

Who should be counseled about the risk of differentiated thyroid carcinoma?

It *is recommended* that childhood, adolescent and young adult cancer survivors treated with radiation therapy that includes the thyroid gland (level A evidence) or therapeutic ¹³¹I-MIBG (level C evidence) should be counseled by their healthcare provider regarding their increased risk for developing differentiated thyroid carcinoma.

It *is recommended* that childhood, adolescent and young adult cancer survivors should be advised to inform their healthcare provider if they detect a thyroid mass, independent of the presence or absence of associated symptoms (expert opinion).

Who should be informed about differentiated thyroid carcinoma surveillance?

It *is recommended* that at-risk survivors (i.e., those treated with radiation therapy that includes the thyroid gland) (level A evidence) should be counseled about options for differentiated thyroid carcinoma surveillance. The decision to commence surveillance should be made by the healthcare provider in consultation with the survivor after careful consideration of the advantages and disadvantages of differentiated thyroid carcinoma surveillance (Box 1) in the context of the survivor's individual preferences.

It *may be reasonable* to inform neuroblastoma survivors who received therapeutic ¹³¹I-MIBG (level C evidence) about options for differentiated thyroid carcinoma surveillance. The decision to commence surveillance should be made by the healthcare provider in consultation with the survivor after careful consideration of the advantages and disadvantages of differentiated thyroid carcinoma surveillance (Box 1) in the context of the survivor's individual preferences.

If the decision to commence surveillance is made, what surveillance modality should be used to detect a thyroid nodule that may represent a differentiated thyroid carcinoma?

It *is recommended* to use neck palpation or thyroid ultrasonography as a screening modality if surveillance for differentiated thyroid carcinoma is planned. Healthcare providers should be aware that both diagnostic tests have advantages and disadvantages and can identify benign as well as malignant nodules resulting in need for invasive procedures (Box 2, Figure 1) (level A evidence). The decision regarding which modality to use should be made by the healthcare provider in consultation with the survivor after careful consideration of the advantages and disadvantages of the two modalities in the context of the practice setting, the health care provider's experience, expertise of local diagnosticians (radiology), and the survivor's preferences.

Ultrasound and FNA and/or biopsy *is recommended* to be performed in centers where there is experience in assessment of thyroid cancers so that appropriate interpretation of radiographic features and clinical risk factors can minimize the number of unnecessary invasive and additional diagnostic procedures. When ultrasound is used for surveillance, the cervical lymph node stations should always be visualized (expert opinion).

If the decision to commence surveillance is made, at what frequency should differentiated thyroid carcinoma surveillance be performed?

It *is reasonable* to commence surveillance for differentiated thyroid carcinoma 5 years after radiation therapy that includes the thyroid gland or therapeutic ¹³¹I-MIBG (level B evidence).

It *is recommended* that even when a childhood, adolescent and young adult cancer survivor does not opt for periodic surveillance with either ultrasonography or palpation, it is appropriate to include examination of the neck as part of a complete physical exam whenever a survivor is assessed by a healthcare provider (expert opinion).

If periodic thyroid palpation is chosen as the screening modality it *may be reasonable* to repeat surveillance for differentiated thyroid carcinoma every 1-2 years (expert opinion; weak recommendation). If thyroid ultrasonography is chosen as screening modality, it *may be reasonable* to repeat surveillance for differentiated thyroid carcinoma every 3-5 years if there are no abnormalities found initially (expert opinion).

What should be done when abnormalities are identified?

Consultation with a thyroid specialist *is recommended* for survivors with a thyroid nodule (detected either by palpation or thyroid ultrasonography, or incidentally noted on other imaging studies (such as CT or MRI)) (expert opinion).

Box 1

Arguments for and against DTC surveillance in at-risk CAYAC survivors (independent of surveillance modality).

Advantages:

- CAYAC survivors undergoing surveillance are likely to have DTC detected at an earlier stage. This may reduce the extent of surgery and/or need for radioiodine therapy, which could decrease overall morbidity, recurrence as well as mortality.
- CAYAC survivors who do not have a DTC detected when they undergo surveillance may benefit by being reassured that they do not have a new cancer.

Disadvantages:

- There is uncertainty about the benefit of early treatment since most DTC can be cured. There are no randomized studies that demonstrate a clear benefit of DTC surveillance.
- Detection of a benign nodule with surveillance (false positive results for DTC) can lead to repeated ultrasounds, fine needle aspiration biopsies or thyroid surgery. These interventions may result in stress and anxiety, as well as inconvenience, costs, and complications of unnecessary biopsies or surgery.
- There is a risk that surveillance will detect an indolent DTC, which may never cause clinical problems and lead to overtreatment.
- False negative results of surveillance may lead to some survivors being falsely reassured that they do not have DTC, when in fact they do.

Abbreviations: DTC: differentiated thyroid carcinoma; CAYAC: childhood, adolescent and young adult cancer.

Box 2Arguments for and against DTC surveillance with neck palpation.

Advantages:

- Quick, inexpensive and non-invasive. High specificity (96–100%) for detecting a thyroid nodule that might represent DTC (many true negatives and few false positives for nodules).

Disadvantages:

- Low sensitivity (17–43%) for detecting a thyroid nodule that might represent DTC (few true positives and many false negatives for nodules).
- Increase in unnecessary invasive procedures due to false positive screening results.
- Detection of DTC at a more advanced stage (compared to thyroid ultrasonography), possibly leading to increased morbidity, recurrence and mortality rate.
- Diagnostic value dependent on experience of the physician (high-interobserver variation).

Arguments for and against DTC surveillance with thyroid ultrasonography.

Advantages:

- Non-invasive.
- High sensitivity (95 to 100%) for detecting a thyroid nodule that might represent DTC (many true positives and few false negatives for nodules).
- High specificity (95 to 100%) for detecting a thyroid nodule that might represent DTC (many true negatives and few false positives for nodules).
- Detection of DTC at an earlier stage (compared to neck palpation).

Disadvantages:

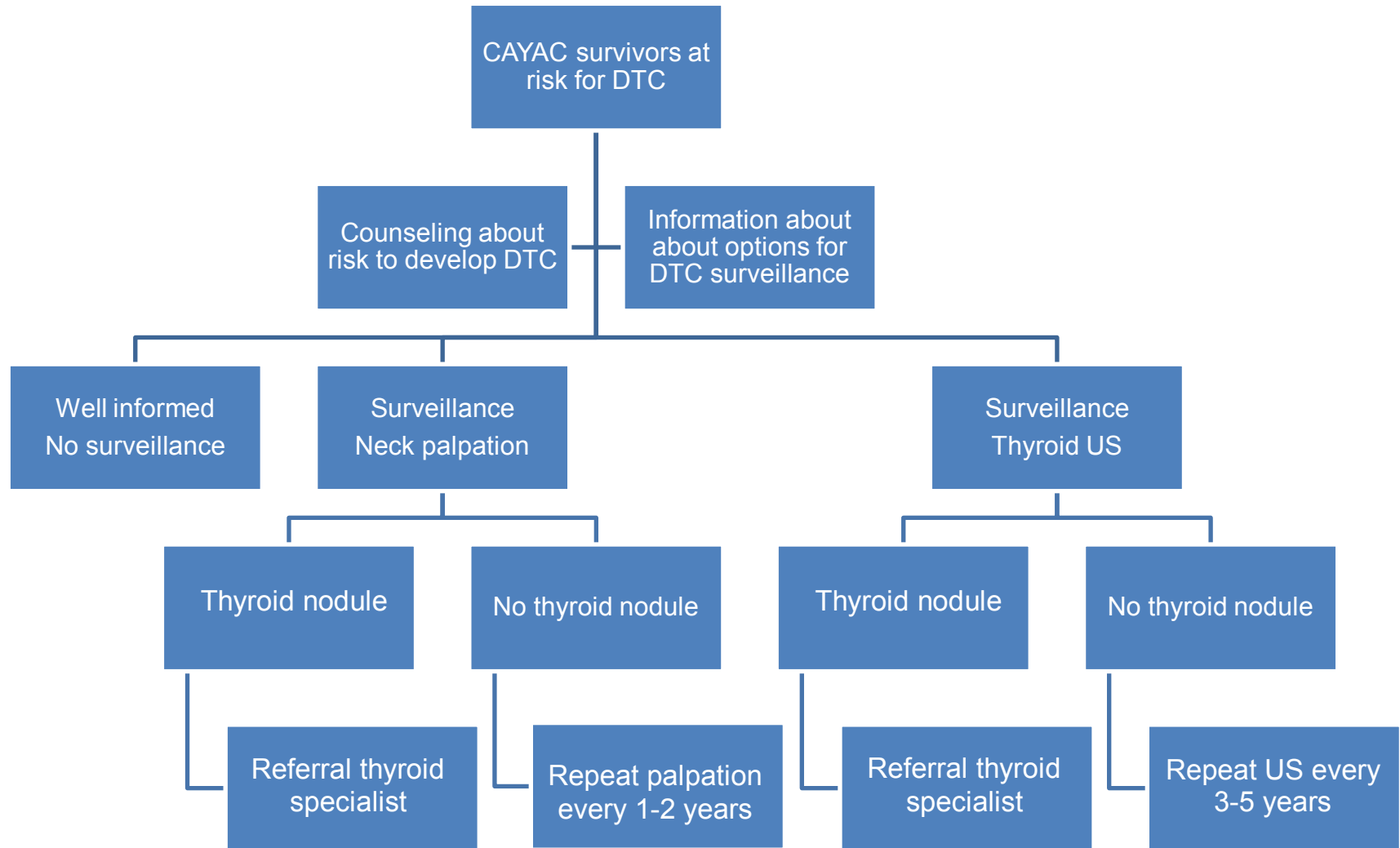
- Poor diagnostic value of ultrasound for predicting whether an identified nodule is a DTC: detection of a high number of benign thyroid nodules and indolent DTC.
- Increase in unnecessary invasive procedures due to false positive screening results.
- Diagnostic value dependent on experience of the ultrasonographer (high-interobserver variation).

Abbreviations: DTC: differentiated thyroid carcinoma.

Publication

Clement SC, Kremer LCM, Verburg FA, Simmons JH, Goldfarb M, Peeters RP, Alexander EK, Bardi E, Brignardello E, Constine LS, Dinauer CA, Drozd VM, Felicetti F, Frey E, Heinzl A, van den Heuvel-Eibrink MM, Huang SA, Links TP, Lorenz K, Mulder RL, Neggess SJ, Nieveen van Dijkum EJM, Oeffinger KC, van Rijn RR, Rivkees SA, Ronckers CM, Schneider AB, Skinner R, Wasserman JD, Wynn T, Hudson MM, Nathan PC, van Santen HM. Balancing the benefits and harms of thyroid cancer surveillance in survivors of Childhood, adolescent and young adult cancer: Recommendations from the international Late Effects of Childhood Cancer Guideline Harmonization Group in collaboration with the PanCareSurFup Consortium. *Cancer Treatment Reviews* 2018;63:28-39.

Figure 1. Options for surveillance of DTC in CAYAC survivors at risk



Abbreviations: DTC: differentiated thyroid carcinoma; US: ultrasonography