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The rising incidence of testicular cancer among young men in Canada, data from 1971–2015

Darren R. Brenner[a,b], Emily Heer[a], Yibing Ruan[a], Cheryl E. Peters[a,b,*]

[a] Department of Cancer Epidemiology and Prevention Research, CancerControl Alberta, Alberta Health Services, Calgary, Alberta, Canada
[b] Departments of Oncology and Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

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ABSTRACT

Background: Testicular cancer is the most common malignancy among young men aged 15–44 in Canada. The goal of this analysis was to examine age-period-cohort effects of testicular cancer incidence between 1971 and 2015.

Methods: Data were collected from the National Cancer Incidence Reporting System and the Canadian Cancer Registry. Birth cohort models were fit using the National Cancer Institute's web tool. Incidence annual percent changes were estimated using NCI's Joinpoint Regression Program.

Results: Incidence of testicular cancer in Canada has increased steadily since 1971. A birth cohort effect was observed for men born in the years after 1945. The rate of testicular cancer peaks at age 35 and drops off with increasing age.

Conclusion: Incidence of testicular cancer has risen dramatically in Canada in recent decades and the cohort effect indicates the need to investigate exposures that have increased since 1945 and that may affect development in young men.

1. Introduction

Testicular cancer (TC) is a relatively rare malignancy in the general population, making up less than 1% of all cancers diagnosed among men. However, it is the most frequently occurring malignancy in young men aged 15–44 in most high-income countries and accounts for 13% of cancers in individuals aged 15–29 in Canada [1]. It is well-documented that the incidence of testicular cancer has been rising at an alarming rate for the past several decades [2]. This increased rate cannot be explained by changing diagnostic practices or definitions, or improved screening, which indicates that there has been a real change in the underlying risk and incidence in the population.

The recent increase in incidence has been seen worldwide, primarily in high-income countries. In the United States, incidence increased by 1.1% per year between 1992 and 2009 and there have been similar increases in many European countries [3]. Notably, while incidence rates in Eastern European countries have previously been lower than in Northern European countries, rates rose rapidly between 2002 and 2007 and are now near equivalent in the two regions [2]. There is also some evidence for a greater increase in rates of non-seminoma type tumors (compared to seminoma), which occur more often in younger men and adolescents [4]. Cohort effects have been documented in several populations, with results indicating an increase in testicular cancer incidence beginning with men born after 1945 [2].

The effect of age, period, and birth cohort have been examined in previous analyses but has not been assessed in the Canadian context since 1999 [5]. Therefore, the goal of this study was to investigate the incidence trends of testicular cancer between 1971 and 2015 in Canada and explore age-period-cohort effects.

2. Methods

Data were collected on testicular cancer cases using ICD-10 codes C62 (C62.0, C62.1, C62.9) for incidence in Canada between 1971 and 2015 [6]. Incidence rates were compiled using the National Cancer Incidence Reporting System (for rates up to 1992) and the Canadian Cancer Registry (CCR) (for rates beyond 1992). The CCR collects data on cancer cases submitted by each province and territory's individual registry. Cancer collection and control is a legislated responsibility within each province and territory, which ensures a high level of quality in the reporting of new cancer cases.

Age-specific annual percent changes in incidence rate were

* Corresponding author at: Department of Cancer Epidemiology and Prevention Research, CancerControl Alberta, Alberta Health Services, Holy Cross Centre, Room 515, Box ACB, 2210-2nd St. SW, T2S3C3 Calgary, Alberta, Canada.
E-mail address: Cheryl.peters@albertahealthservices.ca (C.E. Peters).

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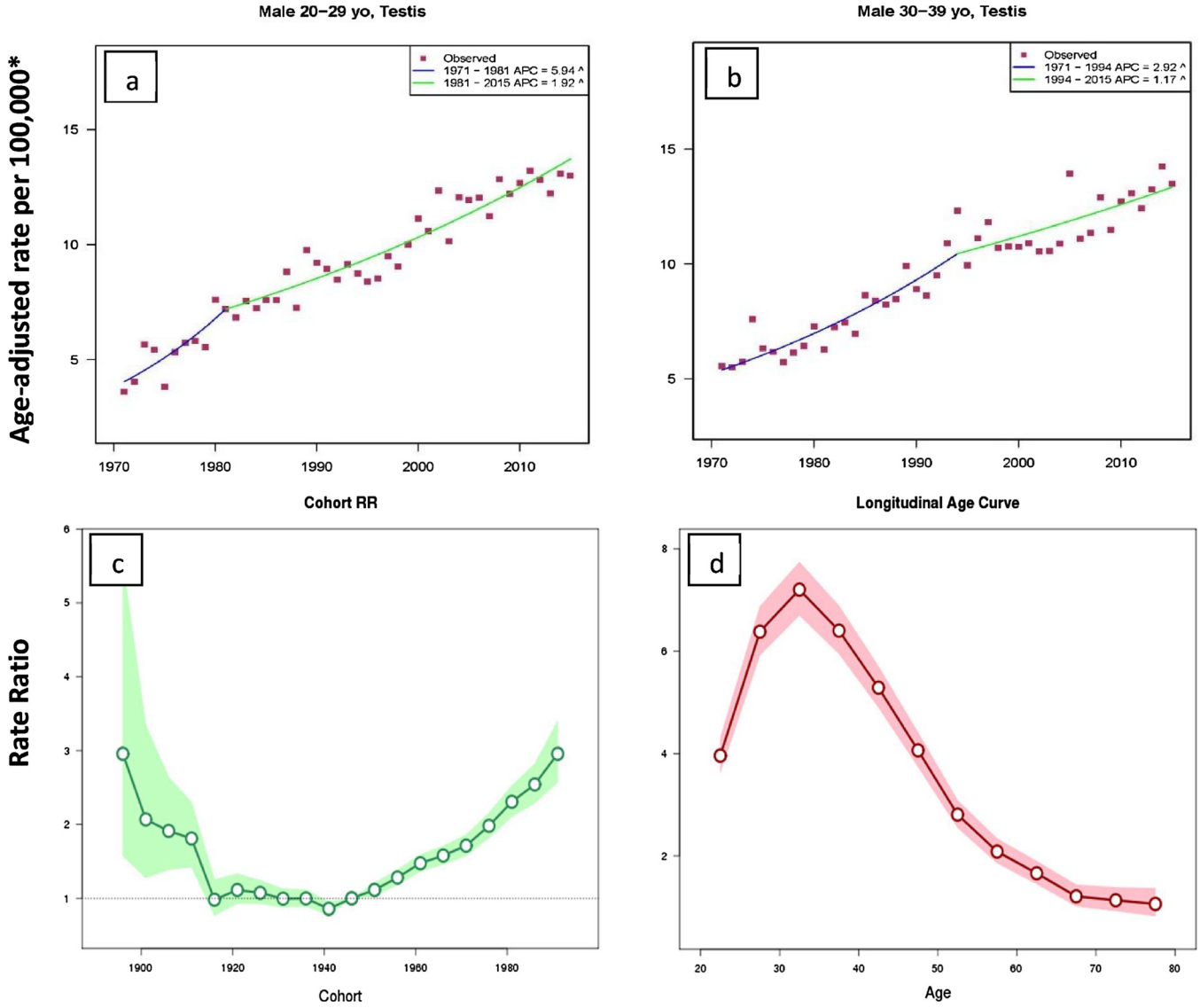

Fig. 1. (a) Age-adjusted incidence rates per 100,000 of testicular cancer in Canadian males aged 20–29 years. Annual percent change (APC) given in legend; (b) Age-adjusted incidence rates per 100,000 of testicular cancer in Canadian males aged 30–39 years. APC given in legend; (c) rate ratio of testicular cancer in Canada by birth cohort 1896–1991; (d) trend of testicular cancer rate by age 20-80.
*Age-adjusted to standard Canadian population, 2011

estimated using the Joinpoint Regression Program (version 4.5.0.1, National Cancer Institute NCI) as described in a previous publication [7]. Birth cohort models were fit using NCI's web tool [8]. Input data were cases and population for 12 five-year age groups (20–79) and 9 five-year periods (1971–2015). Cohort effects are presented as incidence rate ratios with 1946 as the reference cohort.

3. Results

The incidence of testicular cancer in Canada has been increasing since 1971. Incidence in 1971 was approximately 3.77 per 100,000, compared to an incidence of approximately 7.06 per 100,000 in 2015 for all age groups combined. Between 1971 and 1981, the incidence annual percent change (APC) for men aged 20–29 was 5.94, and 1.92 between 1981 and 2015 (Fig. 1a). The changes in incidence among men aged 30–39 was slightly lower but still increased in the same time intervals (Fig. 1b). While the increase in incidence can be seen across time trends, there is evidence for a strong cohort effect that is continuing, with more recent cohorts having higher risk for testicular cancer than men born earlier. Specifically, observed data indicates that there is a dramatic and uninterrupted increase in risk for men born after 1945 (Fig. 1c). Observed data include narrow confidence intervals around estimates for the increasing incidence rates in recent birth cohorts. As expected, we also observed an age effect in these data. The rate of testicular cancer peaks among men aged 35 and drops off considerably as age increases (Fig. 1d).

4. Discussion

Previous studies have found evidence of a cohort effect in testicular cancer incidence. Studies from Western Europe also found that the increase in testicular cancer incidence began in cohorts born after 1945 [9]. A study out of the United States found that, not only was birth cohort associated with higher risk of testicular cancer but the peak age at diagnosis decreased for each successive birth cohort [10]. While we did not investigate this particular trend, it is notable that the incidence among the youngest men had a greater increase than those in older age groups. In the Canadian study mentioned previously [5], the authors found that the effect of birth cohort was a more significant determinant of testicular cancer risk than time period. The present study adds to

existing knowledge by including cohorts born up to 1991, whereas the previous Canadian study stopped at cohorts born in 1964. Although period effects can sometimes be disguised as cohort effects, results from our analysis suggest that we are observing birth cohort effects. The period and cohort effects were both statistically significant ($p < 0.0001$) in the age-period-cohort analysis; however, the age-cohort model explained the testicular cancer incidence better than the age-period model and were similar to the age-period-cohort full model (results available upon request). This suggests that the observed trends were mainly explained by a birth cohort effect rather than a period effect.

Cohort effects lend support to the hypothesis that there is some exposure involved in testicular cancer etiology that changes over time and affects males in development or at a young age. One prenatal exposure that has received attention is increased exposure to estrogens (endogenous, exogenous, or environmental) that can affect gonadal development *in utero* [11]. As many endocrine-disrupting chemicals contain synthetic estrogens and these compounds are prevalent in the Western environment, it is important to pursue this hypothesis further.

Exposures of interests for other conditions of the reproductive system (i.e. prostate cancer, sperm quality, reduced fertility) have included lifestyle factors such as cigarette smoking, recreational drug use, diet [12], ejaculation frequency [13], and occupational exposures [14]. One exposure that appears to show a strong relationship with testicular cancer risk is marijuana use, with several studies pointing toward a positive association [15]. To our knowledge, the association between ejaculation frequency and testicular cancer has not been examined but, given its relationship with other afflictions of the reproductive system, it may be worth investigating. Many of these factors that have not been investigated fully have changed in exposure levels in recent decades, which is relevant to the time frame of increasing incidence seen in this analysis.

Results from examinations of other environmental contaminants have been largely inconsistent and, as the presence of many of these contaminants has decreased in recent years, an association would not explain incidence trends. It would be more useful to examine chemicals and pollutants that may have increased in use in recent decades. Another possibility is that there has been increased awareness of testicular cancer in recent cohorts, which may have led to higher incidence in these groups. However, we suspect that the contribution of this effect is relatively small. Further research should be conducted on this rising incidence, especially considering that rates may be stabilizing in the most recent birth cohorts.

The rising incidence of testicular cancer with no change in diagnostic practices suggests a change in etiologically-relevant exposure, and our current understanding of the causal network of the disease is limited. Several studies have shown that there is evidence of a birth cohort effect in testicular cancer incidence and this analysis of Canadian data adds further evidence of that effect. In response to this information, focus should be placed on early-life or *in utero* exposures that may be involved in the etiology of testicular cancer. With a deeper understanding of the modifiable risk factors of testicular cancer, fewer young men will be exposed to cancer treatment with potentially harmful side effects.

Declaration of interest

No potential conflicts of interest to declare.

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