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Review

# What Has Changed in the 2025 American Thyroid Association Management Guidelines for Adult Patients with Differentiated Thyroid Cancer? Part 3: Long-Term Surveillance, Advanced and Novel Treatments

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**Abstract**

American Thyroid Association (ATA) guidelines for the management of thyroid nodules and differentiated thyroid cancer (DTC) were first published in 1996 and updated in 2006, 2009, and 2015. In 2025, the ATA released a revised version that, for the first time, focuses exclusively on DTC. In our previous reviews, we summarized the updates on preoperative, diagnostic, surgical, and early postoperative management of DTC. In this third and final part, we compare the 2015 and 2025 ATA guidelines with respect to long-term follow-up, TSH suppression strategies, thyroglobulin monitoring, follow-up of low-risk patients. Diagnostic radioiodine whole-body scanning, FDG-PET/CT, dynamic risk stratification, and the management of recurrent or metastatic disease, including local therapies, radioiodine preparation and dosing, and systemic treatments were also highlighted in this part. Particular emphasis is placed on the expanded recommendations for kinase inhibitor therapy, sequencing of systemic agents, targeted therapies (NTRK, RET, ALK, BRAF), redifferentiation approaches, immunotherapy, and supportive care strategies addressing bone and brain metastases, financial toxicity and psychosocial needs. This review provides a comprehensive synthesis of these updates and discusses their implications for individualized long-term management of DTC.

**Keywords:** Advanced treatment strategies, ATA guidelines, differentiated thyroid cancer, long-term surveillance, papillary thyroid cancer

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The American Thyroid Association (ATA) first issued clinical practice guidelines for the management of thyroid nodules and differentiated thyroid cancer (DTC) in 1996, with major revisions subsequently published in 2006, 2009, and 2015.[1–4]

In response to evolving evidence and therapeutic advances, the ATA for the first time divided the guideline development into two separate documents and released the first, focused on the management of DTC in adult patients.[5]

Building upon the updates presented in the 2015 guideline, the most recent version introduces important changes regarding long-term surveillance, adjuvant therapies, and advanced treatment strategies. In this paper, we aim to systematically compare the recommendations of the 2015

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and 2025 ATA guidelines in the context of long-term follow-up, monitoring of disease recurrence, metastatic DTC and the role of novel systemic and targeted therapeutic approaches.

This article represents the third and final part of our review series and concentrates specifically on the guideline updates related to long-term management and advanced treatment modalities for DTC.

The methodology for evidence synthesis, recommendation development, and grading of evidence certainty has been detailed in the first two parts of this review series (Parts 1 and 2). As the methodology is identical, it is not restated here.

## 2025 RECOMMODATIONS

### In patients treated for Differentiated Thyroid Cancer (DTC), the appropriate degree of TSH suppression

In the 2025 revision, Recommendation 45 states that the decision to reduce TSH levels below the reference range should be individualized. This decision should be made by weighing the potential benefits and risks. It is suggested that high-risk patients are likely to benefit more from subnormal TSH levels compared to low-risk patients (see Table 9). (Conditional recommendation, Low-certainty evidence).[5]

In the 2015 revision, this recommendation was provided as Recommendation 59 in five subsections.

In subsection A, it was recommended that, for high-risk thyroid cancer patients, initial TSH suppression should be reduced to below 0.1 mU/L (Strong recommendation, Moderate-quality evidence).

In subsection B, for intermediate-risk thyroid cancer patients, initial TSH suppression was recommended at 0.1–0.5 mU/L (Weak recommendation, Low-quality evidence).

Subsection C states that, TSH could be maintained within the lower part of the reference range (0.5–2 mU/L) during ongoing surveillance for recurrence in low-risk individuals who had undergone remnant ablation and had undetectable serum Tg levels. Similar recommendations were given for low-risk patients without remnant ablation who also had undetectable serum Tg levels (Weak recommendation, Low-quality evidence).

Subsection D indicates that, for low-risk patients who had undergone remnant ablation and had low serum Tg levels, TSH could be maintained at or slightly below the lower limit of normal (0.1–0.5 mU/L) during continued surveillance for recurrence. Comparable guidance applied to low-risk patients without remnant ablation; however, in this group, serum Tg levels might be measurably higher, and ongoing surveillance for recurrence was recommended (Weak recommendation, Low-quality evidence).

Finally, in subsection E, for low-risk patients who had undergone lobectomy, TSH could be maintained in the mid- to lower reference range (0.5–2 mU/L) during ongoing surveillance for recurrence. In such cases, if patients were able to maintain TSH levels within this target range, thyroid hormone therapy might not be necessary (Weak recommendation, Low-quality evidence).[4]

The 2015 ATA guidelines, in Recommendation 59, adopted a risk-based and stepwise approach to TSH suppression in the early management of DTC, stratifying recommendations across high-, intermediate-, and low-risk groups while also taking into account Tg and anti-Tg levels as well as the type of surgical procedure (lobectomy vs. total thyroidectomy).[4] In the new guideline, the decision to reduce TSH below the reference range is recommended on the basis of a potential benefit–risk balance, and it is stated that this should be applied with reference to Table 9, which has been structured similarly to Table 13 of the 2015 guideline. Table 9 specifies TSH targets according to the response-to-therapy categories following initial treatment: excellent response, indeterminate response, biochemical incomplete response, and structural incomplete response. Accordingly, in patients with an excellent response, TSH is recommended to be maintained within the normal reference range. In those with an indeterminate response, TSH is likewise recommended to be kept within the reference range; however, the evidence regarding specific target levels is noted to be inconclusive. In patients with biochemical or structural incomplete response, TSH suppression below the reference range is recommended, although, again, the data regarding optimal target levels are considered inconclusive.[5]

### Duration of TSH suppression below the reference range

In the 2025 revision, Recommendation 45 specifies the following: In subsection A, long-term TSH suppression is not recommended in low- or intermediate-risk patients without biochemical or structural evidence of recurrence (Conditional recommendation, Low-certainty evidence). In subsection B, the balance of benefits and risks of TSH suppression, as well as the TSH targets, should be reassessed over time (Good Practice Statement).[5]

In the 2015 revision, the role of TSH suppression during thyroid hormone therapy in the long-term follow-up of DTC, according to the clinical situation at any point, was addressed in Recommendation 70 across five subsections.

In subsection A, it was recommended that in patients with a structural incomplete response to therapy, the serum TSH

level should be maintained indefinitely below 0.1 mU/L, provided there are no specific contraindications (Strong recommendation, Moderate-quality evidence).

In subsection B, considering the initial ATA risk classification, Tg level, Tg trend over time, and the risks associated with TSH suppression, serum TSH levels for patients with a biochemical incomplete response should be kept between 0.1 and 0.5 mU/L (Weak recommendation, Low-quality evidence).

In subsection C, in patients who initially presented with high-risk disease but who demonstrate either an excellent (clinically and biochemically disease-free) or indeterminate response to therapy, thyroid hormone therapy aiming for serum TSH levels of 0.1–0.5 mU/L may be considered for up to five years; thereafter, the degree of TSH suppression may be reduced with continued surveillance for recurrence (Weak recommendation, Low-quality evidence).

In subsection D, in patients with an excellent or indeterminate response to therapy, particularly those at low risk of recurrence, serum TSH may be maintained within the lower reference range (0.5–2 mU/L) (Strong recommendation, Moderate-quality evidence).

Finally, in subsection E, in patients with an excellent or indeterminate response who have not undergone remnant ablation or adjuvant therapy, with a normal neck ultrasound, low or undetectable suppressed serum Tg, and stable or declining Tg or anti-Tg antibody levels, serum TSH may be allowed to rise into the lower reference range (0.5–2 mU/L) (Weak recommendation, Low-quality evidence).[4]

In the 2015 guideline, Recommendation 70 outlined TSH targets in five subsections, stratified according to the response-to-therapy classification at any point during follow-up. In contrast, the 2025 revision has simplified this to two subsections under Recommendation 46.

In the 2025 guideline, long-term TSH suppression is not recommended in low- or intermediate-risk patients or in those without evidence of recurrence; moreover, the risks and benefits of TSH suppression, as well as the target levels, are advised to be reassessed over time. Overall, the 2025 revision emphasizes a more individualized approach to TSH suppression, with a notable tendency toward reducing the degree of suppression compared to the 2015 guideline.[5]

## The role of serum Tg measurement in the follow-up of differentiated thyroid cancer

In the 2025 revision, this topic is addressed in Recommendation 47, structured into five subsections. In subsection A, it is stated that serum Tg should be measured using an assay calibrated against the BCR-457 standard, and Tg antibodies should be quantitatively assessed with every Tg measurement (Good Practice Statement).

In subsection B, in patients who have undergone total thyroidectomy, with or without RAI, serum thyroglobulin (measured while on thyroid hormone therapy) should be used to monitor response to therapy and to detect recurrence—although its predictive value is higher in those treated with radioactive iodine (RAI) (Strong recommendation, Moderate-certainty evidence).

In subsection C, during the initial follow-up period, serum Tg should be measured every 6–12 months while the patient is on thyroxine therapy, with more frequent testing being appropriate in ATA intermediate- to high-risk patients (Good Practice Statement).

Subsection D states that, in patients who have undergone lobectomy, routine serum Tg measurement during the initial follow-up period while on thyroid hormone therapy is not recommended (see Recommendation 30) (Conditional recommendation, Very low-certainty evidence).

Finally, in subsection E, in patients with circulating Tg antibodies, serial measurement of TgAb levels using the same assay may be useful for disease monitoring. Current Tg immunometric assays and radioimmunoassays are generally affected by TgAb, and Tg measurement by liquid chromatography–tandem mass spectrometry (LC-MS/MS) has low sensitivity. Therefore, Tg measurements alone should not be relied upon in this population; imaging remains the primary modality for surveillance (Conditional recommendation, Low-certainty evidence).[5]

In the 2015 guideline, Recommendation 62 addressed serum Tg measurement across five points.

In point A, it was recommended that serum Tg should be measured using an assay calibrated against the CRM-457 international standard, and Tg antibodies should be quantitatively assessed with each Tg measurement. Ideally, both serum Tg and anti-Tg antibodies should be measured in the same laboratory and by the same method for consistent longitudinal evaluation in a given patient (Strong recommendation, High-quality evidence).

In point B, during initial follow-up, serum Tg should be measured every 6–12 months while the patient is on thyroxine therapy, with more frequent testing considered suitable for ATA high-risk patients (Strong recommendation, Moderate-quality evidence).

The point C states that, in ATA low- and intermediate-risk patients with an excellent response to therapy, the utility of subsequent Tg testing is uncertain, and the interval between serum Tg measurements may be extended to at least 12–24 months (Weak recommendation, Low-quality evidence).

In point D, it was recommended that serum TSH be assessed at least annually in all patients receiving thyroid hormone therapy (Strong recommendation, Low-quality evidence).

Finally, in point E, for ATA high-risk patients (regardless of response to therapy) and for all patients with a biochemical incomplete, structural incomplete, or indeterminate response, serum Tg should be monitored at least every 6–12 months for several years (Weak recommendation, Low-quality evidence).[4]

In the 2015 guideline, Recommendation 63;

A. In ATA low- and intermediate-risk individuals who have undergone remnant ablation or adjuvant therapy and have a negative cervical ultrasound, serum Tg should be assessed during months 6–18 of thyroxine therapy using a sensitive Tg assay (<0.2 ng/mL) or following TSH stimulation to confirm the absence of disease (excellent response) (Strong recommendation, Moderate-quality evidence).

B. In low- and intermediate-risk patients with an excellent response to therapy, repeat TSH-stimulated Tg testing is not recommended (Weak recommendation, Low-quality evidence).

C. In patients showing indeterminate, biochemical incomplete, or structural incomplete responses after additional treatments or spontaneous declines in Tg levels during thyroid hormone therapy, TSH-stimulated Tg testing may be considered later to reassess the response to therapy (Weak recommendation, Low-quality evidence).[4]

In the 2015 guideline, Recommendation 64;

Regular serum Tg measurements during thyroid hormone therapy should be taken into account in the follow-up of DTC patients who have undergone less than total thyroidectomy and in those who have undergone total thyroidectomy but not RAI ablation. Although specific Tg threshold values that effectively differentiate normal remnant thyroid tissue from persistent thyroid cancer are not known, increasing Tg values over time are suggestive of developing thyroid tissue or cancer (Strong recommendation, Low-quality evidence).[4]

In the 2015 revision, Recommendation 62 section A recommended that serum Tg measurement be calibrated according to the CRM-457 international standard, whereas in the 2025 revision, calibration is recommended using the BCR-457 standard (European Commission Institute for Reference Materials). In the 2015 ATA guideline, serum Tg monitoring under thyroid hormone therapy was recommended in RAI-treated patients in Recommendation 62 section E and Recommendation 63 section A, and in non-RAI patients in Recommendation 64. In contrast, the 2025 guideline, in Recommendation 47 section B, recommends in a single point that serum Tg measurement under thyroid hormone therapy should be performed to detect recurrence in all patients, regardless of whether RAI was administered.

In the 2025 revision, Recommendation 47 section C corresponds to 2015 Recommendation 62 section B, updating the initial follow-up schedule: serum Tg should be measured every 6–12 months during thyroxine therapy, with more frequent testing appropriate for ATA intermediate- to high-risk or high-risk patients.

In the 2015 Recommendation 63, in low- and intermediate-risk patients who had received RAI and had a negative cervical ultrasound, Tg measurement was recommended at 6–18 months under thyroxine therapy or after TSH stimulation. In patients with an excellent response, TSH-stimulated Tg testing was not recommended, whereas it was suggested for patients with indeterminate or incomplete responses. Furthermore, in low- and intermediate-risk patients with an excellent response, repeat TSH-stimulated Tg testing was not recommended. In patients showing indeterminate, biochemical incomplete, or structural incomplete responses after additional treatments or spontaneous Tg declines during thyroid hormone therapy, TSH-stimulated Tg testing could later be considered to reassess therapy response.

In the 2015 Recommendation 64, Tg monitoring was recommended in patients who underwent more conservative surgery than total thyroidectomy. Although specific Tg thresholds to reliably distinguish normal remnant thyroid tissue from persistent thyroid cancer were not defined, rising Tg values over time were considered suspicious for growing thyroid tissue or cancer. However, in the 2025 guideline, Recommendation 47 point D newly states that routine serum Tg measurement is not recommended in patients after lobectomy during the initial follow-up period under thyroid hormone therapy. Additionally, in Recommendation 30 point B of the 2025 guideline, a single serum Tg measurement at 6–12 weeks in lobectomy patients, when TSH is within the normal range, may be useful to confirm that Tg is not unexpectedly elevated, although no specific cut-off value is defined.

Finally, in the 2025 ATA guideline, Recommendation 47 point E explicitly notes that circulating anti-Tg antibodies can affect Tg results, whereas in the 2015 guideline, this was mentioned in Recommendation 62 point A.[5]

## Can follow-up be reduced or discontinued in low-risk DTC patients?

In the 2025 revision, six recommendations are provided regarding the follow-up and discontinuation of follow-up in low-risk patients.

1. In low-risk DTC patients treated with total thyroidectomy and RAI who demonstrate a sustained excellent response 5–8 years after initial therapy, routine ultrasound may be discontinued; these patients can subsequently be monitored every 1–2 years using only biochemical markers (Conditional recommendation, Low-certainty evidence).
2. In low-risk DTC patients treated with total thyroidectomy and RAI who demonstrate a sustained excellent response for 10–15 years, routine biochemical follow-up for thyroid cancer is not required; these patients can be considered in complete remission (Good Practice Statement).
3. In low-risk DTC patients treated with total thyroidectomy alone who demonstrate a sustained excellent response 5–8 years after initial therapy, routine ultrasound may be discontinued; subsequent follow-up can be performed every 1–2 years using only biochemical markers (Conditional recommendation, Low-certainty evidence).
4. In low-risk DTC patients treated with total thyroidectomy alone who demonstrate a sustained excellent response for 10–15 years, routine biochemical follow-up for thyroid cancer is not required; these patients can be considered in complete remission (Good Practice Statement).
5. In low-risk DTC patients treated with lobectomy, if the initial ultrasound is negative, subsequent ultrasounds should be performed every 1–3 years for 5–8 years after initial therapy. Nodules in the residual lobe should be monitored according to the ATA thyroid nodule guidelines (Good Practice Statement).
6. In low-risk DTC patients treated with lobectomy, if postoperative Tg is not significantly elevated, additional Tg testing is not routinely recommended (Good Practice Statement).

In the 2015 ATA guideline, Recommendation 70 points D and E emphasized that aggressive TSH suppression is not necessary in low-risk patients with excellent or indeterminate response, and that maintaining TSH between 0.5–2 mU/L is sufficient. However, no recommendations regarding the duration of follow-up were provided.

In contrast, the 2025 ATA guideline has a separate, more detailed recommendation (Recommendation 48) specifically for follow-up of low-risk DTC patients. In patients who underwent total thyroidectomy, whether or not they received RAI, those with a sustained excellent response can discontinue ultrasound monitoring 5–8 years after initial therapy, and those with a sustained excellent response for 10–15 years can be considered in complete remission and removed from follow-up.

In low-risk patients after lobectomy, if the ultrasound is negative, follow-up should be performed every 1–3 years for 5–8 years. In the 2025 revision, Recommendation 47 does not recommend routine Tg measurement under thyroxine therapy, and Recommendation 48 specifies that in low-risk patients after lobectomy, if Tg is not significantly elevated, additional Tg testing is not recommended.[5]

## Diagnostic RAI WBS

In the 2025 guideline, Recommendation 49 addressed diagnostic RAI WBS across four points.

A. In patients who have undergone lobectomy or total thyroidectomy without RAI, whole-body radioiodine scintigraphy (WBS) should not be performed for follow-up purposes (Good Practice Statement).

B. In DTC individuals with low or low–intermediate risk of recurrence who demonstrate an excellent response to therapy, routine diagnostic radioiodine WBS is not necessary during follow-up (Conditional recommendation, Low-certainty evidence).

C. In DTC patients with intermediate–high or high risk of recurrence, diagnostic radioiodine WBS may be performed if there is suspicion of recurrence in order to evaluate the presence of iodine-avid disease. If performed, it should be done using 123I or low-activity 131I (Conditional recommendation, Low- certainty evidence).

D. SPECT-CT radioiodine imaging may be applied in addition to planar imaging to better determine the anatomical localization of radioiodine uptake and to differentiate between potential cancer foci and nonspecific uptake (Conditional recommendation, Low- certainty evidence).[5]

In the 2015 revision, Recommendations 66 and 67 addressed WBS.

In Recommendation 66, following RAI remnant ablation or adjuvant therapy, in low- and intermediate-risk patients who demonstrate an excellent response to therapy—defined as undetectable Tg under thyroid hormone therapy, negative anti-Tg antibodies, and negative ultrasound—routine diagnostic WBS during follow-up is not necessary.

In Recommendation 67, section A, diagnostic WBS performed 6–12 months after adjuvant RAI therapy, following thyroid hormone withdrawal or rhTSH administration, may be used in the follow-up of patients at high or intermediate risk (with higher-risk features) for persistent disease (see risk classification system, section [B19]) and should be performed using 123I or low-activity 131I (Strong recommendation, Low-quality evidence).

In section B, in patients with uptake on planar imaging, SPECT/CT RAI imaging is preferred over planar imaging to better localize RAI uptake anatomically and to distinguish possible tumors from nonspecific uptake (Weak recommendation, Moderate-quality evidence).[4]

In the 2015 revision, following RAI remnant ablation or adjuvant therapy, in low- and intermediate-risk patients who demonstrated an excellent response to therapy—defined as undetectable Tg under thyroid hormone therapy, negative anti-Tg antibodies, and negative ultrasound—routine diagnostic WBS during follow-up was not considered necessary. For high- or intermediate-risk patients, WBS was recommended 6–12 months after RAI therapy, and in patients with uptake on planar imaging, SPECT/CT was recommended to better localize the uptake and differentiate tumors from nonspecific uptake.

In the 2025 revision, WBS is not recommended in low-risk, RAI-untreated total thyroidectomy patients or lobectomy patients who are low–intermediate risk and demonstrate an excellent response to therapy. In intermediate–high and high-risk patients, WBS is recommended only if there is suspicion of recurrence, rather than routinely. SPECT/CT continues to be recommended to differentiate nonspecific tissue from cancer.

### 18FDG-PET/CT Imaging

In the 2025 revision, Recommendation 50 addresses 18FDG-PET/CT in two points.

In point A, 18FDG-PET/CT may be performed in DTC patients with high serum Tg levels and high risk of recurrence, especially in oncocytic thyroid carcinoma or aggressive histology, and in patients with a prior negative RAI imaging history (Conditional recommendation, Moderate- certainty evidence).

In point B, 18FDG-PET/CT may also be used:

(i) As a prognostic tool in individuals at highest risk for fast disease progression and disease-specific mortality, and

(ii) To assess response to therapy after systemic or local treatment of invasive disease (Conditional recommendation, Low-certainty evidence).[5]

In the 2015 revision, Recommendation 68 states:

A. In high-risk DTC patients with negative RAI imaging and higher serum Tg (often >10 ng/mL), 18FDG-PET screening should be taken into consideration (Strong recommendation, Moderate-quality evidence).

B. 18FDG-PET scanning can also be used for the following purposes: (i) initial staging of poorly differentiated thyroid cancers, especially in patients with high serum Tg levels or other imaging findings, such as invasive Hurthle cell carcinoma; (ii) prognostication to identify lesions and patients at highest risk of rapid disease progression and disease-specific mortality in metastatic disease; and (iii) assessing response to treatment following systemic or local therapy in metastatic or locally invasive disease. (Weak recommendation, Low-quality evidence).[4]

Although the recommendations in the two revisions are generally similar, several details are noteworthy. In the 2015 revision, section A was a strong recommendation, whereas in the 2025 revision this point has been downgraded to a conditional recommendation. The 2015 edition addressed patients with rising Tg despite negative imaging, while the 2025 revision includes high-risk DTC patients, particularly those with oncocytic thyroid carcinoma (OTC) or aggressive histology. The recommendation added in point A of the 2025 revision was included in point B of the 2015 revision. In point B of the 2025 revision, the use of 18FDG-PET/CT as a prognostic tool in patients at highest risk for rapid disease progression and disease-specific mortality, and for evaluating response after systemic or local treatment of invasive disease, remains similar to the 2015 revision. Additionally, the term "Hurthle cell carcinoma" used in the 2015 revision has been replaced in the 2025 revision with "Oncocytic thyroid carcinoma" in accordance with the 2022 WHO classification.[6,7]

### Is continuous risk stratification (assessment of response to therapy) useful for long-term disease follow-up and treatment management decisions?

In the 2025 revision, Recommendation 51 addresses this issue. It states that continuous risk stratification (dynamic risk assessment), when used alongside the initial recurrence risk, allows the clinician to provide individualized management recommendations based on changing risk estimates over time and should be used to guide the timing and type of imaging (Good practice statement).[5]

In the 2015 revision, specific details on how surveillance and treatment strategies should be modified over time based on reclassification of response to therapy within the ATA risk categories were not yet defined. In the 2025 revision, it is emphasized as a good practice statement that dynamic risk stratification can directly guide which imaging to perform and when, based on evolving risk assessments.

### When and what type of treatment should be applied for local, regional residual, clinically recurrent, or progressive DTC?

2025 Revision addresses Recommendation 52 subdivided into three sections.

1. A number of considerations should be addressed when deciding whether to do focused central and/or lateral

neck surgery or therapeutic regional neck surgery as part of reoperative therapy. These include the extent of previous surgery(ies), the size and anatomical location of the new disease, its growth rate, patient characteristics and preferences, and the context of overall disease management (Good Practice Statement).

2. For patients with recurrent or residual thyroid cancer, percutaneous ethanol ablation may be a viable alternative therapeutic option, especially if they are at a high risk of reoperation-related complications. (Conditional recommendation, Low-certainty evidence).
3. Radiofrequency ablation (RFA) may be an alternative treatment in recurrent or residual thyroid cancer, particularly in patients at high risk of complications from reoperation (Conditional recommendation, Low-certainty evidence).

In the 2015 guideline, Recommendation 71 strongly recommended therapeutic compartmental central and/or lateral neck dissection in patients with persistent or recurrent disease confirmed by biopsy, where anatomically localized central neck lymph nodes were ≥8 mm and lateral neck nodes were ≥10 mm, performed within previously operated compartments while preserving uninvolved vital structures.

In the 2025 revision, Recommendation 52 point 1 emphasizes that the decision for reoperation should consider multiple factors—including prior surgical extent, lesion size and anatomical location, growth rate, patient-specific factors/preferences, and overall disease context—rather than relying solely on lymph node size criteria.

Additionally, ethanol ablation and RFA were not mentioned in the 2015 guidelines, but in the 2025 revision, they are suggested as conditional, low-certainty alternative therapies for recurrent or residual thyroid cancer.[5]

## Should RAI therapy be used in the treatment of isolated cervical lymph node metastases?

In the 2025 revision, Recommendation 53 addresses this point. It states that for defined isolated cervical lymph node metastases, additional RAI therapy may be considered in cases where local therapy is not feasible, or following local treatment (Conditional recommendation, Low certainty of evidence).[5]

In the 2025 revision, the use of RAI in the treatment of isolated cervical lymph node metastases is presented as a formal recommendation. In the 2015 revision, although the text emphasized that "for regional nodal metastases detected on diagnostic WBS, RAI could be used in patients with low-volume disease or in combination with surgery," it was not included among the official recommendations.[4]

## Should external beam radiotherapy (EBRT) be used in isolated cervical lymph node metastases?

In the 2025 revision, Recommendation 54 addresses EBRT in cervical lymph node metastases:

EBRT delivered with modern techniques such as IMRT or stereotactic radiotherapy may be considered in cases of unresectable locoregional recurrence or when there is extranodal extension or soft tissue involvement (Conditional recommendation, Low certainty of evidence).[5]

In the 2015 guidelines, no recommendation was provided regarding external radiotherapy for locoregional lymph node metastases. In the 2025 revision, however, it is suggested—albeit with low certainty of evidence—that external neck radiotherapy may be considered in cases where locoregional disease is unresectable or when there is extranodal extension and soft tissue involvement.[4]

## Preparation and dosage strategies for RAI therapy in regional and/or distant metastases

In the 2025 revision, Recommendation 55 outlines three points regarding preparation and dosing strategies for RAI therapy in patients with regional and/or distant metastases:

The Section A states that, in patients with renal insufficiency or those over 70 years of age, empirical administration of >5.5 GBq (150 mCi) of $^{131}$I should be avoided due to the increased likelihood of exceeding toxicity thresholds. If doses above this level are being considered, dosimetry should be performed before RAI administration to confirm safety (Strong recommendation, Moderate-certainty evidence).

According to section B, dosimetry-guided RAI administration (either lesion-based or based on the maximal tolerated activity) may be taken into consideration for patients with locoregional or metastatic disease for whom doses greater than 5.5 GBq (150 mCi) are being considered (Conditional recommendation, Moderate-certainty evidence).

Section C indicates that for patients with distant metastatic disease treated with RAI, preparation may be achieved either through rhTSH-mediated TSH stimulation or by LT4 withdrawal (Conditional recommendation, Low-certainty evidence).

It should be noted that in the 2025 revision, point C is presented as a conditional recommendation with a low level of evidence.[5]

In the 2015 revision, Recommendation 73 stated that although dosimetric approaches to the treatment of locoregional or metastatic disease have theoretical advantages, no recommendation could be made regarding the superiority of one method of RAI administration [empirical high activity, blood and/or body dosimetry, or lesional dosim-

etry) over another. In subsection B of the same recommendation, it was emphasized that in patients over the age of 70, empirically administered doses of 131-I exceeding 150 mCi, which could potentially surpass the maximum tolerable tissue dose, should be avoided [Strong recommendation, Moderate-quality evidence).

In the 2025 revision, however, it is specifically recommended that in patients with renal impairment or those over 70 years of age, when doses above 5.5 GBq [150 mCi) are considered, empirical administration should be avoided and treatment should instead be guided by dosimetric assessment.

In the 2015 guideline, Recommendation 74 stated that for patients with distant metastatic disease treated with 131-I, there was insufficient outcome data to recommend routine use of rhTSH-stimulated therapy in all patients. Furthermore, Recommendation 75 noted that recombinant human TSH [rhTSH)–stimulated therapy may be recommended for certain patients who have underlying comorbidities that make iatrogenic hypothyroidism potentially risky, for patients with pituitary disease where serum TSH cannot be elevated, or in cases where treatment delay could be harmful. The activity delivered to these individuals should be at least as high as or higher than what would have been given if the patient had been prepared by hypothyroidism or by a dosimetrically determined activity (Strong recommendation, Low-quality evidence).

In contrast, the 2025 revision provides a more inclusive recommendation, stating that for patients with regional and/or distant metastases, either rhTSH-stimulated TSH elevation or LT4 withdrawal may be used as preparation methods before RAI therapy.[4]

## What RAI dose adjustment strategies should be used in patients with lung metastases?

In the 2025 revision, recommendations for RAI therapy in lung metastases are provided in three points:

A. Pulmonary micrometastases can be treated with RAI, and therapy may be repeated as long as the disease continues to take up RAI and shows a clinical response (Conditional recommendation, Low- certainty evidence).

B. For pulmonary micrometastases, RAI dosing should be either empirical (3.7–7.4 GBq [100–200 mCi]; for patients >70 years, 3.7–5.55 GBq [100–150 mCi]) or estimated using dosimetry to limit whole-body retention at 48 hours to 2.96 GBq (80 mCi) and deliver ≤200 cGy to the bone marrow (Good Practice Statement).

C. RAI can be used to treat radioiodine-avid macronodular metastases, and if an objective benefit is shown, the treatment may be repeated. RAI dosage can be empirical (3.7–7.4 GBq [100–200 mCi]; for patients older than 70 years, 3.7–5.55 GBq [100–150 mCi]) or determined by whole-body dosimetry to keep bone marrow exposure below 200 cGy and 48-hour whole-body retention at 2.96 GBq (80 mCi) (Conditional recommendation, Low-certainty evidence).[5]

In the 2015 revision, Recommendation 77 on the treatment of lung micrometastases was presented in two points, which correspond to points A and B in the 2025 revision. The 2015 guideline specified that therapy could be repeated every 6–12 months, whereas the 2025 revision no longer provides a specific interval for repeat treatment. The recommendation in 2025 is given as a conditional recommendation with low-quality evidence.

For macronodular metastases, the approach in 2015 was described in Recommendation 78, and a similar recommendation appears as point C in the 2025 revision. In 2015, it was emphasized that complete response was uncommon and overall survival was poor; this statement is not included in the 2025 revision.[4]

## RAI dose adjustment strategies in patients with bone metastases

In the 2025 revision, recommendations for RAI therapy and dose adjustment in bone metastases are provided in Recommendation 57, with two points:

According to part A, RAI therapy for iodine-avid bone metastases has been associated with improved survival and is recommended (Strong recommendation, Low-certainty evidence).

Part B states that, the administered activity may be determined either empirically (3.7–7.4 GBq [100–200 mCi]) or using dosimetry (Conditional recommendation, Very low-certainty evidence).

These recommendations are essentially the same as Recommendation 79 in the 2015 revision, with only minor changes in the recommendation strength and evidence level.[5]

## Timing of empirical RAI in Tg-positive, diagnostic RAI scan–negative patients

In the 2025 guideline, this is addressed in Recommendation 58:

A. Patients with stimulated serum Tg <10 ng/mL following thyroid hormone withdrawal or <5 ng/mL following rhTSH (indeterminate response) can be monitored with thyroid hormone therapy alone if there is no structurally identifiable disease. Additional treatment should be saved for situations where serum Tg increases over time or other indications of structural disease progression emerge (Conditional recommendation, Low-certainty evidence).

B. In patients with no targetable tumor on imaging (e.g., cross-sectional imaging and/or 18FDG-PET/CT) but with markedly elevated or rapidly rising serum Tg, empirical (3.7–7.4 GBq, 100–200 mCi) or dosimetry-guided RAI therapy can be considered (Conditional recommendation, Low-certainty evidence).

C. Repeat RAI therapy may be considered for persistent, unresectable disease that localizes following empirical RAI application and shows evidence of a significant tumor shrinkage until the tumor disappears or no longer responds to treatment (Conditional recommendation, Low-certainty evidence).

In the 2015 revision, Recommendations 80–82 presented similar guidance under a single heading. However, 2015 Recommendation 81 included the statement: "The risk of high cumulative RAI activity should be balanced against uncertain long-term benefits. If empirical RAI is given and post-therapy scanning is negative, the patient should be considered RAI-refractory, and further RAI should not be given." This and the corresponding caution in Recommendation 82 regarding high cumulative RAI risk are not included in the 2025 revision.[4,5]

## How is radioactive iodine–refractory (RAIR) DTC classified?

In the 2025 guideline, this is addressed in Recommendation 59:

A. Patients who have not received RAI for ablation or therapy cannot be diagnosed with RAIR DTC. Ablation or therapeutic RAI should be used to assess the disease state of patients who fit the criteria for RAI (Good Practice Statement).

B. Patients with RAIR DTC should not be given additional empirical RAI therapy. Other treatment options should be considered (Good Practice Statement).[5]

In the 2015 guideline, Recommendation 91 classifies RAI-refractory structural DTC in patients who have received appropriate TSH stimulation and iodine preparation into four main categories:

1. Malignant/metastatic tissue that never shows RAI uptake (no uptake outside the thyroid bed on the first therapeutic WBS).
2. Tumor tissue that initially demonstrated RAI avidity but later lost the ability to concentrate RAI (iodine uptake).
3. Heterogeneous uptake, where some lesions show uptake while others do not.
4. Significant RAI uptake is present, but radiologic or clinical progression occurs.

Once a DTC patient is classified as RAI-refractory, there is no indication for further RAI therapy.[4]

In the 2015 revision, the four-item RAIR definition is not explicitly included in the 2025 guideline as a recommendation, although similar explanations appear in the text. In the 2025 revision, it is recommended that for establishing a RAIR diagnosis, RAI therapy should be administered at ablative or therapeutic doses. In section B, it is advised that patients diagnosed as RAIR should not receive empirical RAI therapy, and other treatment options should be considered—this is similar to the 2015 recommendation.

## Which metastatic DTC patients can be monitored without additional treatment?

In the 2025 revision, this is addressed in Recommendation 60:

A. Patients with clinically severe comorbidities or those with RAIR metastatic DTC who are asymptomatic, stable, or minimally progressing can be followed up with serial radiographic imaging every three to twelve months while on TSH-suppressive thyroid hormone therapy (Conditional recommendation, Low certainty evidence).

B. Routine molecular testing is not advised for patients with residual RAIR DTC if systemic therapy or redifferentiation therapy are not planned (Conditional recommendation, Moderate certainty evidence).[5]

This recommendation in the 2025 revision is similar to Recommendation 92 in the 2015 edition.[4,5]

## What is the optimal approach to select the best therapy in RAIR DTC patients considered eligible for systemic treatment?

In the 2025 revision, this is addressed in Recommendation 61:

Before starting systemic treatment for progressive disease, tissue-based biomarker testing should be performed to detect targetable oncogenic alterations (Strong recommendation, Moderate-certainty evidence).[5]

In the 2015 revision, there were no recommendations regarding biomarker testing prior to systemic therapy.

## What is the recommended first-line treatment in progressive RAIR-DTC patients without an actionable oncogenic alteration when systemic therapy is indicated?

In the 2025 revision, this is addressed in Recommendation 62:

In progressive RAIR-DTC patients who do not have an FDA-approved first-line therapy based on an actionable biomarker, a multi-kinase inhibitor (MKI) such as lenvatinib or sorafenib is recommended. Lenvatinib is preferred as first-line therapy in most cases (Strong recommendation, High-certainty evidence).[5]

In the 2015 guideline, Recommendation 96 presented kinase inhibitor therapy as an option to be "considered" only for RAIR

DTC patients with rapidly progressing, symptomatic, or life-threatening disease not amenable to local control. It did not provide specific guidance on which drug to use, only suggesting FDA-approved agents or access through clinical trials.

In contrast, the 2025 guideline strengthens the language from "considered" to "recommended". MKI therapy is now recommended as first-line systemic therapy for progressive RAIR DTC patients who do not have a targetable biomarker for first-line treatment. Specifically, lenvatinib (preferred) and sorafenib are recommended as first-line MKIs.

### Timing of MKI initiation in RAIR DTC patients

In the 2025 revision, this is addressed in Recommendation 63:

A. For symptomatic RAIR DTC patients in whom local therapies such as radiotherapy or surgery are not appropriate, lenvatinib or another MKI should be initiated without delay (Strong recommendation, Moderate-certainty evidence).

B. For asymptomatic RAIR DTC patients with progression over the past 12–14 months and in whom local therapy is not suitable, early initiation of lenvatinib can be considered if the main goal is efficacy. Conversely, if quality of life is the primary concern, delaying lenvatinib initiation and continuing disease monitoring may be the most appropriate approach (Good Practice Statement).[5]

In the 2015 guideline, there was no clear definition or separate recommendation regarding the optimal timing to start MKI therapy in RAIR DTC patients.

### What is the optimal starting dose of lenvatinib in RAIR DTC?

This issue is provided in Recommendation 64 of the 2025 revision. Recommendation 64:

According to part A, for patients starting lenvatinib for progressive RAIR DTC, the recommended starting dose is 24 mg once daily for most patients; a lower starting dose can be considered in selected patients (Strong recommendation, High-certainty evidence).

Part B specifies that, the management of lenvatinib-related adverse events should include dose interruptions and dose reductions as key strategies (Good Practice Statement).[5]

This recommendation was also not included in the 2015 guideline.

### How should adverse effects be managed in patients receiving VEGFR-targeted MKI therapy?

This issue is provided in Recommendation 65 of the 2025 revision. Recommendation 65

For patients undergoing MKI therapy, preventing, minimizing, and promptly managing side effects are crucial. During the first two months of therapy, patients starting MKI medication should be assessed and followed at least every two weeks. After that, they should typically be checked every one to two months (Good Practice Statement).[5]

There was no recommendation regarding this issue in the 2015 edition.

### What is the preferred second-line therapy approach for RAIR DTC patients?

This issue is provided in Recommendation 66 of the 2025 revision. Recommendation 66

In RAIR-DTC patients who experience progression during MKI therapy or cannot tolerate the treatment, Cabozantinib is recommended as a second-line therapy if there is no contraindication to continue the treatment (Strong recommendation, High-certainty evidence).[5]

In the 2015 guideline, Recommendation 97 stated that in the event of failure of initial tyrosine kinase inhibitor therapy, re-evaluation could be considered within therapeutic clinical trials, with a weak recommendation and low-quality evidence. In the 2025 revision, it is clearly recommended that, in the absence of contraindications, Cabozantinib be used as second-line therapy with strong recommendation and high-quality evidence.

In the 2015 guideline, Recommendation 99 advised that unproven agents should primarily be used within therapeutic clinical trials. In the 2025 revision, Recommendations 67–71 more clearly emphasize these agents with low-to-moderate certainty evidence and strong recommendations.

### What is the most appropriate first-line therapy for NTRK fusion–positive RAIR-DTC patients?

In Recommendation 67 of the 2025 revision, it is indicated that, in progressive RAIR-DTC patients harboring an oncogenic NTRK fusion, NTRK-targeted therapy is recommended as first-line treatment (Strong recommendation, Moderate- certainty evidence).[5]

### What is the optimal first-line treatment in RET fusion–positive RAIR-DTC patients?

In the 2025 revision, Recommendation 68 states; In progressive RAIR-DTC patients with oncogenic RET fusion, first-line RET-targeted therapy is recommended (Strong recommendation, Moderate- certainty evidence).[5]

### What is the optimal first-line treatment in ALK fusion–positive RAIR-DTC patients?

Anaplastic lymphoma kinase (ALK)-targeted therapy is advised as the first-line treatment for progressive RAIR-DTC patients with oncogenic ALK fusion, according to Recommendation 69 of the 2025 revision (Strong recommendation, Low- certainty evidence).[5]

## What is the optimal first-line treatment in BRAF V600E–mutated RAIR-DTC patients?

In the 2025 revision, Recommendation 70 states;

A. In progressive RAIR-DTC patients with oncogenic BRAF V600E mutation who are not suitable candidates for lenvatinib, first-line BRAF-targeted therapy may be considered (Conditional recommendation, Moderate-certainty evidence).

B. In BRAF V600E–mutated RAIR-DTC patients who progress during the treatment or cannot tolerate one or more previous MKI therapies, BRAF-targeted therapy is recommended (Strong recommendation, Moderate-certainty evidence).

C. DTC patients with BRAF alterations without V600 mutation should not receive current BRAF-targeted therapies (Strong recommendation, Moderate- certainty evidence).[5]

## What is the optimal first-line treatment in RAIR-DTC patients with other potentially targetable molecular alterations?

In the 2025 revision, Recommendation 71 states:

Progressive RAIR-DTC patients carrying potentially targetable alterations other than NTRK, RET, ALK, or BRAF V600E should be offered participation in a clinical trial or first-line lenvatinib therapy (Conditional recommendation, Low-certainty evidence).[5]

## What is the optimal approach to addressing disease progression in gene-specific therapy for RAIR-DTC?

In the 2025 revision, Recommendation 72 states;

A. Whenever possible, perform surgical or core tumor biopsy to enable NGS testing to identify potential molecular mechanisms of acquired resistance (Good Practice Statement).

B. In patients where tumor biopsy is not feasible, surgical or core biopsy is preferred instead of ctDNA analysis (Conditional recommendation, Low-certainty evidence).

The 2015 ATA guideline did not include a clear definition or separate recommendation for gene-specific RAIR-DTC management.[5]

## What is the role of immunotherapy in RAIR-DTC?

In the 2025 revision, Recommendation 73 states:

In selected patients—such as those whose tumors exhibit high tumor mutational burden or deficiencies in DNA mismatch repair—immune checkpoint inhibitors or other forms of immunotherapy may be considered (Conditional recommendation, Low- certainty evidence).[5]

In the 2015 guideline, immunotherapy was not presented as a recommendation; it was only briefly mentioned that it should be investigated in RAI-resistant thyroid cancer. In the 2025 revision, immunotherapy is presented as a conditional recommendation with low-quality evidence, indicating that it can be applied in selected cases.

## What is the role of kinase inhibitor–mediated redifferentiation therapy in RAIR DTC patients?

In the 2025 revision, Recommendation 74 states:

A. In progressive RAIR DTC patients with targetable mutations, redifferentiation through MAPK pathway blockade can be considered in selected patients. Participation in clinical trials is encouraged (Conditional recommendation, Low certainty evidence).

B. In high-risk, unselected DTC patients, redifferentiation approaches in adjuvant RAI therapy are not recommended (Strong recommendation, Moderate certainty of evidence).[5]

Comparing with the 2015 edition, this appears to be a newly introduced recommendation.

## What is the role of cytotoxic chemotherapy in RAIR DTC?

In the 2025 revision, Recommendation 75 states that in patients with RAIR DTC who are metastatic, rapidly progressive, symptomatic, and/or at imminent risk, and in whom other treatments cannot achieve control, cytotoxic chemotherapy can be considered. However, it is recommended that this treatment preferably be administered within the context of a therapeutic clinical trial (Conditional recommendation, Low-certainty evidence).[5]

According to the 2015 ATA guideline (Recommendation 100), cytotoxic chemotherapy in RAIR DTC patients was suggested for consideration in metastatic, rapidly progressive, symptomatic, or life-threatening disease not controlled by other treatment options (e.g., tyrosine kinase inhibitors). In the 2025 guideline, this recommendation remains unchanged, with the addition that this therapy is preferably administered within the context of a therapeutic clinical trial.[4]

## What is the optimal approach for patients with oligometastatic RAIR DTC?

In the 2025 revision, Recommendation 76 states that for patients with RAIR DTC who have solitary or oligometastatic disease (two to five lesions), focal ablation therapy may be considered. The optimal treatment approach should be determined through evaluation by a multidisciplinary team (Conditional recommendation, Low-certainty evidence).[5]

In the 2015 ATA guideline, oligometastatic RAIR DTC was only briefly mentioned in Recommendation 96 in the con-

text of kinase inhibitor use and was not presented as a formal recommendation. In contrast, the 2025 ATA guideline introduces a completely new Recommendation 76 specifically for the management of patients with solitary or oligometastatic RAIR DTC.[4]

## What is the optimal treatment approach for localized symptomatic RAIR DTC?

In the 2025 revision, Recommendation 77 states: Local therapy is recommended for patients with symptomatic RAIR DTC. Surgical resection, radiotherapy, or percutaneous thermal ablation techniques (e.g., RFA, MWA, cryoablation) can be applied to the disease foci causing symptoms (Conditional recommendation, Moderate-certainty evidence).[5]

In the 2015 ATA guideline, local therapies for managing symptomatic foci in patients with RAIR-DTC were mentioned briefly. Surgical resection, stereotactic body radiotherapy (SBRT), thermal ablation, and radiotherapy were discussed in explanatory text for localized RAIR-DTC, but these approaches were not clearly defined, and recommendation levels were not specified. Recommendation 93 addressed advanced thyroid cancers, noting that methods such as stereotactic radiation and thermal ablation (RFA and cryoablation) could serve as alternatives to surgery in distant metastases.

In the current guideline, Recommendation 77 explicitly includes RFA, MWA, and cryoablation as options for managing symptomatic RAIR-DTC foci, in addition to surgery and radiotherapy. Furthermore, this recommendation is classified as conditional with moderate- certainty evidence, providing a clearer statement on the strength and certainty of the evidence.[4,5]

## In patients with DTC, when should bone-targeted agents be considered?

In the 2025 revision, Recommendation 78 states:

According to part A, in RAIR-DTC patients with symptomatic and/or multiple bone metastases, treatment with bone-modifying agents is advised to reduce the risk of skeletal-related events (Strong recommendation, Low- certainty evidence).

Part B states that administering bone-modifying agents every 3 months instead of monthly may reduce the risk of adverse events such as osteonecrosis of the jaw. However, this approach could increase the risk of symptomatic skeletal events (Conditional recommendation, Low- certainty evidence).[5]

In the 2015 ATA guideline, Recommendation 101, the primary approach for managing bone metastases in RAIR-DTC patients focused on symptom control using local therapies (surgery, radiotherapy) alongside systemic treatments. For widespread or symptomatic bone metastases, bisphosphonates or denosumab were recommended, with prior assessment of renal function, calcium levels, and dental evaluation. In the 2025 ATA guideline, Recommendation 78, it is similarly recommended that bone-modifying agents be used in RAIR-DTC patients with symptomatic or multiple bone metastases. New in 2025 is the additional guidance on the dosing interval of these agents.[4,5]

## What is the optimal treatment in patients with brain metastases?

In the 2025 revision, Recommendation 79 indicates;

A. The primary treatment approach for central nervous system metastases is surgical resection and/or SBRT (Conditional recommendation, Low-certainty evidence).

B. If the metastases are RAI-avid, radioactive iodine may be considered. When RAI is planned, pre-treatment with SBRT and concomitant glucocorticoids is recommended to minimize the effects of TSH-stimulated tumor volume increase and RAI-related inflammatory response (Good Practice Statement).[5]

There is no major difference between the 2015 and 2025 guidelines regarding the management of brain metastases. In the 2015 guideline, Recommendation 94 addressed the approach for DTC patients with brain metastases, and the 2025 revision presents a nearly identical recommendation.[4,5]

## Who should be considered for clinical trials?

In the 2025 revision, Recommendation 80 states that, patients should be informed about participation in prospective clinical trials based on the eligibility criteria of specific studies and the potential benefits of participation. Physicians considering referring patients to clinical trials should review available treatment options and eligibility criteria. This process should preferably involve direct discussions with research center staff and review of materials available at www.clinicaltrials.gov (Good Practice Statement).[5]

There is no significant difference between 2015 Recommendation 95 and 2025 Recommendation 80 regarding which patients should be included in clinical trials. In 2015, the recommendation was supported as a "strong recommendation, moderate-quality evidence," whereas in 2025, although no formal recommendation grade is given, it is presented as a Good Practice Statement.[4,5]

## Management considerations for pregnant patients with DTC

A. The majority of pregnant patients can safely postpone surgery until after delivery. As an exception, surgery may be performed in the second trimester in rare cases with a

significant risk of disease progression (Conditional recommendation, Low-certainty evidence).

B. It is recommended for individuals with DTC throughout pregnancy to have at least one neck ultrasound performed in the early second trimester, and more frequently if clinically required. In some situations, MRI cross-sectional imaging may be performed. Ionizing radiation-intensive imaging techniques ought to be reserved for extremely critical situations (Conditional recommendation, Low-certainty evidence).

C. TSH targets in pregnant patients are generally the same as those set before pregnancy. If there are concerns about potential adverse effects of excessive thyroid hormone on pregnancy, the levothyroxine dose may be adjusted to allow for less TSH suppression. TSH should be monitored approximately every 4 weeks until 16–20 weeks of gestation, and at least once between 26–32 weeks (Good Practice Statement).

D. In pregnant patients with an incomplete response to therapy, follow-up with neck ultrasound and Tg is appropriate; if cross-sectional imaging is needed, MRI is preferred. Pregnant patients with an excellent or indeterminate response category should be monitored in the same way as nonpregnant patients (Conditional recommendation, Low-certainty evidence).[5]

In the 2015 revision, Recommendation 31 summarized the management of malignancy in pregnant patients in a single statement. It is advised that papillary thyroid cancer detected early in pregnancy should usually be monitored with ultrasound. If the tumor shows significant growth before 24–26 weeks of gestation or if suspicious cervical lymph nodes are detected, surgery during pregnancy may be considered. However, if the disease remains stable until mid-gestation, or if the diagnosis is made during the second half of pregnancy, surgery should be delayed until after delivery.[4]

In contrast, the 2025 revision addresses DTC management during pregnancy in more detail under Recommendation 81, divided into four subpoints. Similar to the previous guideline, it recommends delaying surgery until after delivery in the absence of significant disease progression, with the option of surgery in the second trimester if progression occurs. Different from the 2015 guideline, the 2025 update explicitly allows MRI for cross-sectional imaging when necessary during pregnancy, while emphasizing that ionizing radiation should only be used in exceptional situations. Moreover, the 2025 revision introduces clear recommendations on TSH monitoring frequency in pregnant patients with DTC.[5]

## What are the long-term survivorship issues associated with thyroid cancer treatment?

In the 2025 revision, Recommendation 82 states that patients should be informed about potential long-term side effects related to the treatments they have received. In addition, these patients should be monitored during follow-up with appropriate interventions and/or referrals as needed (Good Practice Statement).

In the 2015 ATA guideline, long-term survivorship issues were discussed only within the section on long-term follow-up of DTC, but not presented as a formal recommendation. In contrast, the 2025 revision introduces this topic explicitly as a recommendation.[4,5]

## How should the financial challenges caused by thyroid cancer be addressed?

In the 2025 revision;

According to the part A, patients and families struggling financially due to a thyroid cancer diagnosis should be informed about the resources available to help alleviate this burden (Good Practice Statement).

Part B states that clinicians should be aware that many patients with thyroid cancer face financial hardship arising from the costs of diagnosis, treatment, and follow-up. These issues should be discussed openly with patients and their families (Good Practice Statement).[5]

In the 2015 guideline, there was no direct recommendation regarding financial toxicity.

In contrast, the 2025 revision introduces a new recommendation, emphasizing that the financial burden experienced by patients and their families should be acknowledged and openly discussed.[4,5]

## What are the critical psychosocial issues in thyroid cancer survivors?

In the 2025 revision, Recommendation 84 states:

A. The availability of resources that can assist with their psychosocial needs in relation to the cancer diagnosis should be emphasized to thyroid cancer survivors (Good Practice Statement).

B. Healthcare professionals who treat patients with thyroid cancer should be ready to help them cope with the psychological effects of the diagnosis and course of therapy (Good Practice Statement).[5]

In the 2015 ATA guideline, the psychosocial dimension was addressed only indirectly, mentioned briefly in the explanatory sections, and—similar to financial toxicity—no formal recommendation was provided.

In the 2025 revision, however, unlike the previous guideline, clinicians are now recommended to support thyroid cancer survivors in addressing their psychosocial needs.[4,5]

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