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ORIGINAL ARTICLE

Preferences of patients, clinicians, and healthy controls for the management of a Bethesda III thyroid nodule

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Abstract

Background: Active surveillance is propagated as an alternative for hemithyroidectomy in the management of Bethesda III thyroid nodules.

Methods: A cross-sectional survey questioned respondents on their willingness to accept risks related to active surveillance and hemithyroidectomy.

Results: In case of active surveillance, respondents (129 patients, 46 clinicians, and 66 healthy controls) were willing to accept a risk of 10%–15% for thyroid cancer and 15% for needing more extensive surgery in the future. Respondents were willing to accept a risk of 22.5%–30% for hypothyroidism after hemithyroidectomy. Patients and controls were willing to accept a higher risk on permanent voice changes compared with clinicians (10% vs. 3%, $p < 0.001$).

Conclusion: Real-life risks associated which active surveillance and hemithyroidectomy for Bethesda III nodules are equivalent or less than the risks people are willing to accept. Clinicians accepted less risk for permanent voice changes.

KEYWORDS

active surveillance, Bethesda III, hemithyroidectomy, thyroid nodule, treatment preferences

1 | INTRODUCTION

Thyroid nodules are common in the general population and the prevalence increases with age.[1] Diagnostic evaluation aims to distinguish benign from malignant nodules. Initial assessment consists of an ultrasound and if indicated a fine needle aspiration (FNA) biopsy. The commonly used Bethesda system for classification of cytology results classifies nodules as undiagnostic (Bethesda I), benign (Bethesda II), indeterminate (Bethesda III and

IV), suspicious for malignancy (Bethesda V), and malignant (Bethesda VI). These categories have an estimated malignancy rate of 5%–10%, 0%–3%, 6%–18%, 10%–40%, 45%–60%, and 94%–96%, respectively.[2,3] Indeterminate cytology, comprises 20%–30% of all nodule aspirates.[2,4] In 17%–40% of these indeterminate nodules, a definitive diagnosis will not be established despite additional diagnostic tests, such as a repeated FNA, a core needle biopsy, and molecular testing.[5–9] A hemithyroidectomy is required to obtain a conclusive diagnosis, but at the cost of potential complications. Rare surgical complications include bleeding, wound infection, and laryngeal nerve injury, the latter of which may result in permanent voice changes.[10] Hypothyroidism occurs in 20%–30% of hemithyroidectomy patients and requires lifelong thyroid hormone supplementation.[11]

For Bethesda IV nodules diagnostic surgery is generally the advised approach given the malignancy rate of ~30%, although ultrasound characteristics, molecular testing, and nuclear imaging may be used to select patients who can be followed-up with active surveillance.[12–14] For nodules with a repeated Bethesda III FNA result, active surveillance is increasingly considered an alternative to hemithyroidectomy.[15,16] Recent studies have shown that almost all malignancies detected in Bethesda III nodules are low-risk thyroid malignancies, most commonly the follicular variant of papillary thyroid carcinoma (PTC).[17–19] For low-risk (micro) PTC there is accumulating evidence that active surveillance is safe and will not result in increased morbidity and mortality.[20,21] A meta-analysis showed a pooled proportion for tumor growth to be 4.4% and the rate for metastatic spread to be 1.0% during a mean length of follow-up of 51.7 months.[22] In line with the general trend toward a more conservative approach in patients with low-risk thyroid cancer this observation has led to the suggestion of long-term non-surgical management of patients with asymptomatic Bethesda III nodules as a standard of care.[20,22,23] Active surveillance consists of monitoring the nodule with ultrasound and a repeated FNA on indication. This strategy may avoid unnecessary surgery related complications. However, long-term follow up is required and persisting uncertainty about the nature of their thyroid nodule may cause anxiety in patients. In addition, there remains some uncertainty about the possible effects of delaying treatment in patients with a malignant nodule. International guidelines recommend that the decision between active surveillance and hemithyroidectomy should depend on clinical risk factors, sonographic pattern, and patient preference.[23,24] However, not much is known about patients' preferences in this situation and many experience a significant decisional conflict.[25] As clinicians may influence patients in their choices, it is also interesting to compare the clinicians' perspective with the patients' perspective. Therefore, a willingness to accept experiment was conducted with patients, clinicians and healthy controls. The aim of the current study is to improve clinical management choices on Bethesda III nodules by incorporating patients' and clinicians' treatment preferences. With the current shift toward less aggressive treatment approaches in thyroid cancer, assessing peoples' preferences is of paramount importance to enable the translation of scientific literature into real-world treatment options.

2 | MATERIALS AND METHODS

2.1 | Sample and recruitment

Between August 2019 and July 2020 patients, clinicians and healthy controls were recruited in hospitals across the Netherlands, through press releases on websites of the national endocrine and patient organizations and on social media. Patients who had been diagnosed with a thyroid nodule, recently or in the past, were eligible for inclusion. To assess the effect of having experienced this diagnostic pathway in real-life on the willingness to accept risks, healthy controls (no history of thyroid disease) were included in the survey as well.[26] Clinicians with experience in the treatment of patients with thyroid diseases were eligible for inclusion. Informed consent was obtained before start of the study. No identifiable personal information was collected. This study was approved by the medical ethical board of the Erasmus Medical Centre, Rotterdam (MEC-2018-1666).

2.2 | Experimental design: Willingness to accept

Preferences were investigated by assessing the respondents' willingness to accept (WTA) treatment-related outcomes. The WTA design is an appropriate method for valuing losses, such as losses in quality of life.[27] In the context of the treatment of a thyroid nodule, it is able to quantify the WTA treatment-related risks and adverse events. The WTA method uses explicit questions in a common decisional context, with limited cognitive strain on the respondents.[28–30]

Two relevant outcomes were selected for each treatment option, based on a review of the literature and focus group discussions with patients and clinical experts. For the scenario of active surveillance, the willingness to accept the risk of thyroid cancer and the risk of more extensive surgery in the future were investigated. For the scenario of a hemithyroidectomy the willingness to

accept the risk of permanent voice changes and the risk of hypothyroidism were investigated. For each of these outcomes the WTA value was determined using a multi-step approach with questions in a validated format.[30] Each topic was covered with three questions, consisting of two multiple choice and one open-ended question. First, respondents were asked how much risk they were certainly willing to accept for a specific treatment-related outcome. They were offered a seven-point scale of risk percentages. The presented range of risk percentages for each treatment-related outcome was based on the actual risk, which in turn was derived from literature[10,11,31] (Table 1). Second, respondents were asked how much risk they would certainly *not* be willing to accept, within the same range of percentages as in the first question. Third, respondents were asked for an exact risk percentage, within a specified range defined by the answers on the first and second question. If respondents expressed a WTA of zero percent, they were asked to explain this by either checking a prefilled answer option or use an open text field. The pre-filled answer options consisted of "*this treatment does not appeal to me*" and "*I am not willing to think about this risk in the context of this treatment*." Based on this question, responses were classified as either "*true zero*" or "*protest zero*" responses (see Figure 1 for an example of a WTA question).

Following the WTA questions, respondents were asked to assign importance to the individual outcomes previously explored in the WTA questions. They were offered a 5-points Likert scale and were questioned to what extent these outcomes would influence their treatment choice. The options ranged from very unimportant to very important.

2.3 | Questionnaire

An online survey was created with LimeSurvey version 2.06 (LimeSurvey GmbH, Hamburg, Germany). Patients, clinicians, and controls received the same version of the questionnaire, allowing for valid comparison. Information on age, sex, educational level, and route to survey was collected. Additionally, for patients with a thyroid nodule in the past, questions on the diagnostic work-up, outcome of FNA, and ultimate treatment decision were included in the questionnaire. Educational information was provided on thyroid nodules, diagnostic procedures, and treatment options for Bethesda III nodules (see Data S1). All respondents were asked to imagine they were diagnosed with an indeterminate nodule and were currently facing the decision between a hemithyroidectomy and active surveillance. Respondents were informed about the generally indolent character of thyroid cancer detected in such nodules and the high chance of curation after treatment. An example of a WTA question was included to make respondents familiar with this type of question. The survey was tested in five patients using a think-aloud format with direct verbal feedback. After optimization, the survey was enrolled.

2.4 | Statistical analysis

Respondents who completed at least one out of four WTA questions were included in the final analysis. Protest zero percent responses were excluded from the analysis. The results of the WTA questions were presented as means with the standard deviation and medians with interquartile ranges (IQR). A Fisher exact test was performed to compare medians. The levels of importance, as assessed by Likert scale, were quantified as follows: 1 = very unimportant, 2 = unimportant, 3 = neutral, 4 = important, 5 = very important. For each outcome, mean importance scores were calculated.

3 | RESULTS

3.1 | Respondents' characteristics

The study population consisted of 129 (54%) patients, 46 (19%) clinicians, and 66 (27%) controls. Baseline characteristics are presented in Table 2. In 96 patients (74%), an FNA was performed. The FNA result was reported by 84 (88%) patients and was benign in 47 (49%) patients, malignant in 17 (18%) patients, and indeterminate in

TABLE 1 Risk ranges in WTA questions.

Treatment-related outcome	WTA risk ranges						
Risk of thyroid cancer	0%	5%	10%	15%	20%	25%	>25%
Risk of more extensive surgery	0%	5%	10%	15%	20%	25%	>25%
Risk of permanent voice changes	0%	1%	2%	3%	4%	5%	>5%
Risk of hypothyroidism	0%	10%	20%	30%	40%	50%	>50%

Abbreviation: WTA, willingness to accept.

For the upcoming questions, please imagine you consider active surveillance as the treatment for your thyroid nodule. Active surveillance consists of regular ultrasounds of the neck and on indication a repeated fine needle biopsy. During active surveillance uncertaintly will persist about the nature of your thyroid nodule, whether it is benign or malignant.

The next few questions are about the risk you are willing to accept

Question 1. What would be an acceptable risk for thyroid cancer when you consider active surveillance as a treatment for your thyroid nodule? Take a look at the row below with risk percentages. Please select what risk you are certainly willing to take.

0%	5%	10%	15%	20%	25%	more
○	○	○	○	○	○	○

For example: if you are sure that you are willing to accept a 5% risk for a thyroid malignancy, but not sure if you would accept a 15% risk, please select 5%

Question 2. What risk for thyroid cancer would NOT be acceptable when you consider active surveillance for your thyroid nodule? Take a look at the row below with risk percentages. Please select what risk you are certainly NOT willing to take.

0%	5%	10%	15%	20%	25%	more
○	○	○	○	○	○	○

For example: if you are sure that you are NOT willing to accept a 25% risk for a thyroid malignancy, but a 20% risk might be acceptable, please select 25%

Question 3. You have selected you are willing to take [answer question 1] risk for thyroid malignancy, but not [answer question 2]. What exact risk between [answer question 1] and [answer question 2] for thyroid cancer would you be willing to take when considering active surveillance for your thyroid nodule.

_____ **%**

FIGURE 1 Example of a WTA question. WTA, willingness to accept.

20 (21%) patients. Patients were recruited by their treating clinician ($n = 29$, 22%), reached the survey through the patient organization ($n = 61$, 47%), or via a friend, internet, or (social) media ($n = 39$, 30%). Healthy controls primarily reached the survey via a friend or family ($n = 35$, 53%) and internet or (social) media ($n = 25$, 38%) (Table 2).

3.2 | Willingness to accept—Active surveillance

Patients who had been diagnosed with a thyroid nodule, were willing to accept a median thyroid cancer risk of 10.0% (IQR 5.0–20.0) when presented with a scenario of active surveillance, as opposed to surgery, for their

TABLE 2 Characteristics of respondents.

	Frequencies (%)		
	Patients ($n = 129$)	**Clinicians ($n = 46$)**	**Controls ($n = 66$)**
Sex			
Female	120 (93%)	32 (70%)	44 (67%)
Age (years)			
Mean (range)	51 (18–81)	37 (26–67)	46 (24–77)
Highest level of education			
Elementary	1 (1%)	—	—
Secondary	29 (22%)	—	4 (6%)
Vocational	35 (27%)	—	2 (3%)
Higher	58 (45%)	44 (96%)	57 (86%)
Missing	6 (5%)	2 (4%)	3 (5%)
Diagnostic puncture			
Yes	96 (74%)	—	—
No	32 (25%)	—	—
Unknown or missing	1 (1%)	—	—
Outcome of FNA ($n = 96$)			—
Benign	47 (49%)	—	—
Malignant	17 (18%)	—	—
Indeterminate	20 (21%)	—	—
Unknown or missing	12 (13%)	—	—
Treatment			—
No treatment	35 (27%)	—	—
Surgery	70 (54%)	—	—
Radioactive iodine	31 (24%)	—	—
Radiofrequent ablation	1 (1%)	—	—
Route to survey			—
Asked by treating physician	29 (22%)	—	1 (2%)
Through patient organization	61 (47%)	—	1 (2%)
Via friend or family	9 (7%)	—	35 (53%)
Website, newspaper, flyer	22 (17%)	—	23 (35%)
Social media	8 (6%)	—	2 (3%)
Other	—	—	2 (3%)
Missing	—	—	2 (3%)

Note: Data are presented as *n* (%) or as median (range).
Abbreviation: FNA, fine needle aspiration.

thyroid nodule. Clinicians and healthy controls were willing to accept a median risk of 15.0% (IQR 10.0–21.5) and 10.0% (IQR 5.0–20.0), respectively. Patients would accept a median risk of 15.5% (IQR 7.8–30.0) for a more extensive surgery in the future, similar to the accepted median risk of 15.0% (IQR 10.0–25.0) by clinicians and 15.5% (IQR 10.0–23.8) by controls. There are no statistically significantly differences among participant groups (Table 3).

3.3 | Willingness to accept—Hemithyroidectomy

When presented with the scenario of hemithyroidectomy, as opposed to active surveillance, patients were willing to accept a median risk of 10.0% (IQR 4.0–50.0) for permanent voice changes, comparable to healthy controls who were willing to accept a median risk of 10.0% (IQR 3.0–25.0). In contrast, clinicians were willing to accept a

TABLE 3 Results of the WTA questions.

	WTA percentages			*p*-value (Fisher exact)	
				Patients vs. clinicians	Patients vs. controls
Active surveillance					
Risk of thyroid cancer	Patients (n = 115)	Clinicians (n = 46)	Controls (n = 64)		
Mean % (SD)	17.2 (1.9)	20.5 (2.9)	13.2 (1.4)	0.083	1000
Median % (IQR)	10.0 (5.0–20.0)	15.0 (10.0–21.5)	10.0 (5.0–20.0)		
Risk of more extensive surgery	Patients (n = 112)	Clinicians (n = 41)	Controls (n = 62)		
Mean % (SD)	25.8 (2.6)	18.2 (2.1)	21.9 (2.7)	0.367	1000
Median % (IQR)	15.5 (7.8–30.0)	15.0 (10.0–25.0)	15.5 (10.0–23.8)		
Hemithyroidectomy					
Risk of permanent voice changes	Patients (n = 129)	Clinicians (n = 40)	Controls (n = 66)		
Mean % (SD)	27.0 (2.8)	6.7 (2.5)	20.4 (3.09)	<0.001	0.880
Median % (IQR)	10.0 (4.0–50.0)	3.0 (2.0–4.3)	10.0 (3.0–25.0)		
Risk of hypothyroidism	Patients (n = 76)	Clinicians (36)	Controls (n = 56)		
Mean % (SD)	39.0 (3.2)	31.2 (4.4)	31.3 (2.8)	0.548	0.860
Median % (IQR)	30.0 (15.0–60.0)	22.5 (15.0–36.3)	25.0 (15.0–45.0)		

Abbreviations: IQR, interquartile range; SD, standard deviation; WTA, willingness to accept.

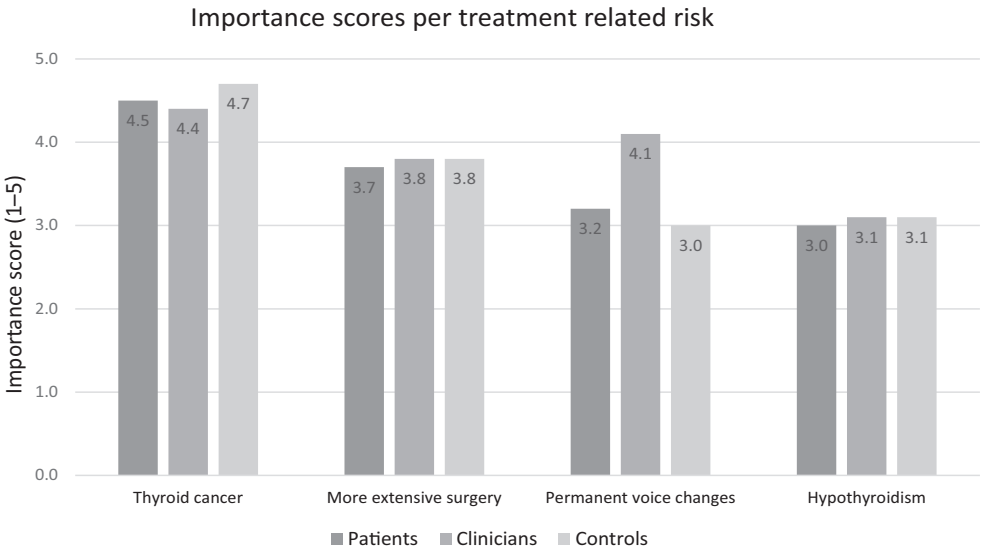

FIGURE 2 Mean importance score assigned to treatment related risks, out of a maximum score of 5. Response value: 1—very unimportant; 2—unimportant; 3—neutral; 4—important; 5—very important.

median risk of 3.0% (IQR 2.0–4.3) on permanent voice changes. This difference between patients and clinicians was statistically significant ($p < 0.001$). Regarding the risk of permanent hypothyroidism, patients would accept a 30.0% (IQR 15.0–60.0) risk, clinicians a 22.5% (IQR 15.0–36.3) risk, and healthy controls a 25.0% (IQR 15.0–45.0) risk. This is not statistically significantly different among participant groups (Table 3).

Patients with a higher education level tended to accept less risk of more extended surgery and permanent voice changes. This trend was not observed for the WTA risk of thyroid cancer and hypothyroidism. The FNA result of the thyroid nodule did not seem to be associated with reported WTA percentages. Across all WTA questions, younger clinicians tended to accept higher risk levels (Table S1).

3.4 | Which outcome influences treatment decision the most?—Importance scores

Among included outcomes, the highest importance score was assigned to thyroid cancer risk. Out of a maximum

score of 5, patients gave a mean score of 4.5 (standard deviation [SD] of 0.1), clinicians 4.4 (SD of 0.1) and controls 4.7 (SD of 0.1). Clinicians considered the risk of permanent voice changes as the second most important outcome influencing treatment choice with a mean score of 3.8 (SD 0.1). Patients and controls rated the risk of more extensive surgery as the second most important outcome, both groups with a mean score of 3.8 (SD 0.1). For patients as well as clinicians, the risk of postoperative hypothyroidism was considered least important, with scores of 3.0 (SD 0.1) and 3.1 (SD 0.2) respectively (Figure 2).

4 | DISCUSSION

Risk acceptance in the management of a Bethesda III thyroid nodule was investigated with a *willingness to accept* experiment. The main finding is that patients, clinicians and healthy controls have similar preferences for the management of a Bethesda III thyroid nodule with regard to the risk of thyroid cancer, more extensive surgery and hypothyroidism. The only exception was the risk of permanent voice changes, which clinicians were less willing to take compared with patients and controls. All risks respondents were hypothetically willing to take were similar or lower compared with the real-life risks.

Respondents were willing to accept a median risk of 10%–15% for thyroid cancer when considering active surveillance for their thyroid nodule. This is in the same range as the actual risk of malignancy in a Bethesda III nodule of 6%–18%.[4] One study showed that when the risk of cancer is higher than 38.6% people favor surgery. That threshold was dependent on the 10 year survival rate and decreased when reducing the hypothetical survival rate.[32] The willingness to accept active surveillance for a potentially malignant Bethesda III thyroid nodule may be lowered by the association of cancer with severe illness and mortality. Although respondents were informed about the indolent behavior of most thyroid cancers arising from Bethesda III nodules and the good prognosis, patients can have difficulty to accept the non-resection of a potential malignancy.[33–35] Interestingly, clinicians are less likely to advise active surveillance to their patients, based on the assumption that patients favor more aggressive treatments.[36,37] In this study we asked clinicians what risk they would tolerate when they were diagnosed with a thyroid nodule themselves. The finding that patients, clinicians, and healthy controls are willing to accept a similar 10% risk of thyroid cancer is informative when discussing management options with patients.

Terminology in conversations is also crucial as people are likely to have a similar emotional response to the diagnosis of an indeterminate nodule compared with patients with aggressive cancers.[34] Furthermore, phrasing a low-risk thyroid neoplasm, as either cancer, tumor or nodule, was found to highly influence decision making. When the disease was labeled as a cancer, participants were more likely to choose surgery, even if this would result in a worse prognosis and accept more adverse events.[33,38] The levels of concerns about cancer do decrease over time in patients with thyroid papillary microcarcinomas under active surveillance with very little treatment regret.[39] Education on the prognosis of thyroid cancer and careful use of terms to describe a thyroid nodule are very important when active surveillance for a Bethesda III nodule is addressed in the clinicians' office.

Patients, clinicians as well as controls were willing to accept a median risk of ~15% for more extensive surgery in the future when considering active surveillance. During a period of active surveillance possible tumor progression may lead to involvement of the contralateral thyroid lobe or cervical lymph nodes, requiring more extensive surgery than what upfront would have been required. Data on progression of Bethesda III nodules during active surveillance is lacking, as studies directly comparing active surveillance versus hemithyroidectomy in indeterminate nodules have not been performed.[40] However, Bethesda III nodules that turn out to be malignant, are almost always made up of low-risk papillary thyroid carcinoma.[17–19] Hence, it is unlikely that small sized Bethesda III nodules will significantly progress during surveillance requiring more extensive surgery.

Clinicians were willing to accept a significantly lower risk of voice changes compared with patients and controls. The risk of laryngoscopy proven, vocal cord paralysis, approximates 1.4%–2% and will persist in 0.6% of patients.[10,41] However, subjective voice changes are reported more frequently.[42,43] Clinicians may be better positioned to understand the impact of voice changes, possibly explaining the difference in the WTA between patients and clinicians. This adverse event may severely impact personal and professional lives.[43] The discrepancy between the WTA of patients and clinicians suggests that counseling of patients on the risk of voice changes requires more explanation than just mentioning the risk percentage. Which factors lead to the difference in willingness to accept need further investigation to optimize treatment decision guidance.

Patients were willing to accept a median risk of 30% for post-surgery hypothyroidism, whereas clinicians and controls accepted a risk of 22.5% and 25.0%, respectively. The actual risk of (sub)clinical hypothyroidism after hemithyroidectomy is ~20%.[11] Clinicians as well as patients assigned lower importance scores to hypothyroidism compared with voice changes. This is in agreement with a study investigating patients' preferences

about the extent of surgery in low-risk thyroid cancer.[44] In that study the risk of voice changes explained 19% of treatment choices, whereas hormone supplementation explained 9% of these choices.[44]

This is the first study that compares preferences in the treatment of Bethesda III thyroid nodules between patients, controls and clinicians. The use of a pilot-tested and multistep design of the questions allowed for a direct assessment of the WTA percentages. This study has several limitations. First, due to the relatively low incidence of Bethesda III nodules, it was not feasible to include only those patients who recently had been diagnosed with such nodule and were about to make a treatment decision at time of participating in the survey. All patients with a history of a thyroid nodule were eligible for inclusion, irrespective of FNA diagnosis, the time since diagnosis and treatment outcome. This may have introduced a bias in patients' preferences. Patients' WTA of treatment-related risks may have been influenced by the outcome of the diagnostic evaluation and treatment of their thyroid nodule. Although the limited number of participating patients prevented a statistical comparison of subgroups, a descriptive analysis did not show an association between FNA outcome and reported WTA levels. By asking respondents to imagine facing an imminent treatment decision for an indeterminate thyroid nodule, the situation of interest was mimicked as best as possible. Second, for patients, data on ultrasonographic characteristics of the thyroid nodules and whether this was communicated with patients was not available. Specific characteristics of the thyroid nodule, such as size, may have affected, for example, the willingness to accept the risk for thyroid cancer. Third, the mode of recruitment of participants may have introduced a selection bias. A large proportion of patients reached the survey through the national patient organization. These patients may not represent the general thyroid nodule patient population, as they may be more involved into their disease than a recently diagnosed patient new to these considerations. Fourth, for each WTA question, the scale of risk percentages was based on the actual real-life risk of that specific outcome. However, the presented risk ranges may have influenced the WTA results. Therefore, the outcomes of the different WTA questions should be interpreted separately and not be compared in absolute terms. Fifth, inaccurate risk perception by respondents cannot be ruled out as numeracy or health literacy was not measured.

In conclusion, this study presents patients', clinicians' and healthy controls' perspectives on risk assessment in clinical management of Bethesda III thyroid nodules. The results show that patients, clinicians and controls are willing to accept risks related to active surveillance for a Bethesda III thyroid nodule that are similar to actual risks reported in literature. The observed discrepancy between patients and clinicians with regard to the willingness to accept voice changes as an adverse event of hemithyroidectomy suggests that counseling on this topic can be further optimized.

AUTHOR CONTRIBUTIONS

Caroline M. J. van Kinschot: Study design, data collection, interpretation of data, and manuscript draft. **Vikas R. Soekhai:** Study design, analysis, interpretation of data, and critical review. **Esther W. de Bekker-Grob:** Study design, interpretation of data, and critical review. **W. Edward Visser:** Study design and critical review. **Robin P. Peeters:** Study design and critical review. **Charlotte van Noord:** Study design, data collection, and critical review. **Tessa M. van Ginhoven:** Study design, data collection, interpretation of data, and critical review.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author [CvK], upon reasonable request.

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REFERENCES

1. Guth S, Theune U, Aberle J, Galach A, Bamberger CM. Very high prevalence of thyroid nodules detected by high frequency (13 MHz) ultrasound examination. *Eur J Clin Invest*. 2009; 39(8):699-706. doi:10.1111/j.1365-2362.2009.02162.x
2. Baloch ZWCD, Gharib H, Alexander EK. Overview of diagnostic terminology and reporting. In: Ali SZ, Cibas ES, eds. *The Bethesda System for Reporting Thyroid Cytopathology: Definitions, Criteria, and Explanatory Notes*. Springer; 2017.
3. Bongiovanni M, Papadakis GE, Rouiller N, et al. The Bethesda system for reporting thyroid cytopathology explained for practitioners: frequently asked questions. *Thyroid*. 2018;28(5): 556-565.
4. Bongiovanni M, Spitale A, Faquin WC, Mazzucchelli L, Baloch ZW. The Bethesda system for reporting thyroid cytopathology: a meta-analysis. *Acta Cytol*. 2012;56(4):333-339. doi:10.1159/000339959
5. Baloch Z, LiVolsi VA, Jain P, et al. Role of repeat fine-needle aspiration biopsy (FNAB) in the management of thyroid nodules. *Diagn Cytopathol*. 2003;29(4):203-206. doi:10.1002/dc.10361
6. Yang J, Schnadig V, Logrono R, Wasserman PG. Fine-needle aspiration of thyroid nodules: a study of 4703 patients with histologic and clinical correlations. *Cancer*. 2007;111(5):306-315. doi:10.1002/cncr.22955

7. Na DG, Kim JH, Sung JY, et al. Core-needle biopsy is more useful than repeat fine-needle aspiration in thyroid nodules read as nondiagnostic or atypia of undetermined significance by the Bethesda system for reporting thyroid cytopathology. *Thyroid*. 2012;22(5):468-475.
8. Durante C, Grani G, Lamartina L, Filetti S, Mandel SJ, Cooper DS. The diagnosis and management of thyroid nodules: a review. *JAMA*. 2018;319(9):914-924.
9. Paschke R, Cantara S, Crescenzi A, Jarzab B, Musholt TJ, Sobrinho SM. European thyroid association guidelines regarding thyroid nodule molecular fine-needle aspiration cytology diagnostics. *Eur Thyroid J*. 2017;6(3):115-129.
10. Rosato L, Avenia N, Bernante P, et al. Complications of thyroid surgery: analysis of a multicentric study on 14,934 patients operated on in Italy over 5 years. *World J Surg*. 2004;28(3):271-276. doi:10.1007/s00268-003-6903-1
11. Verloop H, Louwerens M, Schoones JW, Kievit J, Smit JW, Dekkers OM. Risk of hypothyroidism following hemithyroidectomy: systematic review and meta-analysis of prognostic studies. *J Clin Endocrinol Metab*. 2012;97(7):2243-2255. doi:10.1210/jc.2012-1063
12. Zhu CY, Donangelo I, Gupta D, et al. Outcomes of indeterminate thyroid nodules managed nonoperatively after molecular testing. *J Clin Endocrinol Metab*. 2021;106(3):e1240-e1247.
13. Vriens D, de Koster EJ, de Geus-Oei LF, Oyen WJG. Preoperative stratification of cytologically indeterminate thyroid nodules by [(18)F]FDG-PET: can Orpheus bring back Eurydice? *Eur J Nucl Med Mol Imaging*. 2023;50(4):975-979.
14. Garcia-Lozano CA, Sanabria A. Preliminary report of active surveillance as a conservative strategy for Bethesda IV thyroid nodules. *Thyroid*. 2023;33(1):126-128.
15. Smulever A, Pitoia F. Active surveillance in small cytological indeterminate thyroid nodules: a call to common sense? *Endocrine*. 2021;72(2):505-512.
16. Gorshtein A, Slutzky-Shraga I, Robenshtok E, Benbassat C, Hirsch D. Adherence to active surveillance and clinical outcomes in patients with indeterminate thyroid nodules not referred for thyroidectomy. *Eur Thyroid J*. 2021;10(2):168-173.
17. Liu X, Medici M, Kwong N, et al. Bethesda categorization of thyroid nodule cytology and prediction of thyroid cancer type and prognosis. *Thyroid*. 2016;26(2):256-261.
18. VanderLaan PA, Marqusee E, Krane JF. Features associated with locoregional spread of papillary carcinoma correlate with diagnostic category in the Bethesda system for reporting thyroid cytopathology. *Cancer Cytopathol*. 2012;120(4):245-253.
19. Singh Ospina N, Iñiguez-Ariza NM, Castro MR. Thyroid nodules: diagnostic evaluation based on thyroid cancer risk assessment. *BMJ*. 2020;368:l6670.
20. Leboulleux S, Tuttle RM, Pacini F, Schlumberger M. Papillary thyroid microcarcinoma: time to shift from surgery to active surveillance? *Lancet Diabetes Endocrinol*. 2016;4(11):933-942.
21. Oda H, Miyauchi A, Ito Y, et al. Incidences of unfavorable events in the management of low-risk papillary microcarcinoma of the thyroid by active surveillance versus immediate surgery. *Thyroid*. 2016;26(1):150-155.
22. Saravana-Bawan B, Bajwa A, Paterson J, McMullen T. Active surveillance of low-risk papillary thyroid cancer: a meta-analysis. *Surgery*. 2020;167(1):46-55.
23. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association Guidelines Task Force on thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2016;26(1):1-133. doi:10.1089/thy.2015.0020
24. Perros P, Boelaert K, Colley S, et al. Guidelines for the management of thyroid cancer. *Clin Endocrinol (Oxf)*. 2014;81(Suppl 1):1-122. doi:10.1111/cen.12515
25. Taylor BA, Hart RD, Rigby MH, Trites J, Taylor SM, Hong P. Decisional conflict in patients considering diagnostic thyroidectomy with indeterminate fine needle aspirate cytopathology. *J Otolaryngol Head Neck Surg*. 2016;45:16.
26. Gorin MA, Soloway CT, Eldefrawy A, Soloway MS. Factors that influence patient enrollment in active surveillance for low-risk prostate cancer. *Urology*. 2011;77(3):588-591.
27. Verbooy K, Hoefman R, van Exel J, Brouwer W. Time is money: investigating the value of leisure time and unpaid work. *Value Health*. 2018;21(12):1428-1436.
28. Soekhai V, Whichello C, Levitan B, et al. Methods for exploring and eliciting patient preferences in the medical product lifecycle: a literature review. *Drug Discov Today*. 2019;24(7):1324-1331.
29. Whichello C, Levitan B, Juhaeri J, et al. Appraising patient preference methods for decision-making in the medical product lifecycle: an empirical comparison. *BMC Med Inform Decis Mak*. 2020;20(1):114.
30. Reckers-Droog V, van Exel J, Brouwer W. Willingness to pay for health-related quality of life gains in relation to disease severity and the age of patients. *Value Health*. 2021;24(8):1182-1192.
31. Cibas ES, Ali SZ. The 2017 Bethesda system for reporting thyroid cytopathology. *Thyroid*. 2017;27(11):1341-1346. doi:10.1089/thy.2017.0500
32. Lee DJ, Xu JJ, Brown DH, et al. Determining patient preferences for indeterminate thyroid nodules: observation, surgery or molecular tests. *World J Surg*. 2017;41(6):1513-1520. doi:10.1007/s00268-017-3887-9
33. Dixon PR, Tomlinson G, Pasternak JD, et al. The role of disease label in patient perceptions and treatment decisions in the setting of low-risk malignant neoplasms. *JAMA Oncol*. 2019;5(6):817-823.
34. Pitt SC, Saucke MC, Wendt EM, et al. Patients' reaction to diagnosis with thyroid cancer or an indeterminate thyroid nodule. *Thyroid*. 2020;31(4):580-588.
35. Park JW, Yoo JS, Yun JK, Kim BH, Noh YW, Kim DJ. An online questionnaire survey on preferred timing for the diagnosis and management of thyroid carcinoma in general population in Korea. *Ann Surg Treat Res*. 2016;90(6):297-302.
36. Nickel B, Brito JP, Barratt A, Jordan S, Moynihan R, McCaffery K. Clinicians' views on management and terminology for papillary thyroid microcarcinoma: a qualitative study. *Thyroid*. 2017;27(5):661-671.
37. Burch HB, Burman KD, Cooper DS, Hennessey JV, Vietor NO. A 2015 survey of clinical practice patterns in the management of thyroid nodules. *J Clin Endocrinol Metab*. 2016;101(7):2853-2862. doi:10.1210/jc.2016-1155
38. Nickel B, Howard K, Brito JP, Barratt A, Moynihan R, McCaffery K. Association of preferences for papillary thyroid

cancer treatment with disease terminology: a discrete choice experiment. *JAMA Otolaryngol Head Neck Surg*. 2018;144(10):887-896.
39. Davies L, Roman BR, Fukushima M, Ito Y, Miyauchi A. Patient experience of thyroid cancer active surveillance in Japan. *JAMA Otolaryngol Head Neck Surg*. 2019;145(4):363-370.
40. Force USPST, Bibbins-Domingo K, Grossman DC, et al. Screening for thyroid cancer: US Preventive Services task Force recommendation statement. *JAMA*. 2017;317(18):1882-1887.
41. The British Association of Endocrine & Thyroid Surgeons. Fifth National Audit Report. 2017.
42. Kletzien H, Macdonald CL, Orne J, et al. Comparison between patient-perceived voice changes and quantitative voice measures in the first postoperative year after thyroidectomy: a secondary analysis of a randomized clinical trial. *JAMA Otolaryngol Head Neck Surg*. 2018;144(11):995-1003.
43. Kuhn MA, Bloom G, Myssiorek D. Patient perspectives on dysphonia after thyroidectomy for thyroid cancer. *J Voice*. 2013;27(1):111-114.
44. Ahmadi S, Gonzalez JM, Talbott M, et al. Patient preferences around extent of surgery in low-risk thyroid cancer: a discrete choice experiment. *Thyroid*. 2020;30:1044-1052.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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