Prostate Cancer Incidence and Mortality Rates and Trends in the United States and Canada

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SYNOPSIS

Objective. The purpose of this study was to compare prostate cancer incidence and mortality trends between the United States and Canada over a period of approximately 30 years.

Methods. Prostate cancer incident cases were chosen from the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) Program to estimate rates for the United States white males and from the Canadian Cancer Registry for Canadian men. National vital statistics data were used for prostate cancer mortality rates for both countries, and age-adjusted and age-specific incidence and mortality rates were calculated. Joinpoint analysis was used to identify significant changes in trends over time.

Results. Canada and the U.S. experienced 3.0% and 2.5% growth in age-adjusted incidence from 1969–90 and 1973–85, respectively. U.S. rates accelerated in the mid- to late 1980s. Similar patterns occurred in Canada with a one-year lag. Annual age-adjusted mortality rates in Canada were increasing 1.4% per year from 1977–93 then fell 2.7% per year from 1993–99. In the U.S., annual age-adjusted mortality rates for white males increased 0.7% from 1969–1987 and 3.0% from 1987–91, then decreased 1.2% and 4.5% during the 1991–94 and 1994–99 periods, respectively.

Conclusions. Recent incidence patterns observed between the U.S. and Canada suggest a strong relationship to prostate-specific antigen (PSA) test use. Clinical trials are required to determine any effects of PSA test use on prostate cancer and overall mortality.

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Prostate cancer is the second-leading cause of cancer deaths among men in both the United States and Canada.[1,2] About 189,000 new cases of this disease are projected for U.S. men and 18,200 for Canadian men in 2002; approximately 30,200 deaths from prostate cancer among Americans and 4,300 among Canadians are expected that year.[1,2]

Numerous epidemiologic studies have shown that prostate cancer is rare in men younger than 50 years of age, but thereafter the risk of incident prostate cancer increases significantly with increasing age.[3,4] This disease is likely to become a more prominent and pressing problem in both countries as the percentage of elderly men increases in the United States and in Canada.

The prostate-specific antigen (PSA) test is currently widely used for prostate cancer detection in these two countries.[4,5] The PSA test has been widely used since it became available in 1986, despite the lack of evidence from randomized controlled trials being conducted to determine whether the test is efficacious at reducing prostate cancer mortality.[6–9]

We know of only two studies that describe differences in prostate cancer incidence and mortality rates and trends between countries—the United States and Sweden[10] and the United States and the United Kingdom.[11] Variability in U.S. geographic regions has also been reported.[12] The United States and Canada have different health care systems, yet the time of adoption and extent of use of the PSA test are similar in the two countries. We wished to compare prostate cancer incidence and mortality rates and trends in these two countries.

METHODS

Data sources
In Canada, national surveillance system data on prostate cancer incidence and mortality data are available from 1969; in the U.S., incidence data go back only to 1973. For the United States information, we used prostate cancer incidence data (1973–1999) from the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) Program, and mortality data (1969–1999, underlying cause of death) from the National Center for Health Statistics of the Centers for Disease Control and Prevention. SEER registry data, which cover about 10% of the United States population, are accepted as being of very high quality.[13,14] Information about the SEER registries, including the participating registries, is available elsewhere.[3] Canadian data came from the Health Statistics Division, Statistics Canada, and included prostate cancer inci-

dence (1969–1998) from the Canadian Cancer Registry and prostate cancer mortality (1969–1999) from the Canadian Vital Statistics Database. Canadian incidence data are population-based; all provinces submit high-quality data to the Canadian Cancer Registry.

Prostate cancer is rare among men younger than 50 years of age.[4] We excluded men this age from our age-specific analysis because calculated incidence and mortality rates for this group would be highly erratic and unreliable.

Selection of standard population
Before computing age-adjusted rates for the comparative analysis, we investigated three standard populations commonly used by the cancer registry community (including the North American Association of Central Cancer Registries): Canada-1991, U.S.-1970, and World.[15] We compared the age structures of the standards to the age structure of the SEER population in 1992, the year in which the age-adjusted prostate cancer incidence rate peaked for white American men. Goodness of fit between standards and the empirical population was measured using the index of dissimilarity (ID), calculated as:

$$\{\Sigma_I \text{ [Absolute (Standard population}_I - \text{U.S. SEER population}_I)]\} / 2$$

where I (five-year age group) varies from 1 to 18 (0–4, 5–9 . . . 80–84, 85+).

Index of dissimilarity is a "summary measure of the difference between two age distributions."[16] The standard with the best fit has the lowest ID value [17,18] and minimizes the difference between crude and adjusted rates.[17] ID was 0.03 for the Canada–1991 standard, 0.12 for U.S.–1970 and 0.13 for World. Thus, we chose the Canada–1991 standard for age adjustment in the comparative analysis of incidence. This standard population was used for mortality comparisons as well.

Controlling for the effects of race
In the United States, large differences in age-adjusted prostate cancer incidence rates exist among racial groups (Table 1). For this reason, our cross-national comparisons should control in some way for differences in racial composition. Normally, we would build race into the rate-adjustment process, or compute race-specific rates, but Canadian incidence data were not available by race. Instead, we determined how to prepare United States data for the cross-national comparison, because Canadian data would have to be used "as is."

We began by comparing the racial distribution of all males in the United States and Canada from esti-

Table 1. Age-adjusted incidence rates of prostate cancer in the United States by race (1990–1996) and racial distribution of United States and Canadian populations (1996)

	Prostate cancer incidence rate[a] United States	Racial distribution (%) United States[b]	Canada[c]
All races	151.9	100	100
Black	222.9	12	2
White	147.3	83	88
Asian or Pacific Islander	81.5	4	7
Native American or Aboriginal	46.5	1	3

[a]Per 100,000 men and age-adjusted to the 1970 United States standard population. Data are from the Surveillance, Epidemiology, and End Results program of the National Cancer Institute, 1990–1996.

[b]U.S. Bureau of the Census, July 1, 1996

[c]Canadian Census, 1996

mates and counts for 1996, the last year for which prostate cancer incidence and mortality data for both countries were available. Compared with the United States, Canada had a greater proportion of whites, Asian/Pacific Islanders, and Native American/Aboriginals, and a smaller proportion of blacks (Table 1).

Because the age-adjusted prostate cancer incidence rate was 50% higher for black men than for white in the United States, and the proportion of blacks among the male population was six times higher in the United States than in Canada, we evaluated whether to compare the Canadian rate for all races combined with that for United States whites only. This approach would minimize the effect of the higher-than-average rate for black men in the United States (which probably elevates the U.S. rate for all races combined relative to the Canadian rate for all races combined) but leave uncontrolled the residual effect of non-white rates within the overall Canadian rate. To estimate the magnitude of this residual effect, we compared two scenarios: (1) age- and race-specific SEER prostate cancer incidence rates for 1992–1996 applied to counts of Canadian men 45 years old and older (the only data category closest to our study population available at the time of our analysis), and (2) age-specific SEER prostate cancer incidence rates for whites for 1992–1996 applied to counts of Canadian men ages 45 years and older with all men in Canada assumed to be white. Canadian men of all races combined yields rates only slightly lower than those yielded by Canadian men

assumed to be white. Because this bias was minor and we had estimated its direction, we decided to compare the incidence and mortality rate for Canadian men of all races with the incidence and mortality rate for white American men.

Statistical analyses
United States incidence rates were calculated with SEER*Stat (version 4.2.3).[19] United States mortality data were converted through SEER*Prep (version 1.9)[20] for subsequent use in SEER*Stat. Canadian incidence and mortality rates were calculated using in-house software at Statistics Canada.

We used 10-year age groups (50–59, 60–69, 70–79, 80+ years) for calculations of age-specific incidence and mortality rates. Joinpoint regression analysis was used to describe prostate cancer trends over time, including the amount of increase or decrease for each time interval.[21] This method determines the number of significant joinpoints by performing several permutation tests. We allowed for up to four joinpoints for each model and preserved the type I error rate through a Bonferroni correction. Each trend in the final model was described by an annual percentage change. The rate of change for each trend was tested to determine whether it was significantly different from zero. Observed incidence and mortality rates are represented by symbols and predicted trends from the joinpoint analysis are represented by solid lines in figures.

In the comparison of United States and Canadian incidence and mortality data, we present U.S.-to-Canada rate ratios. A ratio greater than 1.0 indicates U.S. men have a higher rate; conversely, a ratio less than 1.0 indicates Canadian men have a higher rate. We compared data only for the years available for both countries. Thus, incidence comparisons were restricted to 1973–1998 and mortality comparisons were for 1969–1999. Exact confidence intervals for the rate ratios were calculated. Two-sided mid-p-values were used to determine the statistical significance of the U.S.-to-Canada rate ratios.

RESULTS

Age-standardized incidence rates
Joinpoint analysis identified three trends in the Canadian age-standardized prostate cancer incidence rate: an average increase of 3.0% per year for the period 1969–1990, then a more accelerated increase of 12.7% for 1990–1993, and finally a decline of 8.4% for 1993–1996 (Figure 1, Table 2). The rate peaked in 1993, at 140.4 incident cases per 100,000 men.

Five trends in the U.S. age-standardized incidence

Figure 1. Age-standardized[a] prostate cancer incidence and mortality rates, Canada and the United States white population

[a]Standardized to the 1991 Canadian Population

Sources: Canadian Cancer Registry (1969–1998), Statistics Canada (1969–1999), US SEER (1973–1999), US NCHS (1969–1999)

NOTE: Points represent observed rates; lines represent joinpoint regression lines.

rate were identified, the first four of which were significant. The rate increased steadily (2.5% per year for 1973–1985, 6.7% for 1985–1989, and 18.1% for 1989–1992). A steep decline of 12.3% occurred in 1992–1995, then a non-significant increase through 1999 (Figure 1, Table 2). The rate peaked in 1992 at 213.2 cases per 100,000 men.

Both countries experienced a gradual rise in prostate cancer incidence rate, then a rapid increase beginning in 1989–1990. The rapid increase was more dramatic in the United States than in Canada. In all years, the rate was higher in the United States than in Canada.

Age-standardized mortality rates

Canadian age-standardized prostate cancer mortality rates decreased non-significantly at an average of 0.08% per year for the period 1969–1977, increased significantly at 1.4% for 1977–1993, then decreased significantly at 2.7% for 1993–1999 (Figure 1, Table 3). The rate peaked in 1991, at 31.2 deaths per 100,000 men.

Four trends in United States prostate cancer mortality rates were identified, three of which were significant. The rate increased an average of 0.7% for 1969–1987, increased 3.0% for 1987–1991, decreased insignificantly at 1.2% for 1991–1994, and decreased 4.5% for 1994–1999 (Figure 1, Table 3). The rate peaked in 1991, at 29.4 deaths per 100,000 men.

Both countries experienced a significant decline in prostate cancer mortality rate beginning in 1993–1994.

Table 2. Prostate cancer incidence rate[a] joinpoint analyses[b] by country and age

Country	Trend 1 Range of years	Trend 1 APC	Trend 2 Range of years	Trend 2 APC	Trend 3 Range of years	Trend 3 APC	Trend 4 Range of years	Trend 4 APC	Trend 5 Range of years	Trend 5 APC
Canada	1969–1990	3.0[c]	1990–1993	12.7[c]	1993–1996	–8.4[c]	1996–1998	3.7		
Age (years)										
50–59	1969–1977	5.7[c]	1977–1989	2.5[c]	1989–1993	19.5[c]	1993–1998	3.8		
60–69	1969–1989	3.7[c]	1989–1993	16.2[c]	1993–1998	–1.8				
70–79	1969–1989	3.1[c]	1989–1993	8.8[c]	1993–1998	–6.7[c]				
80+	1969–1993	2.1[c]	1993–1996	–11.0	1996–1998	0.9				
United States, SEER, white	1973–1985	2.5[c]	1985–1989	6.7[c]	1989–1992	18.1[c]	1992–1995	–12.3[c]	1995–1999	1.6
Age (years)										
50–59	1973–1989	4.2[c]	1989–1992	29.6[c]	1992–1999	4.1[c]				
60–69	1973–1985	3.3[c]	1985–1989	9.6[c]	1989–1992	23.8[c]	1992–1995	–7.9	1995–1999	1.5
70–79	1973–1986	2.6[c]	1986–1992	12.5[c]	1992–1995	–14.5[c]	1995–1999	0.6		
80+	1973–1987	1.5[c]	1987–1992	7.0[c]	1992–1995	–19.8[c]	1995–1999	–1.8		

[a]Incidence data are from nine Surveillance, Epidemiology, and End Results (SEER) registries covering 9.5 percent of the U.S. population from 1973 to 1999 and from the Canadian Cancer Registry from 1969 to 1998. Rates are per 100,000 men. Overall rates for Canada and U.S. SEER (white) are standardized to the 1991 Canadian population.

[b]Joinpoint analyses of trends allowing for up to four joinpoints

[c]The APC is statistically significantly different from 0 ($p<0.05$).

APC = annual percentage change

In all years, the rate was higher in Canada that in the United States.

Age-specific incidence rates

For Canadians 50–59, 60–69, and 70–79 years old, the prostate cancer incidence rate gradually rose from 1969 until 1989-1990, when the rate increased much more quickly; then the rate declined starting in 1993 (Figure 2, Table 2). For men at least 80 years old, only two significant trends were identified by joinpoint analysis: an average annual increase of 2.1% until 1993, and then the start of an average decline of 11.0%. The incidence rate peaked in 1993–1994 for all four age groups (Figure 2).

Among all age groups, the prostate cancer incidence rate for white American men increased significantly each year through 1992 (Figure 3, Table 2).

Starting in 1986 (70–79 years), 1987 (≥80 years), or 1989 (50–59 and 60–69 years), the rate jumped at least threefold. From 1992 through 1995, the rate decreased 14.5% annually for men 70–79 years old and 19.8% for men at least 80 years old and increased 4.1% among 50–59-year-olds (1992–1999). For men ages 50–59 years, the incidence peaked in 1999; for all other American men, the rate peaked in 1991–1992.

In both Canada and the United States, the prostate cancer incidence rate was higher in each advancing 10-year age group, except that among Americans starting in 1992, the rate was lower among men ages 80 years or older than among men ages 70–79 years. In each age group, the incidence rate was higher among white Americans, except for the last five years in the oldest age group, where Canadian rates were higher.

Figure 2. Age-specific prostate cancer incidence rates, Canada, 1969 to 1998

Source: Canadian Cancer Registry

NOTE: Points represent observed rates; lines represent joinpoint regression lines.

Figure 3. Age-specific prostate cancer incidence rates, United States SEER white population, 1973 to 1999

Source: Surveillance, Epidemiology, and End Results program

NOTE: Points represent observed rates; lines represent joinpoint regression lines.

Age-specific mortality rates

Canadian age-specific prostate cancer mortality rate trends were more gradual than the age-specific incidence trends (Figure 4, Table 3). From 1969 to the mid-1990s, significant positive trends were observed for the oldest three age groups. Among those men, the prostate cancer death rate decreased from 1993 to 1999 by an average of 3.1% per year; a decrease (−4.1% APC) was also experienced by men ages 60–69 over the same period.

In all age groups, the prostate cancer mortality rate for white Americans increased significantly at some point until the early 1990's (Figure 5, Table 3). A measurable increase in the rate occurred among men 60–79 years old in 1984 and among men ages 80 years and older in 1987. Declines began in 1990 for white Americans ages 50–59 years, in 1992 for those ages 60–79 years, and in 1993 for men at least 80 years old.

Prostate cancer mortality rates peaked in 1990–1991, except for the oldest age group (80 years and older), for whom the rate peaked in 1993.

Rate ratios

From 1973 through 1982, age-specific prostate cancer incidence rate ratios declined slightly, then began to increase, and differences in age groups became more apparent (Figure 6). The largest difference between the two countries' incidence rates was among men 50–59 years old, where, in 1988–1992, the rate in the United States was almost 1.9 times the rate in Canada. From 1983 to 1998, generally, the ratios increased with each decreasing 10-year age group. Canadian men had a higher incidence rate than United States white men only in 1993–1998 among those aged 80 years or older (rate ratio [RR] = 0.97, 95% confidence interval [CI] 0.95, 0.99; $p=0.01$). At all other time points, the

Figure 4. Age-specific prostate cancer mortality rates, Canada, 1969 to 1999

Source: Statistics Canada

NOTE: Points represent observed rates; lines represent joinpoint regression lines.

U.S. had significantly higher incidence rates among all age groups.

The range in prostate cancer mortality rate ratios is much smaller than that for incidence rate ratios. With some exceptions among men ages 50–69 years through 1979–1983, prostate cancer mortality rates were higher among Americans than Canadians (Figure 7). However, only among men 60–69 years old in 1974–1978 was this difference statistically significant (RR=1.06, 95% CI=1.01, 1.11; p=0.03). The data appear to show an age effect, as the ratios tended to decrease with increasing age group, except among the oldest men in recent years. Rate ratios in the 1970s were quite variable; beginning in 1979–1983, with a few exceptions, the direction of the ratios became similar in all age groups. Furthermore, the differences between the age groups narrowed considerably over time and by 1994–

1999, the rate ratio was 0.88–0.91 in all groups (p<0.05 for all age groups). Among men ages 70 years and older, the U.S. rates were significantly lower than the Canadian rates for all groups except for a borderline difference among men ages 70–79 in 1969–1973 (p=0.07).

DISCUSSION

The advent of PSA testing resulted in sharp increases in prostate cancer incidence rates in both countries. This is consistent with Legler et al.[5] in the United States and Levy in Canada,[4] who showed that changes in incidence rates have been associated with changes in the use of the PSA test. The Canadian age-standardized prostate cancer incidence rates are similar to the patterns of those for U.S. white men with a year or two

Table 3. Prostate cancer death rate[a] joinpoint analyses[b] by country and age

Country	Trend 1		Trend 2		Trend 3		Trend 4	
	Range of years	APC	Range of years	APC	Range of years	APC	Range of years	APC
Canada	1969–1977	–0.08	1977–1993	1.4[c]	1993–1999	–2.7[c]		
Age (years)								
50–59	1969–1999	0.4						
60–69	1969–1993	1.2[c]	1993–1999	–4.1[c]				
70–79	1969–1993	0.9[c]	1993–1999	–3.1[c]				
80+	1969–1995	1.1[c]	1995–1999	–1.8				
United States, white	1969–1987	0.7[c]	1987–1991	3.0[c]	1991–1994	–1.2	1994–1999	–4.5[c]
Age (years)								
50–59	1969–1990	0.8[c]	1990–1999	–3.6[c]				
60–69	1969–1984	0.5[c]	1984–1992	1.8[c]	1992–1999	–5.6[c]		
70–79	1969–1984	0.2[c]	1984–1992	1.7[c]	1992–1999	–4.4[c]		
80+	1969–1987	1.2[c]	1987–1993	2.9[c]	1993–1999	–3.4[c]		

[a]Death data are from the National Center for Health Statistics (NCHS) covering the entire U.S. population from 1969 to 1999 and from Statistics Canada from 1969 to 1999. Rates are per 100,000 men. Overall rates for Canada and U.S. white population are standardized to the 1991 Canadian population.

[b]Joinpoint analyses of trends allowing for up to four joinpoints

[c]The APC is statistically significantly different from 0 (p<0.05).

APC = Annual percentage change

lag and tend to be lower than the United States' rates. This year or two lag time is consistent with the later introduction (1986 in the U.S. and approximately 1988 in Canada) of PSA testing for screening purposes in Canada.[22]

Our results show higher incidence rates in the United States than in Canada, which may be attributed to a number of factors. First, the incidence data from Canada were population-based whereas the United States data were based on sentinel sites from the SEER program. SEER data may overestimate United States rates because the population residing within the SEER areas is more affluent, has lower unemployment and is much more urban than the rest of the United States population.[23] Urban men may be more likely to have [24] and be diagnosed with prostate cancer due to their access to health services such as the PSA test, transurethral resection of the prostate, etc. Second, PSA testing for screening purposes was likely more aggressive in the United States during the 1990's than it was in Canada. This could be due to the assertive promotion of PSA screening kits by their manufacturers in the U.S. contrasted with the single-payer system in Canada, where marketing was not as widespread.

In contrast, the Canadian Task Force on the Periodic Health Examination,[25] the Canadian Workshop on Screening for prostate cancer (which is largely endorsed by most Canadian health organizations),[26] and the U.S. Preventive Services Task Force[27] all reviewed the evidence for routine use of the PSA test for prostate cancer screening and determined that there was not enough evidence (no decrease in prostate cancer mortality) to recommend its use. Despite the lack of evidence from randomized controlled clinical trials, the American Cancer Society recommended limited use of the PSA test beginning in 1992.[28]

Despite the differences in incidence, mortality rates in the United States and Canada appear similar. Prostate cancer mortality rates remained relatively stable for younger age groups, but increased noticeably in older age groups (ages 80 years and older) during the 30 years of observation. In recent years, rates have been on the decline for younger age groups in both countries. Several factors could account for the overall decrease in prostate cancer mortality rates. Changes in the disease management could explain the reduced mortality in younger men;[11] there could also be misclassification of cause of death.

Feuer et al.[9] suggest that prostate cancer mortality

Figure 5. Age-specific prostate cancer mortality rates, United States white population, 1969 to 1999

Source: US National Center for Health Statistics

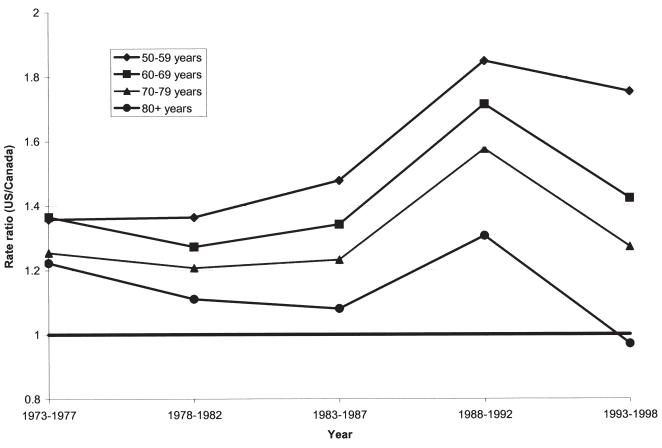NOTE: Points represent observed rates; lines represent joinpoint regression lines.

trends have been affected by cause-of-death misclassification associated with the rising and falling pool of prevalent cases with a fixed proportion having misattributed cause of death within the prevalent pool. Wilt suggests that geographic variation in care coupled with population size variability may partially account for the decline.[7] Variations in prostate cancer care could be caused by differences in health care systems, societal beliefs, physician practices, and patient characteristics.

Gann asserted that mortality rates would need to fall below those of pre-PSA (as a diagnostic tool) levels to provide evidence that PSA screening has lowered mortality from prostate cancer.[29] Tarone et al. point out that mortality rates began to decline before prostate cancer incidence rates peaked,[6] though this does not refute the possibility of a PSA/early detection/

mortality connection. Tarone and colleagues used stage-specific survival rates to demonstrate that detection of high-grade prostate cancers before metastasis may be the reason for a rapid decline in mortality rates. At this point, definitive randomized trials to assess the efficacy of early detection and treatment have not been completed.

Future studies of this nature could use more representative data from the United States when they become sufficiently reliable. Such data will come from state registries in the CDC's National Program of Cancer Registries, which, when fully implemented, will cover 96% of the United States population. Subanalyses comparing neighboring cities in Canada and the United States, and province/state comparisons to explore variations in prostate cancer as well as other cancers would also be worthwhile.

Figure 6. Age-specific prostate cancer incidence rate ratios between the United States SEER white population and Canada, 1973 to 1998

Sources: Canadian Cancer Registry; Surveillance, Epidemiology, and End Results program

NOTE: Points represent observed rates; lines represent joinpoint regression lines.

The robust trends we observe strongly implicate the connection between PSA test use and recent prostate cancer incidence trends in Canada and the United States. A few years' additional data are needed to decide whether the observed decline in both countries' mortality rates will be sustained. It is hoped that clinical trials now in the field will determine the true effect of PSA screening on prostate cancer mortality.

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Figure 7. Age-specific prostate cancer mortality rate ratios between the United States white population and Canada, 1969 to 1999

Sources: Statistics Canada; US National Center for Health Statistics

NOTE: Points represent observed rates; lines represent joinpoint regression lines.

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