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Cosentino G, et al. Ablative versus conservative approach for hyperthyroidism treatment in patients with Graves' orbitopathy: a retrospective cohort study. *Thyroid*. 2025;35(3):298-306; doi: 10.1089/thy.2024.0633. PMID: 39909466

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Thyroid eye disease (TED) is caused by inflammation in the eye muscles in patients with Graves' disease and can result in significant problems with vision that can be hard to treat. Recently, statin use has been associated with lower rates of TED in patients with Graves' disease. The researchers of this study used a large patient database to determine the relationship between statin use and TED.

Chou YT et al. Statin use and the risk of Graves' orbitopathy: a nationwide population-based cohort study. *Thyroid*. 2025;35(2):199-207; doi: 10.1089/thy.2024.0536. PMID: 39804287.

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Why do thyroid cancer outcomes differ across racial and ethnic lines?

Past studies have shown that Black and Hispanic patients often have worse results during thyroid cancer treatment. The researchers wanted to better understand why thyroid cancer outcomes differ across racial and ethnic groups. They measured how much cancer type, treatment differences, and social factors contributed to these differences. They also examined whether the type of surgery patients received affected their chances of doing well.

Fwelo P et al. Disparities in thyroid cancer mortality across racial and ethnic groups: assessing the impact of socioeconomic, clinicopathologic, and treatment variations. *Ann Surg Oncol* 2025;32(2):1158-1175; doi: 10.1245/s10434-024-16569-y. PMID: 39614001.

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Is neck ultrasound required in follow-up of low-risk thyroid cancer in children?

Children and adolescents with thyroid cancer usually have an excellent response to treatment. Although postoperative follow-up with neck ultrasound poses little physical risk, potential harm from overuse can occur because of detection of false-positive or unclear findings, which trigger further investigation, health care expenditures, and patient anxiety. Data on the use of neck ultrasound follow-up in children are particularly lacking. This study examined the risk of thyroid cancer recurrence in children and adolescents and the use of neck ultrasound to follow thyroid cancer low risk patients.

Rao S, et al. Utility of ultrasound surveillance for thyroid cancer in children. *Thyroid* 2025;35(4):406-414; doi: 10.1089/thy.2024.0624. PMID: 39888311.

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How often are thyroid nodules with indeterminate results and negative molecular testing actually cancer?

While most thyroid biopsies show that a nodule is benign (not cancerous), sometimes, the results are unclear (indeterminate). If genetic tests on the cells removed during a biopsy are negative, these nodules are then considered benign. This study looked at how often these indeterminate nodules with negative results on genetic tests are benign and how many actually turn out to be cancer. They also looked at how best to follow these nodules over time.

Nachum S, et al. Thyroid nodules with indeterminate cytology and negative molecular profile: prevalence of malignancy and practice paradigms for surveillance. *Thyroid* 2025;35(3):265-273; doi: 10.1089/thy.2024.0455. PMID: 39874551.

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Incidence and response to treatment for medullary thyroid cancer over time

Medullary thyroid cancer is a relatively uncommon but important form of thyroid cancer. The authors of this study used large European patient databases to evaluate changes in the incidence of medullary thyroid cancer over the last 30 years, as well as to study how surgical treatment for this cancer has changed during this time frame. In particular, these researchers focused on studying the impact changes in surgical treatment have had on the recurrence risk and survival for people diagnosed with medullary thyroid cancer.

Jager EC et al. Trends in the incidence, organization of care, and surgical treatment of medullary thyroid cancer: a population-based study. *Thyroid* 2025;35(1):87-96; doi: 10.1089/thy.2024.0433. PMID: 39705074.

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Editor's Comments

Welcome to another issue of *Clinical Thyroidology for the Public*! In this journal, we will bring to you the most up-to-date, cutting edge thyroid research. We also provide even faster updates of late-breaking thyroid news through X (previously known as Twitter) at [@thyroidfriends](https://twitter.com/thyroidfriends) and on [Facebook](https://www.facebook.com/thyroidfriends). Our goal is to provide patients with the tools to be the most informed thyroid patient in the waiting room. Also check out our friends in the [Alliance for Thyroid Patient Education](https://www.allianceforthyroidpatienteducation.org). The [Alliance](https://www.allianceforthyroidpatienteducation.org) member groups consist of: the *American Thyroid Association*®, *Bite Me Cancer*, the *Graves' Disease and Thyroid Foundation*, the *Light of Life Foundation*, *MCT8 – AHDS Foundation*, *ThyCa: Thyroid Cancer Survivors' Association*, and *Thyroid Federation International*.

We invite all of you to join our [Friends of the ATA](https://www.thyroid.org/donate) community. It is for you that the American Thyroid Association® (ATA®) is dedicated to carrying out our mission of providing reliable thyroid information and resources, clinical practice guidelines for thyroid detection and treatments, resources for connecting you with other patients affected by thyroid conditions, and cutting edge thyroid research as we search for better diagnoses and treatment outcomes for thyroid disease and thyroid cancer. We thank all of the *Friends of the ATA* who support our mission and work throughout the year to support us. We invite you to help keep the ATA® mission strong by choosing to make a donation that suits you — it takes just one moment to give online at: www.thyroid.org/donate and all donations are put to good work. The ATA® is a 501(c)3 nonprofit organization and your gift is tax deductible.

July is [Graves' Disease Awareness Month](https://www.thyroid.org/donate).

In this issue, the studies ask the following questions:

- Do different treatments for Graves' disease affect thyroid eye disease
- Can statin drugs prevent thyroid eye disease?
- Why do thyroid cancer outcomes differ across racial and ethnic lines?
- Is neck ultrasound required in follow-up of low-risk thyroid cancer in children?
- How often are thyroid nodules with indeterminate results and negative molecular testing actually cancer?
- How has the treatment for medullary thyroid cancer changed over time?

We welcome your feedback and suggestions. Let us know what you want to see in this publication. I hope you find these summaries interesting and informative.

— Alan P. Farwell, MD



GRAVES' DISEASE

Hyperthyroidism treatment and thyroid eye disease

BACKGROUND

Hyperthyroidism is a condition whereby the thyroid gland becomes overactive and makes too much thyroid hormone. Graves' disease is an autoimmune condition in which the person produces antibodies that stimulate the thyroid gland to make too much thyroid hormone and causes hyperthyroidism. Some patients with Graves' disease develop thyroid eye disease (sometimes referred to as Graves' eye disease or Graves' orbitopathy). This condition is associated with inflammation of the eye and eye muscles and can cause pain, bulging of the eyes and difficulty moving the eyes which can cause double vision. Treatment of thyroid eye disease (TED) depends on severity and can include high doses of glucocorticoids such as prednisone or methylprednisolone and surgery. A newer medication, teprotumumab/Tepezza™, works differently by blocking a receptor in eye muscles (insulin-like growth factor 1 receptor), and has been markedly effective in the treatment of TED.

Treatment of Graves' disease includes medications (antithyroid drugs), surgery to remove the thyroid and radioactive iodine, which is taken up into the thyroid and destroys it. This study examines the effects of the treatment choice for Graves' disease affected moderate to severe TED and the response of TED to glucocorticoid treatment.

THE FULL ARTICLE TITLE

Cosentino G, et al. Ablative versus conservative approach for hyperthyroidism treatment in patients with Graves' orbitopathy: a retrospective cohort study. *Thyroid*. 2025;35(3):298-306; doi: 10.1089/thy.2024.0633. PMID: 39909466

SUMMARY OF THE STUDY

The study included 49 Italian patients with Graves' disease and moderate to severe TED. The patients were divided into 2 groups for analysis: 24 patients treated with radioactive iodine and 25 with the antithyroid medication methimazole. All patients had moderate to severe TED and received treatment with intravenous high dose glu-

cocorticoids weekly for 12 doses starting at the baseline visit which was approximately 4 weeks after the initial screening visit. Patients that were treated with radioactive iodine received levothyroxine replacement therapy after destruction of the thyroid. The main study endpoint for group comparisons was a composite score of TED activity at 24 weeks compared to baseline. Other outcomes measured overall TED activity and quality of life at 48 and 72 weeks of follow-up. Detailed eye exams to assess TED activity were performed at screening, baseline and every 4 weeks for a total of 72 weeks.

Results showed that the overall response of TED to glucocorticoids was greater in the radioactive iodine treatment group compared to the methimazole group at 24 weeks. However, the proportion of patient responders in the methimazole group increased over time such that at the later time points, there were no differences in eye outcomes. TED specific quality of life was improved at 24 weeks in the radioactive iodine treatment group compared to methimazole treated at 24 weeks but again, these differences were not apparent at the later time points in the study. One patient in the radioactive iodine treatment group and 4 in the methimazole group experienced worsening eye disease at week 24. These data suggest that radioactive iodine treatment for Graves' disease seems to be associated with a faster improvement in TED activity in response to glucocorticoid treatment. However, there were no differences in TED improvements following glucocorticoid therapy when the groups were compared at 48 and 72 weeks. Thus, in the long term, TED responds equally to intravenous glucocorticoid therapy irrespective of whether the patient's hyperthyroidism was treated with radioactive iodine or methimazole. Future studies are needed to confirm these findings.

WHAT ARE THE IMPLICATIONS OF THE STUDY?

This study suggests that radioactive iodine treatment may be associated with a faster improvement in TED following glucocorticoids compared to antithyroid medications.



GRAVES' DISEASE, continued

However, there were no differences in TED response to glucocorticoids at later time points, suggesting that the chosen method of treating hyperthyroidism does not significantly impact TED response to glucocorticoids in the long term. This study shows that patients with Graves'

disease and moderate to severe TED can be treated with radioactive iodine or antithyroid drugs along with steroid without worsening the TED, increasing the options for treatment to normalize their thyroid function.

— Whitney W. Woodmansee MD

ATA THYROID BROCHURE AND WEBSITE LINKS

Hyperthyroidism (Overactive): <https://www.thyroid.org/hyperthyroidism/>

Graves' Disease: <https://www.thyroid.org/graves-disease/>

Radioactive Iodine Therapy: <https://www.thyroid.org/radioactive-iodine/>

Thyroid Eye Disease: <https://www.thyroid.org/thyroid-eye-disease/>

ABBREVIATIONS & DEFINITIONS: FROM ACTIVE LIST

Hyperthyroidism: a condition where the thyroid gland is overactive and produces too much thyroid hormone. Hyperthyroidism may be treated with antithyroid meds (Methimazole, Propylthiouracil), radioactive iodine or surgery.

Graves' Disease: the most common cause of hyperthyroidism in the United States. It is caused by antibodies that attack the thyroid and turn it on.

Radioactive Iodine (RAI): this plays a valuable role in diagnosing and treating thyroid problems since it is taken up only by the thyroid gland. I-131 is the destructive form

used to destroy thyroid tissue in the treatment of thyroid cancer and with an overactive thyroid. I-123 is the non-destructive form that does not damage the thyroid and is used in scans to take pictures of the thyroid (*Thyroid Scan*) or to take pictures of the whole body to look for thyroid cancer (*Whole Body Scan*).

Thyroid Eye Disease (TED): also known as Graves ophthalmopathy. TED is most often seen in patients with Graves' disease but also can be seen with Hashimoto's thyroiditis. TED includes inflammation of the eyes, eye muscles and the surrounding tissues. Symptoms include dry eyes, red eyes, bulging of the eyes and double vision.



GRAVES' DISEASE

Can statin drugs prevent thyroid eye disease?

BACKGROUND

Thyroid eye disease (TED), also known as Graves' orbitopathy, develops in around 25% of patients with Graves' disease. It is caused by inflammation in the eye muscles and can result in significant problems with vision that can be hard to treat. Because of this, strategies to prevent TED are required. Currently, these are limited to recommending stopping smoking, considering selenium supplementation, and considering surgery to remove the thyroid to reduce the level of antibodies that cause Graves' disease.

Statin drugs are very effective drugs aimed at lowering cholesterol levels. They also appear to have other beneficial effects in areas unrelated to lowering cholesterol levels. Recently, statin use has been associated with lower rates of TED in patients with Graves' disease. The researchers of this study used a large patient database to determine the relationship between statin use and TED.

THE FULL ARTICLE TITLE

Chou YT et al. Statin use and the risk of Graves' orbitopathy: a nationwide population-based cohort study. *Thyroid* 2025;35(2):199-207; doi: 10.1089/thy.2024.0536. PMID: 39804287.

SUMMARY OF THE STUDY

The researchers examined the national health insurance database in Taiwan to perform a study of individuals >40 years of age with Graves' disease newly diagnosed between 2010 and 2019. Patients were separated by current statin use at time of the diagnosis of Graves' disease. Patients were followed until one of the study end points was reached: TED diagnosis, switching to a different statin, statin discontinuation for more than 3 months, initiation of any cholesterol-lowering drug in patients not on statins or the end of the study period.

Statin potency and dose were recorded. Other associated factors identified included smoking status, radioactive iodine treatment for Graves' disease, heart disease risk, and obesity. All study information relied on coding in health databases.

There were 102,858 new diagnoses of Graves' disease included in the study. These patients were followed for 4 to 5 years after diagnosis. Some 7073 patients (6.9%) were using statins at the time of Graves' disease diagnosis. Overall, the rate of TED development was 5 cases per 1000 person-years in statin users and 6.75 per 1000 person-years in statin nonusers. The adjusted rate of TED development after statistical analysis was 4.91 cases per 1000 person-years in statin users and 5.15 per 1000 person-years in nonusers. In subgroup analysis, statin use was associated with lower TED incidence in females and in younger patients (ages 40–60 years). No difference in effect was seen by the type of statin or by statin dose.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In this registry-based study of patients with mostly Asian ethnicity, continued statin use at the time of Graves' disease diagnosis was associated with lower rates of subsequent development of TED. However, the absolute effect size was small and was significant only in women in the subgroup analysis. The effect appears independent of type or potency of statin and may be more pronounced in younger individuals (ages 40–60 years). More studies are needed to clarify this effect before any recommendations if statin use in patients with Graves' disease without another indication for statin use. However, these results are promising for patients with Graves' disease.

— Alan Farwell, MD



GRAVES' DISEASE, continued

ATA THYROID BROCHURE LINKS

Graves' Disease: <https://www.thyroid.org/graves-disease/>

Thyroid Eye Disease: <https://www.thyroid.org/thyroid-eye-disease/>

ABBREVIATIONS & DEFINITIONS

Graves' Disease: the most common cause of hyperthyroidism in the United States. It is caused by antibodies that attack the thyroid and turn it on.

Thyroid Eye Disease (TED): also known as Graves ophthalmopathy. TED is most often seen in patients with Graves' disease but also can be seen with Hashimoto's

thyroiditis. TED includes inflammation of the eyes, eye muscles and the surrounding tissues. Symptoms include dry eyes, red eyes, bulging of the eyes and double vision.

Statin Drugs: very effective drugs for lowering high cholesterol and decreasing the risk of heart disease





THYROID CANCER

Why do thyroid cancer outcomes differ across racial and ethnic lines?

BACKGROUND

Thyroid cancer is the most common endocrine cancer in the US. Most people do very well with treatment, but not everyone has the same good outcomes. Past studies have shown that Black and Hispanic patients often have worse results during thyroid cancer treatment. These differences may have multiple causes. For example, some patients may not receive the standard treatments recommended for their condition, or they may be treated by surgeons who perform fewer thyroid operations, which can increase the risk of complications. While past studies have shown differences in outcomes, they often did not specify which types of surgery were done or how this affected the results. Medical factors like the cancer type and size, and whether it has spread, can strongly affect treatment and survival. Social and economic factors like education, income, health insurance, and where someone lives may also affect when and how people are diagnosed or treated. These are called social determinants of health and have not been studied as well.

The researchers wanted to better understand why thyroid cancer outcomes differ across racial and ethnic groups. They measured how much cancer type, treatment differences, and social factors contributed to these differences. They also examined whether the type of surgery patients received affected their chances of doing well.

THE FULL ARTICLE TITLE

Fwelo P et al. Disparities in thyroid cancer mortality across racial and ethnic groups: assessing the impact of socioeconomic, clinicopathologic, and treatment variations. *Ann Surg Oncol* 2025;32(2):1158-1175; doi: 10.1245/s10434-024-16569-y. PMID: 39614001.

SUMMARY OF THE STUDY

This study looked at information from 109,981 people in the US who had surgery for thyroid cancer between 2006 and 2018. The researchers used a large national database with information about cancer diagnosis, treatment, and outcomes. They used a step-by-step approach to see how

different factors influenced the results. First, they looked at basic differences, like age, sex, and marital status. Then they added medical details about the cancer itself, like cancer type and how far it had spread. After that, they looked at differences in treatment. Finally, they added social and economic factors, like where someone lives and their income level. They repeated this process for both thyroid cancer-related deaths and overall deaths, using a special analysis to measure how much each factor explained the differences.

The study found differences in the type of treatment patients received based on race and ethnicity. Hispanic patients were the most likely to receive the recommended kind of surgery (79%), while non-Hispanic Black patients were the least likely (68.9%). People with more advanced cancer were more likely to receive the recommended surgery than those with early-stage cancer (96.6% vs 63.7%). Non-Hispanic Black patients had a higher risk of dying from any cause. Hispanic patients appeared to have a higher risk of dying from thyroid cancer, but when researchers accounted for the socioeconomic factors, this risk was no longer higher. Medical details about the cancer itself explained most of the higher risk seen in Hispanic patients. For non-Hispanic Black patients, social and economic factors explained nearly half of the difference in thyroid cancer-related deaths.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

These findings support earlier research showing that thyroid cancer care and outcomes can differ across racial and ethnic groups. Using a large national database and detailed analysis, the study was able to measure how much of these differences were explained by medical factors like cancer type and treatment, as well as social and economic factors. However, because the study used medical records, it lacked information on why some patients did not get the standard treatment and could not account for other factors like additional health problems, access to care, or trust in the healthcare system.



THYROID CANCER, continued

This study reminds us how important it is for patients and their healthcare teams to talk openly, not only about the cancer but also about any challenges patients face

in getting care. It also highlights the need for care that focuses on the whole person, not just the diagnosis.

— Ebru Sulanc, MD

ATA THYROID BROCHURE LINKS

Thyroid Cancer (Papillary and Follicular): <https://www.thyroid.org/thyroid-cancer/>

ABBREVIATIONS & DEFINITIONS

Papillary Thyroid Cancer: the most common type of thyroid cancer. There are 4 variants of papillary thyroid cancer: classic, follicular, tall-cell and noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

Follicular Thyroid Cancer: the second most common type of thyroid cancer.

Clinicopathologic Factors: Medical details about cancer type, size, and spread.

Socioeconomic Factors: Social and economic circumstances, like income, education, insurance status, and neighborhood.



THYROID CANCER

Is neck ultrasound required in follow-up of low-risk thyroid cancer in children?

BACKGROUND

Thyroid cancer occurs in children and adolescents. Fortunately, children and adolescents usually have an excellent response to treatment, as is often seen with adults. The vast majority of children and adolescents have a very low risk of recurrence of their thyroid cancer. With the excellent response to treatment, less aggressive treatment of the thyroid cancer at the time of initial diagnosis is recommended. This includes removal of only the thyroid lobe containing the cancer (lobectomy) as opposed to removing the entire thyroid gland and a decrease in the use of radioactive iodine therapy. Thus, determining the appropriate means and duration of post-treatment follow up is very important.

Although postoperative follow-up with neck ultrasound poses little physical risk, potential harm from overuse can occur because of detection of false-positive or unclear findings, which trigger further investigation, health care expenditures, and patient anxiety. Data on the use of neck ultrasound follow-up in children are particularly lacking. This study examined the risk of thyroid cancer recurrence in children and adolescents and the use of neck ultrasound to follow thyroid cancer low risk patients.

THE FULL ARTICLE TITLE

Rao S, et al. Utility of ultrasound surveillance for thyroid cancer in children. *Thyroid* 2025;35(4):406-414; doi: 10.1089/thy.2024.0624. PMID: 39888311.

SUMMARY OF THE STUDY

This study examined all patients ≤ 18 years of age with thyroid cancer at a single center classified as either ATA-Excellent response or ATA-Indeterminate response to therapy. The response to therapy was assessed 6–18 months after lobectomy or total thyroidectomy, with or without treatment with radioactive iodine, and then followed with ultrasound. Study end points were development of cancer recurrence in the neck detected by ultrasound.

Between 1998 and 2022, 112 children (78% female, average age at diagnosis, 15 years) were included, with 87% having papillary thyroid cancer. Some 15% of patients were classified initially as ATA-High post-operative risk for cancer recurrence, with the rest ATA-Low risk or ATA-Intermediate risk. The average ultrasound follow-up was 6.4 years, over which time 683 ultrasound studies were performed (around one per patient per year).

None of the 61 patients with a ATA-Excellent risk developed recurrence of thyroid cancer in the nodes of the neck over an average of 6 years of follow-up. However, 29% of these patients had a false-positive ultrasound finding, and 2 required thyroid biopsy for clarification. By contrast, 18% of patients with a posttherapy ATA-Indeterminate response developed thyroid cancer recurrence over an average of 6 years of follow-up, which represented one third of those with at least one indeterminate or abnormal ultrasound finding during follow-up. Of note, 7 of these 9 recurrences were detected by ultrasound.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

In children with ATA-Excellent response to therapy in this study, follow-up with ultrasound had very limited utility to detect recurrent thyroid cancer, with all abnormal ultrasound findings found to be negative for cancer. By contrast, recurrences were detected in ATA-Indeterminate patients using ultrasound. Thus, this study suggests that the risks of unnecessary invasive diagnostic procedures following false positive ultrasound findings may outweigh the perceived benefits of annual ultrasound screening in these low-risk patients. More studies are required to determine the role of ultrasound follow-up in children and adolescents with low risk thyroid cancer.

— Alan P. Farwell, MD



THYROID CANCER, continued

ATA THYROID BROCHURE LINKS

Thyroid Cancer (Papillary and Follicular): <https://www.thyroid.org/thyroid-cancer/>

ABBREVIATIONS & DEFINITIONS

Papillary Thyroid Cancer: the most common type of thyroid cancer. There are 4 variants of papillary thyroid cancer: classic, follicular, tall-cell and noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

Follicular Thyroid Cancer: the second most common type of thyroid cancer.

Thyroid Ultrasound: a common imaging test used to evaluate the structure of the thyroid gland. Ultrasound uses soundwaves to create a picture of the structure of

the thyroid gland and accurately identify and characterize nodules within the thyroid. Ultrasound is also frequently used to guide the needle into a nodule during a thyroid nodule biopsy.

Thyroid Fine Needle Aspiration Biopsy (FNAB): a simple procedure that is done in the doctor's office to determine if a thyroid nodule is benign (non-cancerous) or cancer. The doctor uses a very thin needle to withdraw cells from the thyroid nodule. Patients usually return home or to work after the biopsy without any ill effects.



THYROID NODULES

How often are thyroid nodules with indeterminate results and negative molecular testing actually cancer?

BACKGROUND

Thyroid nodules are very common. Up to 50% of individuals that have any imaging test of the neck will be found to have a thyroid nodule. The concern of any thyroid nodule is whether it is a thyroid cancer. To evaluate this, a thyroid biopsy can be performed. While most biopsies show that the nodule is benign (not cancerous), sometimes, the results are unclear. This is called “indeterminate cytology” and usually means more testing or even surgery is needed to find out if it’s cancer. There are 2 categories of indeterminate nodules: Bethesda III (Atypia of unknown significance, AUS, or follicular lesion of unknown significance, FLUS) and Bethesda IV (Follicular lesion or Hurtle cell lesion).

New genetic tests on the cells removed during a biopsy, like ThyroSeq v3, can help doctors decide if surgery is necessary by checking for cancer-related gene changes. Many nodules come back with negative results on this test, meaning no gene changes linked to cancer were found. These nodules are then considered benign.

This study looked at how often these indeterminate nodules with negative results on genetic tests are benign and how many actually turn out to be cancer. They also looked at how best to follow these nodules over time,

FULL ARTICLE TITLE

Nachum S, et al. Thyroid nodules with indeterminate cytology and negative molecular profile: prevalence of malignancy and practice paradigms for surveillance. *Thyroid* 2025;35(3):265-273; doi: 10.1089/thy.2024.0455. PMID: 39874551.

SUMMARY OF THE STUDY

Doctors reviewed records from 556 people with thyroid nodules that had indeterminate biopsy results (called Bethesda III or IV) and tested negative on the ThyroSeq v3 genetic test. These nodules were grouped based on the kind of negative result they got: 1) Negative, 2) Currently Negative, or 3) Negative but Limited. Researchers looked at what kind of follow-up these patients had, who needed surgery, and which nodules turned out to be cancer.

Overall, 75 patients (13.5%) had surgery. Of these, 15 nodules were cancer and 2 were low-risk cancers. Nodules called “Currently Negative” or “Negative but Limited” were more likely to be operated on than those simply called “Negative.” Cancer risk in these 3 categories were: Negative: 2–18%, Currently Negative: 7–30%, Negative but Limited: 7–33%. Nodules labeled Bethesda IV had higher cancer risk than Bethesda III, even if their molecular test was negative. Most patients were followed without surgery, often with ultrasound, and few needed a second biopsy.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Even when genetic tests are negative, the type of negative result and biopsy category matter. Some patients may still need close follow-up, especially those with Bethesda IV or less certain negative results. This study helps patients and doctors make better decisions about follow-up care. Not all nodules with negative genetic tests are the same, so the follow-up plan should be tailored based on the test subtype and biopsy findings. Most of these nodules can be watched safely with regular check-ups and imaging, instead of surgery.

— Maria Brito, MD, ECNU



THYROID NODULES, continued

ATA THYROID BROCHURE LINKS

Thyroid Nodules: <https://www.thyroid.org/thyroid-nodules/>

Fine Needle Aspiration Biopsy of Thyroid Nodules: <https://www.thyroid.org/fna-thyroid-nodules/>

Thyroid Cancer (Papillary and Follicular): <https://www.thyroid.org/thyroid-cancer/>

ABBREVIATIONS & DEFINITIONS

Thyroid Nodule: an abnormal growth of thyroid cells that forms a lump within the thyroid. While most thyroid nodules are non-cancerous (Benign), ~5% are cancerous.

Thyroid Ultrasound: a common imaging test used to evaluate the structure of the thyroid gland. Ultrasound uses soundwaves to create a picture of the structure of the thyroid gland and accurately identify and characterize nodules within the thyroid. Ultrasound is also frequently used to guide the needle into a nodule during a thyroid nodule biopsy.

Thyroid Biopsy: a simple procedure that is done in the doctor's office to determine if a thyroid nodule is benign (non-cancerous) or cancer. The doctor uses a very thin needle to withdraw cells from the thyroid nodule. Patients usually return home or to work after the biopsy without any ill effects.

Indeterminate Thyroid Biopsy: this happens a few atypical cells are seen but not enough to be abnormal (atypia of unknown significance (AUS) or follicular lesion of unknown significance (FLUS)) or when the diagnosis is a follicular or hurthle cell lesion. Follicular and hurthle cells are normal cells found in the thyroid. Current analysis of thyroid biopsy results cannot differentiate between follicular or hurthle cell cancer from noncancerous adenomas. This occurs in 15-20% biopsies and often results in the need for surgery to remove the nodule.

Molecular Markers: genes and microRNAs that are expressed in benign or cancerous cells. Molecular markers can be used in thyroid biopsy specimens to either to diagnose cancer or to determine that the nodule is benign. The two most common molecular marker tests are the Afirma™ Gene Expression Classifier and Thyroseq™.



THYROID CANCER

Incidence and response to treatment for medullary thyroid cancer over time

BACKGROUND

Medullary thyroid cancer is a relatively uncommon but important form of thyroid cancer. As is the case for all cancers, medullary thyroid cancer can grow over time and may eventually spread out of the thyroid to other parts of the body (a process called metastasis). Metastasis causes significant illness, or even death, and thus treating people diagnosed with medullary thyroid cancer to prevent, or at least control, its growth and spread is very important.

The most critical treatment for medullary thyroid cancer is surgery to remove the whole thyroid gland (called a total thyroidectomy). Because medullary cancer often has spread out of the thyroid to the neighboring neck lymph nodes by the time it is discovered, most experts now recommend surgical removal of these lymph nodes (called a central neck dissection) with the thyroid gland. It also appears increasingly clear that people diagnosed with medullary thyroid cancer who undergo thyroid and central neck dissection surgery under the care of a surgeon who specializes in thyroid surgery (called an endocrine surgeon) have lower risks of surgical complications, lower risk that thyroid cancer will come back after surgery (called recurrence) and better survival.

The authors of this study used large European patient databases to evaluate changes in the incidence of medullary thyroid cancer over the last 30 years, as well as to study how surgical treatment for this cancer has changed during this time frame. In particular, these researchers focused on studying the impact changes in surgical treatment have had on the recurrence risk and survival for people diagnosed with medullary thyroid cancer.

FULL ARTICLE TITLE

Jager EC et al. Trends in the incidence, organization of care, and surgical treatment of medullary thyroid cancer: a population-based study. *Thyroid* 2025;35(1):87-96; doi: 10.1089/thy.2024.0433. PMID: 39705074.

SUMMARY OF THE STUDY

The authors of this research studied two large databases that include the healthcare records for the population of the European country the Netherlands. They specifically reviewed 30 years of patient healthcare information (1989 to 2018) to determine if the rate of medullary thyroid cancer diagnosis changed during this time frame, as well as to see how surgical treatment might have changed and how these changes may have impacted the recurrence rate and survival for people diagnosed with this cancer.

A total of 818 cases of medullary thyroid cancer were identified by the study authors. Review of the associated health care records showed that the incidence of medullary thyroid cancer did not change during the 30-year time course assessed (the risk of developing medullary thyroid cancer stayed between 0.15 and 0.18 per 100,000 people). The probability of thyroid surgery being performed by an experienced surgeon increased from 41% to 86% over the study time course, however, as did the proportion of patients undergoing central neck dissection, rising from 77% to 93%. Although the risk of medullary thyroid cancer recurrence did not change during the study time frame, survival did, improving significantly from 55% to 88%.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This work shows that, for the large European population evaluated, the risk of developing medullary thyroid cancer has stayed the same over time. Thus, the factors that might increase a person's chances of developing this cancer (which are largely unknown) have not expanded, at least not in the Netherlands. Importantly, the authors also found that the increased probability of treatment by an expert surgeon seen over the study time course, with more people undergoing central neck dissection in addition to total thyroidectomy. While this did not decrease the chances of this cancer coming back, the chances of



THYROID CANCER, continued

surviving this cancer improved significantly. These findings show that people whose surgery is performed by an expert surgeon, with a central neck dissection, are more likely to survive in general and that when medullary thyroid cancer does recur after such surgery, this is less likely to cause

death. For these reasons, people diagnosed with medullary thyroid cancer should be referred to an endocrine surgeon for their care and surgery should include both total thyroidectomy and central neck dissection.

— Jason D. Prescott, MD PhD

ATA THYROID BROCHURE LINKS

Thyroid Surgery: <https://www.thyroid.org/thyroid-surgery/>

Thyroid Cancer (Medullary): <https://www.thyroid.org/medullary-thyroid-cancer/>

ABBREVIATIONS & DEFINITIONS

Medullary Thyroid Cancer: a relatively rare type of thyroid cancer that often runs in families. Medullary cancer arises from the C-cells in the thyroid.

Cancer Metastasis: spread of the cancer from the initial organ where it developed to other organs, such as the lungs and bone.

Total Thyroidectomy: surgery to remove the entire thyroid gland.

Lymph Node: bean-shaped organ that plays a role in removing what the body considers harmful, such as infections and cancer cells.

Cancer Recurrence: this occurs when the cancer comes back after an initial treatment that was successful in destroying all detectable cancer at some point.

Central Neck Compartment: the central portion of the neck between the hyoid bone above, and the sternum and collar bones below and laterally limited by the carotid arteries.



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Graves' Disease and Thyroid Foundation

www.gdatf.org

(Toll-free): 877-643-3123

info@ngdf.org

Thyca: Thyroid Cancer Survivors' Association, Inc.

www.thyca.org

(Toll-free): 877-588-7904

thyca@thyca.org

Thyroid Federation International

www.thyroid-fed.org

tfi@thyroid-fed.org

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