The Clinical and Economic Burden of a Sustained Increase in Thyroid Cancer Incidence

Briseis Aschebrook-Kilfoy¹, Rebecca B. Schechter², Ya-Chen Tina Shih³, Edwin L. Kaplan⁴, Brian C.-H. Chiu¹, Peter Angelos⁴, and Raymon H. Grogan⁴

Abstract

**Background:** Thyroid cancer incidence is increasing worldwide at an alarming rate, yet little is known of the impact this increase will have on society. We sought to determine the clinical and economic burden of a sustained increase in thyroid cancer incidence in the United States and to understand how these burdens correlate with the National Cancer Institute’s (NCI) prioritization of thyroid cancer research funding.

**Methods:** We used the NCI’s SEER 13 database (1992–2009) and Joinpoint regression software to identify the current clinical burden of thyroid cancer and to project future incidence through 2019. We combined Medicare reimbursement rates with American Thyroid Association guidelines, and our clinical practice to create an economic model of thyroid cancer. We obtained research-funding data from the NCI’s Office of Budget and Finance.

**Results:** By 2019, papillary thyroid cancer will double in incidence and become the third most common cancer in women of all ages at a cost of $18 to $21 billion dollars in the United States. Despite these substantial clinical and economic burdens, thyroid cancer research remains significantly underfunded by comparison, and in 2009 received only $14.7 million (ranked 30th) from the NCI.

**Conclusion:** The impact of thyroid cancer on society has been significantly underappreciated, as is evidenced by its low priority in national research funding levels.

**Impact:** Increased awareness in the medical community and the general public of the societal burden of thyroid cancer, and substantial increases in research on thyroid cancer etiology, prevention, and treatment are needed to offset these growing concerns. *Cancer Epidemiol Biomarkers Prev;* 22(7); 1252–9. ©2013 AACR.

Introduction

A substantial accumulation of evidence has shown that age-adjusted incidence of thyroid cancer has increased worldwide for many decades (1–7). This trend started as early as 1940 and has steadily increased since that time (8). The increasing thyroid cancer rates were first attributed to the widespread use of external beam radiation to treat benign diseases of the head and neck in the first part of the 20th century. However, increases in the number of non-radiation-induced thyroid cancer cases were reported as early as the 1950s, and contrary to the decrease that was expected, rates of thyroid cancer continued to increase after the routine use of radiation for benign head and neck disease had stopped, suggesting alternative factors were involved (9–12).

After several decades of data accumulation, the prevailing hypothesis for explaining the increase in thyroid cancer shifted to improved surveillance and diagnostics. Population-level data supported this hypothesis by correlating the increasing use of thyroid ultrasound and fine-needle aspiration (FNA), tools that were introduced in the early 1980s for thyroid cancer diagnosis, to the increasing thyroid cancer incidence (13). Now, almost 30 years after the introduction of thyroid ultrasound into clinical practice, thyroid cancer rates continue to increase, suggesting that other factors are involved. The patterns are concerning as there is no evidence of a decrease or plateau in incidence on the horizon. Great debate about the true cause of this increase continues, but what has been the price of this debate?

The decades-long debate over why thyroid cancer is increasing has overshadowed an issue of equal importance: the clinical and economic consequences of the continued increase. There is a paucity of data on the clinical and economic impact of thyroid cancer care. Understanding the magnitude of the clinical and economic burden of thyroid cancer is essential to allow resources to be appropriately prioritized to mitigate the impact of increasing
incidence in thyroid cancer. Such data could change our understanding of the societal burden of thyroid cancer, improve the clinical practice of physicians caring for patients with thyroid cancer, and inform policy changes for future research funding.

We hypothesized that the clinical and economic consequences of a sustained increase in thyroid cancer incidence, regardless of the cause, has been greatly underappreciated; creating a misconception that thyroid cancer is a disease with low clinical and economic burden, subsequently leading to substantial underfunding of thyroid cancer research relative to other cancers. We explored our hypothesis gathering incidence and funding data from the National Cancer Institute’s (NCI) Surveillance, Epidemiology, and End Results database (SEER) and the Office of Budget and Finance. We then used these data in Joinpoint and economic models to predict the economic and clinical impact of thyroid cancer over the next 10 years and correlated these findings with current thyroid cancer research funding data.

Materials and Methods

Incidence data source

We used the NCI’s SEER 13 Registries Database November 2011 Submission (14) to analyze male and female thyroid carcinoma incidence rates from 1992 through 2009. The SEER 13 Registries Database included registries in Atlanta, CT, Detroit, HI, IA, NM, San Francisco-Oakland, Seattle-Puget Sound, UT, Los Angeles, San Jose-Monterey, Rural Georgia, and the Alaska Native Tumor Registry and covered approximately 14% of the U.S. population.

Thyroid cancer cases were coded using the International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) (15), and were stratified into 1 major histologic types: papillary carcinoma (ICD-O-3 codes 8050, 8260, 8340–8341, 8343–8344, 8350), follicular carcinoma (ICD-O-3 codes 8290, 8330–8332, 8335), medullary carcinoma (ICD-O-3 codes 8354–8346, 8510), and anaplastic carcinoma (ICD-O-3 codes 8012, 8020–8021, and 8030–8032); all other ICD-O-3 codes were categorized as other or unknown. To compare thyroid cancer with cancers that are commonly screened for and/or highly funded by the NCI, ICD-O-3 codes were used to identify prostate, lung and bronchus, colorectal, and ovarian cancers (PLCO cancers), as well as cancer of the breast, brain, and pancreas, and leukemia, non–Hodgkin lymphoma (NHL), and melanoma.

Funding data source

We obtained funding data from the NCI’s Office of Budget and Finance for the fiscal year 2009 (16).

Data Analysis

Incidence analysis

Incidence rates (IR) were calculated using SEER*Stat 7.1.0 (17) and expressed per 100,000 person-years, man-years, or woman-years. Age-adjusted rates were standardized to the 2000 U.S. population. Prevalence estimates were also ascertained from SEER*Stat. The NCI’s Joinpoint Regression program version 3.5.2 (18) was used to test the statistical significance of trends and to obtain estimated annual percent change and 95% confidence intervals. Joinpoint regression is a statistical method that describes changing trends over successive segments of time and the rate of increase or decrease within each segment. The most recent annual percent change (APC) was calculated for each cancer site stratified by gender. The calculated APC was applied to the most recent incidence data (2009) to calculate projections for the subsequent 10-year period using the following formula: rate in subsequent year = (rate in current year) + (rate in current year × APC). The age-adjusted temporal trends were then plotted on a linear scale.

Cost analysis

To estimate the total medical costs associated with incident cohorts of patients diagnosed with thyroid cancer between 2010 and 2019, we estimated the average lifetime cost per patient, multiplied this cost by the number of estimated incident cases in a year, and then aggregated over the entire 10-year cohort. A decision model was used to document the clinical pathway for a hypothetical patient diagnosed with thyroid cancer at the median age of diagnosis (50 years old; ref. 19). The model followed the patient for 30 years, reflecting the life expectancy of a 50-year-old in the United States (20). The clinical pathway in the model was primarily based on the American Thyroid Association’s 2009 management guidelines for patients with differentiated thyroid cancer (21), supplemented with inputs from clinicians in our project team (R.B. Schechter, E.L. Kaplan, P. Angelos, and R.H. Grogan). The model also considered the possibility of recurrence and metastasis because these cases were more costly to treat and required more intensive surveillance. Rates of recurrence (30%) and metastasis (5%) were obtained from epidemiology studies (22–25).

Clinical events documented in the model included initial treatment with thyroidectomy and radioactive iodine, maintenance therapy with levothyroxine, office visits and imaging tests associated with diagnosis and surveillance of thyroid cancer, and treatment for a subset of patients with metastasis or recurrence. These events provided information on resource utilization, and each item of resource has its associated ICD-9 diagnosis/procedure code (for hospital admissions), Current Procedural Terminology codes (for outpatient visits), or National Drug Codes (for outpatient prescription drugs). We then used these codes to obtain the “unit cost” or price associated with each item of resource from published sources. Specifically, inpatient costs for each admission diagnosis or ICD-9 procedure were retrieved from the HCUPnet (http://hcupnet.ahrq.gov; ref. 26), an online query system based on data from the AHRQ’s
Healthcare Cost and Utilization Project, outpatient costs from Medicare’s resource-based relative value scales fee schedule (http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched/index.html?redirect=/physicianfeesched/), and drug costs from the Red Book (http://www.redbook.com). We then calculated the total lifetime cost by summing over the product of counts of each resource item by its corresponding unit cost across all resources and applied a 3% annual discount rate for costs occurring after the first year of diagnosis. All costs were reported in 2012 U.S. dollars.

**Funding analysis**

Incidence rate ratios (IRR) and estimated number of cases were used to compare thyroid cancer funding with other cancer sites. The funding disparity is presented as the ratio of funding of the comparison cancer site and other cancer sites. The funding disparity is presented as cases were used to compare thyroid cancer funding with the dominance of papillary thyroid cancer over the other thyroid cancer types and found in the most recent time period a yearly increase of 7.0% for papillary, 1.0% for follicular, 2.0% for medullary, and 1.0% for anaplastic thyroid cancers. We used the APC to make projections by subtype through 2019 and plotted the trends from 1992 through 2019 (Fig. 1). Our projections show that if the current trend continues, the rate of papillary thyroid cancer per 100,000 person-years will be 23.8 in 2019, compared with 15.0 for follicular thyroid cancer, 0.26 for medullary thyroid cancer, and 0.12 for anaplastic thyroid cancer. Even more striking, these data show that the rate of papillary thyroid cancer in women is expected to increase to 37.0 per 100,000 person-years by 2019 (Table 1). Given the dominance of papillary thyroid cancer over the other thyroid cancer subtypes, we chose to restrict subsequent analyses of thyroid cancer to the papillary type. We chose PLCO for comparison of incidence trends as they are the high-incidence cancers for which screening is expected to play a role in incidence trends over time and mortality outcomes. For the PLCO cancers (Table 1), we determined the incidence in 2009 to be 146.7 per 100,000 man-years for prostate cancer, 54.7 per 100,000 person-years for lung cancer (64.9 per 100,000 man-years and 47.5 per 100,000 woman-years), 42.4 person-years for colorectal cancer (48.3 per 100,000 man-years and 37.7 per 100,000 woman-years), and 12.5 per 100,000 woman-years for ovarian cancer. In 2009, the overall incidence of papillary thyroid cancer was 12.1 per 100,000 person-years, with a rate of 18.2 per 100,000 woman-years and 5.8 per 100,000 man-years.

We used the incidence data from 1992 through 2009 to fit trends for the PLCO cancers, and we report the APC for the most recent Joinpoint segment for each cancer site (Table 1). We found an increasing annual incidence for papillary thyroid cancer for both males and females (APC overall: 7.0, APC in males: 6.2, APC in females: 7.3). Conversely, a decreasing incidence was observed for all PLCO cancer sites (APC prostate: −2.1, APC lung: −1.1, APC colorectal: −2.1, APC ovary: −1.4). The APC projections show the incidence of papillary thyroid cancer in females will be 37.0 per 100,000 woman-years by 2019, surpassing ovarian (10.8) and colorectal cancer (30.4) in incidence by 2019 (Fig. 2) to become the third most common cancer in women of all ages after breast (75.0) and lung cancer (42.1). At that time, thyroid cancer will also become the second most common cancer in women under age 45 with an incidence (19.3 per 100,000 years) second only to breast cancer (data not shown).

**Cost**

Using our economic model, we estimate the lifetime cost for a hypothetical cohort of patients with thyroid cancer to be $34,723 per patient. The lifetime cost of patients without metastasis was $33,463 per patient, whereas the cost of those with metastasis was $58,660 per patient. Using the above projected incidence rates, combined with the predicted population size by the Census (27), we calculated the total cumulative cost for thyroid cancers diagnosed between 2010 and 2019 (Table 2). As shown, the total cost for an incident cohort of thyroid
The total medical cost associated with diagnosis, treatment, and management amounted to $18.59 billion dollars (or $21.6 billion undiscounted).
On the basis of these data, the sustained increase in thyroid cancer incidence will be responsible for an additional cost of $4.5 billion dollars (or $7.5 billion undiscounted) over the next 10 years.

Funding

On the basis of incidence rates, we found a significant discrepancy in NCI funding for thyroid cancer compared with the top 10 most funded cancer sites (Table 3). In 2009, thyroid cancer was the seventh most common cancer in incidence in the United States (5th most common excluding melanoma and NHL). In the same year, the NCI allocated $14.7 million to thyroid cancer research, making it the 30th most funded cancer site. By comparison, the 4 cancer sites with the highest incidence rates in 2009 were breast, prostate, lung, and colon. They were also the 4 most highly funded cancer sites, and their funding rank correlated directly with their incidence rates. Leukemia was the fifth most funded cancer and its incidence (8th most common) in 2009 was very similar to that of thyroid cancer (12.4 vs. 13.7 per 100,000), but the discrepancy in funding was striking ($220.6 million vs. $14.7 million). If the increasing incidence in thyroid cancer is not taken into consideration in the future, the discrepancy in funding for thyroid cancer will only worsen (Table 3).

Because thyroid cancer has a high survival rate (28), it also has a prevalence that is higher than many other cancers. To understand how thyroid cancer funding compares to other cancers based on survivorship, we compared funding rates of the top 10 funded cancer types to thyroid cancer as a function of prevalence. On the basis of prevalence estimates and funding in 2009, we found that $30 were spent per American who has survived thyroid cancer in the United States, compared with $217 per breast cancer survivor, $811 per leukemia survivor, $1053 per brain cancer survivor, $270 per NHL survivor, $602 per ovarian cancer survivor, $118 per melanoma survivor, and $2341 per pancreatic cancer survivor (Table 4).

Comment

We found that thyroid cancer imposes a significant clinical and economic burden in the United States. Our data suggest that if current trends are maintained, within the next 10 years, the incidence rate of thyroid cancer would more than double and be as high as 89,500 new cases per year and cost between $18 and $21 billion. Our findings also indicate that although the lifetime cost of thyroid cancer was not high (around $35,000 per patient) compared with other cancers, the overall cost of illness is expected to increase substantially in the next 10 years as a result of the increasing incidence of thyroid cancer. On the basis of thyroid cancer funding data, this burden has been greatly underappreciated, as it is only the 30th most funded cancer even though it is the seventh most common type of cancer. Interestingly, 6 of the 10 most highly funded cancer types are decreasing in incidence, and of the remaining 4 that are increasing, none are increasing at a rate higher than 1.8% per year compared to 6.6% for thyroid cancer (7.0% for the papillary thyroid cancer subtype). We cannot ascertain from our data whether higher levels of research funding directly decrease cancer incidence, but we do show that thyroid cancer is significantly underfunded and at the same time is increasing at a much more rapid rate than almost any other cancer type.

In general, the prognosis for thyroid cancer is good as the 10-year survival rate for papillary thyroid cancer is as high as 97% in some studies (28). A high rate of survival, a relatively younger age at diagnosis, and the increasing

### Table 2. Annual cost estimate and burden on U.S. healthcare system due to rapid increase in thyroid cancer cases

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of thyroid cancer cases</th>
<th>Total cost undiscounted</th>
<th>Total cost discounted</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>40,622.7</td>
<td>$1,410,543,455</td>
<td>$1,410,543,455</td>
</tr>
<tr>
<td>2011</td>
<td>44,357.6</td>
<td>$1,540,228,794</td>
<td>$1,495,367,761</td>
</tr>
<tr>
<td>2012</td>
<td>48,434.6</td>
<td>$1,681,794,187</td>
<td>$1,585,252,321</td>
</tr>
<tr>
<td>2013</td>
<td>52,884.2</td>
<td>$1,836,296,484</td>
<td>$1,680,471,411</td>
</tr>
<tr>
<td>2014</td>
<td>57,739.4</td>
<td>$2,004,883,994</td>
<td>$1,781,313,461</td>
</tr>
<tr>
<td>2015</td>
<td>63,036.2</td>
<td>$2,188,807,646</td>
<td>$1,888,084,703</td>
</tr>
<tr>
<td>2016</td>
<td>68,813.9</td>
<td>$2,389,426,771</td>
<td>$2,001,107,303</td>
</tr>
<tr>
<td>2017</td>
<td>75,115.2</td>
<td>$2,608,223,574</td>
<td>$2,120,724,448</td>
</tr>
<tr>
<td>2018</td>
<td>81,986.7</td>
<td>$2,846,822,633</td>
<td>$2,247,308,075</td>
</tr>
<tr>
<td>2019</td>
<td>89,479.5</td>
<td>$3,106,995,536</td>
<td>$2,381,253,366</td>
</tr>
<tr>
<td>10-year total</td>
<td></td>
<td>$21,614,023,073</td>
<td>$18,591,426,304</td>
</tr>
</tbody>
</table>

NOTE: Discounted estimate is based on a 3% annual discount rate.
Table 3. NCI research funding for thyroid cancer compared with the top 10 most funded cancer sites in 2009 and projections for 2019

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>Funding rank</th>
<th>Funding per year absolute</th>
<th>Funding compared with thyroid&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Incidence rate</th>
<th>IRR compared with thyroid</th>
<th>APC</th>
<th>Incidence rate</th>
<th>IRR compared with thyroid</th>
<th>Funding compared to thyroid normalized for incidence&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>1</td>
<td>$599.5</td>
<td>40.8</td>
<td>68.3</td>
<td>5.0</td>
<td>8.2</td>
<td>0.9%</td>
<td>75.0</td>
<td>25.7</td>
</tr>
<tr>
<td>Prostate</td>
<td>2</td>
<td>$293.9</td>
<td>20.0</td>
<td>66.7</td>
<td>4.9</td>
<td>4.1</td>
<td>-2.1%</td>
<td>54.2</td>
<td>2.1</td>
</tr>
<tr>
<td>Lung</td>
<td>3</td>
<td>$246.9</td>
<td>16.8</td>
<td>54.7</td>
<td>4.0</td>
<td>4.2</td>
<td>-1.1%</td>
<td>49.0</td>
<td>1.9</td>
</tr>
<tr>
<td>Colon/Rectum</td>
<td>4</td>
<td>$264.2</td>
<td>18.0</td>
<td>42.4</td>
<td>3.1</td>
<td>5.8</td>
<td>-2.4%</td>
<td>33.4</td>
<td>1.3</td>
</tr>
<tr>
<td>Leukemia</td>
<td>5</td>
<td>$220.6</td>
<td>15.0</td>
<td>12.4</td>
<td>0.9</td>
<td>16.7</td>
<td>-0.1%</td>
<td>12.2</td>
<td>0.5</td>
</tr>
<tr>
<td>Brain</td>
<td>6</td>
<td>$142.7</td>
<td>9.7</td>
<td>5.9</td>
<td>0.4</td>
<td>24.3</td>
<td>-0.2%</td>
<td>5.8</td>
<td>0.2</td>
</tr>
<tr>
<td>NHL</td>
<td>7</td>
<td>$130.9</td>
<td>8.9</td>
<td>20.0</td>
<td>1.5</td>
<td>5.9</td>
<td>0.4%</td>
<td>20.7</td>
<td>0.8</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>8</td>
<td>$110.1</td>
<td>7.5</td>
<td>6.7</td>
<td>0.5</td>
<td>15.0</td>
<td>-1.4%</td>
<td>5.8</td>
<td>0.2</td>
</tr>
<tr>
<td>Melanoma</td>
<td>9</td>
<td>$103.7</td>
<td>7.1</td>
<td>20.2</td>
<td>1.5</td>
<td>4.7</td>
<td>1.8%</td>
<td>24.2</td>
<td>0.9</td>
</tr>
<tr>
<td>Pancreas</td>
<td>10</td>
<td>$89.7</td>
<td>6.1</td>
<td>12.2</td>
<td>0.9</td>
<td>6.8</td>
<td>1.1%</td>
<td>13.8</td>
<td>0.5</td>
</tr>
<tr>
<td>Thyroid</td>
<td>30</td>
<td>$14.7</td>
<td>Ref.</td>
<td>13.7</td>
<td>Ref.</td>
<td>Ref.</td>
<td>6.6%</td>
<td>Ref.</td>
<td>Ref.</td>
</tr>
</tbody>
</table>

Abbreviation: Ref, reference for comparison (thyroid).

<sup>a</sup>Funding data (in millions) is from NCI’s Office of Budget and Finance for the fiscal year 2009.

<sup>b</sup>Absolute funding illustrates the ratio of funding for cancer sites relative to thyroid cancer without factoring incidence.

<sup>c</sup>Funding is normalized for incidence by dividing the amount of funding for each cancer site by the amount of funding for thyroid cancer divided by the IRR (i.e., $/breast/$/thyroid divided by the IRR for the 2 cancers). For example, each new breast cancer case receives 8.2 times more research funding than each new case of thyroid cancer.

<sup>d</sup>The 2019 projections for funding normalized for incidence show what the funding rate for each cancer site would be relative to thyroid cancer if the funding rates in 2009 are continued at the same rate in 2019.
Our study does have some limitations. The economic model likely underestimates the true cost of thyroid cancer because the model only captured essential care components, it did not include any treatment-related complications or use of novel therapies for metastatic disease. In addition, our unit cost information was based on Medicare payment rates, which tend to be lower than the rates in commercial plans. Our study is also limited by the usual concerns related to analyses of registry data: nonreview of histopathologic diagnoses, potential incomplete data collection, and inconsistencies in tumor classification over time due to changing staging systems. The precision of trend analyses depends on the extent of data available; however, trend analyses ascertained using data such as SEER are based on a relatively large population with extensive historic data and are subsequently more reliable. Also, trend analyses are more accurate if there are no major changes in treatment options that are likely to impact future rates. Accurate projections of cancer rates must also take into consideration geographic and demographic differences in populations. However, it is unlikely that these factors play a significant role in our projections as we used a very large sample size and changes in the population are less likely when using a database as large as SEER.

**Table 4. Amount of cancer research dollars allocated per U.S. citizen alive with a cancer diagnosis in 2009**

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>NCI fundinga</th>
<th>No. of cancer cases</th>
<th>SPP with cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>$599.5</td>
<td>2,761,749</td>
<td>$217.07</td>
</tr>
<tr>
<td>Prostate</td>
<td>$293.9</td>
<td>2,496,784</td>
<td>$117.71</td>
</tr>
<tr>
<td>Lung</td>
<td>$246.9</td>
<td>387,762</td>
<td>$636.73</td>
</tr>
<tr>
<td>Colon/Rectum</td>
<td>$264.2</td>
<td>1,140,161</td>
<td>$231.72</td>
</tr>
<tr>
<td>Leukemia</td>
<td>$220.6</td>
<td>271,880</td>
<td>$811.39</td>
</tr>
<tr>
<td>Brain</td>
<td>$142.7</td>
<td>135,402</td>
<td>$1,053.90</td>
</tr>
<tr>
<td>NHL</td>
<td>$130.9</td>
<td>484,336</td>
<td>$270.27</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>$110.1</td>
<td>182,758</td>
<td>$602.44</td>
</tr>
<tr>
<td>Melanoma</td>
<td>$103.7</td>
<td>876,344</td>
<td>$118.33</td>
</tr>
<tr>
<td>Pancreas</td>
<td>$89.7</td>
<td>38,308</td>
<td>$2,341.55</td>
</tr>
<tr>
<td>Thyroid</td>
<td>$14.7</td>
<td>496,901</td>
<td>$29.58</td>
</tr>
</tbody>
</table>

Abbreviation: PP, per person.

aIn millions.

incidence is resulting in a greater prevalence of thyroid cancer survivors. The majority of these patients will live full lives after their diagnosis, but they will need lifelong surveillance. We are not arguing that thyroid cancer prognosis is similar to the other more common cancer types but simply that the trends and magnitude of persons affected now and in the near future warrant consideration of investment in research to understand the cause and implications of the issue.

Our data also suggest that thyroid cancer is increasingly a major public health issue, particularly for women. The increase in incidence is clearly an important women’s health issue because the thyroid cancer burden is not equally distributed by gender, and we expect the gender difference to widen in the future. An improved understanding of how biologic, environmental, social, and cultural factors contribute to differences in cancer prevention is key to alleviating the observed gender disparity and to identifying opportunities to slow the increasing rates. The control of thyroid cancer is a critical piece of the actionable strategies necessary to reduce the burden of cancer. Furthermore, if we were better able to prognosticate between different types of cancer, we could definitely reduce spending by reducing surgery, follow-up, workup etc., on those patients with more benign forms of the disease.

Our study does have some limitations. The economic model likely underestimates the true cost of thyroid cancer because the model only captured essential care components, it did not include any treatment-related complications or use of novel therapies for metastatic disease. In addition, our unit cost information was based on Medicare payment rates, which tend to be lower than the rates in commercial plans. Our study is also limited by the usual concerns related to analyses of registry data: nonreview of histopathologic diagnoses, potential incomplete data collection, and inconsistencies in tumor classification over time due to changing staging systems. The precision of trend analyses depends on the extent of data available; however, trend analyses ascertained using data such as SEER are based on a relatively large population with extensive historic data and are subsequently more reliable. Also, trend analyses are more accurate if there are no major changes in treatment options that are likely to impact future rates. Accurate projections of cancer rates must also take into consideration geographic and demographic differences in populations. However, it is unlikely that these factors play a significant role in our projections as we used a very large sample size and changes in the population are less likely when using a database as large as SEER.

**Conclusion**

Thyroid cancer diagnosis, treatment, and surveillance have not changed significantly since the introduction of thyroid ultrasound and FNA nearly 30 years ago. Given the continued rapid rate of increase in thyroid cancer, it is unlikely that ultrasound and FNA are the sole source of the increase. A sense of complacency in research and development of new therapies and diagnostic strategies for thyroid cancer has been promoted because it is thought of as a disease with a minimal burden on society. Our data refute this commonly held belief and show a clear clinical and economic burden on society as a result of thyroid cancer. While it is true that most people survive thyroid cancer, recurrences can occur after many years, and patients must live a lifetime of surveillance and worry. The psychological impact of thyroid cancer survivorship has not been well studied, but it is another considerable burden for many patients. On the basis of our data, we believe thyroid cancer should receive a higher priority in funding so that more research on the etiology, prevention, and improved treatment of thyroid cancer might take place.

**Disclosure of Potential Conflicts of Interest**

Y.-C. T. Shih is a consultant/advisory board member on the panel of Genentech CER Oncology. No potential conflicts of interest were disclosed by the other authors.

**Authors’ Contributions**

Conception and design: B. Aschebrook-Kilfoy, Y.-C. T. Shih, P. Angelos, R.H. Grogan

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Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): B. Aschebrook-Kilfoy, R.B. Schechter, R.H. Grogan

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