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Subclinical Hypothyroidism: Who Should Be Treated and Who Can Be Observed?

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Abstract

Subclinical hypothyroidism (SCH), defined by an elevated thyroid-stimulating hormone (TSH) concentration with a normal free thyroxine (FT4), is common, yet whether to treat it remains debated. This narrative review examines the natural history, clinical consequences, and treatment evidence for SCH and proposes a practical approach for identifying patients who should be treated and those who can be reasonably observed. PubMed/Medical Literature Analysis and Retrieval System Online (MEDLINE) and the Cochrane Library were searched from inception between September 1 and October 3, 2026 (last search), supplemented by reference-list screening; English-language adult studies and major guidelines were prioritized, with emphasis on randomized trials, systematic reviews, meta-analyses, and large prospective cohorts. SCH frequently resolves spontaneously or remains stable, particularly when TSH is below 10 mIU/L and thyroid peroxidase antibodies (TPOAb) are negative. Persistent TSH ⩾10 mIU/L and TPOAb positivity predict progression to overt hypothyroidism, and coronary heart disease risk is clearly increased only at TSH ⩾10 mIU/L, with no excess at 4.5-6.9 mIU/L. Randomized trials, conducted mostly in older adults with mild elevation, show that levothyroxine normalizes TSH without improving symptoms, quality of life, or cardiovascular outcomes. Guidelines differ, mainly for TSH below 10 mIU/L. Persistent TSH ⩾10 mIU/L generally favors treatment, whereas many patients with milder elevation, especially older adults, can be observed with scheduled monitoring. Pregnancy and preconception require a separate, timing-based approach. Decisions should be individualized rather than based on a single TSH cutoff. The proposed algorithm synthesizes existing evidence and guidelines and has not been prospectively validated. It should support, not replace, clinical judgment.

Categories: Endocrinology/Diabetes/Metabolism
Keywords: clinical decision-making, levothyroxine, older adults, subclinical hypothyroidism, thyroid peroxidase antibodies, thyrotropin

Introduction And Background

Subclinical hypothyroidism (SCH) is a biochemical condition characterized by an elevated serum thyroid-stimulating hormone (TSH) concentration with a free thyroxine (FT4) concentration within the reference range. It is common. The population prevalence is approximately 5%-10%, although estimates vary with age, sex, iodine status, assay methods, and the TSH cutoff used. SCH is more frequent in women, becomes more common with advancing age, and is more frequent in iodine-sufficient regions [1]. Serum TSH also rises with age; applying a fixed adult upper reference limit can, therefore, increase the classification of SCH in older adults [2]. A biochemical diagnosis alone does not establish that treatment will improve clinical outcomes.

The natural course of SCH is variable, ranging from spontaneous normalization to persistent biochemical abnormality or progression to overt hypothyroidism [3]. Observational data link higher TSH concentrations, particularly ⩾10 mIU/L, to coronary heart disease events [4], whereas randomized evidence, derived mainly from older adults with mild SCH, has not shown meaningful improvement in symptoms, quality of life, or cardiovascular outcomes with levothyroxine [5,6]. Management should, therefore, incorporate the degree and persistence of TSH elevation, age, symptoms, thyroid autoimmunity, cardiovascular risk, comorbidity, and reproductive status.

Existing reviews and guidelines often emphasize whether levothyroxine should be prescribed. This review differs by making observation an explicit management pathway: it defines who can reasonably be monitored without treatment, examines why major guidelines diverge from the trial-based BMJ Rapid Recommendation, and integrates persistence of TSH elevation, age, symptoms, thyroid peroxidase antibodies (TPOAb) status, underlying thyroid disease, cardiovascular and metabolic factors, and reproductive status into a single practical decision framework.

Review

Literature search approach

Relevant scientific literature was identified and reviewed from September 1, 2026, to October 3, 2026, which

was the date of the final search. PubMed/Medical Literature Analysis and Retrieval System Online (MEDLINE) and the Cochrane Library were searched from database inception using combinations of "subclinical hypothyroidism," "thyrotropin," "TSH," "levothyroxine," "natural history," "progression," "cardiovascular," "lipids," "cognition," "older adults," "pregnancy," and "guideline," and reference lists of key articles were also screened. English-language publications relevant to adults with SCH were included, and randomized controlled trials, systematic reviews and meta-analyses, large prospective cohorts, and major society or national guidelines were prioritized. Pediatric literature was excluded, and pregnancy evidence was included only to delineate why pregnancy and preconception require a separate approach. Study selection was clinically focused rather than exhaustive; no protocol was registered, no duplicate screening was performed, and no formal risk-of-bias assessment or quantitative synthesis was undertaken. The manuscript was structured with reference to the Scale for the Assessment of Narrative Review Articles (SANRA), particularly its domains concerning justification of importance, statement of aims, description of the literature search, referencing, scientific reasoning, and presentation of relevant outcome data [7].

Definition, classification, and diagnostic confirmation

SCH is defined biochemically by an elevated serum TSH concentration with an FT4 concentration within the reference range. According to the degree of elevation, it can be classified as mild SCH, with TSH from 4.0 to 9.9 mIU/L, and more severe SCH, with TSH ⩾10.0 mIU/L [1]. Studies differ slightly in their lower cutoff (for example, 4.0 or 4.5 mIU/L); throughout this review, "mild SCH" refers to TSH below 10 mIU/L, and the cutoffs used by individual studies are reported as stated by their authors.

Interpretation of thyroid function tests should consider the substantial interindividual variation in thyroid hormone set points. Individual reference ranges are considerably narrower than population-based laboratory ranges, so an FT4 within the laboratory interval may not represent an individual's usual thyroid status [8]. Age also influences interpretation. A large laboratory-based study of approximately 7.6 million TSH measurements, derived retrospectively from routine requests at 13 Dutch laboratories using indirect methods, showed an age-related increase in the upper TSH reference limit, particularly after age 50 in women and 60 in men, and applying age-specific intervals reduced the classification of subclinical and overt hypothyroidism in older adults [2]. Because these intervals were derived from patients tested for clinical reasons rather than from a screened healthy reference population, their generalizability to other populations, assays, and clinical settings is uncertain.

Because an isolated TSH elevation may be transient, persistence should be confirmed before treatment decisions are made. In patients with an initially elevated TSH and normal FT4, TSH and FT4 should be repeated after approximately two to three months, together with TPOAb testing [1]. TPOAb testing helps identify autoimmune thyroiditis as the cause and provides prognostic information, as positivity is associated with progression to overt hypothyroidism [1,3].

Transient and reversible causes should be considered before labeling SCH as persistent [1]. These include recovery from non-thyroidal illness, when TSH can rise transiently during the recovery phase; the recovery phase of thyroiditis (for example, subacute or postpartum); untreated adrenal insufficiency, in which glucocorticoid deficiency raises TSH; and obesity-associated mild TSH elevation, which may improve with weight loss. Medication- and iodine-related effects are also important, including amiodarone, lithium, iodinated contrast, and immune checkpoint inhibitors, which can cause thyroiditis followed by hypothyroidism. Assay interference should be suspected when results do not fit the clinical picture, including macro-TSH, heterophile antibodies, and biotin supplementation, whose effect depends on the assay design. Factors related to previous thyroid treatment, such as recent radioiodine therapy or thyroid surgery, or inadequate levothyroxine dosing or adherence, should also be considered. Persistent SCH is commonly associated with chronic autoimmune thyroiditis [1].

Natural history and risk of progression to overt hypothyroidism

Patients with SCH may return to euthyroidism, remain biochemically stable, or progress to overt hypothyroidism. A recent systematic review and meta-analysis of eight prospective studies (1,859 individuals; median follow-up 0.5-10 years across studies; progression defined as development of overt hypothyroidism in each study) examined these outcomes. In the only two studies that stratified by TSH, both in older adults with a median follow-up of about two to 2.6 years, patients with TSH ⩾10 mIU/L had a substantially higher risk of progression than those with TSH 4.5-9.9 mIU/L (28 of 68 versus eight of 383 patients; RR 11.38; 95% CI, 4.98-26.03; fixed-effect model, $I^2 = 0\%$). The wide interval reflects the small number of contributing studies, and because only two studies were pooled, the low heterogeneity statistic is not informative; the magnitude of this estimate is therefore imprecise even though its direction is consistent. TPOAb positivity, assessed in all eight studies, was also associated with progression (124 of 689 versus 57 of 1,112 patients; RR 2.53; 95% CI, 1.86-3.44; fixed-effect model, $I^2 = 40\%$). Both factors were associated with a lower likelihood of spontaneous return to euthyroidism (TSH ⩾10 mIU/L: RR 0.20; 95% CI, 0.09-0.42; $I^2 = 0\%$; TPOAb positivity: RR 0.68; 95% CI, 0.60-0.76; $I^2 = 79\%$, indicating substantial heterogeneity). The included studies differed in age, setting, and follow-up, so pooled estimates should be interpreted cautiously [3].

A small long-term prospective cohort of 82 women, followed for a mean of 9.2 years, provides supportive but imprecise evidence on TSH-related progression. The estimated 10-year incidence of overt hypothyroidism rose from 0% with baseline TSH 4-6 mIU/L to 42.8% with TSH >6-12 mIU/L and 76.9% with TSH >12 mIU/L; antibody positivity conferred additional risk [9]. For counseling, the classic 20-year Whickham survey estimated an annual progression to overt hypothyroidism of approximately 4.3% per year in women with both raised TSH and positive thyroid antibodies [10]; this figure comes from a single community cohort measured with older assays and should be treated as an approximate guide, not a precise individual risk. Patients in the Huber cohort were enrolled between 1979 and 1999, and TSH was measured by an immunoradiometric assay, so these thresholds may not map exactly onto current automated immunoassays and reference intervals. Because of its limited sample size, all-female population, and older assay methodology, this study should be interpreted as complementary to, rather than stronger than, the larger contemporary meta-analysis [3].

Progression is not inevitable, particularly in mild SCH. In a pooled analysis of two randomized placebo-controlled trials (TRUST and IEMO 80-plus) in community-dwelling adults aged ⩾65 years, TSH normalized spontaneously in 60.8% of the pretrial screening population (n = 2,335; at least one elevated TSH ⩾4.60 mIU/L; median follow-up about one year), and even among placebo-group participants with persistent SCH confirmed by at least two elevated measurements at least three months apart (n = 361), 39.9% returned to euthyroidism without treatment after one year. Lower TSH, higher FT4, and absence of TPOAb were associated with normalization [11].

SCH is thus a dynamic biochemical condition rather than an inevitably progressive disorder. Marked TSH elevation (particularly ⩾10 mIU/L) and thyroid autoimmunity increase the likelihood of progression, whereas spontaneous normalization is common with milder elevations.

Clinical consequences of untreated SCH

Cardiovascular Outcomes

In an individual-participant data analysis of 55,287 adults from 11 prospective cohorts, the hazard ratio (HR) for coronary heart disease events, compared with euthyroid individuals, was 1.00 (95% CI, 0.86-1.18) for TSH 4.5-6.9 mIU/L, 1.17 (95% CI, 0.96-1.43) for 7.0-9.9 mIU/L, and 1.89 (95% CI, 1.28-2.80) for 10-19.9 mIU/L. Coronary heart disease mortality followed a similar pattern, whereas total mortality was not significantly increased [4]. The same consortium found a similar threshold pattern for heart failure in 25,390 adults from six cohorts: HRs were 1.01 (95% CI, 0.81-1.26) for TSH 4.5-6.9 mIU/L, 1.65 (95% CI, 0.84-3.23) for 7.0-9.9 mIU/L, and 1.86 (95% CI, 1.27-2.72) for 10-19.9 mIU/L [12]. For stroke, an analysis of 47,573 adults from 17 cohorts found no overall association (HR 1.05; 95% CI, 0.91-1.21), but the risk was higher in younger participants, with a HR for stroke events of 3.32 (95% CI, 1.25-8.80) at ages 18-49 years, compared with 1.00 (95% CI, 0.86-1.18) at 65-79 years; the estimates in younger groups are imprecise because they rest on few events [13]. Cardiovascular risk therefore appears most evident at TSH ⩾10 mIU/L, and the stroke findings suggest that age may modify the association, consistent with the age-based approach in Section 8.3.

Lipid Effects

In a meta-analysis of 35 case-control and cohort studies, individuals with mild SCH (TSH <10 mIU/L) had higher total cholesterol, low-density lipoprotein cholesterol (LDL-C), and triglycerides and lower high-density lipoprotein cholesterol (HDL-C) than euthyroid controls. Pooled mean differences were 12.75 mg/dL for total cholesterol, 10.95 mg/dL for LDL-C, 19.27 mg/dL for triglycerides, and −1.81 mg/dL for HDL-C. No significant differences were found in very-low-density lipoprotein (VLDL), apolipoprotein A1, or apolipoprotein B [14]. Because these pooled data come from observational studies (case-control and cohort designs), they show association rather than causation, and residual confounding by factors such as age, sex, body mass index, diet, and other metabolic conditions is likely. Metabolic outcomes beyond the lipid profile, such as insulin resistance and fatty liver disease, were not reviewed in depth.

Symptoms and Quality of Life

Symptoms attributed to hypothyroidism, such as fatigue, mood changes, constipation, and hair loss, are nonspecific. In a population-based study of 376 individuals with SCH and 7,619 euthyroid controls, overall symptom burden did not differ between groups, and within the SCH group TSH was not associated with symptom burden, whereas comorbidity, age, body mass index, and smoking were associated with individual symptoms. Nonspecific symptoms in SCH should, therefore, not automatically be attributed to thyroid dysfunction [15].

Cognitive Function

A meta-analysis of 15 studies including 19,944 adults aged >60 years (1,199 with SCH) found no significant association between SCH and global cognition, executive function, or memory, and prospective data from four studies showed no association with accelerated cognitive decline [16]. These findings apply only to

adults older than 60 years. Studies in younger adults were not included in this meta-analysis and were not systematically reviewed here, so the absence of an association should not be extrapolated to younger patients, in whom the evidence is limited.

Evidence for and against levothyroxine treatment

Symptoms and Quality of Life

In the TRUST trial, 737 adults aged ⩾65 years (mean age 74.4 years) with persistent SCH, defined as TSH 4.60-19.99 mIU/L with normal FT4, were randomized to levothyroxine or placebo. The mean baseline TSH was 6.4 mIU/L, and the trial reported that few participants had a baseline TSH above 10 mIU/L. Levothyroxine lowered TSH at one year (3.63 vs 5.48 mIU/L with placebo), but there were no significant differences in hypothyroid symptom or tiredness scores, and no meaningful benefit across secondary outcomes [5]. Because most participants had mild TSH elevation, these results mainly inform the management of mild SCH in older adults and say little about patients with TSH ⩾10 mIU/L.

A meta-analysis of 21 randomized trials (2,192 non-pregnant adults) agrees: thyroid hormone therapy normalized TSH but was not associated with improvement in general quality of life (standardized mean difference (SMD)−0.11; 95% CI, −0.25 to 0.03) or thyroid-related symptoms (SMD 0.01; 95% CI, −0.12 to 0.14), with moderate- to high-quality evidence [6]. Normalization of TSH does not necessarily translate into symptomatic benefit, particularly in mild SCH.

Cardiovascular Outcomes

In a pooled analysis of two randomized trials including 842 older adults with SCH, levothyroxine reduced TSH but did not significantly alter the risk of cardiovascular events (HR 0.74; 95% CI, 0.41-1.25), atrial fibrillation (HR 0.69; 95% CI, 0.32-1.52), heart failure (HR 0.41; 95% CI, 0.13-1.35), or all-cause mortality (HR 1.28; 95% CI, 0.54-3.03), irrespective of baseline cardiovascular disease or age [17]. Because participants were predominantly older adults with mild TSH elevation, the effect of treatment on cardiovascular outcomes in younger individuals or in those with TSH ⩾10 mIU/L remains uncertain, and for these groups the case for treatment currently rests largely on observational data.

Lipid Effects

A meta-analysis of randomized placebo-controlled trials showed significant reductions in total cholesterol and LDL-C with levothyroxine, without consistent improvement in HDL-C or triglycerides [18]. Whether these changes reduce cardiovascular events remains uncertain.

Potential Harms and Overtreatment

Levothyroxine is generally well tolerated when appropriately dosed, but excessive exposure is a concern, particularly in older adults. In a population-based nested case-control study of adults aged ⩾70 years, higher levothyroxine doses were associated with progressively greater fracture risk [19]. In a nested case-control study of more than 180,000 older users, higher cumulative exposure was associated with atrial fibrillation (adjusted OR 1.08; 95% CI, 1.04-1.11 for medium exposure and 1.29; 95% CI, 1.23-1.35 for high exposure, compared with low exposure) [20]. These two studies included levothyroxine users in general, not specifically patients with SCH, and being observational, they are subject to confounding by indication, since people who receive higher doses may differ in underlying thyroid disease, comorbidity, and baseline risk; they therefore show an association with dose, not proof that treating SCH causes these outcomes. However, randomized trials in older adults with SCH have not shown increased atrial fibrillation when levothyroxine is carefully titrated to keep TSH within the reference range [17]. Careful titration and biochemical monitoring are, therefore, essential.

Harms are not only biochemical. Starting levothyroxine usually implies long-term, often lifelong, medication, with repeated blood tests and clinic visits to maintain the dose, as well as the cost of treatment and monitoring. Treating a mildly abnormal laboratory value in a person without symptoms may also medicalize a finding that would often have resolved or remained stable without treatment, and it can create an expectation of benefit that the trial evidence does not support.

Guideline recommendations: areas of agreement and disagreement

Major guidelines agree that persistence of TSH elevation should be confirmed before treatment and that pregnancy and preconception require separate considerations. They differ mainly in how they weigh observational evidence of progression and cardiovascular risk against randomized evidence showing little symptomatic benefit in predominantly older adults with mild SCH (Table *1*). As of October 2026, the American Thyroid Association (ATA)/American Association of Clinical Endocrinologists (AACE) adult hypothyroidism guideline (2012) and the European Thyroid Association (ETA) Guidelines for SCH (2013) remain the most recent guidance documents addressing non-pregnant adult SCH from those organizations.

The 2014 ATA guideline on the treatment of hypothyroidism focuses mainly on levothyroxine and other thyroid hormone preparations rather than on the decision to treat SCH, and it was therefore not tabulated separately in Table *1*. National Institute for Health and Care Excellence Guideline NG145 (NICE NG145) (published 2019; updated 2023) remains current. The 2019 BMJ Rapid Recommendation takes a more treatment-conservative position [1,21-23].

Guideline	Persistent TSH ≥10 mIU/L	TSH <10 mIU/L (non-pregnant adults)	Older adults
ATA/AACE adult hypothyroidism guideline (2012) [21]	Treatment should generally be considered; individual factors remain important.	Individualize treatment, particularly when symptoms, TPOAb positivity, atherosclerotic cardiovascular disease, heart failure, or cardiovascular risk factors are present.	No single age-only rule; treatment should be individualized, with attention to comorbidity and overtreatment risk.
European Thyroid Association SCH guideline (2013) [1]	LT4 recommended in younger patients (<65–70 years), even without symptoms. In patients >70 years, consider treatment only if there are clear hypothyroid symptoms or high vascular risk.	Consider a monitored LT4 trial in younger symptomatic patients; otherwise observation is appropriate in many patients	Use age-specific TSH ranges where available. For TSH ≥10 mIU/L in patients >70 years, treatment is considered only with clear symptoms or high vascular risk. Wait-and-see is preferred in those >80–85 years with TSH ≤10 mIU/L.
NICE NG145 (2019; updated 2023) [22]	Consider LT4 when TSH is ≥10 mIU/L on two separate occasions three months apart	Consider a six-month LT4 trial only in symptomatic adults <65 years after two abnormal tests three months apart.	No separate blanket recommendation against treatment; age modifies the <10 mIU/L trial recommendation, and monitoring is emphasized
BMJ Rapid Recommendation (2019) [23]	Strong recommendation against thyroid hormones in adults with SCH, including TSH 10–20 mIU/L. It does not apply to TSH >20 mIU/L or to women trying to become pregnant, and it may not apply to young adults (for example, ≤30 years) or patients with severe symptoms.	Strong recommendation against thyroid hormones in adults with SCH (same exceptions).	Informed particularly by trials in older adults with mild SCH; favors avoiding routine treatment.

TABLE 1: Summary of major guideline recommendations for non-pregnant adults with persistent SCH.

TSH: thyroid-stimulating hormone; ATA: American Thyroid Association; AACE: American Association of Clinical Endocrinologists; TPOAb: thyroid peroxidase antibodies; SCH: subclinical hypothyroidism; LT4: levothyroxine; NICE NG145: National Institute for Health and Care Excellence Guideline NG145

The recommendations in Table *1* should be interpreted in the context of the populations and evidence considered by each guideline. The BMJ Rapid Recommendation places greater weight on randomized trial evidence, whereas ATA/AACE, ETA, and NICE also incorporate TSH magnitude, progression risk, symptoms, age, and features of underlying thyroid disease [1,21-23].

These differences largely reflect differing evidence hierarchies. Trial-based recommendations rely on studies conducted mostly in older adults with mild elevation, whereas recommendations favoring treatment at higher TSH levels rely on observational associations with progression and coronary heart disease events. The recommendations in this review follow the middle path: treatment is favored at persistent TSH ⩾10 mIU/L, and observation or a monitored trial is individualized below this level.

Who should be treated?

Patients With Persistent TSH ⩾10 mIU/L

Persistent TSH ⩾10 mIU/L is the clearest indication for considering levothyroxine, particularly in younger adults, after persistence has been confirmed by repeat testing. This is supported by the substantially greater likelihood of progression to overt hypothyroidism and the higher risk of CHD events at this level [3,4].

Levothyroxine may also improve total cholesterol and LDL-C, with more pronounced effects at higher pretreatment TSH [1]. In older adults (>70 years), the ETA advises more cautious individualization, with treatment considered mainly when clear symptoms or high vascular risk are present [1]. Even here, age, comorbidities, and the risk of overtreatment should be considered, and the evidence in this group is largely observational (as outlined in the "Cardiovascular Outcomes" section). Guideline support is not uniform (as discussed in the "Guideline recommendations: Areas of Agreement and Disagreement" section).

Patients With Mild SCH (TSH <10 mIU/L)

In persistent TSH elevation below 10 mIU/L, the decision should be individualized. In adults aged <65 years with persistent symptoms suggestive of hypothyroidism after biochemical confirmation, a time-limited, monitored therapeutic trial of levothyroxine may be considered. NICE suggests a trial of up to six months [22]. Because symptoms are nonspecific and trials have not shown consistent symptomatic benefit, clinical response should be reassessed once TSH has normalized and again at the end of the trial period (about six months), and treatment should be stopped if symptoms have not improved [5,6].

Other factors may shift the balance toward treatment: TPOAb positivity, which suggests autoimmune thyroid disease and a greater likelihood of progression [3]; features of established thyroid disease such as previous thyroid surgery or radioactive iodine treatment; and goiter, dyslipidemia, and diabetes [1]. None of these is an absolute indication, and each must be weighed against the likelihood of spontaneous normalization and the risks of overtreatment. Pregnancy and preconception are managed separately from the general adult pathway, according to the timing-based approach described in the "Pregnancy and Preconception" section below.

The Role of Age

Age is a key modifier. TSH rises with age, and age-specific reference ranges may reduce overdiagnosis; spontaneous normalization is common in older adults, even with repeat-confirmed SCH [1,2,11]. The expected benefit of levothyroxine also diminishes with age in mild SCH: randomized evidence in adults aged ⩾65 years shows no clinically meaningful improvement in symptoms or tiredness [5] and no significant reduction in cardiovascular events [17]. Decisions in older adults should, therefore, weigh TSH level, symptoms, cardiovascular disease, comorbidities, frailty, and the consequences of overtreatment.

The ETA guideline notes that age criteria are used inconsistently across studies, so no robust chronological cutoff can be defined, although many studies show differences between individuals younger than 60-65 years and those older than 70 years. For moderately old patients (approximately 60-70 years), the decision should therefore include a specific evaluation of cardiovascular risk, degree of TSH elevation, comorbidity, and frailty [1]. The age thresholds used in this review (<65 years for a symptomatic levothyroxine trial and >80-85 years for wait-and-see management) follow the sources cited and are intended as guides rather than rigid cutoffs.

European guidance recommends a wait-and-see strategy in individuals aged >80-85 years with TSH ⩽10 mIU/L, with careful follow-up rather than routine levothyroxine [1]. Mild TSH elevation in older adults may partly reflect age-related changes in the hypothalamic-pituitary-thyroid axis rather than clinically important thyroid failure [2]. Persistent TSH ⩾10 mIU/L, progressive biochemical dysfunction, significant symptoms, underlying thyroid disease, or relevant cardiovascular comorbidity may shift the balance toward treatment. When treatment is considered necessary in an older patient, it should be started cautiously and monitored closely (outlined in the "Starting and Titrating Levothyroxine" section below).

Who can reasonably be observed?

Observation is an appropriate initial strategy for many patients with mild SCH, particularly when TSH is persistently elevated but below 10 mIU/L. This is supported by the variable natural history, the frequent spontaneous normalization when elevation is mild and antibodies are absent [3,11], and the lack of consistent benefit from levothyroxine in randomized trials [5,6,17].

Patients are particularly suitable for observation when they have all of the following: mild TSH elevation (<10 mIU/L), minimal or no symptoms attributable to hypothyroidism, negative TPOAb, and no features of progressive thyroid disease. In this review, features of progressive thyroid disease mean a rising TSH trend on serial testing or a falling FT4 [3], goiter [1], or evidence of established thyroid disease such as previous thyroid surgery (including hemithyroidectomy) or radioactive iodine treatment [1,22]. TPOAb positivity is treated as a separate criterion. Increasing age strengthens the case for observation (discussed in the "The Role of Age" section), and in adults aged >80-85 years with TSH ⩽10 mIU/L, wait-and-see is generally preferred [1].

Many patients will meet some but not all of these criteria, and for them the decision is individualized rather than binary. The features are not equal in weight. Persistent TSH ⩾10 mIU/L moves a patient out of the observation group, whereas a single feature such as TPOAb positivity, mild symptoms, or younger age does

not by itself require treatment. For example, an asymptomatic, TPOAb-positive adult of around 50 years with a persistent TSH of 7 mIU/L can reasonably be observed, but with closer surveillance, because TPOAb positivity increases the likelihood of progression [3]. NICE recommends annual TSH and FT4 testing in untreated adults with raised thyroid autoantibodies [22] (discussed in the "Monitoring Untreated Patients" section below). Treatment or a monitored trial should be reconsidered if TSH rises toward ⩾10 mIU/L, FT4 falls, or symptoms develop. When symptoms are the only reason a patient does not meet the observation criteria, and the patient is aged <65 years, a time-limited, monitored levothyroxine trial may be considered (outlined in the "Patients With Mild SCH (TSH <10 mIU/L)" section). Treatment is most reasonable to consider in patients who do not meet several of these criteria at once, for example those with symptoms, TPOAb positivity, and features of progressive thyroid disease, particularly when they are also younger.

Observation is not the absence of follow-up. Patients should undergo periodic reassessment of thyroid function and clinical status (discussed in the "Monitoring Untreated Patients" section). The emergence of persistent TSH ⩾10 mIU/L, progressive biochemical dysfunction, or new factors favoring treatment should prompt reconsideration.

Special populations

Pregnancy and Preconception

Diagnosis and management of SCH during preconception and pregnancy differ from those in non-pregnant adults. The 2026 ATA guideline emphasizes pregnancy-appropriate interpretation of thyroid function and an individualized approach that accounts for the timing and severity of TSH elevation [24]. Its recommendations were graded using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework [24].

The 2026 ATA guideline no longer uses TPOAb status to determine whether levothyroxine should be started for maternal SCH, a change from the 2017 ATA guideline, which took TPOAb status into account in its treatment recommendations [25]. Profound SCH with TSH >10 mIU/L during pregnancy should be treated with levothyroxine. For mild SCH diagnosed in the first trimester, levothyroxine may be considered after shared decision-making; when mild SCH is first diagnosed after the first trimester, levothyroxine should not be offered routinely, and TSH can be reassessed after four to six weeks. This timing-based strategy reflects evidence that treatment initiated after approximately the first trimester has not improved pregnancy or offspring neurocognitive outcomes [24].

For women with SCH identified before conception, the 2026 ATA guideline recommends preferentially postponing attempts at pregnancy, when feasible, and repeating thyroid function after four to six weeks because spontaneous normalization is common. If SCH persists, or waiting six to 12 weeks is not feasible, low-dose levothyroxine (for example, 50 µg/day) can be considered. For women receiving levothyroxine before or during pregnancy, a TSH within the trimester-specific reference range (or the laboratory's pregnancy-appropriate range), and below 2.5 mIU/L, may be targeted. TPOAb testing may still inform counseling about postpartum thyroiditis and future screening, but it is no longer a treatment threshold for SCH [24].

Populations Not Addressed in This Review

This review focuses primarily on non-pregnant adults. Children and adolescents are outside its scope because age-specific diagnostic thresholds and treatment recommendations differ substantially. Patients with major comorbid conditions such as heart failure or chronic kidney disease may require additional individualized consideration; disease-specific guidance should therefore be consulted when these conditions materially affect treatment decisions.

The general framework may also need adjustment in groups in whom SCH is more likely to progress or has a different cause. Patients who have had a hemithyroidectomy or radioactive iodine treatment have reduced thyroid reserve, and established thyroid disease of this kind is among the factors that may shift the balance toward treatment (as discussed in the "Patients With Mild SCH (TSH <10 mIU/L)" section) [1]. In patients receiving amiodarone, lithium, or immune checkpoint inhibitors, SCH may be drug-related, may be transient or progressive depending on the mechanism, and warrants closer TSH and FT4 monitoring; in these patients the decision should be individualized and drug-specific guidance should be consulted.

Practical aspects of treatment and monitoring

Starting and Titrating Levothyroxine

Because most patients with SCH retain residual thyroid function, doses below full replacement are often sufficient, and the starting dose should be matched to the patient. The ETA suggests a weight-related dose of approximately 1.5 µg/kg/day in patients without cardiac disease, which is close to full replacement and is generally appropriate for younger patients with higher TSH values. Older adults and patients with cardiac

disease should generally start with 25-50 µg/day and undergo gradual titration [1]. NICE likewise recommends a cautious starting dose of 25-50 µg/day in adults aged 65 years or older or in those with cardiovascular disease [22]. TSH should be rechecked about two months after starting levothyroxine, with dose adjustments made accordingly, and again after each dose change; once the dose is stable, TSH should be monitored at least annually [1]. For most adults, the ETA aims for a stable TSH in the lower half of the reference range (0.4-2.5 mIU/L) [1], while avoiding TSH suppression and iatrogenic thyrotoxicosis [22]. Because overtreatment carries particular risks in older adults (discussed in the "Potential Harms and Overtreatment" section), the dose should be titrated carefully in this group, with close biochemical monitoring. If levothyroxine was started as a therapeutic trial for symptoms in mild SCH, clinical response should be reassessed once TSH has normalized and at about six months, and discontinuation should be considered if symptoms have not improved despite a normalized TSH [22].

Monitoring Untreated Patients

After a first finding of elevated TSH with normal FT4, thyroid function should be repeated after approximately two to three months to confirm persistence and exclude transient abnormalities [1]. Once persistent SCH is confirmed and a decision is made to manage without levothyroxine, surveillance should reflect the likelihood of progression.

NICE NG145 recommends measuring TSH and FT4 once a year in adults with untreated SCH who have features suggesting underlying thyroid disease, such as previous thyroid surgery or raised thyroid autoantibodies, and once every two to three years in adults without such features [22]. Earlier reassessment is appropriate if symptoms develop or clinical circumstances change.

A progressive rise in TSH, an FT4 below the reference range, persistent TSH ⩾10 mIU/L, or new clinical factors favoring treatment should prompt reconsideration of management [1,22]. Monitoring is an active management strategy, not simply withholding therapy.

Practical clinical decision-making algorithm

Figure *1* summarizes the approach proposed in this review. Management begins with confirmation of persistent biochemical abnormality, with repeat testing after approximately two to three months and TPOAb assessment, rather than treatment on a single elevated TSH [1]. Pregnancy or active pregnancy planning is identified early and managed separately according to the timing-based pathway in the "Special populations" section [24]. In non-pregnant adults with confirmed persistent SCH, TSH magnitude guides initial management: persistent TSH ⩾10 mIU/L generally favors levothyroxine, whereas for TSH <10 mIU/L the decision is individualized by age, symptoms, TPOAb status, and features of progressive thyroid disease, with observation and scheduled monitoring appropriate for many patients (discussed in sections titled "Who should be treated?" and "Who can reasonably be observed?") [1,22]. The algorithm is a synthesis of the evidence and guidelines discussed above and is not a substitute for clinical judgment.

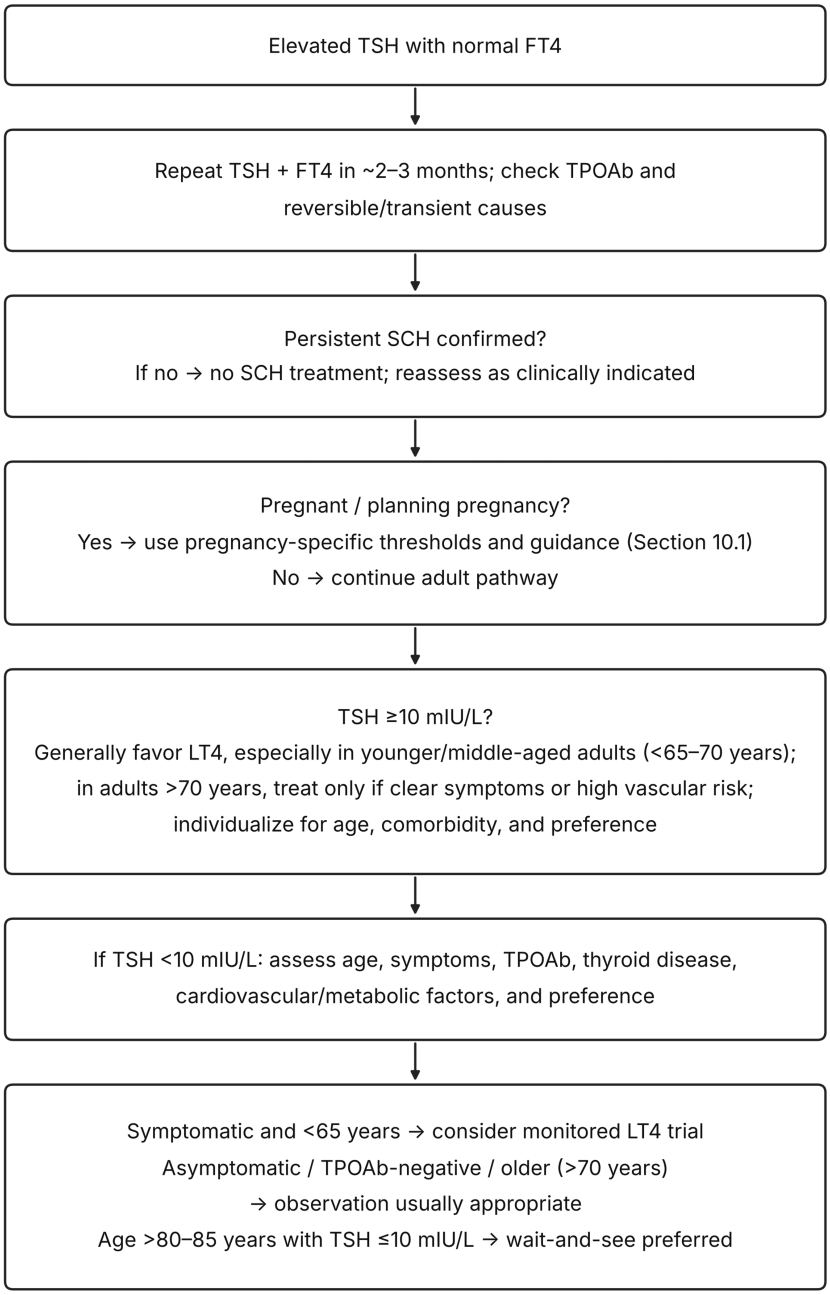


FIGURE 1: Practical algorithm for the evaluation and management of SCH in nonpregnant adults

Proposed clinical decision-making algorithm for SCH in adults. Pregnant patients and those planning pregnancy leave the general adult pathway and are managed according to the timing-based approach in the section titled "Pregnancy and preconception" [24]. The algorithm has not been prospectively validated and does not replace clinical judgment.

TSH: thyroid-stimulating hormone; FT4: free thyroxine; TPOAb: thyroid peroxidase antibody; SCH: subclinical hypothyroidism; LT4: levothyroxine

This is an original figure created by the author using Python/Matplotlib (Python Software Foundation, Wilmington, DE).

Strengths and limitations

Strengths of this review include its focus on both treatment and observation, its use of recent randomized and individual-participant evidence, the comparison of guidelines, and the integration of these data into a

single practical algorithm.

This review has several limitations. First, it is a narrative review rather than a systematic review: although PubMed/MEDLINE and the Cochrane Library were searched and key reference lists were screened, the search was limited to English-language publications, study selection was not exhaustive, duplicate screening was not performed, and no formal risk-of-bias assessment was undertaken; selection bias, including language bias, therefore remains possible. Second, randomized evidence comes predominantly from older adults with mild TSH elevation, limiting direct inference for younger symptomatic adults and patients with persistent TSH ⩾10 mIU/L. Third, studies vary in TSH cutoffs, assays, and definitions of persistence. Fourth, some practical recommendations, including monitoring intervals and the >80-85-year wait-and-see threshold, depend heavily on individual guidelines, which may be revised; the guideline-based content of this review, including Table *1* and the "Pregnancy and preconception" section, reflects guidance available as of the final search date (October 3, 2026). Fifth, the proposed algorithm is an evidence-informed synthesis and has not been prospectively validated. Children and adolescents were outside the scope, and major comorbid conditions such as heart failure and chronic kidney disease were not reviewed in depth.

Conclusions

SCH is a heterogeneous biochemical condition with a variable natural history, from spontaneous normalization to progression to overt hypothyroidism. An elevated TSH alone should not automatically lead to levothyroxine treatment. Confirmation of persistence and consideration of age, degree of TSH elevation, thyroid autoimmunity, symptoms, comorbidities, and reproductive status are essential before treatment decisions are made. Persistent TSH ⩾10 mIU/L generally favors treatment, particularly in younger and middle-aged adults, although guidelines are not unanimous. Many patients with mild SCH can be reasonably observed, especially when asymptomatic, TPOAb-negative, and at low risk of progression. A conservative approach is particularly appropriate in older adults, in whom mild TSH elevation is common, spontaneous normalization is frequent, and randomized trials have shown no consistent symptomatic or cardiovascular benefit.

The main evidence gaps are the lack of randomized trials in younger adults and in patients with persistent TSH ⩾10 mIU/L. Most randomized evidence comes from older adults with mild TSH elevation, so the recommendation to treat persistent TSH ⩾10 mIU/L, particularly in younger and middle-aged adults, rests largely on observational data and guideline recommendations. Trials in younger symptomatic adults and in those with higher TSH, with clinically meaningful outcomes and adequate follow-up, are needed to refine these recommendations. When treatment is considered in mild SCH, it should be individualized, with clinical benefit reassessed after biochemical normalization. Pregnancy and preconception are distinct situations requiring pregnancy-specific, timing-sensitive management rather than the general adult thresholds. Ultimately, management of SCH should move beyond a single biochemical threshold toward an individualized, risk-based approach. This approach should balance the likelihood of progression and potential treatment benefit against the chance of spontaneous normalization and the risks of overtreatment.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Muna M. Mareh

Acquisition, analysis, or interpretation of data: Muna M. Mareh

Drafting of the manuscript: Muna M. Mareh

Critical review of the manuscript for important intellectual content: Muna M. Mareh

Supervision: Muna M. Mareh

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References

1. Pearce SH, Brabant G, Duntas LH, Monzani F, Peeters RP, Razvi S, Wemeau JL: ETA guideline: management of subclinical hypothyroidism. Eur Thyroid J. 2013, 2:215-28. 10.1159/000356507
2. Jansen HI, Dirks NF, Hillebrand JJ, et al.: Age-specific reference intervals for thyroid-stimulating hormones and free thyroxine to optimize diagnosis of thyroid disease. Thyroid. 2024, 34:1346-55. 10.1089/thy.2024.0346
3. Zhang X, Zhang G, Wang S, Jin J, Zhang S, Teng X: The change in thyroid function categories with time in patients with subclinical hypothyroidism: a systematic review and meta-analysis. BMC Endocr Disord. 2024, 24:224. 10.1186/s12902-024-01754-7
4. Rodondi N, den Elzen WP, Bauer DC, et al.: Subclinical hypothyroidism and the risk of coronary heart disease and mortality. JAMA. 2010, 304:1365-74. 10.1001/jama.2010.1361
5. Stott DJ, Rodondi N, Kearney PM, et al.: Thyroid hormone therapy for older adults with subclinical hypothyroidism. N Engl J Med. 2017, 376:2534-44. 10.1056/NEJMoa1603825
6. Feller M, Snel M, Moutzouri E, et al.: Association of thyroid hormone therapy with quality of life and thyroid-related symptoms in patients with subclinical hypothyroidism: a systematic review and meta-analysis. JAMA. 2018, 320:1349-59. 10.1001/jama.2018.13770
7. Baethge C, Goldbeck-Wood S, Mertens S: SANRA-a scale for the quality assessment of narrative review articles. Res Integr Peer Rev. 2019, 4:5. 10.1186/s41073-019-0064-8
8. Andersen S, Pedersen KM, Bruun NH, Laurberg P: Narrow individual variations in serum T(4) and T(3) in normal subjects: a clue to the understanding of subclinical thyroid disease. J Clin Endocrinol Metab. 2002, 87:1068-72. 10.1210/jcem.87.3.8165
9. Huber G, Staub JJ, Meier C, Mitrache C, Guglielmetti M, Huber P, Braverman LE: Prospective study of the spontaneous course of subclinical hypothyroidism: prognostic value of thyrotropin, thyroid reserve, and thyroid antibodies. J Clin Endocrinol Metab. 2002, 87:3221-6. 10.1210/jcem.87.7.8678
10. Vanderpump MP, Tunbridge WM, French JM, et al.: The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham Survey. Clin Endocrinol (Oxf). 1995, 43:55-68. 10.1111/j.1365-2265.1995.tb01894.x
11. van der Spoel E, van Vliet NA, Poortvliet RK, et al.: Incidence and determinants of spontaneous normalization of subclinical hypothyroidism in older adults. J Clin Endocrinol Metab. 2024, 109:e1167-74. 10.1210/clinem/dgad623
12. 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, 126:1040-9. 10.1161/CIRCULATIONAHA.112.096024
13. Chaker L, Baumgartner C, den Elzen WP, et al.: Subclinical hypothyroidism and the risk of stroke events and fatal stroke: an individual participant data analysis. J Clin Endocrinol Metab. 2015, 100:2181-91. 10.1210/jc.2015-1438
14. Treister-Goltzman Y, Yarza S, Peleg R: Lipid profile in mild subclinical hypothyroidism: systematic review and meta-analysis. Minerva Endocrinol (Torino). 2021, 46:428-40. 10.23736/S2724-6507.20.03197-1
15. Carlé A, Karmisholt JS, Knudsen N, et al.: Does subclinical hypothyroidism add any symptoms? Evidence from a Danish population-based study. Am J Med. 2021, 134:1115-1126.e1. 10.1016/j.amjmed.2021.03.009
16. Akintola AA, Jansen SW, van Bodegom D, van der Grond J, Westendorp RG, de Craen AJ, van Heemst D: Subclinical hypothyroidism and cognitive function in people over 60 years: a systematic review and meta-analysis. Front Aging Neurosci. 2015, 7:150. 10.3389/fnagi.2015.00150
17. Zijlstra LE, Jukema JW, Westendorp RG, et al.: Levothyroxine treatment and cardiovascular outcomes in older people with subclinical hypothyroidism: pooled individual results of two randomised controlled trials. Front Endocrinol (Lausanne). 2021, 12:674841. 10.3389/fendo.2021.674841
18. Li X, Wang Y, Guan Q, Zhao J, Gao L: The lipid-lowering effect of levothyroxine in patients with subclinical hypothyroidism: a systematic review and meta-analysis of randomized controlled trials. Clin Endocrinol (Oxf). 2017, 87:1-9. 10.1111/cen.13338
19. Turner MR, Camacho X, Fischer HD, Austin PC, Anderson GM, Rochon PA, Lipscombe LL: Levothyroxine dose and risk of fractures in older adults: nested case-control study. BMJ. 2011, 342:d2238. 10.1136/bmj.d2238
20. Gong IY, Atzema CL, Lega IC, Austin PC, Na Y, Rochon PA, Lipscombe LL: Levothyroxine dose and risk of atrial fibrillation: a nested case-control study. Am Heart J. 2021, 232:47-56. 10.1016/j.ahj.2020.09.016
21. Garber JR, Cobin RH, Gharib H, et al.: Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Endocr Pract. 2012, 18:988-1028. 10.4158/EP12280.GL
22. National Institute for Health and Care Excellence: thyroid disease: assessment and management (NG145) . (2023). Accessed: October 7, 2026: https://www.nice.org.uk/guidance/ng145.
23. Bekkering GE, Agoritsas T, Lytvyn L, et al.: Thyroid hormones treatment for subclinical hypothyroidism: a clinical practice guideline. BMJ. 2019, 365:l2006. 10.1136/bmj.l2006
24. Korevaar TI, Leung AM, Alexander EK, et al.: American Thyroid Association 2026 guidelines for thyroid disease in preconception, pregnancy, and postpartum. Thyroid. 2026, 36:481-544. 10.1177/10507256261445624
25. Alexander EK, Pearce EN, Brent GA, et al.: 2017 guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. Thyroid. 2017, 27:315-89. 10.1089/thy.2016.0457