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The rural disadvantage – prostate cancer outcomes of rural and urban patients over 25 years

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Abstract

Purpose: Prostate cancer is a common malignancy among men, with disparities based on the geographic location. This study aims to evaluate long-term trends in prostate cancer outcomes among rural and urban populations within a universal health care system, providing insights into the persistent disparities in cancer-specific mortality despite supposed equal access to medical coverage.

Methods: A retrospective cohort study was conducted using data from the Alberta Cancer Registry (January 1, 1999 to December 31, 2022) and the Alberta Prostate Cancer Research Initiative (APCaRI) (July 1, 2014 to June 7, 2024). There were 45,602,119 person-years from the Alberta Cancer Registry and 8932 men from APCaRI. The exposure was the place of residence, categorized as urban or rural, based on postal codes at the time of diagnosis and death. The primary outcome was prostate cancer-specific mortality.

Findings: Rural men were diagnosed at an older age (66.7 vs. 68.9, $p<0.001$) and had higher age-adjusted prostate cancer-specific mortality compared to urban men (52.0 vs. 37.6 deaths per 100,000, $p<0.001$). Though both groups showed improvements over time, rural areas consistently had higher age-adjusted mortality rates. Despite a 38% relative increase in prostate cancer specific mortality, rural patients had minimal, though statistically significant differences in PSA (9% vs. 11% >20, $p = 0.008$), stage (40% vs. 46% T2–T4, $p<0.001$) and Gleason Grade Group (11% vs. 14% ≥4, $p<0.001$) at diagnosis.

Conclusions: The study reveals that rural men experienced significantly worse prostate cancer outcomes compared to urban men. These findings highlight the need for targeted health care interventions to improve access to care in rural areas.

KEYWORDS
disparities in health, prostate cancer, rural, urban

INTRODUCTION

Prostate cancer remains one of the most prevalent malignancies among men worldwide, with significant variability in incidence and outcomes based on geographic, socioeconomic, and health care access factors.[1] As health care systems strive to improve patient outcomes, understanding these disparities is essential for developing targeted interventions and policies.

Urban and rural environments present distinct challenges and opportunities in health care delivery, impacting the diagnosis, treatment, and overall management of prostate cancer. Urban areas often exhibit higher concentrations of medical facilities, specialized health care providers, and advanced diagnostic and treatment technologies. In contrast, rural areas frequently face limitations such as reduced access to health care services, fewer specialists, and longer travel distances to medical centers.[2] These differences can contribute to disparities in prostate cancer outcomes, including variations in disease stage at diagnosis, treatment modalities, and overall survival rates.[3,4]

Previous research has identified that rural patients often experience delays in diagnosis and treatment, which can result in more advanced disease at presentation and poorer outcomes.[3,5–7] Moreover, socioeconomic factors, such as income level and education, which often vary between urban and rural populations, play a significant role in influencing health behaviors and access to care.[2,8–10] Despite these recognized disparities, there remains a need for comprehensive analyses that directly compare prostate cancer outcomes between urban and rural settings, especially in a universal health care system.

Although the rural disadvantage in cancer outcomes is well-documented, few studies have systematically examined how these disparities persist or evolve over time in a universal health care setting. Our study aimed to address the Canadian knowledge gap by comparing prostate cancer mortality rates between rural and urban patients in Alberta, Canada, using data from the Alberta Cancer Registry spanning from 1999 to 2022. By leveraging a large, diverse cohort this research aims to elucidate the extent and nature of disparities in prostate cancer diagnosis, treatment, and survival. Understanding these differences is crucial for informing health care policy, resource allocation, and the development of targeted interventions aimed at reducing disparities and improving outcomes for all prostate cancer patients, regardless of their geographic location.

MATERIALS AND METHODS

Patients

A total of 8932 patients were included from the Alberta Prostate Cancer Research Initiative (APCaRI), a prospective cohort collected from the two primary urban urology referral centers in Alberta: the University of Alberta and the University of Calgary. All men diagnosed with prostate cancer and assessed by specialists at these two sites were eligible for inclusion in APCaRI, provided they gave written informed consent. This study included all patients with prostate cancer enrolled from July 1, 2014 to June 7, 2024. At the time of enrollment, patients' home addresses were recorded, and they are followed prospectively at least every 6 months from the time of prostate cancer diagnosis. The APCaRI cohort has been previously described.[11] Due to the relatively short follow-up period for these patients in the APCaRI cohort, long-term prostate cancer-specific mortality was assessed using data collected through Cancer Care Alberta.[12] Cancer Care Alberta collects data on all persons in the province of Alberta, and tracks age of diagnosis, age of death and cancer-specific mortality for many different types of cancers. Rural areas are defined using the Canadian governments definition as "all territory lying outside population centers" and determined using the second character of postal codes in this study. A population center as defined by government Canada "has a population of at least 1000 and a population density of 400 persons or more per square kilometer, based on population counts from the current Census of Population".[13] This study received ethical approval by the relevant health ethics board.

Outcomes

The primary outcome of this study was prostate cancer specific mortality stratified by place of residence (urban vs. rural). Secondary outcomes in this study include age at diagnosis, PSA at diagnosis, initial treatment modality, time from diagnosis to initial treatment, stage, and age at death as well as metastasis free and overall survival.

Statistical Analysis

Mean values and standard deviations are reported for continuous variables and categorical variables are reported as frequencies (%). ANOVA and *T* tests were used to compare continuous variables where appropriate, and chi-square test was used to compare the categorical variables. SPSS version 29 (IBM Corp. Released 2023. IBM SPSS Statistics for Windows, Version 29.0.2.0: IBM Corp) was used for all statistical analysis. A p-value <0.05 was used for statistical significance and all hypothesis tests were based on 2-sided tests. The STROBE reporting guidelines were followed for cohort studies.

RESULTS

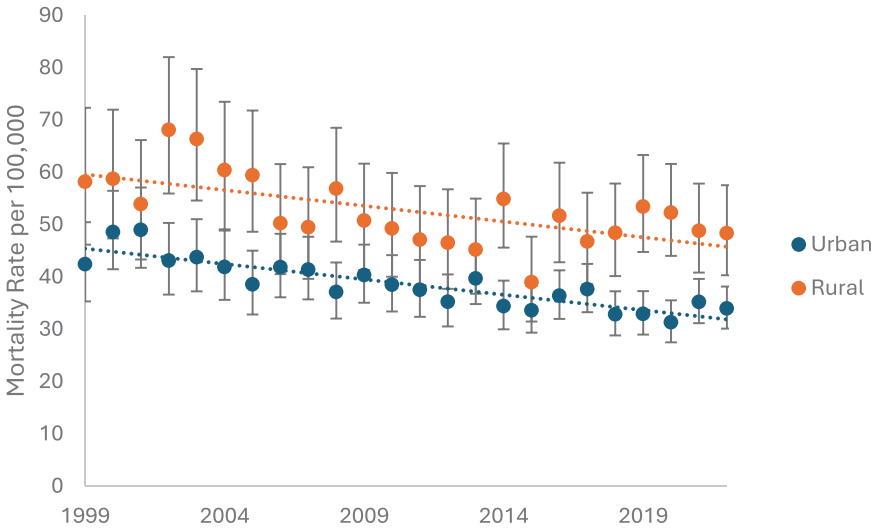
From 1999 to 2022, there were 10,180,230 and 35,421,889 person-years of data available for men living in rural and urban settings, respectively (Table 1). Men living in rural areas were diagnosed with prostate cancer at a significantly later age (66.7 vs. 68.9, $p<0.001$). There was significant difference in age-adjusted mortality rate from prostate cancer for men in rural areas when compared to urban areas (52.0 vs. 37.6 deaths per 100,000, $p<0.001$). In both rural and urban settings, the age-adjusted mortality rate decreased from 1999 to 2022, with urban remaining lower than rural for the duration of the study period (Figure 1). There was no significant difference in the change of

TABLE 1 Cancer Care Alberta prostate cancer demographics and prostate cancer specific survival.

	Urban (n = 35,421,889)	Rural (n = 10,180,230)	p-value
Age at diagnosis, mean (SD)	66.7 (9.8)	68.9 (9.6)	**<0.001**
Age at death due to prostate cancer, mean (SD)	78.6 (9.9)	79.0 (9.5)	**<0.001**
Age-Adjusted Mortality Rate (95% CI)	37.6 (36.5-38.6)	52.0 (50.0-54.0)	**<0.001**

Abbreviations: CI, confidence interval; SD, standard deviation.

FIGURE 1 Age-adjusted prostate cancer-specific mortality rates in Alberta from 1999 to 2022 stratified by living in a rural or urban setting.



mortality rate per year between urban or rural settings. Despite the improvements in prostate cancer-specific survival seen in both rural and urban men, rural men in the year 2022 still had worse age-adjusted prostate cancer-specific mortality than urban men had in 1999.

The APCaRI cohort was then used to examine the differences in patient characteristics at time of prostate cancer diagnosis. Patient demographics and tumor characteristics at the time of prostate cancer diagnosis are shown in Table 2. In the APCaRI cohort, there was no significant difference in age of diagnosis (64.5 vs. 64.8, $p = 0.22$), Charlson Comorbidity Index (91% vs. 93% ≥2, $p = 0.12$) or family history of prostate cancer (27% vs. 31%, $p = 0.08$). Despite being from rural communities, there was a similar time from diagnosis to treatment for rural men when compared to men from urban areas (11.3 vs. 11.0 weeks, $p = 0.88$).

There was a significant difference in self-identified ethnicity between the two groups, with a higher proportion (1% vs. 4%) identifying themselves as Indigenous in the rural cohort, and a higher proportion identifying as Asian (4% vs. <1%) and Black (4% vs. <1%) in the urban cohort. Rural men were diagnosed with a higher Gleason Grade Group (11% vs. 14% ≥GG4, $p = 0.003$), higher clinical stage and higher PSA level at diagnosis (9% vs. 11% PSA >20, $p = 0.008$). Men from rural areas also undergo a different initial treatment modality, with a lower proportion undergoing active surveillance (30% vs. 28%), and radical prostatectomy (29% vs. 25%), with a subsequent increase in primary androgen deprivation therapy (ADT) (5% vs. 8%) and radiation (34% vs. 36%) (p<0.001). When adjusting for prostate cancer risk categories, intermediate risk men continued to show disparities in treatment modality, with a higher proportion of urban men undergoing radical prostatectomy (42% vs. 33%) and active surveillance (17% vs. 14%) and a lower proportion undergoing radiation therapy (35% vs. 40%) and ADT (3% vs. 6%) (p<0.001).[14]

Discussion and Interpretation

In this study of all men in Alberta from 1999 to 2022, we found that there was a significantly higher rate of age-adjusted prostate cancer-specific mortality for men in rural areas when compared with men from urban areas. At diagnosis rural men were similar age, had similar Charlson comorbidity indices and family history of prostate cancer, and had similar time from diagnosis to treatment. Rural men did however have significantly different ethnicity, higher PSA at diagnosis, higher Clinical stage and Gleason Grade groups, with associated differences in initial treatment, with higher rates of radiation and primary ADT when compared to urban men. Both rural and urban men saw a significant decrease in age-adjusted prostate cancer-specific mortality over this time, though at similar rates.

This discrepancy in cancer-specific survival underscores the multifaceted challenges faced by rural populations, including socioeconomic factors, health care access, access to screening, and differences in treatment modalities and follow-up care.[2,4–7] Current Canadian and international prostate cancer guidelines often do not account for the unique challenges faced by rural patients, making it difficult to adhere to them exactly in these areas.[14–16] Rural health care settings frequently lack the specialized medical facilities, advanced diagnostic technologies, and access to specialized care that are more readily

TABLE 2 Patient and tumor characteristics of the Alberta Prostate Cancer Research Initiative (APCaRI) cohort.

	Urban ($n = 7917$)	Rural ($n = 1015$)	*p*-value
Age, mean (SD)	64.5 (7.8)	64.8 (7.7)	0.22
Charlson Comorbidity index, No. (%)			0.12
0	66 (1)	8 (1)	
1	647 (8)	64 (6)	
≥2	7204 (91)	943 (93)	
Ethnicity, No. (%)			**<0.001**
Asian	390 (4)	4 (<1)	
Black	191 (4)	4 (<1)	
Caucasian	5189 (66)	710 (70)	
Indigenous	71 (1)	43 (4)	
Hispanic	48 (1)	0 (0)	
Middle Eastern	13 (<1)	1 (<1)	
Multiracial	8 (<1)	0 (0)	
Other/Unknown	2007 (25)	253 (25)	
Family history of prostate cancer, No. (%)	2135 (27)	317 (31)	0.08
PSA, No. (%), ng/mL			**0.008**
<10	5010 (69)	575 (64)	
10–20	1615 (22)	230 (25)	
>20	681 (9)	101 (11)	
Clinical Stage, No. (%)			**<0.001**
Tx	199 (3)	46 (5)	
T1	4173 (53)	450 (44)	
T2	2711 (34)	388 (38)	
T3/4	471 (6)	83 (8)	
TanyN1	126 (2)	15 (1)	
TanyNanyM1	237 (3)	33 (3)	
Gleason Grade Group			**0.003**
1	2713 (35)	328 (33)	
2	3184 (41)	409 (41)	
3	1130 (14)	130 (13)	
4	297 (4)	38 (4)	
5	518 (7)	99 (10)	
Time from diagnosis to treatment, median (IQR), weeks	11.3 (4.4–19.4)	11.0 (4.9–19.1)	0.88
Initial Treatment			**<0.001**
Active Surveillance	2337 (30)	280 (28)	
Radical Prostatectomy	2295 (29)	252 (25)	
Radiation	2661 (34)	366 (36)	
Primary ADT	425 (5)	83 (8)	
Cryoablation	196 (2)	34 (3)	
Follow up duration, median (IQR), months	39.7 (31.9–78.1)	39.8 (31.7–78.6)	0.79

Abbreviations: ADT, androgen deprivation therapy; IQR, interquartile range; PSA, prostate specific antigen; SD, standard deviation.‘

available in urban centers.[2,7] Consequently, adhering to standardized guidelines can be challenging, leading to delays in diagnosis and treatment, and ultimately contributing to poorer outcomes for rural prostate cancer patients. This is seen in our study where men in rural areas are diagnosed at significantly later age, with correspondingly higher stage and grade of disease.

The higher age-adjusted mortality rate from prostate cancer in rural areas emphasizes the need for targeted interventions to address these disparities. This finding is particularly alarming as it suggests that the impact of rural residence on prostate cancer outcomes persists over an extended period. The observation that both rural and urban areas experienced a decrease in age-adjusted mortality rates from 1999 to 2022, with urban areas consistently maintaining lower rates, indicates that while overall prostate cancer care may be improving, the urban-rural gap remains a persistent challenge. This trend highlights the importance of not only improving overall prostate cancer care but also developing strategies to specifically address the unique needs and challenges of rural populations. This study also found that the effect of rurality on prostate cancer mortality was higher than a recent study using the SEER database looking at several types of cancer which found that 5-year cancer mortality for rural men was 33.9% compared to 31.56% for urban men.[3] The effect of rurality does appear to be less than the effect of racial disparities, which can be as high as 2–3 times for Black men when compared to white men.[17]

The significant difference in self-identified ethnicity between urban and rural cohorts, with a higher proportion of Indigenous men in rural areas, suggests that cultural and socioeconomic factors may also play a crucial role in these disparities. Indigenous populations often experience unique barriers to health care, including historical and systemic inequities, which may contribute to the observed differences in prostate cancer outcomes.[9] This finding underscores the importance of culturally sensitive and tailored health care interventions that address the specific needs of diverse rural populations. Moreover, the higher proportion of Asian and Black individuals in urban areas may indicate disparities in health care access and outcomes within these populations that warrant further investigation.[8,18,19]

There are notable differences in initial treatments between rural and urban men with prostate cancer in Alberta. These differences in treatment approaches may reflect several factors unique to rural health care settings.[2] The lower rates of active surveillance and radical prostatectomy among rural men could be attributed to limited access to specialized urological care and advanced surgical facilities in rural areas. Additionally, the logistical challenges of frequent follow-up visits required for active surveillance may make this option less feasible for rural patients who live far from medical centers. The higher utilization of primary ADT among rural men might be due to the relative ease of administering this treatment in community settings, reducing the need for travel to urban centers. However, it’s important to note that while primary ADT may be more convenient for rural patients, it may not represent the optimal approach for long-term outcomes, particularly for localized diseases. Furthermore, even when adjusted for risk groups, men in rural areas underwent radiation therapy at a higher rate than urban men. Radiation therapy is more readily avail-

able in rural areas in Alberta, with regional centers such as Grande Prairie offering radiation treatments, whereas radical prostatectomy is only offered in the major urban areas in Alberta. These findings highlight the need for improved access to comprehensive prostate cancer care options in rural areas, as well as the importance of patient education and shared decision-making to ensure that treatment choices are based on both clinical factors and patient preferences, rather than solely on geographical constraints.

This study has several limitations that should be considered when interpreting the results. The APCaRI Registry was designed as an opt-in study, requiring participants to provide informed consent, which may have led to selection bias and overrepresentation of patients who are more health-conscious or have better access to health care services. Furthermore, the APCaRI cohort underrepresents rural men, as patient recruitment primarily occurs in urban centers such as Edmonton and Calgary. The similarities of time to treatment between rural and urban men is limited as patients have already met the urologist at the time of their appointments and does not include the wait time prior to urologist assessment. The APCaRI Registry began collecting data in 2014, providing a relatively short (~3.5-year median) follow-up period for assessing long-term outcomes, we incorporated data from Cancer Care Alberta for long-term prostate cancer-specific mortality, which may introduce inconsistencies in data collection methods and quality between the two sources. A key limitation of the Cancer Care Alberta data is the inability to control important clinical parameters such as stage at diagnosis and treatment, precluding a more detailed analysis of these potentially confounding factors. Another limitation is that our data does not provide information on screening rates and access to screening which would almost certainly play a role in the later age, and stage of diagnosis of prostate cancer experienced by rural men.

CONCLUSION

This study demonstrates that rural men experience significantly poorer prostate cancer outcomes over an extended period compared to their urban counterparts. These findings underscore the need for targeted interventions, improved screening and improved health care access in rural areas to address this disparity and enhance the long-term prognosis for rural men diagnosed with prostate cancer.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interests.

ETHICS STATEMENT

This study protocol was approved by the Health Research Ethics Board of Alberta (HREBA.CC-23-0100).

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