial hardship among cancer survivors, including both material and psychological effects, will provide stakeholders with the information required to identify those individuals who are most vulnerable and to develop evidence-based interventions and policies to help reduce the potential for financial hardship.■

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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64% Worried

Among respondents, 64 percent reported being worried about having to pay large bills related to their cancer.

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Characteristic	Number	Percent
AGE (YEARS)		
18–44	1,491	31.8
45–54	1,607	34.3
55–64	1,591	33.9
SEX		
Female	3,135	66.8
Male	1,560	33.2
RACE/ETHNICITY		
Black, non-Hispanic	107	2.3
Hispanic	258	5.5
White, non-Hispanic	4,125	87.8
Other	206	4.4
MARITAL STATUS		
Married or living with a partner	3,253	68.9
Other ^a	1,466	31.1
EDUCATION		
High school or less or other	394	8.4
Some undergraduate college or completed technical or community college	1,375	29.2
Bachelor's degree	1,644	34.9
Advanced degree	1,296	27.5
ANNUAL HOUSEHOLD INCOME		
Less than \$40,000	827	17.5
\$41,000–\$80,000	1,195	25.3
\$81,000–\$120,000	1,007	21.3
More than \$120,000	961	20.4
Other ^b	729	15.5
EMPLOYMENT STATUS		
Full time	2,529	53.9
Part time or student	513	10.9
Not employed	661	14.1
Retired	420	9.0
Other	568	12.1
HEALTH INSURANCE		
Private ^c	3,987	84.5
Public	376	8.0
Uninsured	133	2.8
Other	223	4.7
NUMBER OF CANCER DIAGNOSES		
1	3,496	74.3
2 or more ^d	1,209	25.7
TIME SINCE FIRST CANCER DIAGNOSIS		
Less than 1 year	940	20.3
1–4 years	1,845	39.8
5–9 years	822	17.7
10 years or more	1,026	22.2
TIME SINCE LAST TREATMENT		
Less than 1 year	1,251	27.2
1–4 years	1,312	28.5
5–9 years	906	19.7
10 years or more	1,136	24.7

EXHIBIT 1.

Characteristics Of 4,719 Cancer Survivors Ages 18–64, 2012

SOURCE Authors' analysis of data from the LIVESTRONG 2012 survey. **NOTE** Percentages may not sum to 100 because of rounding. ^aPeople who were single, divorced, widowed, or separated; who preferred not to answer; and for whom answers were missing. ^bPeople who preferred not to answer or said they did not know. ^cPrivate, employer-based, or military insurance. ^dDiagnoses of one or more subsequent primary cancers or of recurrence of the first primary cancer.

	Number	Percent
ALL SURVIVORS		
Ever worried about paying large bills related to cancer	3,002	63.8
Had to borrow money or go into debt ^a	1,583	33.6
Ever filed for bankruptcy ^a	145	3.1
Had to make any other kinds of financial sacrifices ^a	1,864	39.7
SURVIVORS WHO REPORTED GOING INTO DEBT		
Ever worried about paying large bills related to cancer	1,366	86.6
Ever filed for bankruptcy ^a	144	9.1
Had to make any other kinds of financial sacrifices ^a	1,069	68.0

EXHIBIT 2.

Working-Age Cancer Survivors' Responses To Survey Questions About Worry And Sacrifices, 2012

SOURCE Authors' analysis of data from the LIVESTRONG 2012 survey. **NOTES** The numbers and percentages presented are those of the participants who responded "yes" to each question. For all survivors, $N = 4,719$. For survivors who reported going into debt, $n = 1,583$. ^aSurvey question included the phrase "because of your cancer, its treatment, or the lasting effects of that treatment?"

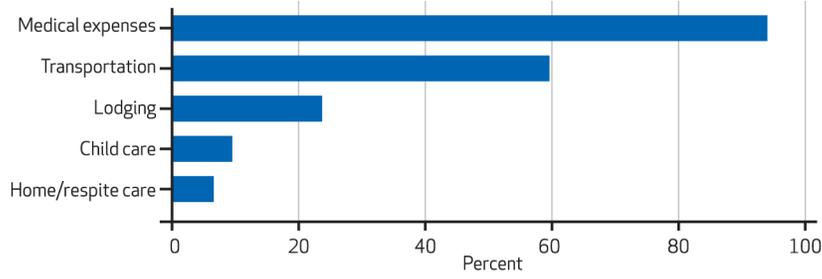


EXHIBIT 3.
Types Of Out-Of-Pocket Spending Among Working-Age Cancer Survivors Who Reported Borrowing Money Or Going Into Debt Because Of Cancer, 2012
SOURCE Authors’ analysis of data from the LIVESTRONG 2012 survey. **NOTES** The percentages presented are those of the 1,583 participants who responded yes to the question, “Have you or has anyone in your family had to borrow money or go into debt because of your cancer, its treatment, or the lasting effects of that treatment?” and who had valid responses to the question, “Because of your cancer, its treatment, or the lasting effects of that treatment, did you have any out-of-pocket costs in the following categories?” Categories are not mutually exclusive. “Medical expenses” include physician copayments, medications, and durable medical equipment.

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Characteristic	Borrowing money or going into debt	Bankruptcy
AGE (YEARS)		
55–64	Ref	Ref
45–54	1.66***	1.86**
18–44	2.07***	1.81**
SEX AND MARITAL STATUS		
Male, married	Ref	Ref
Male, not married	1.37**	1.52
Female, married	1.26	0.83
Female, not married	1.56***	0.99
RACE/ETHNICITY		
White, non-Hispanic	Ref	Ref
Black, non-Hispanic	0.80	2.25
Hispanic	1.41**	0.87
Other	1.00	1.01
ANNUAL HOUSEHOLD INCOME^a		
\$81,000 or more	Ref	Ref
\$41,000–\$80,000	2.46***	2.80***
Less than \$40,000	3.52***	4.50***
Other ^b	0.92	0.49
EMPLOYMENT STATUS		
Full time	Ref	Ref
Part time or student	1.03	1.28
Not employed	1.28**	1.74**
Retired	0.51***	1.00
Other	1.75***	1.34
HEALTH INSURANCE		
Private ^c	Ref	Ref
Public	1.95***	1.82**
Uninsured	2.46***	1.05
Other	1.21	0.99
NUMBER OF CANCER DIAGNOSES		
1	Ref	Ref
2 or more ^d	1.49***	2.00***
TIME SINCE LAST TREATMENT		
Less than 1 year	Ref	Ref
1–2 years	0.92	1.21
3–5 years	0.97	1.71**
6 years or more	0.82**	1.65**

EXHIBIT 4.**Working-Age Cancer Survivors' Risk Factors For Borrowing Money, Going Into Debt, And Bankruptcy, By Various Characteristics, 2012**

SOURCE Authors' analysis of data from the LIVESTRONG 2012 survey. **NOTES** The exhibit shows the results of the final adjusted regression models. Associations between the two outcomes (borrowing money or going into debt and filing for bankruptcy) are based on the 4,504 participants who had valid values for each variable included in the final model. A version of this exhibit including 95% confidence intervals can be found in the Appendix (see Note 35 in text). Significance refers to the difference from the reference category. ^aFor the analyses, annual household income was recategorized as shown in the exhibit. ^bPeople who preferred not to answer or said they did not know. ^cPrivate, employer-based, or military

insurance. ^dDiagnoses of one or more subsequent primary cancers or of recurrence of the first primary cancer. ** $p < 0.05$ *** $p < 0.001$

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