Catalogue no. 82-003-X
ISSN 1209-1367

Health Reports

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Release date: April 17, 2019

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Abstract

Background: Prostate cancer is the most common type of cancer in Canadian men. Screening recommendations have changed substantially over the last 25 years. Since 2011 (United States) and 2014 (Canada), taskforce guidelines have recommended against screening using the prostate-specific antigen (PSA) test in low-risk men of all ages. This work reports on trends in prostate cancer incidence, mortality, and stage at diagnosis in Canada from 1992 to 2015.

Data and methods: Prostate cancer incidence, mortality, and stage at diagnosis were retrieved from Statistics Canada's Canadian Cancer Registry and Canadian Vital Statistics - Death Database. Joinpoint analysis was used to examine trends over time.

Results: The age-standardized incidence rate (ASIR) of prostate cancer peaked in 1993 and 2001, and declined thereafter. From 2011 to 2015, the ASIR declined by 9.3% per year. The age-standardized mortality rate (ASMR) decreased continuously from 1992 to 2015, but fell most rapidly (2.9% per year) after 2001. Data from two provinces show that, from 2005 to 2015, the rate of Stage I and Stage II cancers decreased by 3.2% per year, while the rate of Stage III and Stage IV cancers remained relatively stable.

Interpretation: Incidence of prostate cancer has declined substantially in recent years. Most of the decline seems to be in localized cases (Stage I and Stage II). Changes in incidence have mirrored changes to PSA screening recommendations. Future work should continue to monitor trends over time at the national level, especially as they relate to screening recommendations.

Keywords: Cancer, prostate, prostate-specific antigen, screening, men's health, public health.
DOI: https://www.doi.org/10.25318/82-003-x201900400002-eng

Part of a man's reproductive and urinary systems, the prostate is a small gland just below the bladder.[1] Changes in the cells of the prostate can lead to benign conditions such as prostatitis or benign prostate hyperplasia, pre-cancerous conditions such as prostatic intraepithelial neoplasia, or prostate cancer. Prostate cancer is the most common type of cancer in Canadian men, followed by colorectal, lung, and bladder cancers.[2,3] Recent analyses from the Canadian Cancer Society suggest that 1 in 7 men will be diagnosed with prostate cancer in their lifetime and that 1 in 29 will die from the disease.[2]

Prostate cancer often progresses slowly and, in many cases, can be managed effectively after diagnosis. However, some prostate cancers can become aggressive and lethal, and distinguishing between indolent and lethal forms can be difficult.[2] The majority (75%) of prostate cancers are localized (Stage I or Stage II) at diagnosis.[4] As a result, prostate cancer has one of the highest five-year survival rates of all cancers in Canada (95%).[2] In fact, many older men have prostate cancer without knowing, and prostate cancer itself is not often the cause of mortality.[5] For example, results from autopsy studies around the world show that the majority of older men have evidence of undiagnosed prostate cancer at death.[5]

Screening guidelines for prostate cancer evolved considerably over the past 25 years. In the early 1990s, the prostate-specific antigen (PSA) test was introduced in several countries as a non-invasive blood test to detect early signs of prostate cancer in asymptomatic men. In Canada, PSA testing was introduced in 1993, with further emphasis on the importance of screening in 2001.[6] Although elevated levels of the PSA (typically defined as PSA ≥3 ng/mL) can be a sign of prostate cancer, PSA levels fluctuate naturally, especially with advanced age, and can reflect several other conditions, such as prostatic hyperplasia, prostatitis, or urinary tract infection.[7] In fact, research suggests that widespread PSA testing has resulted in the over-diagnosis of many men who have low-grade, or early-stage, prostate cancer. This has resulted in unnecessary subsequent treatment or testing.[8]

In response to over-diagnoses, the U.S. Preventive Services Task Force (USPSTF) released recommendations in 2008 advising against PSA screening in men over 75 years of age.[9] In 2011, the USPSTF updated its recommendations and advised against PSA screening for asymptomatic men of all ages.[9,10] In 2014, the Canadian Task Force on Preventive Health Care followed with recommendations against PSA screening for healthy men of any age.[8] This also aligns with current recommendations from the United Kingdom, which advises against screening in men over 50 years of age.[11]

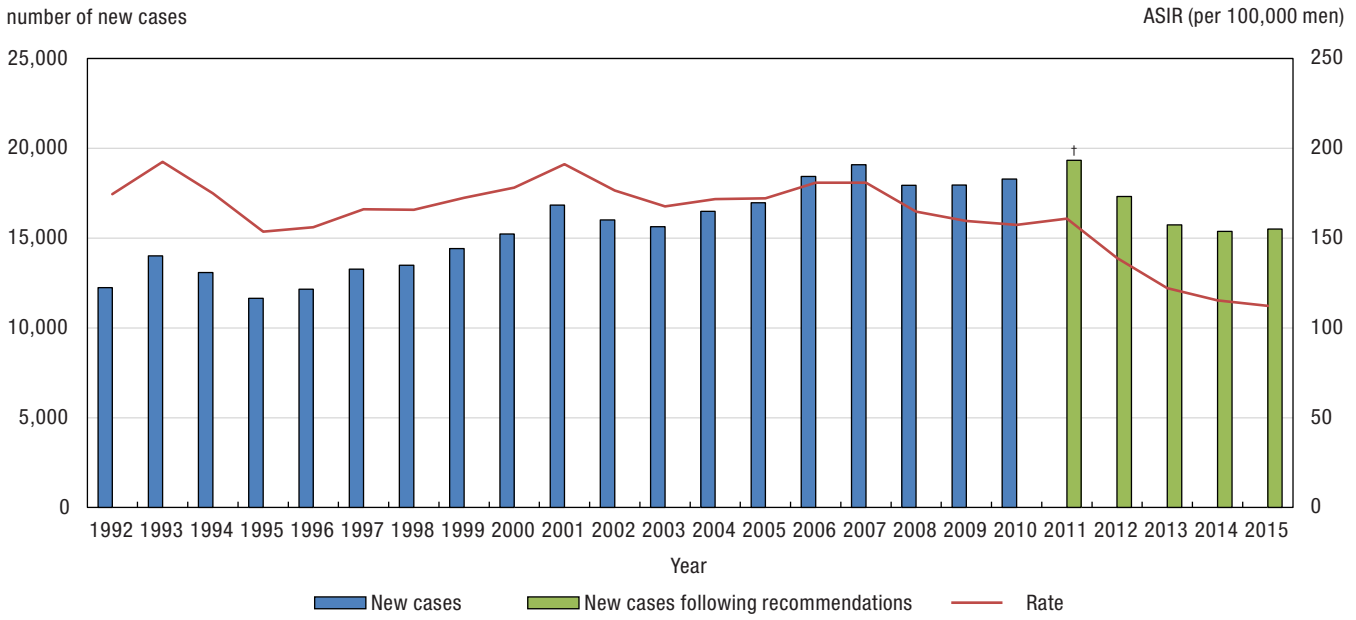
In 2012, Statistics Canada published an initial examination of the impact of changes in PSA screening recommendations on prostate cancer rates.[12] This analysis builds on that work by providing an up-to-date and in-depth analysis of trends in prostate cancer incidence, mortality and stage at diagnosis over time and by age group, including the impact of the updated (2014) Canadian prostate cancer screening guidelines.

Methods

Prostate cancer incidence counts were obtained from the Canadian Cancer Registry (1992 to 2015), and mortality counts were retrieved from the Canadian Vital Statistics - Death

Authors: Allana G. LeBlanc (allana.leblanc@canada.ca), Alain Demers, and Amanda Shaw are with the Adult Chronic Diseases and Conditions Division, Centre for Surveillance and Applied Research, Public Health Agency of Canada, Ottawa, Ontario.

Figure 1
Number of new diagnoses and age-standardized incidence rate of prostate cancer, Canada, 1992 to 2015



ASIR = age-standardized incidence rate
† Recommendations advising against PSA testing for men of all ages were released in the United States in 2011.
Notes: Data from Quebec are not included. Rates are age-standardized to the 2011 Canadian population.
Source: Statistics Canada, Canadian Cancer Registry Database.

Database (1992 to 2015). Both databases maintained by Statistics Canada compile information provided by the provincial and territorial cancer and vital statistics registries. ICD-O-3 morphology code C61 (excluding ICD-O-3 histology codes 905, 9140 and 9590 to 9992) was used to define malignant prostate cancer. The province of Quebec has not submitted cancer incidence data since 2010 and, consequently, is not included in the current analysis. The Quebec mortality data were excluded to ensure consistency with incidence data and to maintain the same population base. Annual population estimates for 1992 to 2015 by region, age, and sex, were extracted from the most recent Canadian population estimates, which included a postcensal estimate for 2017.[13] Statistics Canada adjusts inter- and postcensal estimates for net undercoverage. Rates were age-standardized to the 2011 Canadian standard population, which is based on the final 2011 Canadian postcensal population structure.[14] To ensure confidentiality, incidence and mortality counts not ending in a zero or five were randomly rounded to an adjacent multiple of five. Unrounded counts were used to calculate age-standardized rates and percentages.

Stage at diagnosis coded according to the Collaborative Stage (CS) System, based on the American Joint Committee on Cancer (AJCC) 6th edition, was available for 2005 to 2015 in two Canadian provinces (Alberta and Manitoba). When compared with stage at diagnosis based on AJCC 7th edition (available from 2010 to 2015), approximately 18% of cases classified as Stage II in AJCC 6th edition are considered Stage I in AJCC 7th, and less than 1% of cases classified as Stage IV in AJCC 6th edition are classified as Stage III in AJCC 7th. It is interesting to note that just over 1% of cases classified as Unknown Stage in AJCC 6th are classified as Stage I, Stage II or Stage III in AJCC 7th edition. As a result, stage was categorized as one of the following: Stage I or Stage II (local or locally advanced); Stage III or Stage IV (regional or distant); or Stage Unknown. Cases with no stage information (0.3%) or cases that were considered "unstageable" (0.4%) were excluded from the analysis. The category "Stage Unknown" was assigned to cases where some stage information was available but was insufficient to determine exact stage (e.g., individual did not undergo the full diagnostic workup required to determine stage, or the record of the workup is incomplete). As a large proportion of the Stage Unknown cases were in men over the age of 80 (41%), trend analysis was repeated on men aged 18 to 79 only.

Joinpoint regression models were used to determine whether changes in trends over time were statistically significant (Joinpoint, version 4.2.0.2). The maximum number of joinpoints allowed was set to four. The minimum number of observations from a joinpoint to the start or end of the data, and the minimum number of observations between two joinpoints, were also set at four. For trends by stage at diagnosis, only one joinpoint was allowed due to the short time period examined, while the minimum number of observations from a joinpoint to the start or end of the data, and the minimum number of observations between two joinpoints, were set at

Table 1
Trends in prostate cancer age-standardized incidence and mortality rates, overall, selected age groups, by stage at diagnosis, Canada, 1992 to 2015

	Trend 1			Trend 2			Trend 3			Trend 4		
	Period	APC (%)	P-value	Period	APC (%)	P-value	Period	APC (%)	P-value	Period	APC (%)	P-value
Incidence												
All ages	1992 to 1996	-4.2	0.112	1996 to 2001	3.3	0.176	2001 to 2011	-1.6	0.019	2011 to 2015	-9.3	0.001
Age group												
Under 55	1992 to 2001	10.7	0.000	2001 to 2006	4.8	0.052	2006 to 2011	-0.7	0.716	2011 to 2015	-10.7	0.000
55 to 69	1992 to 2007	2.7	0.000	2007 to 2015	-6.3	0.000	…	…	…	…	…	…
70 and over	1992 to 1996	-6.9	0.001	1996 to 2001	0.1	0.979	2001 to 2011	-2.9	0.000	2011 to 2015	-7.4	0.001
Stage at diagnosis†												
I or II	2005 to 2015	-3.2	0.000	…	…	…	…	…	…	…	…	…
III or IV	2005 to 2009	4.8	0.047	2009 to 2015	-1.0	0.298	…	…	…	…	…	…
Unknown	2005 to 2015	-11.9	0.000	…	…	…	…	…	…	…	…	…
Mortality												
All ages	1992 to 2001	-1.7	0.000	2001 to 2015	-2.9	0.000	…	…	…	…	…	…

… not applicable

† Stage at diagnosis is based on data from two Canadian provinces (Alberta and Manitoba) for 2005 to 2010.

Notes: Data from Quebec are not included. Rates are age-standardized to the 2011 Canadian population. APC represents the average change in age-standardized rate in the given period. A positive APC represents an increase in the rate over time; a negative APC represents a decrease in the rate over time. Empty cells indicate that no other joinpoint was found. APC: annual percentage change

Source: Statistics Canada, Canadian Cancer Registry Database and Vital Statistics Database.

two. SAS (version 9.3) was used to complete all other statistical analysis.

Results

In 2015, there were 15,510 new cases of prostate cancer, accounting for 21% of all cancer diagnoses in Canadian men (excluding Quebec). There were also approximately 3,105 prostate cancer deaths in Canada in 2015 (excluding Quebec), representing 10.6% of cancer deaths. The incidence rate of prostate cancer peaks among men aged 70 to 79 years, while the mortality rate continues to rise with increasing age (data not shown). Over 98% of prostate cancer cases and 99% of prostate cancer deaths are in men over the age of 50.

The incidence count of prostate cancer increased gradually from 1992 to 2011, peaking at 19,325 cases in 2011, before falling to 15,510 cases in 2015 (Figure 1). During the same period, the age-standardized incidence rate (ASIR) of prostate cancer fluctuated, with peaks in 1993 (192.4 per 100,000) and 2001 (191.1 per 100,000). Joinpoint trend analysis revealed that, from 1992 to 2001, there was no significant change in the prostate cancer ASIR (Table 1). From 2001 to 2011, the ASIR decreased by 1.6% per year; from 2011 to 2015, the ASIR declined more rapidly, by 9.3% per year.

Among men aged 55 to 69, the ASIR of prostate cancer peaked in 2001 (511.1 per 100,000) and 2007 (517.2 per 100,000). From 2007 to 2015 the ASIR in men aged 55 to 69 decreased by 6.4% per years (Table 1 and Figure 2). Although prostate cancer is rare in younger men, the ASIR of prostate cancer in men under 55 years also peaked in 2007 (17.5 per 100,000), then flattened, and began to decrease in 2011 at 10.7% per year. For men over 70 years of age, the ASIR of prostate cancer peaked in 1993 (1185.8 per 100,000) then flattened, and began to decline in 2001 and more rapidly after 2011.

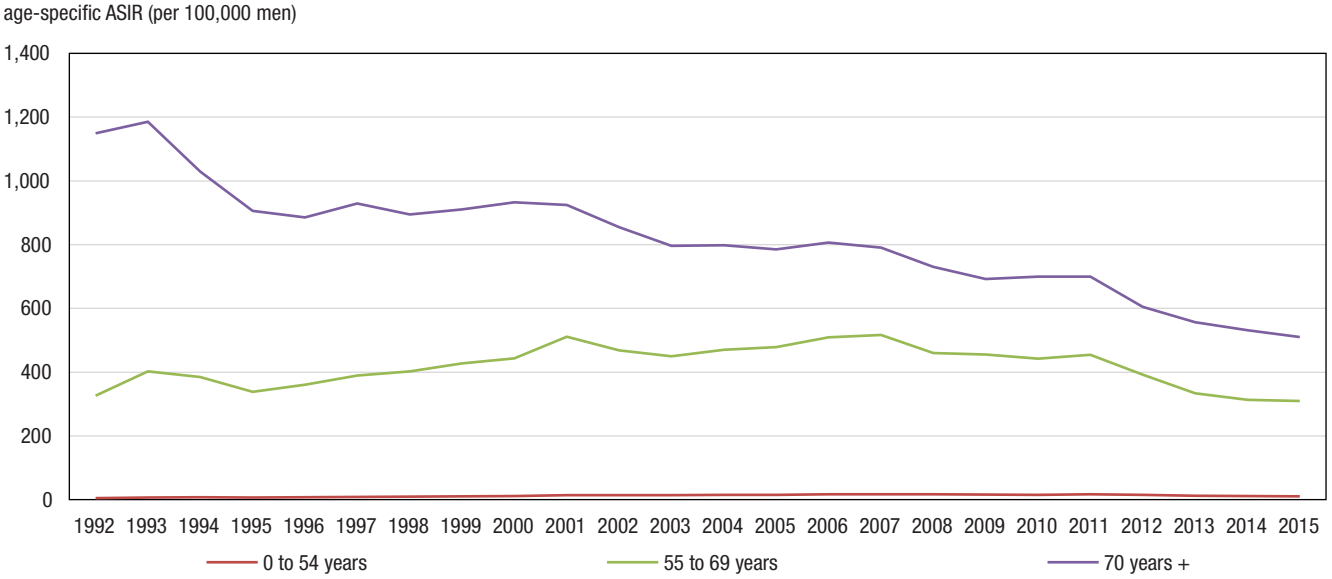
From 1992 to 2015, the number of deaths due to prostate cancer increased, while the age-standardized mortality rate (ASMR) declined substantially (Figure 3). The number of deaths due to prostate cancer in Canada peaked in 2014 at just over 3,200. Trend analyses show that the ASMR decreased by 1.7% per year from 1992 to 2001. It then fell more rapidly, by 2.9% per year, from 2001 to 2015 (Table 1).

In 2015, 71.6% of prostate cancers in Alberta and Manitoba were Stage I or Stage II (local or locally advanced), while 11.2% were Stage III (regional) and 13.5% were Stage IV (distant) (Figure 4). A small portion of cases were categorized as Stage Unknown (3.7%). These results are comparable to national results based on nine provinces and territories using AJCC 7th edition for 2011 to 2015.[4] Trend analyses show that, from 2005 to 2015, the ASIR of Stage I and Stage II prostate cancers decreased by 3.2% per year (Table 1). The ASIR of Stage III and Stage IV cancers rose by 4.8% from 2005 to 2009 and then stabilized from 2009 to 2015 (Table 1). Although rare, the ASIR of Stage Unknown cases decreased by 11.7% per year from 2005 to 2015. Almost identical trends were found when data were restricted to men 18 to 79 years at diagnosis (data not shown).

Discussion

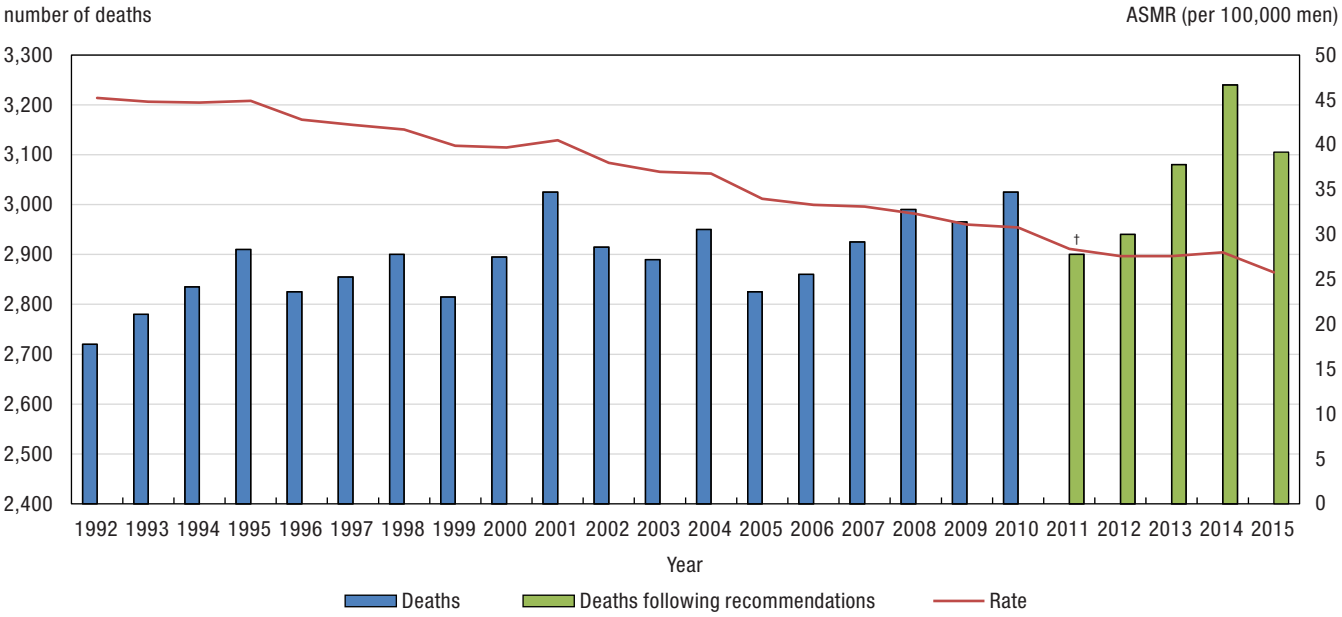
This report presents up-to-date information on prostate cancer incidence, mortality, and stage at diagnosis in Canada. Prostate cancer remains the most common type of cancer among Canadian men, accounting for approximately 21% of cancer diagnoses and 10% of cancer deaths. The incidence rate of prostate cancer has decreased rapidly in recent

Figure 2
Age-standardized incidence rate of prostate cancer by age group, Canada, 1992 to 2015



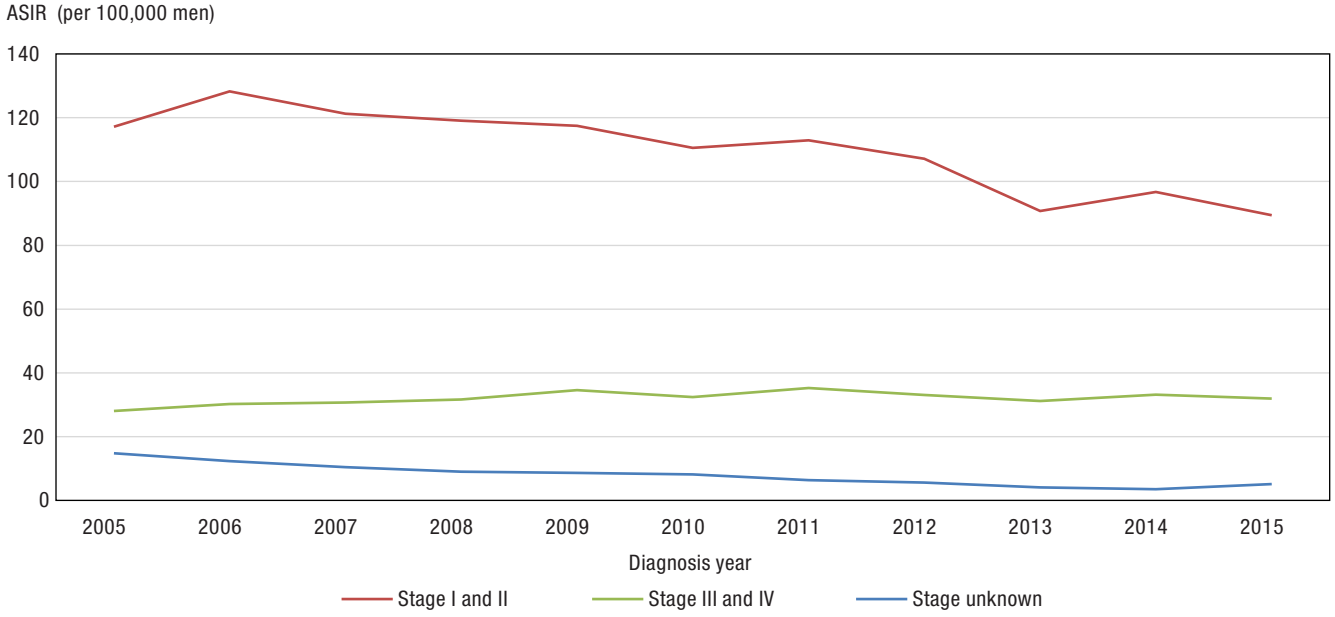
ASIR = age-standardized incidence rate
Notes: Data from Quebec are not included. Rates are age-standardized to the 2011 Canadian population.
Source: Statistics Canada, Canadian Cancer Registry Database.

Figure 3
Number of deaths and age-standardized mortality rate, prostate cancer, Canada, 1992 to 2015



ASMR = age-standardized mortality rate
† Recommendations advising against PSA testing for men of all ages were released in the United States in 2011.
Notes: Data from Quebec are not included. Rates are age-standardized to the 2011 Canadian population.
Source: Statistics Canada, Vital Statistics Database.

Figure 4
Age-standardized incidence rate of prostate cancer, by stage at diagnosis, Alberta and Manitoba combined, 2005 to 2015



ASIR = age-standardized incidence rate
Notes: Rates are age-standardized to the 2011 Canadian population.
Source: Statistics Canada, Canadian Cancer Registry Database.

years, while mortality rates fell consistently from 1992 to 2015. This suggests that changes to screening protocols have not negatively affected patient outcomes. Initial analyses of prostate cancer stage data show that, while the incidence rate for local or locally advanced Stage I and Stage II cases has decreased from 2005 to 2015, the incidence rate of regional or metastatic Stage III and Stage IV cases has remained stable. This is consistent with results from an Ontario hospital, which found that changes in screening recommendations were associated with a decrease in the number of biopsies and new prostate cancer diagnoses, but no change in the number of high-risk (metastatic) cases.[15]

The results of this analysis show that the incidence rate of prostate cancer fluctuated during the 1990s, with peaks in 1993 and 2001 that mirror intensified use of PSA testing in Canada.[2,3,8,16] Since 2001, the incidence rate of prostate cancer has declined, with a more rapid decline beginning in 2011, consistent with the release of revised PSA screening recommendations in the United States (2011) and Canada (2014). This trend is most apparent in men under 70 years of age who have historically been targeted for screening. In 2018 the USPSTF released new recommendations that advocate for individualized, physician-guided screening decisions for men between the ages of 55 and 69 based on individual risk factors as well as a discussion of the benefits and harms of screening.[17,18] The USPSTF continues to recommend against screening for men over 70 years of age,[17,18] while Canada continues to recommend against PSA screening for low-risk men of all ages, although general practice varies from province to province (most provinces do not currently cover the cost of testing).

Recommendations against PSA screening are supported by several large, well-designed, randomized controlled studies. Specifically, results from the European Randomized Study of Screening for Prostate Cancer (ERSPC) and the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO) showed that, while PSA screening decreases the risk of dying from prostate cancer, the decrease is small (approximately 1 death per 1,000), and the benefits of screening do not outweigh the potential harms.[19,20] Results from Martin et al. (2018), showing that offering a single PSA screening to middle-aged men (i.e., between 50 and 59 years) was ineffective in reducing mortality,[21] are consistent with those from the ERSPC and the PLCO, and consequently stimulate additional discussion on the value of widespread screening in healthy men.[22] Given that most known risk factors for prostate cancer are non-modifiable (e.g., age, family history, ethnicity), future work may benefit from examining the efficacy of targeted screening practices among high-risk groups only.

Strengths and limitations

This analysis is a timely update on prostate cancer in Canada. The Canadian Cancer Registry and the Canadian Vital Statistics - Death Database represent the most comprehensive cancer incidence and death databases in Canada and provide important information for national health surveillance. Unfortunately, data from Quebec are not included in the analysis as the province has been unable to submit cancer incidence data to the national

registry since 2010. It will be important to examine the rates and trends of prostate cancer in Quebec compared with the rest of the country once data are available. Further, although this is the first time that trends in stage at diagnosis have been presented for Canada, this information is limited to two Canadian provinces. Since 2010, all Canadian provinces have been submitting cancer stage data to the National Cancer Registry[2] for at least the top four cancer types. Future work should examine trends in stage at diagnosis for all Canadian provinces as information becomes available. Finally, cases in the "Stage Unknown" category may represent a unique sub-group of patients who are older at diagnosis and do not receive a full diagnostic workup.[4] Previous analyses have found this group to be socioeconomically disadvantaged, with lower survival than Stage I and Stage II cancers but higher survival than Stage III and Stage IV cancers.[23] Though the rate of "Stage Unknown" prostate cancers seems to be declining, these cancers should continue to be examined as a unique sub-group with different risk factors and patterns of care.

Conclusion

Prostate cancer remains the most common type of cancer among Canadian men. Incidence counts and rates have decreased significantly in recent years, mirroring recent recommendations against population-based PSA screening. Initial results show the reduction in prostate cancer incidence is primarily due to a reduction in localized cancers (Stage I and Stage II). Future work should include more in-depth analysis, including longer-term trends in stage at diagnosis from more Canadian provinces. ■

Acknowledgement

The authors would like to thank Kristina Sabou for her assistance with an early version of this work.

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