

SEMDSA/ACE-SA Guideline for the Management of Hypothyroidism in Adults

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Abstract

Background: Hypothyroidism is a common clinical condition confronting all healthcare practitioners yet there remains uncertainty about the optimal medication and optimum treatment targets. In addition, many patients remain symptomatic despite using recommended medications and attaining recommended treatment targets.

Methods: All endocrinologists in South Africa who consented to be part of the guideline process were assigned various aspects of the management of patients with thyroid disease. In each section the current literature was reviewed and the level of evidence was graded. This information was then presented at a guideline meeting. Where evidence was lacking a consensus among participants was adopted.

Results: This guideline provides 11 recommendations for the management of primary hypothyroidism, secondary hypothyroidism and subclinical hypothyroidism in adults.

Conclusions: This is the first South African guideline for the management of hypothyroidism in adults and represents a comprehensive review of the current literature in an attempt to provide evidence-based guidance for all healthcare practitioners regarding the many clinical aspects encountered when managing patients with hypothyroidism.

FOREWORD

Thyroid disease is a common clinical problem encountered by all healthcare practitioners. To date there have been no South African guidelines for the management of any aspect of thyroid disease. This guideline represents the first in a series of guidelines reviewing the management of various aspects of thyroid disease. Unless otherwise specified, this guideline pertains to the care of non-pregnant adults with hypothyroidism.

Hypothyroidism is a common clinical problem encountered by all healthcare practitioners. Despite adequate treatment, some patients with hypothyroidism remain symptomatic prompting many healthcare practitioners to question the treatments used and the recommended treatment targets. In addition, frustrated patients often turn to alternative medical supplements in an attempt to improve their symptoms. This is the first South African guideline for the management of hypothyroidism in adults and represents a comprehensive review of the current literature in an attempt to provide evidence-based guidance for all healthcare practitioners regarding the many clinical aspects encountered when managing patients with hypothyroidism. This guideline is not intended to replace professional judgement, experience and appropriate referral. These guidelines are intended to inform general patterns of care that will enhance the management of patients with hypothyroidism. They reflect the best available

evidence at the time, and practitioners are encouraged to keep updated with the latest information. Whilst care has been taken to ensure accuracy, SEMDSA/ Association of Clinical Endocrinologists of South Africa (ACE-SA, a subgroup of SEMDSA) assumes no responsibility for personal or other injury, loss or damage that may result from the information in this publication.

The Guideline development process

The process we followed in developing the guideline was as follows:

1. The SEMDSA executive committee entrusted the guideline process to ACE-SA
2. The broad topic of the management of patients with thyroid disease was divided into smaller sections. ACE-SA then invited all endocrinologists who wanted to be involved in the guideline process to lead the guideline development for a specific section
3. A Guideline Meeting was held in Cape Town on 18th/19th October 2014. The following participants were invited to this meeting:
 - a. All members of ACE-SA who had indicated that they wanted to be involved in the guideline process
 - b. Representatives from the Department of Health

- c. Representatives from the Council of Medical Schemes
 - d. Representatives from Faculty of Consulting Physicians of South Africa, South African Society of Nuclear Medicine, Association of Surgeons of South Africa
 - e. Representatives from Medical Schemes
4. The meeting was funded using unrestricted educational grants from two pharmaceutical companies involved in the field of managing patients with hypothyroidism and hyperthyroidism. Two representatives from each company were allowed observer status at the meeting (i.e. they were not allowed to participate in the proceedings of the meeting).
 5. At the Guideline Meeting, each endocrinologist was required to present the proposed guideline for their allocated section to the audience. The information presented was interrogated and amendments and additions were suggested. The discussions were evidence-based (see box 1), but where evidence was lacking, a consensus among participants was adopted (see box 2).
 6. Two ACE-SA members recorded detailed minutes of the discussions and debates at the meeting.
 7. After the Guideline Meeting, each section was rewritten according to an agreed format and included suggestions made at the Guideline Meeting.
 8. A Writing Group was then convened in Cape Town on the 30th/31st May 2015. At this meeting each section was reviewed. The group decided that the guideline should be published in 4 separate sections: Management of Adult patients with Hypothyroidism, Management of Adult patients with Hyperthyroidism, Management of patients with a Thyroid Nodule and Management of Hypothyroidism and Hyperthyroidism in Pregnancy.
 9. The revised draft guideline for the management of hypothyroidism was then sent to all members of ACE-SA and other societies involved in the management of patients with hypothyroidism.
 10. After receiving final comments, the guideline was amended as required and submitted for publication

Website

An electronic version of these guidelines will be available at www.semDSA.org.za. Any changes after the printing of this edition and before the next will be available on this website. Comments about the guideline can also be sent via the website.

Box 1: Level of Evidence

- | | |
|-----|--|
| IA | Evidence from meta-analysis of randomised controlled trials |
| IB | Evidence from at least one randomised controlled trial |
| IIA | Evidence from at least one controlled study without randomisation |
| IIB | Evidence from at least one other type of quasi-experimental study |
| III | Evidence from non-experimental descriptive studies, such as comparative studies, correlation studies, and case-control studies |
| IV | Evidence from expert committee reports or opinions or clinical experience of respected authorities or both |

Guideline committee: Joel Dave, Ania Kliesiwicz, Tanya Kinvig, Zaheer Bayat, Nazeer Ahmed Mohamed, Zane Stevens, Greg Hough, Helena Oosthuizen, Imran Paruk, Fraser Pirie, MAK Omar, Hilton Kaplan, Sinddeep Bhana, Daksha Jivan, Peter Raubenheimer, Sophia Rauff, Wimpie De Lange, Willie Mollentze, Nasrin Goolam Mahyoodeen, Bill Toet, Aslam Amod.

INTRODUCTION

Hypothyroidism is defined as a condition where the thyroid gland is unable to make adequate thyroid hormone to meet the requirements of the peripheral tissues. In primary hypothyroidism the thyroid gland fails to produce sufficient quantities of thyroid hormone to maintain normal thyroid stimulating hormone (TSH) secretion. This failure of negative feedback results in elevated levels of TSH. In secondary hypothyroidism (1% of all cases of hypothyroidism), disease of either the hypothalamus or pituitary gland results in inadequate TSH production and therefore insufficient stimulation of structurally and functionally normal thyroid gland. In early secondary hypothyroidism the TSH may be normal but is biologically inactive with the hallmark of secondary hypothyroidism being a normal or low TSH and a low free thyroxine (fT4). This guideline provides 11 recommendations for the management of primary hypothyroidism, secondary hypothyroidism and sub-clinical hypothyroidism in adults (see Table 1).

Primary hypothyroidism

Iodine deficiency is the commonest cause of hypothyroidism worldwide.¹ Voluntary salt iodisation was introduced in South Africa in 1954 but achieved minimal reduction in endemic goiter and hypothyroidism.² Mandatory iodisation of table salt at 40-60 ppm in 1995 dramatically improved the situation; a 1998 survey showed that optimal iodine nutrition, determined by urinary iodine concentration (UIC) where iodine deficiency is defined as a UIC < 100 µg/L, was achieved nationally in seven of the nine provinces; with more than adequate iodine intake in two provinces. At that time, 86.4% of households used iodised salt and 62.4% used adequately iodised salt that contained more than 15 ppm of iodine, with low coverage rates (<50%) in the three northern provinces (Limpopo, Mpumalanga and North West).² To maintain a sufficient iodine status, the World Health Organization (WHO), the United Nations Children's Fund (UNICEF) and the International Council for Control of Iodine Deficiency Disorders (ICCIDD) recommend age dependent daily iodine intake: 90 µg for preschool children (0 to 59 months), 120 µg for children (6 to 12 years) and 150 µg for adults (above 12 years). The recommendation for pregnant and lactating women has recently been increased to 250 µg per day.³

Box 2: Strength of recommendation

Weak	Based on poor scientific data or consensus of the Guideline Panel
Moderate	Based on weak scientific data or consensus of the Guideline Panel
Strong	Based on robust scientific data or consensus of the Guideline Panel

The National Health and Nutrition Examination Survey (NHANES III) studied an unselected U.S. population over age 12 between 1988 and 1994 and quoted 0.3% prevalence for overt hypothyroidism.⁴ It is important to note that one has to have a high index of suspicion and at the same time recognise that many of the clinical features of hypothyroidism are non-specific. The severity of symptoms not only depends on the duration of the disease but also the rapidity with which it develops. Autoimmune thyroid disease may affect quality of life, even in euthyroid individuals.^{5,6}

Subclinical hypothyroidism (SCH)

This condition is defined as a repeated serum TSH elevated above the normal range with a persistently normal free T4 and free T3 which is stable over a period of weeks, occurring in the absence of hypothalamic-pituitary disease and no recent non-thyroidal illness. Population prevalence varies between 5 - 10%, depending on the cohort.^{4,7-9} Unfortunately, there is limited data on the

prevalence of SCH in the general population in South Africa.¹⁰ SCH should be considered in 2 categories: those with a TSH > 10 mIU/L and those with a TSH 4.0 - 10.0 mIU/L. It is important to differentiate between younger (< 65 years) and older patients (> 80-85 years) as the TSH increases with age and it is thought that a rising TSH may confer a physiological advantage. SCH is associated with increased coronary heart disease (CHD) risk including both CHD events and mortality from CHD. The risk of CHD events and CHD mortality increases with increasing TSH, particularly with TSH levels > 10.0 mIU/L. Consequently, there is little debate in the literature about treating patients with TSH levels persistently > 10.0 mIU/L.¹¹⁻¹³ Treatment of patients with TSH levels 4.0 – 10 mIU/L is controversial as there are few randomized controlled trials to guide management of this group. Different aspects have been examined including recommendations for thyroxine therapy in individuals with a goitre, those with positive thyroid peroxidase antibodies (TPO Ab), those with an increased cardiovascular risk and in those

Table 1: Recommendations for the management of hypothyroidism

Recommendation	Level of evidence	Strength of recommendation
General		
1 Levothyroxine (LT4) is the treatment of choice for Primary (Overt/Subclinical/Elderly) and Secondary Hypothyroidism	IV	Strong
Subclinical hypothyroidism		
2 Treat patients with persistent elevations of the serum TSH level > 10.0 mIU/L as there is an increased risk of coronary heart disease (CHD) events and CHD mortality with increasing levels of TSH, particularly with TSH levels > 10.0mU/L	1A	Strong
3 Treatment of patients with persistent elevations of serum TSH 4.0–10 mIU/L is controversial. Treatment of patients with cardiovascular disease (CVD), increased risk for CVD, presence of thyroid peroxidase antibodies (TPO Abs), psychiatric illness, pregnancy, type 2 diabetes, dyslipidaemia or symptoms should be considered	IV	Weak
Primary hypothyroidism		
4 The serum TSH level should be used to monitor adequacy of thyroid hormone replacement and should be assessed 4-8 weeks after any dosage change and until the goal TSH is reached and maintained	IIA	Strong
5 The serum TSH level target should be: within the reference range of a 3 rd generation assay of a given laboratory preferably between 0.5-3.0 mIU/L	IA IV	Strong Moderate
6 Liothyronine (Tertroxin [®]) and other forms of thyroid hormone replacement should not be used routinely	IA	Strong
Elderly		
7 Maintain a high index of suspicion for hypothyroidism in elderly patients (> 65 years) as they may lack the typical symptoms and signs	IV	Strong
8 The serum TSH level is higher for elderly individuals (> 65 years) and a higher target TSH level on LT4 replacement therapy of 4.0-6.0 mIU/L may be appropriate in those > 65 years old	IV	Strong
Secondary hypothyroidism		
9 The serum TSH level should NOT be measured in the management of secondary hypothyroidism	IV	Strong
10 The serum fT4 level should be used to monitor adequacy of LT4 replacement therapy and should be assessed 4-8 weeks after any dosage change until the goal fT4 is reached and maintained	IIA	Strong
11 The fT4 target should be maintained within the upper half of the reference range of a given laboratory	IV	Moderate

with symptoms. The currently available data does not provide clear-cut benefit to all groups, hence a number of views exist and consensus panels are suggesting that the key determinant in this group of patients should be good clinical judgement.^{14,15}

Obese patients with SCH should be managed cautiously as TSH levels may increase with increasing obesity and revert to normal levels with weight loss such as occurs following gastric banding and gastric bypass.^{16,17} The AACE strongly recommends against thyroid hormone replacement for treatment of obesity in euthyroid patients.¹⁵

The measurement of TPO Abs is advised by several professional societies and clinical endocrinologists as the presence of elevated TPO Ab titres helps predict progression to overt hypothyroidism. Many patients with chronic autoimmune thyroiditis may have a normal TSH; however, approximately 75% have elevated anti-thyroid antibody titres including anti-thyroglobulin antibodies (Tg Ab), anti-thyroid peroxidase/anti-microsomal antibodies (TPO Ab) and TSH receptor antibodies. In the NHANES survey of a disease-free population, 10.4% of individuals tested positive for Tg Ab and 11.3% for TPO Ab.⁴ A positive TPO Ab test was significantly associated with the development of hypothyroidism, hence the recommendation for measurement of TPO Ab levels.^{14,18} TPO Abs are the most sensitive serologic test for thyroid autoimmunity in subclinical hypothyroidism.¹⁹ Serum concentrations wane with time and therefore repeated antibody measurements do not contribute to management of patients with SCH.²⁰

Screening for SCH is not recommended as there is no consensus on the benefits of therapy.

Elderly patients

The prevalence of hypothyroidism (overt and subclinical) is 10% in men and 16% in women in the age group 65-74 years and increases to 16% and 21% respectively in subjects older than 74 years.⁷ The main causes of hypothyroidism in older adults are autoimmune thyroiditis, postoperative hypothyroidism, and post-radioiodine hypothyroidism.²¹ Serum TSH levels increase with age in both males and females. This increase may result in values above the upper limit of the traditional reference range in elderly persons with normal thyroid function. The prevalence of positive anti-thyroid antibodies also increases with advancing age. TPO Abs and Tg Abs are positive in up to 20% of healthy elderly subjects. Importantly, the presence of thyroid autoantibodies in the elderly does not predict the development of thyroid disease.

LITERATURE REVIEW

Primary hypothyroidism

a. Pharmacological agent:

- *L-thyroxine (LT4) monotherapy*: considered the standard of care despite the absence of randomized clinical trials comparing LT4 to placebo. Withdrawal of LT4 leads to recurrence of the signs and symptoms of hypothyroidism.
- *Combination therapy*: there is increasing evidence to suggest that the TSH level achieved by LT4 is unable to achieve

adequate T3 levels in all tissues prompting some to suggest that combination therapy with LT4 and triiodothyronine would be preferable. However, multiple randomised-controlled trials have shown conflicting results.²²⁻²⁷ In addition, multiple meta-analyses have suggested no clinical benefit of combination therapy concluding that monotherapy with LT4 should remain the treatment of choice.²⁸⁻³⁰ There has also been a suggestion that perhaps treatment of hypothyroidism should be individualized with specific individuals possibly benefiting more from combination therapy.³¹

- *Desiccated thyroid extract (DTE)*: there is some evidence to suggest that treatment with DTE (animal-derived, porcine; contains T4 and T3) may be at least equivalent to LT4 in normalizing TSH levels and improving symptoms in some patients preferring therapy with DTE compared to LT4.³² However, there is a lack of long-term studies proving the safety and efficacy of DTE compared to LT4, and the relative excess of T3 in these preparations often produces supraphysiological levels of T3 which have unknown long-term consequences and which may produce symptoms.³³
 - *Selenium*: selenium is currently being investigated for its possible disease modifying effects in thyroid pathology, including autoimmune diseases. However, the data on the role of selenium supplementation in decreasing TPO Abs and decreasing the risk of hypothyroidism is conflicting. Some studies show a decrease in TPO Abs in autoimmune thyroiditis and a decrease in risk of post-partum hypothyroidism in pregnant patients that have TPO Abs^{34,35} while some studies show no effect.³⁶⁻³⁸ A meta-analysis showed a decrease in TPO Ab titres at 3 months with some improvement in mood and general well-being, however, the data is not sufficiently consistent to recommend routine selenium supplementation.³⁹
 - *Other formulations*: there is no consistent data for the use of any other formulation for the treatment of hypothyroidism, including but not limited to L-tyrosine, Asian ginseng, bladderwrack, Capsaicin, Echinacea and 3,5,3'-Triiodothyroacetic acid.
- b. *Target TSH level*: For many years there has been debate on the target TSH range for treatment of patients with hypothyroidism. Recent studies have shown no clinical benefit of treating to low normal TSH ranges.^{40,41} Consequently, the goal of treatment is to maintain the TSH level in the defined 3rd generation assay range for the specific pathology laboratory, but preferably at 0.5 – 3.0 mIU/L.
- c. *Factors affecting absorption of LT4*: Food and a number of medications affect the absorption of LT4 (see Table II). Randomised-controlled studies show that taking LT4 60 minutes before breakfast or 4 hours after the last meal of the day achieve the best absorption of LT4, but no data shows which of these options is superior.^{42,43}
- d. *Initiating dose of LT4*: Patients with minimal residual thyroid function or those that have had a total thyroidectomy usually require about 1.6 ug LT4/kg daily [44, 45]. Young healthy patients can be initiated with the full dose of LT4 whereas patients with cardiovascular disease should be initiated on

25 ug LT4 daily and healthy patients > 60 years old should be initiated on 50 ug LT4 daily.⁴⁶ Dose adjustments may be required with ageing,^{47,48} weight loss and in pregnancy. In addition, those with subclinical hypothyroidism may require lower doses of LT4.

Secondary hypothyroidism

There are multiple retrospective studies but only one randomized controlled trial (RCT). The RCT showed that using a LT4 dose of 1.6 µg/kg and maintaining the fT4 in the upper half of the reference range obtained the best reduction in symptoms of hypothyroidism.⁴⁹ There are no longterm studies.

Subclinical hypothyroidism

Symptoms: The Colorado Thyroid Disease Prevalence Study, a questionnaire based study in 25,862 subjects, showed a small but significant difference in symptoms between euthyroid patients and those with SCH.⁷ There are a number of small studies looking at improvement of symptoms with thyroxine replacement which do not show any significant benefit. However, one randomised crossover study, using 100 µg LT4 or placebo in 100 subjects with a mean TSH of 6.6mIU/L showed a significant improvement in tiredness.⁵⁰

Dyslipidaemia: Heterogeneous results were obtained in observational studies investigating the relationship between SCH and dyslipidaemia. Data from the Colorado Thyroid Disease Prevalence Study shows a positive relationship between TSH and dyslipidaemia, suggesting that there are already alterations in the lipid profile prior to the development of overt hypothyroidism.⁷ The association of SCH with increasing levels of TC, low density lipoproteins (LDL) and triglycerides (TG) are greatest for TSH levels > 10.0 mIU/L.⁵¹ There is data showing improvement in various lipid parameters with treatment with LT4; however, lipid targets may not be achieved and lipid lowering therapy may still be required.^{52,53}

Coronary heart disease: The Cleveland Clinic Preventative Cardiology Clinic showed that patients with CHD risk, < 65 years and TSH elevation 6.1 - 10.0 mIU/L as well as > 10.0 mIU/L untreated with LT4 had a higher all-cause mortality.⁵⁴ A recent analysis of 3 093 patients (40-70 years old) and 1 642 patients (over 70 years old) from the United Kingdom General Practitioner Research Database with a TSH level 5.01 - 10.0 mIU/L showed that treatment with LT4 reduced CHD event rates over the 7.6 years of follow-up but only in those that were 40-70 years old.⁵⁴ There remains conflicting data on the risk of ischaemic heart disease (IHD) in patients with SCH. Some meta-analyses have shown an increased risk for IHD and cardiovascular mortality in patients < 65 years old^{13,55} and some have not.⁵³ However, there are no RCTs with hard cardiac endpoints. Treatment with LT4 in patients with SCH who are < 65 years old should be considered. There is no data to suggest that this increases risk.⁵⁴ There is also some data to suggest that patients > 65 years old with SCH are also at increased risk for IHD,⁵⁶ although there is no data to suggest that treatment will decrease this risk.⁵⁴ Not all studies have shown that age is a predictor of risk for IHD in patients with SCH and there

is no robust data to suggest that treatment with LT4 reduces risk for IHD.

Psychiatric illness: SCH affects declarative and working memory.⁵⁷ There is some evidence showing that treatment improves mood in younger patients. It is not unreasonable to consider treatment in patients with depression, bipolar mood disorder and cognitive dysfunction. The effect of SCH on cognition and mood in people > 65 years old is unclear.⁵⁸

Type 2 diabetes: There is a reduction in insulin sensitivity in patients with SCH and the possibility of worsening glycaemic control in patients with type 2 diabetes (T2DM). There is some evidence to show that treatment with LT4 improves insulin sensitivity.⁵⁹ Therefore, consider treatment with LT4 in patients with T2DM and SCH. Review glycaemic control 3 months after thyroid targets are achieved to ascertain whether to continue therapy with LT4.

Elderly

Metabolism of thyroid hormone is altered in older people due to altered absorption, reductions in lean body mass and the use of numerous drugs for co-morbid conditions so that the response to replacement doses of levothyroxine should be monitored closely in individuals in this age group.⁶⁰ In addition, elderly patients often lack the typical symptoms and clinical signs associated with hypothyroidism.⁶¹ The TSH level increases with age whereby 40% of people > 80 years old with no thyroid disease have a TSH level > 2.5 mIU/L and 14.5% have a TSH level > 4.5 mIU/L.⁶² This shows that older patients may have an elevated TSH as part of the normal ageing process and not due to thyroid dysfunction. Therefore, some suggest that age-specific reference ranges should be used when interpreting TSH levels but these have not been validated in the South African setting.

Table II: Factors affecting the absorption of LT4

- Bile acid sequestrants (cholestyramine, colestipol, colesevelam)
- Sucralfate
- Cation exchange resins (Kayexelate)
- Oral bisphosphonates
- Proton pump inhibitors
- Raloxifene
- Multivitamins (containing ferrous sulfate or calcium carbonate)
- Ferrous sulfate
- Phosphate binders (sevelamer, aluminum hydroxide)
- Calcium salts (carbonate, citrate, acetate)
- Chromium picolinate
- Charcoal
- Orlistat
- Ciprofloxacin
- H2 receptor antagonists
- Dietary factors:
 - Ingestion with a meal
 - Grapefruit juice
 - Espresso coffee
 - High fibre diet
 - Soybean formula (infants)
 - Soy

CLINICAL PRACTICE RECOMMENDATIONS (see Figure 1)

Primary Hypothyroidism: because primary hypothyroidism accounts for 99% of cases of hypothyroidism, the TSH level is an appropriate screening test. If the TSH is elevated, serum free Thyroxine (fT4) should be measured. Free T3 (fT3) and reverse T3 (rT3) levels are not required for the diagnosis and management of patients with primary hypothyroidism or SCH. Thyroid antibodies are useful to confirm autoimmunity and should only be measured at the time of diagnosis. They play no role in the ongoing management of the patient and should therefore not be measured again.

Secondary hypothyroidism: if secondary hypothyroidism is suspected then fT4 levels should be measured as a screening test

TSH screening: there is no consensus about population screening for hypothyroidism:

- American Thyroid Association recommends that TSH be measured at age 35 years and every 5 years thereafter.⁶³ This is primarily based on the limited accuracy of clinical diagnosis. If only patients with clearly suggestive signs and symptoms were tested then many affected patients will remain undiagnosed.
- American Association of Clinical Endocrinologists suggests screening of older patients (age not specified), especially women⁶⁴
- The U.S. Preventive Services Task Force concluded that evidence is insufficient to recommend for or against routine screening for thyroid disease in adults.⁶⁵

It is recommended that the TSH level should be measured in various clinical situations (see Box 3).

Box 3: Suggested clinical situations in which TSH testing should be considered

- Symptomatic patients
- Autoimmune disease, such as type 1 diabetes
- First-degree relative with autoimmune thyroid disease
- History of neck radiation, radioactive iodine therapy and external beam radiotherapy for head and neck malignancies
- Prior history of thyroid surgery or dysfunction
- Abnormal thyroid examination
- Psychiatric disorders
- Patients taking amiodarone or lithium
- Infertility and repeated miscarriages
- Growth retardation and delayed puberty
- Other
 - Pregnant woman with risk factors
 - Genetic syndromes (e.g. Down's syndrome, Turner syndrome)
 - Hyperprolactinaemia
 - Dyslipidemia
 - Heart failure
 - Chronic constipation
 - Dementia
 - Obesity

Treatment of patients with LT4

- All patients with primary hypothyroidism, secondary hypothyroidism and SCH (TSH > 10 mIU/L) should be treated with LT4 monotherapy.
- Initiate with full replacement doses of LT4 (1.6 µg/kg calculated on lean body mass) in young patients with overt primary or secondary hypothyroidism. Full replacement doses are generally not required in patients with SCH. In these patients 25 to 75 µg is usually sufficient for achieving euthyroid levels. Older patients (> 65 years old) or those with heart failure, ischaemic heart disease or arrhythmias should be initiated on lower doses (12.5 to 25 µg). In patients with secondary hypothyroidism, hypoadrenalism should be excluded first before starting treatment with LT4.
- Repeat TSH level every 4-8 weeks in patients with primary hypothyroidism or SCH.
- Repeat fT4 every 4-8 weeks in patients with secondary hypothyroidism. There is no role for monitoring the TSH level in the management of patients with secondary hypothyroidism so this should not be measured.
- Aim for TSH levels within the normal range of a 3rd generation TSH assay for a specific pathology laboratory, but preferably 0.5 – 3.0 mIU/L. In patients > 65 years old the TSH level should be maintained at 4.0 - 6.0 mIU/L .
- LT4 dose adjustment should generally be no higher than 12.5 to 25 µg per day (either up or down) depending on the TSH level in primary hypothyroidism and fT4 level in secondary hypothyroidism. Serum TSH (primary hypothyroidism) and fT4 (secondary hypothyroidism) should be repeated every 4-8 weeks until the goal is achieved. Thereafter, the TSH (primary hypothyroidism) or fT4 (secondary hypothyroidism) may be measured every 6-12 months.
- Dose requirements of LT4 may change under some circumstances such as pregnancy, weight loss or gain, addition of concomitant medications known to affect LT4 requirements or absorption of LT4 (see Table II) and gastrointestinal disease.
- Excessive LT4 and iatrogenic hyperthyroidism should be avoided as it may lead to adverse outcomes such as atrial fibrillation, heart failure and osteoporosis.⁶⁶⁻⁶⁸ Under-replacement should also be avoided as there may be a detrimental effect on the lipid profile and cardiovascular disease.^{52,69}
- Co-morbidities may be present in elderly patients and drugs often prescribed for these conditions may interfere with the absorption and metabolism of levothyroxine so more frequent monitoring of TSH levels is often required.
- Once target TSH levels are achieved, the TSH level should be repeated at 6-12 monthly intervals. Once a decision has been made to continue lifelong therapy and the patient is clinically and biochemically stable on replacement therapy with LT4 then follow-up with a GP is suggested.
- Once the patient is euthyroid then lipid levels should be checked.
- The use of dessicated thyroid preparations and combination therapy is not advised.

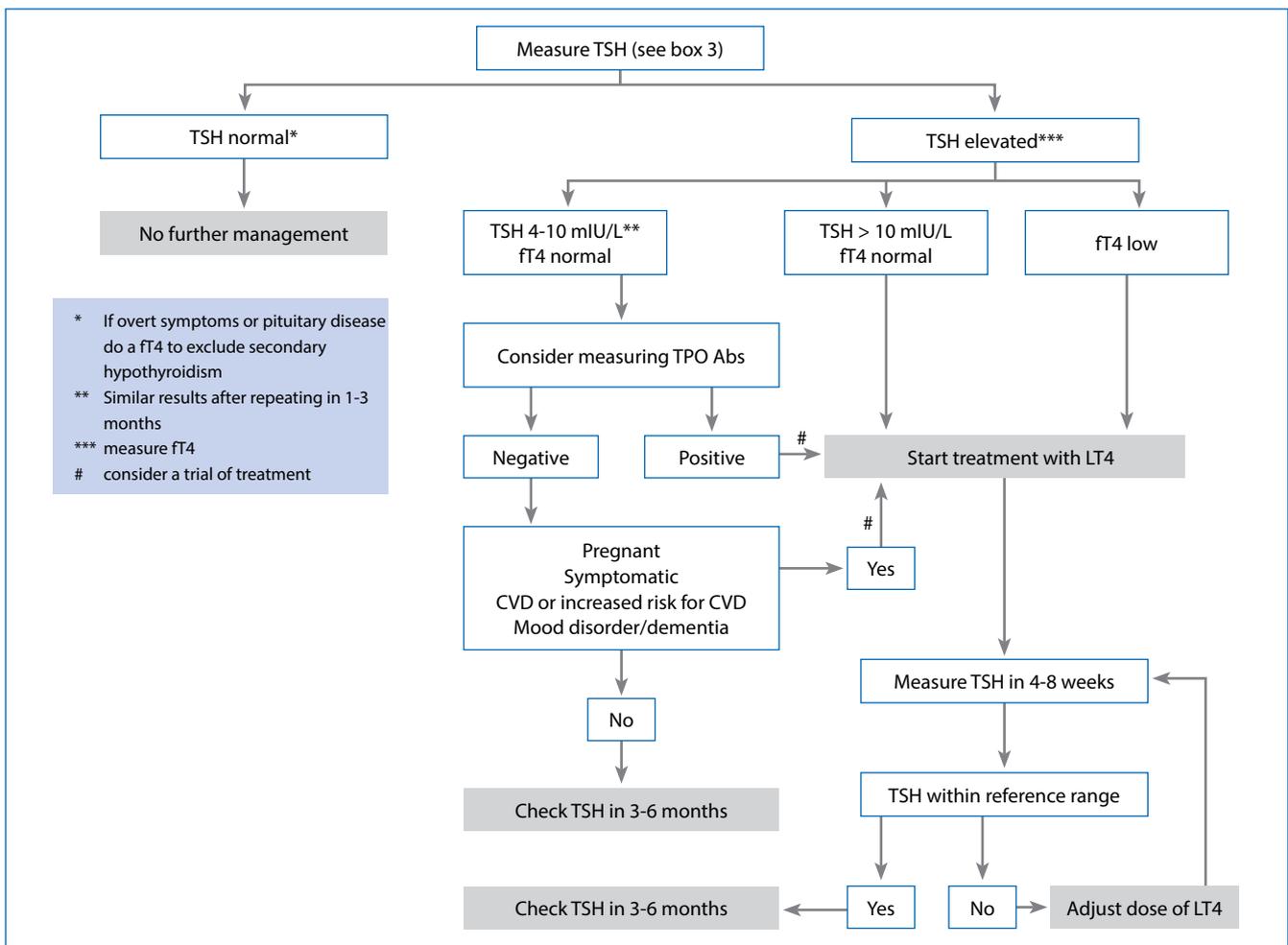


Figure 1: Algorithm for the management of a patient with hypothyroidism

Management of patients with SCH (TSH 4-10 mIU/L, normal ft4)

- If TPO Abs are positive then patients should be treated with LT4 as the presence of TPO Abs appears to confer greater risk of progression to overt hypothyroidism (4.3%/yr. vs 2.6%).⁸
- If TPO Abs are negative then it may be prudent to consider a trial of therapy in patients < 65 years old with: symptoms, pregnancy, psychiatric illness, dyslipidaemia, coronary heart disease or type 2 diabetes.

Referral to a specialist

Referral to an endocrinologist or specialist physician should be considered in patients with hypothyroidism or SCH in the following clinical situations:

- Children

- Patients with poor control, for example lack of control after two dose adjustments
- Planning conception or pregnancy
- Infertility
- Cardiac disease
- Structural abnormalities of the thyroid gland such as nodules or a goitre
- Co-morbid endocrine disorders such as pituitary, adrenal or polyglandular auto-immune disorders
- Unusual thyroid results or unusual causes of hypothyroidism
- Psychiatric disorders

Full list of references are available on request.