

# Trends in the incidence of testicular germ cell cancer in Ontario by histologic subgroup, 1964–1996



*Evidence*

*Études*

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## Abstract

**Background:** Testicular cancer is rare but is notable because it affects mainly young men. The incidence of this disease has been increasing in developed countries throughout the world for several decades. The authors examined trends in the incidence of testicular germ cell cancer in Ontario for the period 1964–1996 according to the 2 main histologic groups, seminoma and non-seminoma.

**Methods:** Data on incident cases of testicular germ cell cancer diagnosed in Ontario residents aged 15–59 years between 1964 and 1996 were extracted from the population-based Ontario Cancer Registry. Annual rates of testicular cancer for the 2 histologic groups were analysed by means of log-linear regression to estimate average annual percent change.

**Results:** Between 1964 and 1996 the incidence of testicular germ cell cancer increased by 59.4%, from 4.01 to 6.39 per 100 000. This corresponded to an average annual increase of about 2% for both nonseminoma and seminoma. The relative increase in incidence was greatest in the lowest age group (15–29 years) for both histologic groups, although the data suggest that the incidence of non-seminoma cancer in this age group began to decline in the early 1990s. The increase in incidence appears to be due to a birth cohort effect, with more recent cohorts of men at increased risk.

**Interpretation:** The rise in the incidence of testicular germ cell cancer, not only in Ontario but also in many developed countries, requires investigation. The search for explanatory factors should focus on exposures whose prevalence may have increased over the past few decades and that are common enough to affect population incidence. The similarity of trends for seminoma and nonseminoma cancer suggests that the underlying risk factors are likely the same.

## Résumé

**Contexte :** Le cancer du testicule est rare, mais il faut le signaler parce qu'il atteint surtout des hommes jeunes. L'incidence de cette maladie est à la hausse dans les pays industrialisés du monde entier depuis plusieurs décennies. Les auteurs ont étudié les tendances de l'incidence du cancer des cellules germinales du testicule en Ontario pendant la période de 1964 à 1996 en fonction des deux principaux groupes histologiques : séminome et non séminome.

**Méthodes :** On a extrait du Registre du cancer de l'Ontario, base de données démographique, des données sur les cas nouveaux de cancer des cellules germinales du testicule diagnostiqués, entre 1964 et 1996, chez des résidents de l'Ontario âgés de 15 à 59 ans. On a analysé les taux annuels de cancer du testicule des deux groupes histologiques au moyen d'une régression loglinéaire pour estimer le pourcentage annuel moyen de changement.

**Résultats :** Entre 1964 et 1996, l'incidence du cancer des cellules germinales du testicule a augmenté de 59,4 % pour passer de 4,01 à 6,39 pour 100 000. Cette augmentation correspond à une augmentation annuelle moyenne d'environ 2 % des cancers non séminomes et des cancers séminomes. L'augmentation re-

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lative de l'incidence a été la plus importante chez les sujets les moins âgés (15 à 29 ans) pour les deux groupes histologiques, même si les données indiquent que l'incidence de cancers non séminomes dans ce groupe d'âge a commencé à diminuer au début des années 90. L'augmentation de l'incidence semble attribuable à un effet de cohorte de naissance qui accroît le risque chez les cohortes plus récentes d'hommes.

**Interprétation :** Il faut enquêter sur la montée de l'incidence du cancer des cellules germinales du testicule constatée non seulement en Ontario, mais aussi dans beaucoup de pays industrialisés. La recherche des facteurs explicatifs devrait porter avant tout sur les expositions dont la prévalence peut avoir augmenté au cours des dernières décennies et qui sont assez communes pour jouer sur l'incidence démographique. La similarité des tendances des cancers séminomes et non séminomes indique que les facteurs de risque sous-jacents sont probablement les mêmes.

**A**lthough testicular cancer is rare, accounting for only 1% of all cancers diagnosed in male residents of Ontario, it is the most commonly diagnosed cancer in men aged 25–34 years.<sup>1</sup> Testicular cancer has a unique age-at-incidence pattern: incidence rises through adolescence, peaking at age 25 to 29, and declines gradually thereafter.<sup>1</sup> Most testicular cancers in young and middle-aged men are germ cell tumours, which are grouped histologically into seminoma and nonseminoma.<sup>2</sup>

The incidence of testicular cancer is increasing in Ontario<sup>1</sup> and in developed countries throughout the world.<sup>3–8</sup> However, reasons for the increasing incidence remain unknown. Despite numerous investigations, little consistent information regarding the etiology of this disease has emerged, apart from the fact that cryptorchidism results in a substantially increased risk.<sup>9,10</sup> However, since cryptorchidism is rare (prevalence less than 3%),<sup>9</sup> changes in its prevalence could not produce the observed increases in the incidence of testicular cancer.

Some researchers have studied risk factors for the 2 main histologic subgroups separately, in part because of their very different age-at-incidence curves. The evidence for differences in etiology is inconclusive, however.<sup>11,12</sup>

Close examination of incidence trends according to the 2 histologic subgroups and age may provide clues about the underlying causes of the increase and whether they are likely to differ by histologic subgroup. In this report we describe the incidence of testicular germ cell cancer in Ontario over the period 1964–1996 according to the 2 main histologic subgroups and discuss how the data may suggest or support etiologic hypotheses.

## Methods

Data were extracted from the Ontario Cancer Registry, a population-based registry that includes all newly diagnosed cancers in residents of Ontario (1996 population 11.25 million<sup>13</sup>) since 1964. The registry, which is maintained by Cancer Care Ontario, routinely receives hospital discharge records, pathology reports and death certificates that mention

cancer, as well as reports from the regional cancer centres, which are also part of Cancer Care Ontario, and the Princess Margaret Hospital. These reports are linked together by means of probabilistic record linkage to create case records. The registry methods are described in more detail elsewhere.<sup>14</sup> The primary site of cancer is coded according to the International Classification of Diseases, 9th Revision (ICD-9)<sup>15</sup> and morphology according to the International Classification of Diseases for Oncology (ICD-O).<sup>16</sup>

We evaluated trends in incidence between 1964 and 1996 for the 2 histologic subgroups and for 3 age groups (15–29 years, 30–44 years and 45–59 years) as well as for all ages (15–59 years) through log-linear modelling of annual rates using the SAS procedure GENMOD (release 6.09, SAS Institute Inc., Cary, NC). Each model included year of diagnosis and categorical variables for all relevant 5-year age groups; the error structure was assumed to be Poisson. We calculated the average annual percent changes and their 95% confidence intervals from the maximum likelihood estimates of the year parameter and its standard error. Quadratic effects were assessed for each model.

We also calculated 3-year moving average rates, age-standardized to the World Standard Population,<sup>17</sup> for graphic presentation of trends.

Age-specific incidence was also examined graphically for cohorts of men born in 1920–1924 through 1965–1969 for both histologic subgroups.<sup>18</sup>

## Results

Between 1964 and 1996, 5156 cases of testicular germ cell cancer (ICD-9 code 186 and ICD-O morphology codes 906 to 910) were diagnosed in Ontario residents aged 15–59 years. About half of the cases (2802 [54.3%]) were seminomas (ICD-O morphology code 906); the mean age at diagnosis was 36 years. The remaining 2354 cases were either nonseminomas (ICD-O morphology codes 907 to 910) or mixed seminoma–nonseminoma tumours; the mean age at diagnosis was 29 years.

Over the study period the incidence of testicular germ cell cancer in males aged 15–59 years rose by 59.4%, from 4.01 per 100 000 in 1964–1966 to 6.39 per 100 000



in 1994–1996 (data not shown). Similar proportional increases were observed for both histologic subgroups (Fig. 1). The incidence trends for the 3 age groups for seminoma and nonseminoma germ cell tumours separately are shown in Fig. 2. Table 1 presents frequencies and age-adjusted rates for 1964–1966 and 1994–1996 as well as the estimated average annual percent change in incidence for

the age and histologic subgroups from the modelling of annual rates. There was an average annual increase of about 2% for both seminomas and nonseminomas. For nonseminomas, there was a statistically significant increase in incidence in the 2 lower age groups (15–29 years and 30–44 years) but not in the higher age group, and rates were highest among males aged 15–29 years. However, the presence of a significant quadratic effect (signify-

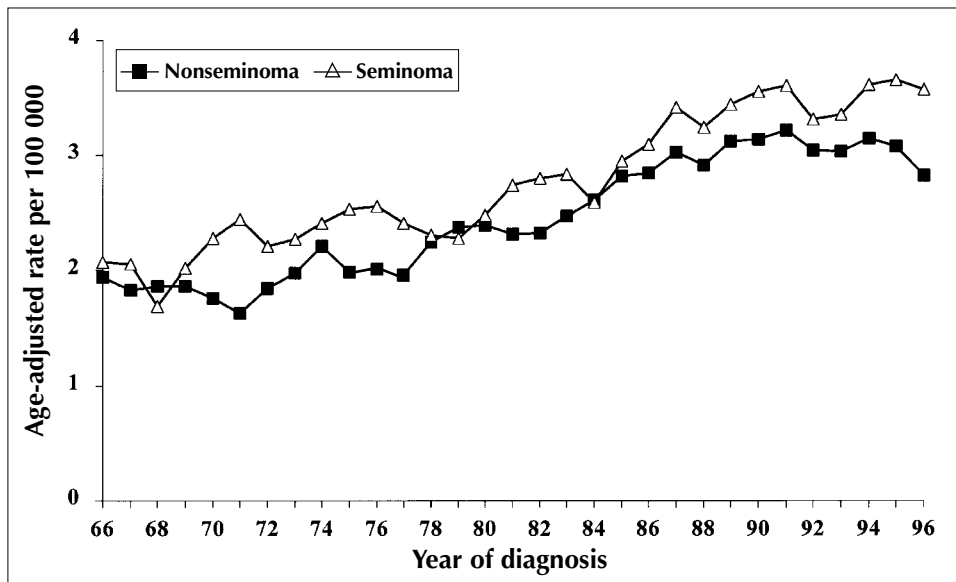


Fig. 1: Incidence of testicular germ cell cancer by histologic subgroup in Ontario residents aged 15–59 years during 1964–1996 (3-year moving average rates).

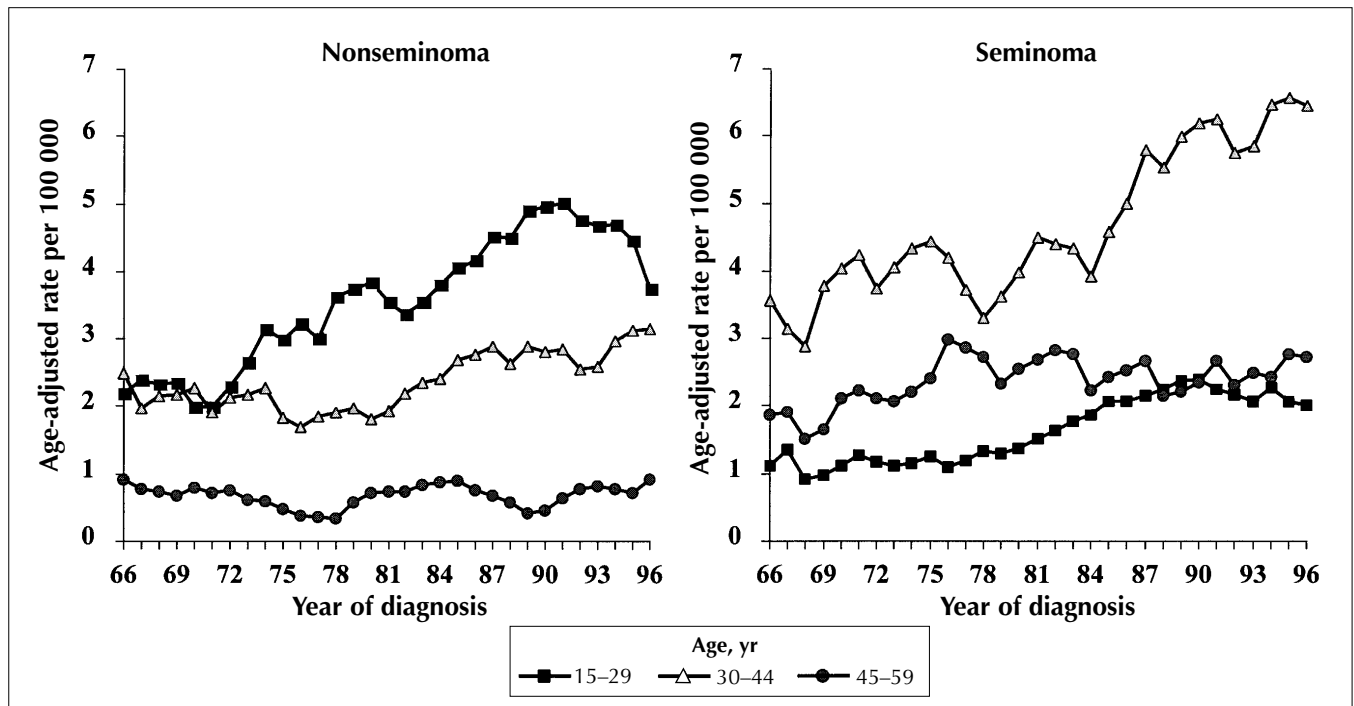


Fig. 2: Incidence of testicular germ cell cancer by age at diagnosis for the 2 main histologic subgroups during 1964–1996 (3-year moving average rates).



ing a nonlinear trend) for those aged 15–29 means the average annual percent increase alone cannot adequately represent the change in incidence over time. After a long period of sustained increase, the incidence of nonseminomas in the lowest age group began to decline in the early 1990s (Fig. 2).

For seminomas, there was a statistically significant increase in incidence among males in all 3 age groups over the study period; rates were highest among those aged 30 to 44.

When age-specific incidence rates by 5-year age group

and 5-year birth cohort were examined, a steady increase in age-specific incidence for both nonseminomas and seminomas was evident among more recently born cohorts (detailed data not shown). Fig. 3 shows 4 of the 10 possible birth cohorts for nonseminomas. In general, at each age, males born more recently had a higher incidence than those born earlier.

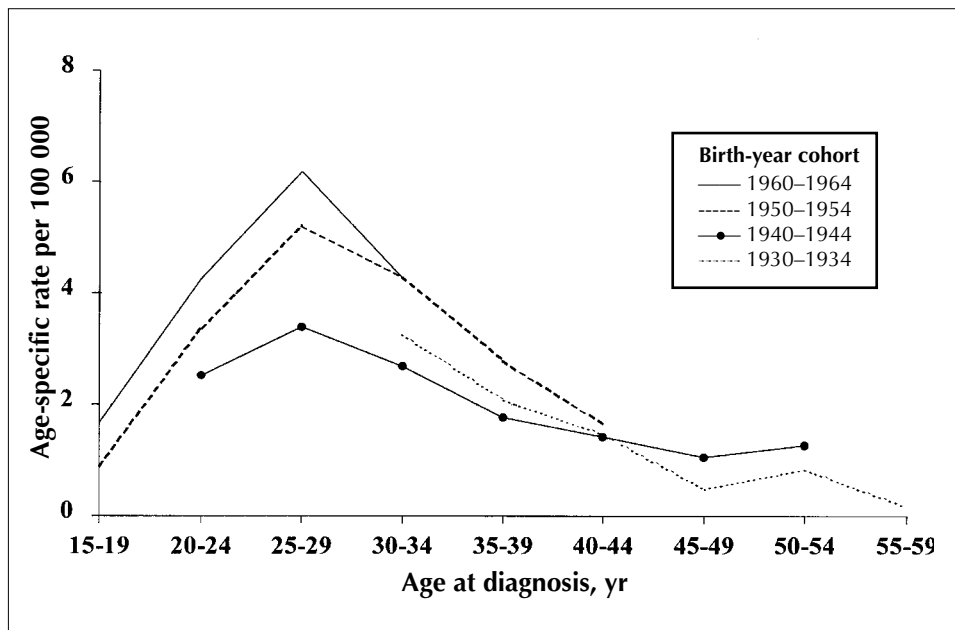
### Interpretation

In Ontario the incidence of testicular germ cell cancer

**Table 1: Frequency, age-adjusted incidence rate and average annual percent change for testicular germ cell cancer in Ontario residents aged 15–59 years by age group and histologic subgroup, 1964–1996**

Histologic subgroup; age, yr	1964–1966		1994–1996		Average annual change (and 95% CI), %*
	No. of cases	Age-adjusted rate	No. of cases	Age-adjusted rate	
<b>Nonseminoma</b>					
15–29	46	2.18	136	3.73	2.37 (1.76 to 2.98)†
30–44	51	2.48	138	3.14	1.46 (0.71 to 2.21)
45–59	14	0.92	25	0.91	0.41 (–1.26 to 2.08)
All ages	111	1.94	299	2.82	1.90 (1.45 to 2.35)
<b>Seminoma</b>					
15–29	23	1.12	79	2.01	2.82 (1.92 to 3.72)
30–44	74	3.56	282	6.45	2.31 (1.76 to 2.86)
45–59	28	1.87	77	2.73	0.98 (0.08 to 1.89)
All ages	125	2.07	438	3.57	2.14 (1.79 to 2.55)

Note: CI = confidence interval.  
\*Estimated by modelling. See the Methods.  
†A significant quadratic effect is also present.



**Fig. 3: Age-specific incidence rates of testicular nonseminoma by year of birth in Ontario residents aged 15–59 years during 1964–1996.**



increased by nearly 60% between 1964 and 1996, whereas the incidence of testicular tumours of other histologic types did not rise (Ontario Cancer Registry unpublished data). The quality of the registry data is good, particularly for testicular cancer.<sup>1</sup> Although registry data sources changed somewhat over the study period, it is unlikely that these changes are responsible for the observed increase, given that few other sites of cancer have shown such trends.<sup>1</sup> In addition, there is no population-based screening for testicular cancer in Ontario, and diagnostic methods for this disease have not changed since at least the late 1970s. Since similar increases in the incidence of testicular cancer have been noted in other jurisdictions, some of which have high-quality long-standing cancer registry systems,<sup>3-8</sup> it seems likely that the changing incidence in Ontario is real.

In considering etiologic factors that may be responsible for this phenomenon, it should be noted that the most important determinants of the risk of cancer for an individual (i.e., those with a high relative risk, such as cryptorchidism) may differ from the most important determinants of population incidence<sup>19</sup> (i.e., those with a high prevalence). The descriptive epidemiology of testicular germ cell cancer suggests several clues to the determinants of incidence. The increase in incidence appears to be due to a birth cohort effect, with more recent cohorts of men at increased risk. A similar cohort phenomenon has been observed in Denmark, other north European countries and Connecticut.<sup>5,7,8</sup> Exposures most likely have changed over time: the intensity of exposure may have increased, or protective factors may have decreased. Candidate risk factors include age at puberty,<sup>20-22</sup> which has declined among more recently born cohorts of men, coincident with the birth cohort phenomenon, and estrogen and estrogen-like substances, whose prevalence may have increased in the environment.<sup>23</sup>

The possibility of different etiologies for seminoma and nonseminoma has been raised because of their distinct age-at-incidence curves. Several investigators have attempted to explore this possibility in etiologic investigations;<sup>9,11,12</sup> however, their results have not proven convincing. In addition, the similarity of secular trends for seminoma and nonseminoma germ cell cancer in Ontario, whether examined cross-sectionally or by cohort, suggests that the risk factors responsible for the increases are likely the same.

In summary, future etiologic investigations should focus on exposures whose prevalence has increased over the past few decades, coincident with the birth cohort phenomenon apparently responsible for the rising incidence of testicular germ cell cancer. The recent decline in the incidence of nonseminoma testicular germ cell cancer in males aged 15 to 29 years requires further observation,

because such a change in incidence may suggest and support etiologic hypotheses.

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