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PII: S0002-9149(20)31229-7
DOI: https://doi.org/10.1016/j.amjcard.2020.11.005
Reference: AJC 24961

To appear in: *The American Journal of Cardiology*

Received date: 21 September 2020
Revised date: 31 October 2020
Accepted date: 3 November 2020

Please cite this article as: Avirup Guha MBBS , Amit Kumar Dey MBBS , Sadeer Al-Kindi MD , P. Elliott Miller MD , Arjun Ghosh MBBS , Amitava Banerjee MBBCh , Juan Lopez-Mattei MD , Nihar R. Desai MD , Brijesh Patel MD , Guilherme H. Oliveira MD, MBA , Marcos de Lima MD , Michael Fradley MD , Daniel Addison MD , Socio-economic Burden of Myocardial Infarction among Cancer Patients, *The American Journal of Cardiology* (2020), doi: https://doi.org/10.1016/j.amjcard.2020.11.005

Socio-economic Burden of Myocardial Infarction among Cancer Patients

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Running Title: Financial toxicity in cancer patients

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Funding: This work was supported in part by NIH grant P30 CA016058, and by K12-CA133250 (DA) grants.

Role of the Funder: The funding source had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclosures: All authors declare no conflicts of interests in relation to the work presented in this manuscript.

Acknowledgements: NIL

Abstract

Cancer patients face a higher risk of future myocardial infarction (MI), even after completion of anticancer therapies. MI is a critical source of physical and financial stress in non-cancer patients, but its impacts associated with cancer patients also saddled with the worry (stress) of potential reoccurrence is unknown. Therefore, we aimed to quantify MI's stress and financial burden after surviving cancer and compare to those never diagnosed with cancer. Utilizing cross-sectional national survey data from 2013-2018 derived from publicly available U.S. datasets, the National Health Interview Survey (NHIS), and economic data from the National Inpatient Sample (NIS), we compared the socio-economic outcomes among those with MI by cancer-status. We adjusted for social, demographic, and clinical factors. Overall, 19,504 (10.2%) of the 189,836 NHIS survey responders reported having cancer for more than 1 year. There was an

increased prevalence of MI among cancer survivors compared to non-cancer patients (8.8% vs. 3.2%, P<0.001). MI was associated with increased financial worry, food insecurity, and financial burden of medical bills (P<0.001, respectively); however, concurrent cancer did not seem to be an effect modifier (P>0.05). There was no difference in annual residual family income by cancer status; however, 3 lowest deciles of residual income representing 21.1% cancer-survivor with MI had a residual income of <$9,000. Myocardial infarction continues to represent an immense source of financial and perceived stress. In conclusion, although cancer patients face a higher risk of subsequent MI, this does not appear to advance their reported stress significantly.

Keywords: Myocardial Infarction; cancer; socio-economic outcomes; financial hardship

Introduction

In the United States (U.S.), the development of myocardial infarction (MI) continues to have dire socio-economic consequences[1]. An alarming 1 in 5 patients with MI is unable to pay their medical bills and report financial hardship from medical expenses[1]. Because of this, many patients and their families live daily with the heavy burden of the financial and psychological impacts of MI. Yet, as these burdens are increasingly detrimental to long-term health, growing calls for enhanced attention to higher-risk populations have been made. Over the last 2 decades, the number of cancer survivors has dramatically risen, with a projected 20 million survivors in the United States by 2025 alone[2]. Unfortunately, with increasing cancer survival, the prevalence of subsequent cardiovascular events[3], including myocardial infarction (MI), has dramatically risen[2,4,5]. Like MI, cancer has also been associated with high material, psychological, and

behavioral healthcare burden[6,7]. This is amplified by recent public health education efforts spreading increasing awareness of the long-term risk and effects of MI in this growing population. Given this burden, it is reasonable to hypothesize that the financial and psychological impacts of MI among cancer patients may be particularly excessive, and this study is aimed to quantify this stress and financial burden.

Methods

Accordingly, we aimed to quantify the financial status and healthcare burden of MI among cancer survivors. Utilizing the NHIS is a dataset compiled by the Center for Disease Control and Prevention (CDC) annually, we sought to quantify patient-reported measures of perceived stress. It is a cross-sectional national survey that uses complex multistage sampling to estimate the non-institutionalized U.S. population. We utilized 6 years of data (2013 through 2018) from the NHIS to study demographics of MI patients with and without cancer as well as to compare the socio-economic outcomes among those with MI and cancer, keeping in mind that the study was limited to those who reported their cancer status to be more than a year[7]. The cost estimate reference of a MI hospitalization was obtained using the 2014-2015 National Inpatient Sample Dataset (NIS). Actual hospitalizations for MI were not utilized in any portion of this study. NIS is managed under the Healthcare Cost and Utilization Project by the Agency for Healthcare Research and Quality (AHRQ). This study was conducted using publicly available data and did not require approval by an institutional review board.

Self-reported data, including heart disease, stroke, hypertension, diabetes mellitus and cancer condition status, was used annually. Specifically, if the interviewee ever responded positively to the question of ever having been told by a doctor that they had a heart attack, they were considered to have had MI (**Figure 1A**). The study was limited to all adults (≥ 18 years)

and reported their cancer status to be more than a year[7]. In the NHIS, cancer history is self-reported at the time of the survey. We defined cancer survivors as those who reported ever having been diagnosed with cancer or a malignancy of any kind by a physician or other health professional. Individuals with only nonmelanoma skin cancer and skin cancer of unknown type were excluded[7].

Financial distress burden[1] was defined using 6 questions regarding the level of worry concerning financial matters of retirement savings, ability to bear the cost of serious illness, ability to maintain a standard of living, ability to pay the cost of regular health care, ability to pay normal monthly bills and affordability with regards to housing costs. The questions were posed on a 4-point scale, and the collective score was converted to quartiles of least worry to most worry. Medication insecurity[1] was defined using the 6 questions which were: 'skipped medication doses to save money?', 'took less medicine to save money?', 'Delayed filling a prescription to save money?', 'Asked doctor for lower cost medication to save money?', 'Bought prescription drugs from another country to save money?', 'Used alternative therapies to save money?'. If there was a 'yes' reply obtained to any of these questions, the interviewee was considered medication insecurity. Food insecurity[1] was obtained from the "Family" file of the NHIS annual survey by the U.S. Department of Agriculture Economic Research Service. The defined scale was then converted into 3 categories - no food insecurity, moderate food insecurity, and high food insecurity. The financial burden of medical bills[1] was a 3-category outcome that included those with no problems with medical bills, those with some problems with medical bills or using a payment plan to pay off medical bills, and those unable to pay medical bills.

The reference for cost estimates of hospitalization for primary diagnosis of MI, using the AHRQ Clinical Classifications Software (CCS) code of 100 for the years 2014-15, was obtained

from the NIS data. The cost for hospitalization was obtained by multiplying the geographic modifier and cost-to-charge ratios to the hospitalization charge. The cost obtained was inflation-adjusted to 2019 ($22,715)[8]. Further, the NHIS provided annual family income[9] using multiple imputation, which was then was averaged across each year (2013 through 2018) and adjusted for inflation estimates based on 2019[8]. Under the Affordable Care Act (ACA), Health and Human Services (HHS) publishes an annual out-of-pocket maximum annually since 2014. As of 2019, the individual out-of-pocket yearly maximum is listed at $7,900[10]. In a report by the American Heart Association[9], MI was considered the most expensive condition treated in the hospital. In another report by the CDC in 2017, annual healthcare expenditure for that year for the entire U.S. population was $10,348 per person[11]. Given these 2 facts, we assumed that the interviewee would have been required to meet the prescribed annual maximum threshold limit assuming they had MI in the same year. Hence, $7,900 was subtracted from the inflation-adjusted yearly family income. If the patient was uninsured, the inflation adjusted cost of MI hospitalization derived from NIS ($22,715) was subtracted from the inflation adjusted annual family income. The residual income was split into deciles and compared after stratification by history of cancer (**Figure 1B**). Financial toxicity was defined as <$9,000 annual residual income.

Covariates included in this study included age, gender, race/ethnicity, family income (based on family income as a percentage of the federal poverty limit from the Census Bureau: high-income [≥400%], middle-income [200% to 400%], low-income [100-200%] and below the poverty line [<100%]), education, insurance status, and geographical region. Cardiovascular risk factors, namely, smoking history, body mass index, hypertension, and diabetes, were collated. Self-reported 34 chronic comorbidities were aggregated and categorized as having 0, 1, or ≥2 comorbidities.

Weighted estimates were presented in our results. The survey-specific Rao-Scott chi-square test was used to assess differences in categorical variables, with survey-weighted proportions used to study outcome prevalence in our study population. Adjusted survey-specific polytomous logistic regression models were used as measures of association between financial distress burden, food insecurity, medication insecurity, and financial burden of medical bills and cancer state. Covariates were adjusted for were age, gender, race, insurance status, and family income. As a sensitivity analysis, the analysis mentioned above was repeated in subgroups of only prostate and breast cancer survivors only. Variance estimation for the entire pooled cohort was obtained from the Integrated Public Use Microdata Series. For all statistical analyses, $P < 0.05$ was considered statistically significant. All analyses were carried out using SAS 9.4 (Cary, NC).

Results

Overall, 19,504 (10.2%) of the 189,836 NHIS survey responders reported having cancer (with or without MI) for more than 1 year. However, on weighted analyses, 19,504 (10.2%) of the 189,836 NHIS survey responders represent 65 million cancer survivors among 639 million survey responders after accounting for survey weights along all strata and clusters. MI was reported by 1,719 (8.8%) survey respondents among those who had cancer. On weighted analyses, this represents 5.6 million cancer survivors who also reported having a MI after accounting for survey weights along all strata and clusters. Among cancer survivors who had prior MI(s), 12%, 4.4%, 7.7%, 28.6%, and 2.9% reported having survived breast, lung, colon, prostate, and lymphoma.

Cancer survivors saw an increase in MI prevalence compared to non-cancer (8.8% vs. 3.2%, $p < 0.0001$). The demographics of cancer survivors who reported having MI are shown in

Table 1 when compared to non-cancer survivors with MI. Cancer survivors with reported MI were more likely older, white, and non-smoker than those with MI but no history of cancer (P-value for all comparison < 0.0001, **Table 1**).

Among the 4 quartiles of financial worry, the lowest quartile of financial worry had 35.7% cancer responders vs. 28.9% non-cancer responders (P < 0.0001). There was a similar number of cancer and non-cancer responders in the middle quartiles (**Figure 2**). However, in the highest worry quartile, cancers responders constituted around 20.3% compared to 26.5% non-cancer responders (P < 0.0001). There was no difference in adherence to medication based on cancer survivor status (71.3% in cancer responders vs. 71.8% in non-cancer responders, P = 0.71).

High food insecurity was seen in 1.7% cancer survivors and 1.9% non-cancer responders, respectively, which was not statistically different. Low food insecurity was seen in 80.4% of cancer survivors and 74.9% of non-cancer responders, respectively. The level of moderate food insecurity was lower in cancer-survivors (17.9%) vs. those without cancer (23.2%, P = 0.0003).

There was no hardship seen in 72.7% of cancer survivors regarding medication insecurity than 68.5% non-cancer responders (P = 0.002). Further, 9.5% of cancer survivors had no hardship from medical bills than 12.8% of non-cancer responders (**Figure 3**).

Cancer survivor status was not significantly associated with any aforementioned study outcomes after adjusting for age, gender, insurance status, and annual income (**Figure 4A**). Cancer survivors reported to have MI from 2013 to 2018 had annual residual family income ranging from $-1992.5 to $139,472 among all deciles combined. Similarly, the non-cancer responders who had MI in the same period had residual yearly income ranging from $-3565.8 - $143,685 among all deciles. The lowest 3 deciles had <$9,000 residual across cancer-survivors

and non-cancer responders (**Figure 4B**). The 3 lowest deciles represent 6,673,562 patients with MI (21.1% cancer-survivors) demonstrated immense financial toxicity associated with MI.

In two additional subgroup analyses in only prostate cancer and breast cancer patients, the study results did not significantly deviate from the aforementioned study outcomes (**supplemental figure 1 and 2**). The lowest 3 deciles had <$9,000 residual across the patients included in both subgroups.

Discussion

In this study, we observed a higher prevalence of reported M.I.s among cancer survivors. There was no difference in the reported amount of financial hardship following MI, even after adjustment for age, gender, insurance status, and annual income. However, the lowest 3 deciles of cancer survivors who had MI, representing ~ 1.4 million patients, had <$9,000 residual family income representing immense financial toxicity with MI. These findings should prompt further investigation into preventive measures among cancer survivors to reduce the burden of MI.

Our study supports the finding of a recent analysis of NHIS spanning from 2013-2017[1], which showed that nearly 3.9 million American adults with cardiovascular disease experience medical bills related to financial hardship. Additionally, our study extends findings from prior research by demonstrating that cancer status does not modify this effect. Moreover, the financial burden of toxicity in estimated health care dollars that plagues the bottom 3 deciles of MI patients was also quantified. It is noted that cancer responders appeared to have less financial worry among those that had a MI. Although the reasons for this are unclear, it is perhaps related to selective resilience and mental preparation following a cancer diagnosis, in terms of familiarity with the healthcare system, and better insurance coverage, among others[12]. Further, it

is also possible cancer patients and providers may not have been aware of the spectrum of cardiac (including MI) associated with their treatments, as recently observed.[20]

The vulnerability of material, psychological, and behavioral domains of cancer survivors are especially concerning due to the increased risk of late and long-term cardiovascular complication of cancer treatment. Therefore, MI, which is one of the adverse complications of many cancer therapies and an outcome of shared risk factors between cardiovascular disease and cancer, may add immensely to all financial toxicity domains in cancer survivors[7]. Keeping this in mind, our study aimed to quantify the residual family income in the era of ACA, where cancer survivors are offered protection of health insurance[13]. Our findings demonstrated that even though cancer patients increasingly are covered by the new provisions of ACA[14], over 6 million are left with <$9,000 residual annual income after a MI. Further changes in health care policies are needed to protect cancer survivors experiencing an MI from financial toxicity. Leveraging cardiovascular prevention guidelines[15] and refining the cancer society guidelines[16,17] about financial burden and toxicity of MI in cancer is paramount.

Several limitations should be acknowledged. First, the NHIS data are based on patient self-report of several critical measures used in the analysis, including income, health status, and health insurance. Hence, they are subject to recall bias. Although the sample is nationally representative, individuals with cancers with shorter survival are less likely to be included in this survey. Because of the nature of the survey's retrospective nature, we could not fully elucidate the true levels of patient and clinician awareness of the elevated risk of subsequent MI[18] or differences in coping strategies (i.e., resilience) with this risk. Also, prior MI report is generally heterogeneous among non-medically trained populations, wherein an abnormal electrocardiogram or verbal report of suspicion of previous MI may be accidentally confused

with medically confirmed or biomarker-positive MI. Moreover, our findings of financial hardship associated with cancer often refer to families of cancer survivors and not individuals[1,19]. Finally, the derived cost of MI from NIS, even though nationally representative, comes with drawbacks of using weighted stratified sampling technique[20].

Conclusion

Cancer patients face an onerous burden of increased myocardial infarction risk, even after completing their cancer treatments. Within this study, the burden of perceived and financial was significant among many Americans who have MI. However, this level of stress is not modified by cancer survivor status. Further research into the clinician and patient awareness of cancer survivorship risks of MI and the optimal coping methods with this risk are needed.

Author Contributions:

AG and DA had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: AG conceived the study concept and the study design was by DA.

Acquisition, analysis, or interpretation of data: AG acquired, analyzed, and interpreted the data.

Drafting of the manuscript: AG and AKD drafted the manuscript.

Critical revision of the manuscript for important intellectual content: All authors provided critical revisions of the manuscript.

Statistical analysis: AG performed analyses.

Study supervision: The study was conducted under the supervision of DA.

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Figure Legends

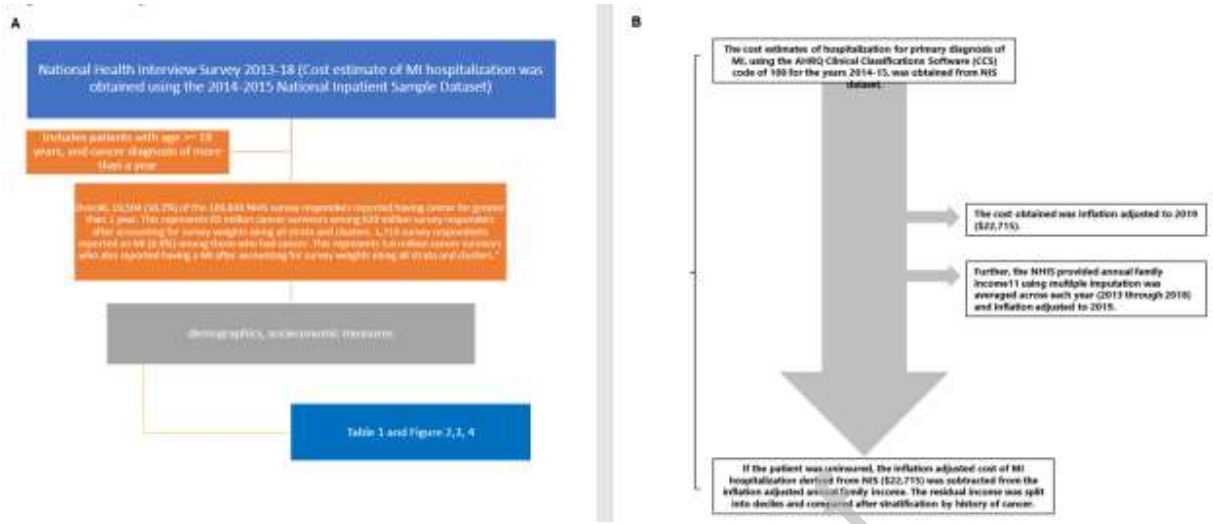

Figure 1A: Consort Diagram**; 1B:** Detailed description of residual income calculation

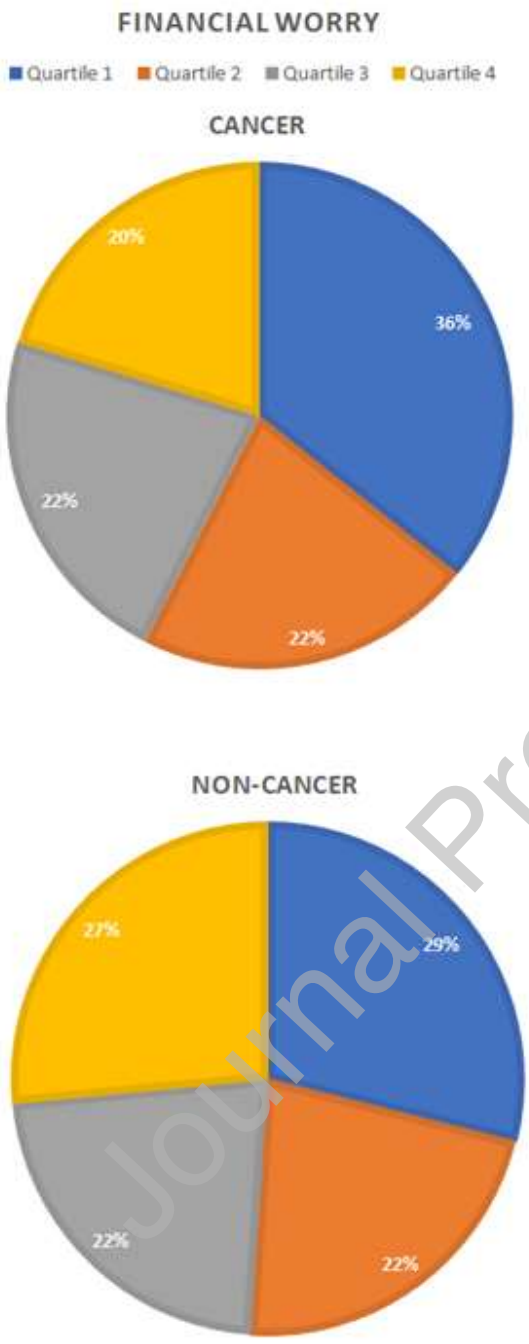

Figure 2: Financial worry measure among cancer survivor vs. non-cancer patients with myocardial infarction

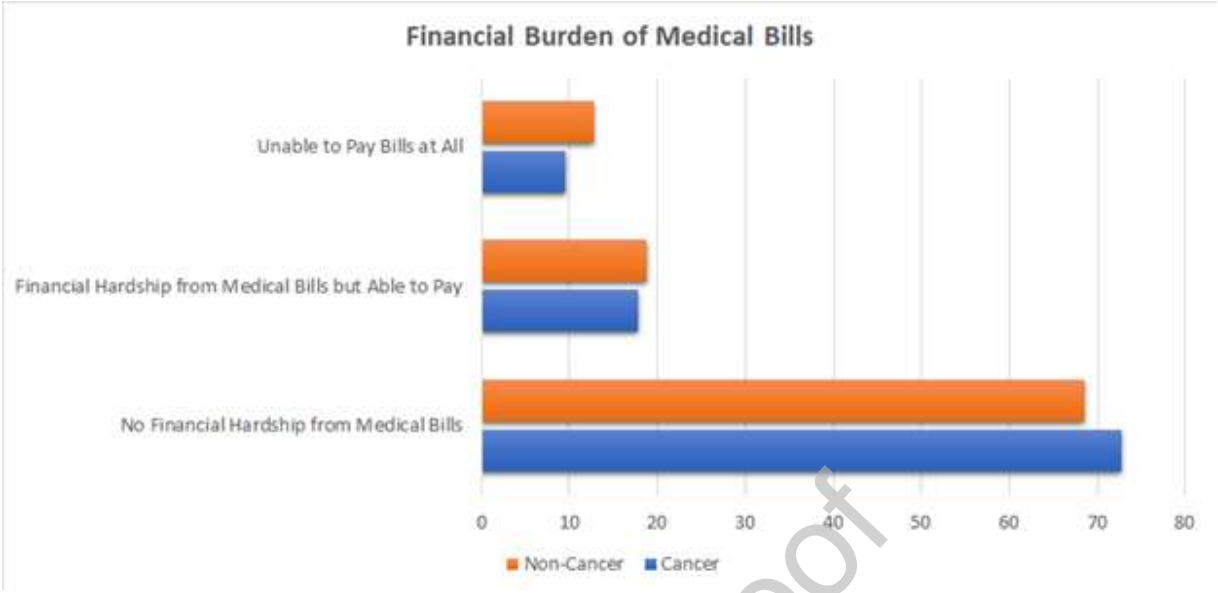

Figure 3: Financial Burden of Medical Bills among cancer survivor vs. non-cancer patients with myocardial infarction

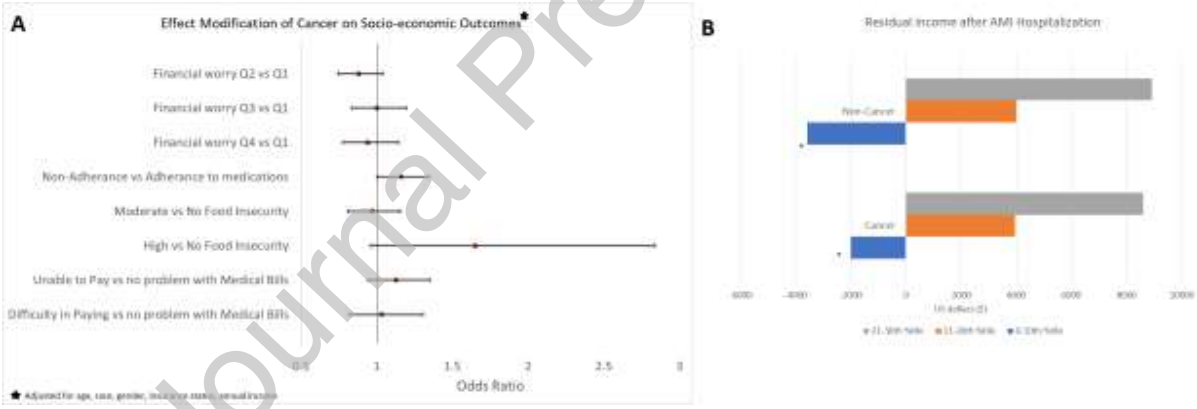

Figure 4A: Cancer survivor status and association with study outcomes after adjustment for age, gender, insurance status, and annual income; **4B:** Cancer survivors reported to have MI from 2013 to 2018 had residual family income ranging from $-1992.5 - $139,472 among all deciles combined. Similarly, the non-cancer responders who had MI in the same period had annual residual income ranging from $-3565.8 - $143,685 among all deciles. The lowest 3 deciles had <$9000 residual across cancer-survivors and non-cancer responders. The 3 lowest deciles

represent 6,673,562 patients with MI (21.1% cancer-survivors) demonstrated immense financial toxicity associated with MI.

Table 1: Demographics of patients with myocardial infarction among cancer survivors and non-cancer responders from 2013-2018.

Variable	**Cancer (N = 1,719)**	**Non-Cancer (N = 5,520)**	**P-value**
Age Group (years)			<0.0001
18-40	1.6 %	3.4 %	
41-65	24.1 %	41.3 %	
65+	74.3 %	55.3 %	
Women	41.1 %	38.6 %	0.21
			<0.0001
Non-Hispanic white	84.8 %	71.7 %	
Non-Hispanic black	7.2 %	13.2 %	
Hispanic	3.9 %	9.2 %	
Other	4.1 %	5.8 %	
BMI (kg/m^2)			0.003
<18	5.1 %	3.6 %	

18 - 25	23.9 %	20.6 %	
26 - 30	34.9 %	35.0 %	
> 30	36.2 %	40.7 %	
Insurance			<0.0001
Insured	98.1 %	95.0 %	0.006
Medicare	25.1 %	25.6 %	
Medicaid	13.2 %	16.8 %	
Private	48.3 %	45.1 %	
Other	13.4 %	12.6 %	
Uninsured	1.9 %	5.0 %	<0.0001
Education			0.01
Less than high school	20.6 %	23.0 %	
High School Graduate/GED recipient	28.6 %	31.6 %	
Some college or associate degree	29.5 %	28.2 %	
Bachelor's degree or higher	21.4 %	17.2 %	
Annual Family Income			0.66
Below poverty line (<100%)	63.4 %	65.4 %	

100-199% of poverty line	29.0 %	27.2 %	
200-399% of poverty line	5.7 %	5.2 %	
400%+ above poverty line	1.9 %	2.2 %	
Region			0.95
Northeast	17.4 %	16.8 %	
South	37.4 %	38.6 %	
West	19.8 %	20.4 %	
Midwest	25.4 %	24.5 %	
Risk Factors			
Smoker			<0.0001
Current	16.8 %	23.3 %	
Former	47.5 %	41.5 %	
Never	35.7 %	35.3 %	
Alcohol drinker			0.32
Current	45.6 %	48.4 %	
Former	34.0 %	32.0 %	
Never	20.3 %	19.7 %	

Hypertension	76.6 %	76.4 %	0.94
Diabetes mellitus	32.6 %	34.5 %	0.65
Emphysema	10.8 %	9.0 %	0.01

BMI = body mass index; GED = General Educational Development. Values reported in the table as (%) for categorical data. P-value less than 0.05 was deemed significant.