Assessment of the epidemiological trends for prostate cancer using administrative data in Ontario

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See related commentary on page 92

ABSTRACT

INTRODUCTION: Studies have shown fluctuations in prostate cancer (PCa) incidence and prevalence over time and by region. Less is known about the most recent epidemiological trends by PCa disease stage.

METHODS: This study was a population-based, sequential, cross-sectional analysis that used administrative health data from Ontario, Canada. After inclusion, patients were classified into non-metastatic (nm) PCa and metastatic (m) PCa. The primary study outcome was a description of temporal trends in the incidence and prevalence of PCa over the study period (2010–2019), stratified by disease state. Crude incidence and prevalence rates were estimated for each year in the study period.

RESULTS: Overall, there were 131 718 men living with PCa in 2019. The incident cohort contained 86 123 patients with nmPCa (n=65 691, 76.3%), mPCa (n=8431, 9.8%), or unknown stage (n=12 001, 13.9%). The prevalence increased from 216 to 253 per 10 000 men between 2010 and 2019, respectively. Between 2011 and 2014, overall PCa incidence decreased from 20.9 to 15.4 per 10 000 men, followed by an increase to 18.8 per 10 000 in 2018. The nmPCa incidence rate was considerably higher compared with mPCa and followed a trend similar to the overall incidence. In contrast, the incidence rate for mPCa demonstrated a continuous increase from 1.5 per 10 000 in 2010 to 2.4 per 10 000 in 2018.

CONCLUSIONS: The overall prevalence of PCa has risen steadily over the last decade, despite fluctuations in nmPCa incidence. The concurrent rise in mPCa and nmPCa requires further study regarding the burden of localized and systemic treatment.

INTRODUCTION

Prostate cancer (PCa) is the most commonly diagnosed non-cutaneous cancer in men in Canada.[1] It accounts for approximately 21% of cancer diagnoses in Canadian males and 10% of cancer deaths.[2,3] PCa impacts patients' quality of life[4] and has a considerable economic burden on the healthcare system, which continues to increase over time.[5]

Through the advent and introduction of new diagnostic and therapeutic options, PCa has become a chronic disease with a generally protracted natural history over the past two decades. Most patients are diagnosed with early-stage disease, a portion of whom will eventually progress to metastatic disease.[2] Further, nearly 25% of patients are initially diagnosed with advanced disease, a number that has risen in developed countries in recent years.[6]

Previous studies show fluctuations in overall PCa incidence over time characterized by incidence peaks (1993 and 2001) and stabilization followed by decline.[2,3,7,8] Geographical variation has also been demonstrated: the age-adjusted rates of PCa ranged from 10.2 (Manitoba) to 12.8 (Prince Edward Island) per 10 000 in 2021.[3] These trends in incidence, partly explained by screening practices,[2] were accompanied by reductions in PCa mortality:[7] it is currently 50% lower compared with its peak in mid-1990s.[3] Although the available global and local reports provide a limited account of incidence and prevalence rates stratified by various PCa disease stages,[2,9] there is a lack of reports examining tem-

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KEY MESSAGES

- Driven by nmPCa cases, the trend toward a decreasing PCa incidence reversed in 2014.
- The incidence of advanced PCa, as well as the overall PCa prevalence, were rising throughout the study period.
- The trends of increased PCa incidence and prevalence may have significant localized and systemic therapeutic implications.

poral trends in more recent years, especially after 2014, when the Canadian Task Force on Preventive Health Care issued recommendations against prostate-specific antigen (PSA) screening for healthy men of any age.[10]

Understanding the burden of PCa through its incidence and prevalence is of interest to cancer program administrators and clinicians.[4,11] The main objective of this study was, therefore, to characterize the distribution of patients with PCa in Ontario over time and by disease stage.

METHODS

Study design

This study was a population-based, sequential, cross-sectional analysis that used administrative health data in Ontario, Canada. Ontario makes up approximately 40% of the national population in Canada, with a provincial population size of almost 14.8 million.[12] The study was conducted using two cohorts: prevalent and incident. The prevalent cohort included men diagnosed with PCa between January 1, 1991, and December 31, 2019. Men who were diagnosed with PCa between January 1, 2010, and December 31, 2019, formed the incident cohort. The study time period was from January 1, 2010, and December 31, 2019; the period was selected based on data availability (2019 was the most recent year for which data was available for analysis) and reasonable duration (i.e., 10 years)

Data source

This study used administrative health service records held by the Institute for Clinical and Evaluative Studies (IC/ES), which captures publicly insured healthcare touch points of Ontarians through multiple linked datasets. As all patient data is anonymized, IC/ES has statutory authority to conduct health services research without consent, thus patient consent was waived. The study received ethics approval from Advarra IRB (Pro00046107).

Data held by IC/ES is collected at the record-level and datasets are linked at the patient level, allowing for longitudinal analysis. This study used the following linked datasets: Ontario Cancer Registry (OCR), Registered Persons Database (RPD), National Ambulatory Care Reporting System (NACRS), Ontario Health Insurance Plan Claims database (OHIP), Ontario Laboratories Information System (OLIS), New Drug Funding Program (NDFP), and Ontario Drug Benefits (ODB).

Inclusion and exclusion criteria

The study included Ontario men diagnosed with PCa who were identified in the OCR database using the International Classification of Diseases for Oncology, third edition, topography code C61.9. Following inclusion into the overall cohort, patients were classified into the following major PCa disease states at the time of diagnosis using the PCa stage flag available in the OCR database: 1) non-metastatic PCa (nmPCa) as stage groups 1–3; and 2) metastatic PCa (mPCa) as stage group 4.

Outcomes

The primary study outcome was a description of temporal trends in the incidence and prevalence of PCa over the study period (2010–2019), stratified by disease state. More specifically, the study analyzed observed prevalence of overall PCa, observed incidence of overall PCa, nmPCa, and mPCa.

Variables

At baseline, the study population was described using patient sociodemographic characteristics (age, socioeconomic status, rurality), health status (Charlson Comorbidity Index [CCI]), and healthcare use (number of visits to a general practitioner [GP], history of hospitalizations, and status of a long-term care (LTC) resident in the year prior to diagnosis).

> “A decline in the overall PCa crude incidence rate in 2010–2014 was followed by an increase in incidence by 2018, driven primarily by nmPCa cases. mPCa crude incidence showed a gradual increase over the entire study period.”

Table 1. Baseline characteristics

Characteristics n (%), mean (SD), or median (IQR)	Total N=74 122	nmPCa n=65 691	mPCa n=8431	p
Age				
Mean ± SD, years	68.02±9.29	67.43±8.92	72.56±10.73	<0.001
Median (IQR), years	68 (62–74)	67 (61–73)	73 (65–81)	<0.001
Age category				
≤50	1836 (2.5%)	1677 (2.6%)	159 (1.9%)	<0.001
50–59	11 778 (15.9%)	10 892 (16.6%)	886 (10.5%)	
60–64	12 950 (17.5%)	11 933 (18.2%)	1017 (12.1%)	
65–69	16 129 (21.8%)	14 821 (22.6%)	1308 (15.5%)	
70–79	22 778 (30.7%)	20 235 (30.8%)	2543 (30.2%)	
80+	8651 (11.7%)	6133 (9.3%)	2518 (29.9%)	
Socioeconomic status and rurality				
Quintile 1	11 700 (15.8%)	10 056 (15.3%)	1644 (19.5%)	<0.001
Quintile 2	14 084 (19.0%)	12 448 (18.9%)	1636 (19.4%)	
Quintile 3	14 804 (20.0%)	13 130 (20.0%)	1674 (19.9%)	
Quintile 4	15 648 (21.1%)	13 954 (21.2%)	1694 (20.1%)	
Quintile 5	17 886 (24.1%)	16 103 (24.5%)	1783 (21.1%)	
Rural	10 479 (14.1%)	9229 (14.0%)	1250 (14.8%)	0.054
Medical care and comorbidity				
Comorbidity (CCI)				
Mean ± SD	0.21±0.74	0.19±0.69	0.36±1.06	<0.001
CCI: 0 or missing	66 142 (89.2%)	59 040 (89.9%)	7102 (84.2%)	<0.001
CCI: 1	3753 (5.1%)	3229 (4.9%)	524 (6.2%)	
CCI: 2	2682 (3.6%)	2253 (3.4%)	429 (5.1%)	
CCI: ≥3	1545 (2.1%)	1169 (1.8%)	376 (4.5%)	
Number of GP visits in year prior to diagnosis				
Mean ± SD	7.10±6.80	6.87±6.49	8.84±8.67	<0.001
Any hospitalization in year prior to diagnosis	29 630 (40.0%)	25 888 (39.4%)	3742 (44.4%)	<0.001
Ever LTC resident	367 (0.5%)	233 (0.4%)	134 (1.6%)	<0.001

*PSA test 3 months prior to PCa diagnosis date; if none is available, then from PSA test 2 months after PCa diagnosis date, using the value closest to PCa diagnosis date. CCI: Charlson Comorbidity Index; IQR: interquartile range; GP: general practitioner; LTC: long-term care; nmPCa: non-metastatic prostate cancer; mPCa: metastatic prostate cancer; PSA: prostate-specific antigen; SD: standard deviation.

Data analysis

Descriptive

Descriptive statistics were used to summarize baseline characteristics. Categorical variables were summarized as counts and proportions (%), and continuous variables are summarized as median and interquartile range (IQR).

For each year in the analysis, 2010–2019, crude prevalence of patients with PCa and each PCa disease state were identified as of January 1. For overall prevalence, for each year of the analysis, patients diagnosed with PCa who were still alive as of January 1 of the year of interest were identified by looking back from January 1 of the year of interest until January 1, 1991.

For crude incidence, all new diagnoses of PCa during each year were identified by patients with a new diagnosis of PCa in CCO records between January 1 and December 31 of the year of interest. Patients were categorized into PCa disease state incidence using the following approach: disease state was assessed as the same or different in the previous year for patients with prevalent PCa. Then, patients with the same disease state as the previous year were excluded from the disease state incidence calculation, whereas patients whose present-year disease state and past-year disease state differed were considered incident cases of their present-year disease state.

Data analysis was undertaken in SAS Enterprise Guide V7.15 (SAS Institute Inc., Cary, NC, U.S.), with the level of significance set at 5%.

RESULTS

Patient demographics and baseline characteristics

After all exclusion criteria were applied, 177 297 men diagnosed with PCa in Ontario between January 1, 1991, and December 31, 2019, formed the overall prevalent cohort. The final incident cohort (i.e., patients diagnosed with PCa between January 1, 2010, and December 31, 2019) consisted of 86 123 patients with nmPCa (n=65 691, 76.3%) and mPCa (n=8431, 9.8%), whereas patients with unknown stage accounted for 13.9% (n=12 001).

Patients with mPCa were older compared with those with nmPCa (mean 72.6 years, standard deviation [SD] 10.7) vs. 67.4 years, SD 8.9, respectively). Patients with mPCa had a higher CCI (mean 0.36 vs. 0.19, p<0.001) and had a higher number of GP visits in a year preceding PCa diagnosis (mean 8.8 vs. 6.9,

p<0.001). Baseline characteristics among nmPCa and mPCa patients are presented in Table 1.

Prevalence and incidence

Prostate cancer prevalence

The observed prevalence has increased both by absolute number and by rate (Figure 1). As such, the number of patients with PCa grew over the reported period from 100 611 in 2010 to 131 718 in 2019 (216 to 253 per 10 000 men, respectively).

Prostate cancer incidence

The incidence trends could only be reported for the 2010–2018 period due to incomplete data by disease stage for 2019. The observed overall PCa incidence rate over the study period revealed a dip in 2011–2014 from 20.9 per 10 000 to 15.4 per 10 000 men. It was followed by a steady growth in the number of new cases, reaching an incidence rate of 18.8 per 10 000 in 2018 (Figure 2).

The nmPCa incidence was considerably higher compared with mPCa. There were two peaks observed for the nmPCa incidence: the 2010 peak at 17.5 per 10 000 was followed by a drop to 12.5 by 2014 and a gradual recovery to a smaller peak of 14.5 per 10 000 by 2017.

In contrast, the incidence rate for mPCa demonstrated a continuous increase from 1.5 per 10 000 in 2010 to 2.4 per 10 000 in 2018 with minor fluctuations over the course. The rate of patients with unknown stage fluctuated from 1–2 per 10 000 throughout most of the study period.

Table 1 (cont'd). Baseline characteristics

Characteristics n (%), mean (SD), or median (IQR)	Total N=74 122	nmPCa n=65 691	mPCa n=8431	p
Hospital setting for care deliver site				
Community hospital	48 809 (65.8%)	43 231 (65.8%)	5578 (66.2%)	0.522
Academic hospital	25 313 (34.2%)	22 460 (34.2%)	2853 (33.8%)	
Prostate cancer characteristics				
PSA at diagnosis*				
Mean ± SD	61.76±388.53	15.36±74.88	393.31±1031.62	<0.001
Biopsy Gleason score				
<7	18 441 (24.9%)	18 389 (28.0%)	52 (0.6%)	<0.001
7	26 002 (35.1%)	25 053 (38.1%)	949 (11.3%)	
>7	12 509 (16.9%)	8881 (13.5%)	3628 (43.0%)	
Grade missing	17 170 (23.2%)	13 368 (20.3%)	3802 (45.1%)	

*PSA test 3 months prior to PCa diagnosis date; if none is available, then from PSA test 2 months after PCa diagnosis date, using the value closest to PCa diagnosis date. CCI: Charlson Comorbidity Index; IQR: interquartile range; GP: general practitioner; LTC: long-term care; nmPCa: non-metastatic prostate cancer; mPCa: metastatic prostate cancer; PSA: prostate-specific antigen; SD: standard deviation.

DISCUSSION

This study used a large, population-based cohort from the province of Ontario to explore epidemiological trends among men with PCa in the period between 2010 and 2019. The study showed that a decline in the overall PCa crude incidence rate in 2010–2014 was followed by an increase in incidence by 2018. This pattern was driven primarily by nmPCa cases, whereas the mPCa crude incidence showed a gradual increase over the entire study period. The overall crude prevalence was also on the rise throughout the entire study period.

In Canada, other groups have assessed trends in PCa diagnosis, finding similar but somewhat more limited results.[2,7,8] Using data from Canadian Cancer Registry, LeBlanc et al showed an overall decline in PCa incidence between 2011 and 2015.[2] As with our data, the trend was driven by decreases in nmPCa. We are likely seeing the expected delayed effects of changes in primary care recommendations regarding PSA screening, combined with a change in the cohort of family physicians to include many now who were educated during times in which PSA screening was discouraged by their guidelines/national organizations. Our findings further build on this study by demonstrating the inflection in incidence, with increase between 2015 and 2018, driven by a growing incidence of both nmPCa and de novo mPCa.

Our findings are largely aligned with recent U.S.-based reports. First, data provided by the U.S. Surveillance, Epidemiology, and End Results (SEER) program show a similar trend in the overall PCa incidence: the age-adjusted rate was in decline until 2014, followed by a gradual increase afterwards.[13,14] Second, studies found that the incidence of mPCa started to increase after the U.S. Preventive Services Task Force (USPSTF) recommended against routine PSA screening, initially for men >75 years of age (2008) and then for all men (2012).[15,16] This confirms previously raised concerns about the long-term negative impact of the recommendations and the underappreciation of advanced strategies to address overdiagnosis and overtreatment.[17,18]

In Canada, the same recommendation was issued in 2014; however, contrary to the U.S., there was no

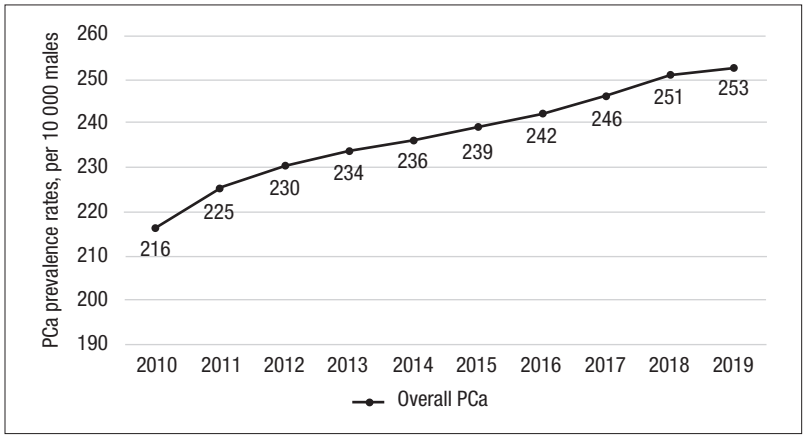

Figure 1. Prevalence rate, 2010–2019 (crude, per 10 000 men). The figure presents prevalence data for overall prostate cancer (PCa).

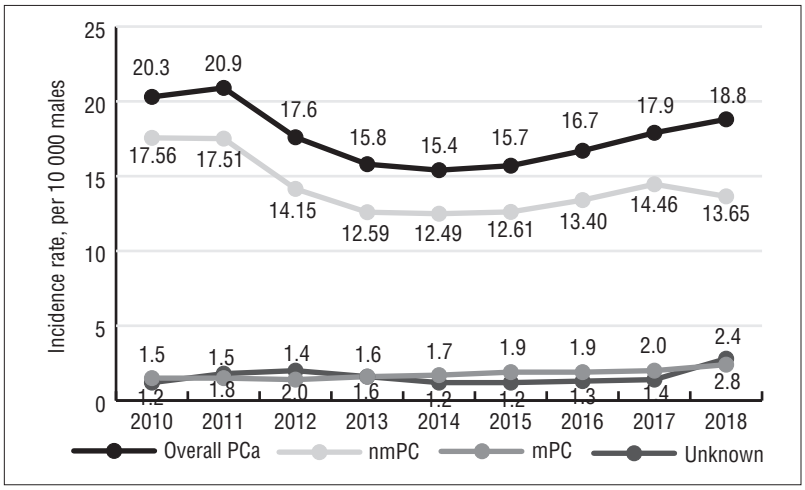

Figure 2. Incidence rate, 2010–2018 (crude, per 10 000 men). The figure presents incidence data for overall prostate cancer and prostate cancer by disease stage (nmPCa: non-metastatic prostate cancer; mPCa: metastatic prostate cancer). Note: Results for 2019 were not reported due to incomplete data by disease stage.

decrease in the overall PCa incidence after the recommendation: the rate began to ascend in the following year. This can, in part, be explained by poor acceptance of the Grade D recommendation by specialist medical communities in Canada and globally, which have issued their own guidance recommending PSA screening for interested patients.[19]

Limitations

The evidence presented in the current study addresses an important gap in the literature, i.e., limited descriptions of epidemiological trends by PCa disease stage, especially in the period after the pivotal recommendation on PCa screening; however, the study has several challenges and limitations worth noting.

First, the authors could not determine epidemiological trends in other disease states, the subsets of nmPCa and mPCa (e.g., patients on local therapy with or without recurrence, castration-sensitive or non-metastatic/metastatic castrate-resistant prostate cancer) due to lack of imaging results, limiting the ability to accurately identify the timing of metastasis development and necessitating use of a proxy definition of metachronous metastatic disease. In turn, PCa disease state proxy definitions included the levels of PSA and testosterone, which too were missing or otherwise limited in the database. IC/ES has taken initiatives to expand data availability and improve capabilities in data science, which are expected to bridge the gaps.[20]

Second, the study results may be affected by the number of patients with unknown stage (13.9%). To a certain extent, the missing information may be explained by delayed data processing at Cancer Care Ontario.

Third, we realize the potential important of mortality data reported alongside disease incidence and prevalence; however, due to data unavailability, we could not report on PCa-specific mortality.

CONCLUSIONS

Prostate cancer is the most common type of cancer among Canadian men. This study showed a reversal of the trend toward a decreasing PCa incidence characterized by a halt in its decline in 2014, followed by a rapid increase afterwards, driven primarily by nmPCa cases. The incidence of advanced PCa rose throughout the study period. These trends of increased PCa incidence and prevalence may have significant localized and systemic therapeutic implications that will require further monitoring and investigation.

COMPETING INTERESTS: Dr. Saad has been an advisory board member for and has received grants/honoraria from Amgen, Astellas, AstraZeneca, Bayer, Janssen, Knight, Myovant, Novartis, Pfizer, Sanofi, and Tolmar; and has participated in clinical trials supported by Astellas, AstraZeneca, Bayer, Janssen, Novartis, Pfizer, and Sanofi. Dr. Bhindi has been an advisory board member for Bayer, Janssen, and Verity Pharmaceuticals; has received speaker honoraria from Bayer, Merck, and Pfizer; and has been a paid consultant for Bayer, Ferring, and Janssen. Dr. Noonan has been an advisory board member for AstraZeneca, EMD Serono, Janssen, Novartis, Roche, and Pfizer. Dr. Ong is part of Janssen's GU Research Consortium; and has received consultation fees from Astellas, Bayer, BMS, EMD Serono, Janssen, Merck, and Pfizer. Ms. Castellano and Ms. Kourkounakisis are employees of Janssen Inc. Dr. Wallis has received consulting fees from Janssen Oncology, Precision Point Specialty LLC, and SESEN Bio; and has received honoraria from Bayer, EMD Serono, Haymarket Media, Healing and Cancer Foundation, Knight Therapeutics, and Tolmar.

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