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International patterns and trends in thyroid cancer incidence, 1973–2002

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Abstract

During the past several decades, an increasing incidence of thyroid cancer has been reported in many parts of the world. To date, no study has compared trends in thyroid cancer incidence across continents. We examined incidence data from Cancer Incidence in Five Continents (CI5) over the 30-year period 1973–2002 from 19 populations in the Americas, Asia, Europe and Oceania. Thyroid cancer rates have increased from 1973–1977 to 1998–2002 for most of the populations except for Sweden, in which the incidence rates decreased about 18% for both males and females. The average increase was 48.0% among males and 66.7% among females. More recently, the age-adjusted international thyroid cancer incidence rates from 1998–2002 varied 5-fold by geographic region for males and nearly 10-fold for females by geographic region. Considerable variation in thyroid cancer incidence was present for every continent but Africa, in which the incidence rates were generally low. Our analysis of published CI5 data suggests that thyroid cancer rates increased between 1973 and 2002 in most populations worldwide and that the increase does not appear to be restricted to a particular region of the world or by the underlying rates of thyroid cancer.

Introduction

Thyroid cancer is a relatively rare neoplasm worldwide, accounting for approximately 1–5% of all cancers in females and less than 2% in males (1). Although the incidence of thyroid cancer is relatively rare, it is the most common endocrine malignancy worldwide (1). While

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the international incidence varies considerably, a fairly consistent female-to-male ratio of three-to-one is observed in almost all geographic areas and ethnic groups (1).

During the past several decades, an increasing incidence of thyroid cancer has been reported in some European countries, the United States, and some parts of the China (3–8); however, no study has provided a comparison of trends in thyroid cancer incidence across continents. The International Agency of Research on Cancer (IARC) has published rates for time periods spanning three decades for 95 registries around the world, enabling the analysis of trends over a relatively longer time period. To understand how thyroid cancer incidence has changed over time across different populations and what factors may be responsible for the observed change, we examined incidence data over the 30-year period 1973–2002 from 19 populations in the Americas, Asia, Europe and Oceania.

Materials and methods

Incidence data

To examine the secular trends in the incidence of thyroid cancer, age-standardized (World Population) incidence rates were obtained from volumes 4–9 of Cancer Incidence in Five Continents (CI5). The CI5 volumes include incidence data reported by selected population-based cancer registries covering areas within Asia, Oceania, Africa, Europe, and the Americas. Volumes 4–9 generally provided data for the 5-year periods 1973–1977, 1978–1982, 1983–1987, 1988–1992, 1993–1997, and 1998–2002. The classification of thyroid cancer was based on ICD-8, ICD-9, and ICD-10 for volumes 4, 5–8, and 9, respectively. There were no changes in the coding of thyroid cancer between the eighth, ninth, and tenth revisions (193). Incidence rates for different histologic subtypes (follicular, papillary, medular, anaplastic, other/ unspecified) were abstracted from volume 9 as incidence rates for specific subtypes was not provided in the earlier volumes.

Populations were chosen for inclusion in our analysis on the basis of the following criteria: (i) availability of rates in the CI5 for time periods at least as far back as 1978–1982; (ii) an absence of changes in population coverage or of warnings regarding data quality; and (iii) a sufficiently large number of registered cases in CI5 volume 9 to enable analyses of recent rates by histologic subtype (trends by histologic subtype are not included in our study). Only one registry from each country was selected; if more than one registry met the basic criteria, the registry with the largest population was included in the analysis. A total of 19 populations were selected: 4 from the Americas, 4 from Asia, 4 from Scandinavia, 5 from elsewhere in Europe and 2 from Oceania. No African or South Asian populations met all the inclusion criteria. However, 5 African countries included in CI5 volume 9 (Algeria, Setif; Egypt, Gharbiah; Tunisia, Center, Sousse; Uganda, Kyadondo Country; Zimbabwe, Harrare) and the registry of Mumbai, India, had rates available which allowed for a broader geographic comparison for recent years.

Data analysis

Thyroid cancer incidence is presented overall and by histologic subtype for males and females separately for selected populations for the time period 1998–2002. Trends in age-standardized (world standard) incidence rates were examined for the time periods 1973–1977, 1978–1982,1983–1987, 1988–1992, 1993–1997, and 1998–2002. The percentage change in thyroid cancer rates between 1973–1977 and 1998–2002 was calculated for each population to show the relative change in incidence between these two periods for males and females separately.

Results

The 1998–2002 age-adjusted thyroid cancer incidence rates varied 5-fold for males and nearly 10-fold for females (Table 1), with the highest rates in the U.S. and Israel for males (3.5 per 100,000 for both countries) and for females (10.0 per 100,000 and 12.1 per 100,000, respectively), and the lowest rates in Uganda for males (0.5 per 100,000) and for females (1.5 per 100,000). The highest rates nor the lowest rates were concentrated in one continent for either males or females. Considerable variation in thyroid cancer incidence was present within every continent with the exception of Africa, in which the incidence rates were generally low. Based on the rates from 1998–2002, the incidence of papillary was the highest, followed by follicular, medular and anaplastic subtypes (Figures 1 and 2).

Thyroid cancer rates increased from 1973–1977 to 1998–2002 (Table 1) for most populations. On average, the populations with increasing rates experienced about a 58.1% increase. The average increase was 48.0% among males and 66.7% among females with the largest increase in Australia, New South Wales for both males (177.8%) and females (252.2%). In contrast, the incidence rates decreased for males in Sweden (18.8%) and for females in Norway, Sweden, and Spain (5.8%, 18.2%, and 25.9%, respectively).

The thyroid cancer rates among each population during the 30-year period 1973–2002 are shown in Figures 2a and 2b. Fairly consistent increasing trends in rates were apparent for most populations, and positive trends were generally stronger among females. There has been, however, a leveling off for trends in the Scandinavian countries.

Discussion

During the period 1973–2002, the incidence rates of thyroid cancer increased among most populations examined. Thyroid cancer incidence among the 19 populations varied more than 5-fold among both males and females. The variation was mainly attributed to papillary thyroid carcinoma. Despite the wide intercountry variation in age-adjusted incidence rates, a consistent female-to-male ratio of three-to-one is observed within most of the countries included in both the earlier (1973–1977) and later (1998–2002) data.

It is currently unclear whether the observed increases in thyroid cancer are real or are due to increased diagnosis. The common use of fine needle aspiration technology in late 1980s in combination with thyroid ultrasound has facilitated the diagnosis of smaller thyroid tumors (14) in areas with access to these technologies. Previously, investigators concluded that the increase in the incidence rates reflects increased detection of subclinical disease, not an increase in the true occurrence of thyroid cancer due to the increase in microcarcinas (14). Because information on tumor size is not available for majority of the registries, we were unable to assess whether the international incidence rates increased for all sizes of thyroid cancer tumors or mainly in cases with smaller size tumors. However, we observed a substantial percent change from 1988–95 to 1996–2005 in the incidence of thyroid cancer for both smaller size tumors and larger size tumors in the SEER 9 database (13), with a 120.85% increase in thyroid microcarcinomas <1cm, and a 56.2% increase for thyroid tumors >4cm. This argues against advanced diagnostic techniques or increased attention to small nodules as the only explanation for the observed increasing trend of thyroid cancer.

The histopathologic classification system for thyroid cancer has evolved over time. In 1988, the World Health Organization (WHO) revised its classification when it was recognized that nuclear features (particularly nuclear inclusions and nuclear folds) are more important than architectural patterns in classifying thyroid cancer (29). As a result, many cancers previously classified as follicular are now categorized as follicular variants of papillary cancer (30). Although changes in classification could impact the distribution of cases by subtype, this point

does not undermine our findings as the total number of cases diagnosed should not be significantly affected.

Most countries have introduced nationwide iodization measures, but there are regional differences in the year iodine supplementation was implemented. In 1990, iodine deficiency affected almost one-third of the world population (33). Following a resolution adopted by the World Summit for Children in 1990, major programs of iodine supplementation were implemented by governments of the affected countries. By April 1999, 68% of the affected populations had access to iodized salt. It has been noted that when iodine supplementation occurs in iodine deficient regions, the proportion of papillary thyroid cancers often increases although the overall rates tend to stay the same (31,32). According to the World Health Organization, of the countries included in this study with available iodine intake data, Denmark, France, Italy, Australia, New Zealand, and Algeria all reported to be iodine deficient (34).

The differences in thyroid cancer rates, particularly among women, in the Scandinavian countries are notable because similar standards of medical care and reporting in the Scandinavian countries reduce the limitations associated with intercountry comparisons. The age-adjusted incidence rate among women in Finland is over twice that reported in Denmark in both time periods of interest (1973–1977 and 1998–2002). Furthermore, the wide variation in percent change over the past three decades in these countries is striking. This suggests that these populations may be experiencing different levels of environmental exposure to a significant risk factor/set of risk factors.

It is also notable that despite the wide intercountry variation in age-adjusted incidence rates, according to the GloboCan 2002 database (35), there is small variation in sex-specific mortality rates by geographic region. Among females, the current thyroid cancer mortality rates for the European, Oceanic, American, and Asian countries included in this analysis is between 0.2 to 1.0 per 100,000 person-years. Similarly, for males, the range in thyroid cancer mortality rates is from 0.1 to 0.7 per 100,000 person-years. Such consistency in mortality burden suggests that differences in incidence may be a function of detection methods. However, as thyroid cancer is known to have a high rate of survival, the intercountry consistency in mortality rate may not necessarily be evidence of artificially inflated rates.

There is emerging evidence that PBDEs alter thyroid hormone homeostasis and cause thyroid dysfunction, and may subsequently play a role in the global increase in thyroid tumorigenesis (36). The use of PBDEs has increased rapidly during the last three decades in the US and other parts of the world, doubling in some areas in less than a decade (15), reaching a global demand of 200,000 tons in 2003 (16). PBDEs are widely used as flame retardants in polyurethane foam, textiles and hard plastics used in applications such as carpet pads, furniture, curtains, televisions, computers and seats in automobiles and airplanes. The impact of these hormone disrupting agents in the etiology of thyroid cancer is of interest as there is strong animal data and evidence of increasing and widespread global exposure. The European Union banned the use of two PBDEs (Penta- and OctaBDE) in 2004 due to increasing evidence that PBDEs may result in thyroid toxicity, liver toxicity, and neurodevelopmental toxicity, and because PBDEs accumulate in human breast milk (37). The State of Washington also passed a bill banning the use of PBDEs in 2007 (38). However, these compounds, like the other previously banned PHAHs (such as PCBs, DDT and HCB), will remain ubiquitous in the environment due to their stability, persistence, and their ability to bioaccumulate.

It is also notable that despite the wide intercountry variation in age-adjusted incidence rates, a consistent female-to-male ratio of three-to-one is observed within most of the countries included in the international comparison in both the earlier (1973–1977) and later (1998–2002) data. Possible explanations for the disparities between males and females with sporadic thyroid

cancers are biological sex differences, differential screening patterns, or gender-specific behavioral differences. One hypothesized mechanism is that increased levels of female hormones during reproductive years, due to pregnancy which increases thyroid stimulating hormone (TSH) levels, potentially leading to thyroid dysplasia and then to cancer (24–27). Experimental evidence shows that TSH stimulation of the thyroid gland can lead to proliferative changes of follicular cells including hypertrophy and hyperplasia, as well as ultimately neoplasia in rodents (28). Our results confirm the previously observed gender disparity and support the need for future research in this area.

In summary, our analysis of published CI5 data suggests that thyroid cancer rates increased between 1973 and 2002 in most populations worldwide, for males and females, and that the increase does not appear to be restricted to a particular region of the world or by the **underlying** rates of thyroid cancer. There is also some indication that the rates may be leveling off in some populations. The worldwide increase in thyroid cancer incidence may be due to changes in the prevalence of important risk factors; epidemiologic investigations describing between population differences and within population trends in the prevalence of suspected risk factors may yield important insights into the causes of the widespread increase in thyroid cancer.

Acknowledgments

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38. Chemical ban puts industry on the defensive. State of Washington bans use of PBDEs. http://seattlepi.nwsource.com/local/311845_pbdes17.html

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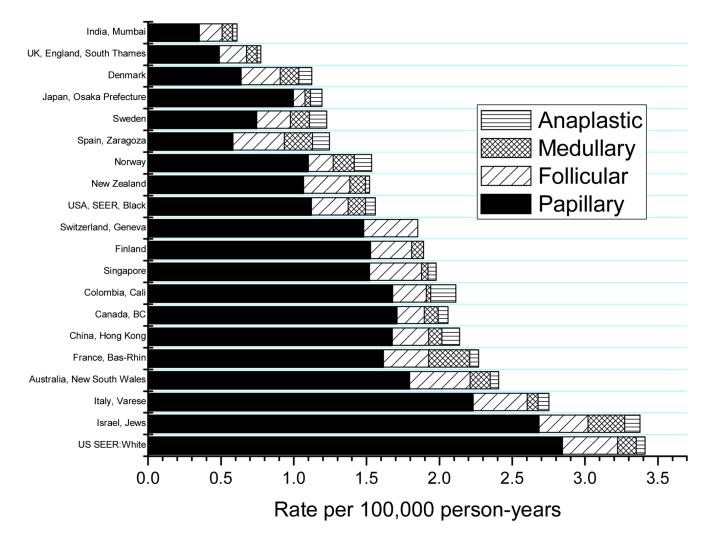


Figure 1. Rates for males from selected populations for the time period 1998–2002 Incidence rates of thyroid cancer for males (per 100,000 person-years) age standardized to the world population for selected populations for the time period 1998–2002. Kilfoy et al.

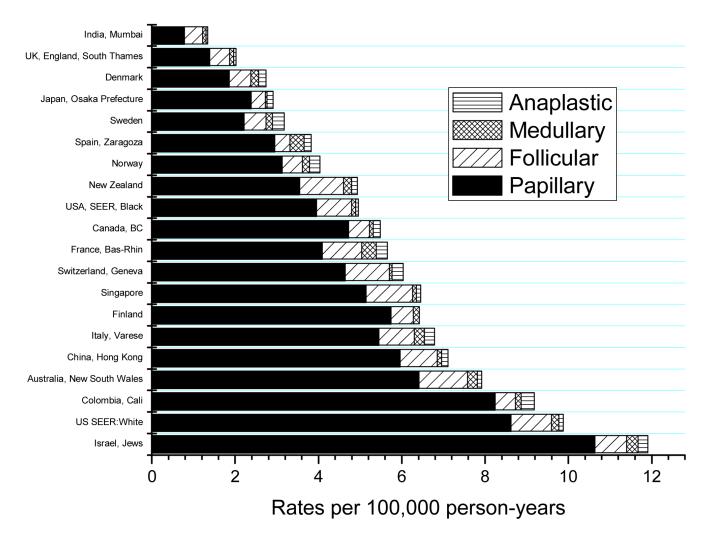


Figure 2. Rate for females from selected populations for the time period 1998–2002 Incidence rates of thyroid cancer for females (per 100,000 person-years) age standardized to the world population for selected populations for the time period 1998–2002.

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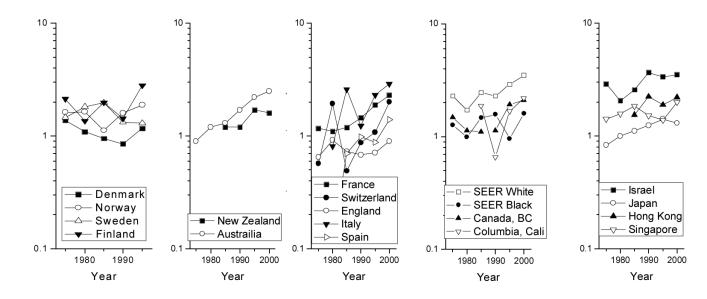
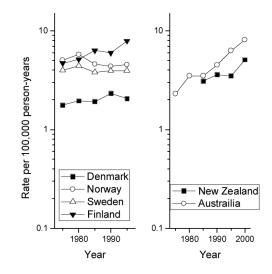


Figure 3.

Trends in age-standardized thyroid cancer rates by continent and area for the time periods 1973–1977 to 1998–2002 for males

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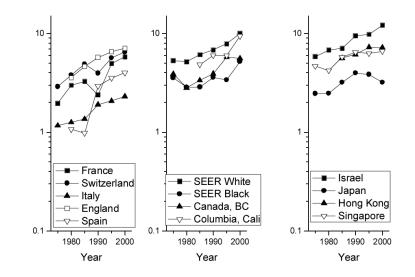


Figure 4.

Trends in age-standardized thyroid cancer rates by continent and area for the time periods 1973–1977 to 1998–2002 for females

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International variation in thyroid cancer inci	roid cancer incic	lence rates,	dence rates, 1973–1977 to 1998–2002	1998–2002						
		1973–1977				1998-2002				
	Males Cases	Rate	Females Cases	s Rate	Males Cases	les Rate	Females Cases	ales Rate	Males % Change	Females % Change
Europe. Scandinavian Countries										
Denmark	168	- ;	330	1.6	210	1.2	524	2.9	20.0	81.3
Norway Sureden	182 463	I.4 الا	558 1158	4.4 4.0	247 407	1.6	649 1031	4.2 2.3	14.3 -18.8	-5.8 -18.2
Finland	221	1.7	684	4.3	384	2.2	1281	7.0	29.4	62.8
Europe, Other										
France, Bas-Rhin	25	0.0	85	2.8	75	2.3	198	5.8	155.6	107.1
Switzerland, Geneva	18	1.9	43	3.5	27	2.0	86	6.5	5.3	85.7
UK, England, Thames	134	0.6	391 105	1.5 2 0	433 15	0.0 0.0	1133	2.3	50.0 15	53.3 oz o
spain, Zaragoza	28	1.2	134	5.4	37	2.7 1.4	123	4.0	16.7	00.0 -25.9
Oceania New Zealand	108	1 2	785	3 1	181	16	508	5 ا	111	5 64 5
Australia, New South	116	0.9	315	2.3	506	2.5	1639	8.1	177.8	252.2
Wales										
Americas										
US SEER:White	766	2.3	2491	5.4 7.7	2216	3.5	6306	10.0 ž č	52.2	85.2
Canada, BC Colomhia. Cali	104 20 (1972–76)	<u>. 1</u>	222 104 (1972–76)	5.0 6.1	271 85	2.1 2.2	450	0.0 9.4	40 46.7	54.1
USA, SEER:Black	47	1.2	173	3.8	121	1.6	494	5.2	33.3	36.8
Asia										
China, Hong Kong	126 (1974–77)	1.6	352 (1974–77)	4.2	447 132	2.2	1557	7.2	37.5 85 7	71.4
Japan, Osawa Frerecuite Singapore	43	0.7 1.3	432 141	3.8 3.8	432 180	0. 1 0	636	5.6 6.6	53.8	73.7
Israel:Jews	193	2.6	472	6.2	474	3.5	1747	12.1	34.6	95.2
Africa										
Algeria, Setif					32	1.4	88	3.6		
Egypt, Unarotan Tunisia, Center, Sousse					00 14	1.1	34	2.0 3.1		
Uganda, Kyadondo County Zimhahwa, Harara					11	0.5	26 15	1.5		
ZIIIIDADWC, IIAIAIC					ţ	T	f	1.0		

Rate is age-standardized to the world population, per 100,000 person-years. Counts, rate for 1978–1982 period. These registries were excluded from the trends analysis due to an absence of data for early time periods, changes in population coverage and/or data quality issues.

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