

Regional Differences in Opinions on Adjuvant Radioactive Iodine Treatment of Thyroid Carcinoma within Canada and the United States

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Objective: To identify regional differences in recommendations for radioactive iodine remnant ablation (RRA) in early stage well-differentiated thyroid carcinoma (WDTC) within Canada and the United States. *Design:* A cross-sectional written survey of a sample of physicians in specialties potentially involved in thyroid cancer care was performed in 2006. Participants were asked if they recommended RRA for a hypothetical 38-year-old woman with a solitary, 1.6-cm papillary carcinoma resected by total thyroidectomy. Exploratory regional comparisons were performed using Student *t* tests or analysis of variance. The regions studied were western Canada, eastern Canada (Ontario, the Maritimes), Quebec, the northeastern United States, the western and midwestern United States, and the southern United States. In a secondary multivariable logistic regression analysis, we explored potential relationships between individual respondent characteristics RRA recommendations. *Main outcome:* Agreement with case-based RRA recommendations was measured on a Likert scale of 1 to 7 (7 = strongest agreement). *Results:* The effective response rate was 56.3% (486/864). There were significant differences in RRA recommendations among the regions studied ($F = 11.99$, 5 df, $p < 0.001$); national boundaries did not explain regional variations. For the sample case, the strongest support for RRA was in Quebec and the southern United States, intermediate support in eastern Canada and the northeastern United States, and the least support in western Canada and the western and midwestern United States. Academic affiliation and surgical specialty were independently inversely associated with strong RRA recommendations. *Conclusions:* There are significant regional differences in physician-based RRA recommendations in early stage WDTC within Canada and the United States. Physician specialty and practice characteristics may influence RRA recommendations.

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Introduction

THE INCIDENCE OF THYROID carcinoma is rising in Canada (1) and the United States (2,3). Early stage papillary thyroid cancer accounts for the majority of the observed increase in incidence of thyroid cancer (2). Recommended treatments for well-differentiated thyroid carcinoma (WDTC), including papillary or follicular cancer, endorsed by international clinical practice guidelines include thyroidectomy, thyroid hormone suppressive therapy, and sometimes adjuvant radioactive iodine remnant ablation (RRA) (4–8). However, the use of RRA in early stage WDTC is controversial. Potential reasons for this controversy include the observation that the risk of thyroid cancer–related mortality is low in this group (2,9) and the fact that there are no randomized controlled trials of RRA with long-term outcome data (10). Pooled analyses of retrospective series suggest that the use of adjuvant RRA in early stage WDTC may be associated with a reduced risk of local regional disease recurrence and distant metastases (10). In a survey of American Thyroid Association (ATA) members performed over a decade ago, 61% of respondents recommended adjuvant RRA for a hypothetical sample case of a 39-year-old woman with a 2.0-cm solitary papillary carcinoma, with no consensus in radioactive iodine dosing (11).

We recently completed the Canadian–American Thyroid Cancer Survey of thyroid cancer–related specialty physicians in Canada and the United States. In this secondary analysis, we explored whether regional differences in the approach to adjuvant radioactive iodine treatment of WDTC currently exist within Canada and the United States. Potential regional differences in treatment of WDTC have great implications for regional cancer resource utilization, given the rising incidence burden of this disease in Canada (1) and the United States (2,3). In another secondary analysis, we explored potential associations between characteristics of individual respondents and strong recommendations for radioactive iodine remnant ablation in early stage thyroid cancer.

Methods

Questionnaire design and distribution to participants

We performed a cross-sectional self-completed written survey mailed to a sample of thyroid cancer–related specialty physicians in Canada and the United States in the year 2006. We presented various statements accompanied by a Likert scale framed on a disagree–agree continuum (12) (using a scale of 1 to 7, with 7 representing the strongest agreement). We also asked some categorical response questions. Test–retest reliability of the survey was established in a subset of 34 individuals who completed the survey a second time approximately 2 weeks after the first administration.

The English-language survey was mailed to 731 thyroid cancer–related specialty physicians in Canada who were listed in active practice in the Canadian Medical Directory (2005 MD Select Software, Scott's Directories, Toronto, Ontario, Canada). The Canadian physicians included those in endocrinology, nuclear medicine, and head and neck surgery (and related specialties). The survey was also mailed to 304 ATA member physicians in the United States whose addresses were listed publicly on the ATA website (13). Canadian physicians whose preferred language was French or who resided

in Quebec also received a French version of the questionnaire. We provided self-addressed, stamped return envelopes to maximize the response rate (14,15). There were two mailings of the survey within Canada and one in the United States. Informed consent for participation in the study was implied by completion of the survey and the study was approved by the University Health Network Research Ethics Board.

Statistical analyses

Descriptive information such as response rates and the degree of agreement with Likert scale questions were described using the number (percent) for categorical variables or the mean (standard deviation, SD) for continuous variables. Numerical Likert scale responses were assumed to be continuous for the purpose of analysis (since analysis of data from rating scales as if they are interval is thought to be acceptable under most circumstances [12]). Student *t* tests were used to compare Likert scale responses between countries. Analysis of variance was used to compare Likert scale responses among regions. Chi-squared analyses were performed in the comparison of categorical responses among regions.

The Canadian regions studied included 1) western Canada (British Columbia, Alberta, Saskatchewan, and Manitoba), 2) eastern Canada (Ontario, New Brunswick, Newfoundland/Labrador, and Nova Scotia), and 3) Quebec. Quebec (Canada) was grouped individually, as it is recognized as a distinct cultural region within Canada. No Canadian thyroid cancer specialty physicians were identified in Prince Edward Island or the Canadian Northern Territories, precluding inclusion in the study. The categorization of states in the United States was based on the U.S. Census Bureau (16). The following U.S. regions were studied: 1) West and Midwest (Arizona, Colorado, Utah, Nevada, California, Oregon, Washington, Indiana, Illinois, Michigan, Ohio, Wisconsin, Minnesota, Missouri, and Nebraska), 2) the Northeast (Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont, New Jersey, New York, and Pennsylvania), and 3) the South (District of Columbia, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, Alabama, Kentucky, Mississippi, Tennessee, Arkansas, Louisiana, Oklahoma, and Texas). No potential participants from the following states were identified on the ATA website: Alaska, Wyoming, Arkansas, Delaware, Hawaii, Idaho, Iowa, Kansas, Montana, New Mexico, North Dakota, South Dakota, and West Virginia, precluding inclusion of these states in the analyses. Data from the three Canadian and three American regions were analyzed concurrently, unless otherwise specified.

In a secondary analysis, a backward conditional logistic regression analysis was performed to identify demographic or practice characteristics of individual respondents that independently predicted of strong agreement with administration of RRA in the sample case of a patient with a 1.6-cm solitary papillary cancer (strong agreement defined by a score 6 or 7 out of 7). The variables included in the initial regression model were: university affiliation (yes/no), gender (male/female), self-reported specialty (surgery or nuclear medicine respectively compared to endocrinology-related specialties), and duration of experience treating thyroid cancer (categorical variable in 5-year increments ranging from <5 years to >20 years, excluding those who do not treat thyroid cancer). The criterion for removal in the stepwise model was set at $\alpha = 0.10$.

The results of the logistic regression analysis were reported as coefficient, corresponding standard errors, estimate of odds ratio and corresponding 95% confidence intervals, and associated *p* values. The goodness-to-fit of the final model was assessed using the Hosmer–Lemeshow test (17).

Missing or uninterpretable responses were excluded from the analyses, unless otherwise specified. All statistical tests were performed using two-sided tests at the 0.05 level of significance. The statistical analyses were performed using SPSS 12.0 (SPSS Inc., Chicago, IL).

Results

Characteristics of participants

We mailed the questionnaire to 731 physicians in Canada and 304 physicians in the United States. There were 128 individuals from Canada and 11 from the United States who returned the coversheet (without completing the questionnaire), indicating that they did not treat thyroid cancer. There were 32 surveys (19 from Canada and 13 from the United States) that were returned to the sender because the physician had retired, died, or moved with no forwarding address. These individuals were excluded from the relevant response rate. For the Canadian sample, the relevant response rate was 52.7% (308/584). For the sample from the United States, the relevant response rate was 63.6% (178/280). The percentage of respondents (*n* = 486) from each region was as follows: western Canada, 37.7% (*n* = 61); eastern Canada, 46.1% (*n* = 152); Quebec, 39.7% (*n* = 95); the western and midwestern United States, 57.4% (*n* = 62); the northeastern United States, 59.6% (*n* = 65); the southern United States, 58.6% (*n* = 51). The baseline characteristics of respondents are shown in Table 1.

The majority of respondents were affiliated with a university. Males comprised the majority of respondents. The largest proportion of respondents from each region was endocrinologists (treating adults). The majority of U.S. respondents had >20 years of experience treating thyroid carcinoma (Table 1).

Opinions on management of a hypothetical case of papillary thyroid cancer

Within the questionnaire, a hypothetical sample case of early stage papillary cancer was described. The case was described as a 38-year-old previously healthy woman who presented with an asymptomatic thyroid nodule, found to be suspicious for papillary cancer on fine needle aspiration biopsy. At total thyroidectomy, a solitary papillary cancer measuring 1.6 cm in maximal diameter was completely resected. The described cancer did not show any tall cell variant, vascular invasion, lymphatic invasion, or extra-thyroidal extension. Resection margins and a limited lymph node dissection were negative for tumor. There was no past history of radiation exposure and the family history was unremarkable. Proposed statements related to this case are shown in Table 2. Agreement with these statements was measured on a scale of 1 to 7 (with 7 representing the strongest agreement).

There were no significant differences in national responses between the Canada and the United States with respect to recommendations on the administration of RRA in the sample case (470 quantifiable responses, *t* = 0.859, 468 df, *p* = 0.391). The mean agreement score out of 7 for administration of RRA in the sample case was as follows: Canada, 5.44 (SD 1.62) (*n* = 294); United States, 5.30 (SD 1.78) (*n* = 176). Given the lack of significance of nationality in explaining RRA recommendations, we proceeded to explore for regional differences

TABLE 1. CHARACTERISTICS OF THE RESPONDENTS FROM CANADA AND THE UNITED STATES

Characteristic ^a	% (no. of responses from each region)						
	Western Canada	Eastern Canada	Quebec Canada	Western and midwestern United States	Northeastern United States	Southern United States	
Gender: male	68.9 (42)	69.7 (106)	70.5 (67)	83.3 (50)	86.2 (56)	78.4 (40)	
University affiliation	90.2 (55)	68.4 (104)	80.0 (76)	85.5 (53)	90.8 (59)	66.7 (34)	
Primary specialty	Endocrinology	47.5 (29)	60.1 (89)	61.3 (57)	83.6 (46)	84.4 (54)	87.2 (41)
	Nuclear medicine	29.5 (18)	18.2 (27)	32.3 (30)	3.6 (2)	3.1 (2)	4.5 (2)
	General surgery ^b	6.6 (4)	4.7 (7)	1.1 (1)	3.6 (2)	6.3 (4)	0 (0)
	Otolaryngology ^b	11.5 (7)	12.8 (19)	0 (0)	3.6 (2)	3.1 (2)	6.4 (3)
	Pediatric endocrinology	3.3 (2)	3.4 (5)	3.2 (3)	1.8 (1)	0 (0)	0 (0)
	Internal medicine	1.6 (1)	0 (0)	2.2 (2)	0 (0)	0 (0)	0 (0)
	Other	0 (0)	0.7 (1)	0 (0)	3.6 (2)	3.1 (2)	2.1 (1)
Years treating thyroid cancer	<5 ^c	17.2 (10)	15.8 (23)	6.5 (6)	1.6 (1)	3.1 (2)	2.0 (1)
	5.1–10	32.8 (19)	15.8 (23)	19.4 (18)	8.1 (5)	10.9 (7)	9.8 (5)
	10.1–15	24.1 (14)	16.4 (24)	26.9 (25)	11.3 (7)	9.4 (6)	15.7 (8)
	15.1–20	10.3 (6)	17.8 (26)	11.8 (11)	21.0 (13)	4.7 (3)	9.8 (5)
	>20	15.5 (9)	34.2 (50)	35.5 (33)	58.1 (36)	71.9 (46)	62.7 (32)

^aMissing or uninterpretable responses were excluded.

^bGeneral surgery or otolaryngology categories required a listing of a subspecialty interest in head and neck.

^cIncludes eight individuals from Canada and one from the United States who reported that they did not currently treat thyroid cancer but completed the survey.

TABLE 2. COMPARISON OF REGIONAL OPINIONS ON MANAGEMENT OF A HYPOTHETICAL CASE OF A 38-YEAR-OLD WOMAN WITH A 1.6-CM SOLITARY PAPILLARY CARCINOMA RESECTED AT TOTAL THYROIDECTOMY^a

Statement	Mean score of agreement on Likert scale (95% confidence interval; no. of responses from each region)						F value (df1, df2) ^b	p value
	Western Canada	Eastern Canada	Quebec Canada	Western and midwestern United States	Northeastern United States	Southern United States		
1. I would consider this patient's risk of thyroid cancer-related mortality as low.	6.24 (5.97, 6.51; 59)	6.25 (6.10, 6.40; 146)	6.26 (6.05, 6.47; 92)	6.48 (6.22, 6.75; 62)	6.43 (6.17, 6.69; 65)	6.10 (5.85, 6.34; 51)	1.23 (5, 469)	0.295
2. I would recommend that this patient receive radioactive iodine remnant ablation (RRA).	4.58 (4.16, 5.00; 57)	5.37 (5.09, 5.65; 144)	6.08 (5.84, 6.31; 93)	4.52 (n = 3.97, 5.06; 62)	5.46 (5.05, 5.87; 63)	6.06 (5.80, 6.32; 51)	11.99 (5, 464)	0.001
3. If the patient expressed a desire to become pregnant in the next couple of years, this issue would influence my recommendation to administer RRA or not.	3.82 (3.33, 4.30; 54)	3.67 (3.33, 4.01; 140)	3.33 (2.92, 3.74; 90)	3.49 (2.96, 4.03; 61)	3.95 (3.47, 4.44; 64)	3.72 (3.19, 4.24; 50)	0.95 (5, 453)	0.451
4. If this patient's resected tumor was a 5.0 cm papillary cancer, I would recommend RRA administration.	6.46 (6.28, 6.63; 59)	6.64 (6.49, 6.79; 144)	6.45 (6.13, 6.76; 92)	6.23 (5.88, 6.58; 61)	6.77 (6.61, 6.92; 64)	6.80 (6.69, 6.92; 51)	2.75 (5, 465)	0.018

^aRespondents were asked how strongly they agreed with each statement on a scale of 1 to 7 (1 representing strongest disagreement and 7 representing strongest agreement); missing or "don't know" or uninterpretable responses were excluded from analysis.

^bdf1 = numerator degrees of freedom (between groups); df2 = denominator degrees of freedom (within groups).

within the two countries, in further combined analyses (Table 2).

There was no significant variability in agreement with a statement that the risk of thyroid cancer-related mortality is low in the sample case presented (Table 2). However, there were significant regional differences in the recommendation for RRA in this case, with the strongest support for RRA expressed in Quebec and the southern United States and the least support from western Canada and the western and midwestern United States (Table 2). Intermediate support for the use of RRA in the sample case was observed in eastern Canada and the northeastern United States. There was no significant regional difference in opinions on whether RRA recommendations should change if the individual described in the sample case expressed a desire to become pregnant in the next couple of years (Table 2). Significant regional differences in RRA recommendations were also observed if the sample case was modified such that a 5.0-cm tumor was resected, with the strongest recommendations supporting RRA in the southern United States and the least regional support in the western and midwestern United States (Table 2). Moreover, for each region studied, general support of RRA was greater in the case of the 5.0-cm tumor compared to the 1.6-cm tumor (as reflected by generally higher mean agreement scores). The dose recommendation for RRA for the sample case (1.6-cm tumor), ranged from strongly discouraging RRA to the use of >100 mCi; however, in each region, the most frequently selected single dose activity was 100 mCi (Table 3). It is important to note that in western Canada, the western and midwestern United States, and the northeastern United States, dose activities ranging from 29.9 to 99 mCi were selected by more than half of respondents. Strong discouragement of RRA use in the sample case in question (1.6-cm primary papillary tumor) was expressed by about 10% of respondents in western Canada and the western/midwestern United States; whereas none of the respondents from Quebec or the southern United States strongly discouraged RRA for the sample case (Table 3).

Opinions on which thyroid cancer patient subgroups should receive RRA and dosing

We asked respondents about their general opinions on RRA, focusing on which patient subgroups should receive RRA and dosing. We observed significant regional differences in opinions on which patients should receive RRA as well as dosing (Table 4). Quebec physicians held the strongest beliefs that all papillary thyroid cancer patients should receive RRA, with lower agreement scores in all other regions. Quebec and southern U.S. physicians most strongly supported RRA administration for primary thyroid cancers >1.5 cm in diameter, with the least support from the western/midwestern United States and western Canada (Table 4). In cases of thyroid cancer with lymph node metastases, physicians from Quebec, eastern Canada, and the southern United States, most strongly supported RRA administration, whereas the least support was observed in the western/midwestern United States (Table 4). Furthermore, respondents from Quebec had the highest mean agreement scores with a statement suggesting that all patients with papillary thyroid cancer should receive ≥ 100 mCi of radioactive iodine for remnant ablation; while the lowest mean agreement scores for this statement were observed in the northeastern United States, western Canada, and the western/midwestern United States.

Relationships between characteristics of individual respondents and recommendations for RRA in the sample case of early stage WDTC

A strong recommendation for RRA for the sample case of a 38-year-old woman with a 1.6-cm solitary papillary carcinoma was independently predicted by the following individual respondent characteristics: non-university affiliation (odds ratio [OR] 1.71, 95% confidence interval [CI] 1.02, 2.88, $p = 0.043$) and physician specialty compared to endocrinology ($p < 0.001$ overall, surgery OR = 0.27 [95% CI 0.15, 0.52, $p < 0.001$], and nuclear medicine OR = 1.47 [95% CI 0.84, 2.58, $p = 0.181$]) (final model $n = 440$, Cox and Snell $r^2 = 0.057$,

TABLE 3. COMPARISON OF REGIONAL OPINIONS ON RADIOACTIVE IODINE DOSING RECOMMENDATIONS FOR REMNANT ABLATION FOR A HYPOTHETICAL CASE OF A 38-YEAR-OLD WOMAN WITH A 1.6-CM SOLITARY PAPILLARY CARCINOMA RESECTED AT TOTAL THYROIDECTOMY

Dose of radioactive iodine recommended for remnant ablation in this case ^a	% positive responses for each choice ^b (no. of responses from each region)					
	Western Canada (n = 49)	Eastern Canada (n = 140)	Quebec Canada (n = 92)	Western and midwestern United States (n = 57)	Northeastern United States (n = 62)	Southern United States (n = 51)
29.9 mCi	22.4 (11)	6.4 (9)	14.1 (13)	21.1 (12)	11.3 (7)	25.5 (13)
30–99 mCi	24.5 (12)	15.0 (21)	9.8 (9)	22.8 (13)	43.5 (27)	17.6 (9)
100 mCi	30.6 (15)	60.7 (85)	62.0 (57)	38.6 (22)	32.3 (20)	49.0 (25)
>100 mCi	2.0 (1)	7.9 (11)	6.5 (6)	1.8 (1)	6.5 (4)	7.8 (4)
Dose per dosimetry	10.2 (5)	5.0 (7)	7.6 (7)	5.3 (3)	1.6 (1)	0 (0)
Strongly recommend against radioactive iodine remnant ablation in this case	10.2 (5)	5.0 (7)	0 (0)	10.5 (6)	4.8 (3)	0 (0)

^aThe participants were asked to select one of the choices shown. Missing or uninterpretable or “don’t know” responses are excluded.

^bThe number of respondents in each region selecting each choice is shown. Upon comparing the responses among regions, the Pearson chi-squared value was 80.33, $df = 25$, $p < 0.001$.

TABLE 4. COMPARISON OF REGIONAL OPINIONS ON THE TOPIC OF WHICH PAPILLARY THYROID CANCER PATIENTS SHOULD RECEIVE RADIOACTIVE IODINE REMNANT ABLATION (RRA) AND DOSING

Statement	Mean score of agreement on Likert scale (95% confidence interval; no. of responses from each region) ^a						F value (df1, df2) ^b	p value
	Western Canada	Eastern Canada	Quebec Canada	Western and midwestern United States	Northeastern United States	Southern United States		
1. All patients with papillary thyroid cancer should receive RRA.	2.67 (2.26, 3.07; 57)	2.92 (2.60, 3.23; 142)	3.77 (3.44, 4.20; 94)	2.41 (1.94, 2.88; 61)	2.71 (2.26, 3.17; 63)	2.73 (2.17, 3.28; 51)	5.07 (5, 462)	<0.001
2. All patients with papillary thyroid cancer with primary tumors >1.5 cm in diameter should receive RRA.	5.23 (4.84, 5.63; 60)	5.87 (5.61, 6.13; 145)	6.42 (6.25, 6.59; 93)	5.08 (4.56, 5.61; 62)	5.67 (5.25, 6.08; 63)	6.22 (5.96, 6.48; 51)	8.88 (5, 468)	<0.001
3. All papillary thyroid cancer patients, who at presentation have local lymph node metastases, should receive RRA.	6.24 (6.01, 6.47; 59)	6.52 (6.38, 6.67; 145)	6.80 (6.70, 6.90; 90)	5.73 (5.22, 6.23; 62)	6.34 (6.00, 6.68; 61)	6.52 (6.21, 6.83; 50)	7.56 (5, 461)	<0.001
4. In adjuvant treatment of papillary thyroid cancer, the dose of radioactive iodine used for remnant ablation should always be ≥ 100 mCi.	3.53 (3.00, 4.07; 45)	4.69 (4.34, 5.03; 127)	5.01 (4.60, 5.42; 93)	3.66 (3.11, 4.21; 62)	3.31 (2.79, 3.82; 62)	4.16 (3.58, 4.74; 49)	8.90 (5, 432)	<0.001

^aScores were based on a Likert scale with scores ranging from 1 (strongly disagree) to 7 (strongly agree); missing or "don't know" or uninterpretable responses were excluded from analysis.

^bdf1 = numerator degrees of freedom (between groups); df2 = denominator degrees of freedom (within groups).

Hosmer–Lemeshow $\chi^2 = 1.064$, 3 df, $p = 0.786$) (Table 5). Gender and duration of experience treating thyroid cancer were conditionally removed from the final logistic regression model (because of lack of a significant association).

Discussion

We observed significant regional differences in opinions on adjuvant radioactive iodine treatment in WDTC among Ca-

nadian and American physicians in specialties involved in thyroid cancer care. Regional differences were not defined by national boundaries. Moreover, we observed regional patterns of responses mirrored between the countries, better defined by east–west differences and distinct cultural regions. For example, the least support for administration of RRA in the case of a young woman with a 1.6-cm papillary thyroid carcinoma was observed in western Canada and the western and midwestern United States. Support of RRA for the sample

TABLE 5. RESULTS OF A MULTIVARIATE LOGISTIC REGRESSION ANALYSIS EXAMINING THE RELATIONSHIP BETWEEN RESPONDENT CHARACTERISTICS AND A STRONG RECOMMENDATION FOR RADIOACTIVE IODINE REMNANT ABLATION (RRA) IN THE SAMPLE CASE OF EARLY STAGE WELL-DIFFERENTIATED THYROID CARCINOMA

Predictor variables in the final model ^a	Odds ratio (95% confidence interval)	p value
No university affiliation of physician	1.71 (1.02, 2.88)	0.043
Respondent specialty (overall)	—	<0.001
Surgery compared to endocrinology	0.27 (0.15, 0.52)	<0.001
Nuclear medicine compared to endocrinology	1.47 (0.84, 2.58)	0.181

^aA backward conditional regression model was performed predicting a strong recommendation for RRA for the sample case of a 38-year-old woman who had a 1.6-cm papillary thyroid cancer resected at total thyroidectomy. The final model included data from 440 physicians (Cox and Snell $r^2 = 0.057$, Hosmer–Lemeshow $\chi^2 = 1.064$, 3 df, $p = 0.786$). Gender and duration of experience treating thyroid cancer were conditionally removed from the final logistic regression model (because of the lack of significance of associations).

case was intermediate in eastern Canada and northeastern United States. Moreover, the highest support for RRA in the sample case was expressed in Quebec, Canada, and the southern United States, potentially reflecting cultural distinct regions within each country. In keeping with the existing published evidence (18,19), respondents agreed that in the sample case of early stage WDTC presented, thyroid cancer-related mortality was considered low, so regional differences in recommendations could not be explained by differences in interpretation of patient risk. Significant regional variability was also observed in opinions on which WDTC patients should receive RRA and RRA dosing. In a multivariable analysis exploring potential relationships between individual respondent characteristics and RRA recommendations in early stage papillary cancer, academic affiliation and surgical specialty were found to be inversely associated with strong RRA recommendations.

In a prior survey of the ATA performed over a decade ago by Solomon *et al.* (11), 61% of respondents recommended RRA for a hypothetical case of a 39-year-old woman with a 2.0-cm solitary papillary carcinoma; there was no consensus on RRA dosing recommendations. Moreover, the existence of regional differences in opinions was not explored in this earlier study. Of note, in an American national cancer database published 9 years ago, only about 38% of WDTC patients were reported to have received postoperative radioactive iodine ablation or therapy (20). The cancer database study findings may also potentially reflect inconsistencies in thyroid cancer care within the United States, although underreporting of RRA administration may have been a limitation of the study. As for the issue of RRA dose recommendations, the existing evidence is not clear-cut. Hackshaw *et al.* (21) recently performed a systematic review and meta-analysis to compare the efficacy of remnant ablation with doses of radioactive iodine of 30 mCi compared with 100 mCi. They observed a significantly higher efficacy of ablation with the larger dose in observational studies but this finding was not borne out in a pooled analysis of randomized controlled trials (21). Hackshaw *et al.* suggested that large randomized controlled trials are required to resolve the radioiodine dosing and guide clinical practice.

Thyroid cancer care is generally performed by specialists from a variety of clinical backgrounds, including endocrinology, nuclear medicine, and surgery, in academic and non-academic settings. This study is the first to explore differences in approach to management of WDTC across disciplines. It is not clear why head and neck surgeons were least likely to recommend RRA in early stage WDTC, relative to other specialists. It is possible that there are differences in opinions on the strength of existing observational evidence on the risks and benefits of RRA. It is also possible that some surgeons may favor alternative follow-up strategies for WDTC (such as neck ultrasounds), in contrast to stimulated thyroglobulin measurements which are meaningful only after RRA. Moreover, less aggressive surgical procedures (such as hemithyroidectomy) in absence of RRA, may be favored by some surgeons in early stage WDTC because of less risk of surgical complications (22). The differences in approach to management of early stage WDTC among specialists is important to acknowledge, given that patients may receive conflicting recommendations among their physicians. As for the differences in recommendations in academic and nonacademic settings that were observed, it is possible that in nonacademic

settings, treating physicians may consider a biochemical follow-up paradigm (using stimulated thyroglobulin measurements) more feasible for their patients with WDTC, rather than a follow-up regime dependent on imaging availability.

In addition to conflicting available observational evidence, the variability in recommendations for RRA in early stage WDTC that we observed could potentially be explained by factors such as physicians' interpretations of existing observational evidence, location of clinical training, clinical experiences, acceptance of existing clinical practice guidelines, influence of international and local opinion leaders in WDTC, and societal or cultural values. These issues were not explored in this substudy. However, the existence of regional differences in opinions on adjuvant radioactive iodine treatment of WDTC is important to recognize, as such findings have implications for future regional cancer resource utilization within Canada and the United States. Moreover, if not acknowledged, strong regional differences in opinions in treatment of WDTC may threaten the success of any proposed national treatment initiatives. It may be useful to repeat a survey of North American physicians involved in thyroid cancer care in the next several years, in an effort to explore conformity with the recently published guidelines of the ATA (4).

This study is the largest survey of Canadian and American thyroid cancer specialty physicians eliciting opinions on the use of RRA for WDTC. An important strength of our study is a high number of responses from physicians from a variety of specialties from across two countries. A limitation of the study is an incomplete response rate and that the opinions of nonresponders are unknown. The presence of unknown sampling bias or nonresponse bias is a possibility with an incomplete response rate. In a prior review of physician nonresponders to surveys in general, nonresponders were found to be generally older and busier, had less interest in the topic of the survey, and were graduates of foreign medical schools (15). Unfortunately, lack of detailed data about nonresponders with respect to these characteristics for all regions, precluded us from exploring systematic differences between nonresponders and responders or issues of sampling bias. Of note, the response rate in our study (56.3%) was similar to that obtained by Solomon *et al.* (11) in a prior physician survey in this area (57.1%). An additional limitation of this study is the lack of detailed information on how many thyroid cancer patients are treated by each respondent each year; such information was not collected as it was thought to be difficult for respondents to reliably ascertain, without detailed review of personal records. An additional potential limitation of the study is that we included responses from specialists other than adult endocrinologists, nuclear medicine physicians, and head and neck surgeons, such as internal medicine physicians, pediatric endocrinologists, and others, who may see fewer thyroid carcinoma cases than some of the other specialty groups. However, in a sensitivity analysis of the primary outcome examining strength of recommendations for RRA in the sample case according to region, the results were not significantly impacted by excluding these specialty groups traditionally less likely to be involved in thyroid carcinoma care. Moreover, the analyses that we have presented should be considered a hypothesis-generating secondary analyses and the clinical importance of our findings are not known.

In summary, it appears that regional differences exist in opinions on the issue of adjuvant RRA treatment of early stage

WDTC within Canada and the United States. The explanation for variation in RRA recommendations among individual physicians could be explored in the form of future qualitative research. Further research should be performed examining whether regional differences in opinions on the treatment of WDTC exist in other parts of the world.

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