Received: 9 January 2023 | Revised: 22 February 2023 | Accepted: 24 February 2023

DOI: 10.1002/cncr.34812

ORIGINAL ARTICLE

Disparities in prostate cancer screening, diagnoses, management, and outcomes between Indigenous and non-Indigenous men in a universal health care system

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Funding information
University Hospital Foundation; Alberta Cancer Foundation; The Bird Dogs

Abstract

Background: Indigenous Peoples have higher morbidity rates and lower life expectancies than non-Indigenous Canadians. Identification of disparities between Indigenous and non-Indigenous men regarding prostate cancer (PCa) screening, diagnoses, management, and outcomes was sought.

Methods: An observational cohort of men diagnosed with PCa between June 2014 and October 2022 was studied. Men were prospectively enrolled in the province-

wide Alberta Prostate Cancer Research Initiative. The primary outcomes were tumor characteristics (stage, grade, and prostate-specific antigen [PSA]) at diagnosis. Secondary outcomes were PSA testing rates, time from diagnosis to treatment, treatment modality, and metastasis-free, cancer-specific, and overall survivals.

Results: Examination of 1,444,974 men for whom aggregate PSA testing data were available was performed. Men in Indigenous communities were less likely to have PSA testing performed than men outside of Indigenous communities (32 vs. 46 PSA tests per 100 men [aged 50–70 years] within 1 year; $p < .001$). Among 6049 men diagnosed with PCa, Indigenous men had higher risk disease characteristics: a higher proportion of Indigenous men had PSA ≥ 10 ng/mL (48% vs. 30%; $p < .01$), TNM stage ≥ T2 (65% vs. 47%; $p < .01$), and Gleason grade group ≥ 2 (79% vs. 64%; $p < .01$) compared to non-Indigenous men. With a median follow-up of 40 months (interquartile range, 25–65 months), Indigenous men were at higher risk of developing PCa metastases (hazard ratio, 2.3; 95% CI, 1.2–4.2; $p < .01$) than non-Indigenous men.

Conclusions: Despite receiving care in a universal health care system, Indigenous men were less likely to receive PSA testing and more likely to be diagnosed with aggressive tumors and develop PCa metastases than non-Indigenous men.

KEYWORDS
disparities in health, Indigenous, outcomes, prostate cancer, screening

INTRODUCTION

Prostate cancer (PCa) is the most common internal malignancy and third most common cause of death in Canadian men.[1] Retrospective evidence suggests that PCa detection occurs less often and with worse overall survival in Indigenous men than non-Indigenous men.[2,3] This is in keeping with Indigenous Peoples in Canada having higher morbidity rates and a lower life expectancy than non-Indigenous Canadians.[4]

Equal access to health care services is critical for reducing social inequalities in health. Despite an equal access health care model in Canada, Indigenous Peoples describe access to health services as difficult and limited.[5] Three frequently reported barriers to health care access among Indigenous Peoples in Canada are substandard quality of care, long wait times, and experiences of racism and discrimination.[6]

In this study, we sought to identify disparities in PCa screening, diagnoses, management, and outcomes between Indigenous and non-Indigenous men.

MATERIALS AND METHODS

PCa characteristics and outcomes

To assess differences in PCa characteristics at diagnosis, treatment approaches, and outcomes between Indigenous and non-Indigenous men, we performed a prospective cohort study by using data collected within the Alberta Prostate Cancer Research Initiative from the two centralized urology referral centers in Alberta (University of Alberta and University of Calgary) between June 2014 and October 2022.[7] The study was approved by the Health Research Ethics Board of Alberta (HREBA.CC-14-0085). The study followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting guideline.

All men assessed by PCa specialists (i.e., urologists, radiation oncologists, and medical oncologists) at these two centers for diagnostic workup and management of PCa were potentially eligible. Men were included if they received a diagnosis of PCa. Ethnicity was determined by self-identification at study entry. Men were prospectively followed at least every 6 months after PCa diagnosis.

The primary outcomes were tumor characteristics (stage, grade, and prostate-specific antigen [PSA]) at diagnosis. Secondary outcomes were PCa screening rates, time from diagnosis to treatment, and treatment modality, as well as metastasis-free, cancer-specific, and overall survivals.

PCa screening by PSA

To assess differences in PSA screening, we examined data from a provincial data repository managed by Alberta Precision Laboratories based on a human research ethics board–approved protocol (HREBA.CC-22-0068). We obtained aggregate PSA testing rates by postal

code (between April 2017 and March 2021) across the Province of Alberta. In accordance with Canadian Urology Association guidelines, PSA testing rates were analyzed for men between the ages of 50 and 70 years, in whom PCa screening is recommended.[8] Postal codes with fewer than 10 men between the ages of 50 and 70 years were excluded to minimize outliers. Indigenous communities (First Nations and Métis settlements) in Treaties 6, 7, and 8 with data available are listed in Table S1. Urban versus rural geographical localization was determined via the postal code, given that the second character in the code denotes a rural region if set as 0 and urban if set as 1–9.[9] PSA testing heatmaps were created with Maptive Software (San Francisco, California). With the use of the heat mapping tool with a radius of 10%, opacity of 80%, and intensity threshold of 20% and including the dissipate option, all data points were plotted separately stratified by postal codes of Indigenous communities versus all other postal codes.

Statistical analyses

Tests, including *t*-tests, X^2 tests (or Fisher exact test when necessary), and Wilcoxon rank sum or median tests, were used as appropriate. A Welch test for unequal variance was used to compare aggregate PSA testing data. Survival analyses for metastasis-free survival, PCa-specific survival, and overall survival were conducted and Kaplan–Meier estimates were calculated. A log-rank test was used to compare the Kaplan–Meier curves. A Cox proportional hazards regression model (with age, ethnicity, PSA, and family history of PCa as covariates) was used to compare the Indigenous group to the non-Indigenous group for metastasis-free survival. The hazard ratio (HR) and the corresponding 95% confidence intervals (CIs) were reported. SPSS (SPSS Statistics for Windows, v. 25.0; IBM Corporation, Armonk, New York) was used to conduct all statistical analysis. Statistical significance was defined as two-sided $p < .05$.

RESULTS

A cohort of 6049 men was diagnosed with PCa and prospectively followed between June 2014 and October 2022. Patient and tumor characteristics at the time of PCa diagnosis are shown in Table 1. There were no differences in age or Charlson comorbidity index between groups. At diagnosis, a higher proportion of Indigenous men had PSA ≥ 10 ng/mL (48% vs. 30%; $p < .01$) and TNM stage ≥ T2 (65% vs. 47%; $p < .01$) and were more likely to have Gleason grade group ≥ 2 (79% vs. 64%; $p < .01$) compared to non-Indigenous men. There was no difference in time from diagnosis to treatment initiation between groups. PCa treatment selection differed between groups, with the largest proportion of Indigenous men choosing radiation therapy (55%) compared to most non-Indigenous men choosing radical prostatectomy (36%) ($p < .01$).

Indigenous men were at a higher risk of developing PCa metastases (HR, 2.3; 95% CI, 1.2–4.2; $p < .01$) than non-Indigenous men (Figure 1). At this intermediate duration of follow-up, there were no differences in PCa-specific survival (HR, 3.0; 95% CI, 0.9–9.4; $p = .07$) or overall survival (HR, 1.2; 95% CI, 0.4–3.1; $p = .76$).

PSA testing data from 1,444,974 men were analyzed (Table 2). Among men aged 50–70 years, there were 13,074 from Indigenous communities and 368,286 from other regions. Men in Indigenous communities were less likely to have PSA testing performed than men outside of Indigenous communities at all potential time intervals of PSA testing according to Canadian guidelines (within 1 year: 32 vs. 46 per 100 men, $p < .001$; within 2 years: 45 vs. 70 per 100 men, $p < .001$; within 4 years: 72 vs. 117 per 100 men, $p < .001$). A heatmap of PSA testing in Indigenous communities versus other communities is shown in Figure 2. To account for a rural versus urban bias, rural Indigenous communities were also compared to all other rural regions, which also showed similarly reduced rates of PSA testing in Indigenous communities at all time intervals (within 1 year: 32 vs. 45 per 100 men, $p < .001$; within 2 years: 45 vs. 69 per 100 men, $p < .001$; within 4 years: 72 vs. 116 per 100 men, $p < .001$).

DISCUSSION

In this multicenter prospective cohort study of 6049 men with PCa, Indigenous men were more likely to be diagnosed with higher stage and higher grade tumors as well as more likely to develop PCa metastases than non-Indigenous men.

Recent studies of PCa outcomes in visible minorities such as African American men show that although African American men have higher PCa-specific mortality, this association dissolves after adjusting for socioeconomic status in a country with private health care systems.[10] Similarly, in a publicly funded (Canadian) health care system, this association with Black ethnicity is nonexistent.[11] Conversely, this study shows that despite the presence of a universal public health care system, Indigenous men experience worse PCa diagnoses and outcomes. Furthermore, Indigenous Peoples comprise 5.1% of the population in the study catchment area; however, only 1.4% of the cohort contains Indigenous men. Although this may be because of a younger average age of Indigenous men in Alberta (average age is 30 vs. 38 years for non-Indigenous men; only 2.8% of men in Alberta aged at least 65 years are Indigenous),[12] it may alternatively highlight barriers in access to care, which may be a cause of the differences in outcomes, given that all men referred for PCa diagnosis and management were eligible for this study. Furthermore, access to primary care physicians and screening programs for multiple diseases may be limited for Indigenous men.

It is unclear whether differences in PCa diagnoses and outcomes are due to disparities in PCa screening or whether is there an underlying difference in tumor biology between Indigenous and non-Indigenous men. In the present study there was no difference in age at diagnosis; however, a greater proportion of Indigenous men

TABLE 1 Patient, tumor, and treatment characteristics between Indigenous and non-Indigenous men diagnosed with prostate cancer.

Characteristic	Indigenous (n = 82)	Non-Indigenous (n = 5967)	p value
Age at diagnosis, mean (SD), years	64.2 (6.8)	64.5 (7.7)	.75
BMI, median (IQR), kg/m^2	28.4 (26.5–32.0)	27.7 (25.1–31.2)	.04
Charlson comorbidity index, No. (%)			.60
0	0 (0)	50 (1)	
1	5 (6)	461 (8)	
≥2	77 (94)	5455 (91)	
Ethnicity, No. (%)			<.01
Asian	0 (0)	342 (6)	
Black	0 (0)	157 (3)	
Caribbean	0 (0)	3 (<1)	
Caucasian	0 (0)	5359 (90)	
First Nations	62 (76)	0 (0)	
Hispanic	0 (0)	48 (1)	
Inuit	0 (0)	0 (0)	
Métis	20 (24)	0 (0)	
Middle Eastern	0 (0)	10 (<1)	
Multiracial	0 (0)	10 (<1)	
Other/unknown	0 (0)	38 (<1)	
Family history of prostate cancer, No. (%)	30 (37)	2065 (35)	.71
PSA, No. (%), ng/mL			<.01
<10	39 (51)	3685 (70)	
10–20	23 (30)	1125 (21)	
>20	14 (18)	487 (9)	
Clinical stage, No. (%)			<.01
T1	26 (34)	2987 (53)	
T2	33 (43)	2070 (37)	
T3/4	9 (12)	356 (6)	
TanyN1	4 (5)	74 (1)	
TanyNanyM1	4 (5)	144 (3)	
Gleason grade group, No. (%)			<.01
1	17 (21)	2100 (36)	
≥2	64 (79)	3789 (64)	
Time from diagnosis to treatment, median (IQR), weeks	9.5 (4.0–15.0)	11.0 (5.0–18.0)	.39
Initial treatment choice, No. (%)			<.01
Active surveillance	10 (13)	1127 (21)	
Prostatectomy	16 (21)	1920 (36)	
Radiation	42 (55)	1776 (23)	
Primary ADT	8 (10)	310 (6)	
Cryoablation	1 (1)	177 (3)	
Follow-up duration, median (IQR), months	37.0 (19.3–64.8)	40.0 (29.0–65.0)	.15

Abbreviations: ADT, androgen-deprivation therapy; BMI, body mass index; IQR, interquartile range; PSA prostate-specific antigen.

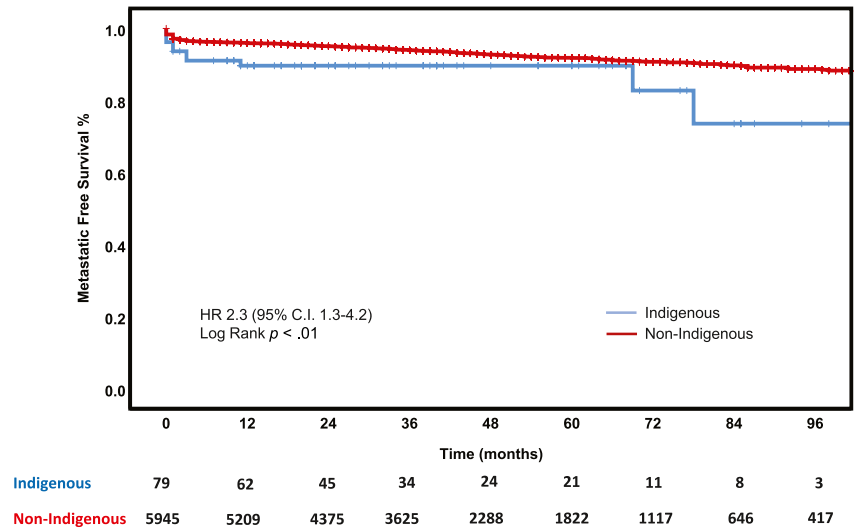

FIGURE 1 Prostate cancer metastasis-free survival stratified by Indigenous men (blue) versus non-Indigenous men (red). HR indicates hazard ratio.

TABLE 2 PSA testing rates for men in Indigenous and other communities.

	Indigenous communities	Other communities	*p* value
Total No. of male sex	59,205	1,385,769	
No. of male sex between ages 50 and 70 years	13,074	368,286	
Total No. of PSA tests performed within 1 year	4359	164,700	
Total No. of PSA tests performed within 2 years	6270	250,118	
Total No. of PSA tests performed within 4 years	10,037	418,428	
PSA tests per 100 males aged 50–70 years per postal code within 1 year, mean (SE)	32 (1)	46 (0.1)	<.001
PSA tests per 100 males aged 50–70 years per postal code within 2 years, mean (SE)	45 (2)	70 (0.3)	<.001
PSA tests per 100 males aged 50–70 years per postal code within 4 years, mean (SE)	72 (4)	117 (0.5)	<.001

Abbreviations: PSA, prostate-specific antigen; SE, standard error.

had PSA ≥ 10 ng/mL at diagnosis, which suggests that there may be differences in access to and rates of PCa screening. The PSA testing data support this hypothesis with an approximately 50% relative reduction in PSA testing for men in Indigenous communities. Importantly, the rural geography of many Indigenous communities did not account for the differences in PSA testing rates. Therefore, lower rates of PCa screening may contribute to more aggressive disease at presentation. In addition, because higher risk tumors are associated with worse oncologic outcomes, this may explain why metastasis-free survival was reduced among Indigenous men.[13] To further address this likely multifactorial discrepancy, further biological studies such as genomic analyses are needed to determine whether there are also differences in tumor biology.

Treatment choices differed between Indigenous and non-Indigenous men with PCa. A higher proportion of Indigenous men underwent primary radiation therapy whereas non-Indigenous men most often selected radical prostatectomy. It is not clear why treatment choices differed between groups; however, differences in body mass index as well as tumor stage and grade may be factors.

A limitation to this study is the intermediate term of follow-up (a median of 40 months), given that longer follow-up may be required to detect differences in PCa-specific and overall survivals. However, the presence of a difference in metastasis-free survival (an important oncological outcome) within intermediate follow-up accentuates that important differences may exist in the access to and quality of PCa care provided to Indigenous men. Another limitation is the lack of an Indigenous community partnership to identify possible reasons for the variance in PSA testing and treatment selection. The research team will consider knowledge translation and mobilization strategies to support Indigenous men, as well as consult Elders regarding interventions for early diagnosis and PCa awareness. Another limitation is the absence of data that assess differences in socioeconomic status and the social determinants of health between Indigenous and non-Indigenous men.

In conclusion, despite receiving care in a universal health care system, Indigenous men were less likely to receive PSA testing and more likely to be diagnosed with aggressive tumors and develop PCa metastases than non-Indigenous men.

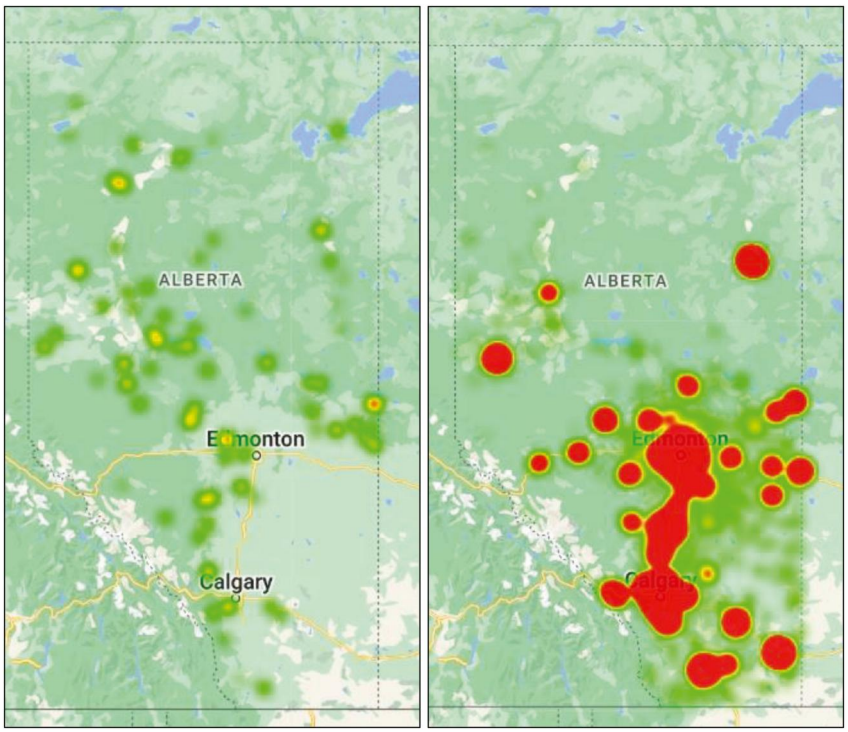

FIGURE 2 Heatmap of PSA testing rates stratified by postal codes in Alberta. Indigenous communities (left); all other communities (right). Red intensity increases with greater PSA testing rates: dense data points are represented in red, medium data points are in yellow, and light data points are in green. PSA indicates prostate-specific antigen.

ACKNOWLEDGMENTS

We recognize that our study takes place on historical and contemporary Indigenous lands, including the territories of Treaties 6, 7, and 8 and the homeland of the Métis. We also acknowledge the many Indigenous people who identify themselves as part of a growing urban community in centers across Alberta. This research was supported in part by the University Hospital Foundation, the Alberta Cancer Board, the Bird Dogs, the Frank and Carla Sojonky Chair in Prostate Cancer Research, and generous donations from Mr. Scott Davis, Mr. Myron Yurko, Mr. Del Sveinsson, and Mr. Leo Broks.

CONFLICT OF INTEREST STATEMENT

Patrick Lightning has been a consultant for the University of Alberta. Stacey Broomfield has been a consultant for the University of Alberta. Adrian Fairey has been a consultant for Alberta Health Services. Michael Kolinsky has been an independent consultant for EMD Serono, AstraZeneca Canada, Ipsen Bioscience, Janssen Biotech, Eisai, Bristol-Myers Squibb Canada, Merck, Astellas Pharma Canada, and Bayer. Christopher J. D. Wallis has been a consultant for Janssen Global Services, EMD Serono, the Genitourinary Research Consortium, Knight Therapeutics, AstraZeneca Canada, Sesen Bio, Precision Point Specialty, Bayer, Tolmar, Merck, and TerSera Therapeutics. Steven Yip has been a consultant for Merck, Novartis, OncoHelix, Ipsen Biopharmaceuticals, AstraZeneca, Janssen Biotech, Bayer, Pfizer Canada, Hoffmann-La Roche, and Bristol-Myers Squibb and has received grants from Janssen Biotech, Bayer, and AstraZeneca. The other authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Alex Kiciak: Conceptualization, formal analysis, writing–original draft, and writing–review and editing. **Wayne Clark:** Conceptualization, writing–original draft, and writing–review and editing. **Maxwell Uhlich:** Data curation, formal analysis, methodology, and software. **Angeline Letendre:** Writing–review and editing. **Randy Littlechild:** Writing–review and editing. **Patrick Lightning:** Writing–review and editing. **Catalina Vasquez:** Data curation, project administration, and writing–review and editing. **Raja Singh:** Data curation, project administration, and writing–review and editing. **Stacey Broomfield:** Data curation and writing–review and editing. **Anais Medina Martin:** Data curation, project administration, and writing–review and editing. **Guocheng Huang:** Writing–review and editing. **Adrian Fairey:** Writing–review and editing. **Michael Kolinsky:** Writing–review and editing. **Christopher J. D. Wallis:** Writing–review and editing. **Christopher Fung:** Writing–review and editing. **Eric Hyndman:** Data curation, funding acquisition, and supervision. **Steven Yip:** Data curation, funding acquisition, and supervision. **Tarek A. Bismar:** Data curation, funding acquisition, and supervision. **John Lewis:** Data curation, funding acquisition, and supervision. **Sunita Ghosh:** Formal analysis, data curation, methodology, and writing–review and editing. **Adam Kinnaird:** Conceptualization,

data curation, formal analysis, funding acquisition, methodology, project administration, resources, supervision, writing–original draft, and writing–review and editing.

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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: Kiciak A, Clark W, Uhlich M, et al. Disparities in prostate cancer screening, diagnoses, management, and outcomes between Indigenous and non-Indigenous men in a universal health care system. *Cancer*. 2023;129(18):2864-2870. doi:10.1002/cncr.34812