JOURNAL OF ADOLESCENT AND YOUNG ADULT ONCOLOGY
Volume 1, Number 2, 2011

DOI: 10.1089/jayao.2011.0014

Examination of the Increase in Thyroid Cancer Incidence Among Younger Women in the United States by Age, Race, Geography, and Tumor Size, 1999–2007

Dawn M. Holman, MPH, CPH,[1] Ashwini Soman, MBBS, MPH,[2] Meg Watson, MPH,[1] Hannah K. Weir, PhD,[1] Katrina F. Trivers, PhD, MSPH,[1] and Mary C. White, ScD[1]

Purpose: Thyroid cancer incidence has been increasing for several decades, but the reasons are not fully understood. Previous surveillance reports have covered less than 26% of the U.S. population. More recent, nationwide data are needed. This study examines thyroid cancer incidence among younger women by age, race/ethnicity, geography, and tumor size. ***Patients and Methods:*** Our study uses nationwide surveillance data to describe incidence rates and recent trends in thyroid cancer among adults aged 20–39 years in the United States during 1999–2007, with a focus on females. ***Results:*** Incidence rates were more than five times higher among females (16.4 per 100,000; 95% confidence interval [CI]: 16.2–16.6) than among males (3.1 per 100,000; 95% CI: 3.1–3.2). Among females, rates were higher among non-Hispanic whites than among other racial/ethnic groups and higher in the Northeast compared with other regions ($p < 0.05$). During 1999–2007, incidence rates increased 5.3% each year among females (95% CI: 4.7–5.9). This increase was observed across five-year age groups, racial/ethnic groups (except American Indians/Alaska Natives), geographic regions, and tumor sizes. ***Conclusion:*** The increase in rates across all tumor sizes suggests that the observed increases cannot be attributed solely to changes in diagnostics or surveillance. In addition, the continued increase in incidence rates in recent years among persons born after 1960 suggests that other, more contemporary factors than those previously proposed may play a contributing role.

Introduction

The increase in the incidence of thyroid cancer in the United States during the past 30 years has been documented in numerous reports.[1–7] Incidence rates have been consistently higher among women than among men for several decades, and this difference has increased over time.[1,2,4,5] In 2007, more than 35,000 people in the United States were diagnosed with thyroid cancer, and approximately one-quarter of them were younger than 40 years of age.[8] Although survival rates following a diagnosis of thyroid cancer are high (as evidenced by low mortality), the treatment and management of thyroid cancer can have long-term effects on survivors' health and quality of life.[8–11] The American Thyroid Association recommends a near-total or total thyroidectomy for tumors more than a centimeter in diameter, and recommends radioactive iodine ablation in addition to surgery for high-risk patients and those with distant metastases.[9] Given improvements in diagnosis and treatment, there is the possibility that some thyroid cancers are being overdiagnosed.[12] The U.S. Preventive Services Task Force does not currently recommend for or against routine screening for thyroid cancer in asymptomatic adults, and there is little evidence that treatment in those without symptoms leads to improved clinical outcomes.[13,14] After treatment, survivors require lifelong thyroid hormone replacement therapy[10] and may have an increased risk for cancers of the salivary gland, stomach, colorectal, breast, prostate, kidney, brain/central nervous system, bone, and adrenal glands, as well as soft tissue sarcoma, non-Hodgkin lymphoma, multiple myeloma, and leukemia (standardized incidence ratio for all second primary malignancies = 1.2; 95% CI: 1.17–1.24).[15] Additionally, the risk for future cancers may be greater for those diagnosed at a young age.[16]

The reasons for the increase in thyroid cancer incidence are not well understood, but several theories have been proposed.

[1]Division of Cancer Prevention and Control, Centers for Disease Control and Prevention, Atlanta, Georgia.
[2]Northrop Grumman Corporation, Atlanta, Georgia.

Changes to coding practices and improvements in diagnostics during the 1970s are thought to play a role in the reported increase in incidence.[17] Among other proposed explanations is the use of medical radiation to treat benign thyroid disease, a practice that occurred from the 1920s to the 1950s.[18] However, the impact of the introduction of newer diagnostic technology and the discontinued use of medical radiation to treat benign thyroid disease would be expected to diminish over time, and thus other factors may be contributing to the continued increase in incidence during recent years, especially among young adults.

Examining incidence rates and recent trends over time among persons born during or after 1960 can aid progress toward understanding more contemporary risk factors for thyroid cancer and may ultimately help identify opportunities for primary prevention.[19] Previous studies have analyzed surveillance data from the National Cancer Institute's (NCI) Surveillance, Epidemiology and End Results (SEER) program and have only covered up to 26% of the U.S. population.[3–5,7,20] As a result, these studies were limited in their ability to examine geographic variation or trends at younger ages (when incidence rates are lowest). More recent, nationwide data are needed. The current study enhances previous research by using combined data from the Centers for Disease Control and Prevention's (CDC) National Program of Cancer Registries (NPCR) and NCI's SEER, which provides greater geographic and regional coverage and greater statistical stability. The purpose of this study is to use nationwide surveillance data to look specifically at recent trends in thyroid cancer among young adults aged 20–39 years in the United States, focusing on females by age, race/ethnicity, U.S. census region, and tumor stage, histology, and size.

Materials and Methods

Data sources

Data from the two federal cancer surveillance programs, CDC's NPCR and NCI's SEER, were used to examine thyroid cancer incidence rates and trends.[8,21,22] Both NPCR and SEER data were collected and reported using standard data items and uniform codes and procedures, as documented by the North American Association of Central Cancer Registries.[23] Combined NPCR and SEER data that meet high quality data standards are published yearly in the *United States Cancer Statistics* (USCS) report and represent official federal statistics on cancer.[8,24] Only cancer incidence data that meet publication criteria for the USCS report were included in this analysis.[25]

The use of combined NPCR/SEER data maximized the population coverage for the analysis. For thyroid cancer incidence rates, NPCR/SEER data for 2003–2007 were used, resulting in population coverage of 97.2% for those years. When assessing recent trends, NPCR/SEER data for 1999–2007 were used, resulting in population coverage of 89.4% for those years. Because tumor size is not included in NPCR data collection, SEER data for 1999–2007 covering only 13.8% of the population were used to assess long-term trends in thyroid cancer incidence rates by tumor size.[26]

NPCR data used in these analyses were reported to CDC as of November 30, 2009.[8] SEER data were reported to NCI as of November 1, 2009, and were made available through SEER's limited-use data file, which was released in April 2010.[8] Data from states that are supported by both NPCR and SEER are presented as reported to CDC as of November 30, 2009.[8] The population denominator data for calculating cancer incidence rates were obtained from the 2000 U.S. Census and modified by SEER for the purpose of improving the accuracy of rates for the population of Hawaii.[27]

Case definition

Cancer cases were coded using the International Classification of Diseases-Oncology (ICD-O), which was in use at the time of diagnosis. ICD-O 2nd Edition (ICD-O-2) was used for 1999–2000 diagnosis years, and ICD-O 3rd Edition (ICD-O-3) was used for 2001–2007 data. The 1999–2000 data were converted to ICD-O-3 codes.[8,28–30] Cases were defined as invasive, microscopically confirmed, primary, malignant, thyroid neoplasm (ICD-O-3 site code C73.9). We defined histologic types of thyroid cancer according to the following ICD-O-3 codes: papillary tumor (8050, 8052, 8130, 8260, 8340-8344, 8450, and 8452), follicular (8290, 8330-8332, and 8335), medullary (8345, 8346, and 8510), or anaplastic (8021).

Statistical analysis

Incidence rates were calculated per 100,000 persons and were age-adjusted to the 2000 U.S. standard population.[31] Given the low case counts among those below the age of 20, the final analyses were limited to those aged 20–39 years. Combined NPCR/SEER data for 2003–2007 were used to calculate age-specific incidence rates by sex and age-specific rates for females by age (20–24 years, 25–29 years, 30–34 years, and 35–39 years); race/ethnicity (non-Hispanic white, Hispanic, black, Asian Pacific Islander [API], and American Indian/Alaska Native [AI/AN]); U.S. census region (Northeast, Midwest, West, and South); U.S. state; tumor stage; and tumor histology. Annual percent change (APC) was calculated by using the least squares method, and 95% confidence intervals (95% CI) were based on the Gamma method and used the Tiwari modification (Tiwari mod).[32] Combined NPCR/SEER data for 1999–2007 were used to calculate APC by sex and to calculate APC for females by age, race/ethnicity, U.S. census region, U.S. state, tumor stage, and tumor histology. SEER data for 1999–2007 were used to calculate APC for females by tumor size. Cancer cases with unknown sex or age were excluded from all analyses. The categories used for race/ethnicity were mutually exclusive. Differences between groups, when noted, are statistically significant at $p < 0.05$. All statistical analyses were conducted with SEER*Stat (version 6.5.2).[33]

Results

Thyroid cancer incidence rates increased significantly over time among young adults aged 20–39 years during 1999–2007. Rates were consistently higher and increased more rapidly over time among females compared to rates among males (Fig. 1). Among females, rates increased an average of 5.3% (95% CI: 4.7–5.9) each year; among males, rates increased an average of 3.8% (95% CI: 3.2–4.8) each year. The absolute change in rates among males was only 1.0 per 100,000, compared to an absolute increase of 6.6 per 100,000 among females. By 2007, rates were more than five times higher among young females (18.4 per 100,000) than among young males (3.6 per 100,000).

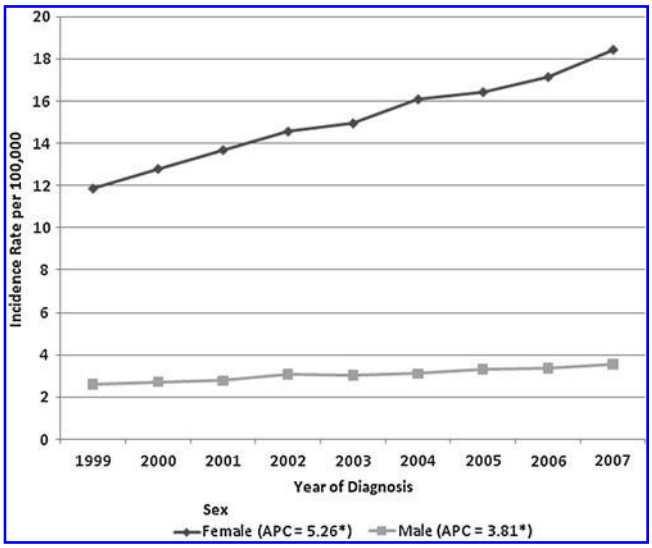

FIG. 1. Age-adjusted incidence rates of thyroid cancer by sex among those aged 20–39 years in the United States, NPCR/SEER 1999–2007. *APC is significantly different from zero ($p < 0.05$). APC, annual percentage change; NPCR, National Program of Cancer Registries; SEER, Surveillance, Epidemiology and End Results program.

Because so few thyroid cancers occurred among young males, all subsequent results focus specifically on females aged 20–39 years. During 2003–2007, there was an average of 16.4 incident cases of thyroid cancer per 100,000 each year, and rates increased an average of 5.3% each year from 1999 to 2007. Most incident thyroid cancers were localized (69.5%) or regional (26.4%) stage at diagnosis, and nearly all (90.2%) were papillary tumors (Table 1). Incident thyroid cancers were distributed across different tumor sizes: 29.1% were less than or equal to 1 centimeter, 30.4% were 1.1–2.0 centimeters, and 32.3% were 2.1–5.0 centimeters. Only 3.5% of tumors were more than 5.0 centimeters. Rates increased significantly over time across all tumor sizes, including those more than 5.0 centimeters in size (Table 1). Furthermore, there was no significant difference in APC when stratifying by tumor size.

Significant differences in rates and trends over time were observed by demographic characteristics (Table 1). Rates were highest among those aged 35–39 years compared to other age groups; the largest percentage increase in rates over time occurred in this age group as well. The lowest rates were among ages 20–24 years. Significant differences were also observed across different racial/ethnic groups, with the highest rates among non-Hispanic whites. The percentage increase in rates over time was not significantly different across racial/ethnic groups. When stratifying by geographic region, the highest rates and APCs of thyroid cancer were seen in the Northeast compared to the other regions. This trend held true for all racial/ethnic groups except for AI/AN (Table 2). The South had the lowest rates overall compared to the other regions (Table 1), but this pattern was not consistent across the different racial/ethnic groups (Table 2). Rates and APCs were also computed for each U.S. state to determine if any states were outliers within their given region. There was modest variation by state, but there were no notable outliers within each region (data not shown).

Rates were consistently higher among those aged 35–39 years compared to other five-year age groups across all racial/ethnic groups, except AI/AN (Table 3), but APCs did not always follow this pattern. Among non-Hispanic whites, those aged 35–39 years had the highest APC compared to other age groups. In all other racial/ethnic groups, APCs were not significantly different across five-year age groups. The pattern of rates increasing with age and over time was consistent across all four geographic regions (Table 4).

Discussion

The results from this study indicate that incidence rates for thyroid cancer have continued to increase in recent years among young adults of both sexes in the United States. In less than a decade, rates have increased more than 50%, with no indication that the rate of increase is slowing or leveling off. The difference in rates by sex has also continued to grow over time. Other notable differences were observed among young women by five-year age group, geographic region, and race/ethnicity. The observation of higher incidence rates among older age groups is consistent with previous literature, which has shown that thyroid cancer incidence rates typically peak around ages 40–59 among women.[4,5]

Reasons for geographic differences in incidence rates are largely unknown and could be due to multiple factors. A study using California Cancer Registry data from 1988–2004 found that Japanese women born outside the United States had a significantly higher rate of thyroid cancer than U.S.-born Japanese women, but among Chinese and Filipina women the U.S.-born women had higher rates.[34] One possible reason for geographic differences in incidence rates could be differences in geographic-specific exposures early in life.

In the current study, rates increased among most racial/ethnic groups and within all geographic regions of the United States. However, non-Hispanic white women consistently had the highest rates, followed by API and Hispanic women. A recent study using SEER data observed similar racial/ethnic patterns in thyroid cancer incidence across all age groups.[35] The use of combined NPCR/SEER data allowed us to provide additional information about these racial/ethnic patterns, including a more detailed age breakdown and a description of the racial/ethnic patterns in each geographic region.

Another notable finding was the increase in the incidence of thyroid tumors of all sizes. Some researchers have proposed that the observed increases are not caused by increases in actual disease but are artifacts of changes in diagnosis and surveillance.[3] For example, improvements in diagnostic techniques, such as the use of ultrasound and thin needle aspiration, have led to an increased ability to detect early-stage cancers, and the coding rules for thyroid cancer were changed in 1988 to include benign-appearing papillary lesions, thus widening the definition of papillary thyroid cancer.[3,6,36–38] If earlier changes in diagnostics and surveillance were the sole reasons for the observed increases, one would expect to observe increases in the rates of only small thyroid tumors and a leveling off of the rate of increase over time, unless physicians are becoming more aggressive in their screening practices over time. However, the increase in rates is occurring across all tumor sizes.[1,4,7,35] Our study results indicate similar trends specifically among younger women, with no indication that the rate of increase is slowing,

Table 1. Incident Case Counts and Rates During 2003–2007 and APC During 1999–2007 for Thyroid Cancer Among Females Aged 20–39 Years in the United States

	N (%)	*Rate (95% CI)*	*APC (95% CI)*
Overall	31,342 (100)	16.4 (16.2, 16.6)	5.3 (4.7–5.9)
Age			
20–24 years	3907 (12.5)	7.9 (7.7, 8.2)	2.1 (0.8, 3.4)
25–29 years	6587 (21.0)	13.9 (13.6, 14.2)	4.0 (3.0, 5.0)
30–34 years	9203 (29.4)	19.2 (17.8, 19.6)	5.0 (4.3, 5.6)
35–39 years	11,645 (37.2)	22.8 (22.4, 23.3)	7.2 (6.4, 7.9)
Race/ethnicity[a]			
Non-Hispanic white	22,103 (70.5)	18.5 (18.2,18.7)	5.4 (4.8, 6.1)
Hispanic	4505 (14.4)	14.0 (13.6, 14.4)	5.4 (3.7, 7.1)
Black	2157 (6.9)	8.2 (7.9, 8.6)	5.0 (2.5, 7.6)
AI/AN	214 (0.7)	9.7 (8.4, 11.1)	3.6 (−2.0, 9.4)
API	1796 (5.7)	15.23 (14.5, 16.0)	6.1 (4.3, 7.9)
Region			
Northeast	7877 (25.1)	22.0 (21.5, 22.5)	7.4 (6.3, 8.4)
Midwest	6875 (21.9)	16.1 (15.8, 16.5)	5.0 (3.9, 6.1)
West	7132 (22.8)	15.9 (15.6, 16.3)	4.7 (3.4, 6.1)
South	9458 (30.2)	13.9 (13.6, 14.2)	4.2 (3.4, 5.0)
Histology[b]			
Papillary	28,259 (90.2)	14.8 (14.6, 14.9)	5.6 (4.9, 6.3)
Follicular	2381 (7.6)	1.2 (1.2, 1.3)	2.3 (1.0, 3.6)
Other[c]	702 (2.3)	0.2 (0.1, 0.2)	2.9 (−1.9, 8.0)
Stage			
Localized	21,797 (69.5)	11.4 (11.3, 11.6)	5.0 (4.2, 5.8)
Regional	8285 (26.4)	4.3 (4.2, 4.4)	7.3 (6.0, 8.7)
Distant	391 (1.2)	0.2 (0.2, 0.2)	2.1 (−2.3, 6.6)
Unstaged	869 (2.8)	0.5 (0.4, 0.5)	−2.8 (−6.7, 1.3)
Tumor size[d]			
≤1 cm	1346 (29.1)	4.8 (4.6, 5.1)	7.2 (5.4, 9.0)
1.1–2.0 cm	1408 (30.4)	5.1 (4.8, 5.3)	5.3 (4.0, 7.0)
2.1–5.0 cm	1495 (32.3)	5.3 (5.1, 5.6)	5.2 (2.6, 7.9)
More than 5.0 cm	164 (3.5)	0.6 (0.5, 0.7)	11.0 (6.0, 16.3)
Unknown	216 (4.7)	0.8 (0.7, 0.9)	−7.2 (−10.5, −3.7)

Note: Rates are per 100,000 and age-adjusted to the 2000 U.S. standard population. Confidence intervals (Tiwari mod) are 95% for rates. Source: Tiwari RC, Clegg LX, Zou Z. Efficient interval estimation for age-adjusted cancer rates. Stat Methods Med Res. 2006;15:547–569.

APC, annual percentage change; AI/AN, American Indian/Alaska Native; API, Asian Pacific Islander; CI, confidence interval.

[a]All races are included in Hispanic ethnicity. White, black, AI/AN, and API are limited to non-Hispanic ethnicity. [b]For analysis of histology, analysis was limited to microscopically confirmed tumors; 99.7% of all tumors were microscopically confirmed. [c]Includes medullary, not otherwise specified, and other. [d]Tumor size is reported on a subset of the population (SEER only).

suggesting that other factors are contributing to the observed increases.

One possible cause for the observed increase in thyroid cancer among young adults is increasing exposure to ionizing radiation, the most well-established risk factor for thyroid cancer.[39–41] Common sources of exposure to ionizing radiation in the United States include medical imaging procedures and natural sources of radiation such as radon.[42] Researchers have estimated that the per capita dose of radiation from medical exposure (not including dental or radiotherapy) increased almost 600% (approximately 3.0 millisieverts) from 1982 to 2006, with the increase largely being attributed to increased use of computed tomography (CT) scans and nuclear medicine.[42] Pediatric diagnostic procedures are among the most rapidly increasing groups of CT procedures.[43,44] Children are more sensitive to radiation than adults and have a longer window of opportunity for expressing radiation damage.[44,45] Dental x-rays are another common source of radiation exposure. Although radiation doses are relatively low, a recent case-control study found that exposure to dental x-rays was significantly associated with an increased risk of thyroid cancer.[46]

Some have also suggested that the increase in thyroid cancer may be in part caused by increases in environmental exposures to chemicals that can interfere with normal thyroid function.[47–51] For example, perchlorate, nitrate, thyocyante, polychlorinated biphenyls (PCBs), bisphenol A (BPA), polybrominated diphenyl ether (PBDE), and phthalates are all thought to alter thyroid function in some manner.[47–53] Perchlorate, phthalate metabolites, and BPA have been detected in measurable amounts in urinary samples, and PCBs and PBDEs have been detected in measurable amounts in serum samples from the U.S. population across all age groups.[54] PBDEs have been measured in breast milk from donors in Texas at levels many times higher than levels measured in women in Europe.[55] Rates of thyroid cancer also tend to be lower in European countries than in the United States, particularly among white women.[49]

Table 2. Incidence Rates and Rate Ratios For Thyroid Cancer Among Females Aged 20–39 Years by Race/Ethnicity and Region in the United States During 2003–2007

Race/ethnicity[a] *Region*	*Cases*	*Rate (95% CI*[b]*)*	*Rate ratio (95% CI)*
Non-Hispanic White			
Northeast	5836	24.4 (23.8, 25.1)	1.6 (1.5, 1.6)
Midwest	5698	17.3 (16.9, 17.8)	1.1 (1.1, 1.1)
West	4288	18.5 (18.0, 19.1)	1.2 (1.1, 1.2)
South	6281	15.8 (15.4, 16.1)	Ref[c]
Hispanic			
Northeast	880	18.3 (17.1, 19.5)	1.3 (1.2, 1.4)
Midwest	434	14.7 (13.3, 16.2)	1.1 (0.9, 1.2)
West	1662	12.3 (11.7, 13.0)	0.9 (0.8, 1.0)
South	1529	14.0 (13.3, 14.7)	Ref
Black			
Northeast	488	10.6 (9.7, 11.6)	1.3 (1.2, 1.5)
Midwest	366	7.5 (6.7, 8.3)	1.0 (0.8, 1.1)
West	167	7.5 (6.4, 8.7)	1.0 (0.8, 1.1)
South	1136	7.9 (7.4, 8.4)	Ref
AI/AN			
Northeast	[d]	[d]	[e]
Midwest	36	10.2 (7.1, 14.2)	1.0 (0.6, 1.5)
West	101	9.8 (7.9, 11.9)	1.0 (0.7, 1.3)
South	66	10.2 (7.9, 13.0)	Ref
API			
Northeast	493	19.8 (18.1, 21.6)	1.5 (1.3, 1.7)
Midwest	189	12.6 (10.9, 14.6)	1.0 (0.8, 1.1)
West	790	14.7 (13.7, 15.8)	1.1 (1.0, 1.3)
South	324	13.3 (11.9, 14.8)	Ref

Note: Rates are per 100,000 and age-adjusted to the 2000 U.S. standard population. Confidence intervals (Tiwari mod) are 95% for rate ratios. Source: Tiwari RC, Clegg LX, Zou Z. Efficient interval estimation for age-adjusted cancer rates. Stat Methods Med Res. 2006;15:547–569.

AI/AN, American Indian/Alaska Native; API, Asian Pacific Islander; CI, confidence interval; Ref, reference.

[a]All races are included in Hispanic ethnicity. White, black, AI/AN, and API are limited to non-Hispanic ethnicity. [b]CI indicates confidence interval for rate ratio. [c]Ref indicates reference group for rate ratios. [d]Statistic not displayed due to fewer than 16 cases. [e]Statistic could not be calculated.

Table 3. Incident Case Counts and Rates During 2003–2007 and APC During 1999–2007 for Thyroid Cancer Among Females Aged 20–39 Years by Race/Ethnicity and Five-Year Age Group in the United States

	N (%)	*Rate (95% CI)*	*APC (95% CI)*
Overall	31,342 (100)	16.4 (16.2, 16.6)	5.3 (4.7–5.9)
Non-Hispanic White			
20–24 years	2749 (12.4)	8.9 (8.6, 9.3)	1.7 (0.1, 3.4)
25–29 years	4507 (20.4)	15.7 (15.2, 16.1)	3.3 (2.0, 4.7)
30–34 years	6456 (29.2)	22.0 (21.0, 22.5)	5.4 (4.8, 6.1)
35–39 years	8391 (38.0)	25.4 (24.9, 25.6)	7.8 (7.0, 8.5)
Hispanic[a]			
20–24 years	608 (13.5)	7.4 (6.8, 8.0)	3.3 (0.7, 5.9)
25–29 years	1092 (24.2)	12.7 (11.9, 13.5)	6.2 (4.2, 8.3)
30–34 years	1352 (30.0)	16.0 (15.2, 16.9)	5.7 (3.2, 8.3)
35–39 years	1453 (32.3)	18.8 (17.8, 19.7)	5.4 (2.7,8.2)
Black			
20–24 years	237 (11.0)	3.3 (2.9, 3.7)	1.2 (−0.8, 3.2)
25–29 years	449 (20.8)	6.7 (6.1, 7.3)	4.1 (−0.6, 9.0)
30–34 years	616 (28.6)	9.4 (8.7, 10.2)	5.2 (3.0, 7.4)
35–39 years	855 (39.6)	12.6 (11.7, 13.4)	6.1 (2.9, 9.4)
AI/AN[b]			
20–24 years	30 (14.0)	4.4 (3.0, 6.3)	—
25–29 years	51 (23.8)	8.7 (6.5, 11.5)	—
30–34 years	56 (26.2)	10.4 (7.8, 13.5)	—
35–39 years	77 (36.0)	14.1 (11.2, 17.7)	—
API			
20–24 years	208 (11.6)	8.5 (7.4, 9.8)	5.7 (−1.6, 13.6)
25–29 years	367 (20.4)	12.7 (11.4, 14.0)	7.2 (3.2, 11.4)
30–34 years	554 (30.8)	16.7 (15.4, 18.2)	4.8 (0.8, 9.0)
35–39 years	667 (37.1)	21.5 (19.9, 23.2)	6.7 (2.9, 10.5)

Note: Rates are per 100,000 and age-adjusted to the 2000 U.S. standard population. Confidence intervals (Tiwari mod) are 95% for rates. Source: Tiwari RC, Clegg LX, Zou Z. Efficient interval estimation for age-adjusted cancer rates. Stat Methods Med Res. 2006;15:547–569.

APC, annual percentage change; AI/AN, American Indian/Alaska Native; API, Asian Pacific Islander; CI, confidence interval.

[a]All races are included in Hispanic ethnicity. White, black, AI/AN, and API are limited to non-Hispanic ethnicity. [b]APCs could not be calculated for AI/AN due to low cell counts when stratifying by age group.

The higher incidence rates and more dramatic increases in rates over time among young women compared to young men suggest that reproductive or hormonal factors could play a role in the etiology of thyroid cancer.[2,56] However, the evidence for a relationship between reproductive and hormonal factors and thyroid cancer has been inconsistent.[56–58] Women tend to be more susceptible than men to thyroid diseases and to the thyroid-disrupting effects of certain chemicals, particularly while pregnant.[52,59,60] Therefore, changes in environmental risk factors, such as an increasing prevalence of endocrine disruptors in the environment, would be expected to have a greater effect on the thyroid health of women than of men.

During the past 30 years, the prevalence of obesity has increased among young men and women, and this increase has been suggested as a potential explanation for the rise in incident thyroid cancer.[57,61,62] However, the association between these metabolic factors and thyroid cancer has been inconsistent and still needs further exploration.[57] The most recent data on obesity in the United States suggest that the increase in rates of obesity is slowing, particularly among women.[61] If obesity is a contributing factor there may be a lagged effect, with subsequent changes in thyroid cancer rates occurring years later.

This study provides a unique contribution to the current literature on thyroid cancer by closely examining recent thyroid cancer incidence rates, trends, and disparities among younger women in the United States. This study benefits from the use of combined NPCR/SEER data, and is the first study to examine incidence rates of thyroid cancer using data that cover approximately 90% or more of the U.S. population, allowing for the comparison of rates and trends by U.S. census region and by demographic subpopulations. This focused approach may further inform plausible hypotheses for contemporary causes of thyroid cancer and reasons for the marked increase in incidence rates in recent years.

Table 4. Incident Case Counts and Rates During 2003–2007 and APC During 1999–2007 for Thyroid Cancer Among Females Aged 20–39 Years by U.S. Census Region and Five-Year Age Group in the United States

	N (%)	*Rate (95% CI)*	*APC (95% CI)*
Overall	31,342 (100)	16.4 (16.2, 16.6)	5.3 (4.7, 5.9)
Northeast			
20–24 years	927 (11.8)	10.4 (9.7, 11.1)	3.4 (0.1, 6.8)
25–29 years	1517 (19.3)	18.3 (17.4, 19.3)	5.5 (4.0, 7.1)
30–34 years	2318 (29.4)	26.0 (24.9, 27.1)	7.8 (5.6,10.0)
35–39 years	3115 (39.5)	30.9 (29.8, 32.0)	9.2 (7.3, 11.1)
Midwest			
20–24 years	878 (12.8)	7.7 (7.2, 8.2)	2.4 (–0.5, 5.4)
25–29 years	1501 (21.8)	14.2 (13.5, 14.9)	3.9 (2.6, 5.1)
30–34 years	1994 (29.0)	18.9 (18.1, 19.8)	3.9 (2.5, 5.4)
35–39 years	2502 (36.4)	22.2 (21.4, 23.1)	7.1 (5.4, 8.9)
West			
20–24 years	970 (13.6)	8.5 (7.9, 9.0)	2.2 (–0.3, 4.7)
25–29 years	1585 (22.2)	13.9 (13.3, 14.6)	3.6 (1.2, 4.7)
30–34 years	2048 (28.7)	18.1 (17.3, 18.9)	4.6 (1.8, 7.4)
35–39 years	2529 (35.5)	21.8 (20.9, 22.6)	6.3 (5.4, 7.2)
South			
20–24 years	1132 (12.0)	6.5 (6.2, 6.9)	0.3 (–0.6, 1.2)
25–29 years	1984 (21.0)	11.6 (11.1, 12.1)	3.5 (1.5, 5.5)
30–34 years	2843 (30.1)	16.5 (15.9, 17.1)	4.1 (3.3, 4.9)
35–39 years	3499 (37.0)	19.4 (18.8, 20.1)	6.0 (4.5, 7.4)

Note: Rates are per 100,000 and age-adjusted to the 2000 U.S. standard population. Confidence intervals (Tiwari mod) are 95% for rates. Source: Tiwari RC, Clegg LX, Zou Z. Efficient interval estimation for age-adjusted cancer rates. Stat Methods Med Res. 2006;15:547–569.

APC, annual percentage change; CI, confidence interval.

The study does have some limitations. Given the ecological design of this study, conclusions about the causes of the observed trends cannot be made. Although it is plausible that the risk factors described above may play a role, better information about the exposure history of persons with thyroid cancer is needed before such hypotheses can be substantiated. This study is also limited by the usual concerns related to registry data, such as the potential for incomplete data collection and inconsistencies in tumor coding. Rates of thyroid cancer among AI/AN may be underestimated in this study due to potential misclassification of race in central cancer registries.[63]

In conclusion, thyroid cancer incidence rates have increased substantially among younger women in the United States in recent years. Rates were significantly higher among non-Hispanic white women compared to other racial/ethnic groups and significantly higher among women living in the Northeast compared to other geographic regions. These descriptive patterns in incidence among this more recent birth cohort may help inform hypotheses about factors currently contributing to the incidence of thyroid cancer in the United States.

Acknowledgments

This research was supported in part by an appointment (Dawn M. Holman) to the Research Participation Program at the Centers for Disease Control and Prevention administered by the Oak Ridge Institute for Science and Education through an interagency agreement between the U.S. Department of Energy and the Centers for Disease Control and Prevention. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Disclosure Statement

No competing financial interests exist.

References

1. Chen AY, Jemal A, Ward EM. Increasing incidence of differentiated thyroid cancer in the United States, 1988–2005. Cancer. 2009;115:3801–3807.
2. Cook MB, Dawsey SM, Freedman ND, *et al*. Sex disparities in cancer incidence by period and age. Cancer Epidemiol Biomarkers Prev. 2009;18:1174–1182.
3. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973–2002. JAMA. 2006;295:2164–2167.
4. 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.
5. Kilfoy BA, Devesa SS, Ward MH, *et al*. Gender is an age-specific effect modifier for papillary cancers of the thyroid gland. Cancer Epidemiol Biomarkers Prev. 2009;18:1092–1100.
6. Ward EM, Thun MJ, Hannan LM, Jemal A. Interpreting cancer trends. Ann N Y Acad Sci. 2006;1076:29–53.
7. Zhu C, Zheng T, Kilfoy BA, *et al*. A birth cohort analysis of the incidence of papillary thyroid cancer in the United States, 1973–2004. Thyroid. 2009;19:1061–1066.
8. Ries LAG, Young JL, Keel GE, *et al*. SEER survival monograph: cancer survival among adults: U.S. SEER Program, 1988–2001, patient and tumor characteristics (NIH Pub. No. 07-6215). Bethesda, MD: National Cancer Institute; 2007.
9. Cooper DS, Doherty GM, Haugen BR, *et al*. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid. 2009;19:1167–1214.
10. Pelizzo MR, Merante BI, Toniato A, *et al*. Diagnosis, treatment, prognostic factors and long-term outcome in papillary thyroid carcinoma. Minerva Endocrinol. 2008;33:359–379.
11. Shaha AR. Implications of prognostic factors and risk groups in the management of differentiated thyroid cancer. Laryngoscope. 2004;114:393–402.
12. Davies L, Ouellette M, Hunter M, Welch. The increasing incidence of small thyroid cancers: where are the cases coming from? Laryngoscope. 2010;120:2446–2451.
13. U.S. Preventive Services Task Force. Screening for thyroid cancer; 1996. Accessed July 29, 2011 from: www.uspreventiveservicestaskforce.org/uspstf/uspsthca.htm
14. U.S. Preventive Services Task Force. Screening thyroid disease: recommendation statement; 2004. Accessed July 29, 2011 from: www.uspreventiveservicestaskforce.org/3rduspstf/thyroid/thyrrs.htm
15. Subramanian S, Goldstein DP, Parlea L, *et al*. Second primary malignancy risk in thyroid cancer survivors: a systematic review and meta-analysis. Thyroid. 2007; 17:1277–1288.
16. Brown AP, Chen J, Hitchcock YJ, *et al*. The risk of second primary malignancies up to three decades after the treatment of differentiated thyroid cancer. J Clin Endocrinol Metab. 2008;93:504–515.

17. Franceschi S, Boyle P, Maisonneuve P, *et al*. The epidemiology of thyroid carcinoma. Crit Rev Oncog. 1993;4:25–52.
18. Zheng T, Holford TR, Chen Y, *et al*. Time trend and age-period-cohort effect on incidence of thyroid cancer in Connecticut, 1935–1992. Int J Cancer. 1996;67:504–509.
19. Bleyer A, O'Leary M, Barr R, Ries LAG. Cancer epidemiology in older adolescents and young adults 15 to 29 years of age, including SEER incidence and survival: 1975–2000 (NIH Pub. No. 06-5767). Bethesda, MD: National Cancer Institute; 2006.
20. National Cancer Institute. SEER data, 1973–2007. Accessed August 6, 2010 from: www.seer.cancer.gov/data
21. Hankey BF, Ries L, Edwards BK. The Surveillance, Epidemiology, and End Results program: a national resource. Cancer Epidemiol Biomarkers Prev. 1999;8:1117–1121.
22. Thoburn KK, German RR, Lewis M, *et al*. Case completeness and data accuracy in the Centers for Disease Control and Prevention's National Program of Cancer Registries. Cancer. 2007;109:1607–1616.
23. Wingo PA, Jamison PM, Hiatt RA, *et al*. Building the infrastructure for nationwide cancer surveillance and control—a comparison between the National Program of Cancer Registries (NPCR) and the Surveillance, Epidemiology, and End Results (SEER) Program (United States). Cancer Causes Control. 2003;14:175–193.
24. Havener L (Ed). Standards for cancer registries volume III: standards for completeness, quality, analysis, and management of data. Springfield, IL: North American Association of Central Cancer Registries; 2004.
25. National Program of Cancer Registries. Achievement of the USCS publication criteria by state and SEER metropolitan area cancer registries, 1999-2007. Accessed July 29, 2011 from: www.cdc.gov/cancer/npcr/uscs/data/00_data_quality.htm
26. National Cancer Institute. Surveillance, Epidemiology and End Results. Number of persons by race and Hispanic ethnicity for SEER participants (2000 Census data). Accessed August 6, 2010 from: www.seer.cancer.gov/registries/data.html#a2
27. National Cancer Institute. Surveillance, Epidemiology and End Results. U.S. population data, 1969–2007. Accessed August 6, 2010 from: www.seer.cancer.gov/popdata
28. Fritz A, Percy C, Jack A, *et al*. International Classification of Diseases for Oncology. 3rd edition. Geneva, Switzerland: World Health Organization; 2000.
29. Percy C, Van Holten V, Muir CM. International Classification of Diseases for Oncology. 2nd edition. Geneva, Switzerland: World Health Organization; 1990.
30. National Cancer Institute. Surveillance, Epidemiology and End Results. ICD conversion programs, ICD-O-2 to 3 and ICD-O-3 to 2. Accessed August 6, 2010 from: www.seer.cancer.gov/tools/conversion
31. National Cancer Institute. Surveillance, Epidemiology and End Results. 2000 U.S. standard population vs. standard million. Accessed August 6, 2010 from: www.seer.cancer.gov/stdpopulations/single_age.html
32. Tiwari RC, Clegg LX, Zou Z. Efficient interval estimation for age-adjusted cancer rates. Stat Methods Med Research. 2006;15:547–569.
33. National Cancer Institute. Surveillance, Epidemiology and End Results. SEER*Stat software. Accessed March 25, 2008 from: www.seer.cancer.gov/seerstat
34. Horn-Ross PL, McClure LA, Chang ET, *et al*. Papillary thyroid cancer incidence rates vary significantly by birthplace in Asian American women. Cancer Causes Control. 2011;22:479–485.
35. Aschebrook-Kilfoy B, Ward MH, Sabra MM, Devesa SS. Thyroid cancer incidence patterns in the United States by histologic type, 1992–2006. Thyroid. 2011;21:125–134.
36. Sprague BL, Andersen SW, Trentham-Dietz A. Thyroid cancer incidence and socioeconomic indicators of health care access. Cancer Causes Control. 2008;19:585–593.
37. Hedinger C, Williams ED, Sobin LH. The WHO histological classification of thyroid tumors: a commentary on the second edition. Cancer. 1989;63:908–911.
38. Verkooijen HM, Fioretta G, Pache JC, *et al*. Diagnostic changes as a reason for the increase in papillary thyroid cancer incidence in Geneva, Switzerland. Cancer Causes Control. 2003;14:13–17.
39. Ron E, Lubin JH, Shore RE, *et al*. Thyroid cancer after exposure to external radiation: a pooled analysis of seven studies. Radiat Res. 1995;141:259–277.
40. Moysich KB, Menezes RJ, Michalek AM. Chernobyl-related ionising radiation exposure and cancer risk: an epidemiological review. Lancet Oncol. 2002;3:269–279.
41. Cardis E, Kesminiene A, Ivanov V, *et al*. Risk of thyroid cancer after exposure to 131I in childhood. J Natl Cancer Inst. 2005;97:724–732.
42. Mettler FA, Thomadsen BR, Bhargavan M, *et al*. Medical radiation exposure in the U.S. in 2006: preliminary results. Health Phys. 2008;95:502–507.
43. Linet MS, Kim KP, Rajaraman P. Children's exposure to diagnostic medical radiation and cancer risk: epidemiologic and dosimetric considerations. Pediatr Radiol 2009;39(Suppl 1):S4–S26.
44. National Cancer Institute. Radiation risks and pediatric computed tomography (CT): a guide for health care providers; 2008. Accessed July 21, 2010 from: www.cancer.gov/cancertopics/causes/radiation-risks-pediatric-CT
45. Shah NB, Platt SL. ALARA: is there a cause for alarm? Reducing radiation risks from computed tomography scanning in children. Curr Opin Pediatr. 2008;20:243–247.
46. Memon A, Godward S, Williams D, *et al*. Dental x-rays and the risk of thyroid cancer: a case-control study. Acta Oncologica. 2010;49:447–453.
47. De Groef B, Decallonne BR, Van der Geyten S, *et al*. Perchlorate versus other environmental sodium/iodide symporter inhibitors: potential thyroid-related health effects. Eur J Endocrinol. 2006;155:17–25.
48. Diamanti-Kandarakis E, Bourguignon J, Guidice LC, *et al*. Endocrine-disrupting chemicals: an Endocrine Society scientific statement. Endocr Rev. 2009;30:293–342.
49. Kilfoy BA, Zheng T, Holford TR, *et al*. International patterns and trends in thyroid cancer incidence, 1973–2002. Cancer Causes Control. 2009;20:525–531.
50. Ward MH, Kilfoy BA, Weyer PJ, *et al*. Nitrate intake and the risk of thyroid cancer and thyroid disease. Epidemiology. 2010;21:389–395.
51. Patrick L. Thyroid disruption: mechanisms and clinical implications in human health. Altern Med Rev. 2009;14:326–346.
52. Jugan M, Levi Y, Blondeau J. Endocrine disruptors and thyroid hormone physiology. Biochem Pharmacol. 2010;79:939–947.
53. Kacsoh B. The Thyroid Gland. In: *Endocrine Physiology*. New York: McGraw-Hill; 2000; pp. 307–359.
54. Centers for Disease Control and Prevention. Fourth national report on human exposure to environmental chemicals.

National Center for Environmental Health, Division of Laboratory Sciences; 2009. Accessed July 22, 2010 from: www.cdc.gov/exposurereport
55. Schecter A, Pavuk M, Papke O, *et al*. Polybrominated diphenyl ethers (PBDEs) in U.S. mothers' milk. Environ Health Perspect. 2003;111:1723–1729.
56. La Vecchia C, Ron E, Franceschi S, *et al*. A pooled analysis of case-control studies of thyroid cancer. III. Oral contraceptives, menopausal replacement therapy and other female hormones. Cancer Causes Control. 1999;10:157–166.
57. Meinhold CL, Ron E, Schonfeld SJ, *et al*. Nonradiation risk factors for thyroid cancer in the US Radiologic Technologists Study. Am J Epidemiol. 2010;171:242–252.
58. La Vecchia C, Bosetti C. Oral contraceptives and neoplasms other than breast and female genital tract. Eur J Cancer Prev. 2009;18:407–411.
59. Golden SH, Robinson KA, Saldanha I, *et al*. Clinical review: prevalence and incidence of endocrine and metabolic disorders in the United States: a comprehensive review. J Clin Endocrinol Metab. 2009;94:1853–1878.
60. Lazarus JH. Thyroid Disease During Pregnancy. In: *Diseases of the Thyroid in Childhood and Adolescence*. Volume 11. Krassas GE, Rivkees SA, Kiess W (Eds). Basel, Switzerland: S. Karger AG; 2007; pp. 25–43.
61. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among U.S. adults, 1999–2008. JAMA. 2010;303:235–241.
62. Almquist M, Johansen D, Bjorge T, *et al*. Metabolic factors and risk of thyroid cancer in the Metabolic syndrome and Cancer project (Me-Can). Cancer Causes Control. 2011;22:743–751.
63. Wiggins CL, Espey DK, Wingo PA, *et al*. Cancer among American Indians and Alaska Natives in the United States, 1999–2004. Cancer. 2008;113(suppl 5):1142–1152.

Address correspondence to:
Dawn M. Holman, MPH, CPH
Epidemiology and Applied Research Branch
Division of Cancer Prevention and Control
Centers for Disease Control and Prevention
4770 Buford Hwy. MS-K55
Atlanta, GA 30341

E-mail: isc6@cdc.gov