Version date: Sept 18, 2024
Version Number: v4
MRP: Dendra Hillier (PMO)

Primary Care Management Pathway
Thyroid Nodule Pathway

Background

Primary care management pathways (PCMP) are being co-developed by primary care physicians (PCP) and specialists to support the management of common, non-urgent conditions for which long wait times to specialty care currently exist. This thyroid nodule pathway will help differentiate patients with high-risk features who require timely specialist assessment from those who can be safely managed by their PCP.

Defining Thyroid Nodules

- Thyroid nodules may be found during a physical examination or incidentally on imaging of the neck. The majority of thyroid nodules are benign. Approximately 5% may be malignant.
- General examination of the thyroid gland may be a part of the routine physical examination. Risk factors for thyroid malignancy include history of head and neck irradiation, total body irradiation for bone marrow transplant, childhood or adolescent exposure to ionizing radiation (e.g., from fallout), family history of thyroid cancer, or rare genetic diseases such as Multiple Endocrine Neoplasia (MEN) 2.
- Differential diagnosis of a thyroid mass include thyroglossal duct cyst, thyroid hemorrhagic cyst, lymph node(s) or parathyroid adenoma. A dedicated thyroid ultrasound is the first line test for differentiation of a thyroid mass. Final work up will be determined by the results of the ultrasound and clinical picture.
- The ultrasound report should characterize the nodule using the Thyroid Imaging Reporting and Data System (TI-RADS). TI-RADS reporting assigns points based on composition, echogenicity, shape, margin and echogenic foci to determine 5 grades. Risk of malignancy, need for ultrasound guided fine needle aspiration (FNA) biopsy, and follow-up is determined by the TI-RADS grade and size of the nodule.

Checklist for work-up of the patient with a thyroid nodule

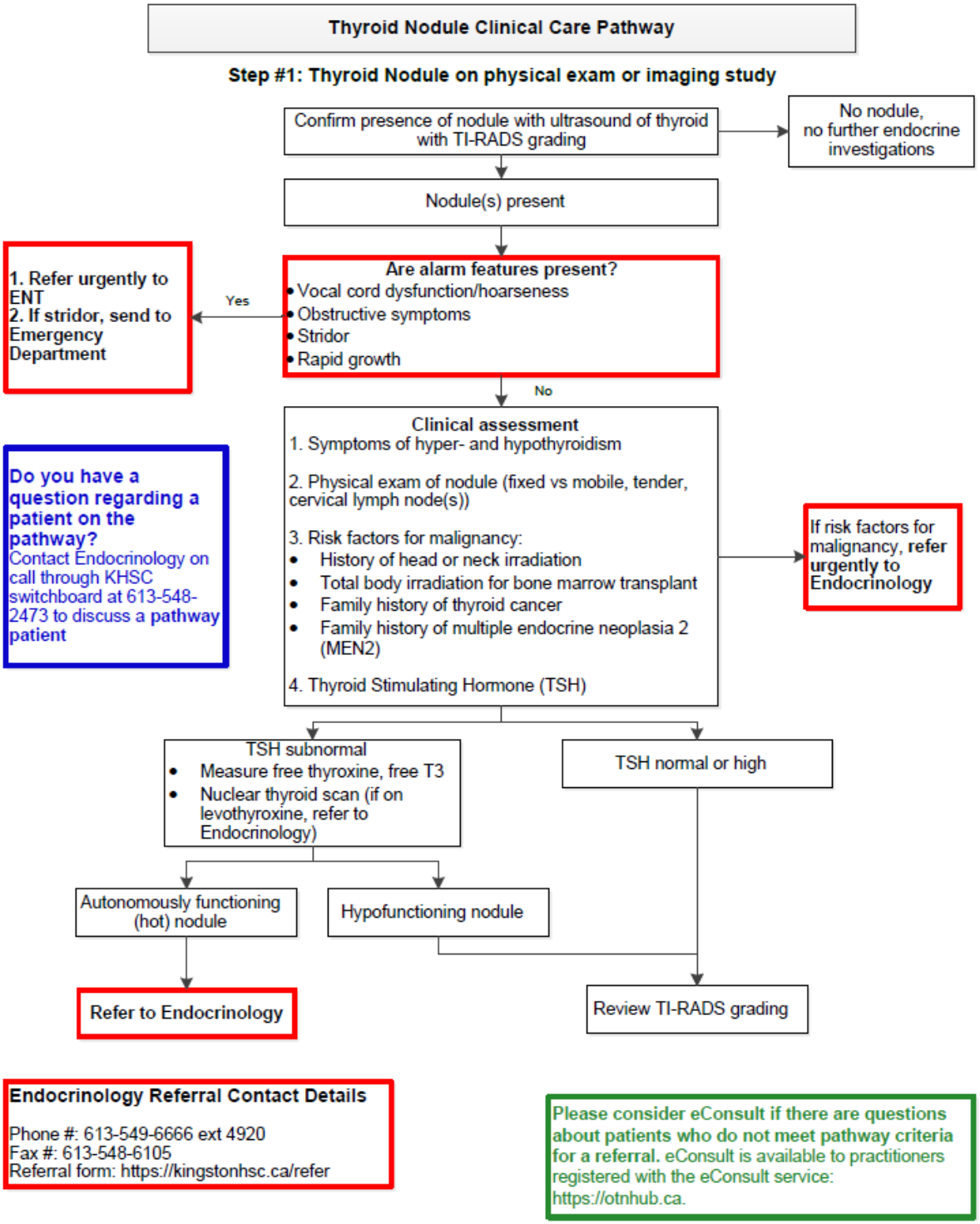
- ✓ Assess for red flag features: change in voice or hoarseness, rapid growth, obstructive symptoms, stridor.
- ✓ Assess for risk factors for malignancy; history of head and neck irradiation, whole body irradiation for bone marrow transplant, childhood or adolescent exposure to ionizing radiation (e.g., from fallout), family history of thyroid cancer, MEN 2.

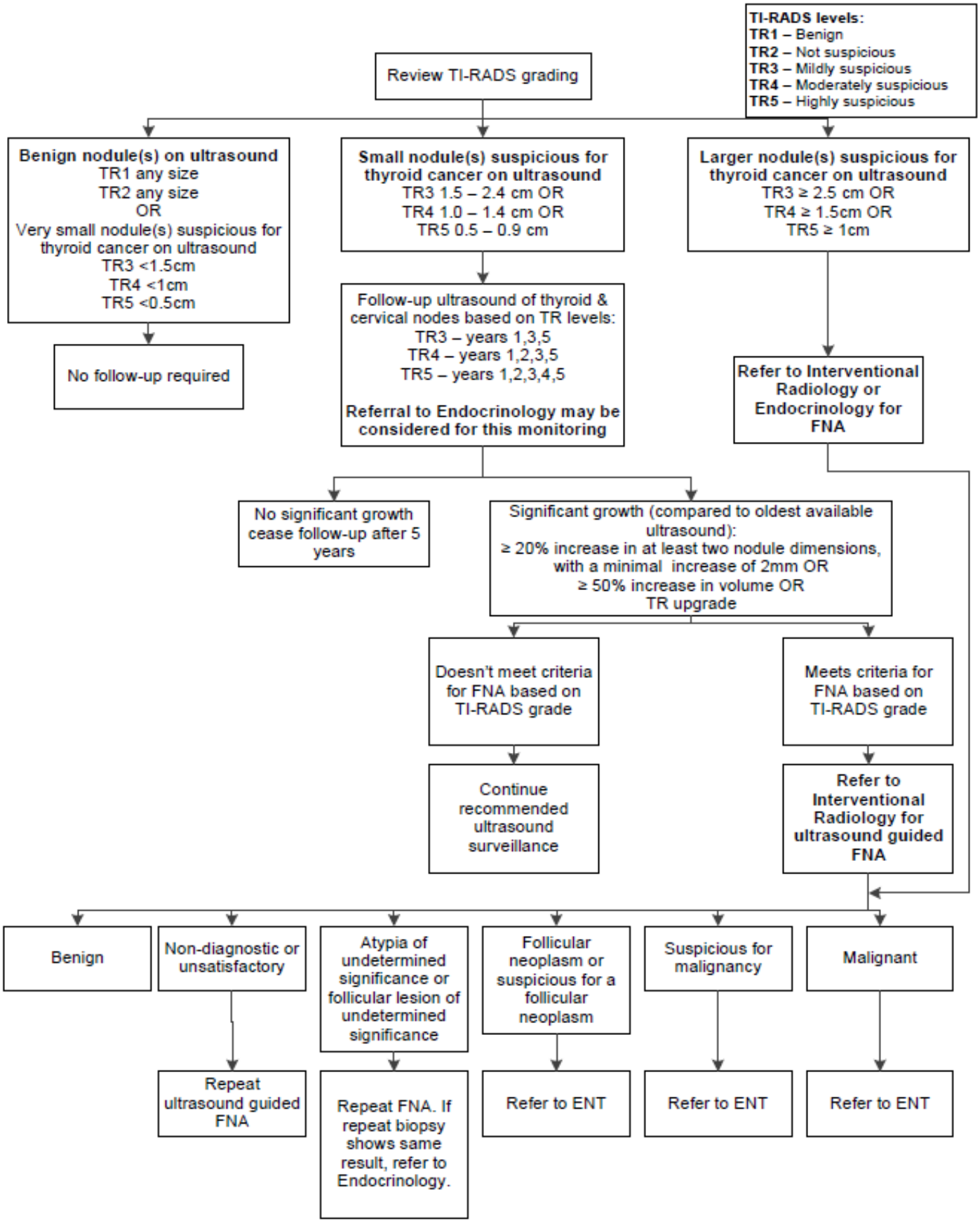
- ✓ Assess patient for symptoms and signs of hyper- or hypothyroidism.
- ✓ Measure TSH (if not already recently done).
- ✓ Assess characteristics of nodule (size, fixed vs. mobile, tender), and presence of cervical nodes.
- ✓ Arrange dedicated thyroid ultrasound with TI-RADS reporting.

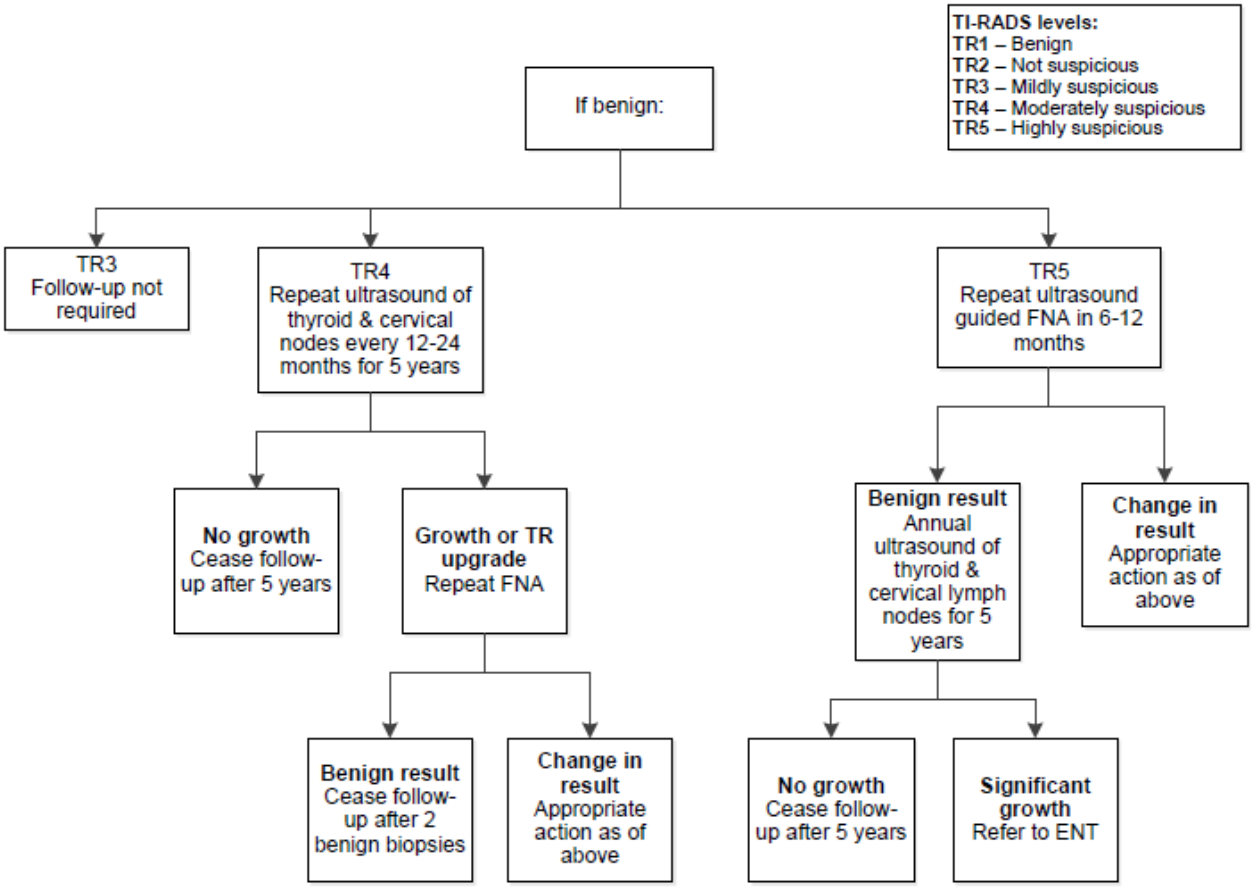
Patient information

It is possible that your patient and/or their family member may express a desire for additional information about the primary care management pathway and their role or experience throughout the process of being on a pathway. Additional information for patient education has been provided in “Appendix B – Patient Information”.

Primary Care Management Pathway – Clinical Flow Diagram
Thyroid Nodules




TI-RADS levels:
TR1 – Benign
TR2 – Not suspicious
TR3 – Mildly suspicious
TR4 – Moderately suspicious
TR5 – Highly suspicious
Review TI-RADS grading
Benign nodule(s) on ultrasound
TR1 any size
TR2 any size
OR
Very small nodule(s) suspicious for thyroid cancer on ultrasound
TR3 <1.5cm
TR4 <1cm
TR5 <0.5cm
No follow-up required
Small nodule(s) suspicious for thyroid cancer on ultrasound
TR3 1.5 – 2.4 cm OR
TR4 1.0 – 1.4 cm OR
TR5 0.5 – 0.9 cm
Follow-up ultrasound of thyroid & cervical nodes based on TR levels:
TR3 – years 1,3,5
TR4 – years 1,2,3,5
TR5 – years 1,2,3,4,5
Referral to Endocrinology may be considered for this monitoring
No significant growth cease follow-up after 5 years
Significant growth (compared to oldest available ultrasound):
≥ 20% increase in at least two nodule dimensions, with a minimal increase of 2mm OR
≥ 50% increase in volume OR
TR upgrade
Doesn't meet criteria for FNA based on TI-RADS grade
Continue recommended ultrasound surveillance
Meets criteria for FNA based on TI-RADS grade
Refer to Interventional Radiology for ultrasound guided FNA
Larger nodule(s) suspicious for thyroid cancer on ultrasound
TR3 ≥ 2.5 cm OR
TR4 ≥ 1.5cm OR
TR5 ≥ 1cm
Refer to Interventional Radiology or Endocrinology for FNA
Benign
Non-diagnostic or unsatisfactory
Repeat ultrasound guided FNA
Atypia of undetermined significance or follicular lesion of undetermined significance
Repeat FNA. If repeat biopsy shows same result, refer to Endocrinology.
Follicular neoplasm or suspicious for a follicular neoplasm
Refer to ENT
Suspicious for malignancy
Refer to ENT
Malignant
Refer to ENT


TI-RADS levels:
TR1 – Benign
TR2 – Not suspicious
TR3 – Mildly suspicious
TR4 – Moderately suspicious
TR5 – Highly suspicious
If benign:
TR3
Follow-up not required
TR4
Repeat ultrasound of thyroid & cervical nodes every 12-24 months for 5 years
TR5
Repeat ultrasound guided FNA in 6-12 months
No growth
Cease follow-up after 5 years
Growth or TR upgrade
Repeat FNA
Benign result
Annual ultrasound of thyroid & cervical lymph nodes for 5 years
Change in result
Appropriate action as of above
Benign result
Cease follow-up after 2 benign biopsies
Change in result
Appropriate action as of above
No growth
Cease follow-up after 5 years
Significant growth
Refer to ENT

Appendix A – Expanded Detail

Thyroid Nodules

1. Thyroid nodules are commonly found incidentally on physical exam or imaging of the neck (US, CT or MRI). The presence of a thyroid nodule should be confirmed with a dedicated ultrasound of the neck and thyroid as this will confirm the presence of the nodule(s), characterize its features, and detect any lymph nodes.
2. When a thyroid nodule or other neck mass is noted, it is important to screen for alarm features or red flags. These include: stridor (may suggest compression of the airway); hoarseness (may suggest compression of the vocal cords by the lesion); obstructive symptoms; or a rapidly growing nodule (may suggest an aggressive malignancy or hemorrhage into a mass).
3. While most cases of papillary thyroid cancer are spontaneous, there are several risk factors. These include a history of head or neck radiation (e.g., treated for lymphoma at a younger age) or radiation fallout from power plant accidents or nuclear weapons (e.g. Chernobyl, Fukushima etc.) There are several hereditary conditions that are associated with an increased risk of papillary thyroid cancer: Cowden syndrome; Familial Adenomatous Polyposis; Carney complex, type 1; and Familial non-medullary thyroid carcinoma (strong family history of papillary thyroid cancer). There are several hereditary conditions that are associated with an increased risk of medullary thyroid cancer. These include MEN 2A (associated with pheochromocytomas and parathyroid gland adenomas; and MEN 2B (associated with pheochromocytomas and benign neuromas). Patients with risk factors for malignancy should be referred to Endocrinology.
4. When investigating a thyroid nodule, a TSH should be requested at baseline. This helps to distinguish if a nodule is non-functional (the majority), or functional (i.e. hot).
5. A normal or elevated TSH is suggestive of a non-functional adenoma. The risk of malignancy in a non-functional adenoma is approximately 5%. Therefore, if the TSH is normal or elevated and the nodule meets criteria for a biopsy, a fine needle aspiration under ultrasound guidance should be arranged. A technetium thyroid scan is not needed.
6. A subnormal TSH may indicate that the thyroid nodule is functional (i.e. hot; shows increased uptake of technetium or radioactive iodine). The risk of malignancy in functional (i.e. hot) nodules is very low and biopsy is not usually indicated. The follicular cells in a functional nodule may be interpreted as highly abnormal as they can resemble thyroid cancer cells when seen under the microscope. However, hot nodules that are suspicious (e.g., irregular borders) should be considered for possible FNA biopsy.
7. Ultrasound guided FNA biopsy is recommended for several reasons. In nodules that have both a cystic and a suspicious solid component, ultrasound helps to ensure that the suspicious solid component of the nodule is biopsied. Ultrasound

allows for visualization of the needle and surrounding structures (e.g. carotid artery, jugular vein and associated lymph nodes).

8. Using TI-RADS grading, patients with the sole recommendation of clinical and ultrasound follow-up may continue to be managed in primary care without the need for specialist referral.
9. Corresponding malignancy risk for TI-RADS categories are:
   TR1 (Benign): < 2%
   TR2 (Not suspicious): < 2%
   TR3 (Mildly suspicious): < 5%
   TR4 (Moderately suspicious): 5 to 20%
   TR5 (Highly suspicious): > 20%
10. Nodules < 5 mm do not need follow-up, even if they are TI-RADS 5 as very unlikely will become a clinically significant malignancy.
11. The cutoff point of 2.5 cm for FNA biopsy in mildly suspicious TR 3 is based on studies showing thyroid carcinomas don't have decreased survival until they reach this threshold.
12. Growth is defined as
    - ≥20% increase in at least two nodule dimensions, with a minimal increase of 2 mm or
    - ≥50% increase in volume.
13. Comparison should be made with the oldest available study, and not only the last one.
14. If there is no change in size for 5 years, a nodule can be considered as benign and further follow up is not needed. If there is interval growth without fulfillment of FNA criteria, the next follow-up should be after 1 year, regardless of TI-RADS category.

Appendix B – Patient Information

PLEASE NOTE: THE FOLLOWING INFORMATION IS MEANT TO BE GIVEN TO THE PATIENT, EITHER AS A HANDOUT OR IN CONVERSATION WITH THEIR PRIMARY CARE PROVIDER.

WHAT ARE THYROID NODULES?

The thyroid is a butterfly-shaped gland in the middle of the neck located below the larynx (voice box) and above the clavicles (collarbones). Thyroid nodules are round or oval-shaped areas within the thyroid. Thyroid nodules are very common; up to half of all people have at least one thyroid nodules, although most are unaware. Thyroid nodules can be caused by many different conditions. Reassuringly, approximately 95% of all thyroid nodules are caused by benign (noncancerous conditions).

HOW WILL MY DOCTOR FOLLOW MY CONDITION?

Diagnostic tests can be used to determine if a thyroid nodule is benign or malignant (cancerous). There are several tests; however, not every person needs all of these tests.

A common first test is a blood test to measure TSH or Thyroid Stimulating Hormone.

- If your TSH level is **normal**, the next step is to have a thyroid ultrasound. Depending on the appearance of the nodule on ultrasound, a fine-needle aspiration (FNA) biopsy may be recommended.
- If your TSH is **lower than normal**, the next step is to have a thyroid scan.
- If your TSH level is **higher than normal**, more blood work to measure your free thyroxine or thyroid hormone level, and to measure levels of thyroid antibodies is sometimes recommended. A FNA biopsy may also be needed.

FNA biopsy uses a thin needle to remove small tissue samples from the thyroid nodule. This test may be performed either in the Interventional Radiology Department of a hospital Diagnostic Radiology Department of in the clinic of an endocrinologist (thyroid specialist). You may feel some pressure and discomfort during the biopsy similar to a wasp sting. Tissue removed during the FNA is examined by a pathologist with a microscope.

The results of a biopsy will be one of the following:

- Benign (noncancerous)
- Malignant (cancerous)
- Suspicious for malignancy
- Indeterminate – this means that the findings are neither clearly benign nor malignant
- Follicular neoplasm
- Follicular lesion or atypia of undetermined significance
- Nondiagnostic or insufficient – In this case, the biopsy does not contain enough tissue to make a diagnosis, and a repeat biopsy is necessary.

The appropriate treatment and follow up depends on the type of thyroid nodule found. Your physician will explain the test results and recommended management with you.

YOU ARE ENROLLED ON A THYROID NODULE CLINICAL PATHWAY. WHAT DOES THIS MEAN?

The thyroid nodule clinical pathway was developed by family doctors, endocrinologists, otolaryngologists, radiologists, and other specialists at Kingston Health Sciences Centre to help with the assessment and monitoring of thyroid nodules. Clinical pathways are an evidence-based tool for common conditions seen frequently by family doctors. The pathways ensure that patients receive standardized care for their conditions. Clinical pathways help identify patients with high-risk features and facilitate early referral to specialists as needed. They also identify patients with low-risk disease who can be monitored by their family doctors.

Appendix C – Endnotes

Links to additional resources for healthcare providers

American Thyroid Association guidelines**.** www.thyroid.org

TI-RADS reporting.
https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/TI-RADS

AACE/ACE/AME Medical Guidelines. Guidelines | American Association of Clinical Endocrinology (aace.com)

ACR Thyroid Imaging. ACR Thyroid Imaging, Reporting and Data System (TI-RADS): White Paper of the ACR TI-RADS Committee - Journal of the American College of Radiology (jacr.org)

Cancer Care Ontario. Thyroid Cancer Pathway Map. https://www.cancercareontario.ca/en/pathway-maps/thyroid-cancer