

# Clinical Thyroidology<sup>®</sup> for the Public



AMERICAN THYROID ASSOCIATION  
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Chaves N et al 2023 Delay in surgery and papillary thyroid cancer survival in the United States: A SEER-Medicare analysis. *J Clin Endocrinol Metab*. Epub 2023 Mar 29. PMID: 36987566.

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In 2020, more than 200,000 patients in China were diagnosed with thyroid cancer. Little is known about the quality of life of thyroid cancer survivors from Mainland China. In this study, the authors examined quality of life measures and identified associated factors in thyroid cancer survivors from Mainland China.

Chen C et al 2023 Health-related quality of life and thyroid cancer-specific symptoms in patients treated for differentiated thyroid cancer: A single center, cross-sectional survey from Mainland China. *Thyroid*. Epub 2023 Feb 15. PMID: 36792949.

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Moleti M et al Preconception thyrotropin levels and thyroid function at early gestation in women with Hashimoto's thyroiditis. *J Clin Endocrinol Metab*. Epub 2023 Jan 9. PMID: 36620924

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Subclinical thyroid disease is described as the presence of abnormal TSH levels with normal blood levels of the thyroid hormones T4 and T3. In order for the diagnosis of subclinical thyroid disease to be accurate, it is important to describe and establish a normal range for blood TSH. This study evaluated the influence of age and sex on thyroid function tests and rates of subclinical thyroid disease.

Yamada S et al. 2023 The impact of age- and sex-specific reference ranges for serum TSH and FT4 on the diagnosis of subclinical thyroid dysfunction: A multi-center study from Japan. *Thyroid*. Epub 2023 Feb 10. PMID: 36772798.

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Yang J et al 2022. The impact of subclinical hyperthyroidism on cardiovascular prognosis in patients undergoing percutaneous coronary intervention. *J Clin Endocrinol Metab* 107:986–997. PMID: 34850030.



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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 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**. The **Alliance** 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*, *Thyroid Cancer Canada*, *Thyroid Cancer Alliance* and *Thyroid Federation International*.

We invite all of you to join our **Friends of the ATA** 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](http://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.

**June is [Thyroid Cancer Awareness Month](#).**

**In this issue, the studies ask the following questions:**

- Does delaying surgery for thyroid cancer affect survival in older patients?
- Does thyroid cancer affect quality of life?
- Is same day discharge after thyroidectomy safe?
- What should the TSH level be in women with Hashimotos that are considering pregnancy?
- Should there be different normal ranges for TSH depending on sex and age?
- What is the effect if subclinical hyperthyroidism on prognosis after a cardiac stent procedure?

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



## THYROID CANCER

# The effect of delayed surgery on survival in older patients with papillary thyroid cancer

### BACKGROUND

Once a cancer is diagnosed and surgery is an option, patients usually proceed with surgery quickly after diagnosis. Waiting a long time from diagnosis to surgery is known to worsen survival in several cancers, such as lung, colorectal, and breast cancer. An exception to this is papillary thyroid cancer. Papillary thyroid carcinoma, the most common type of thyroid cancer, represents a less aggressive type of cancer with an overall good prognosis. Over the last two decades, treatment guidelines for papillary thyroid cancer have changed from total thyroidectomy followed by radioactive iodine therapy recommended for the majority of patients, to total thyroidectomy or lobectomy only for low-risk patients, and to a more recent option of watching without surgery for cancer growth using ultrasound (active surveillance) for very low risk patients with papillary thyroid cancer. The impact of delayed surgery during active surveillance in patients with papillary thyroid cancer has not yet been fully investigated. The aim of this study was to evaluate whether a delay in surgery affects survival in patients older than age 65 diagnosed with papillary thyroid cancer.

### THE FULL ARTICLE TITLE

Chaves N et al 2023 Delay in surgery and papillary thyroid cancer survival in the United States: A SEER-Medicare analysis. *J Clin Endocrinol Metab*. Epub 2023 Mar 29. PMID: 36987566.

### SUMMARY OF THE STUDY

The authors used the U.S. Surveillance, Epidemiology, and End Results (SEER)–Medicare linked data files to identify 8170 Medicare beneficiaries who were diagnosed with papillary thyroid cancer and underwent thyroid surgery between 1999 and 2018. These patients were divided into three groups based on the time to surgery, defined as the time from diagnosis to the date of surgery in days: within the first 90 days (0-90 days), 91 to 180 days (91-180

days), and more than 180 days (>180 days) after diagnosis. Overall survival (OS) and disease-specific survival (DSS) were defined as the time from the date of diagnosis to the time of all-cause mortality and disease-specific mortality, respectively. Age, gender, race and ethnicity, marital status, urban/rural setting, comorbidities, year of diagnosis, cancer stage, number of positive lymph nodes, primary surgery type, radioactive therapy use, and length of follow-up were included in the analysis.

Given their eligibility to receive Medicare, according to the study design, all patients were 65 or older, with an average age of 69 years; 70% of the patients were females, 86% were White and 90% were non-Hispanic. Almost half of the patients had no other significant medical conditions. The patients were followed for an average time of 99 months. The majority of patients (90%) had surgery within the first 90 days after the initial diagnosis, 8% had surgery within 91 to 180 days, and 2% after 180 days. Cancer staging was similar across the three time to surgery groups: 64% of patients had localized disease, 28% had regional disease, and 8% had distant disease.

The estimated overall survival at 1, 5, and 10 years was 95.2%, 81.8%, and 63.2% in the 0-90 days group; 95.7%, 78.6%, and 55.3% in the 91-180 days group; and 98.0%, 67.4%, and 48.9% in the >180 days group. The estimated thyroid cancer-specific survival at 1, 5, and 10 years was 97.8%, 94.4%, and 90.9% in the 0-90 days group; 98.1%, 94.6%, and 87.4% in the 91-180 days group; and 99.5%, 88.1%, and 80.8% in >180 days group.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study suggests that delayed surgery may decrease the overall survival and thyroid cancer-specific survival in older patients with papillary thyroid cancer. Surprisingly, spread of the cancer outside of the neck, which



## THYROID CANCER, continued

would usually prompt more aggressive treatment, were more common in patients with surgery delayed more than 90 and 180 days. However, survival was not affected by the delay in surgery in patients with more advanced

papillary thyroid cancers. Additional research is needed to understand the significance and clinical implications of these findings.

— Alina Gavrilă, MD, MMSC

### ATA RESOURCES

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

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

### 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).

**Thyroidectomy:** surgery to remove the entire thyroid gland. When the entire thyroid is removed it is termed a *total thyroidectomy*. When less is removed, such as in removal of a lobe, it is termed a *partial thyroidectomy*.

**Lobectomy:** surgery to remove one lobe of the thyroid.

**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*).

**SEER:** Surveillance, Epidemiology and End Results program, a nation-wide anonymous cancer registry generated by the National Cancer Institute that contains information on 26% of the United States population. Website: <http://seer.cancer.gov/>

**National Cancer Institute (NCI);** a part of the National Institutes of Health in Bethesda, MD, the NCI is the federal government's primary agency for cancer research and training.

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

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



## THYROID CANCER

# Quality of life considerations in patients treated for thyroid cancer

### BACKGROUND

Thyroid cancer has been one of the fastest rising cancers across the world. Indeed, the number of new cases of thyroid cancer in Mainland China has increased by a lot in recent years. In 2020, more than 200,000 patients in China were diagnosed with thyroid cancer. The treatment of thyroid cancer most often includes surgery to remove part or all of the thyroid gland. If the entire thyroid is removed (total thyroidectomy), patients will be on thyroid hormone replacement, usually levothyroxine, for life. While many patients that only have part of their thyroid removed (partial thyroidectomy) will not be on thyroid hormone, many also do need to be on levothyroxine. Finally, after surgery, some but not all patients may benefit from radioactive iodine treatment. All of these factors, as well as possible complication for surgery, can affect a person's quality of life. However, little is known about the quality of life of thyroid cancer survivors from Mainland China.

In this study, the authors examined quality of life measures and identified associated factors in thyroid cancer survivors from Mainland China.

### THE FULL ARTICLE TITLE

Chen C et al 2023 Health-related quality of life and thyroid cancer-specific symptoms in patients treated for differentiated thyroid cancer: A single center, cross-sectional survey from Mainland China. *Thyroid*. Epub 2023 Feb 15. PMID: 36792949.

### SUMMARY OF THE STUDY

The authors surveyed 373 thyroid cancer survivors from Mainland China. Most of the patients were female (77%), between the ages of 36 and 64 years old (65%) and employed at the time that the survey was completed

(58%). In terms of treatment, most of the surveyed patients underwent a partial thyroidectomy (53%). Further, most patients did not receive radioactive iodine therapy (74%).

Health related quality of life was assessed using the "European Organization for Research and Treatment of Cancer Quality of Life (EORTC QLQ-C30) Questionnaire". This survey found that while patients reported an overall high quality of life, they also reported high levels of the following symptoms: fatigue, pain, insomnia, and financial difficulties.

Thyroid cancer-specific quality of life was assessed using the "Thyroid Cancer-Specific Quality of Life (THYCA-QOL) Questionnaire". Patients reported high levels of the following symptoms: "psychological problems", problems with the scar from thyroid surgery, and voice problems. Factors found to be associated with more thyroid cancer-specific symptoms included hypoparathyroidism, which is a complication of thyroid surgery, lower household income, and higher doses of radioactive iodine treatment.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The study demonstrates that many patients with thyroid cancer experience multiple health-related problems and symptoms after initial treatment for thyroid cancer. All of these factors impact patient's quality of life. More research is needed to understand how to best support thyroid cancer survivor after their initial treatment.

— Debbie Chen, MD





## THYROID CANCER, continued

### ATA RESOURCES

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

Thyroid Hormone Treatment: <https://www.thyroid.org/thyroid-hormone-treatment/>

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

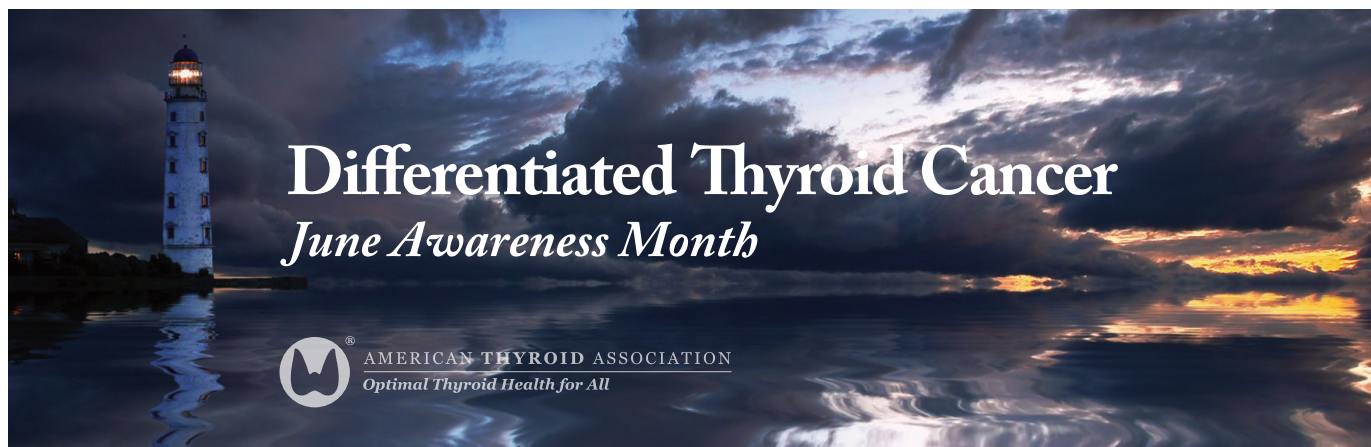
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**Papillary thyroid cancer:** the most common type of thyroid cancer. There are 4 variants of papillary thyroid cancer: classic, follicular, tall-cell and noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP).

**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*).

**Thyroidectomy:** surgery to remove the entire thyroid gland. When the entire thyroid is removed it is termed a *total thyroidectomy*. When less is removed, such as in removal of a lobe, it is termed a *partial thyroidectomy*.

**Thyroid hormone therapy:** patients with hypothyroidism are most often treated with Levothyroxine in order to return their thyroid hormone levels to normal. *Replacement therapy* means the goal is a TSH in the normal range and is the usual therapy. *Suppressive therapy* means that the goal is a TSH below the normal range and is used in thyroid cancer patients to prevent growth of any remaining cancer cells.





## THYROID SURGERY

# Timing of discharge after thyroid surgery differs between hospitals

### BACKGROUND

Thousands of people undergo surgery to remove their thyroid gland (total thyroidectomy) every year. The thyroid is a butterfly-shaped gland located in the front part of the neck that produces thyroid hormone. Common reasons for total thyroidectomy include treatment for thyroid cancer, non-cancerous thyroid enlargement (goiter) and thyroid over-activity (hyperthyroidism). Traditionally, people who undergo total thyroidectomy were admitted to the hospital, at least overnight, to monitor for rare complications that might develop after this surgery. Such complications include internal bleeding at the surgery site and low calcium levels, which can cause numbness, tingling and muscle spasms. By admitting a person to the hospital following total thyroidectomy, thyroid surgeons would hope to identify and treat these rare complications early and so minimize the dangers such complications may pose.

Fortunately, dangerous complications after total thyroidectomy are very rare, especially when this surgery is done by an experienced surgeon (called a high-volume thyroid surgeon). Because of this, many surgeons have started to discharge people who undergo total thyroidectomy from the hospital the same day the surgery is performed (called same day discharge) and a number of studies have shown this practice to be safe. Because most people prefer to be discharged from the hospital as soon as possible after surgery, same day discharge also tends to make most people's surgery experience better. In addition, the less time someone spends in the hospital, the less expensive their surgery will be. For this reason, same day discharge after total thyroidectomy makes the cost of this surgery lower.

The authors of the study described here were interested in understanding how common same day discharge following total thyroidectomy is and also how surgeons decide whether or not same day discharge is appropriate for any given person who undergoes total thyroidectomy.

### FULL ARTICLE TITLE

Hsu S et al 2023 Outpatient endocrine surgery practice patterns are highly variable among US endocrine surgery fellowship programs. *Surgery* 173:76–83. PMID: 36192212.

### SUMMARY OF THE STUDY

The authors of this study asked surgeons enrolled in one of 22 different thyroid surgery training programs in the United States (endocrine surgery fellowships, all run by high-volume thyroid surgeons) how common people who undergo total thyroidectomy at their institutions were discharged from the hospital on the day of surgery. Institutions for which most patients were discharged on the day of total thyroidectomy (high same day discharge rate, >90%) were then compared to institutions for which some (moderate same day discharge rate, 3-89%) and few (low same day discharge rate, <2%) patients were discharged on the day of surgery.

The authors found that 9 of the 20 institutions that participated in their study rarely, if ever, discharged patients from the hospital following total thyroidectomy on the day of surgery (same day discharge rate <2%), while 7 institutions used same day discharge for >90% of patients undergoing total thyroidectomy. The remaining 4 institutions studied used same day discharge following total thyroidectomy on a moderate basis (3-89% of the time). In addition, the authors found that the length of time people undergoing total thyroidectomy were observed before being discharged from the hospital following surgery, even when not admitted to the hospital overnight, varied significantly between institutions. The reasons for deciding to admit a person to the hospital overnight after total thyroidectomy also differed among the institutions studied. The factors most likely to keep the patient overnight were that the patient lived alone, use of anticoagulation/anti-platelet agents, and more extensive surgery into the neck surrounding the thyroid.



## THYROID SURGERY, continued

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Previous studies have shown same day discharge following total thyroidectomy to be safe, cost-effective and preferred by patients. Nonetheless, this study highlights the fact that many institutions have not adopted the practice of same day discharge after total thyroidectomy. The reasons for this are not clear. In addition, previous studies have shown no increased risk of death after total thyroidectomy for

patients who are discharged from the hospital on the day of surgery. The study presented here indicates a need to develop common standards for same-day discharge among institutions where total thyroidectomy is performed, so that all people undergoing thyroid surgery have the safest, most efficient, cost-effective and pleasant surgery experience possible.

— Jason D. Prescott, MD PhD

### ATA RESOURCES

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

### ABBREVIATIONS & DEFINITIONS

**Thyroidectomy:** surgery to remove the entire thyroid gland. When the entire thyroid is removed it is termed a total thyroidectomy. When less is removed, such as in removal of a lobe, it is termed a partial thyroidectomy.

**Goiter:** a thyroid gland that is enlarged for any reason is called a goiter. A goiter can be seen when the thyroid is overactive, underactive or functioning normally. If there are nodules in the goiter it is called a nodular goiter; if there is more than one nodule it is called a multinodular goiter.

**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.





## THYROID DISEASE AND PREGNANCY

# TSH levels may need to be kept lower pre-pregnancy in women with Hashimoto's thyroiditis to ensure normal thyroid hormone levels in early pregnancy.

### BACKGROUND

Thyroid hormone is critical for normal development of the baby, especially in early stages of pregnancy when the baby entirely depends on thyroid hormone coming from mother. Hypothyroidism (low thyroid hormone levels) in pregnancy has been associated with several problems during pregnancy, such as miscarriage, early delivery, and problems with baby's brain development. Hypothyroidism due to Hashimoto's thyroiditis is the most common endocrine disorders affecting pregnant women in developed nations. In women without thyroid disease, thyroid hormone production naturally increases during pregnancy to provide enough thyroid hormone for mother and baby. Women who are already taking levothyroxine for hypothyroidism usually require higher dose of levothyroxine during pregnancy. Women with Hashimoto's thyroiditis who do not require levothyroxine before pregnancy may need levothyroxine during pregnancy, because thyroid hormone production may not increase appropriately due to interference from high levels of thyroid antibody.

Currently, the American Thyroid Association (ATA) recommends keeping blood TSH (thyroid stimulating hormone) levels below 2.5mIU/L during pregnancy in patients who require levothyroxine treatment. For those who are not on levothyroxine before pregnancy, the ATA recommends considering starting levothyroxine for TSH over 4mIU/L, especially if patient has high thyroid antibody levels. Generally, patients are advised to increase their levothyroxine dose by 2 pills a week once pregnant if they were taking levothyroxine before pregnancy. However, it may be too much for some patients. Currently, there is no clear way to tell which patients would require the dose increase and which patients would not. The researchers of this study aimed to determine how many patients with Hashimoto's thyroiditis develop hypo-

thyroidism in early pregnancy, and what pre-pregnancy TSH level would indicate that patients need to increase or start levothyroxine once pregnant.

### THE FULL ARTICLE TITLE

Moleti M et al Preconception thyrotropin levels and thyroid function at early gestation in women with Hashimoto's thyroiditis. *J Clin Endocrinol Metab.* Epub 2023 Jan 9. PMID: 36620924

### SUMMARY OF THE STUDY

The researchers studied 260 women with Hashimoto's thyroiditis who were seen in a single hospital in Italy between 2008-2017. All women had TSH  $\leq$  2.5mIU/L within 6 months of pregnancy and had TSH measured at the time of pregnancy and every 4-6 weeks afterwards during pregnancy.

Among these women, 138 patients had normal thyroid levels without levothyroxine and 122 patients were taking levothyroxine for hypothyroidism before pregnancy. About 30% of these women developed TSH above 2.5mIU/L at their first prenatal visit. However, more women who were not taking levothyroxine before pregnancy developed TSH over 4mIU/L compared to women who were taking levothyroxine before pregnancy (20% vs 10%). The researchers found that women with hypothyroidism from Hashimoto's thyroiditis on levothyroxine pre-pregnancy were 16-times more likely to have TSH  $>$ 2.5mIU/L if their pre-pregnancy TSH was above 1.24mIU/L. For women with Hashimoto's thyroiditis but not on levothyroxine before pregnancy, those who had pre-pregnancy TSH above 1.73mIU/L were 16-times more likely to develop TSH  $>$  2.5mIU/L in early pregnancy, and those who had pre-pregnancy TSH above 2.07mIU/L were 17-times more likely to develop TSH  $>$  4mIU/L in early pregnancy.



## THYROID DISEASE AND PREGNANCY, continued

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

The authors concluded that women with Hashimoto’s thyroiditis require pre-pregnancy TSH levels to be 30-50% lower than 2.5mIU/L to maintain normal thyroid levels in early pregnancy. Although the current ATA guidelines discuss TSH goals for patients who are pregnant, there is no clear guidelines on what pre-pregnancy TSH should be to ensure normal thyroid function in early pregnancy. Early pregnancy is an important

period where a lot of development occurs, but we do not currently have enough information to set pre-pregnancy TSH targets to ensure normal thyroid function in early pregnancy in those at risk of thyroid dysfunction. Results of this study give us potential pre-pregnancy TSH targets for women who have Hashimoto’s thyroiditis and are considering pregnancy in near future. It also emphasizes need for further studies in the care of pregnant women with hypothyroidism starting pre-pregnancy.

— Sun Y. Lee, MD, MSc

### ATA RESOURCES

Thyroid Disease in Pregnancy: <https://www.thyroid.org/thyroid-disease-pregnancy/>

### ABBREVIATIONS & DEFINITIONS

**Hypothyroidism:** a condition where the thyroid gland is underactive and doesn’t produce enough thyroid hormone. Treatment requires taking thyroid hormone pills.

**Hashimotos thyroiditis:** the most common cause of hypothyroidism in the United States. It is caused by antibodies that attack the thyroid and destroy it.

**Levothyroxine (T4):** the major hormone produced by the thyroid gland and available in pill form as Synthroid™, Levoxyl™, Tyrosint™ and generic preparations.

**TSH: thyroid stimulating hormone** — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.

**Miscarriage:** this occurs when a baby dies in the first few months of a pregnancy, usually before 22 weeks of pregnancy.



## SUBCLINICAL HYPOTHYROIDISM

### Age- and sex-specific reference ranges for thyroid function tests reduce misdiagnosis of subclinical thyroid dysfunction.

#### BACKGROUND

Overt thyroid disease is diagnosed when both the TSH and thyroid hormone levels (T<sub>4</sub>, T<sub>3</sub>) are abnormal. In almost all cases, overt thyroid disease is treated. In contrast, subclinical thyroid disease is described as the presence of abnormal TSH levels with normal blood levels of the thyroid hormones T<sub>4</sub> and T<sub>3</sub>. Treatment of subclinical thyroid disease is much less clear.

TSH is very sensitive to changes in thyroid function and is the first hormone to become abnormal and used in assessing thyroid dysfunction. Subclinical hypothyroidism is diagnosed when TSH levels are increased above the normal range while subclinical hyperthyroidism is diagnosed when TSH levels are decreased below the normal range. In order for the diagnosis of subclinical thyroid disease to be accurate, it is important to describe and establish a normal range for blood TSH.

Current TSH ranges used do not account for potential differences due age and sex. As such, this can lead to misdiagnosis of thyroid disease. In addition, there is no agreement in when to start therapy in subclinical hypothyroidism. This study evaluated the influence of age and sex on thyroid function tests and rates of subclinical thyroid disease.

#### THE FULL ARTICLE TITLE

Yamada S et al. 2023 The impact of age- and sex-specific reference ranges for serum TSH and FT<sub>4</sub> on the diagnosis of subclinical thyroid dysfunction: A multi-center study from Japan. *Thyroid*. Epub 2023 Feb 10. PMID: 36772798.

#### SUMMARY OF THE STUDY

This study reviewed thyroid function tests from two hospitals in Japan using three different testing kits. At Takasaki Hidaka Hospital, 14,860 participants (8904 men and 5956 women) were assessed using Siemens kits, and

8132 (4682 men and 3450 women) were assessed using Abbott kits. Those with history of thyroid disease, liver cirrhosis, or renal failure; current use of levothyroxine, antithyroid drugs, insulin, and steroid hormones; and missing data, were not included. At Okamoto Thyroid Clinic, 515 participants (99 men and 416 women) were assessed using Toso Kits. Serum TSH and free T<sub>4</sub> were measured with kits from all manufacturers, while serum free T<sub>3</sub> was measured with Abbott and Toso Kits. Those with history of thyroid disease, elevated antithyroid antibodies, and abnormal thyroid gland findings on ultrasonography were not included.

The study noted an increase in average TSH levels with the age progression in women with all the three kit manufacturers, while men had lower average TSH levels and minor increase with age when compared to women. Free T<sub>4</sub> and T<sub>3</sub> levels did not change with age in women across all three test manufacturers, but serum free T<sub>4</sub> levels in men were higher than in women and slowly decreased with age. However, blood T<sub>3</sub> levels in women did not change.

Diagnosis of subclinical hypothyroidism was high, especially in women, and increased age. Within women aged between 30 to 39 years-old, almost 50% of those participants initially categorized as having subclinical hypothyroidism based on the manufacturer's reference range were categorized as being in the normal range when using reference ranges for age and sex. This number was even higher in women ages 60 to 69 years with up to 78%. On the other hand, there was no difference in the normal range between tests in men ages 30 to 39 and only 5% of men aged 40 to 49 tested normal when the prior tests as indicated having subclinical hypothyroidism. However, the number increased with age and up to 62% of men were categorized as being in the normal range when using reference ranges for age and sex. Interestingly, differences in the diagnosis of subclinical hyperthyroid-



## SUBCLINICAL HYPOTHYROIDISM, continued

ism was very low and only seen in seen in middle-aged patients, with 0.6% in men and 1% in women categorized as being in the normal range when using reference ranges for age and sex.

### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

This study showed that subclinical hypothyroidism is frequently over-diagnosed, especially in those over the

age of 60 years, and women. Over diagnosis is much less frequent when diagnosing subclinical hyperthyroidism. This study shows that there is a need for laboratory reference ranges for age and sex when evaluating thyroid function to accurately diagnosis subclinical thyroid disease.

— Joanna Miragaya, MD

### ATA RESOURCES

Thyroid Function Tests: <https://www.thyroid.org/thyroid-function-tests/>

Thyroid Hormone Treatment: <https://www.thyroid.org/thyroid-hormone-treatment/>

Hypothyroidism (Underactive): <https://www.thyroid.org/hypothyroidism/>

### ABBREVIATIONS & DEFINITIONS

**Overt Hypothyroidism:** clear hypothyroidism an increased TSH and a decreased T4 level. All patients with overt hypothyroidism are usually treated with thyroid hormone pills.

**Subclinical Hypothyroidism:** a mild form of hypothyroidism where the only abnormal hormone level is an increased TSH. There is controversy as to whether this should be treated or not.

**Subclinical Hyperthyroidism:** a mild form of hyperthyroidism where the only abnormal hormone level is a decreased TSH.

**Thyroxine (T4):** the major hormone produced by the thyroid gland. T4 gets converted to the active hormone T3 in various tissues in the body.

**Triiodothyronine (T3):** the active thyroid hormone, usually produced from thyroxine.

**TSH: thyroid stimulating hormone** — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.



## HYPERTHYROIDISM

### The effect of subclinical hyperthyroidism on prognosis after a cardiac stent procedure

#### BACKGROUND

Hyperthyroidism is a condition where the thyroid gland produces high levels of thyroid hormone. This can result in various symptoms, such as weight loss, tremors, anxiety, a fast heart rate, and palpitations. Subclinical hyperthyroidism is considered a milder form of hyperthyroidism. In subclinical hyperthyroidism, the levels of thyroid hormones (T3 and/or T4) are within the normal range, but the TSH level is below normal. This suggests that there is an excess of thyroid hormone in the body even though thyroid hormone levels are normal in routine laboratory tests.

Although subclinical hyperthyroidism may not cause noticeable symptoms or the symptoms may be subtle, research has shown that it can affect the heart muscle and increase the risk of heart problems such as irregular heart rhythms, heart failure, and death. The heart muscle contains receptors for thyroid hormones, establishing a well-known connection between thyroid disease and heart disease. Despite this, limited studies have investigated the heart effects of subclinical hyperthyroidism in patients with preexisting heart disease.

In the present study, the authors specifically examined the association between subclinical hyperthyroidism and outcomes in patients with preexisting heart disease who underwent a cardiac stent procedure.

#### THE FULL ARTICLE TITLE

Yang J et al 2022. The impact of subclinical hyperthyroidism on cardiovascular prognosis in patients undergoing percutaneous coronary intervention. *J Clin Endocrinol Metab* 107:986–997. PMID: 34850030.

#### SUMMARY OF THE STUDY

The researchers examined 8,282 patients with heart disease who had a heart stent procedure at a hospital in

Beijing, China, between January 1, 2013, and December 31, 2013. From this large group of patients they selected 332 individuals who had subclinical hyperthyroidism and compared them to 1,271 patients with normal thyroid function. Subclinical hyperthyroidism was defined as having normal levels of thyroid hormones but abnormally low levels of thyroid-stimulating hormone (TSH) in the blood, specifically below 0.55 mIU/L. When the TSH level was very low i.e., below 0.10 mIU/L, it was called severe subclinical hyperthyroidism. They then followed these patients for 24 months to see if the group with subclinical hyperthyroidism had higher rates of major adverse heart events. Such events included cardiac death, non-fatal heart attack, and need for bypass grafting to a blocked artery in the heart.

After 24 months, the authors found that 11.4% of patients with subclinical hyperthyroidism and 8.8% of patients with normal thyroid function (euthyroid) experienced a major adverse heart event. However, this difference between the two groups was not statistically significant. Furthermore, when comparing patients with severe subclinical hyperthyroidism to patients with normal thyroid function, there was also no significant difference in the number of major adverse heart events. This suggests that even in cases of more severe subclinical hyperthyroidism, there is no increase in the risk of experiencing these serious heart events. Overall, subclinical hyperthyroidism was not identified as a risk factor for having a major adverse heart event in this particular group of patients.

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Doctors have been unsure whether or not to treat subclinical hyperthyroidism, especially in patients who don't have any symptoms. This study shows that patients with subclinical hyperthyroidism and preexisting heart





## HYPERTHYROIDISM, continued

disease do not face a higher risk of adverse outcomes compared to those with normal thyroid function. Although the study only observed patients for 24 months (a relatively short period), these findings help us better

understand the connection between subtle thyroid disease and heart complications. Therefore, perhaps not all patients with subclinical hyperthyroidism need treatment.

— Phillip Segal, MD

### ATA RESOURCES

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

Thyroid Function Tests: <https://www.thyroid.org/thyroid-function-tests/>

### ABBREVIATIONS & DEFINITIONS

**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.

**Subclinical Hyperthyroidism:** a mild form of hyperthyroidism where the only abnormal hormone level is a decreased TSH.

**Thyroxine (T4):** the major hormone produced by the thyroid gland. T4 gets converted to the active hormone T3 in various tissues in the body.

**Triiodothyronine (T3):** the active thyroid hormone, usually produced from thyroxine.

**TSH: thyroid stimulating hormone** — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.



# Clinical Thyroidology® for the Public

## ATA® Alliance for Thyroid Patient Education

**GOAL** The goal of our organizations is to provide accurate and reliable information for patients about the diagnosis, evaluation and treatment of thyroid diseases. We look forward to future collaborations and continuing to work together toward the improvement of thyroid education and resources for patients.



ThyCa: Thyroid Cancer Survivors' Association, Inc.<sup>SM</sup>  
[www.thyca.org](http://www.thyca.org)



MCT8 - AHDS Foundation

THYROID CANCER ALLIANCE



### American Thyroid Association®

[www.thyroid.org](http://www.thyroid.org)

ATA® Patient Resources:

[www.thyroid.org/thyroid-information/](http://www.thyroid.org/thyroid-information/)

Find a Thyroid Specialist: [www.thyroid.org](http://www.thyroid.org)

(Toll-free): 1-800-THYROID

[thyroid@thyroid.org](mailto:thyroid@thyroid.org)

### Bite Me Cancer

[www.bitemecancer.org](http://www.bitemecancer.org)

[info@bitemecancer.org](mailto:info@bitemecancer.org)

### Graves' Disease and Thyroid Foundation

[www.gdatf.org](http://www.gdatf.org)

(Toll-free): 877-643-3123

[info@ngdf.org](mailto:info@ngdf.org)

### Light of Life Foundation

[www.checkyourneck.com](http://www.checkyourneck.com)

[info@checkyourneck.com](mailto:info@checkyourneck.com)

### MCT8 – AHDS Foundation

[mct8.info](http://mct8.info)

[Contact@mct8.info](mailto:Contact@mct8.info)

### Thyca: Thyroid Cancer Survivors' Association, Inc.

[www.thyca.org](http://www.thyca.org)

(Toll-free): 877-588-7904

[thyca@thyca.org](mailto:thyca@thyca.org)

### Thyroid Cancer Alliance

[www.thyroidcanceralliance.org](http://www.thyroidcanceralliance.org)

[www.thyroidcancerpatientinfo.org](http://www.thyroidcancerpatientinfo.org)

Rotterdam, The Netherlands

### Thyroid Cancer Canada

[www.thyroidcancercanada.org](http://www.thyroidcancercanada.org)

416-487-8267

[info@thyroidcancercanada.org](mailto:info@thyroidcancercanada.org)

### Thyroid Federation International

[www.thyroid-fed.org](http://www.thyroid-fed.org)

[tfi@thyroid-fed.org](mailto:tfi@thyroid-fed.org)

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