DOI: 10.1111/jrh.70029

ORIGINAL ARTICLE

THE JOURNAL OF RURAL HEALTH

Risks of adverse health outcomes among older rural prostate cancer survivors in the SEER-Medicare data

Chun-Pin Chang (Esther) PhD[1,2] | Daren Huang MPH[1,2,3] | Shane Lloyd MD[4] | N. Lynn Henry MD, PhD[5] | Brock O'Neil MD[6] | Mia Hashibe PhD[1,2]

[1]Huntsman Cancer Institute, Salt Lake City, Utah, USA

[2]Division of Public Health, Department of Family and Preventive Medicine, University of Utah School of Medicine, Salt Lake City, Utah, USA

[3]Department of Epidemiology, UCLA Fielding School of Public Health, Los Angeles, California, USA

[4]Department of Radiation Oncology, University of Utah, Salt Lake City, Utah, USA

[5]Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, USA

[6]Division of Urology, Department of Surgery, University of Utah, Salt Lake City, Utah, USA

Correspondence
Mia Hashibe, Huntsman Cancer Institute, University of Utah, 2000 Circle of Hope, Salt Lake City, UT 84108.
Email: mia.hashibe@utah.edu

Funding information
National Cancer Institute of the National Institutes of Health, Grant/Award Number: R01CA244326

Abstract

Background: Rural prostate cancer patients face challenges such as greater distance for cancer treatment and care fragmentation. There have been very few studies investigating adverse health outcomes among prostate cancer survivors residing in rural areas. A comprehensive evaluation of adverse health outcomes among rural prostate cancer patients is needed to understand potential health disparities and provide scientific evidence for interventions. The aims of this study were to investigate prevalent and incident adverse health outcomes among older rural prostate cancer survivors compared to urban prostate cancer survivors in the United States.

Methods: The SEER-Medicare linked database was used to identify first primary prostate cancer survivors. Fine-Gray subdistribution hazard models were utilized to estimate hazard ratios (HR) and 95% confidence intervals (CI), comparing rural prostate cancer patients to urban prostate cancer patients.

Results: A total of 37,126 rural prostate cancer survivors and 109,176 urban prostate cancer survivors were identified. We observed that rural prostate cancer survivors had a higher prevalence of rheumatoid arthritis/osteoarthritis (22.1% vs 20.9%; *P*-value <.001) and chronic obstructive pulmonary disease (COPD)/bronchiectasis (14.2% vs 10.5%; *P*-value <.001). A higher incident risk of acute myocardial infarction, COPD/bronchiectasis, hip pelvic fracture, and rheumatoid arthritis/osteoarthritis among rural prostate cancer was observed compared to their urban counterparts >5 years after cancer diagnosis.

Conclusions: This study provides important results on the prevalence and incident adverse health outcomes among older rural prostate cancer survivors. Further investigation into how other factors influence these disparities is warranted.

KEYWORDS
adverse health outcomes, health disparities, prostate cancer, rural disparity, SEER-Medicare

INTRODUCTION

Over 3.5 million men have a history of prostate cancer in the United States.[1] In 2024, there are an estimated 299,010 new cases of prostate cancer diagnosed, and 35,250 men will die from the disease in the United States.[2] Cancer patients residing in rural areas have longer travel distances to oncology centers and experience reduced access to specialized care and advanced cancer treatments.[3] A systematic review, including 25 studies, concluded that rural men were less likely to undergo prostate cancer screening and less likely to be diagnosed with prostate cancer.[4] However, a Surveillance, Epidemiology, and End Results (SEER) cohort study, including 6,653 prostate cancer patients residing in rural areas, reported that rural prostate cancer patients had a higher risk of 10-year mortality from other causes compared to prostate cancer patients residing in urban areas.[5]

Previous research has shown lower adherence to cancer treatment among rural prostate cancer patients.[6–8] Prostate cancer patients residing in rural areas were less likely to receive definitive radiotherapy compared to surgical options and were less likely to be offered curative treatment.[7,8] Rural prostate cancer patients face challenges related to increased travel distances for care and encounter care fragmentation.[8,9] Limited studies have been conducted to investigate adverse health outcomes among prostate cancer survivors residing in rural areas. Our previous studies showed that rural prostate cancer survivors in Utah had a higher risk of heart failure and diseases of the respiratory system, as well as a decreased risk of screen-detected cardiovascular disease (CVD) and diseases of the blood and blood-forming organs.[10,11] Rural prostate cancer survivors in Utah may represent a healthier subgroup compared to those in other parts of the United States, due to factors such as lower smoking rates and a younger population. Therefore, a comprehensive evaluation of adverse health outcomes among rural prostate cancer patients across the United States is needed.

The objective of this study is to investigate the prevalent and incident adverse health outcomes in terms of major diseases among older rural prostate cancer survivors in comparison to older urban prostate cancer survivors in the SEER-Medicare data.

METHODS

Data source

We used the SEER-Medicare linked database from 1999 through 2020 to conduct a cohort study. The SEER-Medicare data, consisting of 2 large population-based sources in the United States, contains information regarding demographics, cancer-related characteristics, and health service claims among Medicare beneficiaries with cancer.[12,13] International Classification of Disease (ICD) codes are available in claims from hospitalizations (Part A), physician/supplier bills (Part B), and institutional outpatient providers (Part B). The study was approved by the Institutional Review Board and received approval for the waiver of consent.

Study population

We included men who were aged ≥66 years and diagnosed with a first primary invasive prostate cancer (SEER site code: 28010; ICD-O-3 site: C61.9, excluding ICD-O-3 histology 9050–9055, 9140, 9590–9993) between 2000 and 2017. To calculate baseline comorbidity scores, we started the eligibility at the age of 66 years old and required enrollment in Part A/B to be continuous a year before cancer diagnosis. Patients from registries of San Francisco-Oakland, Metropolitan Detroit, Metropolitan Atlanta, and Los Angeles were excluded due to the lack of rural area covered by these registries. Patients were excluded if they were (1) identified by autopsy or death certificate, (2) nonadenocarcinoma histology, (3) lost to follow-up or died within 1 year after cancer diagnosis, or (4) not enrolled in Part A and B or enrolled in health maintenance organization (HMO) from a year before cancer diagnosis to the end of SEER follow-up (Figure S1).

Rural residence was determined by the US Department of Agriculture's rural-urban commuting area (RUCA) codes.[14] RUCA secondary codes were linked by patients' census tract at cancer diagnosis. The RUCA 2000 was used for patients diagnosed before 2006, while RUCA 2010 was used for patients diagnosed in 2006 and later. RUCA codes for urban areas were 1.0, 1.1, 2.0, 2.1 3.0, 4.1, 5.1, 7.1, 8.1, 10.1. The rural area included large rural cities/towns (RUCA codes: 4.0, 4.2, 5.0, 5.2, 6.0, 6.1) and small and isolated small rural towns (7.0, 7.2, 7.3, 7.4, 8.0, 8.2, 8.3, 8.4, 9.0, 9.1, 9.2, 10.0, 10.2, 10.3, 10.4, 10.5, 10.6).[15] Each rural prostate cancer patient was matched to up to 3 urban prostate cancer patients by +/− 1 year of diagnosis and age at the time of cancer diagnosis.

We included 22 adverse health outcomes from the Chronic Conditions Data Warehouse (CCW) Chronic Conditions Algorithms: acquired hypothyroidism, acute myocardial infarction, Alzheimer's disease, Alzheimer's disease and related disorders or senile dementia, anemia, asthma, atrial fibrillation, benign prostatic hyperplasia, cataract, chronic kidney disease, chronic obstructive pulmonary disease (COPD) and bronchiectasis, depression, diabetes, glaucoma, heart failure, hip/pelvic fracture, hyperlipidemia, hypertension, ischemic heart disease, osteoporosis, rheumatoid arthritis/osteoarthritis, stroke/transient ischemic attack.[16] We used the adverse health outcome list from 27 CCW Chronic Conditions based on their impact on the Medicare population in terms of prevalence, quality of life, potential for improved disease management, health care utilization and cost, and the feasibility of identification in Medicare claims data.[16] We excluded 5 cancer-related outcomes (breast, colorectal, endometrial, lung, and prostate cancers), resulting in a total of 22 adverse health outcomes. Diagnoses of adverse health outcomes were identified using the ICD-9 and ICD-10 diagnosis codes and processed with the CCW categorizations.[16] To identify incident diagnoses, individuals diagnosed with the diseases before the start of each analysis time period were considered as prevalent cases and were excluded for that specific outcome. Sources of ICD diagnosis codes included hospitalization claims, carrier claims, and outpatient claims. Physicians may have recorded a "rule-out" diagnosis or unconfirmed diagnoses

in physician and outpatient claims. To avoid overestimation of the outcomes, conditions ascertained by physicians and outpatient claims were required to occur twice between 30 and 60 days.

Information on age at cancer diagnosis, year of cancer diagnosis, tumor characteristics, first course of cancer treatment (surgery, radiation, chemotherapy), race, ethnicity, and rural residence was obtained from the SEER cancer file. Since cancer treatment from SEER may not obtain all cancer treatment, we used Common Procedural Terminology/Healthcare Common Procedure Coding System (CPT/HCPCS) codes to identify additional cancer treatment, such as surgery, radiation therapy, and androgen deprivation treatment (ADT),[17] within a year of cancer diagnosis from Medicare claims data.[18] Modified baseline Charlson Comorbidity Index (CCI) was calculated from 1 year before cancer diagnosis up to the time of cancer diagnosis.[19] Cancer diagnosis was excluded from the modified baseline CCI since all patients in our cohort have had cancer. Census tract-level education and income were derived from the census 2000 and the American Community Survey (ACS) 2008-2012 from the SEER-Medicare file. Vital status was obtained from the SEER cancer file and Medicare master beneficiary summary file. Tobacco use disorder, alcohol use disorder, and obesity prior to cancer diagnosis were identified from Medicare claims using Other Chronic Conditions Algorithms.[20]

Statistical analysis

Differences in characteristics between rural and urban prostate cancer survivors were compared using chi-square tests. To account for multiple comparisons in the chi-square tests, the Bonferroni correction was applied when comparing the prevalence of adverse health outcomes between rural and urban prostate cancer survivors. The adjusted significance level of 0.002 was determined by dividing the original alpha level (0.05) by the number of comparisons made (22 adverse health outcomes). Patients who did not develop outcomes of interest were censored at death or the last follow-up date. We used 2 follow-up time periods to evaluate the risk of incident adverse health outcomes: >1 to 5 years and >5 years after a cancer diagnosis. Fine-Gray subdistribution hazard models stratified on matched pairs were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) to account for a competing risk of death.[21] Potential confounding factors were chosen a priori based on the 3 properties of confounders determined by a causal model or directed acyclic graph.[22] We adjusted for matched pair (diagnosis year and diagnosis age), race/ethnicity, baseline CCI, cancer registry region, census-tract income, census-tract education, tobacco use disorder before cancer diagnosis in the model. Adjusting for the cancer registry region accounted for differences in geographic location. A stratified analysis was conducted based on ADT treatment to assess the risk of adverse health outcomes among rural prostate cancer survivors compared to urban prostate cancer survivors. Sensitivity analyses were conducted to examine risks of adverse health outcomes without the adjustment of education and income in the models because education and income may be both confounding factors and mediators between rural residence and risks of adverse health outcomes. As a sensitivity analysis, we restricted our analysis to prostate cancer patients enrolled in Medicaid to estimate the association between death and rural residence. This analysis included patients diagnosed from 2007 and onward, since insurance status from SEER was only available from 2007. Another sensitivity analysis was performed by extending the upper limit of the "rule-out" diagnosis from 60 to 360 days in physician and outpatient claims, to evaluate the potential underestimation of outcomes when using a 60-day upper limit. The proportional hazards assumption was tested for each model by including interactions between the predictors and time in the model. For models where the assumption was violated, flexible parametric survival models with restricted cubic splines were used if the inference was different from the subdistribution hazard model.[23,24] Analyses were performed using SAS (version 9.4, SAS Institute) and Stata (version 17, StataCorp LLC).

RESULTS

A total of 37,126 rural prostate cancer survivors and 109,176 urban prostate cancer survivors were identified in the SEER-Medicare database (Table 1). More than 40% of rural prostate cancer survivors were from cancer registries in the south. In terms of race and ethnicity groups, 87.8% of rural prostate cancer survivors were non-Hispanic White and 82.3% of urban prostate cancer survivors were non-Hispanic White. For census-tract level measures, rural prostate cancer survivors had a higher proportion in the lowest education and income category. The percentage of rural prostate cancer survivors with a baseline CCI score of 0 was slightly higher compared to urban prostate cancer survivors. The percentage of patients who died was higher among rural prostate cancer patients (56.8% vs 53.1%; *P*-value for chi-square < .001). When stratified by cancer stage, rural prostate cancer patients had a higher percentage who died than urban prostate cancer patients at the same stage (data not shown). Median follow-up years were approximately 7 years for both rural and urban prostate cancer survivors, with a range from 1 to 20 years (data not shown; $Q1\text{-}Q3_{rural}$: 3.8-11.1; $Q1\text{-}Q3_{urban}$: 4.1-11.5).

Compared to urban prostate cancer survivors, rural prostate cancer survivors were diagnosed with a distant cancer stage at a slightly higher proportion (Table 2). In addition, rural prostate cancer survivors were diagnosed with stage IV cancer at a higher proportion (7.7% vs 6.9%) compared to urban prostate cancer survivors, although AJCC stage had a relatively higher proportion of missing values than cancer stage (missing for AJCC stage: 24.4%; missing for cancer stage: 4.0%). Rural prostate cancer survivors had a higher percentage receiving surgery and ADT, and a lower percentage receiving radiation therapy compared to urban prostate cancer survivors (Table 2).

Figure 1 shows the prevalence of adverse health outcomes at cancer diagnosis in rural and urban prostate cancer survivors. While the percentage differences in most diseases were less than 1% between rural and urban prostate cancer survivors, rural survivors had a higher prevalence of rheumatoid arthritis/osteoarthritis (22.1% vs 20.9%; *P*-value < .001) and COPD/bronchiectasis (14.2% vs 10.5%; *P*-value

TABLE 1 Demographic characteristics of prostate cancer survivors (n = 146,302), stratified by rural residence, diagnosed from 2000 to 2017, included patients with match pairs only in the SEER-Medicare data.

	Rural (n = 37,126)		Urban (n = 109,176)		
	n	%	n	%	*p*-value[a]
Race and ethnicity					<.001
Non-Hispanic White	32,585	87.8	89,867	82.3	
Non-Hispanic Black	2,385	6.4	8,996	8.2	
Hispanic (any race)	1,489	4.0	5,865	5.4	
Non-Hispanic Asian	129	0.3	2,307	2.1	
Non-Hispanic American Indian/Alaska Native	205	0.6	284	0.3	
Non-Hispanic Hawaiian/Pacific Islander	22	0.1	145	0.1	
Unknown	311	0.8	1,712	1.6	
Census-tract education[b]					<.001
≤35% had college education	9,629	25.9	10,863	9.9	
>35%-55% had college education	17,502	47.1	30,915	28.3	
>55%-70% had college education	7,573	20.4	30,830	28.2	
>70% had college education	2,422	6.5	36,568	33.5	
Census-tract household income[c]					<.001
<$50,000	30,223	81.4	39,366	36.1	
$50,000 to <$60,000	4,086	11.0	17,387	15.9	
$60,000 to <$70,000	1,894	5.1	14,424	13.2	
$70,000+	922	2.5	37,994	34.8	
Baseline Charlson Comorbidity Index					<.001
0	22,392	60.3	64,646	59.2	
1	8,563	23.1	25,177	23.1	
2+	6,171	16.6	19,353	17.7	
Tobacco use disorder before cancer diagnosis					<.001
No	34,536	93.0	103,691	95.0	
Yes	2,590	7.0	5,485	5.0	
Alcohol use disorder before cancer diagnosis					.834
No	36,271	97.7	106,641	97.7	
Yes	855	2.3	2,535	2.3	
Obesity before cancer diagnosis					.543
No	34,668	93.4	101,848	93.3	
Yes	2,458	6.6	7,328	6.7	
Vital status					<.001
Alive	16,050	43.2	51,185	46.9	
Dead	21,076	56.8	57,991	53.1	
Cancer registry region					<.001
West	12,794	34.5	44,371	40.6	
South	15,895	42.8	24,700	22.6	
Northeast	833	2.2	36,120	33.1	
Midwest	7,604	20.5	3,985	3.7	

[a] *P* for chi-square.
[b] Included individuals with some college education and college education at least 4 years.
[c] Unknown N <11.

TABLE 2 Clinical characteristics of prostate cancer survivors (n = 146,302), diagnosed from 2000 to 2017 in the SEER-Medicare data.

	Rural (n = 37,126)		Urban (n = 109,176)		
	n	%	n	%	*p*-value[a]
Cancer stage					<.001
Localized	30,983	86.5	90,887	86.9	
Regional	3,120	8.7	9,153	8.8	
Distant	1,729	4.8	4,521	4.3	
Unknown/missing[b]	1,294		4,615		
AJCC					<.001
Stage I	4,521	16.4	13,153	16.2	
Stage II	19,159	69.6	57,622	70.8	
Stage III	1,740	6.3	5,008	6.2	
Stage IV	2,110	7.7	5,596	6.9	
Unknown/missing[b]	9,596		27,797		
Grade					<.001
Grade 1	2,560	7.2	6,716	6.4	
Grade 2	17,060	47.9	51,958	49.8	
Grade 3	15,837	44.5	45,448	43.5	
Grade 4	122	0.3	279	0.3	
Unknown/missing	1,547		4,775		
Received surgery					<.001
No	25,371	70.0	77,989	72.5	
Yes	10,863	30.0	29,535	27.5	
Unknown	892		1,652		
Received radiotherapy					<.001
No	18,638	51.8	51,497	48.0	
Yes	17,335	48.2	55,845	52.0	
Unknown	1,153		1,834		
Androgen deprivation treatment					<.001
No	20,879	56.2	63,386	58.1	
Yes	16,247	43.8	45,790	41.9	

Abbreviations: AJCC, American Joint Committee on Cancer; NOS, not otherwise specified.
[a]*P* for chi-square.
[b]Missing for AJCC stage: 24.4%; missing for cancer stage: 4.0%.

< .001). On the other hand, lower prevalence was observed among rural prostate cancer survivors for benign prostatic hyperplasia, glaucoma, hyperlipidemia, and hypertension with *P*-value < .001.

To assess the risk of incident adverse health outcomes, we excluded prevalent cases from each analysis (Table S1). Compared to urban prostate cancer survivors, rural prostate cancer survivors had a higher risk of acute myocardial infarction >1 to 5 years after cancer diagnosis (Table 3). In addition, higher risks of acute myocardial infarction, COPD and bronchiectasis, hip pelvic fracture, and rheumatoid arthritis/osteoarthritis among rural prostate cancer were observed >5 years after cancer diagnosis (Table 3). In the analysis stratified by ADT, an increased risk of rheumatoid arthritis/osteoarthritis was only observed among rural prostate cancer survivors who did not receive ADT >5 years after cancer diagnosis (HR: 1.10, 95% CI: 1.04, 1.17; Table S2). Among rural prostate cancer survivors, 7.0% of those who received ADT developed hip/pelvic fractures, whereas 5.0% of those who did not receive ADT developed hip/pelvic fractures (Table S2). However, we did not observe an association between hip pelvic fracture and rural prostate cancer survivors, regardless of whether they received ADT or not (Table S2). A lower risk was observed for Alzheimer's disease, anemia, chronic kidney disease, diabetes, and hyperlipidemia among rural prostate cancer survivors compared to urban prostate cancer survivors >1 to 5 years after cancer diagnosis (Table 3). Beyond 5 years after cancer diagnosis, rural residence was associated with a

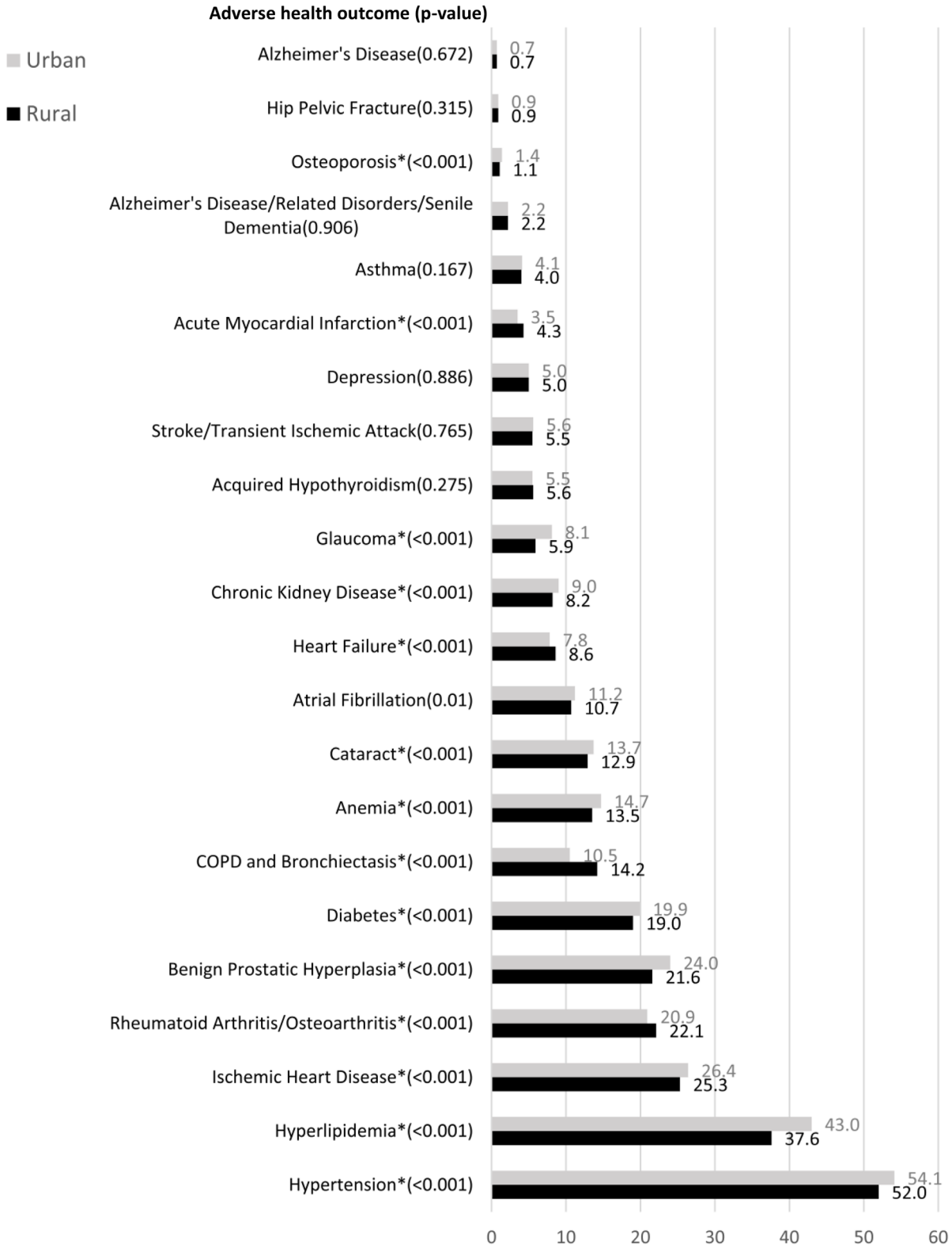

FIGURE 1 Prevalence of adverse health outcomes among prostate cancer survivors at cancer diagnosis in the SEER-Medicare data, stratified by rural and urban. *P for chi-square <.002 (adjusted for multiple comparisons).

TABLE 3 The risks of incident diseases among rural prostate cancer survivors compared to urban prostate cancer survivors in the SEER-Medicare data, stratified by follow-up periods.

	>1 to 5 years after cancer diagnosis					>5 years after cancer diagnosis				
	Rural		Urban			Rural		Urban		
Adverse health outcomes	n	%	n	%	HR (95% CI)[a]	n	%	n	%	HR (95% CI)[a]
Acquired hypothyroidism	1,467	4.3	4,027	4.3	0.96 (0.90, 1.02)	1,958	9.3	4,201	9.0	0.98 (0.93, 1.04)
Acute myocardial infarction	1,639	4.7	4,023	4.1	**1.11 (1.04, 1.18)**	1,950	9.0	4,127	8.4	**1.08 (1.02, 1.15)**
Alzheimer's disease	1,021	2.8	3,006	2.8	**0.92 (0.85, 0.99)**	1,742	7.6	4,033	7.5	**0.94 (0.88, 0.99)**
Alzheimer's disease and related disorders or senile dementia	2,581	7.2	6,721	6.6	1.00 (0.95, 1.05)	4,405	20.2	9,697	19.4	0.99 (0.95, 1.03)
Anemia	6,366	21.9	15,292	22.2	**0.94 (0.91, 0.97)**	5,497	37.4	10,052	37.4	0.98 (0.94, 1.02)
Asthma	870	2.5	2,602	2.7	0.94 (0.87, 1.02)	834	3.8	1,966	4.0	1.07 (0.98, 1.17)
Atrial fibrillation	3,325	10.4	8,486	10.4	0.99 (0.95, 1.04)	4,069	22.0	8,706	22.9	1.00 (0.96, 1.04)
Benign prostatic hyperplasia	2,143	8.2	5,219	8.6	1.03 (0.98, 1.09)	2,779	18.1	6,051	20.5	1.01 (0.96, 1.06)
Cataract	3,954	12.6	9,772	12.4	1.03 (0.99, 1.08)	3,668	21.9	7,616	23.1	1.04 (0.99, 1.09)
Chronic kidney disease	5,043	15.6	12,815	15.4	**0.94 (0.91, 0.98)**	6,747	36.7	14,348	38.0	**0.92 (0.89, 0.95)**
Chronic obstructive pulmonary disease and bronchiectasis	3,392	11.2	7,120	9.2	1.03 (0.99, 1.08)	3,167	17.8	5,481	15.0	**1.11 (1.05, 1.16)**
Depression	2,137	6.2	5,582	5.9	0.95 (0.90, 1.01)	2,545	12.1	5,924	12.8	**0.93 (0.88, 0.97)**
Diabetes	2,512	8.8	5,904	8.9	**0.93 (0.88, 0.98)**	2,040	12.6	3,914	12.9	**0.92 (0.87, 0.99)**
Glaucoma	1,078	3.1	3,956	4.3	0.94 (0.88, 1.01)	1,026	4.9	3,079	6.9	0.95 (0.88, 1.03)
Heart failure	3,871	11.8	9,093	10.5	1.03 (0.98, 1.07)	4,668	24.1	9,291	22.4	1.00 (0.97, 1.05)
Hip pelvic fracture	905	2.5	2,366	2.2	0.95 (0.88, 1.03)	1,315	5.8	2,571	4.8	**1.11 (1.03, 1.19)**
Hyperlipidemia	4,408	24.6	9,194	28.5	**0.94 (0.90, 0.98)**	2,286	37.0	3,477	41.2	0.95 (0.90, 1.02)
Hypertension	3,738	35.4	6,018	37.2	**0.93 (0.89, 0.98)**	1,695	52.2	2,174	53.1	0.99 (0.92, 1.07)
Ischemic heart disease	4,051	16.2	8,434	15.8	0.99 (0.95, 1.03)	3,181	25.2	5,498	25.1	1.05 (1.00, 1.11)
Osteoporosis	804	2.2	2,605	2.5	0.92 (0.85, 1.00)	999	4.4	2,408	4.6	0.99 (0.92, 1.07)
Rheumatoid arthritis/osteoarthritis	4,484	16.7	9,902	16.1	1.03 (0.99, 1.06)	3,649	27.3	6,457	27.1	**1.08 (1.03, 1.13)**
Stroke/transient ischemic attack	2,012	5.8	5,664	6.0	0.98 (0.93, 1.03)	2,270	10.8	5,168	11.2	1.00 (0.95, 1.06)

Note: Text with bold indicates statistical significance ($P < .05$).

Abbreviations: CI, confidence interval; HR, hazard ratio.

[a]Models adjusted for matched pair (diagnosis year and diagnosis age), race and ethnicity, baseline Charlson Comorbidity Index, cancer registry region, census-tract income, census-tract education, tobacco use disorder before cancer diagnosis. Urban residence was the referent group.

TABLE 4 Risks of death among prostate cancer patients in the SEER-Medicare data.

	All	All-cause deaths, n (%)	HR (95% CI)[a,b]	HR (95% CI)[c]
Residence				
Urban	109,176	57,991 (53.1)	Reference	Reference
Large rural city/town	18,134	10,167 (56.1)	**1.05 (1.02, 1.08)**	0.97 (0.94, 1.00)
Small and isolated small rural town	18,992	10,909 (57.4)	**1.08 (1.05, 1.11)**	0.98 (0.95, 1.01)

Note: Text with bold indicates statistical significance ($P < .05$).
Abbreviations: CI, confidence interval; HR, hazard ratio.
[a]Models adjusted for cancer diagnosis age, cancer diagnosis year, race and ethnicity, baseline Charlson Comorbidity Index, cancer stage, cancer registry, surgery, and radiotherapy.
[b]P for trend $< .001$.
[c]Additionally adjusted for census-tract education and census-tract income.

decreased risk of Alzheimer's disease, chronic kidney disease, diabetes, and depression compared to urban residence (Table 3). When education and income were removed from the adjustment, more diseases were positively associated with rural prostate cancer survivors at >1 to 5 years and 5 years after cancer diagnosis, such as heart failure and ischemic heart disease (Table S3). When we extended the upper limit for the rule-out diagnosis from 60 to 360 days, the associations remained similar (Table S4). However, an increased risk of COPD and bronchiectasis was observed, while lower risks of hyperlipidemia and hypertension were no longer evident at >1 to 5 years after cancer diagnosis (Table S4).

The risk of death was 1.05-fold higher among prostate cancer patients from large rural cities/towns and 1.08-fold higher among prostate cancer patients from a small and isolated rural town compared to urban prostate cancer patients, with a dose-response relation (P for trend $< .001$, Table 4). After additionally adjusting for education and income, no association was observed between death and residence. Interaction between race/ethnicity and rural residence on the risk of death were not observed. When we restricted the analysis to prostate cancer patients who enrolled in Medicaid, no association was observed between death and residence (data not shown).

DISCUSSION

In this cohort study, health disparities were observed among rural prostate cancer survivors compared to urban prostate cancer survivors. For example, the prevalence (4.3%) and incidence (for >1 to 5 years after cancer diagnosis: 4.7%; for >5 years after cancer diagnosis: 9.0%) of acute myocardial infarction were higher among rural prostate cancer survivors compared to urban prostate cancer survivors. The risk of death was very modest at 1.05-fold higher in large rural cities/towns and 1.08-fold higher in small and isolated rural towns compared to urban areas among prostate cancer patients. However, after adjusting for education and income, the risk of death was not associated with rural residence.

Consistent with the previous studies,[10,11] we observed that a higher percentage of rural prostate cancer survivors were diagnosed at a distant cancer stage compared to urban prostate cancer survivors.[3] Diagnosis at an advanced stage could be attributed to lower prostate cancer screening rates among rural men.[4] Additionally, a lower percentage of rural prostate cancer survivors received radiotherapy, possibly due to increased travel distances for care.[8,9] Mitigating these challenges for rural prostate cancer survivors could help minimize these disparities.

We observed that rural prostate cancer survivors had a higher prevalence of COPD and bronchiectasis at cancer diagnosis and a higher risk of COPD and bronchiectasis >5 years after cancer diagnosis. A similar association between rural residence and the risk of incident COPD was also observed among prostate cancer survivors in Utah in a previous study.[11] Rural men may have experienced a higher risk of COPD compared to urban men regardless of cancer status. Previous studies showed that the prevalence and mortality rates of COPD were higher among rural populations compared to urban residents.[25,26] Patients with COPD in rural areas were more likely to be uninsured and to face obstacles to care due to cost. Further research and surveillance on COPD among rural prostate cancer survivors are needed.

Rural prostate cancer survivors had a higher risk of incident hip pelvic fractures compared to urban prostate cancer patients >5 years after their cancer diagnosis in this study. ADT, commonly used to treat advanced prostate cancer, accelerates the decline in bone mineral density, increasing the risk of fractures.[27] A previous study showed that rural prostate cancer patients were less likely to undergo bone mineral density testing before receiving ADT.[28] Although we observed that rural prostate cancer survivors who received ADT had a higher percentage of developing hip pelvic fractures compared to rural prostate cancer survivors who did not receive ADT, we did not observe an association between rural residence and hip pelvic fractures when stratified by ADT. Our study may not have enough power to detect a difference if the association was weak among rural prostate cancer survivors who received ADT.

The relationship between rheumatoid arthritis and prostate cancer is complex. Rheumatoid arthritis might raise the risk of prostate cancer, possibly due to treatments for rheumatoid arthritis.[29–31] Conversely, a previous study found a link between ADT and new diagnoses of rheumatoid arthritis in older prostate cancer patients, attributed to the suppressive effects of ADT on the immune system.[17] In our study, rural prostate cancer survivors had a higher prevalence of rheumatoid arthritis/osteoarthritis at cancer diagnosis, as well as a higher risk of rheumatoid arthritis/osteoarthritis > 5 years after cancer diagnosis. However, an increased risk of rheumatoid arthritis/osteoarthritis among rural prostate cancer survivors compared to urban prostate cancer survivors was only observed among those who did not receive ADT. The risk of rheumatoid arthritis/osteoarthritis may be weaker in rural prostate cancer survivors with potentially lower ADT adherence or shorter ADT duration compared to urban prostate cancer survivors who received ADT. Further studies exploring the dosage and duration of ADT among rural prostate cancer survivors compared with those in urban areas, as well as distinguishing between rheumatoid arthritis and osteoarthritis, will be helpful to clarify this association.

Rural prostate cancer survivors had a higher prevalence of acute myocardial infarction at cancer diagnosis and a higher risk of incident acute myocardial infarction for >1 to 5 years and >5 years after cancer diagnosis. In our previous study in Utah, the percentage of incident acute myocardial infarction was higher among rural prostate cancer survivors compared to urban prostate cancer survivors.[10] However, an increased risk of acute myocardial infarction among rural prostate cancer survivors was not observed.[10] This discrepancy could be attributed to sample size limitations, the younger population, or the generally healthier population in Utah. In another study, older patients with acute myocardial infarction in rural hospitals had a higher risk of 30-day mortality compared to older patients in urban hospitals.[32]

Several adverse health outcomes had a lower prevalence among rural prostate cancer survivors compared to urban prostate cancer survivors, such as hyperlipidemia, benign prostatic hyperplasia, and glaucoma. A lower incidence among rural prostate cancer survivors was observed for Alzheimer's disease, chronic kidney disease, and diabetes. However, it is important to note that patients with these conditions may not be captured in our study if they did not seek medical care, as these conditions may not warrant immediate medical attention.

The risks of death were moderately higher for rural prostate cancer patients living in small, isolated rural towns and large rural cities/towns compared to urban prostate cancer patients, before accounting for census-tract education and income. Our previous finding showed that socioeconomic status (SES) is an important prognostic factor for death.[10] Addressing disparities in SES may lead to an improvement in the disparity in all-cause mortality. We did not observe an association between death and residence when we restricted the analyses to prostate cancer patients who enrolled in Medicaid. This implies that the risk of death was similar between older rural and urban prostate cancer patients with low income, although Medicaid enrollment from SEER may be underreported.[33]

The limitations of the study include the restriction to patients aged 66 years and older due to the use of SEER-Medicare data. Therefore, the results are not generalizable to younger rural prostate cancer patients, but 65.7% of prostate cancer patients are diagnosed at 65+ years of age.[34] Additionally, the results may not apply to rural prostate cancer patients with supplemental insurance plans, since we excluded Medicare beneficiaries with HMO to ensure capturing of events in Medicare claims. Events covered by supplemental insurance would be missed for these patients. Furthermore, within Medicare claims, the possibility of missed claims or inaccurate ICD coding exists. If the percentage of missed claims or inaccurate ICD coding is similar between rural and urban prostate cancer patients, there may be an underestimation of the risks of adverse health outcomes. Tobacco use disorder, alcohol use disorder, and obesity prior to cancer diagnosis were identified using ICD diagnosis codes and procedure codes in Medicare claims. These measures are expected to be incomplete with limited sensitivity, thus we expect an underestimation of their prevalence. Finally, we were unable to adjust for factors such as physical activity, which cannot be captured even with a proxy, as it would require self-report. We used ICD codes to capture tobacco use disorder as a proxy for tobacco smoking habit. Census-tract income and education reflect the average income and education of the patients' living areas. Individual-level education and income would be better for confounder adjustment.

Despite these limitations, we identified differences in the prevalence and incidence of adverse health outcomes among older rural prostate cancer survivors in comparison to older urban prostate cancer patients. Leveraging a robust cohort study design mitigated the influence of recall bias on our results. The utilization of SEER data provided a reliable source, encompassing cancer information such as cancer diagnosis, stage, and treatment. The utilization of longitudinal claims records from Medicare enabled us to comprehensively assess incident adverse health outcomes across a long follow-up period.

In conclusion, this study provides important results on the prevalent and incident adverse health outcomes among older rural prostate cancer survivors. Disparities were observed for rural prostate cancer patients compared to urban prostate cancer patients, particularly for acute myocardial infarction and risk of death, with education and income potentially contributing to these differences. Understanding the diseases that rural prostate cancer patients experience more frequently may help to tailor cancer survivorship care for rural residents. Further studies to understand the possible role of lower medical care-seeking behaviors in the lower prevalence of some diseases are needed for rural prostate cancer survivors.

ACKNOWLEDGMENTS

This research was supported by the National Cancer Institute of the National Institutes of Health (NIH) under Award Number R01CA244326. The content is solely the responsibility of the authors and does not represent the official views of the NIH. This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors. The authors acknowledge the efforts of the National Cancer Institute; the Office of Research, Development and Information, CMS; Information Man-

agement Services (IMS), Inc.; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database. The collection of cancer incidence data used in this study was supported by the California Department of Public Health as part of the statewide cancer reporting program mandated by California Health and Safety Code Section 103885; the National Cancer Institute's Surveillance, Epidemiology and End Results Program under contract HHSN261201000140C awarded to the Cancer Prevention Institute of California, contract HHSN261201000035C awarded to the University of Southern California, and contract HHSN261201000034C awarded to the Public Health Institute; and the Centers for Disease Control and Prevention's National Program of Cancer Registries, under agreement # U58DP003862-01 awarded to the California Department of Public Health. The ideas and opinions expressed herein are those of the author(s) and endorsement by the State of California Department of Public Health, the National Cancer Institute, and the Centers for Disease Control and Prevention or their Contractors and Subcontractors is not intended nor should be inferred. The authors acknowledge the efforts of the National Cancer Institute; the Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc.; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database. The computational resources used were partially funded by the NIH Shared Instrumentation Grant 1S10OD021644-01A1.

CONFLICT OF INTEREST STATEMENT

The authors report no conflict of interest.

DATA AVAILABILITY STATEMENT

The datasets used to conduct this study are available upon approval of a research protocol from the National Cancer Institute. Instructions for obtaining these data are available at https://healthcaredelivery.cancer.gov/seermedicare/obtain/.

ORCID

Chun-Pin Chang (Esther) PhD https://orcid.org/0000-0002-0878-997X

Mia Hashibe PhD https://orcid.org/0000-0002-6903-2049

REFERENCES

1. American Cancer Society. *Cancer Treatment & Survivorship Facts & Figures 2022–2024*. American Cancer Society; 2022.
2. American Cancer Society. Cancer Facts & Figures 2024. Atlanta, GA: American Cancer Society; 2024.
3. Zahnd WEJW, James AS, Izadi SR, et al. Utility and generalizability of multistate, population-based cancer registry data for rural cancer surveillance research in the United States. *Cancer Epidemiol Biomarkers Prev*. 2018;27(11):1252-1260.
4. Obertova Z, Brown C, Holmes M, Lawrenson R. Prostate cancer incidence and mortality in rural men–a systematic review of the literature. *Rural Remote Health*. 2012;12(2):2039.
5. Stolzenbach LF, Deuker M, Colla-Ruvolo C, et al. Differences between rural and urban prostate cancer patients. *World J Urol*. 2021;39(7):2507-2514.
6. Desch CEPL, Newschaffer CJ, Hillner BE, et al. Factors that determine the treatment for local and regional prostate cancer. *Med Care*. 1996;34(2):152-162.
7. Muralidhar V, Rose BS, Chen YW, Nezolosky MD, Nguyen PL. Association between travel distance and choice of treatment for prostate cancer: does geography reduce patient choice? *Int J Radiat Oncol Biol Phys*. 2016;96(2):313-317.
8. Baldwin LM, Andrilla CH, Porter MP, Rosenblatt RA, Patel S, Doescher MP. Treatment of early-stage prostate cancer among rural and urban patients. *Cancer*. 2013;119(16):3067-3075.
9. Skolarus TA, Zhang Y, Hollenbeck BK. Understanding fragmentation of prostate cancer survivorship care: implications for cost and quality. *Cancer*. 2012;118(11):2837-2845.
10. Nielsen S, O'Neil B, Chang CP, et al. Determining the association of rurality and cardiovascular disease among prostate cancer survivors. *Urol Oncol*. 2023;41(10):429. e415-429 e423.
11. Huang D, Chang CE, Newman M, et al. Adverse health outcomes among rural prostate cancer survivors: a population-based study. *Cancer Epidemiol*. 2023;86:102430.
12. Enewold L, Parsons H, Zhao L, et al. Updated overview of the SEER-Medicare data: enhanced content and applications. *J Natl Cancer Inst Monogr*. 2020;2020(55):3-13.
13. Warren JL, Benner S, Stevens J, et al. Development and evaluation of a process to link cancer patients in the SEER registries to national Medicaid enrollment data. *J Natl Cancer Inst Monogr*. 2020;2020(55):89-95.
14. Rural-Urban Commuting Area Codes. November 28, 2022. https://www.ers.usda.gov/data-products/rural-urban-commuting-area-codes.aspx
15. Rural Health Research Center. November 28, 2022. http://depts.washington.edu/uwruca/ruca-uses.php
16. Chronic Conditions Warehouse. 27 CCW Chronic Conditions Algorithms: MBSF_CC_{YYYY} File. 2022.
17. Yang DD, Krasnova A, Nead KT, et al. Androgen deprivation therapy and risk of rheumatoid arthritis in patients with localized prostate cancer. *Ann Oncol*. 2018;29(2):386-391.
18. Noone AM, Lund JL, Mariotto A, et al. Comparison of SEER treatment data with Medicare claims. *Med Care*. 2016;54(9):e55-64.
19. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383.
20. Chronic Conditions Warehouse. Other Chronic Conditions Algorithms: MBSF_OTH CC_{YYYY} File. 2021.
21. Austin PC, Fine JP. Practical recommendations for reporting Fine-Gray model analyses for competing risk data. *Stat Med*. 2017;36(27):4391-4400.
22. Hernan MA, Hernandez-Diaz S, Werler MM, Mitchell AA. Causal knowledge as a prerequisite for confounding evaluation: an application to birth defects epidemiology. *Am J Epidemiol*. 2002;155(2):176-184.
23. Lambert PC, Royston P. Further development of flexible parametric models for survival analysis. *Stata J*. 2009;9(2):265-290.
24. Orsini N. Review of flexible parametric survival analysis using Stata: beyond the Cox model by Patrick Royston and Paul C. Lambert. *Stata J*. 2013;13(1):212-216.
25. Ruvuna L, Sood A. Epidemiology of chronic obstructive pulmonary disease. *Clin Chest Med*. 2020;41(3):315-327.
26. Gaffney AW, Hawks L, White AC, et al. Health care disparities across the urban-rural divide: a national study of individuals with COPD. *J Rural Health*. 2022;38(1):207-216.
27. Shahinian VB, Kuo YF, Freeman JL, Goodwin JS. Risk of fracture after androgen deprivation for prostate cancer. *N Engl J Med*. 2005;352(2):154-164.
28. Hu J, Aprikian AG, Vanhuyse M, Dragomir A. Contemporary population-based analysis of bone mineral density testing in men

initiating androgen deprivation therapy for prostate cancer. *J Natl Compr Canc Netw*. 2020;18(10):1374-1381.
29. Beydon M, Pinto S, De Rycke Y, et al. Risk of cancer for patients with rheumatoid arthritis versus general population: a national claims database cohort study. *Lancet Reg Health Eur*. 2023;35:100768.
30. Wheeler AM, Roul P, Yang Y, et al. Risk of prostate cancer in US veterans with rheumatoid arthritis. *Arthritis Care Res (Hoboken)*. 2023;75(4):785-792.
31. Ou J, Zou L, Wu Y, et al. Causal inference between rheumatoid arthritis and prostate cancer. *Clin Exp Med*. 2023;23(8):4681-4694.
32. Loccoh EC, Joynt Maddox KE, Wang Y, Kazi DS, Yeh RW, Wadhera RK. Rural-urban disparities in outcomes of myocardial infarction, heart failure, and stroke in the United States. *J Am Coll Cardiol*. 2022;79(3):267-279.
33. Chan JK, Gomez SL, O'Malley CD, Perkins CI, Clarke CA. Validity of cancer registry Medicaid status against enrollment files: implications for population-based studies of cancer outcomes. *Med Care*. 2006;44(10):952-955.
34. U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; 2024. https://www.cdc.gov/cancer/dataviz

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Chang (Esther) C-P, Huang D, Lloyd S, Henry NL, O'Neil B, Hashibe M. Risks of adverse health outcomes among older rural prostate cancer survivors in the SEER-Medicare data. *J Rural Health*. 2025;41:e70029. https://doi.org/10.1111/jrh.70029