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Substance use disorder and its effects on outcomes in men with advanced stage prostate Cancer

Sumedha Chhatre, Ph.D[1], **David S. Metzger, Ph.D**[1], **S. Bruce Malkowicz, MD**[2], **George Woody, M.D**[1], and **Ravishankar Jayadevappa, Ph.D**[2,3]

[1] Department of Psychiatry, University of Pennsylvania, Philadelphia PA 19104

[2] Department of Surgery, University of Pennsylvania, Philadelphia PA 19104

[3] Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia PA 19104

Abstract

Background—Substance use disorder in cancer patients has implications for outcomes. Study objective was to analyze the effects of type and timing of substance use on outcomes in Medicare elderly with advanced prostate cancer.

Methods—Observational cohort study using Surveillance, Epidemiology, and End Results (SEER) Medicare linked data from 2000-2009. Among men diagnosed with advanced prostate cancer between 2001 and 2004, we identified those with a claim for substance use disorder in pre-cancer diagnosis year, one-year post-cancer diagnosis and four additional years. Outcomes were health services use, cost and mortality.

Results—Prevalence of substance use disorder was 10.6%. The category 'drug psychoses and related' had higher inpatient hospitalizations (OR=2.3, CI=1.9, 2.8), outpatient hospital visits (OR=2.6, CI=1.9, 3.6) and emergency room visits (OR=1.7, CI=1.2, 2.4). Substance use disorder in follow-up-phase had higher inpatient hospitalizations (OR=2.0; CI=1.8, 2.2), outpatient hospital visits (OR=2.0; CI=1.7, 2.4) and emergency room visits (OR=1.7; CI=1.5, 2.1). Compared to those without substance use, 'drug psychoses and related' category had seventy percent higher cost, and substance use disorder in follow-up phase had sixty percent higher cost. Hazard of all-cause mortality was highest for 'drug psychoses and related' (HR=1.3; CI=1.1, 1.7) and for substance use disorder in treatment phase (HR=1.5; CI=1.3, 1.7).

Conclusions—: Intersection of advanced prostate cancer and substance use disorder may adversely affect outcomes. Incorporating substance use screening and treatments into prostate cancer care guidelines and coordination of care is desirable.

Keywords

Advanced prostate cancer; Medicare elderly; substance use disorder

Corresponding Author: Sumedha Chhatre, Ph.D. 3535 Market St., Suite 4051 Philadelphia PA 19104 Tel: 215-746-7348 rasu@mail.med.upenn.edu.

Conflicts of Interest: None

INTRODUCTION

The number of Americans over the age of 65 is expected to double between 2000 and 2050. As prostate cancer incidence increases exponentially with advancing age, there may be a surge in older prostate cancer patients [1], which will pose a challenge to our healthcare system. Like most elderly, elderly prostate cancer patients will likely acquire a higher number of maladies, both physical and psychosocial, with advancing age. Substance use disorder is an important comorbidity. An estimated 23.9 million people in the U. S. were current drug users in 2012 [2]. Prescription drug use is a recent trend in substance use in the U.S. and is now the second most common form of illegal substance use [2]. The exact prevalence of substance use disorder in elderly is uncertain. However, estimates indicate that by 2020, there will be approximately 4.5 million older adults with substance use [3, 4]. Health problems related to substance use disorder can reach unprecedented levels in the baby boomer generation as it reaches Medicare eligibility. Compared to the younger adults, the proportion of older adults seeking treatment for substance use disorder for the first time is on the rise [5].

Despite these trends, the issue of substance use disorder remains understudied in cancer treatment [6], and patients' alcohol and drug use assessments continue to be sketchy [7]. Advanced prostate cancer care involves combinations of drugs, surgery, radiation therapy and palliative care [8]. Many patients with advanced prostate cancer experience cancer related pain and impaired outcomes [9, 10]. The intersection of aging and advanced disease stage may exacerbate the potential for substance use, leading to adverse outcomes [3, 6, 11-14]. Objective of this study was to analyze the prevalence and modifying effects of substance use disorder on health services use, cost of care and mortality in fee-for-service Medicare elderly with advanced prostate cancer. We hypothesized that the timing and the type of substance use disorder will have varying effects on outcomes.

MATERIALS AND METHODS

Data

The Surveillance, Epidemiology and End Results (SEER)-Medicare data are the linkage of two large population-based sources of data and provide detailed information about Medicare beneficiaries with cancer. The SEER program of National Cancer Institute collects data on cancer incidence, treatment and mortality from sixteen SEER sites and encompasses 26% of the population of the USA. Of persons aged 65 years and older, diagnosed with cancer and enrolled in SEER registries, 93% have a match in Medicare enrollment records [15].

Study Cohort

For this retrospective case-control design, we used SEER-Medicare linked data to create a cohort of men, aged 66 years or older, and diagnosed with advanced prostate cancer between 2001 and 2004. The local institutional review board approved the study. Advanced prostate cancer cases were identified from the SEER Patient Entitlement and Diagnosis Summary (PEDSF) file by selecting regional or distant codes for the variable 'Summary stage 2000' (summ2k1). The summary stage variable is derived from Collaborative Stages (CS) for

2004+ and extent of disease (EOD) prior to that, and is used in most SEER publications [16]. We excluded men who were younger than 66 years at the time of diagnosis in order to ensure sufficient claims for medical care prior to the diagnosis of prostate cancer that are necessary to adjust for pre-diagnosis co-morbidity. With date of prostate cancer diagnosis as the anchor, we defined following phases of care: pre-diagnosis phase is the year prior to prostate cancer diagnosis, cancer treatment phase is the one-year period after prostate cancer diagnosis and follow-up phase is up to four years beyond treatment phase.

Type of Substance use disorder: The key independent variable in our analyses was substance use disorder. Substance use disorder was defined using International Classification of Diseases, 9th Edition (ICD-) codes of 291.xx (Alcoholic psychosis and related); 292.xx (Drug psychoses and related); 303.xx (Alcohol dependence syndrome); 304.xx (Drug dependence); and 305.xx (Non-dependent use of drugs). Among our cohort of advanced prostate cancer patients, we identified those with at least one Medicare inpatient or outpatient claim for any of these codes. Timing of substance use disorder - We created three exclusive categories based on the time of identification of substance use disorder: pre-phase, treatment-phase, and follow-up phase substance use disorder.

Outcomes

The main outcomes of our study were health services use, cost of care and mortality. The SEER-Medicare linked data yields data on inpatient hospitalization, outpatient hospital visits (including emergency room or ER visits), physician or provider services, durable medical equipment, home health services, skilled nursing facility use and hospice care. For this study, we defined health service use as number of inpatient hospitalizations, number of outpatient hospital visits and number of emergency room visits. We operationalized cost of care as reimbursements received from Medicare [17-19]. Total cost were calculated as sum of reimbursements from inpatient hospitalizations, outpatient hospital visits, physician or provider services, durable medical equipment, home health services, and hospice care. Using the PEDSF file of SEER, we obtained all-cause mortality data reported both by SEER and by Medicare. For SEER reported mortality, we constructed date of death using the SEER month of death and SEER year of death. Since SEER does not report day of death, we assigned the middle of the month i.e., 15 as the day of death. For Medicare reported mortality, Medicare day, month and year of death yielded the date of death. A patient was coded deceased if SEER and/or Medicare reported the patient as deceased. Time to death was the time between prostate cancer diagnosis and death. We censored those patients who were alive at the end of five-year follow-up. The variable ‘SEER cause-specific death classification’ was used to establish if the death was prostate-cancer specific.

Covariates

From the PEDSF file, we used socio-demographic characteristics, disease severity, medical co-morbidity and type of prostate cancer treatment to adjust our measures of association. Elixhauser co-morbidity index was derived using Medicare inpatient claims for the one-year period prior to prostate cancer diagnosis [20]. Procedure codes helped identify prostate cancer treatments from Medicare claims, leading to following exclusive categories of

treatments: surgery, radiation therapy, multimodal therapy and no treatment/watchful waiting.

Statistical Analysis

We first tested for differences in the demographic and clinical characteristics of patients with and without substance use disorder from our cohort of elderly advanced prostate cancer patients, using t-tests and χ^2-tests, as appropriate. For assessing the health service use, negative binomial models were used [21]. The dependent variables were count data on number of total inpatient hospitalizations, outpatient hospital visits and ER visits. To analyze the association of substance use disorder with cost of care, we used a two-part model. The first part consisted of logistic regression to model the odds of incurring any cost. In the second part, we used non-zero costs to model the association between substance use and cost using a generalized linear model (GLM) with log-link and gamma distribution variance function [21]. For analyzing the association between substance use disorder and mortality, we used Cox regression models. We used three sequential sets of models to study the effect of substance use disorder on health service use, cost of care and mortality, In Model-1 we estimated the unadjusted association of substance use disorder with outcomes. In Model-2, we adjusted for socio-demographic attributes and Elixhauser comordibidity score [20,22]. Type of treatment for prostate cancer may affect outcomes; however, in our assessment of the relationship of substance use disorder with outcomes, treatment assignments are non-random. In order to minimize the bias due to type of prostate cancer treatment, we used propensity score analysis. Using multinomial logistic regression, we estimated for each patient, the propensity of receiving a particular prostate cancer treatment as a function of demographic and clinical characteristics [23]. We compared the t-statistics for these covariates before and after adjusting with propensity score, in order to observe the extent of matching of the different prostate cancer treatment groups. In Model-3, we used type of treatment and propensity score as covariates. In all our analysis, the reference category was ‘those without a substance use disorder’. We used Statistical Analysis System (SAS), Version 9.3 (SAS Institute, Cary, NC, USA) for data analysis.

RESULTS

We identified 14,277 fee-for-service Medicare patients, aged 66 or older and diagnosed with advanced stage prostate cancer between 2001 and 2004. From this cohort, we identified 1509 (10.6%) patients with a diagnosis of substance use disorder. The prevalence of substance use disorder was 1.8% in pre-phase, 4.2% in cancer treatment phase, and 4.6% in the follow-up phase. As frequencies of two categories of substance use disorder, ‘alcoholic psychosis and related’ and ‘drug dependence’ were very small, we excluded them from analysis. Therefore, three major categories of substance use disorder in our analysis were as following: drug psychoses and related (n=136), alcohol dependence syndrome (n=142), and non-dependent use of drugs (n=1201).

In Table 1, we present the comparison of advanced prostate cancer patients with and without substance use disorder. Compared to those without a substance use disorder, those with substance use disorder were younger (mean age 74.5 years, SD.5.6 vs. mean age 72.4 years,

SD.5.6) and had a higher proportion of African Americans (11.3% vs 17.6%). Those with substance use disorder were less likely to be married, and be from metro area. Comparison of clinical characteristics showed that those with substance use disorder had higher medical co-morbidity, and were more likely to have a higher grade of prostate cancer, compared with those without substance use disorder. Finally, those with a substance use disorder were more likely to have received multimodal treatment, and less likely to have received surgery alone, compared to those without substance use disorder.

Table 2 shows the unadjusted outcomes for across different categories of substance use disorder. Highest proportion of patients from ‘drug psychoses and related’ category had used inpatient services and outpatient services. This group also had higher number of inpatient and outpatient episodes, higher cost of care, higher all-cause mortality and higher prostate cancer specific mortality. On the other hand, those with ‘non-dependent use of drug’ had higher ER usage.

Association between substance use disorder and health service use

Inpatient hospitalizations: As shown in Table 3, compared to those without a substance use disorder, all types of substance use categories were associated with higher inpatient use. Especially, the category of ‘drug psychoses and related’ had the highest number of inpatient hospitalizations (OR=2.3, CI=1.9, 2.8). Substance use disorder in follow-up-phase had the highest inpatient hospitalizations (OR=2.0; CI=1.8, 2.2).

Outpatient hospital visits: We observed a pattern similar to inpatient hospitalizations. The category of ‘drug psychoses and related’ had the highest number of outpatient visits (OR=2.6, CI=1.9, 3.6). Substance use disorder identified in the treatment phase (OR=2.0; CI=1.7, 2.3) and in follow-up phase was associated with statistically significant higher outpatient visits (OR=2.0; CI=1.7, 2.4).

ER visits: Compared to those without a substance use disorder, the category of ‘drug psychoses and related’ had higher ER visits (OR=1.7, CI=1.2, 2.4). Substance use disorder in follow-up phase had the highest ER visits (OR=1.7; CI=1.5, 2.1).

Association between substance use disorder and cost of care

Table 4 presents the results of two-part models for cost of care. Part 1 consists of logistic models where the binary dependent variable was ‘any cost’. Compared to the reference category of those without a substance disorder, all types of substance use had higher odds of incurring any cost. Especially, the categories of ‘alcohol dependence syndrome’ and ‘non-dependent use of drugs’ had four times higher odds of incurring any cost. With regard to timing, substance use disorder in cancer treatment phase had very high odds of incurring any cost (Or=7.6, CI=4.7, 12.0).

Part 2 consists of GLM models with log-link and gamma distribution, for those with nonzero costs. Table 4 shows the results of Part 2 models. Costs were higher for all types of substance use. The category of ‘drug psychoses and related’ had seventy percent higher cost that those without a substance use disorder. Additionally, substance use disorder in the follow-up phase had sixty percent higher cost compared to the reference category.

Association between substance use disorder and mortality

All-cause mortality: Figures 1 and 2 show the Kaplan-Meier survival curves. The log-rank statistic (<0.0001) indicates difference in survival probabilities between various substance use categories. Similarly, log-rank statistic indicated differences in probabilities of survival between timing of substance use disorder (<0.0001). The category of 'drug psychoses and related' had the highest hazard of all-cause mortality (HR=1.3; CI=1.1, 1.7). The hazard of mortality was lower for 'non-dependent use of drugs' (HR=0.82; CI=0.69, 0.96). The hazard of mortality was also high for substance use disorder in the pre-phase and in the treatment phase (HR=1.2; CI=1.1, 1.4; and HR=1.5; CI=1.3, 1.7, respectively). We observed comparable results for analysis that focused on prostate cancer-specific mortality (data not shown).

DISCUSSION

Our results provide important evidence regarding intersection of age, advanced prostate cancer and substance use disorders. The prevalence of substance use disorder in our cohort of elderly fee-for-service Medicare patients with advanced prostate cancer was 10.6 percent. Another important observation was that the type of and timing of substance use disorder had strong association with outcomes. Though not most frequently observed, the category of 'drug psychoses and related' had the strongest association with health service use, cost of care and all-cause mortality. Additionally, substance use disorder identified after the diagnosis of prostate cancer had the highest impact on health service use and cost of care. One possible explanation is that pain and psychiatric comorbidities, especially anxiety and depression may influence substance use in this period, and the interaction of these factors may ultimately affect outcomes [24-26]. Past and current substance use disorder in cancer patients can affect their treatment and pain management, and thus complicate the disease management [14, 27]. A study of substance use disorder in patients with chronic myelogenous leukemia or myelodysplastic syndrome found that lifetime cocaine use was associated with a six-fold increased risk of death [6].

We note some limitations of our study. SEER-Medicare linked data has been used to study cancer-related health services and costs, including for prostate cancer [15, 17,18]. In our study, the sample consists only of men aged 66 years and older who lived in a SEER region and were fee-for-service. The SEER-Medicare linked database does not include patients with Medicare advantage or Part C. Furthermore, while the age and sex distribution for persons 66 years and older is comparable with that of older adults in the US, the SEER regions have a higher proportion of non-white persons. Mortality rates derived from SEER data may not be representative of national data on cancer mortality rates [15]. Administrative data has become an important source of information for public health and health services research, but are subject to error [28]. Our sample did not capture men from the 50-64 years age group who also are at risk for prostate cancer. We also did not include 'surrogate' alcohol disorders as part of our substance use disorder group. Finally, substance use disorder may be under-reported in the Medicare claims leading to conservative estimates of the association of substance use disorder with health services use and cost of care.

In conclusion, substance use disorder among Medicare elderly prostate cancer patients can pose unique challenges to effective and efficient care. Substance use disorder can be multifaceted and chronic, and therefore demands intense management similar to that for cancer. There is an urgent need to identify the missed opportunities for identifying and treating substance use disorder among elderly prostate cancer patients. As a first step, guidelines for prostate cancer care can incorporate screening for substance use disorder as a recommendation. Enhanced screening and coordinated care may help early identification of elderly prostate cancer patients with substance use disorder, facilitate appropriate treatments and clinical management and thus, lead to improved outcomes.

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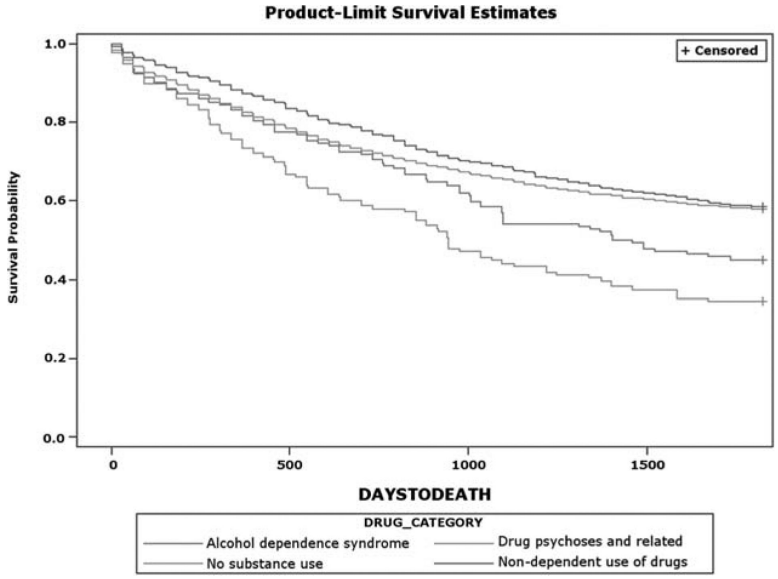

Figure 1.
Survival curve for type of substance use

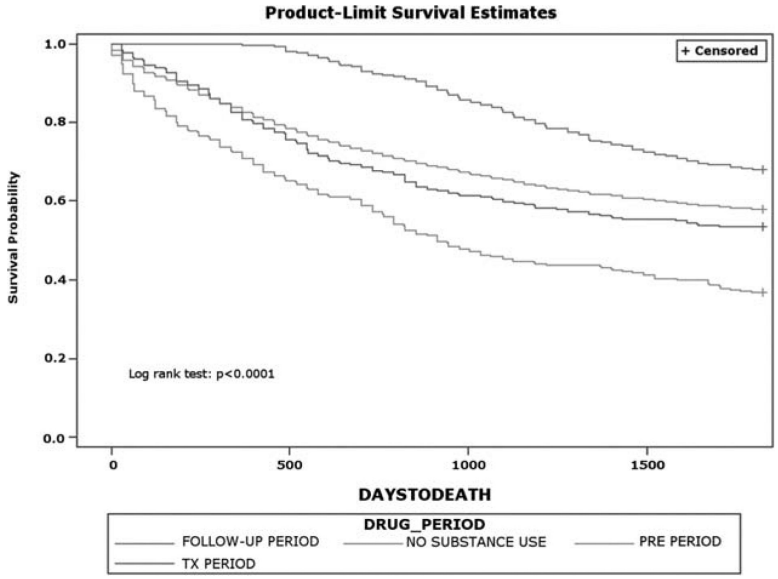

Figure 2.
Survival curve for time of substance use

Table 1

Comparison of demographic and clinical characteristics (n=14,277)

Characteristics	Without a substance use disorder (n =12,768)	With a substance use disorder (n=1,509)	*P* Value
Mean age at diagnosis (Standard deviation)	74.5 (6.9)	72.4 (5.6)	<.0001
Mean census track median income (Standard deviation)	43026 (16623)	37458 (15923)	<.0001
Ethnicity (%)			
White	10208 (79.9)	1127 (74.7)	<.0001
African American	1430 (11.2)	266 (17.6)	
Hispanic	1130 (8.9)	116 (7.7)	
Marital status (%)			
Married	9038 (70.8)	900 (59.6)	<.0001
Single/separated/divorced	3185 (24.9)	537 (35.7)	
Unknown	545 (4.3)	71 (4.7)	
Geographic area (%)			
Metro	11190 (87.7)	1237 (79.8)	<.0001
Non-metro	1570 (12.3)	304 (20.2)	
Elixhauser comorbidity index (%)			
0	11446 (89.7)	1228 (81.4)	<.0001
≥1	1327 (10.4)	282 (18.7)	
Grade (%)			
Moderately differentiated	4242 (33.2)	475 (31.5)	<.0001
Poorly differentiated	6232 (48.8)	752 (49.8)	
Other	2294 (17.9)	282 (18.7)	
Treatment (%)			
Surgery	2902 (22.7)	273 (18.1)	<.0001
Radiation	1252 (9.8)	144 (9.5)	
Multimodal	5803 (45.5)	893 (59.2)	
No treatment/watchful waiting	2811 (22.0)	199 (13.2)	

Table 2

Unadjusted, health service use, costs and mortality outcomes (n=14247)

	Without a substance use disorder (n =12,768)	Non-dependent use of drugs (n=1201)	Drug psychoses and related (n-136)	Alcohol dependence syndrome (n=142)
Any health service use (%)				
Inpatient hospitalizations				
0	40.2	15.8	13.2	14.8
1-3	47.2	57.6	48.5	53.5
≥4	12.6	26.6	38.2	31.7
Outpatient hospital visits				
0	55.9	32.8	23.5	28.2
1-3	24.8	34.1	25.7	35.9
≥4	19.3	33.1	50.7	35.9
ER visits				
0	48.5	28.6	38.2	40.9
1-3	16.6	20.5	26.5	23.2
≥4	34.9	50.9	35.3	35.9
Costs in $ mean (standard deviation), median				
Total cost	44345 (86192)	73383 (110766)	76654 (112827)	65420 (79492)
	18141	39973	34381	39527
Mortality (%)				
All-cause	41.7	41.4	65.4	54.9
Prostate cancer specific	28.5	25.9	39.7	28.9

Table 3

Association between health service use and substance use

	Hospitalizations* OR (95% CI)	Outpatient Visits* OR (95% CI)	ER Visits* OR (95% CI)
Type of substance use disorder*			
Model 1: Unadjusted			
Alcohol dependence syndrome	2.0 (1.6, 2.4)	1.6 (1.2, 2.3)	1.1 (0.70,1.5)
Drug psychoses and related	2.4 (2.0, 2.9)	2.7 (1.9, 3.8)	1.3 (0.89, 1.8)
Non-dependent use of drugs	1.8 (1.7, 1.9)	1.7 (1.5, 1.9)	1.4 (1.5,1.8)
Model 2: Adjusted for socio-demographic characteristics and geographic area			
Alcohol dependence syndrome	1.9 (1.6, 2.3)	1.8 (1.3, 2.5)	1.1 (0.76, 1.5)
Drug psychoses and related	2.3 (1.9, ,2.8)	2.7 (1.9, 3.8)	1.3 (0.90, 1.8)
Non-dependent use of drugs	1.7 (1.6, 1.9)	1.8 (1.6, 2.1)	1.5 (1.3, 1.7)
Model 3: Adjusted for treatment, clinical characteristics and propensity score			
Alcohol dependence syndrome	1.9 (1.6, 2.3)	1.8 (1.3, 2.4)	1.2 (0.85, 1.7)
Drug psychoses and related	2.3 (1.9, 2.8)	2.6 (1.9, 3.6)	1.7 (1.2, 2.4)
Non-dependent use of drugs	1.7 (1.6,1.8)	1.8 (1.6, 2.0)	1.5 (1.3, 1.7)
Period in which substance use disorder was identified*			
Model 1: Unadjusted			
Pre prostate cancer diagnosis	1.7 (1.5, 1.9)	1.8 (1.4, 2.2)	1.1 (0.86, 1.4)
Cancer treatment phase	1.8 (1.6 1.9)	1.8 (1.5, 2.1)	1.5 (1.2, 1.7)
Follow-up phase	2.0 (1.8, 2.2)	1.7 (1.4, 2.1)	1.8 (1.5, 2.2)
Model 2: Adjusted for socio-demographic characteristics and geographic area			
Pre prostate cancer diagnosis	1.4 (1.2, 1.6)	1.6 (1.3, 2.0)	1.1 (0.90, 1.4)
Cancer treatment phase	1.8 (1.6, 1.9)	2.0 (1.7, 2.3)	1.4 (1.1, 1.6)
Follow-up phase	2.1 (1.9, 2.3)	2.0 (1.7, 2.4)	1.7 (1.4, 2.0)
Model 3: Adjusted for treatment and clinical characteristics, and propensity score			
Pre prostate cancer diagnosis	1.4 (1.2, 1.6)	1.6 (1.3, 1.9)	1.1 (1.0,1.4)
Cancer treatment phase	1.8 (1.5,1.9)	2.0 (1.7, 2.3)	1.4 (1.2, 1.6)
Follow-up phase	2.0 (1.8,2.2)	2.0 (1.7, 2.4)	1.7 (1.5,2.1)

** For all models, reference category is those without a substance use disorder

* Negative binomial models

Table 4

Association between, cost, mortality and substance use

	Total cost (Two-part model)* Estimate (SE)		All-cause mortality§ HR (95% CI)
	Part 1 OR (95% CI)	Part2 OR (95% CI)	
Type of substance use disorder **			
Model 1: Unadjusted			
Alcohol dependence syndrome	4.6 (2.3, 9.5)	1.2 (0.99, 1.5)	0.97 (0.66, 1.4)
Drug psychoses and related	3.9 (2.0, 7.8)	1.4 (1.2, 1.8)	1.8 (1.5, 2.7)
Non-dependent use of drugs	4.9 (3.8, 6.4)	1.4 (1.3, 1.5)	0.68 (0.58, 0.80)
Model 2: Adjusted for socio-demographic characteristics and geographic area			
Alcohol dependence syndrome	4.6 (2.3, 9.5)	1.2 (1.0, 1.5)	0.89 (0.61, 1.3)
Drug psychoses and related	3.6 (1.8, 7.2)	1.5 (1.2, 1.9)	1.3 (1.0, 1.6)
Non-dependent use of drugs	4.7 (3.7, 6.1)	1.3 (1.2, 1.4)	0.80 (0.68, 0.94)
Model 3: Adjusted for treatment, clinical characteristics and propensity score			
Alcohol dependence syndrome	4.1 (1.9, 8.5)	1.2 (1.0, 1.5)	0.84 (0.57, 1.2)
Drug psychoses and related	3.4 (1.7, 6.8)	1.7 (1.4, 2.1)	1.3 (1.1, 1.7)
Non-dependent use of drugs	4.3 (3.3, 5.6)	1.3 (1.2, 1.4)	0.82 (0.69, 0.96)
Period in which substance use disorder was identified **			
Model 1: Unadjusted			
Pre prostate cancer diagnosis	3.0 (2.1, 4.4)	1.1 (0.95, 1.3)	1.8 (1.6, 2.1)
Cancer treatment phase	8.3 (5.5, 13.2)	1.2 (1.1, 14)	1.1 (1.0, 1.3)
Follow-up phase	4.4 (3.1, 6.2)	1.7 (1.5, 1.9)	0.14 (0.09, 0.19)
Model 2: Adjusted for socio-demographic characteristics and geographic area			
Pre prostate cancer diagnosis	2.5 (1.7, 3.8)	1.1 (0.94, 1.2)	1.4 (1.2, 1.6)
Cancer treatment phase	8.1 (5.1, 12.8)	1.2 (1.1, 1.3)	1.3 (1.1, 1.5)
Follow-up phase	4.4 (3.1, 6.3)	1.6 (1.4, 1.8)	0.18 (0.12, 0.25)
Model 3: Adjusted for treatment and clinical characteristics, and propensity score			
Pre prostate cancer diagnosis	2.3 (1.6, 3.4)	1.1 (0.95, 1.2)	1.2 (1.1, 1.4)
Cancer treatment phase	7.6 (4.7, 12.0)	1.2 (1.1, 1.3)	1.5 (1.3, 1.7)

	Total cost (Two-part model)* Estimate (SE)		All-cause mortality§ HR (95% CI)
	Part 1 OR (95% CI)	Part2 OR (95% CI)	
Follow-up phase	3.9 (2.7, 5.6)	1.6 (1.4, 1.7)	0.18 (0.13, 0.26)

*Two part model. Part 1 is logistic model and Part 2 is Generalized Linear Model, gamma distribution with log-link

§Cox proportional hazard model

**For all models, reference category is those without a substance use disorder

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