Proceedings of ICEGEE 2026 Symposium: AI-Based Medicine and Biological Data Analysis
DOI: 10.54254/2753-8818/2026.AU32359

# *How Thyroid Dysfunction Contributes to Weight Gain and Obesity-Like Phenotypes: A PubMed-based Literature Review (2015–2025)*

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***Abstract.*** Obesity is a major public health challenge, and thyroid dysfunction is a common endocrine disorder frequently linked to weight change. This PubMed-based review (2015–2025) synthesises epidemiological, mechanistic, and clinical evidence on how thyroid states contribute to weight gain and obesity-like phenotypes. Epidemiological studies indicate that weight shifts after thyroid-related treatment are typically modest (e.g., small average gains after thyroidectomy) but heterogeneous, supporting a role for thyroid-state transitions alongside background weight drift. Mechanistically, reduced thyroid hormone signalling can lower resting energy expenditure and alter substrate metabolism, while impaired brown adipose tissue thermogenesis may further reduce energy output. Clinically, diagnosis should rely on TSH with FT4 and recognition of pitfalls such as obesity-related TSH shifts and central hypothyroidism. Treatment should restore euthyroidism without using thyroid hormones as weight-loss agents, given the limited benefit and potential harms from overtreatment; persistent obesity should be addressed using evidence-based obesity care pathways.

***Keywords:*** Thyroid dysfunction, Hypothyroidism, Weight gain, Obesity

## 1. Introduction

Thyroid hormones regulate resting energy expenditure, substrate utilisation and thermogenesis, making them biologically plausible contributors to weight regulation. However, observed thyroid–obesity associations are often small and confounded, and obesity itself can influence thyroid markers. This review summarises evidence from 2015–2025 PubMed literature across four domains: (1) epidemiological links between thyroid-related treatment and weight trajectories, (2) mechanisms via basal metabolism and brown adipose tissue thermogenesis, (3) clinical manifestations and diagnostic pitfalls, and (4) treatment implications, including risks of overtreatment and management of persistent obesity after thyroid correction.

Searches were conducted in PubMed for English-language studies published between 2015 and 2025, prioritising systematic reviews/meta-analyses, prospective cohorts, randomised trials and major clinical guidelines that directly tested thyroid–weight relationships rather than incidental

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findings. Evidence was selected to support each subsection and then synthesised to highlight where results are consistent, where heterogeneity persists, and how to translate the findings into realistic clinical interpretation and management.

## 2. Epidemiological evidence

Recent evidence (2015–2025) suggests thyroid-related treatment can shift weight trajectories, but average changes are small. A meta-analysis of thyroidectomy cohorts reported modest post-operative weight gain (about +2.13 kg overall) with substantial heterogeneity, with larger gains in younger patients and in surgery for hyperthyroidism [1]. A separate meta-analysis pooling population cohorts also found mild weight increases across thyroid indications, indicating that background weight drift and individual factors can coexist with treatment effects [2]. Prospective cohort data further suggest that treatment for overt hyperthyroidism may be followed by increased obesity risk compared with the general population, and that radioactive iodine with subsequent hypothyroidism is linked to additional excess gain [3]. Together, these data support a plausible association between thyroid-state transitions and modest weight change, motivating mechanistic explanations in the following chapters.

## 3. Mechanisms of basal metabolism, substrate metabolism and heat generation (BAT / CIT)

Thyroid hormones influence body weight largely by setting resting energy expenditure and directing substrate metabolism across tissues. T3 signalling via thyroid hormone receptors regulates transcription linked to mitochondrial biogenesis, oxidative enzymes and ATP-demand pathways (e.g., ion pumping), thereby determining basal ATP turnover [4,5]. Tissue-level thyroid tone also depends on local activation and inactivation of thyroid hormones, so reduced thyroid function can lower intracellular T3 action beyond circulating changes. When TH signalling is reduced, oxidative capacity and lipid oxidation tend to decline, favouring reduced fuel clearance and relatively greater energy storage. However, clinical syntheses show TH–BMI associations are heterogeneous and often mild, implying confounding and suggesting that basal and substrate mechanisms alone are insufficient to explain all obesity-like phenotypes [6]. This supports considering thermogenesis as an additional energy-output pathway [7].

Some studies have shown that thermodynamic capacity provides a more direct energy output pathway. Thermogenic capacity, especially cold-induced thermogenesis (CIT) in brown adipose tissue (BAT), provides a more direct energy-output pathway linking thyroid status to weight regulation. Cold exposure activates sympathetic outflow; norepinephrine stimulates β-adrenergic receptors, triggering cAMP/PKA signalling, lipolysis and delivery of fatty acids to mitochondria [8,9]. Fatty acids both fuel oxidation and activate UCP1, which uncouples the proton gradient from ATP synthesis and dissipates energy as heat. Thyroid hormones support this pathway by enhancing local T3 signalling, increasing UCP1 expression, mitochondrial biogenesis and adrenergic responsiveness, thereby modulating CIT. Human studies indicate that correcting hypothyroidism can restore impaired thermogenesis, but large inter-individual variation in BAT means CIT cannot explain all weight outcomes; overall effects likely reflect combined contributions of basal metabolism, thermogenesis and clinical factors such as body composition and fluid balance [6,7].

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## 4. Clinical manifestations

Some reports indicate that weight gain is often described as one of the clinical manifestations of hypothyroidism. However, its diagnostic specificity is poor, and it cannot be used as a sole criterion for diagnosing thyroid disease [10]. Hypothyroidism is commonly accompanied by symptoms such as fatigue, cold intolerance, constipation, dry skin, and decreased exercise tolerance, which highly overlap with obesity-related complaints and various chronic diseases. This significantly weakens the discriminatory power of inferences based solely on symptoms. Consequently, standard clinical assessment prioritizes biochemical confirmation using thyroid function tests, with the combined interpretation of TSH and FT4 serving as the central step to confirm hypothyroidism and to stratify overt versus subclinical phenotypes. From an evidence-synthesis perspective, this diagnostic framing also aligns with the observation that thyroid-related weight effects are typically modest at the population level. Those changes labeled as "weight gain" may reflect shifts in body composition or fluid balance rather than large increases in fat mass.

These clinical features directly influence how we interpret epidemiological associations, because the same "weight gain" phenotype can be caused by multiple pathways, such as energy intake, physical activity, comorbidities, and medications. Without strict thyroid subtyping, confounding and misattribution are more likely to occur. Therefore, a more prudent approach is to present weight changes along with their possible components, such as changes in fluid retention and fat mass. It is also essential to anchor the findings against an objective thyroid condition, rather than relying on symptom impressions.

## 5. Diagnostic pathways and pitfalls

In obesity assessment, guidelines usually recommend structured endocrine screening, but also emphasize that correction of endocrine abnormalities usually contributes little to weight loss. This means that obesity should not be over-attributed to thyroid dysfunction [11]. A common pitfall is to directly diagnose primary hypothyroidism upon seeing a slightly elevated TSH level, ignoring that obesity itself may be related to a slight increase in TSH. In this case, FT4 must be combined with the clinical context to avoid reflexively prescribing levothyroxine. A more critical pitfall is central hypothyroidism. TSH may be normal or low, or even not rise as expected, so diagnosis depends on identifying a decrease in FT4 in the appropriate context, combined with clues from pituitary disease, drug effects, and other hormone axes [12]. Finally, subclinical hypothyroidism requires a clear risk-benefit trade-off. Relevant guidelines emphasize careful selection of treatment subjects and clarify that thyroid hormones should not be used as a means of weight loss to avoid risks such as iatrogenic hyperthyroidism due to overtreatment [13].

Overall, these pitfalls collectively support a more standardized diagnostic pathway. This involves first using biochemical evidence, such as TSH and FT4, along with necessary follow-up examinations to accurately define thyroid status, before discussing weight intervention strategies. This can reduce missed diagnoses and unnecessary medication.

## 6. Correction of thyroid abnormalities

Correction of confirmed hypothyroidism is clinically necessary, but expectations for weight improvement should generally be conservative, as weight changes often reflect adjustments in fluid and body composition rather than significant fat reduction. Prepost clinical evidence suggests that achieving euthyroidism can normalize thyroid-related symptoms and metabolic homeostasis, yet

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measurable changes may occur primarily in lean mass or fluid compartments without guaranteeing parallel improvements in insulin sensitivity [14]. Importantly, in patients already treated with levothyroxine, randomized dose-adjustment studies that move TSH within the reference range show little clinically meaningful change in resting energy expenditure or body composition, arguing against dose escalation as a weight-loss strategy [15]. This is very important for clinical communication: treatment goals should prioritize achieving biochemical targets and symptom control, while weight and waist circumference should be monitored as outcome indicators that may lag behind endocrine correction. For thyroidectomy-associated weight gain, perioperative lifestyle and nutritional support (e.g., structured dietitian counseling) may help mitigate post-operative weight drift, indicating that endocrine correction alone is rarely sufficient for long-term weight control [16]. In summary, the evidence in this section supports a more realistic conclusion that treating thyroid disease aims to restore endocrine health. However, when overweight/obesity is clinically significant, additional weight-targeted interventions are often still necessary.

## 7. Risks of overtreatment and abuse

Because the treatment window between normal thyroid function and iatrogenic hyperthyroidism can be narrow, overtreatment itself poses a significant clinical risk, especially when thyroid hormones are used for "weight loss" rather than "disease correction." One of the best-studied scenarios is TSH suppression therapy for differentiated thyroid cancer. Its oncological benefits need to be weighed against the potential systemic hyperthyroidism effects of long-term exposure [14]. Systematic reviews and meta-analyses consistently indicate an association between TSH suppression and lower bone mineral density, with the signal most evident in postmenopausal women. However, patterns in premenopausal women and men are less consistent [17,18]. Therefore, a more reasonable approach is risk stratification management. A "minimum effective inhibition intensity" should be adopted based on recurrence risk, with targets dynamically adjusted over time, and bone health monitoring (such as DXA follow-up and fracture risk assessment) should be included in high-risk populations. From a weight management perspective, the "measurable cost" of poor bone health further reinforces the core boundaries of this paper. Thyroid hormones should not be used for weight loss because the potential short-term weight changes cannot justify their long-term harm. Therefore, this section does not negate thyroid treatment itself, but emphasizes safe medication and dosage control based on indications, and avoids iatrogenic complications caused by over-attributing weight problems to thyroid conditions.

## 8. Evidence-based treatment of abnormal weight

When thyroid function has been corrected but obesity persists, the clinical question should shift from whether the thyroid causes weight gain to how to manage obesity as a chronic disease in the context of corrected endocrine status. Major obesity guidelines frame lifestyle therapy as the foundation (dietary energy deficit, physical activity, and behavioral support), with escalation to anti-obesity pharmacotherapy or metabolic/bariatric surgery based on BMI thresholds, comorbidities, and patient-centered goals [19,20]. Within this framework, thyroid assessment still has value and a role in ruling out true endocrine causes and ensuring adequate replacement therapy. However, further "adjusting thyroid hormone levels" should not be the default next step in weight control. Instead, clinicians should systematically characterize obesity-related phenotypes and risks (cardiometabolic risks, sleep apnea, fatty liver, mental health, and weight-gain drugs, etc.) and select intervention strategies that can affect appetite, energy intake, and long-term adherence accordingly.

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This approach helps communicate a clear boundary: correcting hypothyroidism addresses endocrine homeostasis, whereas obesity treatment addresses sustained energy imbalance and downstream complications that may remain even after thyroid normalization.

Among existing treatment options, GLP-1 receptor agonists are a prime example. When lifestyle interventions alone are insufficient, treatments targeting the biological mechanisms of obesity can be used to manage persistent obesity. In the STEP 1 randomized controlled trial, once-weekly semaglutide 2.4 mg plus lifestyle intervention achieved substantially greater mean weight loss than placebo plus lifestyle (approximately −14.9% vs −2.4%). It markedly increased the proportion of participants reaching clinically meaningful weight-loss thresholds [21]. Beyond weight reduction, the trial also reported improvements in cardiometabolic risk factors, supporting the rationale that treating obesity can reduce downstream morbidity even when thyroid status is already corrected. For a review article on the topic of thyroid, its significance is not semaglutide treatment for thyroid disease, but rather that it suggests there is an evidence-based pathway for treating residual obesity without resorting to raising thyroid hormone levels. In practice, therapy choice should be individualized by contraindications, tolerability, access, and risk profile, and delivered as an adjunct to lifestyle therapy with long-term follow-up [19-21].

## 9. Discussion

Across studies, thyroid dysfunction can contribute to weight change through reduced energy expenditure, altered thermogenesis and shifts in body composition or fluid balance, but average effects are typically modest and heterogeneous. Clinically, careful phenotyping (TSH plus FT4) is essential to avoid misattribution and overtreatment, particularly in obesity where mild TSH elevations and central hypothyroidism may complicate interpretation.

A recurring theme is that apparent 'weight gain' may reflect more than fat mass; clinicians and researchers should consider oedema, lean-mass changes and the time course of weight recovery after thyroid-state transitions. The treatment literature also supports separating endocrine goals from weight-management goals: restoring euthyroidism improves endocrine health, while persistent obesity usually requires standard lifestyle interventions and, when appropriate, evidence-based anti-obesity pharmacotherapy or bariatric approaches. Current evidence remains limited by variable definitions of thyroid status, inconsistent adjustment for confounders, short follow-up and a lack of direct measures of body composition and BAT activity. Future longitudinal studies integrating endocrine profiles with imaging-based thermogenesis and robust body-composition phenotyping may better clarify causal pathways and identify subgroups most likely to experience clinically meaningful weight change.

## 10. Conclusion

This article, by integrating PubMed evidence from 2015–2025, assesses whether and how thyroid dysfunction contributes to weight gain and obesity-like phenotypes. In epidemiological studies, treatment-induced changes in thyroid status were associated with measurable changes in weight and body composition, but the overall magnitude was generally small. Mechanistic evidence supports a relatively consistent pathway: decreased thyroid hormone signaling downregulates basal metabolic rate, alters lipid/glucose substrate utilization, and limits thermogenesis in brown adipose tissue and peripheral tissues. Clinically, weight changes are more of a "clue" than a diagnostic criterion; therefore, assessment should focus on thyroid function tests (TSH combined with FT4) and identifying diagnostic pitfalls such as obesity-related TSH fluctuations and central hypothyroidism.

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Treatment-wise, correcting the underlying thyroid disease is necessary for endocrine health, but increasing or abusing thyroid hormones as a weight-loss method is unjustified and potentially harmful. If obesity persists after restoring thyroid function, management should revert to evidence-based obesity treatment pathways, including dietary and behavioral interventions, pharmacological therapy, and procedural protocols where necessary. The main limitations of the existing evidence are the heterogeneity of the population and outcome indicators and the residual confounding. Therefore, future studies need to follow up for a longer period of time and standardize indicators such as energy expenditure, heat production and body composition.

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