Subclinical hyperthyroidism in nonpregnant adults

Author: Douglas S Ross, MD
Section Editor: David S Cooper, MD
Deputy Editor: Jean E Mulder, MD

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: Aug 2022. | **This topic last updated:** Mar 12, 2021.

INTRODUCTION

Subclinical hyperthyroidism is defined biochemically as normal serum free thyroxine (T4) and triiodothyronine (T3) concentrations in the presence of a subnormal thyroid-stimulating hormone (TSH) (<0.5 mU/L). The term overt hyperthyroidism refers to patients with elevated levels of free T4, T3, or both and a subnormal TSH concentration. Both subclinical and overt hyperthyroidism are biochemical definitions since hyperthyroid symptoms are nonspecific and may be present in patients with subclinical disease and absent in those with overt disease, especially older adults.

Subclinical hyperthyroidism in nonpregnant adults will be discussed here. Overt hyperthyroidism and hyperthyroidism during pregnancy are discussed separately.

- (See "Overview of the clinical manifestations of hyperthyroidism in adults".)
- (See "Diagnosis of hyperthyroidism".)
- (See "Graves' hyperthyroidism in nonpregnant adults: Overview of treatment".)
- (See "Treatment of toxic adenoma and toxic multinodular goiter".)
- (See "Hyperthyroidism during pregnancy: Clinical manifestations, diagnosis, and causes".)
- (See "Hyperthyroidism during pregnancy: Treatment".)

EPIDEMIOLOGY

Several large studies have examined the prevalence of subclinical hyperthyroidism [1-7]. The results of these studies, primarily in subjects over age 55 to 60 years, can be summarized as

follows:

- The prevalence of subclinical hyperthyroidism in the community varies between 0.7 and 12.4 percent. This variability is in part due to differences in the definition of low serum TSH values and in the patient populations studied. In the Third National Health and Nutrition Examination Survey (NHANES III) from the United States, which excluded individuals with known thyroid disease, 0.7 percent of 16,533 people had subclinical hyperthyroidism (TSH <0.1 mU/L) [8].

- Subclinical hyperthyroidism is more common in areas of the world with mild to moderate iodine deficiency. In addition, subclinical thyroid dysfunction is more common in females, smokers, and older adults [8,9].

ETIOLOGY

The causes of subclinical hyperthyroidism are the same as the causes of overt hyperthyroidism, and like overt hyperthyroidism, subclinical hyperthyroidism can be persistent or transient (table 1). Common causes of subclinical hyperthyroidism include excessive thyroid hormone therapy (exogenous subclinical hyperthyroidism), autonomously functioning thyroid adenomas and multinodular goiters (endogenous subclinical hyperthyroidism), or Graves' disease (endogenous subclinical hyperthyroidism). (See "Disorders that cause hyperthyroidism".)

Exogenous subclinical hyperthyroidism — As many as 10 million people in the United States and possibly as many as 200 million people worldwide are taking thyroid hormone. All are at risk for subclinical hyperthyroidism, whether intentional or unintentional. Among patients taking T4, as many as 25 percent have low serum TSH values [10,11], and in one study, 5.8 percent were under 0.1 mU/L [12]. (See "Exogenous hyperthyroidism".)

Many of these patients have hypothyroidism, and in them, subclinical hyperthyroidism is not the goal of thyroid hormone therapy. However, subclinical hyperthyroidism is the goal of thyroid hormone therapy in patients with thyroid cancer and in some patients with solitary thyroid nodules, multinodular or diffuse goiters, or a history of head and neck irradiation. In these patients, the benefits of TSH suppression are thought to outweigh the risks of subclinical hyperthyroidism. (See "Differentiated thyroid cancer: Overview of management", section on 'Thyroid hormone suppression' and "Thyroid hormone suppressive therapy for thyroid nodules and benign goiter".)

Endogenous subclinical hyperthyroidism — Autonomously functioning thyroid adenomas and multinodular goiters are the most common causes of endogenous subclinical

hyperthyroidism. Among patients over age 55 years, hyperthyroidism due to multinodular goiters was subclinical in 57 percent of patients, while hyperthyroidism due to Graves' disease was subclinical in only 6 percent of patients [13]. In another study, 22 percent of patients with multinodular goiter had subclinical hyperthyroidism, while 28 percent of those with subclinical hyperthyroidism had autonomous area(s) on thyroid imaging [14].

Subclinical hyperthyroidism also occurs in patients with thyroiditis [15], and it has been reported in 63 percent of clinically euthyroid patients with Graves' ophthalmopathy (euthyroid Graves' disease) [16] and 4 percent of those with Graves' disease in remission [17]. It may also be seen in patients with early Graves' disease prior to the onset of more overt hyperthyroidism. In addition, healthy pregnant women (especially in the first trimester) and those with hyperemesis gravidarum (or trophoblastic disease) who have high serum chorionic gonadotropin concentrations may have subclinical hyperthyroidism. (See "Hyperthyroidism during pregnancy: Clinical manifestations, diagnosis, and causes", section on 'hCG-mediated hyperthyroidism'.)

CLINICAL FINDINGS

Most patients with subclinical hyperthyroidism have no clinical manifestations of hyperthyroidism, and those symptoms that are present (eg, tachycardia, tremor, dyspnea on exertion, weight loss) are mild and nonspecific. Many patients have a multinodular goiter with autonomy (toxic nodular goiter) or mild Graves' disease. Most patients are detected through routine screening of thyroid function.

Subclinical hyperthyroidism is associated with an increased risk of atrial fibrillation and, primarily in postmenopausal women, a decrease in bone mineral density (BMD) (table 2). (See 'Potential consequences of subclinical hyperthyroidism' below.)

DIAGNOSIS

The diagnosis of subclinical hyperthyroidism is based upon biochemical testing alone. Subclinical hyperthyroidism is defined as:

- Normal serum free T4 and T3
- Low TSH

It may occur in the presence or absence of mild symptoms of hyperthyroidism.

If the serum TSH concentration is below normal (<0.5 mU/L in many laboratories), the TSH measurement should be repeated along with a serum free T4 and T3 to make the diagnosis of subclinical hyperthyroidism.

Because the serum TSH concentration can be transiently reduced, a serum TSH measurement, along with a free T4 and T3, should be repeated after one to three months to confirm the diagnosis.

Once the diagnosis of subclinical hyperthyroidism has been established, the cause should be identified (table 1). (See 'Identifying the cause' below.)

Differential diagnosis — Other causes of the combination of low serum TSH and normal free T4 and T3 concentrations include the following:

- Central hypothyroidism – Some patients with central hypothyroidism have low serum TSH and normal (but usually low or low-normal) free T4 and T3 concentrations. (See "Diagnosis of and screening for hypothyroidism in nonpregnant adults", section on 'Secondary and tertiary (central) hypothyroidism' and "Central hypothyroidism", section on 'TSH low'.)

- Nonthyroidal illness – Euthyroid patients with nonthyroidal illness, especially those receiving high-dose glucocorticoids or dopamine, may have low serum TSH and low-normal free T4 and T3 concentrations. (See "Thyroid function in nonthyroidal illness".)

- Recovery from hyperthyroidism – Serum TSH concentrations may remain low for up to several months after normalization of serum T4 and T3 concentrations in patients treated for hyperthyroidism or recovering from hyperthyroidism caused by thyroiditis. (See "Graves' hyperthyroidism in nonpregnant adults: Overview of treatment", section on 'Thyroid function tests' and "Painless thyroiditis", section on 'Laboratory findings'.)

- Due to a shift in the distribution of normal TSH values, approximately 3 percent of healthy Black people have a serum TSH <0.4 mU/L, although it would be unusual for the TSH to be <0.1 mU/L [8,18]. This can mimic subclinical hyperthyroidism.

- Ingestion of 5 to 10 mg of biotin can cause artifactually low serum TSH levels in assays using biotin-streptavidin affinity systems in their design [19-21]. Thyroid tests should be repeated at least two days after discontinuation of biotin supplements.

IDENTIFYING THE CAUSE

In patients with risk factors for complications of subclinical hyperthyroidism (eg, age ≥65 years, cardiovascular disease, osteoporosis) and/or with TSH <0.1 mU/L, the cause of subclinical hyperthyroidism should be determined (table 1) in order to inform management. Patients without risk for complications whose TSH levels are 0.1 mU/L to the lower limit of normal do not require additional evaluation, since observation alone is appropriate management (algorithm 1). (See 'Management' below.)

Patients at high risk for complications and/or TSH <0.1 mU/L should be questioned about symptoms of hyperthyroidism (eg, tremor, palpitations, heat intolerance), in addition to a past history of thyroid disease, exposure to iodine-containing radiographic contrast media or herbal products containing iodine, use of medications that may suppress TSH (T4, high-dose glucocorticoids), and biotin ingestion. Women of childbearing age should be questioned about the possibility of pregnancy.

All patients should be examined for the presence of thyroid gland enlargement and/or nodularity.

In patients not taking T4 or other medications that suppress TSH who have persistently subnormal TSH values, autonomously functioning thyroid adenomas and multinodular goiters are the most common causes of subclinical hyperthyroidism. Graves' disease and thyroiditis are less common.

- **Thyroid testing** – If the diagnosis is not apparent based on the clinical presentation, diagnostic testing is indicated in patients at high risk for complications of subclinical hyperthyroidism in whom we are considering treatment and can initially include any of the following, depending on available expertise and resources (see "Diagnosis of hyperthyroidism", section on 'Determining the etiology'):

  - Measurement of thyrotropin receptor antibodies (TRAb, also called TSI, TBII, or TBI). If the antibodies are positive, it confirms the diagnosis of Graves' disease. If negative, it does not distinguish among the etiologies, as TRAb may not be elevated in patients with mild Graves' disease.

  - Determination of the radioactive iodine uptake scan (table 1). (This can be the initial test or a secondary test in patients with negative TRAb.)

    If the scan shows one or more focal areas of increased uptake, this could account for the low serum TSH (autonomously functioning thyroid adenoma or multinodular goiter, respectively). If there are focal areas of increased uptake, a thyroid ultrasound would then be useful in delineating the presence of discrete nodules.

A high or relatively high 24-hour uptake (relative to the low serum TSH value) that is diffuse is suggestive of Graves' disease.

In patients with low or no uptake on radioiodine scan, the etiology of subclinical hyperthyroidism may be thyroiditis or recent iodine exposure.

- Measurement of thyroidal artery blood flow on Doppler ultrasonography is useful to distinguish Graves' disease from thyroiditis in overt hyperthyroidism; its utility in subclinical hyperthyroidism has not been validated.

- **Other tests** – In postmenopausal women or other patients at risk for osteoporosis, bone densitometry may be useful in making a decision to treat subclinical hyperthyroidism or to monitor. (See "Osteoporotic fracture risk assessment" and "Clinical manifestations, diagnosis, and evaluation of osteoporosis in postmenopausal women".)

POTENTIAL CONSEQUENCES OF SUBCLINICAL HYPERTHYROIDISM

Patients with subclinical hyperthyroidism may progress to overt hyperthyroidism. The skeleton and the cardiovascular system are the major target tissues adversely affected by subclinical hyperthyroidism, although abnormalities in other systems have been reported (table 2).

Progression to overt hyperthyroidism — There are conflicting data regarding the frequency of progression from subclinical to overt hyperthyroidism, with annualized rates of approximately 0.5 to 8 percent [1,4,22-25]. Progression to overt hyperthyroidism appears to be related to the degree of subclinical hyperthyroidism and the underlying disease. As examples:

- In a population-based study from Scotland, 2024 adults with at least two suppressed (<0.4 mU/L) serum TSH levels measured four months apart with normal free or total T4 and total T3 were identified [25]. In the first year of observation, the overall progression rate from subclinical to overt hyperthyroidism was 6.1 percent. For patients with stable subclinical hyperthyroidism who did not progress after one year, progression rates at two, five, and seven years were 0.6, 0.7, and 0.5 percent, respectively. Although the proportion of patients who progressed to overt hyperthyroidism was small, progression was approximately twice as common in patients with serum TSH <0.1 mU/L compared with those with TSH between 0.1 and 0.4 mU/L.

- In a New Zealand study of 96 patients with endogenous subclinical thyrotoxicosis (TSH <0.25 mU/L), progression to overt hyperthyroidism occurred in 8 percent at one year and increased to 26 percent at five years. At five years, overt hyperthyroidism was seen in 9, 21,

and 61 percent of patients whose subclinical hyperthyroidism was due to Graves' disease, nodular goiter, and autonomous nodules, respectively [22].

- In a Brazilian study of 48 women <65 years who had TSH ≤0.1 mU/L (confirmed by repeat measurement six to eight weeks later), 20 percent with nodular disease and 40 percent with Graves' disease progressed from subclinical to overt hyperthyroidism over a two-year period [23]. In a separate study of women ≥60 years with only minimal thyrotoxicosis (TSH 0.1 to 0.4 mU/L), progression to overt hyperthyroidism was uncommon (approximately 1 percent yearly) [24].

- In a study from the United Kingdom, 20.3 percent of patients with subclinical hyperthyroidism and TSH <0.1 mU/L progressed to overt hyperthyroidism over an average of 32 months compared with 6.8 percent of those with TSH 0.1 to 0.39 mU/L [26].

- In the Framingham Study of adults >60 years with a TSH <0.1 mU/L, only 4.3 percent of patients progressed to overt hyperthyroidism after four years [1].

Spontaneous recovery has also been described in patients with subclinical hyperthyroidism. When studied weeks to one year later, 40 to 60 percent of subjects with subclinical hyperthyroidism had normal values [2,4]. This is most likely to occur in subjects with only slightly subnormal serum TSH values (eg, between 0.1 and 0.5 mU/L) when first studied. In an analysis of a primary care network that included 422,242 persons without known thyroid disease, 52 percent who had a serum TSH concentration <0.35 mU/L at baseline had a normal TSH subsequently in the absence of treatment [27].

Bone and mineral metabolism — Thyroid hormone directly stimulates bone resorption, and overt hyperthyroidism is associated with increased bone resorption (and to a lesser extent, low bone formation), low bone density, and an increase in fracture [28]. The changes are greatest in cortical bone (wrist), least in trabecular bone (lumbar spine), and intermediate in mixed cortical-trabecular bone (hip).

Endogenous and exogenous subclinical hyperthyroidism are also associated with reduced bone density, particularly in cortical-rich bone in postmenopausal women. The risk of fracture appears to be related to the degree of TSH suppression and to specific patient factors (eg, older age) that confer an increased risk of osteoporotic fracture. This topic is reviewed separately. (See "Bone disease with hyperthyroidism and thyroid hormone therapy", section on 'Subclinical hyperthyroidism'.)

Cardiovascular effects — Overt hyperthyroidism is associated with an increased risk of atrial fibrillation, heart failure, pulmonary hypertension, and angina (see "Cardiovascular effects of

hyperthyroidism"). Patients with subclinical hyperthyroidism also have an increased risk of atrial fibrillation and, in addition, have more subtle cardiac findings including increases in heart rate, cardiac contractility, and left ventricular mass [29,30].

The presence of cardiovascular findings in subclinical hyperthyroidism is variable, likely due to the degree of TSH suppression, the underlying disease, and individual sensitivity to thyroid hormone excess.

The degree of TSH suppression that predicts adverse cardiovascular effects is unknown. However, in one small study of exogenous subclinical hyperthyroidism, cardiovascular parameters that were abnormal at higher doses became normal when the dose of T4 was adjusted so that the TSH measured approximately 0.1 mU/L [31].

Atrial fibrillation — In a meta-analysis of patient-level data from five prospective cohort studies (8711 participants, 810 with endogenous subclinical hyperthyroidism), subclinical hyperthyroidism was associated with an increased risk of atrial fibrillation (hazard ratio [HR] 1.68, 95% CI 1.16-2.43) [32]. The risk was higher for TSH levels <0.1 mU/L compared with 0.1 to 0.44 mU/L (HRs 2.54 versus 1.63).

The cumulative incidence of atrial fibrillation in patients with subclinical hyperthyroidism is illustrated by the findings of a prospective cohort study of approximately 2000 adults over age 60 years (without atrial fibrillation) followed for 10 years [7]. For subjects with serum TSH values <0.1 mU/L, 0.1 to 0.4 mU/L, or within the normal range, the cumulative incidence of atrial fibrillation was 28, 16, and 11 percent, respectively (figure 1) [7].

In biochemically euthyroid individuals, both serum TSH and free T4 concentrations may also be associated with atrial fibrillation risk. In a population-based study of 1426 subjects, euthyroid individuals with a TSH in the lowest quartile had a higher risk of atrial fibrillation than those in the highest quartile [33]. However, in an analysis of 30,085 individual participant data from 11 prospective cohorts who were euthyroid or had subclinical hypothyroidism, there was no correlation between serum TSH and atrial fibrillation, but serum free T4 concentrations in the highest compared with the lowest quartile was associated with an increased risk of atrial fibrillation (HR 1.45, 95% CI 1.26-1.66) [34].

Guidelines for the management of atrial fibrillation in patients with hyperthyroidism are discussed separately. (See "Atrial fibrillation in adults: Selection of candidates for anticoagulation".)

Coronary heart disease — In the meta-analysis described above (22,437 participants, 718 with endogenous subclinical hyperthyroidism), the risk of coronary heart disease events was higher

in patients with endogenous subclinical hyperthyroidism (HR 1.21, 95% CI 0.99-1.46) [32]. Similar findings were reported in a population-based study from Scotland, which was not included in the meta-analysis [35]. Endogenous subclinical hyperthyroidism was associated with an increased risk of nonfatal cardiovascular disease (HR 1.39, 95% CI 1.22-1.58) [35]. In a 2017 meta-analysis (71,808 participants, 2300 with subclinical hyperthyroidism), the relative risk (RR) for coronary heart disease was 1.20, 95% CI 1.02-1.42 [36].

Heart failure — Subclinical hyperthyroidism is also associated with an increased risk of heart failure [37-39]. In a cohort of older adults aged 70 to 82 years with a history of vascular disease (5316 participants, 71 with subclinical hyperthyroidism, five taking T4), the risk of heart failure over 3.2 years of follow-up was higher compared with euthyroid controls (HR 2.93, 95% CI 1.37-6.24) [37], and in a pooled analysis of individual data from six prospective cohort studies (25,390 participants, 648 with subclinical hyperthyroidism), patients with TSH levels <0.10 mU/L had a higher risk of heart failure than euthyroid controls (16 events in 154 participants [10.4 percent] versus 1762 events in 22,674 [7.8 percent]; HR 1.94, 95% CI 1.01-3.72) [38]. The risk persisted (HR 1.80, 95% CI 1.04-3.13) when those using thyroid hormone were excluded from the analysis.

Other — Subclinical hyperthyroidism has several other effects on cardiac function, all similar to but less severe and less frequent than those in overt hyperthyroidism. These include sinus tachycardia, premature atrial complex (PAC; also referred to a premature atrial beat, premature supraventricular complex, or premature supraventricular beat), increase in left ventricular mass index, increase in cardiac contractility, impaired endothelial function, reduced exercise tolerance, reduced heart rate variability, and an increase in markers of coagulation [29,30,40-43].

Mortality — There appears to be an increased risk of mortality in patients with subclinical hyperthyroidism. Overall, the increased risk appears to be small but increases with the degree of TSH suppression.

- **Exogenous and endogenous subclinical hyperthyroidism** – In a meta-analysis of five population-based studies examining the association between subclinical hyperthyroidism (both endogenous and exogenous with TSH less than 0.3 to 0.5 mU/L) and cardiovascular and all-cause mortality, the risk for all-cause and cardiovascular mortality was not significant (RRs 1.12, 95% CI 0.89-1.42 and 1.19, 95% CI 0.81-1.76, respectively) [44]. In contrast, two other meta-analyses (both endogenous and exogenous subclinical hyperthyroidism) showed a significantly increased risk of all-cause mortality (HR 1.41, 95% CI 1.12-1.79 and RR 1.27, 95% CI 1.07-1.51, respectively) and coronary heart disease mortality (RR 1.45, 95% CI 1.12-1.86) [36,45]. In a mathematical model designed a priori to explore mortality risk, the excess mortality after diagnosis of subclinical hyperthyroidism

depended upon age, with an increase beyond the age of 60 years. However, in a subsequent population-based study, subclinical hyperthyroidism was associated with reduced survival only in individuals <65 years [46].

- **Endogenous subclinical hyperthyroidism** – Serum T3 levels are higher in patients with endogenous than exogenous subclinical hyperthyroidism, and this may confer a higher mortality risk [29]. In the meta-analysis of 10 prospective cohort studies described above (52,674 participants, 2188 with endogenous subclinical hyperthyroidism) that included only patients with endogenous subclinical hyperthyroidism, there was an increased risk of both total (HR 1.24, 95% CI 1.06-1.46) and cardiovascular (HR 1.29, 95% CI 1.02-1.62) mortality in patients with endogenous subclinical hyperthyroidism [32]. The risk of cardiovascular mortality was higher for TSH levels <0.1 mU/L compared with levels between 0.1 and 0.44 mU/L (HRs 1.84 versus 1.24).

- **Exogenous subclinical hyperthyroidism** – In a study evaluating only patients with exogenous subclinical hyperthyroidism, there was an increased risk of cardiovascular or overall mortality only in patients with fully suppressed TSH levels [47]. In this cohort study of 17,684 patients (mean age 61.6 years) taking T4 replacement therapy, TSH levels were fully suppressed (<0.03 mU/L) or low (0.04 to 0.4 mU/L) in 6 and 21 percent of patients, respectively. Compared with patients with normal TSH, patients with suppressed TSH concentrations (<0.03 mU/L) had increased cardiovascular morbidity and mortality (adjusted HR 1.37, 95% CI 1.17-1.60), whereas those who had serum TSH levels between 0.04 and 0.4 mU/L had a smaller increase in risk that was not significant (adjusted HR 1.10, 95% CI 0.99-1.23).

Dementia — Some [35,48-52], but not all [53-57], case-control and population-based cohort studies suggest that subclinical hyperthyroidism is a risk factor for dementia. A pooled analysis of five prospective cohort studies reported an increased risk of dementia in patients with subclinical hyperthyroidism compared with euthyroidism (adjusted risk ratio 1.67, 95% CI 1.04-2.69) [58]. (See "Neurologic manifestations of hyperthyroidism and Graves' disease", section on 'Encephalopathy'.)

Quality of life — Quality of life may be impaired in some patients with subclinical hyperthyroidism, particularly those with endogenous subclinical hyperthyroidism [29]. Variability in findings is likely related to differences in patient populations, duration of subclinical hyperthyroidism, and degree of TSH suppression.

- **Exogenous subclinical hyperthyroidism** – In patients with exogenous subclinical hyperthyroidism, disturbances in sleep and decreases in some physical components have

been reported with [57] or without [55,59-61] significant effect on mood or mental health. As examples:

- In hypothyroid patients randomly assigned to the usual dose of T4 (euthyroid group) versus higher-dose T4 (subclinical hyperthyroid group), the Short Form 36 (SF-36) physical component and general healthy subscale were slightly worse in the subclinical hyperthyroid group [61]. In contrast, mental health, mood, and motor learning were improved.

- In a six-month, randomized trial of T4 titrated to establish continuation of TSH suppression versus normalization of TSH in 24 patients with a history of differentiated thyroid carcinoma, there were no significant changes in any SF-36 components in either group [60].

On the other hand, in a nonblinded study in which subjects were given a T4 dose that was 50 mcg greater or less than their optimal dose (based on thyrotropin-releasing hormone [TRH]-stimulated TSH testing), patients on the higher dose had improved "well-being" using a visual analog scale compared with baseline [62].

- **Endogenous subclinical hyperthyroidism** – In patients with endogenous subclinical hyperthyroidism, scores for both the physical and mental health components appear to be lower than in euthyroid control subjects [63]. The low scores were due to symptoms related to thyroid hormone excess (palpitations, nervousness, tremor, and sweating).

MANAGEMENT

Patients on T4 for the treatment of hypothyroidism — Both low bone density and atrial fibrillation can result in substantial morbidity in older adult patients, and therefore, subclinical hyperthyroidism should be avoided. Patients receiving thyroid replacement therapy who have TSH concentrations below normal should have their dose adjusted to maintain a normal serum TSH concentration (approximately 0.5 to 5.0 mU/L). (See "Treatment of primary hypothyroidism in adults", section on 'Older patients or those with coronary heart disease' and "Treatment of primary hypothyroidism in adults", section on 'Goals of therapy'.)

Patients on suppressive T4 therapy — Subclinical hyperthyroidism is unavoidable when thyroid hormone is given to suppress TSH secretion in an attempt to prevent or reduce goiter growth or prevent recurrence of thyroid cancer since it is the goal of therapy. However, the adverse effects of suppressive therapy can be minimized by treatment with the lowest dose of T4 necessary to meet the desired goal [31,64].

In many, but not all, patients with thyroid cancer, subclinical hyperthyroidism is the goal of thyroid hormone therapy. In these patients, the benefits of TSH suppression are thought to outweigh the risks of subclinical hyperthyroidism. This topic is reviewed elsewhere. (See "Differentiated thyroid cancer: Overview of management", section on 'Thyroid hormone suppression'.)

Candidates for suppressive therapy and goal TSH levels in patients with benign thyroid disease are reviewed in detail separately. (See "Thyroid hormone suppressive therapy for thyroid nodules and benign goiter".)

Postmenopausal women taking suppressive doses of thyroid hormone should receive calcium and vitamin D supplementation if needed, and consideration should be given to instituting antiresorptive therapy to prevent bone loss. Drug options for prevention of osteoporosis are reviewed elsewhere. (See "Bone disease with hyperthyroidism and thyroid hormone therapy", section on 'Prevention and treatment of reduced bone density' and "Calcium and vitamin D supplementation in osteoporosis".)

Endogenous subclinical hyperthyroidism — There are few data to guide clinical decisions regarding the treatment of patients with endogenous subclinical hyperthyroidism. We base our decision to treat on clinical risk for complications of subclinical hyperthyroidism and the degree of TSH suppression. In some patients, the values are normal on retesting weeks or months later, such that intervention should not be considered unless persistently low TSH values are documented [2,4].

Our approach below is largely consistent with guidelines from the American Thyroid Association (ATA) [65] and the European Thyroid Association [66].

Patients at high risk for complications — In patients at high risk for skeletal or cardiac complications (eg, older patients ≥65 years of age, patients with or at risk for cardiovascular disease, or postmenopausal women with or at risk for osteoporosis), we use the following approach (algorithm 1):

- If the serum TSH value is <0.1 mU/L, we treat the underlying cause of subclinical hyperthyroidism.
- If the serum TSH is 0.1 to 0.5 mU/L, we suggest treatment, especially if there is underlying cardiovascular disease, if the bone density is low, or if the patient has hyperthyroid symptoms. We are also more likely to consider treatment if a thyroid radionuclide scan shows one or more focal areas of high uptake (ie, evidence of autonomy) since subclinical

hyperthyroidism due to an autonomous nodule is likely to progress to overt hyperthyroidism as the nodule grows.

Observation is an alternative in asymptomatic patients, especially in the absence of an autonomous nodule on thyroid scan, in patients with normal bone density, in patients who are taking osteoporosis drugs to reduce bone turnover, and in patients who are taking beta-adrenergic blocking drugs for other reasons. In observed patients, we measure TSH, free T4, and total T3 every six months and obtain bone density measurements every two years.

Patients at low risk for complications — In patients at low risk for complications of hyperthyroidism (eg, individuals <65 years, premenopausal women), we use the following approach (algorithm 1):

- If the serum TSH value is persistently <0.1 mU/L, we suggest treating the underlying cause of subclinical hyperthyroidism, especially if the patient has symptoms suggestive of hyperthyroidism and if the patient's thyroid radioiodine scan shows one or more focal areas of increased uptake.

  Observation is an alternative in asymptomatic patients, especially in the absence of an autonomous nodule on thyroid scan and in patients taking osteoporosis drugs or beta-adrenergic blocking agents.

- If the TSH is between 0.1 to 0.5 mU/L, observation alone is appropriate. We measure TSH, free T4, and T3 every six months.

Potential benefits of treatment include improvement in certain cardiovascular parameters and in bone mineral density (BMD). However, there are no studies evaluating the long-term benefits of correcting subclinical hyperthyroidism, particularly studies with clinically important endpoints such as cardiovascular disease and fracture. As an example, in a prospective but uncontrolled study of patients with subclinical hyperthyroidism, antithyroid drugs reduced heart rate, premature atrial and ventricular complexes, left ventricular mass index, interventricular septal thickness, and left ventricular posterior wall thickness [67]. Similar improvements in hemodynamic parameters were seen in other studies following radioiodine therapy [68,69].

In two other nonrandomized studies, postmenopausal women with nodular goiter and subclinical hyperthyroidism treated with antithyroid drugs or radioiodine for two years had higher bone density than similar women who were not treated [70,71].

Thus, in some patients with subclinical hyperthyroidism, normalization of TSH results in improvement in surrogate outcomes. Long-term clinical trials are required to determine if correcting subclinical hyperthyroidism improves cardiovascular or skeletal outcomes.

Treatment options — The treatment options for patients with subclinical hyperthyroidism are the same as those for overt hyperthyroidism and depend upon the underlying etiology. Beta-adrenergic antagonist drugs are useful to control symptoms of adrenergic overactivity (eg, palpitations, tremor). (See "Beta blockers in the treatment of hyperthyroidism".)

In patients with Graves' disease or nodular thyroid disease with autonomy, treatment options include thionamides, radioiodine, or surgery. The treatment of these conditions is reviewed separately. (See "Graves' hyperthyroidism in nonpregnant adults: Overview of treatment" and "Treatment of toxic adenoma and toxic multinodular goiter" and "Radioiodine in the treatment of hyperthyroidism".)

In patients with low or no uptake on radioiodine scan, the etiology of subclinical hyperthyroidism may be thyroiditis, exogenous thyroid hormone intake, or iodine exposure (table 1). Most patients with thyroiditis and iodine exposure require no treatment since thyroid dysfunction is rarely severe and is transient. However, thyroid tests should be monitored, initially every four to eight weeks, until normalization. Symptomatic patients may benefit from beta-adrenergic antagonists. (See "Painless thyroiditis" and "Iodine-induced thyroid dysfunction", section on 'Iodine-induced hyperthyroidism'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Hyperthyroidism".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Hyperthyroidism (overactive thyroid) (The Basics)")
- Beyond the Basics topics (see "Patient education: Hyperthyroidism (overactive thyroid) (Beyond the Basics)" and "Patient education: Antithyroid drugs (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- Most patients with subclinical hyperthyroidism have no clinical manifestations of hyperthyroidism, and those symptoms that are present (eg, tachycardia, tremor, dyspnea on exertion, weight loss) are mild and nonspecific. (See 'Clinical findings' above.)
- The diagnosis of subclinical hyperthyroidism is based upon biochemical testing alone. Subclinical hyperthyroidism is defined biochemically as normal serum free thyroxine (T4) and triiodothyronine (T3) concentrations in the presence of a subnormal thyroid-stimulating hormone (TSH). (See 'Diagnosis' above.)
- The most common causes of subclinical hyperthyroidism are treatment with T4 (exogenous) and autonomously functioning thyroid adenomas and multinodular goiters (endogenous) (table 1). (See 'Etiology' above.)
- Subclinical hyperthyroidism is associated with an increased risk of atrial fibrillation and, primarily in postmenopausal women, a decrease in bone mineral density (BMD). In addition, patients with subclinical hyperthyroidism may progress to overt hyperthyroidism. Data regarding overall mortality and dementia are variable. (See 'Potential consequences of subclinical hyperthyroidism' above.)
- Patients receiving thyroid replacement therapy for the treatment of hypothyroidism and who have TSH concentrations below normal should have their dose adjusted to maintain a normal serum TSH concentration (approximately 0.5 to 5.0 mU/L). (See 'Patients on T4 for the treatment of hypothyroidism' above.)
- For patients with thyroid cancer and in some patients with benign nodular thyroid disease, subclinical hyperthyroidism is the goal of thyroid hormone therapy. The adverse effects of suppressive therapy can be minimized by treatment with the lowest dose of T4 necessary to meet the desired goal. (See 'Patients on suppressive T4 therapy' above.)

For patients with endogenous subclinical hyperthyroidism at high risk for cardiac or skeletal complications (eg, older adults ≥65 years, patients with or at risk for cardiovascular disease, or postmenopausal women with or at risk for osteoporosis) and who have a TSH concentration less than 0.1 mU/L, we recommend treatment of the underlying cause of subclinical hyperthyroidism (algorithm 1) (**Grade 1C**). (See 'Patients at high risk for complications' above.)

For similar patients who have TSH values between 0.1 and 0.5 mU/L, we suggest treatment especially if the bone density is low, if there is underlying cardiovascular disease, if the patient has hyperthyroid symptoms, or if the radionuclide scan shows one or more focal areas of increased uptake (**Grade 2C**). Observation is an alternative in asymptomatic patients, especially in the absence of an autonomous nodule on thyroid scan, in patients with normal bone density, in patients who are taking osteoporosis drugs to reduce bone turnover, and in patients who are taking beta-adrenergic blocking drugs for other reasons. In observed patients, we measure TSH, free T4, and T3 every six months and obtain a bone density every two years. (See 'Patients at high risk for complications' above.)

- For patients with endogenous subclinical hyperthyroidism at low risk for cardiac or skeletal complications (young individuals, premenopausal women) and TSH values less than 0.1 mU/L, we suggest treatment, especially if the patient has hyperthyroid symptoms or if the radionuclide scan shows one or more focal areas of increased uptake (algorithm 1) (**Grade 2C**). Observation is an alternative in asymptomatic patients, especially in the absence of an autonomous nodule, and in patients taking osteoporosis drugs or beta-adrenergic blocking agents. (See 'Patients at low risk for complications' above.)

  For low-risk patients who have a TSH value between 0.1 and 0.5 mU/L, we suggest observation (**Grade 2C**). We measure TSH, free T4, and T3 every six months.

- The treatment options for patients with subclinical hyperthyroidism are the same as those for overt hyperthyroidism and depend upon the underlying etiology. (See 'Treatment options' above.)

REFERENCES

1. Sawin CT, Geller A, Kaplan MM, et al. Low serum thyrotropin (thyroid-stimulating hormone) in older persons without hyperthyroidism. Arch Intern Med 1991; 151:165.

2. Eggertsen R, Petersen K, Lundberg PA, et al. Screening for thyroid disease in a primary care unit with a thyroid stimulating hormone assay with a low detection limit. BMJ 1988; 297:1586.
3. Bagchi N, Brown TR, Parish RF. Thyroid dysfunction in adults over age 55 years. A study in an urban US community. Arch Intern Med 1990; 150:785.
4. Parle JV, Franklyn JA, Cross KW, et al. Prevalence and follow-up of abnormal thyrotrophin (TSH) concentrations in the elderly in the United Kingdom. Clin Endocrinol (Oxf) 1991; 34:77.
5. Franklyn JA, Black EG, Betteridge J, Sheppard MC. Comparison of second and third generation methods for measurement of serum thyrotropin in patients with overt hyperthyroidism, patients receiving thyroxine therapy, and those with nonthyroidal illness. J Clin Endocrinol Metab 1994; 78:1368.
6. Sundbeck G, Jagenburg R, Johansson PM, et al. Clinical significance of low serum thyrotropin concentration by chemiluminometric assay in 85-year-old women and men. Arch Intern Med 1991; 151:549.
7. Sawin CT, Geller A, Wolf PA, et al. Low serum thyrotropin concentrations as a risk factor for atrial fibrillation in older persons. N Engl J Med 1994; 331:1249.
8. Hollowell JG, Staehling NW, Flanders WD, et al. Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). J Clin Endocrinol Metab 2002; 87:489.
9. Belin RM, Astor BC, Powe NR, Ladenson PW. Smoke exposure is associated with a lower prevalence of serum thyroid autoantibodies and thyrotropin concentration elevation and a higher prevalence of mild thyrotropin concentration suppression in the third National Health and Nutrition Examination Survey (NHANES III). J Clin Endocrinol Metab 2004; 89:6077.
10. De Whalley P. Do abnormal thyroid stimulating hormone level values result in treatment changes? A study of patients on thyroxine in one general practice. Br J Gen Pract 1995; 45:93.
11. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. Arch Intern Med 2000; 160:526.
12. Taylor PN, Iqbal A, Minassian C, et al. Falling threshold for treatment of borderline elevated thyrotropin levels-balancing benefits and risks: evidence from a large community-based study. JAMA Intern Med 2014; 174:32.

13. Díez JJ. Hyperthyroidism in patients older than 55 years: an analysis of the etiology and management. Gerontology 2003; 49:316.
14. Rieu M, Bekka S, Sambor B, et al. Prevalence of subclinical hyperthyroidism and relationship between thyroid hormonal status and thyroid ultrasonographic parameters in patients with non-toxic nodular goitre. Clin Endocrinol (Oxf) 1993; 39:67.
15. Charkes ND. The many causes of subclinical hyperthyroidism. Thyroid 1996; 6:391.
16. Kasagi K, Hatabu H, Tokuda Y, et al. Studies on thyrotrophin receptor antibodies in patients with euthyroid Graves' disease. Clin Endocrinol (Oxf) 1988; 29:357.
17. Murakami M, Koizumi Y, Aizawa T, et al. Studies of thyroid function and immune parameters in patients with hyperthyroid Graves' disease in remission. J Clin Endocrinol Metab 1988; 66:103.
18. Boucai L, Surks MI. Reference limits of serum TSH and free T4 are significantly influenced by race and age in an urban outpatient medical practice. Clin Endocrinol (Oxf) 2009; 70:788.
19. Barbesino G. Misdiagnosis of Graves' Disease with Apparent Severe Hyperthyroidism in a Patient Taking Biotin Megadoses. Thyroid 2016; 26:860.
20. Sharma A, Baumann NA, Shah P. Biotin-Induced Biochemical Graves Disease: A Teachable Moment. JAMA Intern Med 2017; 177:571.
21. Li D, Radulescu A, Shrestha RT, et al. Association of Biotin Ingestion With Performance of Hormone and Nonhormone Assays in Healthy Adults. JAMA 2017; 318:1150.
22. Schouten BJ, Brownlie BE, Frampton CM, Turner JG. Subclinical thyrotoxicosis in an outpatient population - predictors of outcome. Clin Endocrinol (Oxf) 2011; 74:257.
23. Rosario PW. The natural history of subclinical hyperthyroidism in patients below the age of 65 years. Clin Endocrinol (Oxf) 2008; 68:491.
24. Rosario PW. Natural history of subclinical hyperthyroidism in elderly patients with TSH between 0.1 and 0.4 mIU/l: a prospective study. Clin Endocrinol (Oxf) 2010; 72:685.
25. Vadiveloo T, Donnan PT, Cochrane L, Leese GP. The Thyroid Epidemiology, Audit, and Research Study (TEARS): the natural history of endogenous subclinical hyperthyroidism. J Clin Endocrinol Metab 2011; 96:E1.
26. Das G, Ojewuyi TA, Baglioni P, et al. Serum thyrotrophin at baseline predicts the natural course of subclinical hyperthyroidism. Clin Endocrinol (Oxf) 2012; 77:146.
27. Meyerovitch J, Rotman-Pikielny P, Sherf M, et al. Serum thyrotropin measurements in the community: five-year follow-up in a large network of primary care physicians. Arch Intern Med 2007; 167:1533.
28. Ross DS. Hyperthyroidism, thyroid hormone therapy, and bone. Thyroid 1994; 4:319.

29. Biondi B, Cooper DS. The clinical significance of subclinical thyroid dysfunction. Endocr Rev 2008; 29:76.
30. Cooper DS, Biondi B. Subclinical thyroid disease. Lancet 2012; 379:1142.
31. Mercuro G, Panzuto MG, Bina A, et al. Cardiac function, physical exercise capacity, and quality of life during long-term thyrotropin-suppressive therapy with levothyroxine: effect of individual dose tailoring. J Clin Endocrinol Metab 2000; 85:159.
32. Collet TH, Gussekloo J, Bauer DC, et al. Subclinical hyperthyroidism and the risk of coronary heart disease and mortality. Arch Intern Med 2012; 172:799.
33. Heeringa J, Hoogendoorn EH, van der Deure WM, et al. High-normal thyroid function and risk of atrial fibrillation: the Rotterdam study. Arch Intern Med 2008; 168:2219.
34. Baumgartner C, da Costa BR, Collet TH, et al. Thyroid Function Within the Normal Range, Subclinical Hypothyroidism, and the Risk of Atrial Fibrillation. Circulation 2017; 136:2100.
35. Vadiveloo T, Donnan PT, Cochrane L, Leese GP. The Thyroid Epidemiology, Audit, and Research Study (TEARS): morbidity in patients with endogenous subclinical hyperthyroidism. J Clin Endocrinol Metab 2011; 96:1344.
36. Sun J, Yao L, Fang Y, et al. Relationship between Subclinical Thyroid Dysfunction and the Risk of Cardiovascular Outcomes: A Systematic Review and Meta-Analysis of Prospective Cohort Studies. Int J Endocrinol 2017; 2017:8130796.
37. Nanchen D, Gussekloo J, Westendorp RG, et al. Subclinical thyroid dysfunction and the risk of heart failure in older persons at high cardiovascular risk. J Clin Endocrinol Metab 2012; 97:852.
38. Gencer B, Collet TH, Virgini V, et al. Subclinical thyroid dysfunction and the risk of heart failure events: an individual participant data analysis from 6 prospective cohorts. Circulation 2012; 126:1040.
39. Selmer C, Olesen JB, Hansen ML, et al. Subclinical and overt thyroid dysfunction and risk of all-cause mortality and cardiovascular events: a large population study. J Clin Endocrinol Metab 2014; 99:2372.
40. Yavuz DG, Yazici D, Toprak A, et al. Exogenous subclinical hyperthyroidism impairs endothelial function in nodular goiter patients. Thyroid 2008; 18:395.
41. Dörr M, Robinson DM, Wallaschofski H, et al. Low serum thyrotropin is associated with high plasma fibrinogen. J Clin Endocrinol Metab 2006; 91:530.
42. Demir T, Akinci B, Comlekci A, et al. Levothyroxine (LT4) suppression treatment for benign thyroid nodules alters coagulation. Clin Endocrinol (Oxf) 2009; 71:446.

43. Eustatia-Rutten CF, Corssmit EP, Heemstra KA, et al. Autonomic nervous system function in chronic exogenous subclinical thyrotoxicosis and the effect of restoring euthyroidism. J Clin Endocrinol Metab 2008; 93:2835.
44. Ochs N, Auer R, Bauer DC, et al. Meta-analysis: subclinical thyroid dysfunction and the risk for coronary heart disease and mortality. Ann Intern Med 2008; 148:832.
45. Haentjens P, Van Meerhaeghe A, Poppe K, Velkeniers B. Subclinical thyroid dysfunction and mortality: an estimate of relative and absolute excess all-cause mortality based on time-to-event data from cohort studies. Eur J Endocrinol 2008; 159:329.
46. van de Ven AC, Netea-Maier RT, de Vegt F, et al. Associations between thyroid function and mortality: the influence of age. Eur J Endocrinol 2014; 171:183.
47. Flynn RW, Bonellie SR, Jung RT, et al. Serum thyroid-stimulating hormone concentration and morbidity from cardiovascular disease and fractures in patients on long-term thyroxine therapy. J Clin Endocrinol Metab 2010; 95:186.
48. Kalmijn S, Mehta KM, Pols HA, et al. Subclinical hyperthyroidism and the risk of dementia. The Rotterdam study. Clin Endocrinol (Oxf) 2000; 53:733.
49. Tan ZS, Beiser A, Vasan RS, et al. Thyroid function and the risk of Alzheimer disease: the Framingham Study. Arch Intern Med 2008; 168:1514.
50. Ceresini G, Lauretani F, Maggio M, et al. Thyroid function abnormalities and cognitive impairment in elderly people: results of the Invecchiare in Chianti study. J Am Geriatr Soc 2009; 57:89.
51. Döbert N, Hamscho N, Menzel C, et al. Subclinical hyperthyroidism in dementia and correlation of the metabolic index in FDG-PET. Acta Med Austriaca 2003; 30:130.
52. Aubert CE, Bauer DC, da Costa BR, et al. The association between subclinical thyroid dysfunction and dementia: The Health, Aging and Body Composition (Health ABC) Study. Clin Endocrinol (Oxf) 2017; 87:617.
53. van der Cammen TJ, Mattace-Raso F, van Harskamp F, de Jager MC. Lack of association between thyroid disorders and Alzheimer's disease in older persons: a cross-sectional observational study in a geriatric outpatient population. J Am Geriatr Soc 2003; 51:884.
54. de Jong FJ, den Heijer T, Visser TJ, et al. Thyroid hormones, dementia, and atrophy of the medial temporal lobe. J Clin Endocrinol Metab 2006; 91:2569.
55. Roberts LM, Pattison H, Roalfe A, et al. Is subclinical thyroid dysfunction in the elderly associated with depression or cognitive dysfunction? Ann Intern Med 2006; 145:573.
56. Moon JH, Ahn S, Seo J, et al. The effect of long-term thyroid-stimulating hormone suppressive therapy on the cognitive function of elderly patients with differentiated thyroid

carcinoma. J Clin Endocrinol Metab 2014; 99:3782.

57. Samuels MH, Kolobova I, Smeraglio A, et al. The effects of levothyroxine replacement or suppressive therapy on health status, mood, and cognition. J Clin Endocrinol Metab 2014; 99:843.
58. Rieben C, Segna D, da Costa BR, et al. Subclinical Thyroid Dysfunction and the Risk of Cognitive Decline: a Meta-Analysis of Prospective Cohort Studies. J Clin Endocrinol Metab 2016; 101:4945.
59. Schlote B, Schaaf L, Schmidt R, et al. Mental and physical state in subclinical hyperthyroidism: investigations in a normal working population. Biol Psychiatry 1992; 32:48.
60. Eustatia-Rutten CF, Corssmit EP, Pereira AM, et al. Quality of life in longterm exogenous subclinical hyperthyroidism and the effects of restoration of euthyroidism, a randomized controlled trial. Clin Endocrinol (Oxf) 2006; 64:284.
61. Samuels MH, Schuff KG, Carlson NE, et al. Health status, mood, and cognition in experimentally induced subclinical thyrotoxicosis. J Clin Endocrinol Metab 2008; 93:1730.
62. Carr D, McLeod DT, Parry G, Thornes HM. Fine adjustment of thyroxine replacement dosage: comparison of the thyrotrophin releasing hormone test using a sensitive thyrotrophin assay with measurement of free thyroid hormones and clinical assessment. Clin Endocrinol (Oxf) 1988; 28:325.
63. Biondi B, Palmieri EA, Fazio S, et al. Endogenous subclinical hyperthyroidism affects quality of life and cardiac morphology and function in young and middle-aged patients. J Clin Endocrinol Metab 2000; 85:4701.
64. Biondi B, Cooper DS. Benefits of thyrotropin suppression versus the risks of adverse effects in differentiated thyroid cancer. Thyroid 2010; 20:135.
65. Ross DS, Burch HB, Cooper DS, et al. 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. Thyroid 2016; 26:1343.
66. Biondi B, Bartalena L, Cooper DS, et al. The 2015 European Thyroid Association Guidelines on Diagnosis and Treatment of Endogenous Subclinical Hyperthyroidism. Eur Thyroid J 2015; 4:149.
67. Sgarbi JA, Villaça FG, Garbeline B, et al. The effects of early antithyroid therapy for endogenous subclinical hyperthyroidism in clinical and heart abnormalities. J Clin Endocrinol Metab 2003; 88:1672.

68. Faber J, Wiinberg N, Schifter S, Mehlsen J. Haemodynamic changes following treatment of subclinical and overt hyperthyroidism. Eur J Endocrinol 2001; 145:391.
69. Kaminski G, Michalkiewicz D, Makowski K, et al. Prospective echocardiographic evaluation of patients with endogenous subclinical hyperthyroidism and after restoring euthyroidism. Clin Endocrinol (Oxf) 2011; 74:501.
70. Mudde AH, Houben AJ, Nieuwenhuijzen Kruseman AC. Bone metabolism during anti-thyroid drug treatment of endogenous subclinical hyperthyroidism. Clin Endocrinol (Oxf) 1994; 41:421.
71. Faber J, Jensen IW, Petersen L, et al. Normalization of serum thyrotrophin by means of radioiodine treatment in subclinical hyperthyroidism: effect on bone loss in postmenopausal women. Clin Endocrinol (Oxf) 1998; 48:285.

Topic 7881 Version 26.0

GRAPHICS

Causes of hyperthyroidism

Hyperthyroidism with a normal or high radioiodine uptake
Autoimmune thyroid disease
Graves' disease
Hashitoxicosis
Autonomous thyroid tissue (uptake may be low if recent iodine load led to iodine-induced hyperthyroidism)
Toxic adenoma
Toxic multinodular goiter
TSH-mediated hyperthyroidism
TSH-producing pituitary adenoma
Non-neoplastic TSH-mediated hyperthyroidism
Human chorionic gonadotropin-mediated hyperthyroidism
Hyperemesis gravidarum
Trophoblastic disease
Hyperthyroidism with a near absent radioiodine uptake
Thyroiditis
Subacute granulomatous (de Quervain's) thyroiditis
Painless thyroiditis (silent thyroiditis, lymphocytic thyroiditis)
Postpartum thyroiditis
Amiodarone (also may cause iodine-induced hyperthyroidism)
Checkpoint inhibitor-induced thyroiditis
Radiation thyroiditis
Palpation thyroiditis
Exogenous thyroid hormone intake
Excessive replacement therapy
Intentional suppressive therapy
Factitious hyperthyroidism
Ectopic hyperthyroidism

Struma ovarii
Metastatic follicular thyroid cancer

Major causes of hyperthyroidism according to the presence of a high or low radioiodine uptake. High uptake indicates increased new hormone synthesis by the thyroid, whereas low uptake indicates release of preformed hormone, exogenous ingestion, or extrathyroidal hormone synthesis.

TSH: thyroid-stimulating hormone.

Graphic 76972 Version 6.0

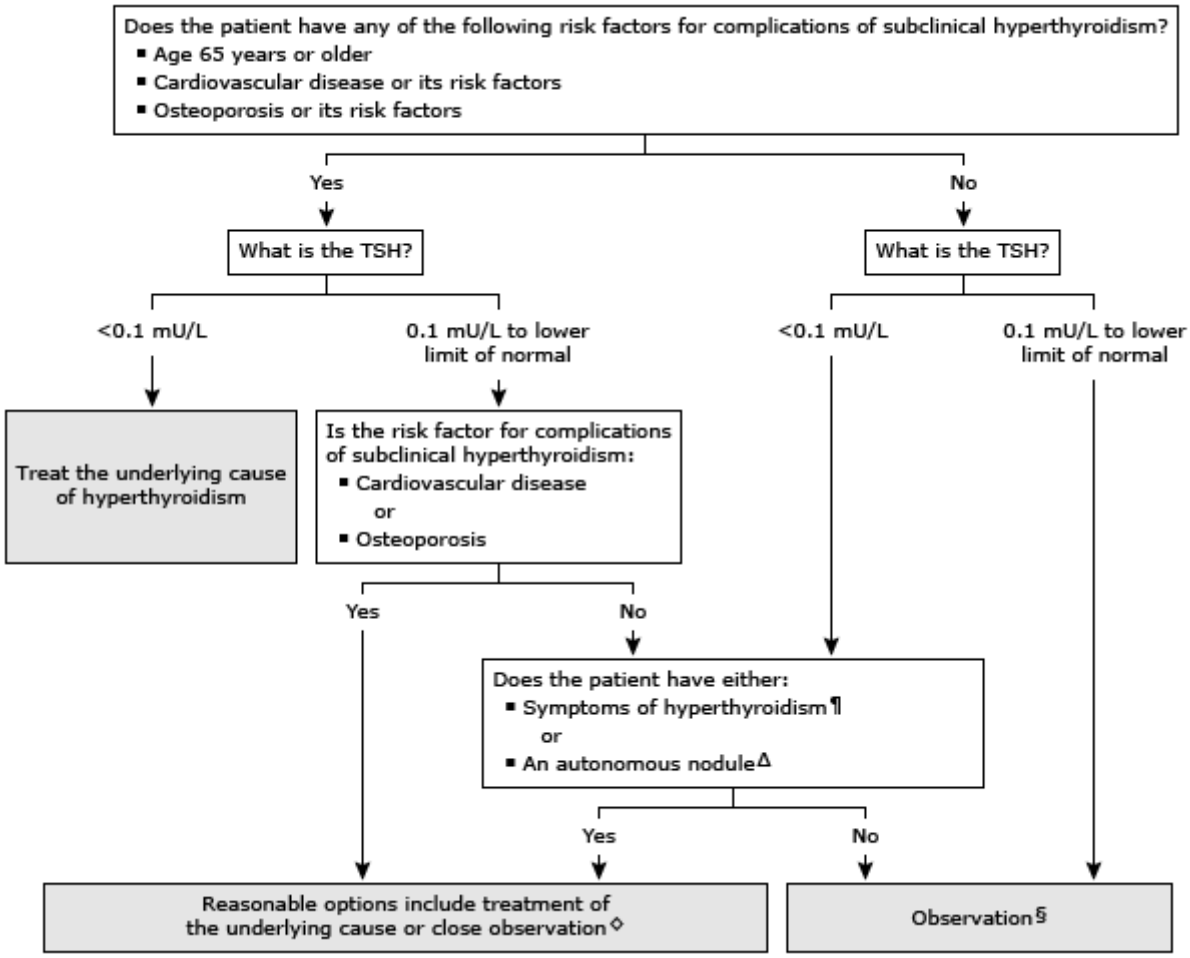
Clinical manifestations of subclinical hyperthyroidism

Bone disease
Decreased bone density, especially in postmenopausal females
Increased fracture risk
Biochemical markers of increased bone resorption
Increased urinary pyridinoline and deoxypyridinoline excretion
Increased urinary hydroxyproline excretion
Heart disease
Increased incidence of atrial fibrillation
Increased heart rate and incidence of atrial premature beats
Increased cardiac contractility
Increased left ventricular mass index and septal and posterior wall thickness
Laboratory abnormalities
Decrease in serum total and LDL cholesterol concentrations
Increased serum concentrations of hepatic enzymes and creatine kinase
Increased serum concentration of SHBG
Other
Decreased time asleep at night
Improved mood

LDL: low-density lipoprotein; SHBG: sex hormone-binding globulin.

Graphic 79602 Version 5.0

Indications for treatment of endogenous subclinical hyperthyroidism in nonpregnant adults*



TSH: thyroid-stimulating hormone.

* Subclinical hyperthyroidism is defined as a normal serum free thyroxine (T4) and triiodothyronine (T3) in the presence of a subnormal TSH, confirmed on repeated measurement over a three- to six-month period.

¶ Symptoms of hyperthyroidism include palpitations, tremulousness, heat intolerance, and insomnia (refer to UpToDate topics on hyperthyroidism).

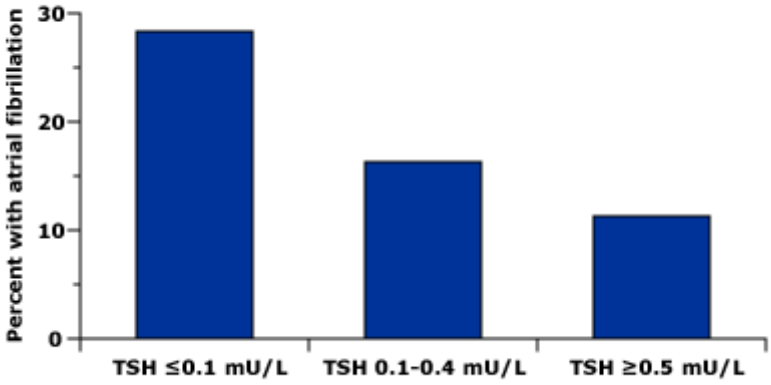
Δ A radionuclide scan showing one or more focal areas of increased uptake is consistent with autonomy and is a risk factor for progression to overt hyperthyroidism.

◇ There are insufficient data for or against treatment of subclinical hyperthyroidism in patients with TSH between 0.1 and the lower limit of normal and in younger patients (<65 years of age) with TSH <0.1 mU/L. A decision for individual management is based upon patient characteristics and preferences (refer to UpToDate topics on subclinical hyperthyroidism).

§ Check TSH, free T4, and T3 every six months.

Graphic 109938 Version 2.0

Increased incidence of atrial fibrillation in subclinical hyperthyroidism



Cumulative incidence of atrial fibrillation in subjects over age 60 years according to the serum concentration of TSH. The risk of atrial fibrillation was increased almost threefold in the subjects with marked suppression of TSH (left panel) as compared with those who had normal serum TSH concentrations and were presumably euthyroid (right panel); patients with slightly low serum TSH concentrations (middle panel) had a lesser increase in risk.

TSH: thyroid-stimulating hormone.

Data from: Sawin CT, Geller A, Wolf PA, et al. Low serum thyrotropin concentrations as a risk factor for atrial fibrillation in older persons. N Engl J Med 1994; 331:1249.

Graphic 55024 Version 4.0

Contributor Disclosures

Douglas S Ross, MD Consultant/Advisory Boards: Arbor Pharmaceuticals [Hypothyroidism];IBSA Pharma Inc [Hypothyroidism];Medullary Thyroid Cancer Registry Consortium [Thyroid cancer];Spectrix Therapeutics, LLC [Hypothyroidism]. All of the relevant financial relationships listed have been mitigated. **David S Cooper, MD** No relevant financial relationship(s) with ineligible companies to disclose. **Jean E Mulder, MD** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy