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## Trends in the Management of Localized Papillary Thyroid Carcinoma in the United States (2000–2018)

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**Background:** In response to evidence of overdiagnosis and overtreatment of papillary thyroid carcinoma (PTC), the 2009 and 2015 American Thyroid Association (ATA) adult guidelines recommended less extensive surgery (lobectomy vs. total thyroidectomy) and more restricted use of postsurgical radioactive iodine (RAI) in management of PTC at low risk of recurrence. In 2015, active surveillance was suggested as a viable option for some <1-cm PTCs, or microcarcinomas. The 2015 ATA pediatric guidelines similarly shifted toward more restricted use of RAI for low-risk PTCs. The impact of these recommendations on low-risk adult and pediatric PTC management remains unclear, particularly after 2015.

*Methods:* Using data from 18 Surveillance, Epidemiology, and End Results (SEER) U.S. registries (2000–2018), we described time trends in reported first-course treatment (total thyroidectomy alone, total thyroidectomy+RAI, lobectomy, no surgery, and other/unknown) for 105,483 patients diagnosed with first primary localized PTC (without nodal/distant metastases), overall and by demographic and tumor characteristics.

**Results:** The declining use of RAI represented the most pronounced change in management of PTCs <4 cm (44–18% during the period 2006–2018), including microcarcinomas (26–6% during the period 2007–2018). In parallel, an increasing proportion of PTCs were managed with total thyroidectomy alone (35–54% during the period 2000–2018), while more subtle changes were observed for lobectomy (declining from 23% to 17% during the period 2000–2006, stabilizing, and then rising from 17% to 24% during the period 2015–2018). Use of nonsurgical management did not meaningfully change over time, impacting <1% of microcarcinomas annually during the period 2000–2018. Similar treatment trends were observed by sex, age, race/ethnicity, metropolitan vs. nonmetropolitan residence, and insurance status. For pediatric patients (<20 years), use of RAI peaked in 2009 (59%), then decreased markedly to 11% (2018), while use of total thyroidectomy alone and, to a lesser extent, lobectomy increased. No changing treatment trends were observed for  $\geq$ 4-cm PTCs.

*Conclusions:* The declining use of RAI in management of low-risk adult and pediatric PTC is consistent with changing recommendations from the ATA practice guidelines. Post-2015 trends in use of lobectomy and nonsurgical management of low-risk PTCs, particularly microcarcinomas, were more subtle than expected; however, these trends may change as evidence regarding their safety continues to emerge.

Keywords: clinical guidelines, papillary thyroid carcinoma, treatment trends

#### Introduction

**I** N THE UNITED STATES, the incidence of papillary thyroid carcinoma (PTC), the most common histological type of thyroid cancer, rose sharply from the 1980s to mid-2010s,

driven primarily by an increase in small localized tumors (1,2). In contrast, thyroid mortality rates remained fairly stable (3). These trends have raised concerns about substantial overdiagnosis and overtreatment of low-risk PTCs, defined broadly as small PTCs, often found incidentally,

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without evidence of metastasis or local invasion or other aggressive pathological features (4–7).

In 2015, the American Thyroid Association (ATA) created the term "very low-risk" to refer specifically to localized PTCs <1 cm (known as papillary thyroid microcarcinomas, or PTMCs); these tumors are typically indolent and come with an excellent prognosis (8).

In response to these concerns, the 2009 and, to a greater extent, 2015 ATA adult treatment guidelines adopted a less is more approach to the management of low-risk and very lowrisk PTCs (4,9,10). In 2009, the ATA no longer recommended postsurgical radioactive iodine (RAI) ablation for very low-risk PTCs (10). Total thyroidectomy alone was indicated as the preferred treatment, with support for lobectomy in certain cases.

In 2015, recommendations to avoid RAI ablation were strengthened and extended to larger (1-4 cm) low-risk PTCs (4). Lobectomy was indicated as the preferred treatment for very low-risk PTCs and as an equivalent option to total thyroidectomy for larger (1-4 cm) low-risk PTCs. Active surveillance (no surgery with regular ultrasound follow-up) was indicated as an option for selected patients with very low-risk PTC (4), following emerging evidence of the safety and effectiveness of this approach (11,12).

The 2015 ATA pediatric guidelines recommended total thyroidectomy as the preferred surgical option for the majority of children, regardless of PTC size, followed by RAI only in selected cases (local invasion or nodal/metastatic disease) (13). This recommendation for more restricted use of RAI marked a major shift in management of pediatric PTC (14,15).

The impact of the 2009 ATA adult treatment guidelines for low-risk PTCs on trends in clinical practice has been reported previously, with evidence of reduction in use of RAI (16). Less is known about the impact of the 2015 guidelines, although increased performance of lobectomy and reduction in RAI for PTCs <2 cm were reported through 2016, only 1 year after publication of the 2015 guidelines (16).

It remains unclear whether and how PTC management, particularly RAI use, has continued to change with time and whether these trends differ by patient demographics or for larger-sized tumors (7,16–20). To our knowledge, the impact of the 2015 ATA pediatric guidelines on clinical practice has not yet been described.

Therefore, we aimed to comprehensively assess U.S. trends (2000–2018) in management of localized PTC by tumor size and patient demographics, including age, sex, race/ ethnicity, metropolitan versus nonmetropolitan residence, and insurance status (available between 2007 and 2016).

#### Methods

Using data from 18 Surveillance, Epidemiology, and End Results cancer registries (SEER-18), covering 28% of the U.S population, we identified patients diagnosed with first primary PTC localized to the thyroid gland (without extrathyroidal extension or nodal or distant metastasis) between 2000 and 2018 (21). PTC was defined using International Classification of Diseases for Oncology, third edition codes (8050, 8260, 8340–8344, 8350, and 8450–8460). Thyroid cancers with unknown histology, size, or nodal/metastasis extension were excluded.

SEER collects information on first-course therapy, defined as therapy received before recurrence or cancer progression, by reviewing medical records. If multiple surgery procedures are recorded, the most invasive, extensive, or definitive surgery within the first-course therapy is reported in SEER. Thus, if a lobectomy performed for a suspicious nodule is followed by a completion thyroidectomy (i.e., because pathology diagnosis indicated a PTC), the surgical procedure reported in SEER would be total thyroidectomy (22).

We classified patients according to first-course therapy as follows: total thyroidectomy followed by RAI, total thyroidectomy alone (no record of RAI), lobectomy, no surgery (unknown if under an active surveillance protocol), and other/unknown therapy. Surgery procedures were identified using codes from the RX Summ—Surgery Primary Site SEER variable: total thyroidectomy included "Removal of a lobe and partial removal of the contralateral lobe," "Subtotal or near total thyroidectomy," "Total thyroidectomy," and "Thyroidectomy not otherwise specified"; lobectomy included "Removal of less than a lobe" and "Lobectomy and/or isthmusectomy"; and no surgery included "No surgery of primary site."

The other/unknown treatment group included "Surgery, not otherwise specified," "Unknown if surgery was performed," or "Not specified local tumor destruction" (which likely captured radiofrequency ablation and other types of tumor ablation techniques). Subjects receiving RAI were identified using the value "radioisotope" from the radiation recode variable. Patients receiving other types of radiation therapies (e.g., radiation beam) were included in the other/ unknown category.

We evaluated treatment trends for localized PTC during the period 2000–2018, overall and by tumor size (<1, 1 to <2, 2 to <4, and  $\geq$ 4 cm). For PTCs <4 cm (low-risk cases), we stratified by age at diagnosis (<20, 20–54, and  $\geq$ 55 years), sex, race/ethnicity (Hispanic [all races] or non-Hispanic White, Black, Asian/Pacific Islander, or Native American/ American Indian/Alaska Native), patients' residence at diagnosis (metropolitan/nonmetropolitan county), and insurance status [private insurance/Medicare or uninsured/Medicaid, available for years 2007–2016 from the SEER November 2018 submission (23)].

Hispanic patients were not subdivided by race/ethnicity due to the small number of Hispanic Black (n=139), Asian/ Pacific Islander (n=111), or American Indian/Alaska Native (n=56) groups. Pediatric patients were defined as those diagnosed before age 20 years (1,4). Metropolitan counties were those with populations of >250,000 individuals. Treatment trends for subjects with unknown values of age, sex, race/ethnicity, residence, or insurance status are not shown.

Analyses were conducted using SEER\*Stat software (version 8.3.9), and graphs were made using R software (version 4.0.5) (24,25). To test the statistical significance of apparent changes in trends of treatment proportions, we estimated annual percentage changes and identified inflection points in the trends using Joinpoint regression (Joinpoint Regression Program, version 4.8.1.0) (26).

Ethical approval was not required for use of anonymized publicly available data.

#### Results

We identified 105,483 patients diagnosed with localized PTC (Table 1). The majority (98%, N=98,880) of PTCs were <4 cm, and 49,131 (50%) were <1 cm. Among patients

#### THYROID CANCER TREATMENT IN THE UNITED STATES (2000-2018)

| Characteristics               | Total<br>thyroidectomy<br>with RAI, N (%) | Total<br>thyroidectomy<br>alone, N (%) | Lobectomy,<br>N (%) | No surgery,<br>N (%) | Other/unknown<br>therapy,<br>N (%) |
|-------------------------------|---|--|---------------------|----------------------|------------------------------------|
| Based on November 2020 SEER d | lata submission                           |  |                     |                      |                                    |
| Total                         | 36,592                                    | 46,400                                 | 18,434              | 1269                 | 2788                               |
| Sex                           | ,   | ,                                      | ,                   |                      |                                    |
| Female                        | 29,175 (80)                               | 38,558 (83)                            | 14,633 (79)         | 932 (73)             | 2190 (78)                          |
| Age, years                    |   |  |                     | . ,                  |                                    |
| <20                           | 538 (1)                                   | 576 (1)                                | 221 (1)             | 9 (0.7)              | 40 (1)                             |
| 20–54                         | 24,186 (66)                               | 28,626 (62)                            | 11,256 (61)         | 741 (58)             | 1814 (65)                          |
| ≥55                           | 11,868 (32)                               | 17,198 (37)                            | 6957 (38)           | 519 (40)             | 934 (34)                           |
| Size, cm                      |   |  |                     |                      |                                    |
| <1                            | 8630 (24)                                 | 27,023 (58)                            | 12,404 (66)         | 311 (25)             | 763 (27)                           |
| 1 to <2                       | 13,535 (37)                               | 11,456 (25)                            | 2977 (16)           | 470 (37)             | 942 (34)                           |
| 2 to <4                       | 10,815 (30)                               | 6135 (13)                              | 2261 (12)           | 345 (27)             | 813 (29)                           |
| ≥4                            | 3612 (10)                                 | 1786 (4)                               | 792 (4)             | 143 (11)             | 270 (10)                           |
| Race/ethnicity                |   |  |                     |                      |                                    |
| Non-Hispanic White            | 24,117 (66)                               | 31,208 (67)                            | 12,596 (68)         | 693 (55)             | 1815 (65)                          |
| Hispanic (all races)          | 5770 (16)                                 | 6666 (14)                              | 2397 (13)           | 267 (21)             | 445 (16)                           |
| Non-Hispanic Black            | 2298 (6)                                  | 3558 (8)                               | 1298 (7)            | 72 (6)               | 193 (7)                            |
| Non-Hispanic API              | 4000 (11)                                 | 4225 (9)                               | 1841 (10)           | 193 (15)             | 297 (11)                           |
| Non-Hispanic AI/AN            | 198 (0.5)                                 | 235 (0.5)                              | 95 (0.5)            | 9 (0.7)              | 21 (0.7)                           |
| Non-Hispanic unknown race     | 209 (0.6)                                 | 508 (1)                                | 207 (1)             | 35 (3)               | 17 (0.6)                           |
| Geographical location         |   |  |                     |                      |                                    |
| Metropolitan county           | 33,019 (90)                               | 41,774 (90)                            | 16,325 (89)         | 1185 (93)            | 2471 (89)                          |
| Nonmetropolitan county        | 3540 (10)                                 | 4586 (10)                              | 2085 (11)           | 78 (6)               | 314 (11)                           |
| Unknown                       | 33 (0.1)                                  | 40 (0.1)                               | 24 (0.1)            | 6 (0.5)              | 3 (0.1)                            |
| Based on November 2018 SEER d | lata submission                           |  |                     |                      |                                    |
| Insurance status <sup>a</sup> |   |  |                     |                      |                                    |
| Uninsured <sup>b</sup>        | 509 (2)                                   | 746 (2)                                | 229 (2)             | 62 (7)               | 51 (3)                             |
| Medicaid <sup>b</sup>         | 1957 (8)                                  | 2984 (10)                              | 1003 (9)            | 121 (14)             | 156 (9)                            |
| Insured                       | 20,555 (88)                               | 26,312 (86)                            | 9251 (85)           | 622 (73)             | 1414 (85)                          |
| Unknown insurance status      | 275 (1)                                   | 712 (2)                                | 356 (3)             | 49 (6)               | 43 (3)                             |

| TABLE 1. CHARACTERISTICS OF THE S | STUDY POPULATION   | BY REPORTED FIRST COURSE |
|-----------------------------------|--------------------|--------------------------|
| of Treatment Modalit              | TIES DURING THE PE | riod 2000–2018           |

<sup>a</sup>Available only for the 2007–2016 period from the 2018 SEER submission.

<sup>b</sup>Combined in the analysis.

AI/AN, American Indian and Alaska Native; API, Asian/Pacific Islander; RAI, radioactive iodine; SEER, Surveillance, Epidemiology, and End Results.

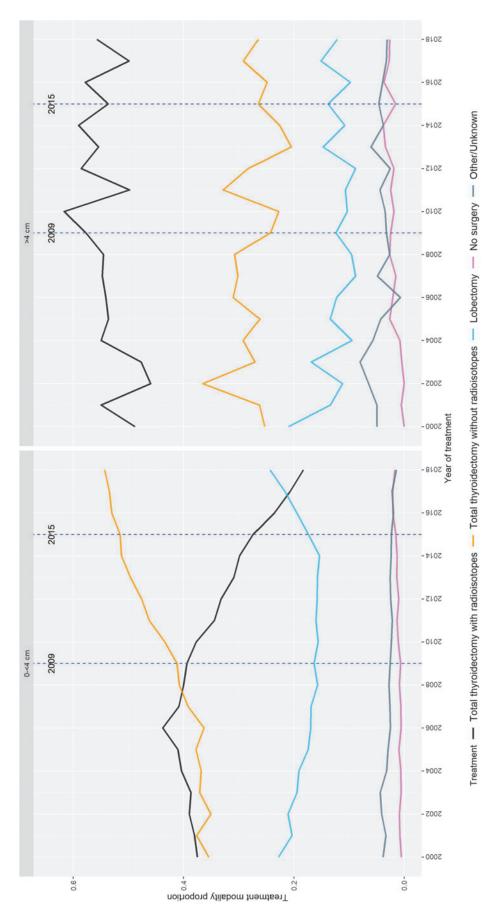
treated with total thyroidectomy+RAI, 80% were female; 66% were non-Hispanic White; 1% were aged <20 years, 66% 20–54 years, and  $32\% \ge 55$  years; and most (90%) resided in metropolitan counties. Demographic characteristics were similarly distributed across other first-course treatment modalities. During the period 2007–2016, the proportion of patients with no insurance or covered by Medicaid was 10– 12% in the RAI, total thyroidectomy alone, lobectomy, or other/unknown therapy groups; this proportion was almost doubled (21%) in the no-surgery group (23).

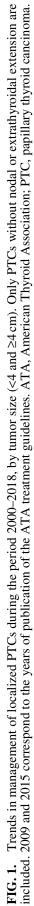
For PTCs <4 cm, the reported use of total thyroidectomy+RAI slightly increased between 2000 (38%) and 2006 (44%), then declined markedly (to 18% in 2018), whereas total thyroidectomy alone increased from 35% to 54% (2000– 2018), and lobectomy increased from 17% to 24% (2015– 2018). For PTCs  $\geq$ 4 cm, there was no measurable change in reported treatment modality utilization during the period 2000–2018; most were managed using total thyroidectomy+ RAI (55%) or total thyroidectomy alone (27%) (Fig. 1).

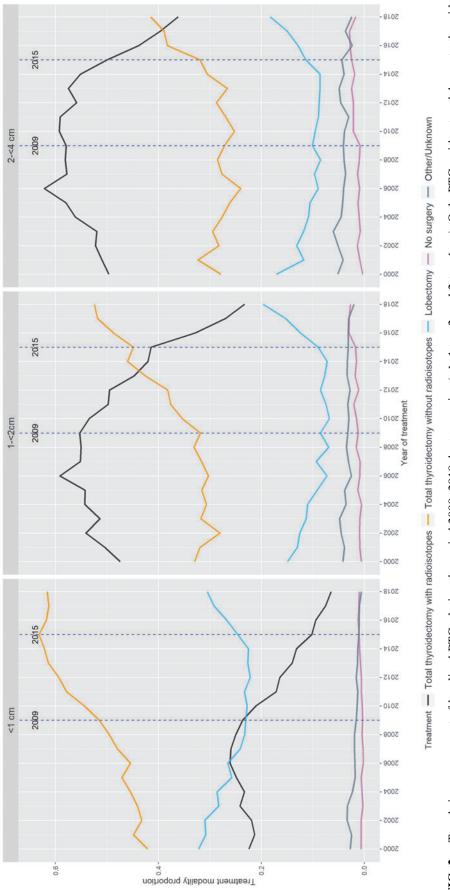
Figure 2 shows reported treatment trends for PTCs <1, 1-2, and 2–4 cm. For PTCs <1 cm, the use of total thyroidectomy+RAI rose slightly after 2000 (22%), peaked in 2007 (26%), and then declined to 6% by 2018; total thyroidectomy alone increased slightly (2000–2007, from 42% to 48%), peaked in 2015 (63%), and subsequently stabilized through 2018; lobectomy declined from 32% to 23% (2000–2009), stabilized (2009–2014), and increased to 30% (2014–2018); and nonsurgical management was used for <1% of cases during the period 2000–2018.

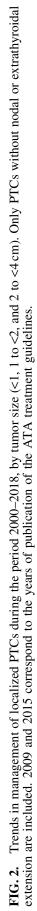
Similar treatment patterns were observed for PTCs 2 to <4 cm. Total thyroidectomy+RAI peaked in 2006 ( $\sim$ 60%), then fell to 23% for 1 to <2 cm and to 36% for 2 to <4-cm PTCs. The decline in RAI use was steeper after 2015 (Supplementary Material). Total thyroidectomy alone increased from 32% (2009) to 52% (2018) for PTCs 1 to <2 cm and from 27% (2011) to 42% (2018) for PTCs 2 to <4 cm. Lobectomy increased during the period 2015–2018, from 9% to 20% for 1 to <2 cm and from 11% to 18% for 2 to <4 cm.

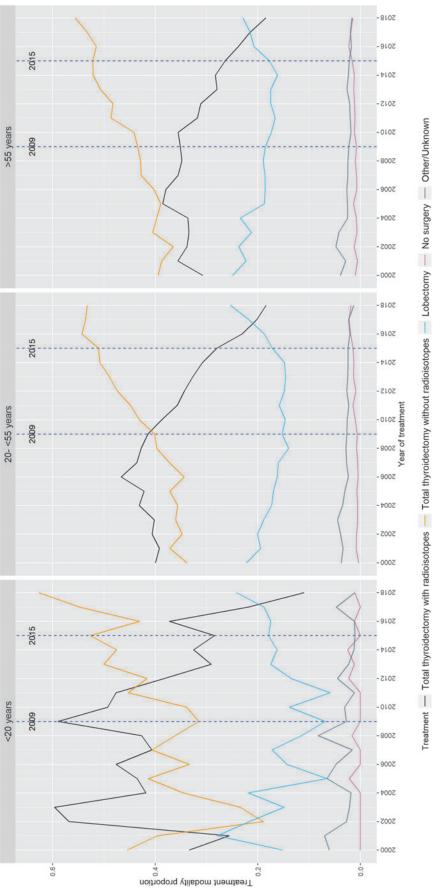
Combining PTCs <4 cm, treatment trends were similar by age (Fig. 3), sex (Fig. 4), race/ethnicity (Fig. 5), metropolitan/ nonmetropolitan residence (Fig. 6), and insurance status (Fig. 7). Before 2010, the reported use of total thyroidectomy+RAI was higher in younger versus older patients (peaking at 59% in 2009 for pediatric patients), but by 2018, the use of RAI was below 20% across all age groups and lowest for pediatric patients (11%).



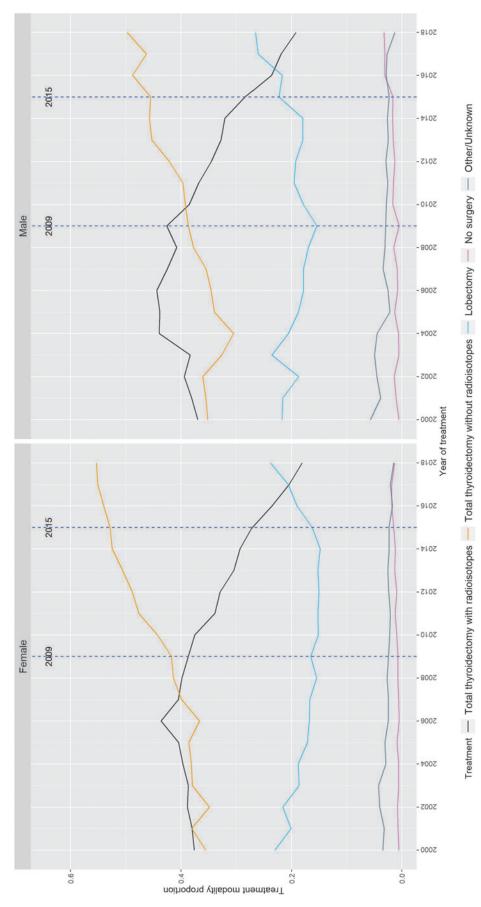


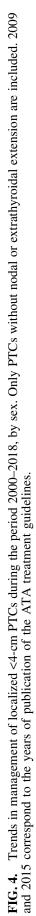


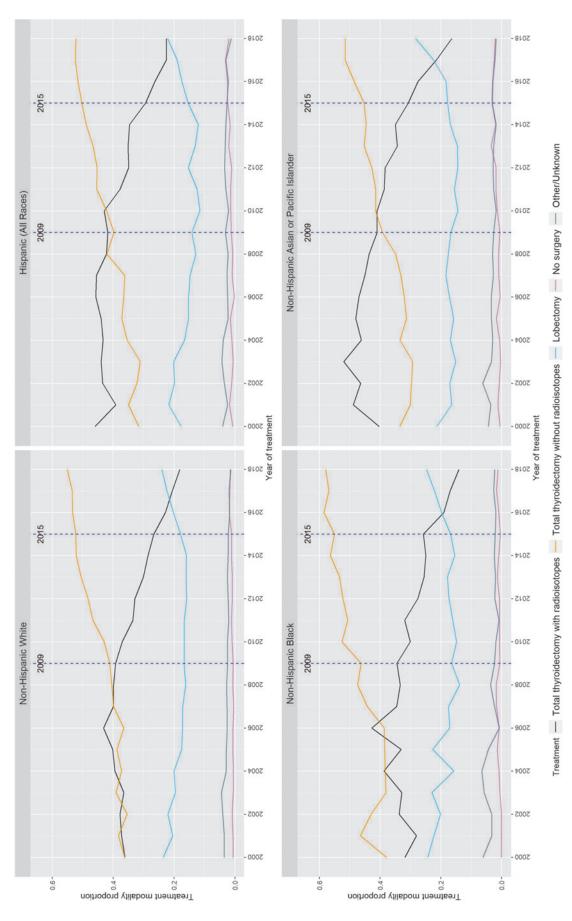




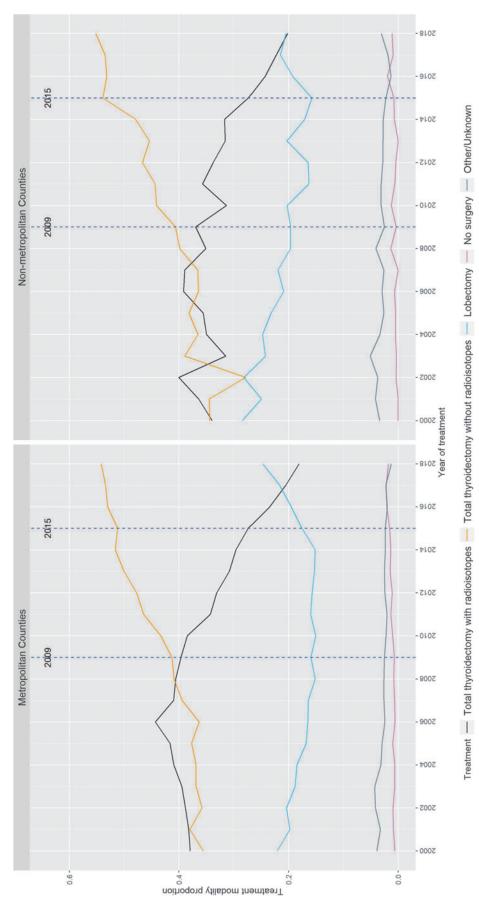


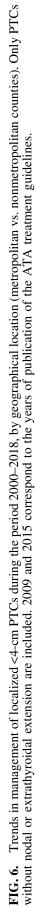


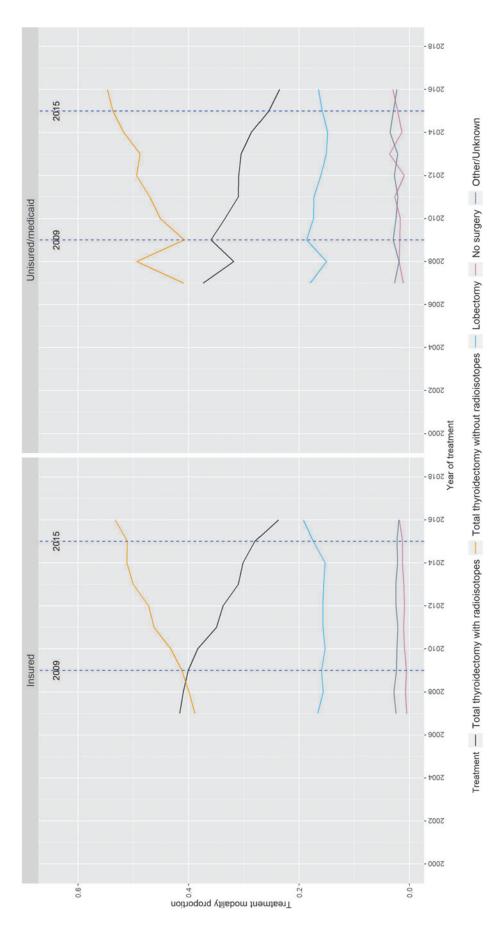


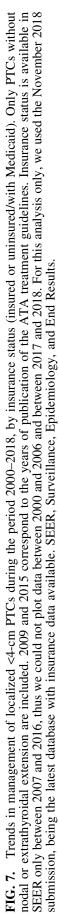












Thyroidectomy+RAI use appeared highest among non-Hispanic Asian/Pacific Islanders and Hispanics and lowest among non-Hispanic Black patients. For non-Hispanic American Indian/Alaska Native patients (data not shown in figures due to small numbers), reported use of total thyroidectomy+RAI decreased from 50% (2008–2010) to 15% by 2018, while total thyroidectomy alone (36% in 2008–2010 to 53% in 2018) and lobectomy (10% in 2014–2015 to 25% in 2018) increased.

A slightly greater increase in lobectomy during the period 2015–2016 was observed among patients covered by private insurance/Medicare versus Medicaid/no insurance. No insurance data were available after 2016.

#### Discussion

During the period 2000–2018, major changes were observed in the reported management of low-risk (<4 cm, localized) PTCs in the United States. RAI declined substantially during the period 2006–2018, most notably for PTMCs. The proportion of patients receiving thyroid-ectomy alone increased over time, while use of lobectomy increased slightly after 2015. Nonsurgical management was used for <1% of PTMCs annually during the period 2000–2018, with no meaningful changes over time. Similar trends were observed by patient sex, age, race/ethnicity, metropolitan versus nonmetropolitan residence, and insurance status. No changes in treatment trends were observed for  $\geq$ 4-cm PTCs.

These changes, especially the declining RAI use, appear to reflect new guidance published in the 2009 and 2015 ATA treatment guidelines. These guidelines encouraged the deescalation of treatment for low-risk pediatric and adult PTCs (those considered unlikely to pose a risk of disease recurrence, persistence, or mortality), with the goal of limiting treatment interventions yielding fewer benefits than risks (4,10,13).

Although RAI treatment of unifocal PTC <1 cm (or multifocal when all foci are <1 cm) has been discouraged since the 2009 guidelines (10), we observed that RAI use declined for all PTCs <2 cm, suggesting more cautious management of small PTCs more broadly. RAI use markedly decreased for PTCs 2 to <4 cm after 2015, when explicit recommendations were made against its use for PTCs <4 cm (4). Still, by 2018, one of five patients with low-risk PTC, including 6% of PTMCs, was reported to have been treated with RAI, suggesting that overtreatment of low-risk PTC with RAI remains a common occurrence.

Consistent with this, studies have shown large variation in adherence to the treatment guidelines regarding the use of RAI, with physician preference or specialty, hospital volume, and patient preference, including worry about cancer progression or death, being predictive of RAI use (27–29). RAI may be indicated for low-risk PTC under some circumstances (e.g., history of high-dose neck irradiation in childhood or adolescence, hereditary syndromes, and contralateral nodularity); however, without information on treatment indication, we could not determine whether RAI use was inappropriate in these cases.

The use of lobectomy increased slightly during the period 2014–2018, consistent with ATA recommendations in support of less extensive surgical management of low-risk tu-

mors; however, the magnitude of increase after 2015 was more subtle than expected. The 2009 guidelines referred to lobectomy as an option for select very low-risk tumors (unifocal, localized, and <1-cm PTC with no aggressive features), while the 2015 adult guidelines considered lobectomy as the preferred treatment option for PTMC and as an option equivalent to total thyroidectomy for larger low-risk (1 to <4 cm) PTCs.

By 2018, lobectomy was performed in around 25% of localized PTCs and 30% of PTMCs. Considering the growing evidence in support of the safety of lobectomy for low-risk PTC (7,30), it is reasonable to predict that its use will increase in the coming years, although it is unclear how other factors might influence future trends. Multiple factors, including physician preferences, patient volumes, and number of years in practice, and patient factors, including disease stage, comorbid conditions, preferences, and access to care, appear to influence decisions regarding the extent of surgical management (31–37).

Based only on 1 year of data (2015–2016), a steeper increase in lobectomy was observed for patients with private insurance/Medicare than those with Medicaid or no insurance, suggestive of socioeconomic disparities in the optimal management of low-risk PTC.

About 1% of adult patients with a diagnosis of PTMC were reported to have been treated without surgery each year. It was not possible to identify the exact proportion of these patients who were managed under an active surveillance protocol because the no surgery group also included patients unable to receive surgery for different reasons, including serious comorbidities or financial hardship; nonetheless, this number appears to have been very small.

Compared with other treatment groups, the no surgery group included a higher proportion of uninsured or Medicaid patients, suggesting lack of access to care rather than active surveillance, as uninsured patients may be less likely to be considered as candidates for active surveillance due to the long-term follow-up requirements (6). Thus, it appears that active surveillance was a very uncommon management strategy for low-risk PTCs, including PTMCs, at least through 2018.

A recent study suggested that while most physicians consider active surveillance to be an appropriate option, less than half reported using it (38), and they infrequently offered it to patients (39). Other barriers for implementation of active surveillance include patient preferences and worry and physician concern over loss to follow-up or malpractice lawsuits (38,40). Active surveillance was only recently introduced in the 2015 ATA guidelines as a viable management option for very low-risk PTC.

In comparison, it took over 20 years for active surveillance to become the preferred treatment option for low-risk prostate cancer (41,42). There is uncertainty regarding the costeffectiveness of a management strategy that requires lifetime medical surveillance, especially for patients diagnosed at younger ages, including many thyroid cancer patients (41,43).

With the increasing number of ongoing clinical trials (41,44,45), it is reasonable to expect an increasing trend for active surveillance in the coming years, although specific decision aid tools (46) or other interventions may be needed to facilitate discussions between clinicians and patients on this topic (47).

The 2015 pediatric thyroid cancer guidelines recommended more restricted use of RAI for low-risk PTCs <4 cm, reflecting a major shift in practice (13–15), perhaps partially influenced by changes to the adult treatment guidelines. It may also reflect growing evidence on the late effects of RAI, including risk of second cancers (48–50). Before 2009, RAI was used more frequently in management of pediatric versus adult PTC, but its use in pediatric PTC then declined precipitously, dropping below adult levels by 2018.

Strengths of this study include reliance on a populationbased dataset with large and representative coverage of the general U.S. population. The inclusion of three calendar years of data after the 2015 ATA guidelines for management of adult and pediatric PTC enabled a more robust assessment of the impact of the most recent recommendations on actual clinical practice. These data also allowed for comparison of treatment trends for low-risk PTC in children versus adults, for whom treatment guidelines are written and published separately by independent guideline committees.

However, we acknowledge the limitations of using SEER data in analyzing treatment practices (51). As the SEER registries provide information only on first-course cancer therapy, the use of more extensive therapy (total thyroidectomy with or without RAI) may have been underestimated if, for instance, such therapies were delayed and performed after disease recurrence or progression. Radiation therapy may also have been underascertained if recorded outside the medical records examined by the registries.

The SEER database has been used to monitor trends and appropriateness of the use of RAI (16,48,52); however, the sensitivity and specificity of this data source for thyroid cancer treatment are unknown. In a comparison between SEER and Medicare data on reporting of radiotherapy for other cancer types, the overall sensitivity was 80%, while specificity was high (91%), meaning that some underestimation of radiation treatment is to be expected, while overestimation is less likely (53). Since we do not expect the validity of these data to change largely over time, the trends described here likely reflect a true reduction in RAI use.

Our estimations are in line with a recent analysis of the National Cancer Database (2004–2016) (54), which also reported decreased utilization of RAI, especially for PTMCs without nodal/metastatic extension (<10% after 2015) (20). In SEER, completion thyroidectomy is coded as total thyroidectomy. Thus, we could not assess if changes in recent guidelines have led to an increase in completion thyroidectomy. This coding protocol also underestimates the number of patients initially selected for lobectomy.

We could not accurately identify nonoperative procedures, such as radiofrequency or other types of ablation techniques, as they are not specifically coded in the SEER database. Rather, these were included in the other/unknown treatment category, which accounted for <1% of patients during the study period.

An additional limitation is the small sample size for the pediatric population and for some race/ethnicity groups (e.g., American Indian/Alaska Native), which prevented finer stratification of these data. SEER collects limited data on socioeconomic indicators, and insurance type was not available after 2016 or before 2007. This, in addition to the lack of information on treatment indication, preferences (physician and patient), treatment facility, and other factors influencing access to care, limited our ability to highlight potential barriers in adherence to the guidelines.

#### Conclusions

Between 2000 and 2018, trends in the reported management of low-risk PTCs in the United States, particularly the decline in RAI use, appeared to correspond to changes in clinical recommendations for management of adult and pediatric differentiated thyroid cancer. Although the use of lobectomy and nonsurgical management did not increase to the extent expected after 2015, it is likely that these options will be more frequently used in the coming years.

There remains a need for studies evaluating patientand physician-specific factors that drive treatment decisionmaking and to identify barriers to the de-escalation of treatment.

#### Authors' Contributions

E.P. was involved in analysis, interpretation, drafting of the article, and approval of the final version; J.A.S. and C.M.K. were involved in concept, interpretation, critical review of the manuscript, and approval of the final version; Y.C. was involved in analysis, interpretation, critical review of the manuscript, and approval of the final version; and S.J.S. and A.B.G. were involved in interpretation, critical review of the manuscript, and approval of the final version.

#### **Author Disclosure Statement**

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All other authors have no disclosure to report.

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#### **Supplementary Material**

Supplementary Material

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