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ADDITIONAL HEALTHCARE EXPENDITURES OF DEPRESSION FOR ELDERLY CANCER PATIENTS WITH DEPRESSION

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DEDICATION

To my parents, Wei Gu & Aijun Xue

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by

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ADDITIONAL HEALTHCARE EXPENDITURES OF DEPRESSION FOR ELDERLY CANCER PATIENTS WITH DEPRESSION

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Background: The risk of depression is high for cancer patients and a large portion of cancer patients are age 65 and over. Both depression and cancer are economically burdensome and depression is associated with healthcare expenditure increase for elderly patients. However, whether comorbid depression affects healthcare expenditures in elderly cancer patients from payers' and patients' perspectives is largely unknown. **Objective:** To investigate whether depression is associated with higher healthcare expenditure among elderly cancer patients from both payers' and patients' perspectives and, and determine whether depression is associated with higher probability of having high out-of-cost burden. **Methods**: From the Medicare Current Beneficiary Survey (MCBS)-Medicare database, we identified breast, lung and prostate cancer patients aged 65 years or older who were newly diagnosed between 2007 and 2012 using Medicare claims. Presence of depression was based on self-reports from the surveys. Healthcare expenditures included expenditures incurred in the cancer diagnosis year and the subsequent calendar year. High out-of-cost burden was referred to as out-of-pocket cost as over 10% of respondent's income. For the analyses of healthcare expenditures, generalized linear models (GLM) and two-part models were used to examine the impact of depression on healthcare expenditures when controlling for all other covariates assessed in

the study. We stratified the analyses by healthcare service types and payers. For the analyses of high out-of-pocket cost burden, logistic regression was used to estimate whether depression was associated with higher probability of having high out-of-pocket cost burden. **Results**: Of the 710 elderly breast, lung and prostate cancer patients identified, 128 (18%) reported depression. The results revealed that elderly cancer patients with depression had $11,454 higher overall total healthcare expenditures. From Medicare's perspective, elderly patients with depression incurred $8,280 higher expenditures, $4,327 higher medical provider expenditures and $870 higher expenditures on other services. They were also more likely to use inpatient services and other services. From the patients' perspective, they had higher healthcare expenditures, medical provider expenditures and other expenditures ($1,270, $654 and $465, respectively). For high out-of-pocket cost burden, although the unadjusted result was significant, the adjusted result was not. **Conclusions**: Elderly patients with depression had significantly higher healthcare expenditures from the payers' perspective. Although they did not have higher out-of-pocket cost burden, they did have higher healthcare expenditures from patients' perspectives and over different expenditure types. These findings provide compelling evidence for policy makers, physicians and researchers to develop guidelines for and conduct studies of depression screening, diagnosis and treatment for geriatric cancer populations.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

BACKGROUND

Statement of the Problem

It has been shown that the risk of depression is higher for cancer patients than those with stroke, diabetes and heart disease.[1, 2] Moreover, many studies have suggested that patients' short-term and long-term physical and mental health are negatively impacted by the coexistence of cancer and depression. [3-5]Therefore, understanding the mental health need among cancer patients is a vital task to improve holistic wellbeing for cancer patients. Additionally, as a result of the aging population in the United States and the high prevalence of cancer among the elderly, the majority of cancer survivors is 65 and over; it is projected that, by 2040, 73% of 26.1 million cancer survivors will be 65 years or older.[6] Considering the serious negative impact of coexisting depression on cancer patients, it is important to study the association between cancer and depression among the elderly.

This study focuses on three most prevalent cancers: breast cancer, lung cancer and prostate cancer. In particular, prostate cancer is the most prevalent among males, and breast cancer is the most prevalent among females. Lung cancer ranks the second in both males and females.[7] The goal of the study is to understand the economic impact of depression on elderly cancer patients through these three important types of cancers.

As one of the most economically burdensome disorders, depression is usually associated with excess healthcare expenditures. In particular, it has been shown that depression is associated with increase in direct health care costs for the elderly patients with depression. [8, 9]However, the healthcare expenditures of depression, in addition to cancer

itself, from the perspective of both payers and patients is largely unknown for elderly cancer patients, which is a quite unsatisfactory situation.

Therefore, it is vital to study the additional healthcare expenditure of depression among elderly depressed breast, prostate and lung cancer patients.

Objectives

The overall objective of this study is to estimate the additional healthcare expenditures of depression for elderly breast, prostate and lung cancer patients with depression from both the payer and patients' perspectives. In addition, this study will examine how elderly depressed breast, prostate and lung cancer patients are adherent on antidepressant therapy and related factors. In particular, the aims of this study are:

Aim 1. From payer's perspective, determine if elderly breast, lung and prostate cancer patients with depression have more healthcare expenditures than those without depression

- Hypothesis: elderly breast, lung and prostate cancer patients with depression will incur higher healthcare expenditures than those without depression in payer's perspective

Aim 2. From patients' perspective, determine if elderly breast, lung and prostate cancer patients with depression have more out-of-pocket healthcare expenditures than those without depression

- Hypothesis: elderly breast, lung and prostate cancer patients with depression will incur higher out-of-pocket healthcare expenditures than those without depression

Aim 3. Determine if elderly breast, lung and prostate cancer patients with depression are more likely to have high out-of-pocket cost burden than those without depression

- Hypothesis: depression will be significantly associated with increased odds of high out-of-pocket cost burden

Public Health Significance

There is a high prevalence of depression among elderly cancer patients. Considering the fact that cancer and depression is each associated with very high expenditures, it is important to study the healthcare expenditures when the two coexist, which is not clear from existing studies. The result of the Aims 1 and 2, by examining the overall health expenditures from both payer and patients' perspectives will bridge this important gap in the literature. Additionally, the result will increase the awareness of depression issues for elderly cancer patients and help evaluate relevant depression prevention/management interventions for this population. Also, the expenditure estimates can be used in cost-effectiveness studies of interventions addressing depression for elderly cancer patients: the reduction of depression related healthcare costs would partially offset the intervention costs. The result of Aim 3, examining whether depression is associated with a high out-of-pocket cost burden, will strengthen the importance of studying individual financial burden for this population.

Literature Review

High Proportion of Elderly Patients with Breast, Lung and Prostate Cancer

It is estimated that 62% of the cancer survivors living in the U.S. are 65 years or older in 2016. By 2040, the proportion of elderly cancer survivors will grow to 73% and the absolute number will become close to 30 million.[6] Like most cancers, breast, lung and prostate cancers are diseases of the elderly people. In the U.S., the median age of diagnosis is about 62 for female breast cancer, 68 for male breast cancer;[10] 70 for lung cancer and 66 for prostate cancer.[10] Such high concentration of cancer among the elderly reinforces the importance of understanding how this disease affects the overall clinical and economic wellbeing of this population. This paper is specifically interested in exploring the intersection of cancer and depression among those 65 and older.

High Prevalence of Depression among Breast, Prostate and Lung Cancer Patients

Cancer often places significant psychological burdens on patients not only at the time of diagnosis but also during treatment and afterwards. Indeed, many studies show that cancer patients are more likely have depression.[11-13] Furthermore, depression symptoms of cancer patients are frequently ignored by clinicians and viewed to be the normal psychological reactions of cancer diagnosis and treatments. It has been shown that detection rate of depression is low among cancer patients and the rate of depression is often underestimated.[14, 15] For example, in a large study of over 1,100 cancer patients, physicians only correctly identified 33% of patients with mild to moderate depression, and only 13% of patients with severe depression were diagnosed.[15] As a result, the actual rate of depression among cancer patients are likely to be higher than the reported numbers in existing studies.

Breast, prostate and lung cancers are all highly associated with depression and depression can appear at any time during the course of the cancers. For example, a study reported the prevalence of depression among breast cancer patients ranged from 1.4% to 46%. [16] For lung cancer, it is also reported that about 11% to 44% of lung cancer patients suffered from depression.[16] In a study estimating longitudinal changes in depression symptoms, 38% had depression symptoms at baseline and 14% more developed "new-onset depression symptoms" during treatment.[17] For prostate cancer, "the lifetime prevalence of major depressive disorder in adults in the U.S." is 17%. [18]An article identified 50,147 elderly patients with newly diagnosed prostate cancer found that 8.54% of them were diagnosed with depression following their prostate cancer diagnosis. [19]A meta-analysis identifying 27 journal articles and with a pooled sample size of 4,494 prostate patients identified pre-treatment, on-treatment and post-treatment depression prevalence of 17.27%, 14.70% and 18.44%, respectively.[20]

Negative Impact of Depression on Breast, Lung and Prostate Cancer Patients

Depression has negative impact on many aspects of cancer patients' outcomes. For example, depression has been linked to higher mortality, poorer quality of life, and poorer treatment adherence for cancer patients in general. [3-5]

Similar negative impact of depression has been found on breast, lung and prostate cancer. For example, a study found that breast cancer patients with depression had lower overall quality of life. [21]Additionally, depression reduces likelihood of breast cancer patients' adherence to their medical treatments.[21, 22]

For lung cancer, it has been shown the depression affected the functional status negatively. [23]Also, depression has been shown to decrease survival among patients recently diagnosed lung cancer.[24]

For prostate cancer, depression also reduces treatment effectiveness, and lowers the survival.[25]

High Healthcare Expenditures of Breast, Lung and Prostate Cancer and Depression

Depression is one of the most economically burdensome disorders worldwide. Moreover, studies have suggested that the already excessive healthcare cost of depression has increased rapidly in recent years; the extra economic burden for patients with major depressive disorder had increased by 21.5% from 2005 to 2010 in the U.S..[26, 27]

It is also well-known that cancer is a very expensive disease for both the patients and the society as a whole. For instance, a study projected that the cost of cancer in the US would reach $173 billion in 2020, representing a 40% increase from 2010. In 2010, the annualized mean net costs of female breast cancer care for elderly patients was $23,078 in initial phase, $2,207 in continuing phase, and $62,856 in last year of life for cancer death. The annualized mean net costs of female lung cancer care for elderly patients was $60,533 in initial phase, $8,130 in continuing phase, and $92,524 in last year of life for cancer death. For male lung cancer patients, the numbers were $60,885, $7,591 and $95,318, respectively, and for elderly prostate cancer patients, the numbers were $ 19,710, $3,201 and $ 62,242, respectively. The national cost of care for female breast cancer patients is $16.50 billion, which is the highest cost among all cancers. The national costs of care for lung cancer and prostate cancer, $12.12 billion and $11.85 billion, respectively, which rank 4th and 5th among all cancers. It is

projected that the national costs in continuing phase for prostate and female breast cancers would rank the top in 2020.[28]

Additionally, for breast cancer, a synthesis of published evidence in 2009 estimated the "lifetime per-patient costs" of breast cancer varied from $20,000 to $100,000.[29]Also, a study about the economic burden of lung cancer in 2005 estimated that the overall costs, from diagnosis to no more than two years after diagnosis, were about $46,000.[30] Moreover, some research estimated lifetime costs for prostate cancer patients enrolled in Medicare at $110,520 in 2004 U.S. dollars, about 31% of which is prostate cancer-related.[31]

Additional HealthCare Expenditures of Depression for Breast, Lung and Prostate Cancer Patients

Although depression is associated with an increase in direct health care costs for elderly patients with depression[8, 9], only a few studies have examined the healthcare expenditures of depression for cancer patients. In a recent paper about cancer patients aged 21 years and older, a study showed that those with depression had more than 30% greater one-year healthcare expenditures compared with those without depression. They found depression increased many types of health care expenditures, including total, outpatient, and prescription expenditures; depression also increased their emergency service utilization.[32]

In terms of elderly cancer patients, a paper about prostate cancer showed that among elderly prostate cancer patients, those with depression had significantly "higher inpatient pharmacy, physical therapy and laboratory costs in all phases"; additionally, they had higher medical and surgical supply costs, except for the terminal phase, compared with those without depression.[19]

Overall, the existing studies either did not examine the overall health care expenditures including both the payer's and patients' perspectives or did not focus on elderly cancer patients or did not examine multiple types of cancers as this study proposes to do. Hence, the healthcare expenditures of depression, in addition to cancer itself, from the perspective of both payers and patients is not studied well for elderly cancer patients.

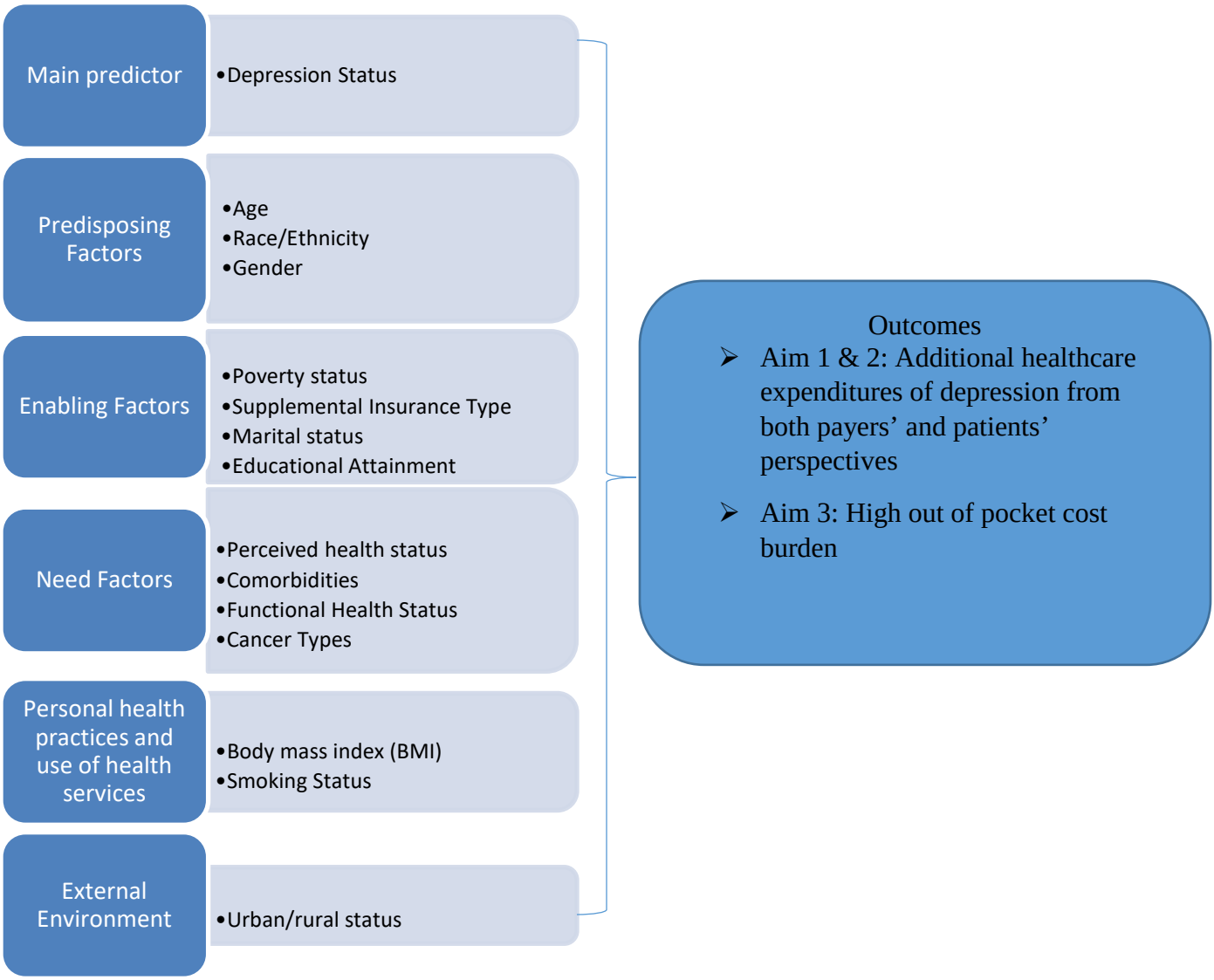
Conceptual Model

This study utilized an expanded Andersen Behavioral Model as the conceptual framework.[33] Concisely, the model is composed of five main constructs 1) predisposing factors; 2) enabling factors; 3) need factors; 4) personal health practices and use of health services; 5) the external environment. As a result of the flexibility of the model, it can be easily to be applied to analyze the relationship between various patient characteristics, detection of depression as well as the healthcare expenditures associated with depression.

Variable selection for this study (Figure 1) was guided by published studies[34-36] that adopted the Anderson Behavioral Model while taking into consideration data elements available in Medicare Current Beneficiary Survey (MCBS)-Medicare. A valuable list of factors associated with health service utilization for adult cancer survivors are summarized in a recent review paper on Andersen Behavioral Model. [34]Additionally, some studies employed this model to assess the relationship of different factors and healthcare expenditures[35, 36]. For example, a study using Medicaid data examined the "association between depression treatment and healthcare expenditures among adults with Type 2 Diabetes Mellitus and depression", taking "coexisting chronic physical conditions" into account, used this model to select independent variables other than the main predictor: "gender, race and age" as

predisposing factors; “Medicaid eligibility status” as enabling factors; “ mental health conditions” as individual’s level of need; “healthcare-seeking behaviors and total baseline healthcare expenditures” as personal health practices and use of health services; “state of residence, community level healthcare infrastructure and community level social determinants of health variables” as external environment[35]. Another study using MCBS data examined the association between depression treatment and healthcare expenditure also used this model as the conceptual framework to select variables other than the main predictor: “gender, race and age” as predisposing factors; “marital status, education, poverty status, and prescription drug coverage” as enabling factors; “perceived health status and functional status” as individual’s level of need; “smoking status, body mass index (BMI), depression treatment, and the baseline year log-transformed health expenditures” as personal health practices and use of health services; “metro status” as external environment[36].

Figure 1: List of Covariates included in the analyses


Main predictor
•Depression Status
Predisposing Factors
•Age
•Race/Ethnicity
•Gender
Enabling Factors
•Poverty status
•Supplemental Insurance Type
•Marital status
•Educational Attainment
Need Factors
•Perceived health status
•Comorbidities
•Functional Health Status
•Cancer Types
Personal health practices and use of health services
•Body mass index (BMI)
•Smoking Status
External Environment
•Urban/rural status
Outcomes
➢ Aim 1 & 2: Additional healthcare expenditures of depression from both payers' and patients' perspectives
➢ Aim 3: High out of pocket cost burden

METHODS

Data Source

The 2007-2013 Medicare Current Beneficiary Survey (MCBS)-Medicare data sponsored by the Centres for Medicare & Medicaid Services (CMS) was used. The data was generated by sampling a nationally representative sample of non-institutionalized Medicare beneficiaries, who are surveyed continuously. The data set had two types of files: Access to Care (MCBS/AC) and Cost and Use (MCBS/CU). MCBS/CU files linking Medicare claims to survey-reported events were used. The data set contained comprehensive and detailed information on patient demographics, socioeconomic status, access to healthcare, healthcare utilization, and self-reported health status and symptoms, and is linked to the Medicare claims to the survey.[37]

Study Design

This was a retrospective cohort study examining Medicare Current Beneficiary Survey (MCBS) respondents (age>=65) diagnosed with breast, lung or prostate cancer between January 2007 and December 2012.The study captured depression status based on self-reports from survey data no later than subsequent follow-up calendar year after cancer diagnosis and collected their expenditures information between January 2007 and December 2013.

Analyses

For Aim1 & 2: Determine if elderly breast, lung and prostate cancer patients with depression have more healthcare expenditures than those without depression from payer's and patients' perspective, respectively.

First, patient characteristics and healthcare expenditures were compared by patients' depression status, using the Chi-square tests for categorical variables and t-test for continuous variables.

Then, this study applied multivariate analysis that included the depression status as one of the covariates. The presence of depression was defined by two questions in the survey: (1). were you depressed the last 12 months? (2). did you lose interest the last 12 months? A patient was considered to have depression if he/she responded positively to both of the questions.

Since healthcare expenditures were highly skewed, the logarithmic transformation with ordinary least squares (log OLS) regression ($\ln(Y_i) = X_i\beta + \varepsilon_i$.) and a general linear model (GLM)($ln\, E(y_i|x_i) = x_i\beta$) were considered. Compared to log OLS model, GLM has advantages in the ways that it avoids needing the smearing estimator for retransforming model estimates of the difference in mean expenditures, and avoids retransformation bias of log OLS models, so GLM was chosen.

Then, Park test (Diagnostics for variance functions) was used to select one of the GLM models. The variance functions is below:

$$var(y_i|x_i) = \alpha[E(y_i|x_i)]^{\lambda}$$

Because $\lambda = 2$ in our study, so gamma model was used.[38]

The change in healthcare expenditures associated with depression were calculated as the difference between the exponentiation of the sum of the intercept and the parameter estimate for depression and exponentiation of the intercept. The percent change in healthcare expenditures associated with depression was calculated as exponentiation of the parameter estimate for depression minus one ($e^{\beta} - 1$).

When stratifying the analyses by healthcare service types, there were a large number of zeros for some of the expenditure categories such as inpatient and other health services categories of Medicare healthcare expenditures. To deal with this issue, two-part models, logistic models estimated in the first part and GLMs with gamma distribution and log link in the second part, were also used to estimate adjusted healthcare expenditures.

This study detected multicollinearity issue by computing variance inflation factor (VIF) to quantify how much the variance is inflated.

All statistical analyses were adjusted for the MCBS complex survey design and performed by using survey sampling and analysis procedures in SAS Enterprise Guide version 6.1 (e.g., surveyfreq, surveymeans) (SAS Institute Inc, Cary, NC and Stata 14.2(e.g., svy glm) (StataCorp, College Station, TX)

For Aim 3: Determine if elderly breast, lung and prostate cancer patients with depression are more likely to have high out-of-pocket cost burden than those without depression

This study used multivariate logistic regression to estimate significant predictors to high out-of-pocket cost burden. The equation is below.

$$logit[\pi(x)] = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 \ldots + \beta_i x_i$$

First, patient characteristics were analyzed by patients' depression status, using the Chi-square tests. The high out-of-pocket cost burden rate was also compared by depression status, according to the independent variables of the five factors of the expanded Anderson Behaviour Model.

Then, this study included all independent variables in the multivariate logistic regression regardless of the univariate logistic regression results, because these variables are based on theories and empirical evidence. For independent categorical variables, the reference group year of cancer diagnosis (2007–2009), gender (male), age in years at diagnosis (65–74) and race/ethnicity (Non-Hispanic white),marital status (married), educational attainment (less than high school), poverty status measured as income (inflated to constant 2017 dollars, adjusting for annual consumer price index for medical care services [39]) to percentage of the federal poverty level (less than 200%),supplemental insurance coverage type (private insurance with drug coverage)[40],cancer site (lung), perceived health status (excellent/very good/good), functional status limitations(the number of activities of daily living (ADLs) with limitations [none limitation]),the number of comorbid health conditions(none or 1 condition). (current), BMI (underweight or normal),[41] and metro status (metropolitan).

This study tested for multicollinearity by computing variance inflation factor (VIF) to quantify how much the variance is inflated.

All statistical analyses were adjusted for the MCBS complex survey design and performed by using survey sampling and analysis procedures in SAS Enterprise Guide version 6.1 (e.g., surveyfreq, surveymeans) (SAS Institute Inc, Cary, NC and Stata 14.2(e.g., svy glm) (StataCorp, College Station, TX)Measurement/Measures

In terms of cohort creation, three types of cancer and depression were the key variables. For depression, the study will define the patient as having depression symptoms via two questions in the survey: (1). were you depressed the last 12 months? (2). did you lose interest the last 12 months? A patient was considered to have depression if he/she responded positively to both of the questions. The combination of these two questions was found to have 91% sensitivity and 86% specificity in detecting depression in cancer and palliative care and hence is a good measure of depression presence based on patient self-report.[42] The three types of diagnosed cancers were defined by ICD-9-CM code in Medicare Claims data: breast cancer (174.x), lung cancer (162.x), and prostate cancer (185.x). The "newly diagnosed" cases were identified by using a 12-month wash-out period.

Outcome measures and independent variables by specific aims

Aim 1. From payer's perspective, determine if elderly breast, lung and prostate cancer patients with depression have more healthcare expenditures than those without depression

In this aim, the outcome variable was Medicare payments, which was described in Table 1. Medicare payments included all healthcare services, including inpatient, skilled nursing facility, hospital outpatient, home health, hospice, prescription drugs, and medical provider. Payments were measured over the cancer diagnosis year as well as the subsequent calendar year. The independent variables included depression status and the five factors the expanded Anderson Behaviour Model, which were controlled for in the analysis and described in Table 2.

Aim 2. From patients' perspective, determine if elderly breast, lung and prostate cancer patients with depression have more out-of-pocket healthcare expenditures than those without depression

In this aim, the outcome variable was out-of-pocket (OOP) expenditures and described in Table 1. OOP expenditures included all personal expenditures for both Medicare covered and non-covered healthcare services, including inpatient, skilled nursing facility, outpatient, medical providers, prescription drugs, home health, hospice and dental services. OOP expenditures were measured over the cancer diagnosis year and the subsequent calendar year. The independent variable included depression status and the five factors in expanded Anderson Behaviour Model, which were controlled in the analysis and described in Table 2.

The components of healthcare expenditures for Aim 1 and Aim 2 are defined in the following way: Inpatient expenditures are payments for care received for inpatient hospital events (admissions). Skilled nursing facility are payments for care received for short-term facility stays. Hospital outpatient expenditures are the payments for services received in outpatient settings. An outpatient setting means "outpatient department or outpatient clinic of a hospital". Inpatient, skilled nursing facility and hospital outpatient expenditures are payments for the facility costs only. The provider payments would be included in medical provider expenditures- the payments for services received from medical providers, unless the medical providers were actually employed by the facility. Medical providers include practitioners "such as chiropractors, podiatrists, audiologists and optometrists; mental health professionals such as psychiatrists, psychologists and clinical social workers; therapists such as physical therapists, speech therapists, occupational therapists, and intravenous and

respiratory therapists; other medical practitioners such as nurses and paramedics; and other places offering medical care, such as clinics, neighborhood health centers, infirmaries and urgent care centers." Home health and hospice expenditures are payments for services received from health professionals in home health and hospice settings. The health professionals include "nurses, doctors, social workers, therapists and hospice workers". Prescribed medicine expenditures are expenses for all prescription medications "except those provided by the doctor or practitioner as samples and those provided in an inpatient setting." Dental expenditures are the payments for dental services.[43]

Aim 3. Determine if elderly breast, lung and prostate cancer patients with depression are more likely to have high out-of-pocket cost burden than those without depression

In this aim, the outcome variable was high out-of-pocket cost burden and described in Table 1. High out-of-pocket cost burden was referred to as out-of-pocket cost as over 10% of respondent's income.[40, 44] The income question is "what is you and your spouse's total income?", so the income value was divided by two if a respondent reports income for both himself/herself and the spouse.

The main predictor was depression status. Other potential determinants of high out-of-pocket cost burden included the five factors in expanded Anderson Behaviour Model, which were controlled in the analysis and described in Table 2.

Table 1: Outcome measures

Aim	**Measures**	**Definition**	**Measurement**
Aim 1	Healthcare expenditures of payer's perspective	Medicare payments	Continuous variable:2017 Dollars

Aim 2	Healthcare expenditures of patients' perspective	Patients' self-report out-of-pocket expenditures	Continuous variable:2017 Dollars
Aim 3	High out of pocket cost burden	Patients' out-of-pocket cost is over 10% of the personal income[40, 44]	Categorical Variable: Yes or No

Table 2: Independent Variables

Independent Variables	**Definitions**	**Measurement**
Main Predictor		
Depression Status	Patients' depression status	Categorical Variable: Yes or No
Predisposing characteristics		
Age Group	Patients' age group at cancer diagnosis	Categorical Variable: 65-74 years old, 75+ years old
Race/ethnicity	Patients' race/ethnicity	Categorical Variable: Non-Hispanic White, , other
Gender	Patients' gender	Categorical Variable: Male, Female
Enabling Factors		
Poverty Status	income (inflated to constant 2017 dollars, adjusting for annual consumer price index for medical care services[39]) to federal poverty level	Categorical variable: less than 200%, greater than or equal to 200%
Supplemental insurance	Patients' supplemental insurance	Categorical Variable: Private insurance with drug coverage; public with drug coverage; Medical insurance only; drug insurance only; None
Marital status	Patients' marital status at cancer diagnosis	Categorical Variable: Other(Single/separated/divorced), Married

Educational Attainment	Patients' educational attainment	Categorical Variable: Less than High School; High School graduate; Greater than High School
Need Factors		
Number of comorbid health conditions	Patients comorbid chronic conditions, including heart disease, stroke/brain hemorrhage, hypertension, diabetes mellitus, arthritis, mental disorder other than depression, neurological conditions, and lung disease	Categorical Variable: None or one condition; more than one condition
Cancer Type	Cancer type	Categorical Variable: Breast, Lung, Prostate
Perceived health status	Patients' perceived health status	Categorical Variables: fair or poor, good, very good or excellent
Functional Health Status Limitations	Patients' number of activities of daily living (ADLs) with limitations	Categorical Variables: none, at least one limitation
Personal health practices and use of health services		
Smoking Status	Patients' smoking status	Categorical Variable: Current, Past, Never
Body mass index (BMI)	Patients' BMI	Categorical Variable: under-weight or normal, overweight, obese
External Environment		
Metro status	Indicator of whether patients living in metropolitan	Categorical Variable: metropolitan, non-metropolitan

Study Cohort

This study considered all Medicare Current Beneficiary Survey (MCBS) respondents (age>=65) between January 2007 and December 2012; and collected their expenditures

information between January 2007 and December 2013.The participants in the cohort were elderly breast, lung and prostate cancer patients (age>=65 years).

The inclusion/exclusion criteria:

Inclusion criteria:

- Respondents newly diagnosed with cancer(breast, lung or prostate) using a one-year wash-out period and at least 65 years old at the diagnosis between January 2007 and December 2012
- Respondents with continuous enrollment in Medicare Part A and Part B
- Respondents enrolled in Medicare at least 1 year before cancer diagnosis
- Respondents having "at least 1 inpatient or 2 outpatient or medical provider claims with a qualifying cancer diagnosis"[40]
- Respondents' outpatient or provider claims have to be at least 30 days apart

Exclusion criteria:

- Respondents with Medicare Advantage Plans
- Respondents with missing social-demographic information
- Respondents who resided in long-term care facilities
- Respondents who were lost follow up during the study period

Sample Size Calculation

To calculate the sample size, a generally accepted power of 0.80, and an alpha level of 0.05 were used. For Aims 1 and 2, multiple regression sample size calculation in PASS 15[45] was used. Other parameters including a total of 22 controlled variables, one tested independent variable, the squared multiple correlation coefficient assumed by the null

hypothesis(β_0^2), squared multiple correlation coefficient where 0.8 power is calculated(β_1^2), were entered into the sample size calculation for multiple regression in PASS 15[45]. This study set β_0^2 to 0. Based on the study results, the coefficient of depression status was 0.3, thus 0.09 was used for β_1^2. The result indicated that 106 observations would be sufficient. This study actually had 710 observations, which is beyond the sample size calculation result; so the sample size is not a concern here.

For Aim 3, logistic regression sample size calculation in PASS 15[45] was used. Other parameters including the baseline probability at the study population mean(P_0), odds ratio , one categorical independent variable of interest, percent of N (the percent of sample with depression in this study),R-Squared of independent variable of interest with other controlled variables(R^2) were entered into the sample size calculation for logistic regression in PASS 15[45]. Based on the study results, P_0 was 0.4, odds ratio was 1.8, N was 20% and R^2 was 0.08. The result indicated that 692 observations would be sufficient. This study actually had 710 observations, which is more than the sample size calculation result; so the study has sufficient sample size here.

Data Collection

For identifying study cohort, this study used data from the Cost and Use files of MCBS-Medicare for years 2007 through 2012. This study captured cancer diagnosis using claims and depression presence using survey part. For healthcare expenditures collection, this study used data from the Cost and Use files of MCBS-Medicare for years 2007 through 2013. For Aim1, it examined healthcare expenditures in the year of diagnosis and subsequent calendar year

using claims. For Aims 2 and 3, it examined out-of-pocket expenditures in the year of diagnosis and subsequent calendar year using surveys.

Data Management

The de-identified datasets were stored on the secure server in University of Texas MD Anderson Cancer Center and the data was stored on a secured and encrypted format. The desktop was protected by strong security systems in University of Texas MD Anderson Cancer Center.

All statistical analyses were conducted in SAS Enterprise Guide 6.1 (SAS Institute, Cary NC) and/or Stata version 14 (Stata Corporation, College Station, TX). This study was reviewed by the Institutional Review Board (IRB) at University of Texas School of Public Health to ensure appropriate study design and data management.

Human Subjects, Animal Subjects, or Safety Considerations

The MCBS Data is a de-identified data. Hence, this research qualifies for minimal risk.

Summary and Implications

There were some limitations associated with the data and study design. First, MCBS data was not linked to cancer registry data, so this used medical claims to identify different cancer types, which might cause potential misclassification. Second, some information such as out of pocket payments were based on self-report, which might be subject to recall bias. However, MCBS data has been considered as a principle resource for assessing out of pocket cost for Medicare beneficiaries, which is a reliable resource for this study.[40] Moreover,

MCBS has taken some measures to minimize the recall bias: for example, the respondents are requested to take their facilitating records of all their healthcare events to the interviews. Third, this study was an observational retrospective cohort study, which may have unmeasured confounding factors than cannot be controlled for.

In terms of implications, the study evaluated the additional health care expenditures of depression in both payer and patients' perspective and estimate the high out-of-pocket burden among elderly cancer patients. The key findings of this study, not previously documented in other studies of elderly Medicare beneficiaries with cancer and depression, will allow us to better understand the impact of depression on elderly cancer patients. By estimating the additional healthcare expenditures associated with depression for elderly cancer patients and identifying the population with cancer and depression who are at risk of high out-of-pocket cost burden, this study will not only promote the awareness of the psychological needs of elderly cancer patients among all stakeholders, such as policy makers, clinicians, patients and their families, but also further the progress of targeted interventions to improve depression management and evaluations of depression-relevant interventions for this population.

Timeline

Task	**Month in 2018**											
	1	2	3	4	5	6	7	8	9	10	11	12
Proposal Writing and Defense	■	■	■	■								
IRB Approved					■							
Data Clean and Merge						■						
Data Analysis							■	■	■	■		
Dissertation Writing										■	■	■
Dissertation Defense												■

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JOURNAL ARTICLE – 1

Association between depression and healthcare expenditures among elderly cancer patients

Introduction

Studies have shown that the risk of depression is higher for cancer patients than for those with stroke, diabetes and heart disease.[1, 2] While the reported prevalence of depression among cancer patients has varied by study design and definitions of depression, a previous meta-analysis reported a pooled mean prevalence ranging from 8% to 24%.[3] Moreover, cancer patients' short-term and long-term physical and mental health are negatively impacted by depression comorbidity, as depression has been linked to higher mortality, poorer quality of life, and poorer treatment adherence for cancer patients in general.[4-6] Additionally, as a result of the aging population in the United States and high prevalence of cancer among the elderly, a large portion of cancer patients are 65 and over; it is projected that by 2040 approximately 70% of those diagnosed with cancer will be 65 years or older.[7] Therefore, addressing the mental health needs of elderly cancer patients is vital to improve the wellbeing of both this population and society as a whole.

In addition to being one of the most economically burdensome disorders overall, depression is usually associated with excess healthcare expenditures. In particular, it has been shown that depression is associated with increased direct healthcare costs for elderly patients with depression. [8, 9] However, only a few studies have examined the healthcare expenditures of depression for cancer patients.

One paper focusing on the nonelderly military population showed that military healthcare beneficiaries with both cancer and depression had significantly higher annual healthcare costs compared with those who only had cancer ($16,212 vs $7,728). Moreover, patients with cancer and depression also had more inpatient, outpatient and medication services utilization.[10] A recent paper about adult cancer patients aged older than 21 years, showed that compared with those without depression, those with depression had about 32% greater one-year total healthcare expenditures including all third-party payments and out-of-pocket expenditures by patient or family. In particular, depression increased many types of healthcare expenditures, such as total, outpatient, and prescription expenditures for cancer patients. But this paper did not stratify the analyses by payers.[11] A more recent paper from the University of California San Diego Healthcare System, examining healthcare charges for cancer patients in the first year after diagnosis, found that depressed individuals had 113% higher total annual healthcare charges compared to those without depression.[12]

In terms of the impact of depression on elderly cancer patients' healthcare expenditure, a study examining the association of depression with increased healthcare costs among prostate cancer patients, showed that those with depression had about 30% higher costs compared with those without depression from Medicare's perspective during the year after cancer diagnosis.[13] Also, patients with depression had more hospitalization, outpatient and emergency services utilization.

Limitations of existing studies include failure to examine overall healthcare expenditures stratified by payers' and patients' perspectives, or failure to focus on elderly cancer patients;

most did not examine multiple cancer types. Hence, the healthcare expenditure associated with depression in the context of multiple cancer types from the perspective of both payers and patients is not well studied for elderly cancer patients.

Methods

Conceptual framework

This study utilized an expanded Andersen Behavioral Model as the conceptual framework.[14] The model is composed of five main constructs: 1) predisposing factors, which include gender, race/ethnicity, age at diagnosis and year of cancer diagnosis; 2) enabling factors, which include supplemental insurance type, marital status, educational attainment and poverty status; 3) need factors, which include number of comorbidities, cancer site, perceived health status and functional status; 4) personal health practices and use of health services, which include smoking status and body mass index (BMI); and 5) external environment, measured as metro status in this study.

Study design

This is a retrospective cohort study that examined the healthcare expenditures associated with depression for elderly cancer patients. In this study, we identified cancer diagnosis based on Medicare claims between January 2007 and December 2012; captured depression status based on self-reports from survey data either in the year of cancer diagnosis or the subsequent calendar year; and measured healthcare expenditures in the year of diagnosis and subsequent calendar year after cancer diagnosis.

Data source

This study used 2007-2013 Cost and Use files of Medicare Current Beneficiary Survey (MCBS)-Medicare sponsored by the Centers for Medicare & Medicaid Services (CMS). MCBS-Medicare is generated by sampling a nationally representative sample of Medicare beneficiaries, who are surveyed up to three rounds per year for four successive years. The data set contains two types of files that are released annually: Access to Care (MCBS/AC) and Cost and Use (MCBS/CU). The MCBS/CU files were used because they link Medicare claims to survey-reported events. Therefore, the data contains "complete expenditure and source of payment data on all healthcare services," even if the services are not covered by Medicare. Additionally, the data set contains comprehensive and detailed information on patient demographics, socioeconomic status, healthcare utilization, and self-reported health status and symptoms.[15]

Ascertainment of study cohort

The algorithm to identify cancer patients was based on clinical diagnoses in claims. The beneficiaries were considered to be diagnosed with cancer based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) (140-172, 174-208, 225, 227.3 and 227.4) and were required to have at least one inpatient or two outpatient claims or medical provider claims with a cancer diagnosis based on the ICD-9-CM codes. The service date between the two outpatient claims was required to be at least 30 days. Additionally, all patients included in the analytical sample had to be continuously enrolled in

Medicare Parts A and B without Medicare Advantage enrollment and not reside in a long-term care facility during the study period so as to ensure the completeness of Medicare claims and prescribed medicine event (PME) files. Patients who were lost to follow-up during the study period were excluded. Newly diagnosed cases were identified by using a 12-month wash-out period.

If clinical diagnosis codes indicated more than one cancer site, this study applied a hierarchical process to assign beneficiaries to the cancer site that is more likely to have been the primary tumor location. For instance, a patient with diagnosis codes for both lung and brain cancer would be assigned to the lung cancer group. [16, 17] Lastly, this study only included beneficiaries belonging to groups of breast, lung and prostate cancer sites with ICD-9-CM codes as 174.x, 162.x, and 185.x, respectively.

Identification of depression

This study defined the patient as having depressive symptoms via two questions in the survey: (1). "In the last 12 months, how much of the time did you feel sad, blue or depressed? "(2). "In the last 12 months, have you had 2 weeks or more when you lost interest or pleasure in the things that you usually cared about or enjoyed?" A patient was considered to have depression if he/she responded "all of the time" or "most of the time" to the first question, and/or answered "yes" to the second question.[18, 19] The combination of these two questions was found to have 91% sensitivity and 86% specificity in detecting depression in cancer and palliative care and hence is a good measure of the presence of depression based on patient self-report.[20]

Dependent variables

The dependent variables included total healthcare expenditure, healthcare expenditure by service types, and payer types. The total healthcare expenditures were combined by MCBS from all payers' payments and respondents' out-of-pocket (OOP) payments, and include payments for different services types, including prescribed medicines, dental, home health, hospice, hospital inpatient, skilled nursing facility, medical provider, and hospital outpatient. In addition to total healthcare, we also analyzed subtypes of expenditures by healthcare services and payers. The healthcare services included inpatient (hospital inpatient and skilled nursing facility), hospital outpatient, medical providers, prescribed medicines, and other (i.e., home health, dental, and hospice). The payers included Medicare, other third-parties (i.e., other public [Medicaid, Veterans Affairs Health Insurance], individually purchased insurance, employer-sponsored insurance, and other payments) and patients' OOP expenditures. The expenditures were inflated to constant 2017 dollars, adjusting for annual consumer price index for medical care services.[21]

The measurement period for expenditures included the year of diagnosis and subsequent follow-up calendar year after cancer diagnosis. While it would have been ideal to measure expenditures in the 12 months following cancer diagnosis, some expenditures include service types and payers that are only reported on an annual basis, such as dental services, OOP costs and other third-party payers.

Other independent variables

Besides depression status, the other independent variables belonging to the five constructs in the expanded Andersen Behavioral Model were also identified by self-reports from the survey data. Predisposing characteristics were: year of cancer diagnosis (2007–2009; 2010–2012), gender (female; male), age in years at diagnosis (65–74; 75 and over) and race/ethnicity (Non-Hispanic white; other). Enabling characteristics included marital status (married; other), educational attainment (less than high school; high school; greater than high school), poverty status measured as income inflated to constant 2017 dollars, adjusting for annual consumer price index for medical care services [21] and converted to percentage of the federal poverty level (less than 200%; greater than or equal to 200%) and supplemental insurance coverage type (private insurance with drug coverage; public with drug coverage; medical insurance only; drug insurance only; none)[17]. Need characteristics included: cancer site (breast; lung; prostate), perceived health status (excellent/very good/good; fair/poor), functional status limitations(the number of activities of daily living (ADLs) with limitations [none limitation; ≥1 limitation]) and the number of comorbid health conditions, including heart disease, stroke/brain hemorrhage, hypertension, diabetes mellitus, arthritis, mental disorder other than depression, neurological conditions, and lung disease (none or 1 condition;>1 condition). Personal health practices and use of health services included smoking status (current; past; never), BMI (underweight or normal, defined as BMI <25 kg/m2; overweight, defined as BMI ≥25- 29.9 kg/m2; obese/morbid obese, defined as BMI ≥ 30 kg/ m2).[22] External environment was captured by metro status (metropolitan; non-metropolitan).

Statistical analyses

The chi-square test for categorical variables and t-test for continuous variables were used to analyze patient characteristics and healthcare expenditures by patients' depression status; the tests were weighted using cross-sectional sampling weights.[23] To estimate different types of adjusted additional expenditures associated with depression, generalized linear model (GLM) regressions with gamma distribution and log link, determined by modified park test[24], were used. This approach has an advantage compared to log-cost regression (log OLS model) in the way that it evaluates transformation of the difference in mean cost, and avoids retransformation bias of log OLS models[24]. In the regression analysis, depression status and all other independent variables were included.

In the analysis of healthcare expenditure by service types and payer types, we observed a large number of zeros for some of the expenditure categories such as inpatient and other health services categories of total healthcare expenditures. When the proportion of zero expenditures was non-negligible, we adopted two-part models [24] with multivariable logistic regressions in the first part and GLMs with gamma distribution and log link in the second part. The first part modeled the probability of utilizing certain services, and adjusted odds ratios (AOR) and 95% confidence intervals (CIs) were provided. The second part estimated the adjusted effect of depression among those who had non-zero expenditures.

All statistical analyses were accounted for the MCBS complex survey design and were performed by using survey sampling and analysis procedures (e.g., surveyfreq, surveymeans) in SAS Enterprise Guide version 6.1 (SAS Institute Inc, Cary, NC) and Stata 14.2 (e.g., svy glm) (StataCorp, College Station, TX).

Results

The sample included 710 elderly beneficiaries who were newly diagnosed with breast, lung and prostate cancer, among which 128 (17.7%) had depression. The description of the study sample by depression status is provided in Table 1. Statistically significant differences were found with respect to supplemental insurance, perceived health status, functional status, and number of comorbid health conditions. Specifically, patients with both public insurance and drug coverage were more likely to report depression (35.8%) compared with those with both private insurance and drug coverage (16.9%), medical insurance only (13.9%) and other supplemental insurance (18.1%). More patients perceiving fair/poor health status reported depression (32.7%) compared with those perceiving excellent/very good/good health (13.6%). Additionally, patients with at least one functional status limitation were more likely to report depression (35.7%) compared to those with no limitations (15.1%); and those with more than one comorbid health condition were more likely to report depression (20.9%) compared with those with none or one comorbid condition (11.1%).

In Table 2, unadjusted total healthcare expenditures were compared between the patients with depression and those without, presented as total overall expenditures and stratified by service types and payers. For the categories of expenditures containing zeros, the comparison were also performed among the patients with non-zero expenditures. Overall, the total healthcare expenditure was significantly higher for patients with depression ($70,918 vs $44,106). In analyses stratified by healthcare service types, patients with depression spent significantly more in medical provider services ($25,052 vs $16,068). Regarding users of other services,

those with depression also spent significantly more ($8,653 vs $3,559). In analysis stratified by payers, patients with depression had significantly more Medicare payments ($48,875 vs $28,856). Additionally, Medicare and OOP expenditures — representing the most important payer and patient perspectives, respectively — were compared between the two groups by service types. In sub-service type analyses for Medicare healthcare expenditures, patients with depression had significantly more medical provider expenditures ($15,566 vs $10,832) and other services expenditures in beneficiaries who used these services ($12,218 vs $7,077). In sub-service type analyses for OOP healthcare expenditures, patients with depression had significantly more medical provider expenditures ($3,028 vs $1,903).

Tables 3-5 provides results from adjusted regressions controlling for all the independent variables described in the methods section. Table 3 presents the adjusted total healthcare expenditures and percent change associated with depression from GLM and two-part models, overall and stratified by service types and payers. The results showed that significant differences were found in total healthcare expenditures and also in some total expenditure categories. Patients with depression had $11,454 higher total healthcare expenditures, which corresponded to 34.5% greater total healthcare expenditures. Among different service types, patients with depression had 45.9% higher medical provider expenditures and were significantly more likely to have inpatient services (AOR, 2.94; 95% CI, 1.82–4.74) compared with those without depression. In users of other services, patients with depression had 50.1% greater other services expenditure. In terms of payers, patients with depression not only

incurred $8,280(43.8%) more expenditures from Medicare's perspective, but also $1,270(32.9%) higher expenditures from patients' perspective.

Adjusted Medicare healthcare expenditures and percent change associated with depression from GLM and two-part models stratified by service types are presented in Table 4. From Medicare's perspective, among different healthcare services, patients with depression had 36% higher medical provider healthcare expenditures. Patients with depression were highly significantly more likely to use inpatient services (AOR, 2.7; 95% CI, 1.59–4.58) and other services (AOR, 2.55; 95% CI, 1.59–4.09). For patients who used other services, depression was associated with 47.2% greater other services expenditure.

Table 5 displays the adjusted OOP healthcare expenditures and percent change associated with depression from GLM and two-part models stratified by healthcare service types. From the patients' perspective, patients with depression had 47.1% and 53% higher medical provider and other healthcare expenditures, respectively. No significant results were found in inpatient and other services, which is possibly because of the small sample size.

Discussion

The current study used MCBS data, a nationally representative survey of Medicare beneficiaries, to estimate the incremental expenditures associated with depression for elderly breast, lung and prostate cancer patients. In this sample, the depression rate was 18% (19% for breast, 19% for lung and 16% for prostate). These rates fall in the range of 8% to 24%, which was estimated from a meta-analysis of depression prevalence among cancer patients assessed

by diagnostic interviews and self-report instruments.[3] The prevalence rate of 18% in this study is higher than a previous paper (14%) by Pan et al.[11] This is plausible because the previous paper used International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes to capture clinical diagnosis of depression, while this study used a self-report instrument. It has been shown that the detection rate of depression is low among cancer patients and depression is often underdiagnosed because their depression symptoms are frequently ignored by clinicians and viewed to be a normal psychological reaction of cancer diagnosis and treatment.[25, 26] For example, in a large study of over 1,100 cancer patients, physicians only correctly identified 33% of patients with mild to moderate depression, and only 13% of patients with severe depression were diagnosed.[26]Also, a recent paper found that depression prevalence was highest by self-reported symptoms scales, followed by diagnostic interviews and ICD-9-CM codes based on claims databases.[27] Depression rates vary broadly by cancer type and patient age; our study focused on the elderly while previous papers included adults of all ages and did not distinguish cancer types.

Since the prevalence of self-reported depression is high for elderly cancer patients in this study, and depression is often unrecognized, it is essential to improve depression screening and diagnosis for this population. While some instruments such as the Geriatric Depression Scale (GDS)[28] are commonly used to identify depression in the elderly, few studies have assessed their accuracy in the geriatric cancer setting. Considering the complexity and difficulty to identify and detect depression for geriatric cancer populations [29], more research is needed to find or develop accurate, appropriate and validated depression measurement tools.

Our study found that depression was associated with 34.5% greater adjusted total healthcare expenditures, which is consistent with a prior study using 2006-2009 Medical Expenditure Panel Survey data on cancer patients older than 21 years, where the percent increase associated with depression in total expenditures was about 30%.[11] In terms of service subtypes of total healthcare expenditures, depression was associated with greater adjusted medical provider and other services expenditures (45.9 % and 50.1%, respectively). Also, depression was associated with higher likelihood of inpatient services use (AOR=2.94). These findings confirm that depression is correlated with excess healthcare expenditure and utilization for elderly cancer patients, and the higher expenditures are concentrated on certain services.

When stratified by payers, depression was associated with 43.8% greater adjusted Medicare healthcare expenditures, which is higher than a previous paper (about 30%) about elderly prostate cancer patients from the Medicare perspective [13]. The lower rate identified in that study may be explained by methodology, as the researchers only focused on prostate cancer while the current study included two more cancer types, which may have more influence on the expenditures. When diving deeper into the subtypes, significant findings were found in medical provider, inpatient and other services, suggesting that, as with total healthcare expenditures, the excess is mainly attributable to certain services.

From the patients' perspective, depression was associated with 32.9% higher OOP expenditures. The OOP expenditures did not include premiums since premiums are separated from actual spending.[17]. When expenditures on different service types were analyzed, significant findings were found for medical provider and other services. These findings stress

that the excess financial burden of depression is not only placed on the healthcare system but also on the patients themselves, indicating that comorbid depression can aggravate the personal financial burden that cancer patients already face.

Subtype analyses from three aspects (i.e., total [all payers], Medicare and OOP expenditures) all highlighted higher expenditures in the category of medical provider services for elderly cancer patients with depression. In terms of total and Medicare analyses, depression was associated with increased inpatient services use. These results are consistent with previous studies irrespective of cancer diagnosis. For example, two studies of cancer patients using military and Medicare populations demonstrated that cancer patients with depression had more hospitalizations.[10, 13] Also, depression is associated with increased risk of hospitalization in patients with heart failure. [30]

It is noteworthy that the estimated expenditures from our study can also contribute to the evaluations of depression-relevant interventions for this population, because the estimates can be applied in cost-effectiveness studies of interventions addressing depression for elderly cancer patients: the reduction of depression related healthcare cost would partially offset the intervention costs.

Since cancer patients with depression incurred substantially higher healthcare utilization and expenditures from payers' and patients' perspectives than their counterparts without depression, it is possible that managing and treating depression effectively in cancer patients could improve health outcomes and potentially reduce healthcare expenditures. While

depression treatment may contribute to higher short-term expenditures (e.g., psychotherapy, psychotropic medications); expenditures could decrease in the long term. Currently, very few studies have examined whether depression treatment has an impact on reducing expenditures in the long-term. One study demonstrated that depression treatment (antidepressants, psychotherapy and both) increased healthcare expenditures for elderly breast, colorectal and prostate cancer patients from Medicare's perspective in the short term but had no effect on long-term expenditures, however, the study's follow-up period of two years after depression diagnosis may not have been long enough[31]. Encouragingly, studies about patients with other co-occurring chronic conditions and depression have shown positive results in reducing costs with depression treatment. For instance, a study about patients with comorbid conditions and type 2 diabetes mellitus along with depression showed that depression treatment (antidepressants, psychotherapy and both) decreased healthcare expenditures significantly during 12 month period after depression diagnosis.[32] Another study focusing on patients with depression and diabetes showed reduced trends for 5-year mean total medical expenditures when comparing depression collaborative care and usual care.[33] Future research needs to examine whether depression treatment in elderly cancer patients can lower healthcare expenditures, especially in the long run, from payers' and patients' perspectives; the depression treatment modalities best suited for this often vulnerable population need to be elucidated.

This study has many strengths. It makes a significant contribution to the existing literature by estimating the healthcare expenditures associated with depression in the elderly cancer population from payers' and patients' perspectives. Also, by examining multiple expenditure

categories, our results detail where the excess economic burden of depression originated from in our study cohort. Additionally, because MCBS data links survey to Medicare fee-for-service claims, this study adjusted for a comprehensive list of independent variables, including patient-level health factors that are generally not available in claims data, such as functional status, general health status and personal health practices. Moreover, this study captured complete healthcare expenditures including both Medicare and non-Medicare expenditures.

There are some limitations associated with the data and study design. Firstly, some information such as OOP payments are based on self-report, which may be subject to recall bias. However, MCBS data is an established principle source for assessing OOP cost for Medicare beneficiaries, which is a reliable resource for this study.[17] Moreover, MCBS includes measures to minimize recall bias: for example, the respondents are requested to take their facilitating records of all their healthcare events to the interviews. Secondly, this study is an observational retrospective cohort study, so the results cannot imply causation. Additionally, this study may have unmeasured confounding factors that cannot be controlled for. These unmeasured confounding factors may include cancer severity such as stage at diagnosis, which is not available in MCBS data. Although depression can happen during any stage of cancer, but many studies showed a higher prevalence of depression with advanced stage cancer.[34, 35] Also, some studies showed that cancer costs were higher for cancer patients whose stage at diagnosis were more advanced.[36] So the additional healthcare expenditures of depression may be underestimated.

Thirdly, the study sample was restricted to fee-for-service Medicare beneficiaries and the results may not be generalizable to other Medicare beneficiaries.

This study has many important and unprecedented implications. To our best knowledge, it is the first study to provide a national estimate of depression prevalence in elderly patients with breast, lung, and prostate cancer, which are the three most common cancer types in the US, and the excess healthcare cost and utilization burden associated with depression for this population. This study adds to our understanding of the notable economic burden imposed by depression on cancer patients. Additionally, our findings reveal the psychological needs of many elderly cancer patients and their associated higher expenditures; the data may stimulate interest among many stakeholders including policy makers, clinicians, patients and their families. Also, the findings highlight the importance of effective depression screening, diagnosis, treatment and management. In terms of screening and diagnosis, specific screening/diagnostic criteria need to be implemented with standardized instruments validated in elderly cancer patients with depression. In terms of depression treatment and management, more research is needed to investigate whether treating depression has an impact on cost-reduction over a longer period for both the healthcare system and patients, and to verify the efficacy of different depression treatments. Additionally, as recommended by other studies, [37-39] integrated collaborative care treatment models need to be emphasized in the near future to monitor and treat depression in cancer patients.

Conclusions

In this sample of elderly breast, lung and prostate cancer patients, patients with depression incurred significantly higher healthcare expenditures from payers' and patients' perspectives and across different expenditure types. These findings provide compelling evidence for policy makers and clinicians to improve depression screening, diagnosis and treatment in geriatric oncology.

Disclosure

The authors have declared no conflicts of interest.

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Table 1.Characteristics of elderly cancer patients by depression status

	Without Depression		With Depression	
Characteristics	N	Wt%	N	Wt %
Total	582	82.3	128	17.7
Predisposing				
Year of cancer diagnosis				
2007-2009	317	83.9	63	16.1
2010-2012	265	80.7	65	19.3
Gender				
Female	234	79.5	56	20.5
Male	348	84.2	72	15.8
Age				
65-74	177	79.4	48	20.6
75 and over	405	84	80	16
Race/ethnicity				
Non-Hispanic white	520	82.9	112	17.1
Other	62	76.8	16	23.2
Enabling				
Marital status				
Married	349	82.8	75	17.2
Other	233	81.2	53	18.8
Educational attainment				
Less than high school	114	77.9	34	22.1
High school	213	85.3	39	14.7
Greater than high school	255	81.8	55	18.2
Poverty status				
LT 200% FPL	435	84.8	79	15.2
GE 200% FPL	147	74.8	47	25.2
Supplemental insurance**				
Private insurance with Rx	237	83.1	51	16.9
Public insurance with Rx	53	64.2	27	35.8
Medical Insurance only	259	86.1	42	13.9
Other	33	81.9	8	18.1
Need				
Cancer site				
Breast	208	80.8	44	19.2
Lung	67	80.6	19	19.4

Prostate	307	83.7	64	16.3
Perceived health status* **				
Excellent/very good/Good	475	86.4	75	13.6
Fair/poor	107	67.3	53	32.7
Functional status limitation* **				
None	426	84.9	78	15.1
≥1	156	64.3	50	35.7
Number of comorbid health conditions **				
None or 1	195	88.9	28	11.1
>1	387	79.1	100	20.9
Personal health practices and use of health services				
Smoking Status				
Current	38	77.9	11	22.1
Past	319	79.9	76	20.1
Never	225	86.6	41	13.4
BMI				
Underweight/normal	206	80.4	54	19.6
Overweight	258	83.7	49	16.3
Obese/morbid obese	118	82.5	25	17.5
External Environment				
Metro status				
Metropolitan	414	82.5	87	17.5
Non-Metropolitan	168	81.5	41	18.5

***P < .001, **.001 ≤ P < .01, *.01 ≤ P < .05

Note: Wt%, Weighted percentage; LT, less than; GE, greater than or equal to; FPL, federal poverty level; Rx, prescription coverage; BMI, body mass index.

Table 2. Unadjusted healthcare expenditures by depression status

	Full sample		In users			
	Without Depression (N=582)	With Depression (N=128)	Without Depression		With Depression	
Healthcare Expenditures	Mean(SE) $	Mean(SE) $	N(%)	Mean(SE)$	N(%)	Mean(SE)$
Total healthcare expenditures						
Overall***	44106(2116)	70918(5759)				
By service types						
Medical provider***	16068(934)	25052(2609)				
Hospital outpatient	8050(658)	8006(865)				
Prescribed medicine	7891(485)	10188(1242)				
Inpatient***	9424(925)	21184(2817)	206(35%)	28743(1890)	77(60%)	35712(3785)
Other*****†	2658(237)	6488(1613)	430(74%)	3559(286)	97(76%)	8653(2152)
By payers						
Medicare***	28856(1716)	48875(4150)				
Out-of-pocket(patient)	6511(291)	9442(1516)				
Other third-party payers	7950(402)	11722(2053)	559(96%)	8232(407)	124(97%)	12031(2099)
Medicare healthcare expenditures						
By service types						
Medical Provider******	10832(700)	15566(1545)				
Hospital outpatient	5766(501)	5949(673)				
Inpatient**	8134(842)	17874(2608)	198(34%)	25658(1850)	75(59%)	31072(4458)
Prescribed medicine	3000(375)	5258(1108)	299(51%)	5868(624)	69(54%)	9659(1969)
Other**††	1124(189)	4228(750)	103(18%)	7077(932)	48(38%)	12218(1652)
Out-of-pocket healthcare expenditures						
By service types						
Medical provider******	1903(122)	3028(348)				
Prescribed medicine	1639(98)	1667(189)				
Other	2067(158)	4020(1316)				
Inpatient	391(117)	320(87)	74(13%)	3290(911)	27(21%)	1685(441)
Hospital outpatient	499(77)	408(113)	359(62%)	823(112)	80(63%)	659(191)

***P < .001, **.001 ≤ P < .01, *.01 ≤ P < .05, indicating significant difference between those with and without depression among th3 full sample.

†††P < .001, ††.001 ≤ P < .01, †.01 ≤ P < .05, indicating significant difference between those with and without depression among patients with non-zero expenditures.

Note: SE, Standard Error

Table 3. Adjusted effect of depression on total healthcare expenditures, overall and stratified by service types and payers

	AOR[95% CI]	Coefficient (SE)	$ Change	% Change
Overall		0.30(0.09)**	11454	34.5
By service types				
Medical provider		0.38(0.1)***	8213	45.9
Hospital outpatient		-0.79(0.14)	-617	-7.6
Prescribed medicine		-0.07(0.11)	-217	-6.5
Inpatient‡	2.94[1.82,4.74]***	0.05(0.11)	1061	5.3
Other‡	1.05[0.65,1.69]	0.41(0.16)*	405	50.1
By Payers				
Medicare		0.37(0.1)***	8280	43.8
Out-of-pocket(patient)		0.28(0.13)*	1270	32.9
Other		0.23(0.15)	2613	26.1

***P < .001, **.001 ≤ P < .01, *.01 ≤ P < .05

‡ Because a large number of patients did not have expenditures in these categories of expenditures, two-part models, with logistic regressions in the first part and GLMs with gamma distribution and log link in the second part were used to estimate the adjusted effect of depression.

Note: SE, Standard Error

Table 4. Adjusted effect of depression on Medicare healthcare expenditures, stratified by service types

	AOR[95% CI]	Coefficient(SE)	$ Change	% Change
Medical provider		0.31(0.1)*	4327	36
Hospital outpatient		-0.02(0.14)	-97	-2.1
Inpatient‡	2.7[1.59,4.58]***	0.05(0.12)	922	4.8
Prescribed medicine‡	0.88[0.53,1.46]	-0.07(0.17)	-76	-6.7
Other‡	2.55[1.59,4.09]*	0.39(0.17)*	870	47.2

***P < .001, **.001 ≤ P < .01, *.01 ≤ P < .05

‡ Because a large number of patients did not have expenditures in these categories of expenditures, two-part models, with logistic regressions in the first part and GLMs with gamma distribution and log link in the second part were used to estimate the adjusted effect of depression.

Note: SE, Standard Error

Table 5. Adjusted effect of depression on out-of-pocket healthcare expenditures, stratified by service types

	AOR [95% CI]	Depression(SE)	$ Change	% Change
Medical provider		0.39(0.16)*	654	47.1
Prescribed medicine		-0.02(0.1)	-10	-2.3
Other		0.43(0.2)*	465	53
Inpatient‡	1.71[0.97,3.01]	-0.54(0.35)	-1025	-41.8
Hospital outpatient‡	1.05[0.58,1.92]	-0.26(0.22)	-342	-23

***P < .001, **.001 ≤ P < .01, *.01 ≤ P < .05

‡ Because a large number of patients did not have expenditures in these categories of expenditures, two-part models, with logistic regressions in the first part and GLMs with gamma distribution and log link in the second part were used to estimate the adjusted effect of depression.

Note: SE, Standard Error

TECHNICAL REPORT OF PROPOSED AIM 3

Depression and high out-of-pocket cost burden among elderly cancer patients

Results

In table 1, the rates of high-out-of-pocket cost burden were compared by depression status in total and according to predisposing, enabling, need, personal health practices and use of health services and the external environment factors. Overall, the depressed group was significantly more likely to have high out-of-pocket cost burden (53% vs 38.12%, p=0.023) compared to the non-depressed group. When stratified by other covariates, the depressed group was more likely to have high out-of-pocket cost burden in the groups of males, aged 75 and over years old, other race/ethnicity, other married status, high school, public insurance with drug, prostate cancer, fair/poor health status, more than one comorbid health condition, never smokers, underweight/normal and metropolitan.

Table 2 presented the unadjusted effect of depression. The unadjusted effect was significant with an odds ratio of 1.83 (95% confidence interval: 1.08-3.09, p=0.024).Compared to the non-depressed group, the odds of having high out-of-pocket cost burden in the depressed group was 1.83 times that in the non-depressed group.

Table 3 presents the adjusted effect of depression. When controlling for the other independent variables, the effect became not significant-the adjusted odds ratio was 1.54 and the 95% confidence interval was 0.86-2.74(p=0.144).

Discussion

In the sample of 710 elderly breast, lung and prostate cancer patients, 128 (18%) reported depression. In the depressed group 53% had high out-of-pocket cost burden while in the non-

depressed group 38% had. When estimating the relationship between depression and high out-of-pocket cost burden, the unadjusted effect was significant while the adjusted effect was not significant and the odds ratio became smaller, from 1.83 to 1.54.

There might be some possible explanations. One possible explanation is that some covariates were confounders, which were correlated with both depression and high-out-of-pocket cost burden and deflated the true estimate of the relationship. As confounding is a major threat to internal validity, in the absence of randomization, we used the multivariable logistic regression to account for their effects to avoid a false positive error. [1, 2]

Other reasons can impact the p-values as well. In particular, we suspect that the relatively small sample size can be a possible explanation. Both the random error and the overall variability are generally reduced as the sample size increases, which may enable us to detect even relatively small differences between groups. Our sample size provided power to detect an OR equal to or greater than 1.83,but was too small to provide a statistically reliable estimate of the smaller observed adjusted OR of 1.54.[3]

Additionally, we defined the high out-of-pocket cost burden as the out-of-pocket cost, excluding insurance premiums, amounted to 10% or more of the person's annual income. The 10% threshold is set because previous papers used the same rule[4, 5.] A recent study also named it as "underinsurance", an indicator of the level of patients' own financial burden. Moreover, that study defined another indicator - "high total cost burden", which means the sum of out-of-pocket cost and the insurance premiums amounting to 20% or more of the annual income.[6] However, there were a lot of missing values in the insurance premiums in

MCBS data, so we cannot estimate the relationship between depression and high total cost burden.

Further research using different data sources is needed. Since depression already proved to increase the financial burden for general elderly in previous studies[7, 8] and in cancer patients in Aim 2 in our study, it is still possible to be associated with high out-of-pocket cost burden (underinsurance) and/or high total cost burden.

Conclusion

After adjusting for other covariates, depression was not significantly associated with high out-of-pocket cost burden. Further research is needed to explore the topic about depression and elderly cancer patients' financial burden.

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Table 1. Rates of high out-of-pocket cost burden by patients' characteristics

	Without Depression		With Depression		
Characteristics	Weighted Rates	95% Confidence Interval	Weighted Rates	95% Confidence Interval	P-Value
Total rates	38.12	(34.5,41.87)	53	(41.72,63.98)	0.023
Year of cancer diagnosis					
2007-2009	37.07	(31.45-43.05)	50.29	(36.58-63.95)	0.079
2010-2012	39.16	(33.74-44.86)	55.14	(39.29-70.02)	0.074
Gender					
Female	40.26	(34-46.84)	49.21	(35.65-62.89)	0.223
Male	36.64	(31.9-41.65)	56.59	(42.31-69.85)	0.015
Age					
65-74	37.43	(30.27-45.18)	46.35	(27.77-66.01)	0.415
75 and over	38.56	(33.77-43.58)	58.83	(47.81-69.02)	0.003
Race/ethnicity					
White	38.57	(34.66-42.63)	50.73	(39.03-62.35)	0.077
Other	33.93	(24.58-44.73)	67.23	(33.34-89.33)	0.045
Marital status					
Married	42.9	(37.97-47.97)	54.07	(38.63-68.77)	0.211
Other	29.46	(23.5-36.22)	51.25	(36.56-65.73)	0.005
Educational attainment					
Less than high school	41.68	(33.07-50.84)	50.18	(41.1-75.08)	0.079
High school	45.27	(38.39-52.34)	67.35	(49.13-81.5)	0.018
Greater than high school	31.28	(26.03-37.06)	41.49	(25.86-59.05)	0.276
Poverty status					
LT 200% FPL	34.31	(30.33-38.53)	46.36	(32.18-61.15)	0.141
GE 200% FPL	50.76	(42.19-59.28)	64.72	(47.53-78.79)	0.157
Supplemental insurance					
Private insurance with Rx	32.34	(26.36-38.96)	48.03	(32.64-63.8)	0.071
Public insurance with Rx	34.95	(23.22-48.85)	68.98	(45.61-85.5)	0.013
Medical Insurance only	42.46	(36.03-49.17)	50.53	(34.02-66.92)	0.419
Other	51.24	(31.63-70.48)	43.01	(12.39-80.11)	0.703
Cancer site					
Lung	44.09	(30.26-58.9)	72.4	(49.29-87.63)	0.034
Breast	41.08	(34.28-48.24)	46.04	(30.67-62.19)	0.567

Prostate	34.69	(29.83-39.88)	53.57	(38.36-68.15)	0.027
Perceived health status					
Excellent/very good/Good	33.77	(29.41-38.41)	37.28	(25.53-50.76)	0.638
Fair/poor	58.53	(48.72-67.71)	76.95	(62.09-87.19)	0.042
Functional status limitation					
0	34.31	(30.09-38.79)	47.79	(33.25-62.72)	0.098
>=1	50.1	(42.83-57.36)	61.78	(45.55-75.74)	0.187
Number of comorbid health conditions					
0-1	27.01	(21.11-33.84)	35.65	(17.33-59.42)	0.45
>1	43.99	(38.89-49.22)	57.34	(45.77-68.16)	0.06
Smoking Status					
Current	39.78	(24.69-57.09)	49.94	(22.21-77.68)	0.55
Past	40.14	(34.4-46.17)	50.32	(38.89-67.22)	0.13
Never	35.02	(28.88-41.71)	53.17	(39.25-66.6)	0.02
BMI					
Underweight/normal	28.76	(23.17-35.09)	46.69	(30.7-63.39)	0.016
Overweight	40.1	(34.2-46.31)	50.86	(36.01-65.56)	0.218
Obese/morbid obese	49.71	(41.14-58.29)	69.24	(43.02-87.03)	0.144
Metro status					
Metropolitan	34.56	(30.38-39)	51.52	(37.29-65.51)	0.038
Non-Metropolitan	48.1	(41.51-54.75)	56.85	(41.36-71.1)	0.341

Note: LT, less than; GE, greater than or equal to; FPL, federal poverty level; Rx, prescription coverage; BMI, body mass index.

Table 2. Univariate regression results

	Odds ratio (95% Confidence Interval)	P-value
Depression (Ref=No)		
Yes	1.83(1.08-3.09)	0.024

Table 3. Multivariable logistic regression modeling of depression and high out-of-cost burden

	Odds ratio (95% Confidence Interval)	P-value
Depression (Ref=No)		
Yes	1.54(0.86-2.74)	0.144
Year of cancer diagnosis (Ref=2007-2009)		
2010-2012	1.10(0.77-1.58)	0.587
Gender(Ref=Male)		
Female	0.88(0.33-2.34)	0.794
Age at diagnosis, years (Ref=65-74 years)		
75 and over	1.41 (0.94-2.12)	0.100
Race/ethnicity (Ref= White)		
Other race	0.75(0.39-1.45)	0.386
Marital status (Ref=Other)		
Married	2.92(1.83-4.69)	0.000
Educational attainment(Ref=Less than high school)		
High school	1.55(0.93-2.60)	0.095
Greater than high school	0.94(0.94-0.57)	0.79
Poverty Status (Ref=LT 200% FPL)		
GE to 200% FPL	0.4(0.24-0.67)	0.001
Supplemental insurance(Ref= Private insurance with Rx)		
Public insurance with Rx	0.86 (0.39-1.88)	0.697

Medical Insurance only	1.43 (1.00-2.05)	0.052
Other	1.40 (0.72-2.74)	0.322
Cancer Site(Ref=Lung)		
Breast	1.03(0.45-2.39)	0.937
Prostate	0.60(0.31-1.17)	0.133
Perceived Health Status(Ref= Excellent/very good/Good)		
Fair/Poor	2.69(1.79-4.04)	0.000
Functional status limitation(Ref=0)		
At least one	1.28(0.86-1.91)	0.224
Number of comorbid health conditions(Ref=0-1)		
>1	1.58(1.06-2.36)	0.024
Smoking Status(Ref=Current)		
Past	1.03(0.51-2.10)	0.930
Never	1.03(0.49-2.16)	0.933
BMI(Ref= Underweight/normal)		
Overweight	1.52(1.01-2.29)	0.046
Obese/morbid obese	2.03(1.24-3.30)	0.005
Metro Status(Ref=Metropolitan)		
Non-Metropolitan	1.41(0.98-2.03)	0.060

Note: LT, less than; GE, greater than or equal to; FPL, federal poverty level; Rx, prescription coverage; BMI, body mass index.