



# Trends in Pediatric Thyroid Cancer Incidence in the United States, 1998-2013

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**BACKGROUND:** Pediatric differentiated thyroid cancer (DTC) rates have increased over time in the United States and worldwide. Improvements in imaging for the diagnosis of DTC have been hypothesized as a potential driver of these increases. This study stratifies temporal trends in pediatric DTC by stage and tumor size to assess whether rates of large, late-stage cancers, which are likely to be clinically meaningful, are increasing over time. **METHODS:** Age-standardized incidence rates (ASRs) of DTC and annual percent changes (APCs) in primary DTC rates were estimated for 0- to 19-year-olds with data from 39 US cancer registries during 1998-2013. **RESULTS:** During 1998-2013, 7296 cases of DTC were diagnosed (6652 papillary cases and 644 follicular cases). APCs of pediatric DTCs significantly increased by 4.43%/y [95% CI, 3.74%/y-5.13%/y], primarily because of increases in papillary histologies. Increasing trends were observed for children aged 10 to 19 years for both sexes and for non-Hispanic whites, non-Hispanic blacks, and Hispanics. Rates increased significantly over the time period for all tumor stages (APC<sub>localized</sub>, +4.06%/y [95% CI, 2.84%/y-5.29%/y]; APC<sub>regional</sub>, +5.68%/y [95% CI, 4.64%/y-6.73%/y]; APC<sub>distant</sub>, +8.55%/y [95% CI, 5.03%/y-12.19%/y]) and across tumor sizes (APC<sub><1 cm</sub>, +9.46%/y [95% CI, 6.13%/y-12.90%/y]; APC<sub>1-2 cm</sub>, +6.92%/y [95% CI, 4.31%/y-9.60%/y]; APC<sub>>2 cm</sub>, +4.69%/y [95% CI, 2.75%/y-6.67%/y]). **CONCLUSIONS:** Significantly increasing rates of DTC over time among 10- to 19-year-olds in the United States are unlikely to be entirely explained by increases in medical surveillance during childhood because rates of large and late-stage DTC are increasing over time. Future studies should examine environmental and other factors that may be contributing to rising DTC rates. *Cancer* 2019;0:1-9. © 2019 American Cancer Society.

**KEYWORDS:** epidemiology, incidence, pediatrics, registries, thyroid cancer.

## INTRODUCTION

Representing 2% to 4% of all pediatric malignancies, differentiated thyroid cancer (DTC) is rare among children and adolescents aged 0 to 19 years.<sup>1,2</sup> Pediatric thyroid cancer rates are also much lower than rates in adults, with pediatric thyroid cancer representing only 2.3% of all thyroid cancer diagnoses.<sup>3</sup> As observed in thyroid cancer occurring during adulthood, an increased incidence of pediatric thyroid cancer over the last decades has been reported in the United States and worldwide.<sup>2,4</sup> In the United States, the incidence rate for 2001-2009 was 6.83 per million with a significant annual percent change (APC) of 4.9%/y.<sup>2</sup> A similar increase was observed when the analysis was restricted to papillary thyroid cancers, which represent the vast majority of DTCs.<sup>5</sup>

In adult DTC, it has been debated whether observed increases in DTC rates are driven by overdiagnosis from screening practices and/or improved imaging or are possibly due to changes in the prevalence of environmental risk factors.<sup>3,6</sup> Incidentally detected DTCs are likely to be smaller, early-stage tumors, whereas larger, late-stage tumors are more likely to be symptomatic and clinically detected. Thus, tumor size and stage can be used as proxies to differentiate increases due to incidental detection during medical surveillance from increases due to the clinical workup of patients with specific symptoms or palpable neck lesions.<sup>3</sup> However, overdiagnosis is less likely to occur in children than adults because thyroid nodule screening would be rarely required for this age group,<sup>7</sup> and medical imaging of the neck would not be usually performed for other clinical purposes.<sup>8</sup>

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These data are based on the December 2015 data submission of the North American Association of Central Cancer Registries. Support for cancer registries is provided by the state, province, or territory in which the registry is located. In the United States, registries also participate in the Surveillance, Epidemiology, and End Results Program (National Cancer Institute), the National Program of Cancer Registries (Centers for Disease Control and Prevention), or both. In Canada, all registries submit data to the Canadian Cancer Registry, which is maintained by Statistics Canada.

Additional supporting information may be found in the online version of this article.

See editorial on pages 1-2 and 1-3, this issue.

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The rarity of pediatric DTC, the lack of information on histologic features, or both have prevented prior studies from analyzing trends by tumor size or cancer stage at diagnosis.<sup>2,9-12</sup> The only prior study to examine DTC trends during 1984-2010 by tumor size in children and young adults included patients 30 years old or younger. Because 85% of the DTC cases occurred among 20- to 30-year-olds, conclusions about the pediatric population were limited.<sup>13</sup>

The current study used 39 US population-based state and metropolitan cancer registries (covering approximately 80% of the US population) to assess pediatric DTC incidence rates and calendar trends during 1998-2013 overall and by age group, sex, histologic type, race/ethnicity, tumor stage, and tumor size.

## MATERIALS AND METHODS

### Study Population

The data were obtained from the North American Association of Central Cancer Registries, which has provided cancer incidence data since 1995 from cancer registries that participate in the National Program of Cancer Registries (Centers for Disease Control and Prevention) and the Surveillance, Epidemiology, and End Results Program (National Cancer Institute). To maximize both the number of years of follow-up and the number of registries included in the analysis, data spanning 1998-2013 from 39 registries were used in this analysis: Alabama, Alaska, Arizona, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Atlanta, Hawaii, Idaho, Illinois, Indiana, Iowa, Kentucky, Louisiana, Maine, Massachusetts, Michigan, Missouri, Montana, Nebraska, New Jersey, New Mexico, New York, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, Texas, Utah, Washington, West Virginia, Wisconsin, and Wyoming. The analysis was approved by the North American Association of Central Cancer Registries (NAACCR) Institutional Review Board.

### Case Definition

DTC cases were classified according to the *International Classification of Diseases for Oncology, Third Edition (ICD-O-3)*, by topography (C73) and histology: papillary (histologic codes 8050, 8052, 8130, 8260, 8340-8344, 8450, and 8452) and follicular (*ICD-O-3* codes 8290, 8330-8332, and 8335). Cases were restricted to children (aged 0-19 years) who were diagnosed with a primary DTC. Second primary DTCs were excluded because of the known impact of cancer treatment, especially radiotherapy, on thyroid cancer risk.<sup>14</sup>

Tumor size was collected routinely between 2004 and 2013 with the introduction of collaborative stages; thus, trends by tumor size are restricted to this time period. Tumor size was categorized as <1, 1 to 2, or >2 cm: 93% of the cases had the size reported. The tumor stage at diagnosis had high rates of missingness in certain included registries, so we restricted stage-specific analyses to the 25 registries that had at least 50% completeness: the stage was known for 97% in these registries. The stage at diagnosis was defined as localized (limited to the thyroid gland), regional (tumor extension beyond the limits of the thyroid gland or spreading by more than 1 lymphatic or vascular supply route), distant (extracervical metastasis), or unknown.<sup>15</sup>

### Statistical Analyses

All incidence rates were age-standardized to the 2000 US standard population and expressed per million person-years of follow-up according to sex, age at diagnosis (0-9, 10-14, or 15-19 years), race/ethnicity (Hispanic, non-Hispanic white, non-Hispanic black, or non-Hispanic other), histologic subtype (papillary or follicular), and tumor size and stage at diagnosis as calculated with the National Cancer Institute's SEER\*Stat software package (version 8.2.1; National Cancer Institute, Bethesda, Maryland). Trends in DTC incidence rates during 1998-2013 were estimated with APCs and corresponding confidence intervals (CIs) with Joinpoint software (version 4.5.0.1). Graphically, trends are presented with a 3-year moving average for each calendar year. Statistical significance was determined on the basis of a *P* value  $\leq .05$ .

## RESULTS

Between 1998 and 2013, a total of 7296 childhood DTCs (age-standardized incidence rate [ASR], 6.66/million) occurred in 39 US cancer registries, including 6652 cases of papillary thyroid cancer (91%; ASR, 6.07/million) and 644 cases of follicular thyroid cancer (9%; ASR, 0.59/million). Girls (*n* = 6028 [83%]; ASR, 11.3/million), 15- to 19-year-olds (*n* = 5578 [76%]; ASR, 20.1/million), and non-Hispanic whites (*n* = 4990 [68%]; ASR, 7.67/million) represented the majority of the cases. Approximately half of the cases were reported in the last 6 years of the 16-year study period, with 599 cases in 2013. Frequencies, ASRs, and APCs for all DTCs by age group categories are presented in Table 1. ASRs calculated for the beginning (1998-2000) and end (2011-2013) of the study period are presented in Supporting Table 1 for sex, histology

**TABLE 1.** ASRs and APCs of Differentiated Thyroid Cancer in Children and Adolescents, 1998-2013, According to Age Category

Variable	All						0-9 y			10-14 y			15-19 y		
	No.	ASR (95% CI)	APC (95% CI)	No.	ASR (95% CI)	APC (95% CI)	No.	ASR (95% CI)	APC (95% CI)	No.	ASR (95% CI)	APC (95% CI)	No.	ASR (95% CI)	APC (95% CI)
Total	7296	6.66 (6.51 to 6.81)	4.43 (3.74 to 5.13)	267	0.52 (0.46 to 0.58)	0.81 (-2.15 to 3.86)	1451	5.32 (5.05 to 5.6)	5.44 (4.19 to 6.70)	5578	20.06 (19.54 to 20.60)	4.33 (3.52 to 5.15)			
Sex															
Female	6028	11.3 (11.02 to 11.59)	4.34 (3.39 to 5.30)	168	0.67 (0.57 to 0.78)	2.15 (-1.90 to 6.37)	1141	8.57 (8.08 to 9.08)	5.27 (3.95 to 6.61)	4719	34.93 (33.94 to 35.94)	4.18 (3.16 to 5.22)			
Male	1268	2.26 (2.14 to 2.39)	4.94 (3.23 to 6.67)	99	0.38 (0.31 to 0.46)	-0.10 (-5.31 to 5.40)	310	2.22 (1.98 to 2.48)	5.67 (2.77 to 8.64)	859	6.01 (5.61 to 6.42)	5.18 (3.47 to 6.92)			
Histologic type															
Papillary	6652	6.07 (5.92 to 6.22)	4.65 (3.87 to 5.43)	245	0.48 (0.42 to 0.54)	-0.05 (-3.30 to 3.32)	1279	4.69 (4.44 to 4.95)	5.67 (4.48 to 6.88)	5128	18.44 (17.94 to 18.96)	4.61 (3.73 to 5.51)			
Follicular	644	0.59 (0.54 to 0.64)	2.08 (0.41 to 3.78)	22	0.04 (0.03 to 0.06)	— <sup>a</sup>	172	0.63 (0.54 to 0.73)	4.15 (0.51 to 7.93)	450	1.62 (1.47 to 1.78)	0.88 (-1.49 to 3.30)			
Race and ethnicity <sup>b</sup>															
Hispanic, all races	1414	6.21 (5.89 to 6.54)	5.10 (3.50 to 6.73)	65	0.54 (0.42 to 0.69)	-1.68 (-8.48 to 5.62)	311	5.33 (4.75 to 5.95)	4.97 (1.94 to 8.09)	1038	18.24 (17.14 to 19.38)	5.58 (3.90 to 7.28)			
Non-Hispanic, white	4990	7.67 (7.45 to 7.88)	4.45 (3.76 to 5.15)	172	0.59 (0.50 to 0.68)	1.70 (-1.55 to 5.07)	951	5.94 (5.57 to 6.33)	5.72 (4.16 to 7.31)	3867	23.31 (22.58 to 24.05)	4.21 (3.40 to 5.03)			
Non-Hispanic, black	350	2.31 (2.07 to 2.57)	3.78 (1.34 to 6.27)	14	0.20 (0.11 to 0.33)	— <sup>a</sup>	79	2.07 (1.64 to 2.58)	— <sup>a</sup>	257	6.70 (5.91 to 7.57)	4.25 (1.90 to 6.66)			
Non-Hispanic, other	419	6.35 (5.75 to 6.99)	4.61 (1.89 to 7.41)	12	0.38 (0.20 to 0.67)	— <sup>a</sup>	89	5.54 (4.45 to 6.81)	3.98 (-0.16 to 8.30)	318	18.87 (16.85 to 21.06)	4.88 (1.65 to 8.22)			

Abbreviations: APC, annual percent change; ASR, age-standardized incidence rate; CI, confidence interval.

ASRs are expressed as cases per million person-years, and APCs are expressed as the percentage per year.

<sup>a</sup>There were too few cases for APCs to be estimated.<sup>b</sup>Race and ethnicity status missing = 3; non hispanic/unknown status = 120.

**TABLE 2.** ASRs and APCs of Differentiated Thyroid Cancer in Children and Adolescents, 1998-2013

Variable	No.	All Patients			
		ASR (95% CI)	APC (95% CI)		
Size		Beginning: 2004-2006	End: 2011-2013	Whole period: 2004-2013	
<1 cm	751	0.75 (0.63 to 0.88)	1.44 (1.28 to 1.62)	1.08 (1.00 to 1.16)	9.46 (6.13 to 12.90)
1-2 cm	1298	1.41 (1.25 to 1.58)	2.37 (2.16 to 2.58)	1.87 (1.76 to 1.97)	6.92 (4.31 to 9.60)
>2 cm	2695	3.26 (3.02 to 3.52)	4.5 (4.22 to 4.8)	3.88 (3.74 to 4.03)	4.69 (2.75 to 6.67)
Unknown	367	0.56 (0.46 to 0.67)	0.54 (0.45 to 0.65)	0.53 (0.48 to 0.59)	-0.79 (-4.47 to 3.03)
Stage at diagnosis <sup>a</sup>		Beginning: 1998-2000	End: 2011-2013	Whole period: 1998-2013	
Local	1751	2.58 (2.27 to 2.93)	4.49 (4.07 to 4.94)	3.44 (3.28 to 3.60)	4.06 (2.84 to 5.29)
Regional	1493	2.16 (1.88 to 2.48)	4.23 (3.82 to 4.66)	2.94 (2.79 to 3.10)	5.68 (4.64 to 6.73)
Distant	118	0.14 (0.07 to 0.24)	0.43 (0.31 to 0.59)	0.24 (0.19 to 0.28)	8.55 (5.03 to 12.19)
Unknown	98	0.21 (0.13 to 0.33)	0.11 (0.05 to 0.2)	0.19 (0.16 to 0.24)	-4.09 (-9.06 to 1.15)

Abbreviations: APC, annual percent change; ASR, age-standardized incidence rate; CI, confidence interval.

The periods for which data were available are shown. ASRs are expressed as cases per million person-years, and APCs are expressed as the percentage per year.

<sup>a</sup>The analysis for the stage at diagnosis is restricted to a subset of 25 registries that had greater than 50% completeness for the time period under study.

type, and race and ethnicity and in Table 2 for tumor size and stage at diagnosis.

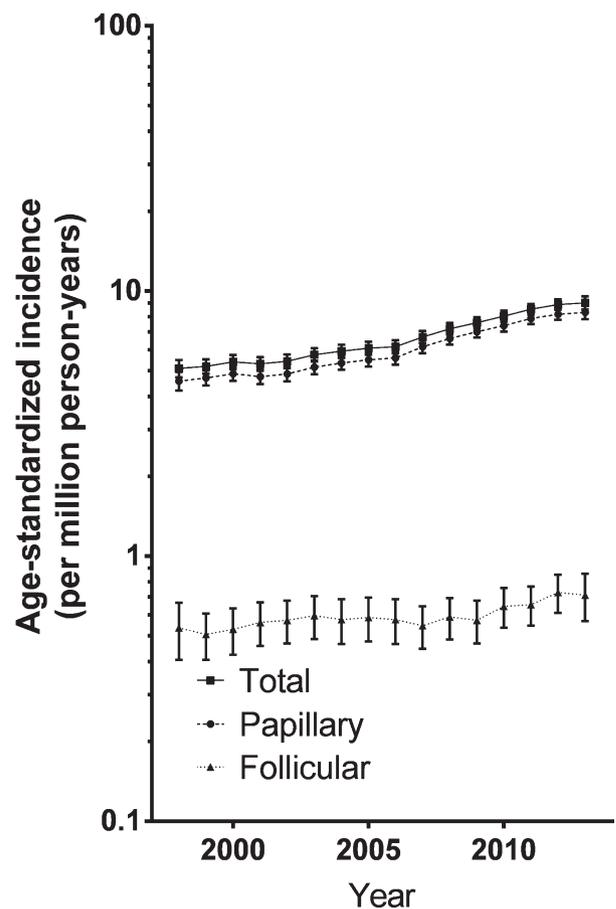
Overall, pediatric DTC incidence rates significantly increased by 4.43%/y (95% CI, 3.74%/y-5.13%/y) from 4.77/million (95% CI, 4.26/million-5.33/million) in 1998 to 8.82/million (95% CI, 8.13/million-9.56/million) in 2013 (Fig. 1). The trends reported for all DTCs were largely driven by papillary histologic types (Fig. 1), but significant increasing trends were also reported for follicular histologic subtypes (APC, +2.08%/y [95% CI, 0.41%/y-3.78%/y]).

Age-specific incidence rates for all DTCs by sex are presented in Figure 2. From 1998 to 2013, significant increasing trends were observed only for 10- to 19-year-olds (Table 1 and Fig. 2). Significant increasing trends were observed for both sexes (Fig. 2) and for all races/ethnicities (Fig. 3).

Rates increased significantly over the time period for both localized tumors (APC<sub>localized</sub>, +4.06%/y [95% CI, 2.84%/y-5.29%/y]) and more aggressive tumors (APC<sub>regional</sub>, +5.68%/y [95% CI, 4.64%/y-6.73%/y]; APC<sub>distant</sub>, +8.55%/y [95% CI, 5.03%/y-12.19%/y]). Rates for tumors less than 1 cm in size (APC<sub><1 cm</sub>, +9.46%/y [95% CI, 6.13%/y-12.90%/y]) increased more rapidly than rates for tumors larger than 2 cm (APC<sub>>2 cm</sub>, +4.69%/y [95% CI, 2.75%/y-6.67%/y]; Figs. 4 and 5 and Table 2).

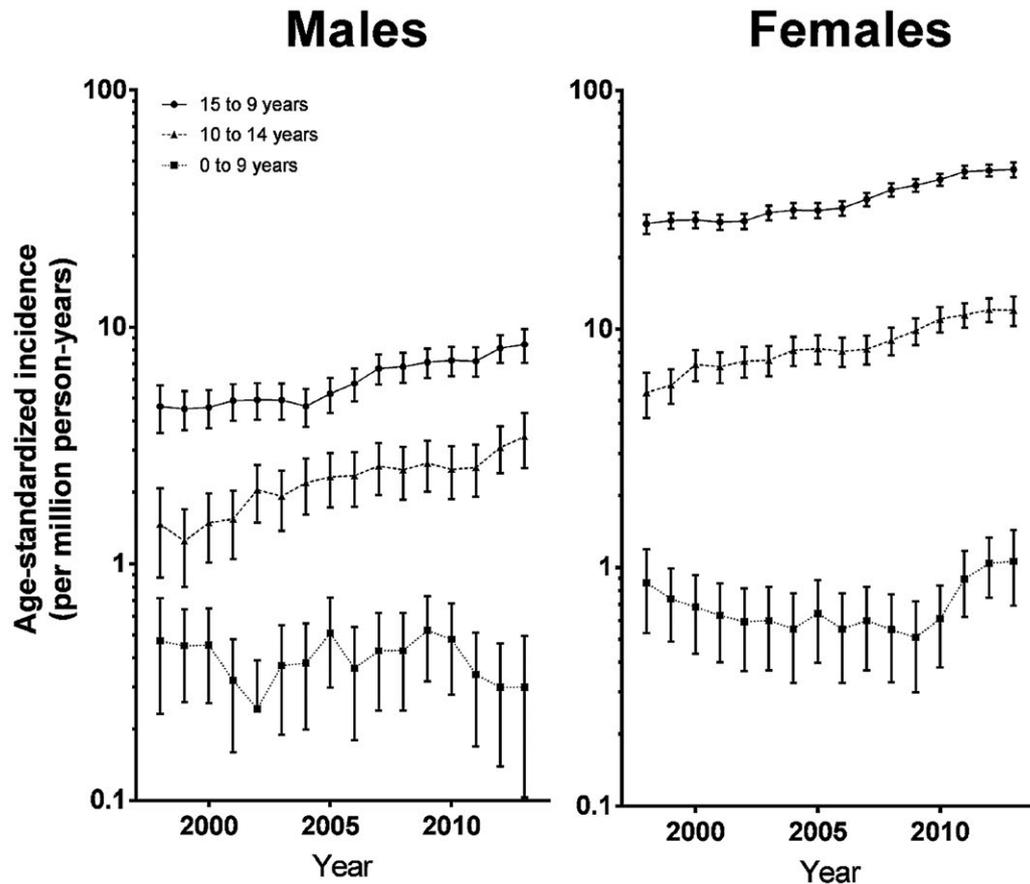
## DISCUSSION

With 7296 available cases from 39 US cancer registries covering approximately 80% of the US population, this study included 1.5 times more cases than the next largest study to date.<sup>2</sup> During 1998-2013, rates of DTC increased significantly among children and adolescents aged 10



**Figure 1.** Trends in differentiated thyroid cancer incidence by histology: 3-year moving average.

to 19 years and across sexes and all races/ethnicities. Because the rates for both smaller, early-stage tumors and larger, later stage tumors increased significantly over time, rising rates are unlikely to be entirely explained by



**Figure 2.** Trends in differentiated thyroid cancer incidence by age and sex: 3-year moving average. Error bars that would have crossed the x-axis have been truncated at 2013.

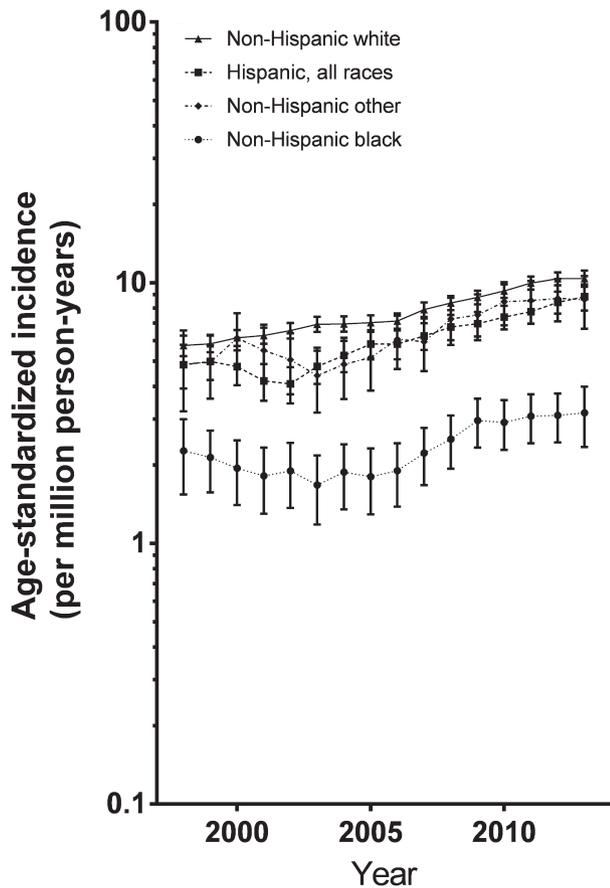
increases in the follow-up of thyroid conditions or other conditions that involve imaging of the neck or thyroid palpation and more sensitive diagnostic technology; environmental and individual factors may also have affected rising trends.

The incidence of DTC is known to vary widely according to age, sex, and race/ethnicity. Very low in the first years of life, the incidence rates increase dramatically in adolescence, and they are generally higher in girls than boys.<sup>5</sup> This study is consistent with prior findings, with rates increasing from 0.52 to 20.06 per 1,000,000 person-years in the 0- to 9-year and 15- to 19-year age groups, respectively. The observed highest rates of incidence in girls and non-Hispanic whites and the observed lowest rates in non-Hispanic blacks are consistent with previous reports.<sup>2,5,10,12</sup>

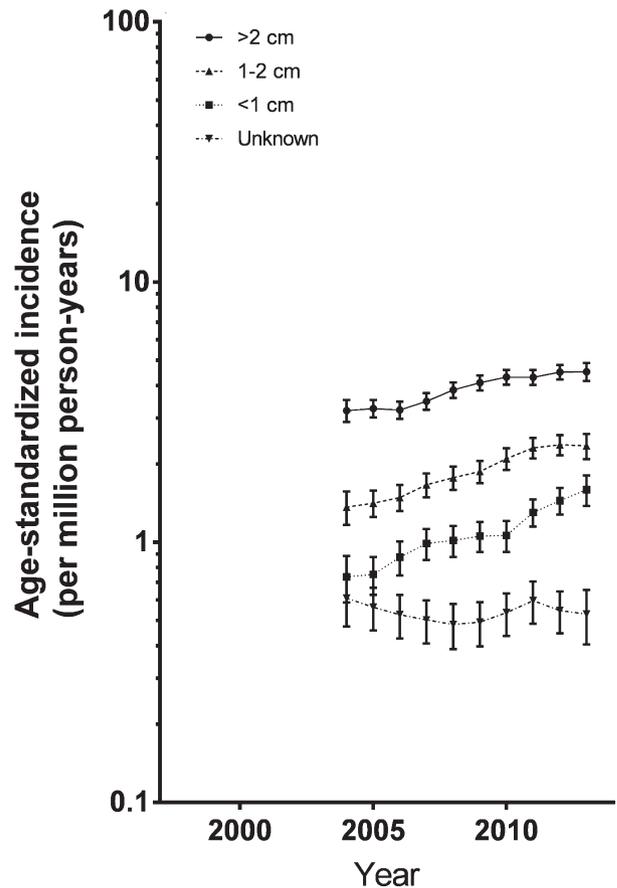
We observed a significant increase in pediatric DTC incidence of 4.43%/y during the period 1998-2013, and this was consistent with the increasing trend of 4.9%/y reported in a previous analysis in the United

States of 4812 cases collected in 47 population-based state cancer registries during 2001-2009.<sup>2</sup> In our study, the observed increasing rates over time in all DTC incidence were driven by papillary histologies (91% of all cases). However, rates of follicular DTC also increased significantly by 2.08%/y.

The main objective of our study was to investigate whether trends in DTC in children and adolescents were consistent with increased medical surveillance and subsequent incidental detection of small and indolent DTCs. In adulthood, the observed increase in DTC rates has been suspected to be linked to the introduction and increasing widespread use of diagnostic ultrasonography and fine-needle aspiration biopsies starting in the 1980s. Indeed, these technologies are able to detect incidental cancers, mostly localized and/or small tumors that are unlikely to have presented clinically.<sup>6,16-18</sup> However, growing evidence of a true increase in DTC in adults is now supported by increasing rates of larger and advanced-stage DTCs over the past several decades.<sup>3</sup> We



**Figure 3.** Trends in differentiated thyroid cancer incidence by race and ethnicity.



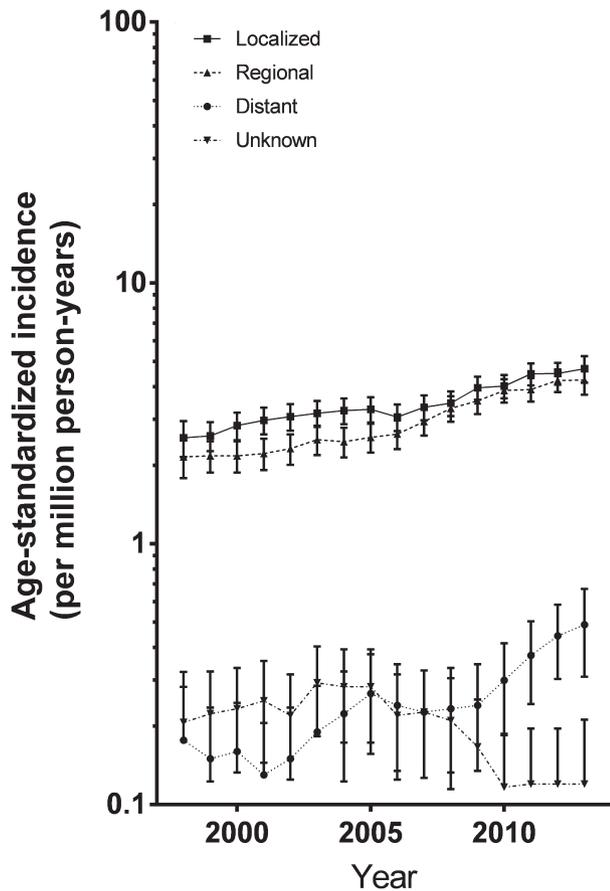
**Figure 4.** Trends in differentiated thyroid cancer incidence by tumor size: 3-year moving average. The study period is limited to 2004-2013, during which tumor size was routinely collected.

have shown for the first time that similar patterns have occurred among children and adolescents, with rates of DTC increasing across stages and tumor sizes. Moreover, we have observed that the annual increases in the rates of distant DTC are higher than those observed for localized or regionally extended DTC. A prior study reported significant increases in DTC rates for all tumor sizes in girls and for tumors >1 cm for boys; however, only 15% of the patients were younger than 20 years, and this precluded a comparison with our study.<sup>13</sup> From a clinical point of view, the likelihood of an overdiagnosis effect is smaller in children and adolescents than adults because this population is not usually subjected to thyroid screening or medical imaging of the neck for other indications.<sup>8</sup> However, the significant annual increases in the rates of small and local-stage DTCs suggest that we might not be able to rule out a contribution of overdiagnosis to rising pediatric DTC rates.

Age-specific trends in thyroid cancer rates in the pediatric population have seldom been studied because of

the rarity of thyroid cancer during childhood, especially before the age of 10 years. The large number of cases available in our study, due to the substantially longer period and larger population studied, allowed us to conduct such analyses in contrast to previous studies.<sup>2,9,13</sup> No significant increase in DTC rates among 0- to 9-year-olds was observed, although only 267 DTC cases occurred in this age group. For older age groups, our results confirmed the increasing trends reported previously among 10- to 14-year-olds<sup>13</sup> and 15- to 19-year-olds.<sup>2,11,13</sup> Consistent with prior studies, we observed significant increases in DTC rates among non-Hispanic white and black children.<sup>2,11</sup>

Observed differences in trends across demographic subgroups may result from 1 or more factors. These might include socioeconomic disparities and associated differential access to medical care. Another possibility could be differences in environmental or exogenous exposures. Host factors (obesity, hormonal factors, or other physiological factors) may be important. Genetic variation or



**Figure 5.** Trends in differentiated thyroid cancer incidence by stage at diagnosis: 3-year moving average. The analysis is limited to the 25 registries that had at least 50% completeness for this variable, considering only these 25 registries, the stage was known for 97% of cases. Error bars that would have crossed the x-axis have been omitted.

gene-environment interactions may also play a role. In our analysis, increasing rates were observed mostly after the age of 10 years and were not restricted to 1 race/ethnicity or sex. Accordingly, global environmental or behavioral factors rather than socioeconomic status or genetic background are more likely to explain this increase.

Studies examining etiological factors associated with thyroid cancer have generally focused on adult thyroid cancers.<sup>19</sup> Large epidemiological studies of DTC risk factors among children are needed to provide insight into etiology. However, known risk factors for thyroid carcinogenesis among adults may also be associated with childhood DTC. Ionizing radiation is the best known risk factor for thyroid cancer. Elevated rates of DTC were observed after the Chernobyl accident in 1986,<sup>20</sup> during the follow-up of atomic bomb survivors,<sup>21</sup> and after medical exposure.<sup>22</sup> Indeed, diagnostic imaging during

childhood has been associated with a 7-fold increase in thyroid cancer per gray among adults.<sup>22</sup> Increased risks associated with computed tomography (CT) scan exposure have also been reported,<sup>23</sup> but the association with diagnostic imaging using lower radiation doses (ie, conventional radiology procedures and dental x-rays) is still unclear.<sup>24</sup> It should be noted that although the studies highlighted here focused on childhood exposure to radiation, thyroid cancers were diagnosed at any time, including adulthood. The increased radiation exposure of children resulting from the large increase in medical diagnostic imaging use over time in pediatrics, especially diagnostic procedures associated with high radiation doses (eg, CT scans),<sup>25</sup> might have contributed to rising pediatric DTC rates. Indeed, between 1996 and 2005, the use of CT scans tripled for children 5 to 14 years old in the United States, and approximately 4.25 million pediatric CTs are performed annually.<sup>26</sup> Some previous analyses of increasing pediatric DTC trends have hypothesized that radiotherapy for prior malignancies may be contributing to rising rates<sup>10,11</sup>; however, this could not be the case in our study because we restricted the analysis to first primary thyroid cancers.

Rates of pediatric DTC are higher in girls than boys, and these differences are even greater after the beginning of puberty.<sup>2,13</sup> The predominance in girls is hypothesized to be related to sex hormone changes during puberty influencing thyroid carcinogenesis. Indeed, estrogen is known to be a potent growth factor for both benign and malignant thyroid cells. It exerts its growth-promoting effect through a classic genomic and nongenomic pathway mediated via a membrane-bound estrogen receptor.<sup>27</sup> Obesity, through estrogen-related pathways and insulin-resistance mechanisms, is also likely to affect thyroid carcinogenesis, as suggested by the positive association of obesity in childhood and adulthood with adult DTC reported in epidemiological studies.<sup>28-30</sup> Thus, the epidemic of obesity reported in the United States<sup>31</sup> and in other developed countries might explain part of the observed increase in pediatric DTC rates, although studies focused on examining associations between obesity and childhood DTC risk are needed. Other environmental risk factors such as endocrine-disrupting chemicals (eg, pesticides, bisphenol A, perchlorate, and polybrominated diphenyl ethers) have been hypothesized as potential risk factors for DTC because of their effect on thyroid hormone metabolism,<sup>32,33</sup> although these associations have not been consistently observed.<sup>34</sup>

The strengths of this study include the large number of cases available, even for the youngest age group;

the quality standards of the North American Association of Central Cancer Registries; and the coverage of approximately 80% of the US population. Information on tumor size and stage allowed us to study a potential overdiagnosis effect on rising rates of pediatric DTC. Although information on tumor stage was incomplete, once we restricted the analyses to the 25 registries with more complete stage data, stage information was available for 97% of the cases. The variation of completeness of these variables over the study period might have had a small impact on size-specific incidence trends. However, the consistency of the results for both tumor size and cancer stage is not in favor of such a bias. Other limitations included a relatively short study period (15 years) and the possible increase in the quality of case ascertainment over time, which might have influenced increasing trends. Last, cancer registries do not collect information on risk factors such as medical radiation exposure and obesity, and this prevents the evaluation of the role of these potential risk factors in increasing rates of DTC.

Rates of pediatric DTC increased significantly between 1998 and 2013 among both boys and girls and across racial and ethnic groups. This trend is unlikely to be explained solely by increased medical surveillance or improved detection because small, early-stage tumors and larger, late-stage tumors have increased over the study period. Additional studies are needed to explore environmental, dietary, and genetic factors that might be involved in the physiopathology of pediatric thyroid cancer, although these studies will be challenging because of the rarity of these cancers.

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## CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

## AUTHOR CONTRIBUTIONS

**Marie-Odile Bernier:** Conceptualization, formal analysis, methodology, project administration, visualization, writing—original draft, and writing—review and editing. **Diana R. Withrow:** Conceptualization, data curation, formal analysis, methodology, software, writing—original draft, and writing—review and editing. **Amy Berrington de Gonzalez:** Conceptualization, funding acquisition, methodology, writing—original draft, and writing—review and editing. **Clara J. K. Lam:** Resources, writing—original draft, and writing—review and editing. **Martha S. Linet:** Methodology, writing—original draft, and writing—review and editing. **Cari M. Kitahara:** Conceptualization, methodology, writing—original draft, and writing—review and editing. **Meredith S. Shiels:** Conceptualization, formal analysis, methodology, supervision, validation, writing—original draft, and writing—review and editing.

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