

Increasing Incidence of Thyroid Cancer in Puerto Rico, 1985-2004

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Objective: Thyroid cancer has become one of the fastest growing malignancies in several countries worldwide. Few studies have examined thyroid cancer trends in Puerto Rico, and those studies have been conducted over relatively short time frames. This study aimed to describe both overall thyroid cancer incidence trends by age, sex, and histology, and the mortality rate by age and sex in Puerto Rico for the period of 1985 to 2004.

Methods: Using the Central Cancer Registry of Puerto Rico database, we conducted a retrospective study of patients with thyroid cancer diagnosed from January 1, 1985, to December 31, 2004.

Results: The overall incidence rate of thyroid cancer increased from 3.0 to 7.0 per 100,000 population (a 2.3-fold increase), with an annual percent change (APC) of 5.3% ($p < 0.05$) during the period of 1985 to 2004. Incidence rates were higher for females (rising from 4.7 in 1985 to 10.5 per 100,000 women in 2004) compared to those for males (rising from 1.1 in 1985 to 3.0 per 100,000 men in 2004). The rising trend was mostly due to an increase in the incidence of papillary thyroid cancer, which rose from 2.4 to 6.0 per 100,000 population (a 2.5-fold increase), with an APC of 5.7% ($p < 0.05$). The overall mortality rate of thyroid cancer was very low (0.4 in 1985 and 0.3 per 100,000 population in 2004), with a non-significant APC of -1.1% ($p > 0.05$).

Conclusion: The incidence of thyroid cancer in Puerto Rico increased significantly from 1985 to 2004, mostly due to an increase of papillary cancer. However, the mortality remained low. [*P R Health Sci J* 2011;30:109-115]

Key words: Thyroid cancer, Epidemiology, Incidence, Mortality, Puerto Rico

The thyroid is the largest endocrine gland and the most common site of all primary endocrine cancers. Thyroid carcinoma is an uncommon malignancy with a high cure rate (1). It accounts for about 1% of all new cancers in the United States population (2). In Puerto Rico, thyroid cancer is relatively uncommon among males; however, among women it is the sixth most common cancer, representing 3.7% of all total cancers for the period of 2000 to 2004 (3). Differentiated thyroid carcinoma, which includes papillary and follicular histologies, is the most common form of thyroid cancer and accounts for about 95% of all cases. Women are affected by differentiated thyroid cancer 2 to 3 times more frequently than are men (4, 5, 6). Even though deaths from this cancer account for only 0.2% of all cancer deaths per year (2), it is responsible for more deaths than all other endocrine cancers combined.

There has been an increasing trend in the incidence of thyroid cancer in the United States, Europe, and other developed countries over the last 30 years (4, 5, 7). According to data reported in the National Cancer Institute's Surveillance, Epidemiology, and End Results program (SEER), thyroid

cancer in patients younger than 65 years old is the cancer with the second greatest increase in incidence (annual percentage change [APC] = 3.6%); in patients 65 and older, it ranks third in increasing incidence (APC = 2.6%) for the period of 1992 to 2000 (8). The reasons for this upward trend remain both unclear and controversial. Some studies have suggested that the increase could be explained by the use of new diagnostic modalities and an increase in medical surveillance (5, 9). Nevertheless, other studies contend that this explanation cannot completely explain the rising incidence of this carcinoma because increased surveillance would be expected to increase the discovery of

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predominantly subclinical disease. On the contrary, incidence reports indicate an increase in the number of tumors (of all sizes and stages) being found as well (6, 10).

The incidence of thyroid cancer varies by race and ethnicity. Detailed analysis of epidemiological data from SEER by different authors has found that non-Hispanic whites have twice the increase in incidence compared to Hispanic whites. Consistent among all sex and racial/ethnic groups is the rise in the incidence rate of papillary carcinoma (6, 10).

There are few studies describing the epidemiology of thyroid cancer in Puerto Rico. The first report in the literature dates back to the year 1952, at which time an incidence of 0.3 per 100,000 population was reported (11); by 1975, this had increased to 3.9 per 100,000, as documented by the Department of Health (12). The rest of the publications detail mostly small series of patients or case reports (13, 14). The scarcity of publications on thyroid cancer trends in Puerto Rico supports the need to address this information gap, especially since this type of malignancy is at present the sixth most common cancer among the Puerto Rican female population (3).

The understanding of the patterns of increased cancer incidence and the estimates of disease burden in specific groups has important implications, from both the clinical and the public health viewpoints because such understanding may lead to the improvement of diagnostic methods, the identification of previously unrecognized risk factors, and a better distribution of resources for cancer-prevention and -control efforts in high-risk populations. Thus, the aim of our study was to ascertain both the overall thyroid cancer incidence trends (classifying them by age, sex, and histology) and the mortality rate (classified by age and sex) in Puerto Rico from 1985 to 2004.

Methods

Data Sources

Data regarding invasive malignant neoplasms of the thyroid were obtained from the Puerto Rico Central Cancer Registry (PRCCR) (15), a population-based cancer registry that has been collecting information on newly diagnosed cancer cases in Puerto Rico since 1951. Using the third edition of the International Classification of Disease for Oncology (ICD-O-3) (16), we identified all of the incident cases consisting of a malignant neoplasm of the thyroid [categorized according to definitions established by the SEER Site Recode, thyroid site (17)] that had been reported in Puerto Rico from January 1, 1985, to December 31, 2004. All thyroid cancer cases diagnosed since 2001 were coded according to the third edition of the International Classification of Disease for Oncology (ICD-O-3) (16). Cases from 1985 to 2000 that had originally been identified using the previous edition (ICD-O2) were converted to ICD-O-3 codes. Thyroid tumors were categorized by histology subtype according to ICD-O3 as follows: papillary (codes 8050,

8052, 8130, 8260, 8340-8344, 8450, 8452), follicular (codes 8290, 8330-8332, 8335), medullary (codes 8345, 8346, 8510), anaplastic (code 8020-8021), and all histological types together (all ICD-O-3 codes for thyroid cancer). Cancer mortality data for Puerto Rico were obtained from the PR Department of Health from death certificates that had been executed by the Division of Statistical Analysis, Auxiliary Secretariat for Planning and Development (18). Causes of death were coded and classified according to the International Classification of Diseases (ICD-9: code 193; or ICD-10: code C73). Once we obtained approval from the University of Puerto Rico Research Ethics Board, we identified 2,810 cases of thyroid cancer and reviewed all records. Patients with malignancies other than primary thyroid malignancies were excluded.

Statistical analysis

Age-adjusted and age-specific incidence and mortality rates and their 95% confidence intervals (CIs) were calculated using Surveillance Research Program National Cancer Institute SEER*Stat software v.6.4.4 (19). Rates were age-adjusted to the 2000 PR population provided by the United States Census Bureau (19). The Annual Percentage Changes (APCs) were estimated using Joinpoint Regression software (20), which involved fitting a least squares regression line to the natural logarithm of the rates to describe changing trends of incidence and mortality from 1985 to 2004. Statistical significance was determined as a p -value <0.05 .

Results

Study population

A total of 2,810 incident cases (collected between January 1, 1985, and December 31, 2004, inclusive) of thyroid cancer were identified using the database of the Cancer Registry of Puerto Rico. Of these, 2,258 (80.4%) represented female patients and 552 (19.6%) represented male patients. Thirty-three cases, identified by death certificates, were excluded from the study because of a lack of histological evidence available on record. The median age at diagnosis for thyroid cancer in males was 53 years, significantly higher (χ : 1.78, $p < 0.05$) as compared to females (48 years). Papillary carcinoma (80.6%) was the most common histological type, followed by follicular carcinoma (10.8%) (Table 1). Overall, more than half of the thyroid cancer cases in Puerto Rico occurred in individuals who were from 20 to 49 years of age. The diagnosis of thyroid cancer in males tended to occur at older ages than it did in females (Table 2).

The average age-specific rates were higher among women than they were in men across all age groups, and the female-to-male rate ratio declined consistently from more than 9 at ages 15 to 19 to 4.1 at ages 50 to 54, approaching 1.5 at ages 80 to 84 (Figure 1). Females showed a rapid increase in the rate of diagnosis of thyroid cancer starting at age 15, followed by a

plateau at age 45 and then a smooth decrease after age 70. In the male population, however, there was a gradual increase after the age of 20, which increase reached a peak at 75 and then gradually decreased thereafter.

Table 1. Distribution of thyroid cancer cases by histologic type in Puerto Rico, 1985-2004

Histology type	Overall n (%)	Male n (%)	Female n (%)
Papillary	2264 (80.6)	424 (76.8)	1840 (81.5)
Follicular	304 (10.8)	59 (10.7)	245 (10.9)
Medullary	90 (3.2)	34 (6.2)	56 (2.5)
Anaplastic	24 (0.9)	5 (0.9)	19 (0.8)
Other*	128 (4.6)	30 (5.4)	98 (4.3)
All Thyroid cancers	2,810	552	2,258

*Cases diagnosed by death certificate only; 33 cases were not included.

Incidence and mortality time trend: 1985-2004

The age-adjusted rate for thyroid cancer showed an increasing trend, rising from 3.0 per 100,000 in 1985 to 7.0 per 100,000 population in 2004, a 2.3-fold increase with an APC of 5.3% (95% CI: 4.2%-6.4%; $p < 0.05$) over the study period (Figure 2). Thyroid cancer incidence rates were consistently 3 to 4 times higher among females than they were among males; nevertheless, the highest increase in the incidence trend was observed among males (APC = 5.5%; $p < 0.05$) with females coming in slightly lower (APC = 5.2%; $p < 0.05$) (Table 2). The increase of overall incidence of thyroid cancer was chiefly due to an increase in papillary cancer, which increased from 2.4 to 6.0 per 100,000 population, a 2.5-fold increase, with an APC of 5.7% (95% CI: 4.5%-6.9%; $p < 0.05$) during the period of 1985 to 2004. There was no significant ($p > 0.05$) trend in the incidence of other histological types, such as follicular or poorly differentiated (medullary and anaplastic analyzed together) cancer (Figure 3). The rates for other specified and unspecified histologic types were not plotted because they were low and cannot provide an explanation for the trends in the more common histologic types. Trends of thyroid cancer by tumor size and stage at diagnosis could not be analyzed due to an excessive amount of missing information (approximately 20% staging data and 40% tumor-size data).

Despite the significant increase in the incidence of thyroid cancer, the mortality rate showed a non-significant downward trend (APC = -1.1%, $p > 0.05$) throughout the study period (Figure 2). A similar non-significant decrease in the mortality trend was observed among females and males. In

Table 3, mortality rate is presented by age and sex, but because the mortality rate was so low, APC could not be estimated in several age groups. Also, the mortality rate could not be analyzed based on histology type because this kind of data was not available on death certificates.

Age-specific time trend: 1985-2004

Consistent increasing overall incidence rates of thyroid cancer were apparent across all ages and both genders (Table 2). Between 1985 and 2004, the incidence of thyroid cancer rose significantly in all age groups except for the youngest (0-19 years) and oldest (80+ years) age groups, in which groups the APCs were not estimated because of the lack of cases (each group consisting of 3.3% of the total number of thyroid cancer cases). In females and males, the most rapid growth was observed in those individuals ranging in age from 35 to 49 years, with an APC of 7.8% and an APC of 11.2%, respectively. However, among females, the highest incidence rates occurred among persons ranging in age from 35 to 49 years (from 6.8 in 1985 to 20.4 per 100,000 women in 2004), while in males, these

Table 2. Thyroid cancer in Puerto Rico (1985-2004): Distribution and age-adjusted and age-specific incidence rates by sex.

Age group	Overall n (%)	Age-specific rate (95% CI)		Overall trend APC% (95% CI) 1985-2004
		1985	2004	
ALL				
0-19	95 (3.4)	0.3 (0.1-0.8)	0.5 (0.2-1.1)	~
20-34	614 (21.9)	4.5 (3.1-6.3)	4.9 (3.5-6.6)	2.5* (0.4-4.5)
35-49	845 (30.1)	4.3 (2.8-6.4)	13.0 (10.6-15.8)	8.2* (5.9-10.5)
50-64	694 (24.7)	3.6 (2.0-6.0)	12.9 (10.3-16)	6.9* (5.3-8.6)
65-79	470 (16.7)	5.1 (2.6-8.9)	11.5 (8.2-15.6)	5.0* (3.3-6.6)
80+	92 (3.3)	1.7 (0.9-4)	9.3 (4.6-16.6)	1.4 (-3.0-6.0)
All ages*†	2810	3.0 (2.4-3.7)	7.0 (6.2-7.8)	5.3* (4.2-6.4)
MALE				
0-19	15 (2.7)	0 (0.0-0.6)	0.2 (0.0-0.9)	~
20-34	79 (14.3)	1.4 (0.4-3.2)	1.2 (0.4-2.8)	3.8 (-0.9-8.8)
35-49	141 (25.5)	1.5 (0.4-3.8)	4.7 (2.7-7.5)	11.2* (6.5-16.2)
50-64	151 (27.4)	0.5 (0.0-3.0)	5.8 (3.4-9.3)	6.8* (3.9-9.8)
65-79	142 (25.7)	4.5 (1.5-10.5)	7.5 (3.9-13.2)	4.7* (1.2-8.2)
80+	24 (4.3)	0 (0.0-14.2)	10.5 (3.424.5)	~
All ages*†	552	1.1 (0.6-1.8)	3.0 (2.3-3.9)	5.5* (4.3-6.7)
FEMALE				
0-19	80 (3.5)	0.6 (0.2-1.6)	0.9 (0.3-2.0)	~
20-34	535 (23.7)	7.4 (5.0-10.5)	8.4 (5.9-11.6)	2.5* (0.6-4.4)
35-49	704 (31.2)	6.8 (4.2-10.5)	20.4 (16.3-25.3)	7.8* (5.6-10.1)
50-64	543 (24.0)	6.3 (3.4-10.8)	18.9 (14.6-24.1)	7.0* (4.9-9.0)
65-79	328 (14.5)	5.7 (2.3-11.7)	14.6 (9.8-21)	5.1* (3.2-7.0)
80+	68 (3.0)	3.0 (0.1-16.6)	8.5 (3.1-18.4)	0.7 (-3.5-5.0)
All ages*†	2258	4.7 (3.7-5.9)	10.5 (9.1-11.9)	5.2* (4.0-6.5)

*†Annual rates presented for selected years; †Rates were age-standardized to the Puerto Rico 2000 standard population using the direct method, and confidence intervals (Tiwari mod) are 95% for rates; Annual percent change (APC) was estimated using Joinpoint regression models; *p-value < 0.05; ~Not enough cases to make estimate, as no cases were reported for some years.

occurred in older persons ranging in age from 65 to 79 (from 4.5 in 1985 to 7.5 per 100,000 men in 2004).

also accompanied by a marked increase in thyroid cancer cases in these populations.

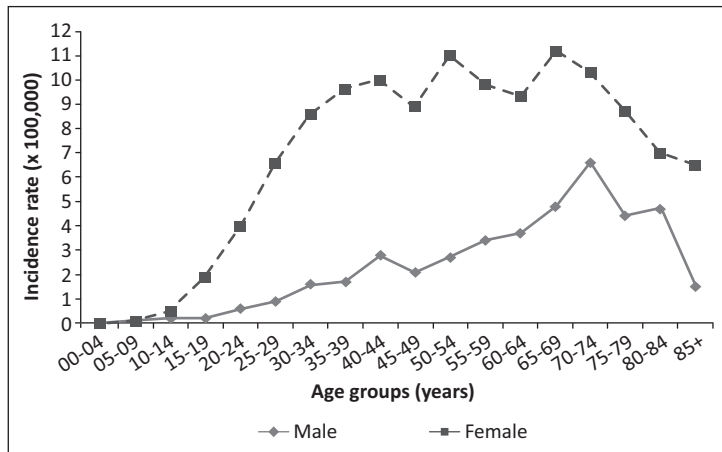


Figure 1. Thyroid cancer average age-specific incidence rates by sex in Puerto Rico (1985-2004). Rates are per 100,000.

Discussion

To our knowledge, this is the first published detailed report describing the incidence trends and mortality rates (over a 20-year period) of thyroid cancer in the Puerto Rican population. Historical data report thyroid cancer incidence rates of 0.3 per 100,000 population in 1948 (11). Based on recent data regarding the incidence rates of invasive thyroid cancer, our report shows a steady increase in those rates, rising from 3.0 per 100,000 population in 1985 to 7.0 per 100,000 in 2004. This rise in incidence rates of thyroid cancer was observed in both sexes in Puerto Rico, though predominantly in women, and across all age groups, except for young patients (0-19 age group). The increase in the overall incidence of thyroid carcinomas was mostly due to an increase in papillary cancer, which makes up the vast majority of cases and accounts for the significant increase in this trend seen in both sexes and all age groups, excepting for the younger and older groups. Reports from the United States and other developed countries have presented similar observations. The incidence rate of thyroid cancer in the United States has experienced a 2.4-fold increase, rising from 3.6 per 100,000 population in 1973 to 8.7 per 100,000 in 2002 (5), which increase is almost exclusively due to an increase in papillary cancer. Our population showed a similar 2.3-fold increase during the period of 1985 to 2004, also attributable to a rise in papillary tumors. In Canada, the incidence rates of thyroid cancer in men and women doubled, going from 3.5 and 1.1 per 100,000 population, respectively, in 1970 to 7.2 and 2.2 per 100,000 population (respectively) in 1994 to 96 (4), which growth was

The overall mortality for thyroid cancer was very low and remained so throughout the study period. There were few reported deaths from thyroid cancer, especially in age groups younger than 50, and the only significant change in the overall death rate was a decrease (APC = -4.9%) in that of the 50 to 64 years age group. The mortality rate in our population was very low, as is also seen in Canada (21) and in the United States, at 0.5 per 100,000 population for the span of years covering from 1973 to 2002 (5). This low rate may be caused by earlier diagnoses resulting from increased diagnostic scrutiny, more access to best standards of care, or overdiagnosis brought about by a proliferation in the use of neck imaging and fine-needle aspiration biopsies, both of which have become standards of care and whose use are revealing disease that, until their employment, remained subclinical (4, 9, 22).

The reason for the increasing incidence in papillary thyroid tumors is not clear, but it seems to be multifactorial. A possible and frequently mentioned explanation is the increased exposure to radiation, which is a major known risk factor for thyroid cancer. The use of high-dose ionizing radiation treatment for benign childhood conditions of the head and neck in the 1920s and 30s has been associated with an increased risk of differentiated thyroid cancer, especially in those patients with papillary cancer (23, 24). Other radiation exposure that is well-documented is associated with the radioactive spill from nuclear weapons or from nuclear power plant accidents such as occurred in Chernobyl in 1986 (25). At present, computed tomography scanning and other radiologic modalities are the primary sources of such exposure (26). Of concern is the

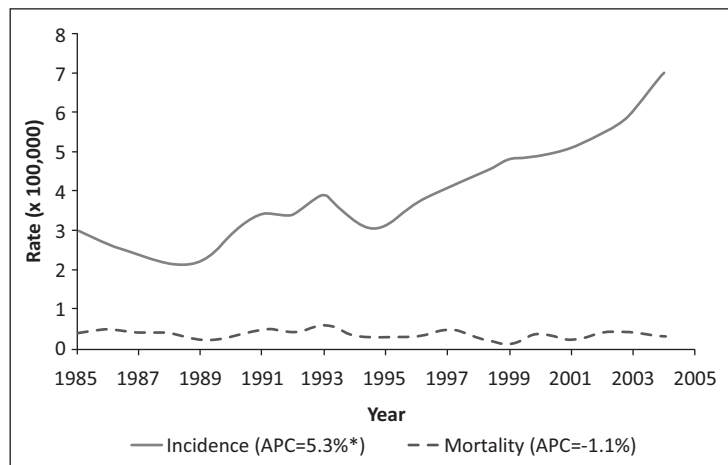


Figure 2. Thyroid cancer incidence and mortality rates in Puerto Rico (1985-2004). Rates are per 100,000 and age-adjusted to the 2000 Puerto Rico population. Annual percentage change (APC) was estimated using Joinpoint regression models (*p<0.05).

use of medical radiation technology in the pediatric population, which is especially sensitive to radiation (27). Another potential explanation for the increase in papillary cancer is the fact our population lived in an iodine-sufficient area and iodine excess has been associated with papillary thyroid carcinoma mediated by activation of the oncogenic T1799A BRAF mutation (28, 29). This association between iodine excess and papillary tumors has also been suggested in epidemiologic studies in Europe and in the United States (30-33). The significant increase in this histological type may also have been partially affected by a change in diagnostic criteria in 1988, when a new WHO classification system was introduced, and tumors with follicular features were reclassified (based on their nuclear characteristics) as papillary carcinoma (34).

Widespread use of imaging and diagnostics techniques has increased over the past decades with the introduction of thyroid ultrasound and fine-needle aspirations in the 1980s (35), which in part could be a potential explanation for the increase in thyroid cancer incidence observed in Puerto Rico. In addition, the new and improved screening methods have become more sensitive in detecting asymptomatic and smaller thyroid carcinomas at an early stage, which might affect the trends over time. However, incidence rates across all ages and sex are increasing over time, except for those pertaining to younger and older age groups, which could suggest a real increase in the occurrence of thyroid cancer, a reflection of heightened diagnostic scrutiny, or both. To better verify the previous, further research is needed, especially in relation to age-/sex-related risk factors, thyroid biology, tumor characteristics, and other factors.

Our study results of age-specific analyses have revealed that the greatest annual percent changes were seen in males aged 35 to 49 years and females aged 50 to 64 years. The age of menopause among Puerto Rican women is approximately 51.4 years (36), and the fastest rising incidence rates of thyroid cancer observed in Puerto Rican women were found during the immediate post-menopausal years, which would suggest a possible association with fluctuating hormonal levels. Some publications suggest that irregular menses, miscarriages, parity, and early menopause appear to augment the incidence of well-differentiated thyroid cancers (37-39). However, other studies indicate that the hypothesis of reproductive risk factors and hormonal exposures provides only limited support to the increased

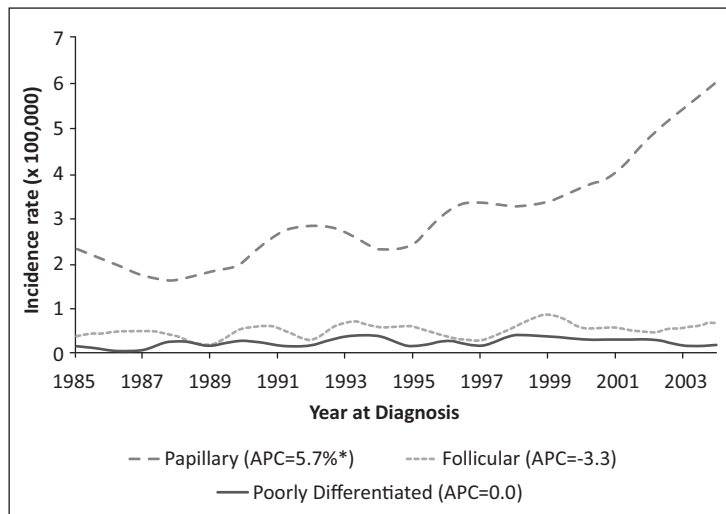


Figure 3. Thyroid cancer incidence rates by histology in Puerto Rico (1985-2004). Rates are per 100,000 and are age-adjusted to the 2000 Puerto Rico population. Poorly differentiated histologies are based on medullary and anaplastic carcinomas grouped together. Annual percentage change (APC) was estimated using Joinpoint regression models (*p<0.05).

Table 3. Distribution and age-adjusted and age-specific mortality rates by sex for thyroid cancer in Puerto Rico, 1985-2004.

Age Group	Overall cases n (%) 1985-2004	Age-specific rate (95% CI)		Overall trend APC% (95% CI) 1985-2004
		1985	2004	
ALL				
0-19	0 (0.0)	0.0 (0.0-0.3)	0.0 (0.0-0.3)	~
20-34	5 (2.1)	0.1 (0.0-0.7)	0.0 (0.0-0.4)	~
35-49	13 (5.3)	0.0 (0.0-0.6)	0.0 (0.0-0.5)	~
50-64	49 (20.2)	1.0 (0.3-2.6)	0.3 (0.0-1.1)	-4.9* (-8.4, -1.1)
65-79	117 (48.1)	1.7 (0.5-4.4)	1.7 (0.6-3.7)	-0.21 (-4.0, 3.7)
80+	59 (24.3)	3.4 (0.4-12.2)	5.1 (1.9-11)	1.18 (-2.1, 4.6)
All ages*†	243	0.4 (0.2-0.7)	0.3 (0.2-0.6)	-1.1 (-3.3, 1.1)
MALE				
0-19	0 (0.0)	0.0 (0.0-0.6)	0.0 (0.0-0.6)	~
20-34	2 (2.2)	0.0 (0.0-1.0)	0.0 (0.0-0.9)	~
35-49	6 (6.5)	0.0 (0.0-1.4)	0.0 (0.0-1.0)	~
50-64	22 (23.9)	0.5 (0.0-3.0)	0.3 (0.0-1.9)	~
65-79	47 (51.1)	0.9 (0.0-5.0)	1.3 (0.2-4.5)	~
80+	15 (16.3)	0.0 (0.0-14.2)	4.2 (0.5-15.2)	~
All ages*†	92	0.2 (0.0-0.6)	0.3 (0.1-0.6)	-1.9 (-5.2, 1.6)
FEMALE				
0-19	0 (0.0)	0.0 (0.0-0.6)	0.0 (0.0-0.6)	~
20-34	3 (2.0)	0.2 (0.0-1.4)	0.0 (0.0-0.9)	~
35-49	7 (4.6)	0.0 (0.0-1.2)	0.0 (0.0-0.9)	~
50-64	27 (17.9)	1.5 (0.3-4.3)	0.3 (0.0-1.6)	~
65-79	70 (46.4)	2.4 (0.5-7.1)	2.0 (0.5-5.2)	~
80+	44 (29.1)	6 (0.7-21.6)	5.6 (1.5-14.4)	~
All ages*†	151	0.6 (0.3-1.2)	0.4 (0.2-0.7)	-1.4 (-4.1, 1.4)

*Annual rates presented for selected years; †Rates were age-standardized to the Puerto Rico 2000 standard population using the direct method, and confidence intervals (Tiwari mod) are 95% for rates; *p-value <0.05; Annual percent change (APC) was estimated using Joinpoint regression models; ~Not enough cases to make estimate, as no cases were reported for some years.

thyroid cancer risk in women (40, 41). The difference in sex-/age-specific incidence patterns observed in Puerto Rico should be considered by future studies in order to better understand and identify the risk factors associated with the rise in thyroid carcinomas. Finally, the environment (42), diet (43), wireless telecommunication (44), and genetics (29), among others, may present unsuspected novel risk factors that increase the incidence of thyroid cancer, especially the papillary type.

The limitations of this study include the fact that it is a record review and some data are unknown. The high rates of unknowns in tumor size (39.1%) prevent us from determining whether the increased incidence pertains mainly to subclinical tumors, as described by Davis, et al (6) versus pertaining to small and large tumor sizes, as reported by Yu et al (8). Moreover, 19.6% of all cases registered have unknown staging at the time of diagnosis, which fact also precludes us from evaluating trends over time by stage. Another limitation is the fact that mortality rate cannot be analyzed based on histologic type because the data in the death certificates do not specifically include the histologic type of thyroid cancer that caused the death of the individual.

Conversely, the major strength of this study is the fact that the data were gathered from the Puerto Rico Cancer Registry, which is a population based-registry with well-validated, high quality data. Also, this is the first report on the incidence and mortality of thyroid cancer in Puerto Rico consisting of a fairly lengthy study period and that can be used as a guide for future studies on thyroid cancer in the Puerto Rican population. In order to evaluate specific thyroid cancer patterns, studies that address tumor size and staging at the moment of diagnosis are needed. Furthermore, studies evaluating changes in risk factors or the medical practices pertaining to the diagnosis of thyroid cancer might be able to answer the question as to why the incidence of thyroid cancer is increasing.

This study provides clinical and public health professionals with a better understanding of both the incidence and the distribution of thyroid cancer in Puerto Rico, setting the scene for future studies addressing the risk factors for this disease in Puerto Rico. These future studies will help in the identification of specific groups and potential health disparities as well as improve the allocation of the already scarce resources for cancer prevention and control to a high-risk population.

In conclusion, our data show that the incidence of thyroid carcinoma in Puerto Rico increased significantly from 1985 to 2004. This is almost entirely due to a rise in papillary cancer, as has also been seen in other countries. However, the mortality rate remained low for the aforementioned period. It remains unclear how much of the noted increase in thyroid cancer incidence is related to the augmented detection of subclinical disease resulting from the frequent utilization of ultrasonography and fine needle aspiration biopsies, to a worldwide increment in radiation exposure, or to a true increase in thyroid cancer. Further studies investigating the relationship between environmental

chemicals, hormones, and other potential risk factors and the development of thyroid cancer are warranted.

Resumen

Objetivo: El cáncer de tiroides se ha convertido en una de las malignidades de más rápido crecimiento en varios países en el mundo. Hay muy pocas publicaciones sobre las tendencias de este cáncer en Puerto Rico, y dichos estudios fueron realizados por periodos de tiempo relativamente cortos. El objetivo de este estudio fue describir la incidencia global del cáncer de tiroides por edad, sexo e histología, y la mortalidad por edad y sexo en Puerto Rico entre los años 1985 y 2004. **Métodos:** Utilizando la base de datos del Registro Central de Cáncer de Puerto Rico, se hizo un estudio retrospectivo de pacientes con cáncer de tiroides diagnosticados desde el 1 de enero de 1985 hasta el 31 de diciembre de 2004. **Resultados:** La incidencia total de cáncer de tiroides aumentó de 3.0 a 7.0 por 100,000 habitantes (2.3 veces más) con un cambio porcentual anual (CPA) de 5.3% ($p < 0.05$) durante el periodo de 1985 a 2004. La incidencia fue más alta en las mujeres (4.7 en 1985 a 10.5 por 100,000 habitantes en 2004) cuando se compara con los hombres (1.1 en 1985 a 3.0 por 100,000 hombres en 2004). El aumento de esta incidencia fue debido mayormente al cáncer papilar de tiroides, el cual aumentó de 2.4 a 6.0 por 100,000 habitantes (2.5 veces más) con un CPA de 5.7% ($p < 0.05$). La mortalidad del cáncer de tiroides fue baja (0.4 en 1985 y 0.3 por 100,000 habitantes en 2004), con un CPA no significativo de -1.1% ($p > 0.05$). **Conclusión:** La incidencia de cáncer de tiroides en Puerto Rico aumentó significativamente durante el período de 1985 a 2004, mayormente debido al cáncer papilar de tiroides. Sin embargo, la mortalidad se mantuvo baja.

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References

1. Franceschi S, Boyle P, Maisonneuve P, et al. The epidemiology of thyroid carcinoma. *Crit Rev Oncog* 1993;4:25-52.

2. Miller BA, Ries LAG, Hankey BF, et al, eds. SEER Cancer Statistics Review: 1973-1990. Bethesda, MD: National Cancer Institute. NIH Publications; 1993. No. 93-2789.
3. Torres-Cintrón M, Ortiz AP, Pérez-Irizarry J, et al. Incidence and mortality of the leading cancers types in Puerto Rico: 1987-2004. *PR Health Sci J* 2010;29:317-329.
4. Lui S, Semenciw R, Ugnat A-M, Mao Y. Increasing thyroid cancer incidence in Canada, 1970-1996: time trends and age-period cohort effects. *Br J Cancer* 2001;85:1335-1339.
5. Davies L, Welch HG. Increasing Incidence of Thyroid Cancer in the United States, 1973-2002. *JAMA* 2006;295:2164-2167.
6. Enewold L, Zhu K, Ron E, et al. Rising thyroid cancer incidence in the United States by demographic and tumor characteristics, 1980-2005. *Cancer Epidemiol Biomarkers Prev* 2009;18:784-791.
7. Leenhardt L, Grosclaude P, Chérié-Challine L. Thyroid Cancer Committee Increased Incidence of Thyroid Carcinoma in France: A True Epidemic or Thyroid Nodule Management Effects? Report from the French Thyroid Cancer Committee. *Thyroid* 2004;14:1056-1060.
8. Howlader N, Noone AM, Krapcho M, et al, eds. SEER Cancer Statistics Review, 1975-2008. National Cancer Institute. Bethesda, MD. Available at: http://seer.cancer.gov/csr/1975_2008/, based on November 2010 SEER data submission, posted to the SEER web site, 2011.
9. Kent WDT, Hall SF, Isotalo PA, et al. Increased incidence of differentiated thyroid cancer and detection of subclinical disease. *CMAJ* 2007;177:1357-1361.
10. Yu GP, Li JC, Branovan D, McCormick S, Schantz SP. Thyroid cancer incidence and survival in the national cancer institute surveillance, epidemiology, and end results race/ethnicity groups. *Thyroid* 2010;20:465-473.
11. Fuentes R. Cancer of the thyroid gland in Puerto Rico. *Bol Asoc Med P R* 1952;44:370-372.
12. Martínez I. Cáncer en Puerto Rico. Departamento de Salud, Estado Libre Asociado de Puerto Rico, 1975; 78.
13. Ydrach AA, Marcial VA, Velázquez Vera J, Moscol JA. Undifferentiated carcinoma of the thyroid: case reports and review of the PR Cancer registry experience from 1970-1974. *Bol Asoc Med PR*, 1980;72:353-359.
14. Muñoz MB and Sorrentino R. Carcinoma of the thyroid at the University (District) Hospital. *Bol Asoc Med P R* 1965;57:346-350.
15. Puerto Rico Central Cancer Registry. Comprehensive Center Cancer of the University of Puerto Rico. Incidence Case File (December 2010), Division of Epidemiology, PR Department of Health.
16. Fritz A, Jack A, Percy C, Parkin M, Sobin L. International Classification of Diseases for Oncology, 3rd Edition. Geneva, Switzerland. World Health Organization; 2000.
17. National Cancer Institute Surveillance Research Program. SEER Incidence Site Recode ICD-O-3 (1/27/2003) Definition. US National Institutes of Health, Bethesda, Maryland.
18. Puerto Rico Mortality File. Puerto Rico Department of Health: Division of Statistical Analysis, Auxiliary Secretariat for Planning and Development, 2010.
19. SEER* Stat software (www.seer.cancer.gov/seerstat) version 6.4.4. [computer program]. Version 6.4.4.
20. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med* 2000;19:335-351.
21. Marrett LD, De P, Airia P, Dryer D. Steering Committee of Canadian Cancer Statistics 2008. Cancer in Canada in 2008. *CMAJ* 2008;179:1163-1170.
22. Burgess JR, Tucker P. Incidence Trends for Papillary Thyroid Carcinoma and Their Correlation with Thyroid Surgery and Thyroid Fine-Needle Aspirate Cytology. *Thyroid* 2006;16:47-53.
23. Hanford JM, Quimby EH, Frantz VK. Cancer arising many years after radiation therapy. Incidence after irradiation of benign lesions in the neck. *JAMA* 1962;181:404-410.
24. Janower ML, Miettinen OS. Neoplasms after childhood irradiation of the thymus gland. *JAMA* 1971;215:753-756.
25. Stezhko VA, Buglova EE, Danilova LI, et al. A cohort study of thyroid cancer and other thyroid diseases after the Chernobyl accident: objectives, design and methods. *Radiat Res* 2004;161:481-492.
26. Wartofsky L. Increasing world incidence of thyroid cancer: Increased detection or higher radiation exposure? *Hormones (Athens)* 2010;9:103-108.
27. Sinnott B, Ron E, Schneider AB. Exposing the thyroid to radiation: a review of its current extent, risks, and implications. *Endocr Rev* 2010;31:756-773.
28. Guan H, Ji M, Bao R, et al. Association of high iodine intake with the T1799A BRAF mutation in papillary thyroid cancer. *J Clin Endocrinol Metab*. 2009;94:1612-1617.
29. Patel KN, Singh B. Genetic considerations in thyroid cancer. *Cancer Control* 2006;13:111-118.
30. Harach HR, Escalante DA, Onativia A, et al. Thyroid carcinoma and thyroiditis in an endemic goiter region before and after iodine prophylaxis. *Acta Endocrinol (Copenh)* 1985;108:55-60.
31. Knobel M, Medeiros-Neto G. Relevance of iodine intake as a reputed predisposing factor for thyroid cancer. *Arq Bras Endocrinol Metabol* 2007;51:701-712.
32. Lind P, Langsteger W, Molnar M, Gallowitsch HJ, Mikosch P, Gomez I. Epidemiology of thyroid diseases in iodine sufficiency. *Thyroid* 1998;8:1179-1183.
33. Langsteger W, Koltringer P, Wolf G, et al. The impact of geographical, clinical, dietary and radiation-induced features in the epidemiology of thyroid cancer. *Eur J Cancer* 1993;29A:1547-1553.
34. Hedinger CE, Williams ED, Sobin LH. Histological typing of thyroid tumors (histological classification of tumors, no. 11), 2nd ed. World Health Organization International. Berlin, Germany: Springer Verlag; 1988.
35. Rojeski MT, Gharib H. Nodular thyroid disease. Evaluation and management. *N Engl J Med* 1985;313:428-436.
36. Ortiz AP, Harlow S, Sowers M, Romaguera J. Age at natural menopause in a sample of Puerto Rican women. *PR Health Sci J* 2003;22:337-342.
37. Preston-Martin S, Bernstein L, Pike MC, et al. Thyroid Cancer among young women related to prior thyroid disease and pregnancy history. *Br J Cancer* 1987;55:191-195.
38. McTiernan A, Weiss NS, Daling JR. Incidence of thyroid cancer in women in relation to reproductive and hormonal factors. *Am J Epidemiol* 1984;120:423-435.
39. Franceschi S, Fassina A, Talamini R, et al. The influence of reproductive and hormonal factors on thyroid cancer in women. *Rev Epidemiol Sante Publique* 1990;38:27-34.
40. Mack WJ, Preston-Martin S, Bernstein L, Qian D, Xiang M. Reproductive and hormonal risk factors for thyroid cancer in Los Angeles County females. *Cancer Epidemiol Biomarkers Prev* 1999;8:991-997.
41. Memon A, Darif M, Al-Saleh K, Suresh A. Epidemiology of reproductive and hormonal factors in thyroid cancer: evidence from a case-control study in the Middle East. *Int J Cancer* 2002;97:82-89.
42. Kolonel LN, Hankin JH, Wilkens LR, et al. An epidemiologic study of thyroid cancer in Hawaii. *Cancer Causes Control* 1990;1:223-234.
43. Franceschi S, Levi F, Negri E, et al. Diet and thyroid cancer: A pooled analysis of four European case-control studies. *Int J Cancer* 1991;48:395-398.
44. World Health Organization, International Agency for Research on Cancer. Volume 80: Non-ionizing radiation, Part 1, Static and extremely low-frequency (ELF) electric and magnetic fields. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. 2002: Lyon, France.