



# African Head and Neck Society Clinical Practice guidelines for thyroid nodules and cancer in developing countries and limited resource settings

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## Abstract

**Background:** International thyroid nodule and cancer management guidelines generally fail to take into account potential limitations in diagnostic and treatment resources.

**Methods:** Thyroid cancer specialists from the African Head and Neck Society and American Head & Neck Society Endocrine Section developed guidelines for diagnosis and management of thyroid nodules and cancer in low resource settings. Recommendations were based on literature review and expert opinion, with level of evidence defined.

**Results:** Using the ADAPTE process, diagnostic and treatment algorithms were adapted from the National Comprehensive Cancer Network (NCCN). Low resource settings were simulated by systematically removing elements such as availability of laboratory testing, hormone replacement, imaging, and cytopathology from NCCN guidelines.

**Conclusions:** Successful management of thyroid nodules and cancer in low resource settings requires adaptation of treatment methodologies. These guidelines define specific scenarios where either more or less aggressive intervention for thyroid pathology may be advisable based on limited available resources.

## KEYWORDS

clinical guidelines, developing countries, low resource settings, thyroid cancer, thyroid nodules

## 1 | INTRODUCTION

Thyroid nodules are common and are estimated to occur in at least 33% of the population.<sup>1</sup> Studies suggest that approximately 95% of thyroid nodules are benign and will not progress to malignant disease.<sup>2,3</sup> However, the rate of malignancy within thyroid nodules may be higher in low resource settings,<sup>4</sup> specifically since nodules are more frequently detected when clinically apparent rather than incidentally. Moreover, approximately 90% of malignant thyroid cancers are well-differentiated histological variants,<sup>5</sup> with the majority diagnosed as papillary (PTC), follicular (FTC), or Hürthle cell thyroid cancers (HTC). In iodine sufficient regions, PTCs are by far the most common subtype, while follicular cancers have been

reported as relatively more common in iodine deficient regions.<sup>6,7</sup> Because differentiated cancers are generally slow-growing and have a good prognosis,<sup>8,9</sup> treatment of differentiated thyroid cancer has become more conservative with observation being a reasonable option for small (<1 cm) low-risk PTCs in patients with reliable follow-up,<sup>10</sup> and less extensive surgery and less frequent use of radioactive iodine employed for low risk differentiated cancers.<sup>11,12</sup>

Many thyroid nodules and cancers are diagnosed incidentally by ultrasound (U/S) and other imaging modalities. However, radiological screening for thyroid nodules and cancers is not recommended.<sup>13</sup> Because the majority of thyroid nodules are not life threatening and hence do not require surgery, investigation of a thyroid nodule is

directed at identifying the minority of cases that require thyroid surgery, as opposed to observation or simple reassurance. The principal diagnostic tools used for thyroid nodules and cancers and to avoid unnecessary surgery are thyroid U/S and fine needle aspiration cytology (FNAC).<sup>14</sup>

International guidelines for management of thyroid nodules and cancers such as those of the American Thyroid Association (ATA) and National Comprehensive Cancer Network (NCCN) assume the availability of thyroid stimulating hormone (TSH) assays, U/S, FNAC, thyroid scans, radioactive iodine (RAI), thyroid and calcium monitoring and replacement, and reliable follow-up.<sup>15,16</sup> However, in low resource settings, such as those found in developing countries, these studies and interventions frequently are not available or are unaffordable.<sup>7,17</sup> Compliance and/or scheduling of follow-up examinations may also be unreliable. Hence, international guidelines for management of thyroid nodules and cancers often cannot be applied to low resource settings.

Without resource-appropriate guidelines for thyroid nodules and cancers, domestic surgeons (and even volunteer surgeons visiting from higher-resource settings) have little guidance with regard to best practice when working in limited-resource settings. Failure to take resource limitations into account may lead to inappropriate surgery, over-investigation or, in the worst-case scenario, even have life-altering or fatal consequences associated with unforeseen perioperative complications or postoperative sequelae. Herein are presented diagnostic and treatment guidelines for management of thyroid nodules and thyroid cancer in low resource settings.

## 2 | METHODS

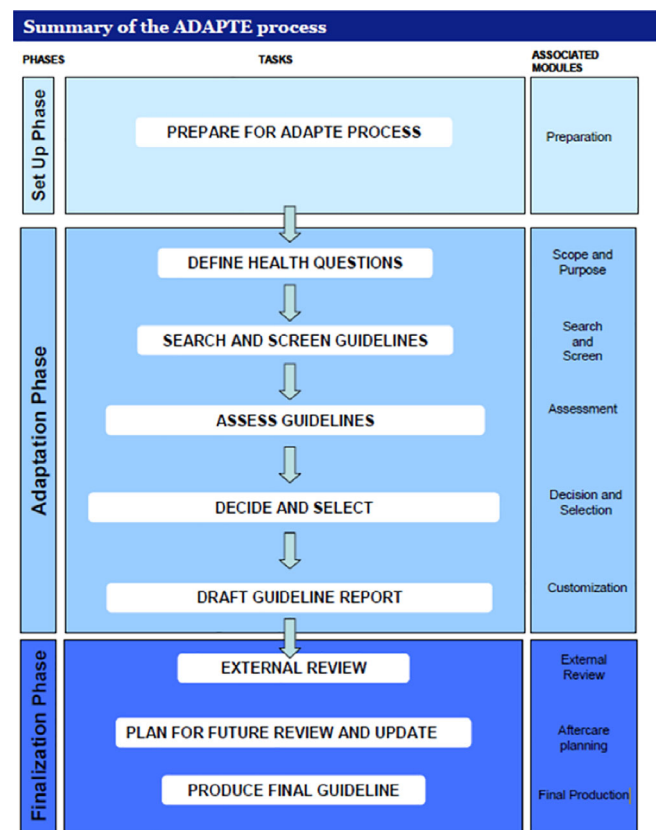
The African Head and Neck Society (AfHNS) convened a task force of thyroid specialists to review thyroid nodule and thyroid cancer management guidelines for low resource settings, with a particular focus on preoperative, perioperative, and postoperative decision making. This international collaboration included otolaryngologists and general surgeons with expertise in head and neck endocrine surgery from across the globe, including members of the AfHNS and American Head & Neck Society (AHNS) Endocrine Section. The task force met in Cape Town in December 2018.

A comprehensive literature review using the PubMed and Cochrane libraries was performed. The search strategy used the following algorithm: (“thyroid cancer” or “thyroid neoplasm” or “thyroid nodule” or “thyroid carcinoma”) and (“evaluation” OR “diagnosis” or “imaging” or “management” or “treatment” or “neck dissection” or

“surgery”) and (“developing” or “resource poor” or “low resource” or “underdeveloped” or “less developed” or “emerging” or “third world”) and (“Countries” or “Nations” or “Area” or “Region”).

The information gathered in this literature review guided the development of task force recommendations—with supplementation by expert opinion and society guidelines when information regarding a particular subject was lacking. In particular, the 2018 NCCN Clinical Practice Guidelines for thyroid carcinoma were used as a framework and adapted for limited resource settings. Low resource scenarios were created by systematically removing elements, such as availability of TSH, U/S, RAI, and so on, from the NCCN diagnostic and management criteria. The task team used the ADAPTE process, a validated systematic approach to amending evidence-based clinical practice guidelines (Figure 1), to modify diagnostic and treatment protocols developed for resource-rich environments to account for the constraints of low resource settings.<sup>18</sup> Each recommendation that was developed was categorized based on the level of evidence and consensus, similar to system utilized by the NCCN<sup>16</sup>:

Category 1: high level evidence and uniform consensus of the authors.



**FIGURE 1** Summary of the ADAPTE process used to create low resource guidelines for thyroid nodule and cancer management [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

Category 2A: lower-level evidence with uniform consensus of the authors.

Category 2B: lower-level evidence with consensus (not uniform) of the authors.

Category 3: any level of evidence where there is significant disagreement between the authors.

It should be noted that there are many reasons why a particular resource could be considered “unavailable,” including a lack of technology or equipment, delays in availability of resources, and/or poor quality of available resources. In this study, we consider low-resource environments as any setting where particular resources are either physically unavailable, financially unavailable, or practically unavailable if the quality of the test is poor on account of inadequate equipment (eg, ultrasound or FNA equipment) or expertise (eg, radiologist/surgeon experienced with thyroid ultrasound or pathologist capable of interpreting thyroid cytopathology). Therefore, a low resource setting can refer to a rural or less developed region within a more developed country, or to a particular patient for whom resources are inaccessible even within an otherwise resource-rich region.

### 3 | RECOMMENDATIONS

#### 3.1 | Evaluation of thyroid nodule or mass in low resource settings

Nodularity of the thyroid gland is common in the general population, and the majority of thyroid nodules are benign and do not require surgical excision.<sup>3,19</sup> Nodules may be detected on incidental neck palpation or by U/S imaging, with the important caveat that standardized screening for healthy adults is not recommended by the U.S. Preventative Services Task Force.<sup>13</sup> Thyroid cancer is estimated to be present in approximately 5% of thyroid nodules,<sup>3,20</sup> although this rate may be higher in low resource settings.<sup>4</sup>

To rule out thyroid cancer, the standard diagnostic workup consists of a thyroid U/S with FNAC.<sup>15,16</sup> Ultrasound is universally agreed to be the most sensitive and specific initial imaging modality for thyroid nodules, and while U/S is generally available in most settings, the quality of the U/S varies substantially with the experience of the ultrasonographer. Additionally, in high-resource settings, indeterminate thyroid nodules can be evaluated with molecular genetics to aid in risk stratification,<sup>15</sup> but this resource-intensive and expensive technology is almost never available in low resource settings.

Serum TSH is standardly checked to evaluate thyroid function at the time of thyroid nodule evaluation. When TSH is not available, clinical signs and symptoms may

be used to determine the probability of a hyperthyroid or euthyroid/hypothyroid state. A clinically validated method is Wayne's Index, with reported positive predictive value of 95% and negative predictive value of 90%<sup>21,22</sup> (Table 1). In situations of hyperthyroidism, a radioactive iodine uptake test may be employed to evaluate the functionality of a thyroid nodule.<sup>23</sup> As any combination of these studies may not be available in low resource settings (Figure 2), clinicians must often rely on alternative clinical evaluation and diagnostic criteria.

**Recommendation 1:** When U/S is unavailable, the history and physical examination of the thyroid and neck may yield features suggestive of higher risk of malignancy, such as rapid growth, firm mass, thyroid asymmetry, cervical lymphadenopathy, recent onset of hoarseness, and vocal cord paralysis. When U/S is unavailable, these high-risk clinical features are indications for FNAC.

Level of evidence: 2A.

**Recommendation 2:** CT or MRI should be considered to assess a thyroid nodule only when U/S is not available. These imaging modalities have poorer sensitivity and specificity and are more expensive than U/S.

Level of evidence: 1.

**Recommendation 3:** Clinical signs and symptoms may be used to determine the probability of a hyperthyroid or euthyroid/hypothyroid state when TSH testing is not available. Wayne's Index can be used as a clinically validated assessment score.

Level of evidence: 2A.

**Recommendation 4:** Other than a rapidly growing thyroid mass, biopsy of a thyroid nodule is typically not urgent, and referral to a better-resourced center for FNAC is recommended if possible.

Level of evidence: 1.

**Recommendation 5:** If referral for FNAC is not possible, clinical and U/S findings may be employed to risk-stratify thyroid nodules using the Thyroid Imaging Reporting and Data System (TI-RADS) (<http://tiradscalculator.com/>). Patients with high-risk clinical and sonographic features are advised to have surgery with histopathologic review of the thyroid specimen.

Level of evidence: 1.

#### 3.2 | Surgical options for thyroid tumors in low-resource settings

Surgical intervention may be indicated for thyroid nodules or cancer in low resource settings for either diagnostic evaluation or definitive management. While FNAC is the preferred diagnostic methodology, a diagnostic lobectomy (or nodulectomy in select cases) may be performed

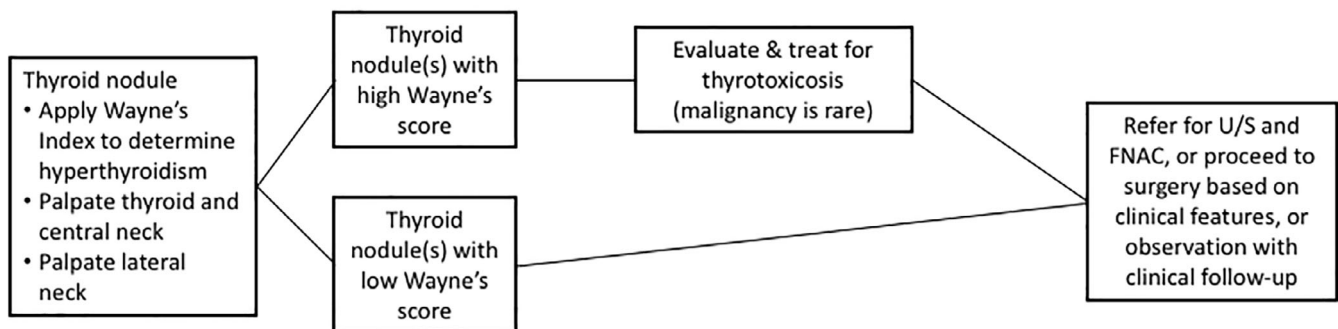
Symptoms	Score	Signs	Present	Absent
Preference for cold	5	Hyperkinesia	4	-2
Excessive sweating	3	Atrial fibrillation	4	0
Appetite increased	3	Palpable thyroid	3	-3
Weight decreased	3	Pulse >90 beats/min	3	0
Palpitations	2	Bruit over thyroid	2	-2
Tiredness	2	Exophthalmos	2	0
Nervousness	2	Lid retraction	2	0
Dyspnea on effort	1	Hands hot	2	-2
Appetite decreased	-3	Lid lag	1	0
Weight increased	-3	Hands moist	1	-1
Preference for heat	-5	Pulse >80 beats/min	0	-3

**TABLE 1** Clinical assessment scores for Wayne's Index

Note: Score of >19 indicates hyperthyroidism; score of <11 indicates euthyroid state.

### AfHNS guidelines for evaluation of a thyroid nodule / mass

Scenarios	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
	Available investigations															
Ultrasound	X		X	X	X				X	X	X	X				
TSH	X	X		X	X		X	X			X		X			
Thyroid scan	X	X	X		X	X		X	X					X		
FNAC	X	X	X	X		X	X			X					X	



**FIGURE 2** Guidelines for evaluation of a thyroid mass without U/S, TSH, thyroid scan, and FNAC [Color figure can be viewed at wileyonlinelibrary.com]

to determine tumor histopathology when FNAC is unavailable. Complete thyroid lobectomy is preferred over thyroid nodulectomy in cases where adequate thyroid hormone is available, unless the nodule is located in the isthmus, wherein a thyroid isthmusectomy may be performed.

However, situations in which patients do not have access to thyroid hormone monitoring and replacement require careful consideration. On the one hand, approximately 25% of thyroid lobectomy patients ultimately develop hypothyroidism,<sup>24,25</sup> with resultant quality of life implications in patients who are not adequately supplemented with thyroid hormone. On the other hand, all other things considered, it is generally safest to perform a complete thyroid lobectomy with identification of the

recurrent laryngeal nerve (RLN), rather than a thyroid nodulectomy, where the RLN may not be identified and therefore could be at increased risk for injury. Additionally, when considering a thyroid nodulectomy, the location of the nodule within the thyroid gland is an important factor, with superficially located anterior, superior, and inferior thyroid nodules posing much less risk of nerve injury with excision than posterior nodules. In a low-resource setting without access to thyroid hormone, a surgeon must carefully weigh the risk of lifelong hypothyroidism with the risk of RLN injury, considering the size and location of the thyroid nodule.

For diagnosed thyroid carcinoma, surgical resection is generally recommended as a primary form of treatment in the vast majority of cases.<sup>16</sup> However, in a low-



resource setting, the degree of thyroid resection should be carefully considered in light of how the extent of thyroid surgery may influence perioperative complications and long-term quality of life. Total thyroidectomy is not recommended in settings without adequate thyroid hormone and/or calcium monitoring and replacement. As approximately 25% of thyroid lobectomies patients have been found to develop hypothyroidism,<sup>24,25</sup> even thyroid lobectomies must be carefully evaluated in low resource settings. Similarly, hypoparathyroidism can be a fatal perioperative complication and remains a possible contraindication to total thyroidectomies when adequate supplementation is unavailable.

In environments where total thyroidectomy cannot be safely performed due to aforementioned resource constraints, a thyroid lobectomy or subtotal thyroidectomy may be considered. The Dunhill procedure is a type of subtotal thyroidectomy procedure that involves complete removal of one thyroid lobe with preservation of the superior and posterior thyroid on the contralateral side. With this procedure, the posterior thyroid tissue near the cricothyroid joint is preserved, with the intent of not disturbing the RLN, although failure to identify the nerve does potentially pose increased risk of injury. Similarly, the intent of preservation of the superior and posterior thyroid tissue is to increase the likelihood of preservation of the superior parathyroid glands, which are generally located along the posterosuperior aspect of the gland. Risks of subtotal thyroidectomy include hemorrhage, RLN injury, tumor recurrence, and the understanding that any future revision surgery will be more challenging in a setting of incomplete thyroid removal.<sup>26</sup>

**Recommendation 6:** Surgeries less than total thyroidectomy should be performed when a patient does not have reliable access to postoperative thyroid or calcium monitoring and replacement.

Level of evidence: 2A

**Recommendation 7:** If FNAC is not available, an open surgical excisional biopsy may be performed in patients with high-risk clinical and sonographic features. For patients with access to thyroid hormone monitoring and replacement, diagnostic complete thyroid lobectomy should be performed rather than nodulectomy.

Level of evidence: 2A.

**Recommendation 8:** For patients without access to thyroid hormone monitoring and replacement, a thyroid nodulectomy may be considered in the diagnostic evaluation and management of thyroid nodules. Nodules in the thyroid isthmus or positioned anteriorly within the thyroid are most favorable for diagnostic nodulectomy, as risk to the RLN and parathyroid glands are lower for nodules in these locations. It must be recognized that while nodulectomy may decrease incidence of

postoperative hypothyroidism as compared to thyroid lobectomy, risk of injury to the RLN may be increased depending on the location of the nodule within the thyroid, the trajectory of the RLN, and the experience of the surgeon. Nodulectomy for posteriorly located thyroid nodules should be avoided due to higher risk of RLN injury.

Level of evidence: 2B.

**Recommendation 9:** Subtotal thyroidectomy (eg, Dunhill procedure) is a surgical option for patients with benign thyroid goiters and thyroid cancers who require bilateral thyroid surgery but who cannot undergo total thyroidectomy due to lack of access to thyroid or calcium monitoring and replacement.

Level of evidence: 2A.

### 3.3 | Management of papillary thyroid cancer in low-resource settings

PTC accounts for approximately 85% of all thyroid carcinomas, although this rate is lower in iodine deficient regions due to a higher incidence of FTC.<sup>6,7</sup> PTC is a well-differentiated thyroid cancer that is generally associated with slow tumor growth and good prognosis and outcomes.<sup>27</sup> Most cases of PTC occur sporadically, but some known risk factors include radiation exposure to the neck and genetic syndromes including familial adenomatous polyposis and Cowden syndrome.<sup>28,29</sup>

Initial management of PTC is often stratified based on tumor size. Large tumors (>4 cm) generally are recommended for total thyroidectomy with possible central neck dissection, whereas small tumors (<4 cm) may be treated by either a lobectomy or total thyroidectomy.<sup>16</sup> High-risk tumor features include large tumor size (>4 cm), significant gross extrathyroidal or extranodal extension, bulky cervical lymph node metastases, and distant metastases. Postoperative RAI presupposes that the thyroid gland has been removed, and therefore these high-risk features often become indications for upfront total thyroidectomy.<sup>15</sup> However, in low resource settings wherein RAI is not available, the decision for total thyroidectomy should not be based upon indications for postoperative RAI.

In appropriately resourced settings, elective central neck dissection is generally only recommended for larger (> 4 cm) papillary thyroid cancers, and often it is not recommended electively in any circumstance.<sup>30</sup> In low-resource settings, especially in environments where calcium monitoring and replacement are not readily available, all four parathyroid glands cannot be put at risk, as the risk of harm from life-threatening hypoparathyroidism and hypocalcemia outweigh any potential benefit.

Therefore, when calcium monitoring and replacement are not available, unilateral papillary thyroid cancer can safely be treated with unilateral surgery (thyroid ± central lymph node dissection in appropriate cases), whereas modifications to the surgical plan must be made for cases with bilateral disease such that all four parathyroid glands are not put at significant risk (typically precluding total thyroidectomy and/or bilateral central compartment dissection). Additionally, since gross intraoperative assessment of lymph nodes generally has poor correlation with final pathology, surgeons in low resource environments should especially exercise caution in putting all four parathyroid glands at risk in any situation based on presence of intraoperatively identified lymph nodes.

**Recommendation 10:** In situations when thyroid and calcium replacement are unavailable, management of PTC may be stratified based on the extent of disease. For a tumor less than 2 cm in size with no gross extrathyroidal extension in a patient less than 55 years old, observation with follow-up U/S may be most appropriate. For thyroid cancers larger than 2 cm that do not extend to the contralateral lobe, the recommended surgery is either a lobectomy or nodulectomy. In cases where more extensive disease is present bilaterally, a subtotal thyroidectomy may be performed if the disease can be completely excised while still preserving sufficient thyroid remnant and avoiding putting all four parathyroid glands at risk. A unilateral central neck dissection may

be performed in patients with clinically apparent or FNA proven lymph node metastases (Figure 3).

Level of evidence: 2A.

**Recommendation 11:** In an environment wherein RAI is unavailable, a thyroid lobectomy is recommended for unilateral PTC, regardless of tumor size, extra-thyroidal or extranodal extension, or distant metastasis. In patients with bilateral thyroid disease and/or bilateral cervical lymph node involvement, total thyroidectomy with or without central neck dissection may be indicated. In instances of lateral neck lymphadenopathy, a respective lateral neck dissection (levels II-Vb) should also be performed (Figure 4).

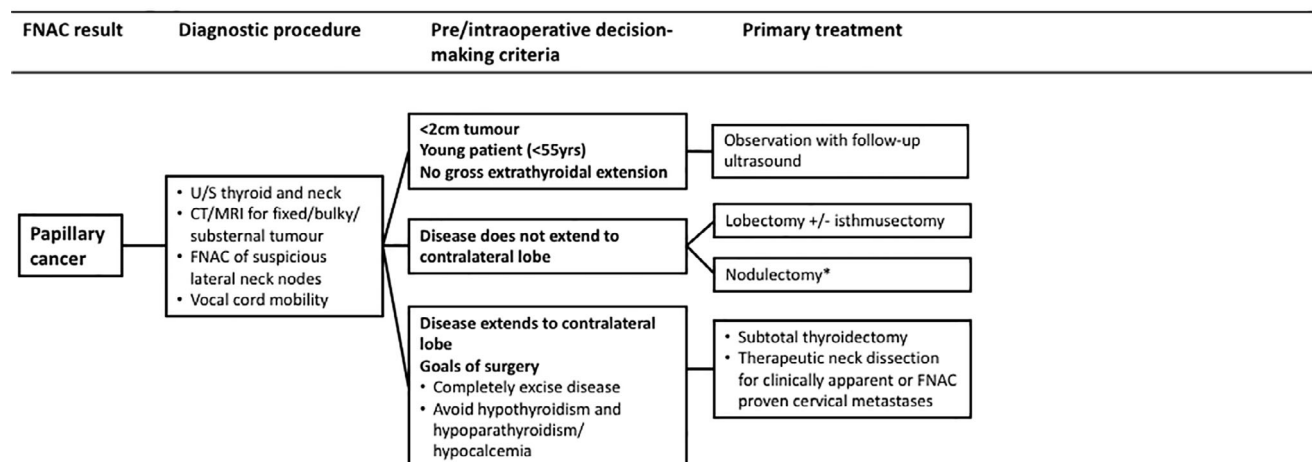
Level of evidence: 2A.

### 3.4 | Management of follicular and Hürthle cell carcinomas in low-resource settings

FTC represents approximately 10% of thyroid carcinoma, and HTC makes up <2% of thyroid cancers.<sup>31</sup> Lymphatic involvement is rarely observed for FTC whereas HTC has a propensity for both vascular and lymphatic spread.<sup>32</sup> The Bethesda System is commonly used to report thyroid cytopathology and direct treatment options. Bethesda Stage III corresponds to a follicular lesion or atypical cells of undetermined significance, while Bethesda IV indicates

#### AfHNS thyroid management guidelines: papillary/suspicious for papillary carcinoma

Scenarios	1	2	3	4	5	6	7	8
	Available							Unavailable or poor follow-up
Thyroid monitoring/replacement	X		X	X	X			
Ca <sup>++</sup> monitoring / replacement	X	X		X		X		
Radioactive iodine therapy	X	X	X				X	

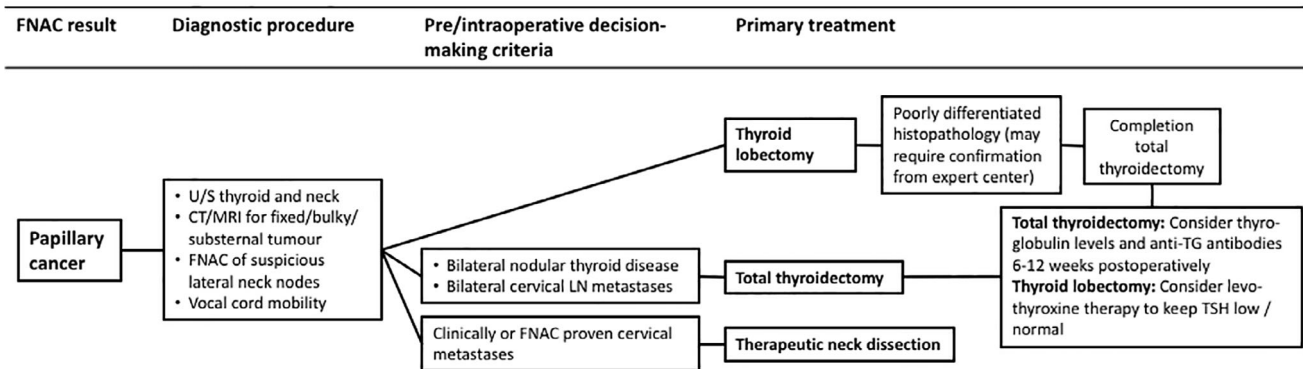


\*While thyroid lobectomy would almost always be preferred over nodulectomy in situations with adequate thyroid hormone monitoring and replacement, in low-resource settings where thyroid hormone monitoring and replacement is not available, nodulectomy may be considered in cases where nodules are located superficially and anteriorly in the thyroid lobe. It must be recognized that while nodulectomy may decrease incidence of postoperative hypothyroidism as compared to thyroid lobectomy, risk of injury to the recurrent laryngeal nerve may be increased depending on the location of the nodule within the thyroid, the trajectory of the recurrent laryngeal nerve, and the experience of the surgeon.

**FIGURE 3** Management algorithm for PTC in setting without calcium or thyroid hormone replacement [Color figure can be viewed at wileyonlinelibrary.com]

## AfHNS thyroid management guidelines: papillary/suspicious for papillary carcinoma

Scenarios	1	2	3	4	5	6	7	8
	Available							Unavailable or poor follow-up
Thyroid monitoring/replacement	X		X	X	X			
Ca <sup>++</sup> monitoring / replacement	X	X		X			X	
Radioactive iodine therapy	X	X	X				X	



**FIGURE 4** Management recommendations for PTC in setting without access to RAI therapy [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

cytopathology identified as a follicular neoplasm or Hürthle cell lesion/neoplasm.<sup>33</sup> However, cytopathology from FNAC cannot be used reliably to distinguish between benign and malignant follicular growths, since the diagnosis requires histopathologic evidence of vascular or capsular invasion.<sup>34</sup> Thus, Bethesda Stage III and IV classified FNAC specimens have only an approximate 15% and 25% risk of ultimately representing a thyroid carcinoma.<sup>35</sup>

While the Bethesda system is commonly employed to risk stratify nodules in resource-rich environments, cytopathology is often not available in low resource environments. In these situations, if U/S is available, the TI-RADS classification can be employed to risk stratify nodules based on ultrasonographic features.<sup>36</sup> If neither cytopathology or U/S are available, then the clinician must use clinical exam findings such as growth, firmness, presence of associated lymphadenopathy, and vocal cord paralysis/voice changes in order to risk stratify patients with thyroid nodules/masses.

**Recommendation 12:** In a low-resource setting without thyroid hormone and/or calcium monitoring and replacement, indeterminate (Bethesda III and IV) thyroid lesions/neoplasms should generally be observed, unless the lesion demonstrates highly suspicious ultrasonographic features or demonstrates growth over time. With growth or suspicious ultrasonographic features, thyroid lobectomy (or nodulectomy in select cases) may be considered. The decision for diagnostic thyroid lobectomy for larger or posteriorly located Bethesda III and IV nodules should be counterbalanced with the understanding that patients with chronically low thyroid hormone (without access to thyroid hormone replacement and monitoring) may have decreased quality of life.

Level of evidence: 2A

**Recommendation 13:** In a low-resource setting without thyroid hormone and/or calcium monitoring and replacement, if a diagnostic lobectomy (or nodulectomy in select cases) indicates minimally invasive follicular carcinoma or follicular carcinoma with vascular invasion, or if surgical pathology is unavailable, completion thyroidectomy is not recommended (Figure 5).

Level of evidence: 2A.

**Recommendation 14:** In a low-resource setting without thyroid hormone and/or calcium monitoring and replacement, subtotal thyroidectomy should only be considered for follicular lesions/neoplasms if there is bilateral disease, and if the disease can be completely excised while still preserving sufficient thyroid remnant and avoiding putting all four parathyroid glands at risk (Figure 5).

Level of evidence: 2A

**Recommendation 15:** In the event that postoperative RAI is not available when considering surgery for a neoplasm suspicious for FTC or HTC, total thyroidectomy should be performed only in cases of bilateral tumor extension or bilateral cervical lymph node metastases.

Level of evidence: 2A.

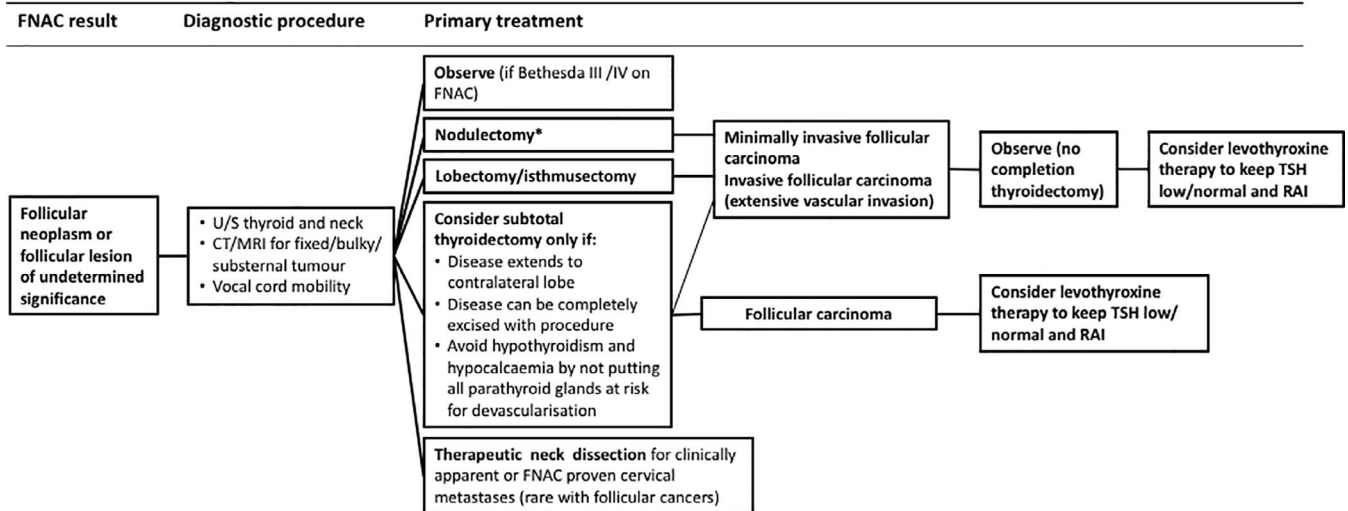
### 3.5 | Management of medullary thyroid cancer in low-resource settings

Medullary thyroid cancer (MTC) is a rare neuroendocrine tumor of the parafollicular (C) cells of the thyroid gland, representing about 2% of thyroid carcinoma cases.<sup>37</sup> The majority of MTC occur sporadically, but



**AfHNS thyroid management guidelines: Follicular neoplasm/carcinoma**

Scenarios	1	2	3	4	5	6	7	8
	Available							
Thyroid monitoring/replacement	X		X	X	X			Unavailable or poor follow-up
Ca <sup>++</sup> monitoring / replacement	X	X		X		X		
Radioactive iodine therapy	X	X	X				X	



\*While thyroid lobectomy would almost always be preferred over nodulectomy in situations with adequate thyroid hormone monitoring and replacement, in low-resource settings where thyroid hormone monitoring and replacement is not available, nodulectomy may be considered in cases where nodules are located superficially and anteriorly in the thyroid lobe. It must be recognized that while nodulectomy may decrease incidence of postoperative hypothyroidism as compared to thyroid lobectomy, risk of injury to the recurrent laryngeal nerve may be increased depending on the location of the nodule within the thyroid, the trajectory of the recurrent laryngeal nerve, and the experience of the surgeon.

**FIGURE 5** Management guidelines for FTC without calcium or thyroid hormone replacement [Color figure can be viewed at wileyonlinelibrary.com]

approximately 25% of cases are hereditary, associated with a *RET* proto-oncogene mutation and multiple endocrine neoplasia type 2 (MEN2) syndrome.<sup>35</sup> Total thyroidectomy and central compartment dissection are recommended for MTC management by the NCCN and ATA guidelines,<sup>16,37</sup> but this is predicated on availability of calcium and thyroid hormone monitoring and replacement after surgery. Elective lateral neck dissection has been variably advocated based on serum calcitonin levels,<sup>38</sup> although recent investigation suggests that observation of the lateral neck in the absence of ultrasonographically apparent neck disease results in similar biochemical cure and ultimate locoregional control.<sup>39</sup>

**Recommendation 16:** When thyroid and calcium monitoring and replacement are not available, a total thyroidectomy cannot be performed for MTC. In these situations, a lobectomy may be considered for unilateral MTC thyroid disease, with consideration for an ipsilateral central neck dissection. For bilateral MTC thyroid disease, subtotal thyroidectomy may be considered, if the disease can be completely excised while still preserving sufficient thyroid remnant and avoiding putting all four parathyroid glands at risk. Depending upon the burden of bilateral disease, the risks of hypothyroidism and

hypocalcemia must be balanced with desire for complete tumor removal.

Level of evidence: 2A.

**Recommendation 17:** In the absence of radiographically apparent disease in the lateral neck, elective lateral neck dissection for MTC is generally not recommended. For patients who do not have access to ultrasound and/or cross-sectional imaging of the lateral neck, elective lateral neck may be considered, especially in cases wherein there is gross disease in the ipsilateral central neck.

Level of evidence: 2A.

**4 | CONCLUSIONS**

Successful management of thyroid neoplasms in low-resource settings often requires adaptation of existing treatment paradigms. Standard evaluation of thyroid nodules is predicated on the availability of U/S, serum TSH, thyroid scans, and/or FNAC. Clinical findings and assessment scores such as Wayne’s Index provide an alternative method for evaluating thyroid function in the absence of serum TSH. Similarly, clinical identification of the features of malignant thyroid masses such as rapid growth,

firm mass, thyroid asymmetry, cervical lymphadenopathy, recent onset of hoarseness, and vocal cord paralysis takes on greater significance in the absence of conventional diagnostic imaging and FNAC.

While definitive surgical resection is the standard of care for thyroid neoplasms and cancers, extent of thyroid surgery should be carefully considered in low-resource settings, especially among populations without access to calcium and thyroid hormone replacement or radioactive iodine. For patients with thyroid cancer, appropriate surgery must be tailored based on a number of factors including histopathology, disease extension, and resource availability, as perioperative complications such as hypocalcemia and/or hypothyroidism may be worse than not treating the disease at all. Referral to higher-resourced environments is occasionally an option and highly encouraged when possible, but more often than not patients in low-resource environments simply do not have access to higher levels of care.

Detailed discussion of cost of specific technologies, medications, and procedures in various low resource settings, as well as general solutions for lack of health care resources globally, are largely beyond the scope of these guidelines. However, the advent of portable U/S in particular represents a unique opportunity to introduce relatively low-cost technology for the basic evaluation of thyroid masses.<sup>40</sup> Telectytopathology represents another example of how the integration of technology and education may contribute to bridging resource gaps in the evaluation and treatment of thyroid nodules and cancers.<sup>41</sup> The integration of new lower cost technologies into low resource health care environments should ideally be accompanied by educational collaborations between developed and developing countries.<sup>42,43</sup>

The complete set of AfHNS thyroid nodule and cancer treatment algorithms can be found at the following link: <https://developingworldheadandneckcancerguidelines.com/>. Overall, these conjoint AfHNS and AHNS Endocrine Section guidelines provide a systematic methodology of evaluating and treating thyroid nodules and cancers while operating within the constraints of limited resource environments.

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**How to cite this article:** Zafereo M, Yu J, Onakoya PA, et al. African Head and Neck Society Clinical Practice guidelines for thyroid nodules and cancer in developing countries and limited resource settings. *Head & Neck*. 2020;42:1746–1756. <https://doi.org/10.1002/hed.26094>