

RISING RISK OF TESTICULAR CANCER BY BIRTH COHORT IN THE UNITED STATES FROM 1973 TO 1995

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ABSTRACT

Purpose: Recent epidemiological studies have demonstrated an increasing incidence of testicular cancer in white men which appears to be correlated with the period of birth. Because this birth cohort phenomenon can explain etiological factors in testicular cancer, we determine whether this trend is present throughout the United States based on an analysis of testicular cancer incidence by birth cohort.

Materials and Methods: Testicular cancer incidence was obtained from the National Cancer Institute Surveillance, Epidemiology and End Results database from 1973 to 1995. Numbers of cases were extracted and grouped by 5-year birth cohorts for all testicular germ cell neoplasms. Poisson regression analysis with variables of age, time of diagnosis and birth cohort were used to determine relative risk. Poisson models were compared using computer log linear model software.

Results: Between 1973 and 1995 the incidence of testicular cancer in the United States increased 51% (3.61 to 5.44/100,000). Analysis of Poisson models revealed that birth cohort was strongly associated with relative risk of testicular cancer ($p = 0.001$). In addition, peak age at diagnosis decreased for each successive birth cohort.

Conclusions: The overall incidence of testicular cancer in white men and the relative risk of testicular cancer have been increasing in the United States. This trend is strongly associated with birth cohort in concordance with previously reported European data. Moreover, testicular cancer is being diagnosed at a younger age as evidenced by a shift to the left in the age of peak incidence. These unique epidemiological patterns offer a basis for analysis of potential etiological factors.

KEY WORDS: testicular neoplasms, epidemiology, testis

Testicular cancer accounts for 1% of all malignancies in men in the United States and 7,200 new cases were predicted to occur in the nation in 1998.¹ Epidemiological studies in the United States and Europe have revealed an increasing incidence of testicular germ cell neoplasms during the last 40 years.^{2,3} Testicular cancer exhibits a peak incidence rate in white men 30 to 35 years old with a marked decline thereafter until it begins to rise again at age 65. However, for unknown reasons the incidence of testicular cancer is significantly lower in black Americans.^{4,5} A large number of studies have investigated possible risk factors for testicular cancer. The only factor proved to increase the risk of testicular cancer is cryptorchidism, which occurs in approximately 10% of cases⁶ and is associated with a 5 to 10-fold increased risk.^{7,8} Studies have supported weaker associations between inguinal hernia, low birth weight, early birth order and a sedentary lifestyle, and subsequent testicular cancer.^{6,9-11}

Despite extensive study no specific etiological factors have been identified to explain the increasing incidence of testicular cancer for the last 40 years. A recent review of cancer registries in 6 European countries revealed a steady increase in the incidence of testicular cancer in each beginning after World War II.² The increasing relative risk in these populations closely correlated with when patients were born, that is a birth cohort phenomenon. After analyzing data from the Connecticut tumor registry Zheng et al also noted that birth cohort closely correlated with a rising incidence of testicular cancer in white men.³ The striking birth cohort phenomenon

in Europe as well as Connecticut suggests that unknown prenatal or postnatal factors may explain the rising incidence of testicular cancer. We determine if the changing incidence of testicular cancer in white men in the United States followed a birth cohort pattern on a national level.

MATERIALS AND METHODS

Testicular cancer incidence data from 1973 to 1995 for the United States from the National Cancer Institute Surveillance, Epidemiology and End Results (SEER) database served as the basis for this analysis. The database has served as a validated source of cancer incidence data for epidemiological studies since inception in 1973 and represents a collection of 9 population based cancer registries in the United States. The initial reporting areas beginning in 1973 were Connecticut, Iowa, New Mexico, Utah and Hawaii, and the metropolitan areas of Detroit and San Francisco-Oakland. The program was expanded from 1974 to 1975 to include the metropolitan areas of Atlanta and a 13-county area around Seattle-Puget Sound. Using the computer software supplied with the latest SEER data, population data were extracted from accompanying SEER census files. Site and histology codes were based on the International Classification of Disease for Oncology (ICD-0-2).

The numbers of cases of testicular cancer and total population were extracted from the database and grouped by 5-year periods of year and diagnosis, and in 5-year age groups for all testicular cancers and 2 histological subgroups of seminoma and nonseminoma. These data were allocated

into 5-year birth cohorts starting in 1929 using methods outlined by Clayton and Schifflers.^{12,13} In addition to simple trend analysis, Poisson regression models were used to fit the data which were analyzed in a manner similar to that of Bergström et al² using an age-period-cohort analysis. The number of incidental cases is a variable with a Poisson distribution that is a function of variables of age, period and birth cohort.^{12,13} Different estimates were determined from maximum likelihood models using generalized log-linear model statistical software. An age linear birth cohort (drift) model, which assumes that rates increase at the same rate each year, and an age birth cohort model, which assumes an independent component of rate change for each year, were used. The log linear chi-square test was used in the evaluation of these models. The age drift model offers substantial improvement compared to an age adjusted model because it uses only 1 additional degree of freedom while accounting for a much larger percentage of variation (see table).

RESULTS

Testicular cancer was reported between 1973 and 1995 in 11,322 white (95%) and 642 nonwhite (5%) men. In white men there were 6,005 seminomas (53%) and 5,317 nonseminomas (47%). The standardized incidence rates for all testicular cancer in white men and the 2 major histological subgroups are shown in figure 1. There was a steady increase in the rate of testicular cancer in the United States with seminoma tracking closely with overall incidence. From 1973 to 1995 the incidence of testicular cancer increased from 3.61 to 5.44/100,000 (51%), including 1.89 to 2.8/100,000 for seminomas (48%) and 1.72 to 2.63/100,000 for nonseminomas (53%).

Figure 2 shows incidence rates by birth cohort and age at diagnosis for all testicular cancer. Because SEER data collection began in 1973, there are no incidence data during the peak age at diagnosis for birth cohorts before 1940 and after 1968. However, for birth cohorts between 1945 and 1968 there is a clear increase in the incidence rates for testicular cancer. In addition, there is a trend toward a younger peak age of incidence for more recent birth cohorts for which data are available before and after the peak age at diagnosis, which is represented in figure 2 as a shift to the left in the incidence curves. This shift is also seen when seminoma rates are analyzed as an individual subset. Each birth cohort is represented by a separate line on figure 2, and these lines are incomplete for birth cohorts before 1940 and after 1968 because the database only includes cases from 1973 to 1995.

Birth cohort risks are shown in the table and figure 3, which provides relative risks by birth cohort with 1944 as the reference group. Relative risks for all testicular cancer, seminoma and nonseminoma are increased for each birth cohort after 1944. Based on the available data, this trend appears to continue up to the present but, since the 1974 birth cohort has not yet matured to span the peak age at diagnosis, it is too early to conclude this with confidence.

DISCUSSION

Our results and previously reported data confirm a steady increase in the incidence of testicular cancer in the United

	Age	Age Drift	Age Birth Cohort	% Annual Change by Birth Yr.
Seminoma:				
Deviance	267.5	115.1	47.9	3.1
Degrees of freedom	55	54	41	
p Value		<0.001	0.28	
Nonseminoma:				
Deviance	194.1	119.8	40.6	2.1
Degrees of freedom	68	67	47	
p Value		<0.001	0.79	

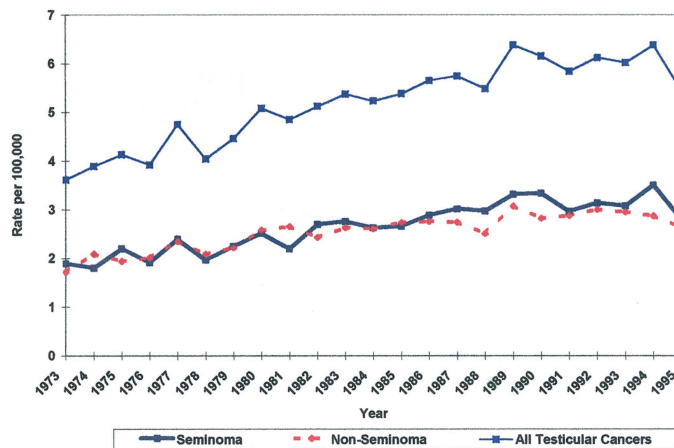


FIG. 1. Age standardized rates in 1980 of testicular cancer by histology for white men.

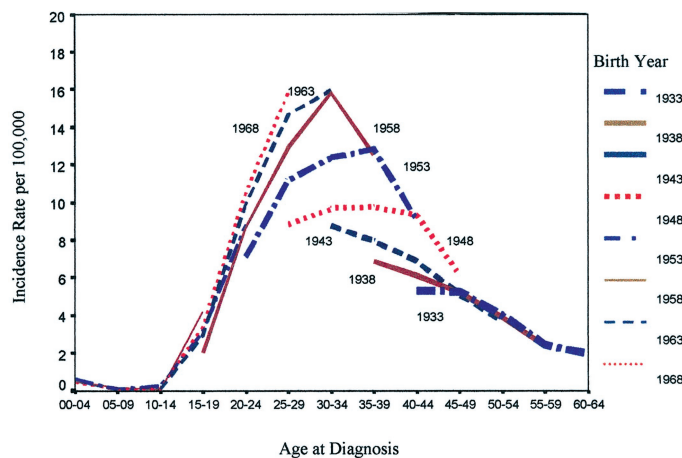


FIG. 2. Testicular cancer rates by birth cohort versus age at diagnosis.

States after 1944. Efforts to explain this phenomenon have led others to investigate the effect of birth cohort on the incidence of testicular cancer. A birth cohort phenomenon occurs when a cohort or study group shares a common period of birth and a similar risk of a disease. Unlike most other cancers, testicular cancer has a peak incidence in the third decade of life which suggests a latency period that involves some prenatal or postnatal stimulatory event influencing tumor development. The widespread observation of a birth cohort correlation for testicular cancer suggests that early or prolonged exposure to some carcinogenic stimuli might be required for the development of testicular cancer. Bergström et al evaluated testicular cancer incidence data from 6 northern European countries and reported that birth cohort was the most powerful predictive factor to explain the increasing risk observed.² After analyzing data from the Connecticut Tumor Registry Zheng et al reached a similar conclusion.³

Our descriptive epidemiological study based on the SEER database confirms that a birth cohort phenomenon is involved in the increasing incidence of testicular cancer on a national level in the United States. In concordance with the European and Connecticut studies the data also show that the incidence of testicular cancer is increasing in the United States as a whole and that birth cohort strongly correlates with the relative risk.

In addition to the overall increased incidence of testicular cancer and the birth cohort association, this analysis demonstrates a decrease, that is shift to the left, in the age for peak incidence of testicular cancer, which implies that more cases

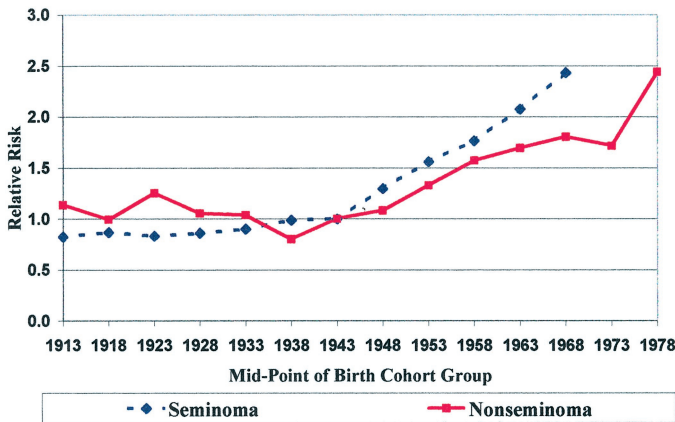


FIG. 3. Relative risk of testicular cancer by birth cohort (1943 = 1.0).

are being diagnosed at earlier ages for each successive birth cohort. If the age of peak incidence is shifting to younger age groups, then successive birth cohorts may reach the peak age of incidence during identical years causing an overlap phenomenon. This overlap could possibly account for a transient elevation in the total number of reported cases and, if this is true, a return to baseline incidence rates might occur after the shift to earlier ages at diagnosis has stabilized. Lead time bias, that is early detection, might explain a shift to the left in age specific incidence curves of any disease process. However, there are no screening tests for testicular cancer to account for this effect.

Neither the rising incidence of testicular nor the decline in the age of peak incidence can be clearly explained with available data. However, it is possible that changing environmental or socioeconomic risk factors during the last 40 years may have a role. Occupational exposure to extreme temperatures may be a risk factor for testicular cancer independent of other potential confounding factors, although not all authors report this finding.^{5,14} Experimental and human data suggest hormonal risk factors for testicular cancer. Prenatal exposure of mice to diethylstilbestrol produces a number of adverse effects on the testes and related structures, including cryptorchidism, inflammation and adenocarcinoma.⁹ However, a number of case control studies have investigated the relationship between in utero exposure to diethylstilbestrol and subsequent testicular cancer in humans, and collectively failed to support an association.^{7,8} Conditions which increase maternal estrogen levels during pregnancy, such as twin pregnancies, primigravid state and obesity, have been associated with increased risk of testicular cancer.^{15,16} Finally, the use of fertility promoting hormonal agents is becoming increasingly more common¹⁷ and these agents have been shown to increase the risk of some childhood cancers.¹⁸ That the incidence of any of these factors is changing with time may explain the now consistently reported increasing incidence of testicular cancer and the observed birth cohort phenomenon.

CONCLUSIONS

The increasing incidence of testicular cancer in white men in the SEER database is consistent with prior reports from Europe, and birth cohort groupings correlate strongly with

the relative risk of testicular cancer. In addition, age at peak incidence of testicular cancer seems to be decreasing. It does not appear that the end points in these trends have occurred, and the incidence of testicular cancer in more recent birth cohorts will require longer followup. However, the birth cohort phenomenon observed in all large databases may offer a unique opportunity to study potential etiological factors which might be responsible for these findings.

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