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Authors
Lim, Hyeyeun
Devesa, Susan S
Sosa, Julie A
et al.

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Trends in thyroid cancer incidence and mortality in the United States, 1974–2013

Hyeyeun Lim, PhD[1], **Susan S. Devesa, PhD**[2], **Julie A. Sosa, MD**[3], **David Check, BS**[2], **Cari M. Kitahara, PhD**[1]

[1]Radiation Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD

[2]Biostatistics Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD

[3]Section of Endocrine Surgery, Department of Surgery, Duke University Medical Center #2945, Seeley Mudd Building #484, 10 Searle Center Drive, Durham, NC

Abstract

Importance: Thyroid cancer incidence has more than tripled in the United States over the last four decades, driven largely by increases in papillary thyroid cancer. It is unclear whether the rising incidence of papillary thyroid cancer has been related to thyroid cancer mortality trends.

Objective: To compare trends in thyroid cancer incidence and mortality by tumor characteristics at diagnosis.

Design, setting, and participants: Trends in thyroid cancer incidence and incidence-based mortality rates were evaluated using data from the Surveillance, Epidemiology, and End Results-9 cancer registry program.

Exposures: Tumor characteristics.

Main outcomes and measures: Log-linear regression was used to calculate annual percent changes in age-adjusted thyroid cancer incidence and incidence-based mortality rates by histologic type and Surveillance, Epidemiology, and End Results stage for cases diagnosed during 1974–2013.

Correspondence to: Cari M. Kitahara, PhD, MHS, 9609 Medical Center Drive, Rm 7E-536, Bethesda, MD 20892, kitaharac@mail.nih.gov, Phone: 240-276-7406.

Author Contributions:
Access to data: Drs. Lim and Kitahara had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study Concept and design: Lim, Kitahara
Acquisition, analysis, or interpretation of data: All authors
Drafting of the manuscript: Lim, Sosa, Kitahara
Critical revision of the manuscript for important intellectual content: All authors
Statistical analysis: Lim
Technical support: Devesa, Check
Study supervision: Kitahara

Conflict of Interest Disclosures: Hyeyeun Lim, Susan S. Devesa, David Check and Cari M. Kitahara declare no competing interests. Julie A. Sosa is on the Data Monitoring Committee of the Medullary Thyroid Cancer Consortium Registry, which is sponsored by Astra Zeneca, Eli Lilly, GlaxoSmithKline and Novo Nordisk.

Results: Among 77,276 patients (mean age at diagnosis, 48 [standard deviation=16] years; 58,213 [75%] women) diagnosed with thyroid cancer from 1974–2013, papillary thyroid cancer was the most common histologic type (64,625 cases), and 2,371 deaths from thyroid cancer occurred during 1994–2013. Thyroid cancer incidence increased, on average, 3.6% per year (95% confidence interval 3.2–3.9%) during 1974–2013 (from 4.56 per 100,000 person-years in 1974–77 to 14.42 per 100,000 person-years in 2010–13), primarily driven by increases in papillary thyroid cancer (annual percent change=4.4%, 95% confidence interval 4.0–4.7%). Papillary thyroid cancer incidence increased for all stages at diagnosis (4.6% per year for localized, 4.3% per year for regional, 2.4% per year for distant, 1.8% per year for unknown). During 1994–2013, incidence-based mortality increased 1.1% per year (95% confidence interval 0.6–1.6%) (from 0.40 per 100,000 person-years in 1994–97 to 0.46 per 100,000 person-years in 2010–13) overall and 2.9% per year (95% confidence interval 1.1–4.7%) for distant papillary thyroid cancer.

Conclusions and Relevance: Among patients in the United States diagnosed with thyroid cancer from 1974–2013, the overall incidence of thyroid cancer increased 3% annually, with increases in the incidence rate and thyroid cancer mortality rate for advanced-stage papillary thyroid cancer. These findings are consistent with a true increase in the occurrence of thyroid cancer in the United States.

Introduction

In the United States, thyroid cancer incidence rates have more than tripled between 1975 and 2013, with papillary thyroid cancer (PTC), the most common and least aggressive histologic type, accounting for most of the new cases[1]. Some investigators have suggested that over-diagnosis, or the increased ability to detect and diagnose small, indolent tumors that would never otherwise cause symptoms or require treatment, explains a substantial proportion of the increase[2–5].

However, there is growing evidence in support of a true increase in the occurrence of thyroid cancer. An analysis of Surveillance, Epidemiology and End Results (SEER) cancer registry data from 1980–2005 revealed substantial increases in the incidence of advanced-stage PTCs and PTCs >5 cm in diameter; these tumors are generally large enough to be detected via palpation or to cause symptoms[6]. The rates of increase for the largest (>5 cm) and the smallest PTCs (≤1 cm) were nearly equal among white women, a group considered to be particularly susceptible to over-diagnosis[6]. While thyroid cancer mortality rates are much lower relative to incidence, providing the impression of stability over time[2–5], thyroid cancer mortality rates have increased significantly since the late 1980s (0.7% per year, $P<0.001$)[1]. These trends are consistent with temporal changes in the prevalence of some risk factors, including obesity and non-current smoking[7].

As advanced-stage PTC is less amenable to treatment than localized PTC, the rising mortality rates may be a direct consequence of the trends in advanced-stage PTC. To address this question, the current analysis used SEER data during 1974–2013 to systematically compare thyroid cancer incidence and mortality trends by demographic and tumor characteristics at the time of diagnosis.

Methods

Data sources

Thyroid cancer cases diagnosed during 1974–2013 were ascertained from the SEER cancer incidence file maintained by the National Cancer Institute[8]. The file includes information from nine high-quality, population-based registries (SEER-9: Connecticut, Iowa, New Mexico, Utah, Hawaii, Detroit, San Francisco-Oakland, Atlanta, and Seattle-Puget Sound) that include approximately 10% of the U.S. population. Demographic and cancer diagnosis information was available for each case. Data on nationwide and SEER-9 thyroid cancer deaths were derived from information recorded in death certificates and ascertained from the National Center for Health Statistics[9].

The incidence-based mortality file uses cancer registry information from the SEER-9 cancer incidence file to link characteristics of the cancer at diagnosis with death certificate information[10,11]. Thus, unlike traditional mortality rates, incidence-based mortality rates can be examined according to variables recorded at diagnosis (e.g., histology, stage, tumor size). The incidence-based mortality analysis was restricted to deaths during 1994–2013 and diagnoses during 1974–2013 to ensure maximum data for those deaths and to prevent underestimation of the incidence-based mortality rates in the earliest years.

Demographic characteristics

Demographic characteristics of interest for this analysis included gender, race, and age at diagnosis. This information was originally abstracted from medical records and submitted to regional or state cancer registries. Information on age at thyroid cancer death was abstracted from death certificates.

Tumor characteristics

Thyroid cancer cases (International Classification of Diseases for Oncology version 3 topography code C73) were classified according to histologic type[12]: PTC (histologic codes 8050, 8260, 8340–8344, 8350, 8450–8460), follicular thyroid cancer (FTC, 8290, 8330–8335), medullary thyroid cancer (MTC, 8345,8510–8513), anaplastic thyroid cancer (ATC, 8020–8035), others (including unspecified, poorly specified [e.g., insular], and others).

SEER Historic Stage A was used to classify cases according to stage at diagnosis: localized (limited to the thyroid gland), regional (tumor extension beyond the limits of the thyroid gland or spread by more than one lymphatic or vascular supply route), distant (extracervical metastasis), and unknown stage[13]. Cases diagnosed since 2004 additionally were classified as Stage I-IV (or unknown) according to the American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) Tumor-Node-Metastasis (TNM) staging system, 6th edition, which accounts for age at diagnosis (<45 and ≥45 years, for PTC and FTC), tumor size (T stage), extent of spread to the regional lymph nodes (N stage), and presence or absence of distant metastases (M stage)[14]. Although AJCC/TNM stage information was not available for the entire study period, it is the staging system most used for thyroid cancer in clinical practice and is more readily interpretable than SEER stage.

Tumor size has been recorded in SEER since 1983 using three different schemes: Extent of Disease-4 codes for 1983–1987, Extent of Disease-10 codes for 1988–2003, and Collaborative Staging codes for 2004–2013. These codes were combined to categorize cases diagnosed during 1983–2013 by tumor size[15].

Data analysis

Only microscopically-confirmed cases and the first matching record were selected, and cases identified only from autopsy records or death certificates were excluded. Incidence and mortality rates were calculated using SEER*Stat version 8.3.2[16]. All rates were age-adjusted to the 2000 U.S. standard population and expressed per 100,000 person–years. Incidence-based mortality rates were calculated as number of thyroid cancer deaths among cases diagnosed in the SEER-9 registries over person-time at risk among individuals in the SEER areas. Standardized dimensions were used for the y- and x-axes, in which a slope of 10 degrees represents a change of 1% per year[17]. Rates for thyroid cancers with missing or unknown histology, stage, or size were calculated and plotted separately from the known values. Rate differences were calculated to evaluate the degree to which reductions or increases in rates for thyroid cancers with unknown stage or size may have affected trends for thyroid cancers with known values. The National Cancer Institute’s Joinpoint Regression Analysis program, version 4.2.0[18], calculated annual percentage changes (APCs) and 95% confidence intervals (CIs) to quantify trends in incidence and mortality, overall and by demographic and tumor characteristics, using T-tests to determine whether APCs were statistically significantly different from zero. The program also selected the best-fitting log-linear regression model to identify calendar years (i.e., the “joinpoints”) when APCs changed significantly, allowing for the minimum number of “joinpoints” necessary to fit the data.[18] Statistical significance was assessed at the $P<0.05$ alpha level, and all hypotheses were two-sided.

Results

Of the 79,409 thyroid cancer cases diagnosed among residents of the SEER-9 areas during 1974–2013, 77,276 (97%) met the case definition and were included in the incidence analysis (Table 1). Women (75%) and whites (82%) comprised the majority of the cases. Mean age at diagnosis was 48 (standard deviation=16) years. The most common histologic types were PTC (84%) and FTC (11%). Of the eligible cases, 2,371 died of thyroid cancer during 1994–2013 and were included in the incidence-based mortality analysis. Of the deaths, 57% occurred in women and 81% in whites. Compared with all cases, patients who died of thyroid cancer were more likely to have been diagnosed at older ages, with non-PTC histologies, and advanced-stage and/or larger tumors. Among those who died of thyroid cancer, the median time between thyroid cancer diagnosis and death was 25 months; 19% survived >10 years after diagnosis. Among PTC patients who died of thyroid cancer, 27% survived >10 years after diagnosis.

Of the 77,276 cases occurring during 1974–2013, 10% were diagnosed in years prior to the availability of tumor size data starting in 1983, and 51% were diagnosed prior to the availability of AJCC/TNM stage information starting in 2004 (Table 1). Of the 2,371 incidence-based mortality deaths occurring during 1994–2013, 3% had been diagnosed in years prior to the availability of tumor size data and 66% were diagnosed prior to the availability of AJCC/TNM stage information. During the years in which specific tumor characteristics were reported to the registries, SEER stage (1974–2013) was unknown for 2% of cases and 5% of deaths, tumor size (1983–2013) was unknown for 13% of cases and 31% of deaths, and AJCNN/TNM stage (2004–2013) was unknown for 5% of cases and 6% of deaths.

A comparison of the agreement between SEER Historic Stage A, tumor size, and AJCC/TNM stage among PTC cases diagnosed between 2004 and 2013 by age (<45 and ≥45 years) is shown in eTable 1. In general, more advanced stage was associated with larger tumor size. There was greater agreement of SEER stage with size and AJCC/TNM stage for patients aged ≥45 years compared with younger patients, reflecting the differences in AJCC/TNM staging guidelines for PTC patients diagnosed before and after age 45 [14].

Trends in thyroid cancer incidence by demographic and tumor characteristics are described in Table 2, with joinpoints denoted as Trends 1–5. Trends by selected tumor characteristics are shown graphically in Figures 1a-1c. Thyroid cancer incidence rates increased over the study period (from 4.56 [95% CI 4.40–4.73] per 100,000 in 1974–77 to 14.42 [95% CI 14.20–14.64] per 100,000 in 2010–13), rising 3.6% (95% CI 3.2–3.9%) per year, on average. Rates increased 6.7% (95% CI 6.1–7.2%) per year during 1997–2009, but did not increase during 2009–2013 (APC=1.8%, 95% CI −0.7–4.4%). Thyroid cancer incidence rates increased for all sex, race, and age groups. Significant increases were observed for PTC (APC=4.4%, 95% CI 4.0–4.7%), FTC (APC=0.6%, 95% CI 0.2–0.8%), and MTC (APC=0.7%, 95% CI 0.2–1.1%). PTC incidence increased significantly for every stage and tumor size category. During 2009–2013, incidence rates did not increase significantly for overall, localized, Stage I, or small (≤2 cm) PTCs, while there was no evidence of a reduction in the increase for regional, distant, or large PTCs.

Thyroid cancer incidence-based mortality rates were underestimated in the earliest calendar years, but consistent with observed nationwide and SEER-9 thyroid cancer mortality rates during 1994–2013 (Figure 2a, eTable 2). Thyroid cancer incidence-based mortality increased, on average, 1.1% (95% CI 0.6–1.6%) annually during 1994–2013 (Table 3; Figure 2a), from 0.40 (95% CI 0.36–0.44) per 100,000 in 1994–97 to 0.46 (95% CI 0.43–0.50) per 100,000 in 2010–13. Positive APCs were observed for most demographic subgroups and statistically significant for females, whites, blacks, and patients diagnosed after age 79. By histologic type, the annual increase in incidence-based mortality rates was restricted to patients diagnosed with PTC (1.7%, 95% CI 0.6–2.9%). Positive APCs were observed for PTCs of all known stages at diagnosis, but were statistically significant only for patients with distant (2.9%, 95% CI 1.1–4.7%) and/or Stage IV (APC=12.9%, 95% CI 7.2–19.0%) disease (Table 3; Figure 2b). Positive APCs occurred for PTCs of all known sizes, with significant increases for tumors ≤2 and >2-≤4 cm (Table 3; Figure 2c).

Rate differences were calculated for PTCs by known/unknown values of SEER stage and tumor size (eTables 3 and 4). The incidence rate for unstaged PTC increased by 0.07 (95% CI 0.04–0.10) from 1974–77 to 2010–13, indicating that the observed increase in PTC with known SEER stage was underestimated by this amount. PTC with unknown tumor size declined by 0.57 (95% CI 0.49–0.65) from 1994–97 to 2010–13, which may have overestimated the observed increase in PTC with known tumor size by this amount; however, apart from PTCs >4 cm, the observed increases for PTCs with known tumor sizes were much larger. The unstaged PTC mortality rate declined by −0.01 (95% CI [−0.01–0.01]) from 1994–97 to 2010–13, indicating that the increase in mortality for PTCs with known SEER stage was overestimated by this amount. The mortality rate for PTCs with unknown tumor size decreased by 0.02 (95% CI 0.00–0.04) since 1998–2001, which may have overestimated mortality rates for PTC with known tumor size by this amount.

The annual numbers of cases or deaths and incidence and incidence-based mortality rates used in this analysis are provided in eTables 5-16.

Discussion

To our knowledge, the current study is the first to describe U.S. trends in thyroid cancer mortality by demographic and tumor characteristics at diagnosis and to systematically compare trends in thyroid cancer incidence and mortality rates by these characteristics. The main finding from this study was the significant increase in thyroid cancer incidence-based mortality from 1994 to 2013 (about 1.1% per year, on average) for thyroid cancer patients overall and those who were diagnosed with advanced-stage PTC (2.9% per year). This finding appears to be associated with the increasing incidence of advanced-stage PTC (3.5% per year since 1981).

The results of this study challenge the prevailing notion that all of the increase in PTC incidence in the United States is related to over-diagnosis[2,4,19], resulting from the introduction and increasing widespread use of diagnostic ultrasound and other imaging modalities and fine-needle aspiration biopsies that have allowed for incidental detection and diagnosis of localized and/or small (<2 cm) cancers that are mostly indolent[20]. Such changes could account for the rapid increases in the incidence rates for localized and/or small PTCs, which have been previously observed[2,4,6,19,21]. Likewise, the deceleration in rates for localized, but not advanced, PTC incidence rates since 2009, as observed previously[19,21], may be explained by less aggressive diagnostic work-up of small thyroid tumors in recent years due to a rising awareness of the problems associated with over-treatment of low-risk thyroid cancers[15,19,22]. However, the significant, albeit less rapid, increase in advanced-stage and larger PTC incidence rates and increasing thyroid cancer mortality rates among patients diagnosed with advanced-stage PTC is incompatible with the notion that over-diagnosis is solely responsible for the changing trends in PTC incidence. Thus, trends in PTC incidence may be explained by two underlying processes, the dominant one being over-diagnosis, and the other being a small but actual increase in PTC incidence, possibly resulting from changes in exposure to environmental risk factors[7].

Additional epidemiologic research is needed to identify the specific environmental factors that have contributed to increasing rates of PTC, namely those with greater aggressive potential. Ionizing radiation exposure in childhood is the most established risk factor for PTC[23], and exposure has increased in the U.S. general population in recent decades, due primarily to more widespread use of diagnostic medical exams[24]. However, studies of changes in radiation-related somatic mutations have shown declines in the proportion of PTCs with radiation signatures, such as *RET/PTC* rearrangements, over time, whereas point mutations, such as *BRAF* or *RAS* that are more likely to have a non-radiation etiology, have increased[25–28]. There is growing evidence suggesting that changes in obesity and smoking prevalence have contributed to rising thyroid cancer rates[7]. Paralleling trends in thyroid cancer incidence, obesity prevalence has increased threefold among U.S. adults between 1960 and 2012, with the fastest rate of increase between 1980 and 2010[29]. In contrast, the prevalence of daily cigarette smoking has significantly decreased in the United States since 1980[30]. Epidemiologic studies have consistently found positive associations between excess adiposity in childhood and adulthood and subsequent risk of thyroid cancer, including PTC[31,32], while current smoking consistently has been associated with a 30–40% reduction in thyroid cancer risk, independent of obesity and other risk factors[33]. Obesity and smoking could influence thyroid cancer development via insulin resistance, thyroid hormone, and estrogen-related pathways[34,35]. Together, these factors have been estimated to be related to >40% of all new cases of thyroid cancer annually in the United States [7]. Endocrine-disrupting chemicals (e.g., pesticides, bisphenol A) also have been suspected to contribute to thyroid cancer incidence trends through their effects on thyroid hormone metabolism[36]. However, evidence in support of a causal association between environmental chemicals and thyroid cancer risk is currently lacking, largely due to the challenges in studying exposures that are ubiquitous and for which long-term exposure is extremely difficult to measure accurately.

The increasing mortality rates among patients with advanced-stage PTC suggest that for patients with these high-risk tumors, there should be renewed focus on aggressive transdisciplinary management that includes surgery, adjuvant radioactive iodine, and, when indicated for the 5–10% of patients who develop progressive disease, systemic therapy. While there is continued debate about the appropriate extent of surgery for low-risk tumors, total thyroidectomy and adjuvant radioactive iodine are indicated for high-risk disease[15]. Thorough preoperative imaging should be used to evaluate the neck for nodal metastases to inform whether simultaneous lymphadenectomy is necessary, and prophylactic central neck dissection should be considered for large and advanced tumors. Sorafenib and lenvatinib are approved for the management of advanced, iodine-resistant differentiated thyroid cancer including PTC, but unfortunately neither has been shown yet to afford a survival advantage, likely due to the indolent natural history of the disease[37,38]. Clinical trials to optimize the development and use of novel systemic therapies are necessary.

This study has several important limitations. Due to the descriptive nature of this study, it is only possible to speculate about potential explanations for the observed thyroid cancer trends. Individual-level environmental exposures and lifestyle-related factors were not captured by registries, nor were methods of thyroid cancer detection. While changes in mortality and incidence-based mortality rates capture secular trends in detection, diagnosis, and case ascertainment, as well as treatment and associated survival, the current study did not evaluate the influence of treatment on these trends. Analyses relying on tumor size and AJCC/TNM stage data were restricted to the years in which the information was reported to the registries. APC estimates for incidence-based mortality by tumor size and AJCC/TNM stage may be artificially inflated as this information was only available for cases diagnosed during 1983–2013 and 2004–2013, respectively, leaving a shorter latency period between diagnosis and death; however, the results generally agree with estimates by SEER stage. The results of an analysis evaluating the effect of unknown stage and size data during the study period suggest that the increasing incidence rates of PTC with unknown SEER stage information underestimated, rather than overestimated, the true increase in PTC incidence for known SEER stages. Unknown SEER stage data could only explain, at most, about one-third of the observed increase in mortality due to advanced-stage PTC. As specimens have been cut more finely and smaller tumors that are incidental findings have become better documented, the reduction in unknown size data over time most likely overestimated the observed trends for the smallest, rather than largest, PTCs. Finally, some results were based on small numbers of cases or deaths. It will be important to continue monitoring thyroid cancer incidence and mortality rates over time to see if the observed trends persist.

Conclusion

Among U.S. patients diagnosed with thyroid cancer from 1974–2013, the overall incidence of thyroid cancer increased 3% annually, with increases in the incidence rate and thyroid cancer mortality rate for advanced-stage PTC. These findings are consistent with a true increase in the occurrence of thyroid cancer in the United States.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Howlader N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Review, 1975–2013, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2013/, based on November 2015 SEER data submission, posted to the SEER web site, 4 2016. Accessed June 1, 2016.
2. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973–2002. JAMA 2006;295(18):2164–2167. [PubMed: 16684987]
3. Kent WD, Hall SF, Isotalo PA, Houlden RL, George RL, Groome PA. Increased incidence of differentiated thyroid carcinoma and detection of subclinical disease. CMAJ 2007;177(11):1357–1361. [PubMed: 18025426]
4. Davies L, Welch HG. Current thyroid cancer trends in the United States. JAMA Otolaryngol Head Neck Surg 2014;140(4):317–322. [PubMed: 24557566]
5. Vaccarella S, Franceschi S, Bray F, Wild CP, Plummer M, Dal Maso L. Worldwide Thyroid-Cancer Epidemic? The Increasing Impact of Overdiagnosis. N Engl J Med 2016;375(7):614–617. [PubMed: 27532827]
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(3):784–791. [PubMed: 19240234]

7. Kitahara CM, Sosa JA. The changing incidence of thyroid cancer. Nat Rev Endocrinol 2016;12(11):646–653. [PubMed: 27418023]
8. Surveillance Epidemiology and End Results (SEER) Program (www.seer.cancer.gov). SEER*Stat Database: Incidence - SEER 9 Regs Research Data, Nov 2015 Sub (1973–2013) <Katrina/Rita Population Adjustment> - Linked To County Attributes - Total U.S., 1969–2014 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released 4 2016, based on the November 2015 submission.
9. Surveillance Epidemiology and End Results (SEER) Program (www.seer.cancer.gov). SEER*Stat Database: Mortality - All COD, Aggregated With State, Total U.S. (1969–2013 <Katrina/Rita Population Adjustment>, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released 4 2016. Underlying mortality data provided by NCHS (www.cdc.gov/nchs).
10. Chu KC, Miller BA, Feuer EJ, Hankey BF. A method for partitioning cancer mortality trends by factors associated with diagnosis: An application to female breat cancer. J Clin Epidemiol 1994;47(12):1451–1461. [PubMed: 7730854]
11. Surveillance Epidemiology and End Results (SEER) Program (www.seer.cancer.gov). SEER*Stat Database: Incidence-Based Mortality - SEER 9 Regs Research Data, Nov 2015 Sub (1973–2013) <Katrina/Rita Population Adjustment> - Linked To County Attributes - Total U.S., 1969–2014 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released 4 2016, based on the November 2015 submission.
12. Forman D, Bray F, Brewster DH, et al., eds. Cancer incidence in five contintents, volume X [electronic version]. Lyon, France: International Agency for Research on Cancer;2013. http://ci5.iarc.fr. Accessed June 1, 2016.
13. Young JL RS Jr, Ries LAG, Fritz AG, Hurlbut AA SEER Summary Staging Manual - 2000: Codes and Coding Instructions, National Cancer Institute, NIH Pub. No. 01–4969, Bethesda, MD, 2001.
14. Adjusted AJCC stage 6th edition. Surveillance Epidemiology and End Results Program; http://seer.cancer.gov/seerstat/variables/seer/ajcc-stage/6th/.Accessed August 1, 2016.
15. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid 2016;26(1):1–133. [PubMed: 26462967]
16. Surveillance, Epidemiology, and End Results (SEER) Program. SEER*Stat Software 2016; https://seer.cancer.gov/seerstat/. Accessed April 30, 2016.
17. Devesa SS, Donaldson J, Fears T. Graphical presentation of trends in rates. Am J Epidemiol 1995;141(4):300–304. [PubMed: 7840107]
18. Surveillance, Epidemiology, and End Results (SEER) Program. Joinpoint Trend Analysis Software 2016; https://surveillance.cancer.gov/joinpoint/, 2016. Accessed August 1, 2016.
19. Morris LG, Tuttle RM, Davies L. Changing Trends in the Incidence of Thyroid Cancer in the United States. JAMA Otolaryngol Head Neck Surg 2016;142(7):709–711. [PubMed: 27078686]
20. Sosa JA, Hanna JW, Robinson KA, Lanman RB. Increases in thyroid nodule fine-needle aspirations, operations, and diagnoses of thyroid cancer in the United States. Surgery 2013;154(6):1420–1427. [PubMed: 24094448]
21. Mao Y, Xing M. Recent incidences and differential trends of thyroid cancer in the United States. Endocr Relat Cancer 2016;23(4):313–322. [PubMed: 26917552]
22. Kim BW, Yousman W, Wong WX, Cheng C, McAninch EA. Less is More: Comparing the 2015 and 2009 American Thyroid Association Guidelines for Thyroid Nodules and Cancer. Thyroid 2016;26(6):759–764. [PubMed: 27141822]
23. Dal Maso L, Bosetti C, La Vecchia C, Franceschi S. Risk factors for thyroid cancer: an epidemiological review focused on nutritional factors. Cancer Causes Control 2009;20(1):75–86. [PubMed: 18766448]
24. Fazel R, Krumholz HM, Wang Y, et al. Exposure to low-dose ionizing radiation from medical imaging procedures. N Engl J Med 2009;361(9):849–857. [PubMed: 19710483]
25. Romei C, Fugazzola L, Puxeddu E, et al. Modifications in the papillary thyroid cancer gene profile over the last 15 years. J Clin Endocrinol Metab 2012;97(9):E1758–E1765. [PubMed: 22745248]

26. Mathur A, Moses W, Rahbari R, et al. Higher rate of BRAF mutation in papillary thyroid cancer over time. Cancer 2011;117(19):4390–4395. [PubMed: 21412762]
27. Jung CK, Little MP, Lubin JH, et al. The increase in thyroid cancer incidence during the last four decades is accompanied by a high frequency of BRAF mutations and a sharp increase in RAS mutations. J Clin Endocrinol Metab 2013;99(2):E276–E285. [PubMed: 24248188]
28. Kowalska A, Walczyk A, Kowalik A, et al. Increase in Papillary Thyroid Cancer Incidence Is Accompanied by Changes in the Frequency of the BRAFV600E Mutation: A Single-Institution Study. Thyroid 2016;26(4):543–551. [PubMed: 26889698]
29. Centers for Disease Control and Prevention. Prevalence of Overweight, Obesity, and Extreme Obesity Among Adults: United States, 1960–1962 Through 2011–2012 http://www.cdc.gov/nchs/data/hestat/obesity_adult_11_12/obesity_adult_11_12.htm. Accessed August 1, 2016.
30. Ng M, Freeman MK, Fleming TD, et al. Smoking prevalence and cigarette consumption in 187 countries, 1980–2012. JAMA 2014;311(2):183–192. [PubMed: 24399557]
31. Kitahara CM, McCullough ML, Franceschi S, et al. Anthropometric Factors and Thyroid Cancer Risk by Histological Subtype: Pooled Analysis of 22 Prospective Studies. Thyroid 2016;26(2):306–318. [PubMed: 26756356]
32. Kitahara CM, Gamborg M, de González AB, Sørensen TI, Baker JL. Childhood height and body mass index were associated with risk of adult thyroid cancer in a large cohort study. Cancer Res 2014;74(1):235–242. [PubMed: 24247722]
33. Kitahara CM, Linet MS, Freeman LEB, et al. Cigarette smoking, alcohol intake, and thyroid cancer risk: a pooled analysis of five prospective studies in the United States. Cancer Causes Control 2012;23(10):1615–1624. [PubMed: 22843022]
34. Almquist M, Johansen D, Björge T, et al. Metabolic factors and risk of thyroid cancer in the Metabolic syndrome and Cancer project (Me-Can). Cancer Causes Control 2011;22(5):743–751. [PubMed: 21380729]
35. Wiersinga WM. Smoking and thyroid. Clin Endocrinol (Oxf) 2013;79(2):145–151. [PubMed: 23581474]
36. Pellegriti G, Frasca F, Regalbuto C, Squatrito S, Vigneri R. Worldwide increasing incidence of thyroid cancer: update on epidemiology and risk factors. J Cancer Epidemiol 2013;2013.
37. Schlumberger M, Tahara M, Wirth LJ, et al. Lenvatinib versus placebo in radioiodine-refractory thyroid cancer. N Engl J Med 2015;372(7):621–630. [PubMed: 25671254]
38. Brose MS, Nutting CM, Jarzab B, et al. Sorafenib in radioactive iodine-refractory, locally advanced or metastatic differentiated thyroid cancer: a randomised, double-blind, phase 3 trial. Lancet 2014;384(9940):319–328. [PubMed: 24768112]

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KEY POINTS SECTION

Question:

What have been the trends in U.S. thyroid cancer incidence and mortality, and have they differed by tumor characteristics at diagnosis?

Findings:

In this analysis of 77,276 thyroid cancer patients diagnosed during 1974–2013 and 2,371 thyroid cancer deaths during 1994–2013, average annual increases in incidence and mortality rates, respectively, were 3.6% and 1.1% overall and 2.4% and 2.9% for patients diagnosed with advanced-stage papillary thyroid cancer.

Meaning:

Thyroid cancer incidence and mortality rates have increased for patients diagnosed with advanced-stage papillary thyroid cancer in the United States since 1974, suggesting a true increase in the occurrence of thyroid cancer.

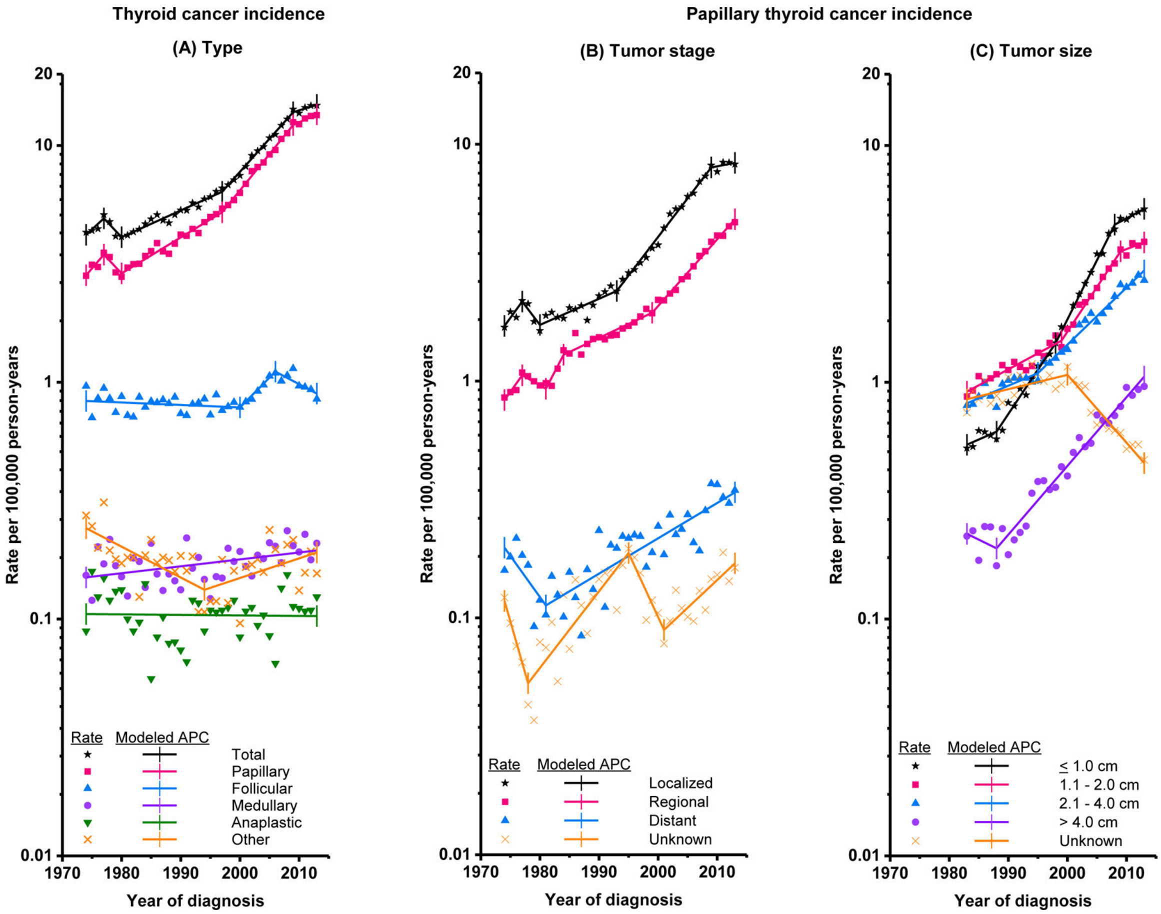

Figure 1.

Trends in annual thyroid cancer incidence rates (cases per 100,000 person-years). (A) Thyroid cancer incidence, overall and by histologic type (1974–2013) (B) Papillary thyroid cancer incidence by SEER Historic Stage A at diagnosis (1974–2013) (C) Papillary thyroid cancer incidence by tumor size at diagnosis (1983–2013). Tumor size was not recorded for cases diagnosed 1974–1982. Rates are age-adjusted to the 2000 U.S. standard population. Each line represents the annual percent change (APC).

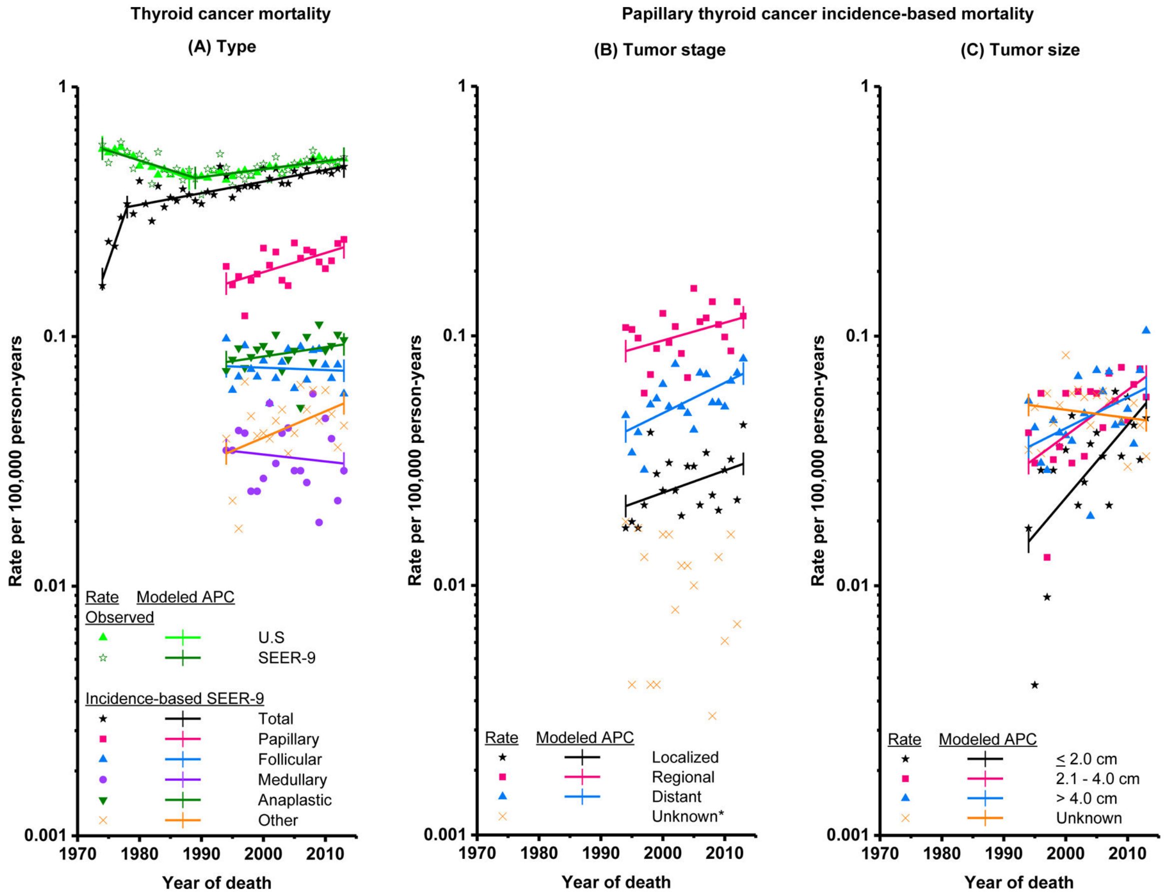

Figure 2.

Trends in annual thyroid cancer mortality rates (deaths per 100,000 person-years). (A) Observed total U.S. thyroid cancer mortality (1974–2013), observed SEER-9 thyroid cancer mortality (1974–2013), thyroid cancer incidence–based mortality, overall (1974–2013) and by histologic type (1994–2013), based on cases diagnosed during 1974–2013 (B) Thyroid cancer incidence-based mortality by SEER Historic Stage A at diagnosis (1994–2013), based on papillary thyroid cancer cases diagnosed during 1974–2013 C) Thyroid cancer incidence-based mortality by tumor size at diagnosis (1994–2013), based on papillary thyroid cancer cases diagnosed during 1983–2013. Tumor size was not recorded for cases diagnosed 1974–1982. Rates are age-adjusted to the 2000 U.S. standard population. Each line represents the annual percent change (APC). *APCs were not calculated if 0 deaths occurred in one or more years.

Table 1.

Thyroid cancer incidence (1974–2013) and incidence-based mortality (1994–2013): the SEER-9 Registry Database

	Incidence								Incidence based mortality							
Characteristic at diagnosis	**Thyroid cancer**				**Papillary thyroid cancer**				**Thyroid cancer**				**Papillary thyroid cancer**			
	No. of cases [a]	**%**	**Rate** [b]	**95% CI**	**No. of cases** [a]	**%**	**Rate** [b]	**95% CI**	**No. of deaths** [c]	**%**	**Rate** [b]	**95% CI**	**No. of deaths** [c]	**%**	**Rate** [b]	**95% CI**
Overall	77,276	100	7.98	7.93, 8.04	64,625	100.0	6.66	6.61, 6.71	2,371	100	0.44	0.42, 0.46	1063	100	0.20	0.19, 0.21
Gender																
Male	19,063	24.7	4.20	4.14, 4.26	15,074	23.3	3.28	3.23, 3.33	1,017	42.9	0.44	0.41, 0.47	464	43.7	0.20	0.18, 0.22
Female	58,213	75.3	11.63	11.53, 11.72	49,551	76.7	9.92	9.83, 10.01	1,354	57.1	0.44	0.41, 0.46	599	56.3	0.19	0.18, 0.21
Race																
White	63,479	82.1	8.18	8.12, 8.24	53,219	82.4	6.85	6.80, 6.91	1,914	80.7	0.43	0.41, 0.45	841	79.1	0.19	0.18, 0.20
Black	4,582	5.9	4.88	4.73, 5.03	3,473	5.4	3.64	3.52, 3.77	143	6	0.32	0.27, 0.38	48	4.5	0.11	0.08, 0.15
Others [d]	8,442	10.9	9.14	8.95, 9.34	7,305	11.3	7.85	7.66, 8.03	312	13.2	0.59	0.52, 0.66	173	16.3	0.33	0.28, 0.38
Age (years)																
<20	1,794	2.3	0.62	0.59, 0.65	1,512	2.30	0.52	0.49, 0.55	-	-	-	-	-	-	-	-
20–39	23,877	30.9	8.00	7.89, 8.09	21,106	32.7	7.06	6.97, 7.16	102	4.3	0.02	0.02, 0.02	47	4.4	0.01	0.01, 0.01
40–59	32,188	41.7	13.28	13.14, 13.43	27,727	42.9	11.45	11.32, 11.59	631	26.6	0.11	0.10, 0.12	314	29.5	0.06	0.05, 0.06
60–79	16,877	21.8	13.15	12.95, 13.35	12,825	19.8	9.92	9.75, 10.10	1,148	48.4	0.22	0.21, 0.24	515	48.4	0.10	0.09, 0.11
≥80	2,540	3.3	8.81	8.47, 9.16	1,455	2.3	5.05	4.79, 5.31	479	20.2	0.09	0.08, 0.10	184	17.3	0.03	0.03, 0.04
Histologic type																
Papillary	64,625	83.6	6.66	6.61, 6.71					1,063	44.8	0.20	0.19, 0.21				
Follicular	8,359	10.8	0.87	0.85, 0.89					404	17	0.08	0.07, 0.08				
Medullary	1,685	2.2	0.18	0.17, 0.18					189	8	0.04	0.03, 0.04				

Characteristic at diagnosis	Incidence								Incidence based mortality							
	Thyroid cancer				Papillary thyroid cancer				Thyroid cancer				Papillary thyroid cancer			
	No. of cases[a]	%	Rate[b]	95% CI	No. of cases[a]	%	Rate[b]	95% CI	No. of deaths[c]	%	Rate[b]	95% CI	No. of deaths[c]	%	Rate[b]	95% CI
Anaplastic	975	1.3	0.11	0.10, 0.11					471	19.9	0.09	0.08, 0.10				
Other[e]	1,632	2.1	0.17	0.17, 0.18					244	10.3	0.05	0.04, 0.05				
SEER Historic Stage A																
Localized	45,919	59.4	4.75	4.71, 4.79	39,971	61.9	4.13	4.09, 4.17	280	11.8	0.05	0.05, 0.06	143	13.5	0.03	0.02, 0.03
Regional	25,835	33.4	2.66	2.62, 2.69	21,435	33.2	2.20	2.17, 2.23	1,045	44.1	0.19	0.18, 0.21	566	53.2	0.11	0.10, 0.11
Distant	3,658	4.7	0.39	0.37, 0.40	2,045	3.2	0.21	0.20, 0.22	922	38.9	0.17	0.16, 0.18	308	29.0	0.06	0.05, 0.06
Unknown	1,864	2.4	0.19	0.18, 0.20	1,174	1.8	0.12	0.11, 0.13	124	5.2	0.02	0.02, 0.03	46	4.3	0.01	0.01, 0.01
AJCC/TNM stage[f]																
Stage I	25,580	67.4	8.91	8.80, 9.02	23,974	71.5	8.34	8.24, 8.45	17	0.7	0.01	0.003, 0.01	-	-	-	-
Stage II	2,870	7.6	0.92	0.89, 0.96	2,091	6.20	0.67	0.64, 0.70	-	-	-	-	-	-	-	-
Stage III	4,562	12.0	1.46	1.42, 1.50	3,821	11.4	1.22	1.18, 1.25	45	1.9	0.02	0.01, 0.02	24	8.7	0.01	0.01, 0.01
Stage IV	3,045	8.0	1.01	0.97, 1.04	2,111	6.3	0.69	0.66, 0.72	680	28.7	0.23	0.21, 0.25	218	77.6	0.07	0.06, 0.08
Unknown	1,881	5.0	0.62	0.59, 0.65	1,541	4.6	0.51	0.48, 0.53	49	68.1	0.02	0.01, 0.02	19	6.9	0.01	0.00, 0.01
Tumor size (cm)[g]																
≤1	19,943	28.6	2.50	2.47, 2.54	19,257	32.5	2.42	2.38, 2.45	71	3.1	0.01	0.01, 0.02	53	5.2	0.01	0.01, 0.01
>1-≤2	18,113	26.0	2.26	2.23, 2.29	16,477	27.8	2.05	2.02, 2.09	188	8.2	0.04	0.03, 0.04	130	12.9	0.02	0.02, 0.03
>2-≤4	16,031	23.0	2.00	1.97, 2.03	12,772	21.6	1.59	1.56, 1.61	483	21.1	0.09	0.08, 0.10	274	27.2	0.05	0.05, 0.06
>4	6,713	9.6	0.85	0.83, 0.87	3,973	6.7	0.50	0.48, 0.51	852	37.1	0.16	0.15, 0.17	278	27.5	0.05	0.05, 0.06

	Incidence								Incidence based mortality							
Characteristic at diagnosis	Thyroid cancer				Papillary thyroid cancer				Thyroid cancer				Papillary thyroid cancer			
	No. of cases [a]	%	Rate [b]	95% CI	No. of cases [a]	%	Rate [b]	95% CI	No. of deaths [c]	%	Rate [b]	95% CI	No. of deaths [c]	%	Rate [b]	95% CI
Unknown	8,879	13.0	1.12	1.10, 1.14	6,721	11.4	0.84	0.82, 0.86	700	30.5	0.13	0.12, 0.14	276	27.3	0.05	0.05, 0.06

Abbreviations: AJCC/TNM, American Joint Committee on Cancer/Tumor-Node-Metastasis; APC, annual percent change; CI, confidence interval

- Statistic suppressed due to <16 cases/deaths in the time interval

[a] Cases included first primary tumors that matched the selection criteria, were microscopically confirmed, were not identified only from autopsy records or death certificates.

[b] Rates were calculated as number of cases or deaths per 100,000 person-years and age-adjusted to the 2000 U.S. standard population.

[c] Based on cases diagnosed during 1974–2013.

[d] Includes American Indian/Alaskan Native and Asian/Pacific Islander.

[e] Includes other specified, poorly differentiated, and other types.

[f] Based on cases diagnosed during 2004–2013 and deaths during 2004–2013.

[g] Based on cases diagnosed during 1983–2013 and deaths during 1994–2013.

Table 2.

Trends in thyroid cancer incidence rates [a] (1974–2013): the SEER-9 Registry Database

	Overall		Trend 1			Trend 2			Trend 3			Trend 4			Trend 5		
Characteristic at diagnosis	**APC (95% CI)**	***P* value**	**Year**	**APC (95% CI)**	***P* value**	**Year**	**APC (95% CI)**	***P* value**	**Year**	**APC (95% CI)**	***P* value**	**Year**	**APC (95% CI)**	***P* value**	**Year**	**APC (95% CI)**	***P* value**
Total	3.6 (3.2, 3.9)	<0.001	1974–77	5.5 (1.4, 9.8)	0.01	1977–80	−5.9 (−13.1, 1.9)	0.10	1980–97	2.6 (2.3, 2.9)	<0.001	1997–09	6.7 (6.1, 7.2)	<0.001	2009–13	1.8 (−0.7, 4.4)	0.20
Gender																	
Male	3.1 (2.7, 3.5)	<0.001	1974–80	−2.9 (−5.9, 0.2)	0.07	1980–98	2.5 (1.8, 3.2)	<0.001	1998–13	5.6 (4.7, 6.4)	<0.001						
Female	3.7 (3.3, 4.1)	<0.001	1974–77	5.8 (0.7, 11.2)	0.03	1977–80	−5.3 (−14.2, 4.6)	0.30	1980–96	2.6 (2.2, 3.0)	<0.001	1996–09	6.7 (6.1, 7.4)	<0.001	2009–13	1.6 (−1.5, 4.8)	0.30
Race																	
White	3.8 (3.4, 4.2)	<0.001	1974–77	6.2 (2.2, 10.4)	<0.001	1977–80	−5.9 (−12.9, 1.6)	0.10	1980–97	2.9 (2.6, 3.2)	<0.001	1997–09	7.0 (6.5, 7.6)	<0.001	2009–13	1.4 (−1.1, 3.9)	0.30
Black	3.4 (2.8, 4.0)	<0.001	1974–88	−1.3 (−2.8, 0.3)	0.10	1988–13	5.4 (4.7, 6.1)	<0.001									
Others [b]	1.5 (1.1, 1.9)	<0.001	1974–96	−0.2 (−0.9, 0.4)	0.50	1996–13	3.9 (2.9, 5.0)	<0.001									
Age (years)																	
<20	1.9 (1.3, 2.4)	<0.001	1974–06	1.1 (0.5, 1.7)	<0.001	2006–13	9.8 (3.4, 16.7)	0.003									
20–39	3.0 (2.6, 3.3)	<0.001	1974–82	−1.4 (−3.1, 0.3)	0.10	1982–93	1.8 (0.6, 3.1)	0.005	1993–13	4.7 (4.3, 5.2)	<0.001						
40–59	3.9 (3.5, 4.3)	<0.001	1974–81	−1.2 (−3.9, 1.5)	0.40	1981–95	2.8 (1.7, 3.9)	<0.001	1995–13	6.2 (5.5, 6.9)	<0.001						
60–79	4.2 (3.8, 4.6)	<0.001	1974–96	2.2 (1.8, 2.7)	<0.001	1996–09	7.7 (6.5, 8.9)	<0.001	2009–13	0.8 (−5.2, 7.2)	0.80						
≥80	2.3 (1.8, 2.7)	0.002	1974–96	1.0 (0.1, 2.0)	0.03	1996–13	4.1 (2.7, 5.5)	<0.001									

	Overall		Trend 1			Trend 2			Trend 3			Trend 4			Trend 5		
Characteristic at diagnosis	**APC (95% CI)**	***P* value**	**Year**	**APC (95% CI)**	***P* value**	**Year**	**APC (95% CI)**	***P* value**	**Year**	**APC (95% CI)**	***P* value**	**Year**	**APC (95% CI)**	***P* value**	**Year**	**APC (95% CI)**	***P* value**
Histologic type																	
Papillary	4.4 (4.0, 4.7)	<0.001	1974–77	6.9 (1.5, 12.6)	0.01	1977–80	−5.9 (−15.2, 4.4)	0.20	1980–97	3.6 (3.2, 4.0)	<0.001	1997–09	7.3 (6.6, 8.1)	<0.001	2009–13	2.6 (−0.7, 6.1)	0.10
Follicular	0.6 (0.2, 0.8)	<0.001	1974–00	−0.2 (−0.7, 0.2)	0.30	2000–06	6.0 (0.8, 11.4)	0.03	2006–13	−3.0 (−5.9, −0.1)	0.05						
Medullary	0.7 (0.2, 1.1)	0.005															
Anaplastic	−0.1 (−0.7, 0.6)	0.80															
Other[c]	−0.6 (−1.3, 0.0)	0.06	1974–94	−3.0 (−4.6, −1.7)	<0.001	1994–13	1.9 (0.2, 3.7)	0.03									
<u>Papillary</u>																	
SEER Historic Stage A																	
Localized	4.6 (4.1, 5.1)	<0.001	1974–77	8.2 (0.0, 17.2)	0.05	1977–80	−7.3 (−20.9, 8.7)	0.30	1980–93	2.6 (1.6, 3.5)	<0.001	1993–09	7.8 (7.1, 8.5)	<0.001	2009–13	1.1 (−3.8, 6.3)	0.70
Regional	4.3 (4.0, 4.6)	<0.001	1974–77	8.4 (1.4, 15.9)	0.02	1977–81	−3.3 (−9.5, 3.4)	0.30	1981–84	11.7 (−2.2, 27.5)	0.10	1984–99	2.8 (2.1, 3.4)	<0.001	1999–13	6.7 (6.0, 7.4)	<0.001
Distant	2.4 (1.7, 3.2)	<0.001	1974–81	−7.7 (−15.0, 0.3)	0.06	1981–13	3.5 (2.6, 4.4)	<0.001									
Unknown	1.8 (0.9, 2.7)	<0.001	1974–78	−18.2 (−33.2, 0.1)	0.05	1978–95	7.7 (5.1, 10.4)	<0.001	1995–01	−11.8 (−23.6, 1.7)	0.08	2001–13	5.6 (1.7, 9.6)	<0.001			
AJCC/TNM stage[d]																	
Stage I	5.8 (4.5, 7.1)	<0.001	2004–09	8.2 (5.7, 10.7)	<0.001	2009–13	2.6 (−0.7, 6.1)	0.10									
Stage II	3.9 (0.6, 7.3)	0.03															

	Overall		Trend 1			Trend 2			Trend 3			Trend 4			Trend 5	
Characteristic at diagnosis	**APC (95% CI)**	***P* value**	**Year**	**APC (95% CI)**	***P* value**	**Year**	**APC (95% CI)**	***P* value**	**Year**	**APC (95% CI)**	***P* value**	**Year**	**APC (95% CI)**	***P* value**	**Year**	**APC (95% CI)**	***P* value**
Stage III	9.2 (6.6, 11.9)	<0.001	2004–06	26.0 (7.8, 47.3)	0.01	2006–13	6.5 (4.3, 8.7)	<0.001									
Stage IV	5.2 (3.3, 7.2)	<0.001															
Unknown	−3.9 (−6.4, −1.3)	0.009															
Tumor size (cm)[e]																	
≤1	9.3 (8.8, 9.8)	<0.001	1983–88	2.6 (−1.0, 6.3)	0.15	1988–98	9.0 (7.4, 10.6)	<0.001	1998–08	12.2 (10.6, 13.8)	<0.001	2008–13	3.1 (−0.5, 6.9)	0.09			
>1-≤2	5.4 (4.9, 5.9)	<0.001	1983–99	3.1 (2.6, 3.7)	<0.001	1999–09	9.1 (7.6, 10.6)	<0.001	2009–13	2.2 (−2.5, 7.2)	0.40						
>2-≤4	4.5 (4.2, 4.9)	<0.001	1983–95	2.5 (1.4, 3.6)	<0.001	1995–13	5.7 (5.1, 6.3)	<0.001									
>4	6.1 (5.4, 6.7)	<0.001	1983–88	−2.8 (−9.7, 4.6)	0.40	1988–13	6.9 (6.2, 7.6)	<0.001									
Unknown	−1.8 (−2.6, −1.0)	<0.001	1983–00	1.4 (0.4, 2.4)	0.005	2000–13	−6.4 (−7.7, −5.1)	<0.001									

Abbreviations: AJCC/TNM, American Joint Committee on Cancer/Tumor-Node-Metastasis; APC, annual percent change; CI, confidence interval.

[a]Rates were calculated as number of cases per 100,000 person-years and age-adjusted to the 2000 U.S. standard population.

[b]Includes American Indian/Alaskan Native and Asian/Pacific Islander.

[c]Includes other specified, poorly differentiated, and other types.

[d]Based on cases diagnosed during 2004–2013.

[e]Based on cases diagnosed during 1983–2013.

Table 3.

Trends in observed thyroid cancer mortality rates [a] (total U.S. and SEER-9) and thyroid cancer incidence-based mortality rates [a] (1994–2013): the SEER-9 Registry Database

Characteristic at diagnosis	Overall	
	APC (95% CI)	*P* value
Observed		
Total U.S	0.9 (0.7, 1.5)	<0.001
SEER-9	1.0 (0.4, 1.5)	<0.001
Incidence-based [b]		
Total	1.1 (0.6, 1.6)	<0.001
Gender		
Male	1.0 (−0.1, 2.1)	0.10
Female	1.2 (0.4, 2.0)	0.01
Race		
White	0.9 (0.3, 1.6)	0.01
Black	3.8 (0.2, 7.6)	0.04
Others [c]	−0.2 (−2.4, 2.2)	0.90
Age (years)		
<20	-	-
20–39	-	-
40–59	1.4 (0.0, 2.8)	0.05
60–79	0.8 (−0.2, 1.8)	0.10
≥80	1.3 (0.5, 2.1)	0.002
Histologic type		
Papillary	1.7 (0.6, 2.9)	0.01
Follicular	−0.2 (−1.6, 1.2)	0.80
Medullary	−0.7 (−3.2, 1.9)	0.60
Anaplastic	0.9 (−0.4, 2.2)	0.20
Other [d]	2.4 (−0.1, 5.1)	0.06
Papillary (incidence-based)		
SEER Historic Stage A [b]		
Localized	2.1 (−0.1, 4.2)	0.06
Regional	1.7 (−0.3, 3.6)	0.09
Distant	2.9 (1.1, 4.7)	0.003
Unknown	-	-
AJCC/TNM stage [e]		
Stage I	-	-
Stage II	-	-

Characteristic at diagnosis	Overall	
	APC (95% CI)	*P* value
Stage III [f]	14.5 (−6.1, 39.7)	0.20
Stage IV [f]	12.9 (7.2, 19.0)	<0.001
Unknown [f]	16.5 (−3.4, 40.4)	0.09
Tumor size (cm) [g]		
≤2	6.8 (2.4, 11.4)	0.004
>2-≤4	4.3 (1.3, 7.3)	0.01
>4	2.8 (−0.1, 5.9)	0.06
Unknown	−0.6 (−2.7, 1.5)	0.50

Abbreviations: AJCC/TNM, American Joint Committee on Cancer/Tumor-Node-Metastasis; APC, annual percent change; CI, confidence interval.

- APC could not be calculated due to 0 deaths in at least one year.

[a]Rates were calculated as number of deaths per 100,000 person-years and age-adjusted to the 2000 U.S. standard population.

[b]Based on deaths during 1994–2013 and cases diagnosed during 1974–2013.

[c]Includes American Indian/Alaskan Native and Asian/Pacific Islander.

[d]Includes other specified, poorly specified, and other types.

[e]Based on deaths during 2004–2013 and cases diagnosed during 2004–2013.

[f]APCs were calculated during 2005–2013 due to 0 deaths in 2004.

[g]Based on deaths during 1994–2013 and cases diagnosed during 1983–2013.