

Cite as: Archiv EuroMedica. 2025. 15; 2. DOI [10.35630/2025/15/2.205](https://doi.org/10.35630/2025/15/2.205)

Received 16 February 2025;
Accepted 8 April 2025;
Published 14 April 2025

SUPPLEMENTATION OF IRON, SELENIUM, ZINC AND IODINE IN HYPOTHYROIDISM

¹Mikołaj Szewczykowski  , ¹Magdalena Dorobek

,

¹Ewa Otręba , ¹Tomasz Klinkosz ,

²Aleksander Walukiewicz , ³Filip Ogończyk-Mąkowski 

¹F. Ceynowa Specialist Hospital in Wejherowo, Poland

²Mikołaj Kopernik Hospital, Gdansk, Poland

³Provincial Polyclinical Hospital of Marcin Kacprzak in Płock, Poland



[download article \(pdf\)](#)

 m.szewczykowski98@gmail.com

ABSTRACT

Aims: Hypothyroidism is a disease that affects numerous people all over the world. The treatment is based on supplementation of thyroid hormones, however recent clinical trials, meta-analyses, and systematic reviews provide new insights about the role of micronutrients in this disease. Nevertheless, there are inconsistencies in the literature regarding the efficacy and necessity of supplementing these micronutrients in patients with hypothyroidism. The motivation to broach this topic was the dynamic growth of the dietary supplements market and the interest we observed among patients regarding the use of supplements in our clinical practice. Our goal is to evaluate the latest literature regarding the role of supplementation of iron, selenium, zinc and iodine in patients with hypothyroidism and its practical significance for healthcare professionals.

Methods: The literature review was conducted using the PubMed and Google Scholar database. Publications from 2016–2024 were searched using specific keywords.

Results: Hypothyroidism negatively affects iron metabolism, conversely iron deficiency impacts negatively the thyroid function. However, we have found only one prospective study showing benefits of iron supplementation in hypothyroidism patients. Selenium supplementation in hypothyroidism reduces TSH levels, this effect is intensified by co-supplementation of myo-inositol. No impact of selenium supplementation on T3 and T4 levels was described; also the impact on quality of life is controversial. There is still a lack of definitive evidence regarding the positive effects of zinc supplementation in hypothyroidism. Although both iodine deficiency and excessive iodine intake can lead to hypothyroidism, the impact of iodine supplementation specifically in patients with hypothyroidism remains unclear.

Conclusions: The microelements have clinical impact on function, metabolism and conversion of thyroid hormones; however the effectiveness of supplementation in hypothyroidism has not been broadly examined.

Keywords: hypothyroidism, dietary supplements, iron, selenium, zinc, iodine

INTRODUCTION

EPIDEMIOLOGY AND ETIOLOGY OF HYPOTHYROIDISM

Hypothyroidism is a common endocrine disease worldwide, caused by an under-secretion of thyroid hormones. The prevalence rate of overt hypothyroidism in the general population varies from 0.2% to 5.3% in Europe and from 0.3% to 3.7% in the USA [1]. In the Polish population over 60 years old the prevalence of hypothyroidism was estimated to be 13.9% (19.4% in women and 6.3% in men) [2]. Reported incidence rate of spontaneous hypothyroidism is 3.5–5.0 per 1000 women and 0.6–1.0 per 1000 men [1]. In Europe the prevalence of undiagnosed subclinical hypothyroidism varies between 0.5% and 12.5% and the prevalence of undiagnosed overt hypothyroidism varies between 0.1% and 3.2% [3]. Women are ten times more likely to develop hypothyroidism than men. Black individuals are reported to have the lowest prevalence of hypothyroidism and those of dual heritage and white individuals to have a higher prevalence [1]. Hypothyroidism presents also more often in people over the age 65 years old [4]. Leading causes of primary hypothyroidism are iodine deficiency and autoimmune thyroiditis [1,5]. Some other factors that can lead to this condition are radiation therapy, thyroid gland removal surgeries and some medications [4].

CLINICAL PRESENTATION OF HYPOTHYROIDISM

The most common consequences of thyroid hormone deficiency are chronic fatigue, weight gain, increased sensitivity to cold, constipation, voice distortion, dry skin and loss of hair. Within the cardiovascular system bradycardia, hypertension, dyslipidemia and changes in the ECG may occur. Patients can also present with memory loss, impaired coordination and signs of depression. Musculoskeletal changes include weakness, cramps in the muscles, and joint pain [4,6,7,8].

DIAGNOSIS AND TREATMENT OF HYPOTHYROIDISM

The main diagnostic tools for detecting hypothyroidism are laboratory tests of thyroid stimulating hormone (TSH) and free thyroxine (fT4). Hypothyroidism is diagnosed when TSH levels exceed reference values and fT4 levels fall below reference values. Additional laboratory tests that can indicate autoimmune cause of hypothyroidism are increased levels of antithyroid antibodies such as antithyroperoxidase antibody (TPOAb) and antithyroglobulin antibody (TgAb). Although it is worth noting that these antibodies are prevalent in more than 10% of the general population and their presence is not always associated with thyroid disease. The treatment of hypothyroidism involves the supplementation of thyroid hormones, mostly in the form of levothyroxine (L-T4). Patients should take the tablet of L-T4 on an empty stomach and not eat anything for the next hour. The optimal daily dose in overt hypothyroidism is 1,5-1,8 µg per day. Therapy targets include both normalization of TSH levels and reduction of mental and physical symptoms [4,5].

AIM OF THE STUDY

Recent clinical trials, meta-analyses, and systematic reviews provide new insights about the role of micronutrients in hypothyroidism. Nevertheless there are inconsistencies in the literature regarding the efficacy and necessity of supplementing these micronutrients in patients with this disease. Additionally, there is a growing interest among the patients in the topic of dietary supplementation, which leads to their increased consumption [9]. Considering these factors, our goal is to evaluate the latest literature regarding the role of supplementation of iron, selenium, zinc and iodine in patients with hypothyroidism and its practical significance for healthcare professionals. A new literature review will help consolidate the latest findings and provide a more comprehensive analysis.

METHODS

The literature review was conducted using the PubMed and Google Scholar database. Publications from 2016–2024 were searched combining following phrases: „hypothyroidism“, „epidemiology“, „iron“, „iron deficiency“, „supplementation“, „iron supplementation“, „selenium“, „selenium deficiency“, „selenium supplementation“, „zinc“, „zinc deficiency“, „zinc supplementation“, „Iodine“, „Iodine deficiency“, „Iodine supplementation“.

RESULTS OF SELECTION

During our research we have found one study regarding iron supplementation, five studies regarding selenium supplementation, three studies regarding selenium + myo-inositol-3 co-supplementation, three studies regarding zinc supplementation, one study regarding zinc + magnesium + vitamin A co-supplementation. Additionally, we have included one publication from October 2015 regarding iron supplementation.

CONTENT OF THE REVIEW

IRON

The role of iron in the human body

Iron is a crucial part of hemoglobin, which transports oxygen in the circulatory system [10]. Each hemoglobin molecule contains four iron atoms; consequently, insufficient dietary intake of this element disrupts erythropoiesis, resulting in a reduction of hemoglobin concentration below 13 g/dl for men and 12 g/dl for women, enabling the diagnosis of anemia [11]. Typical biochemical finding in patients with iron deficiency (ID) is low serum ferritin (SF) concentration - this indicator is broadly used in the studies regarding anemia and iron metabolism [12].

Epidemiology

ID is the most common nutritional deficiency in the world, around 2 billion people in the world suffer from this condition [12], mainly young women and children [13]. Over 60% of anemia cases are caused by ID, the condition is more prevalent in young children and women in reproductive age [11].

The role of iron in the thyroid function

In addition to the role in erythropoiesis, iron is essential in many other metabolic processes in the human body, some regarding thyroid hormones (Figure 1. and Figure 2.) [14]. It was established that iron shortage results in reduced free triiodothyronine (fT3) and fT4 levels in both pregnant and non-pregnant women [12,15], although the effects of ID on TSH levels remain inconsistent [12,15,16]. ID was also associated with an elevated risk of the prevalence of antithyroglobulin antibodies [12,15,16]. In O’Kane’s (2018) systematic review two studies have shown an increase in fT4 and no significant change in fT3 in patients supplementing iron, thyroid disease was an exclusion criterion in this review [14].

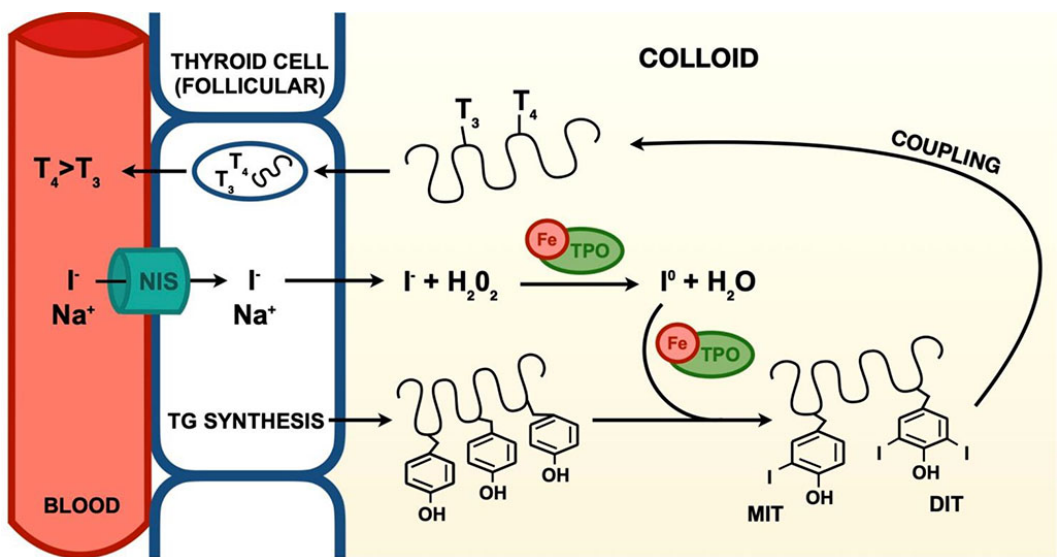


Figure 1. Process of the synthesis of the thyroid hormones in the thyroid gland. Iron deficiency reduces thyroid peroxidase (TPO) activity. NIS - sodium/iodide cotransporter, MIT - monoiodotyrosine, DIT - diiodotyrosine [14,51].

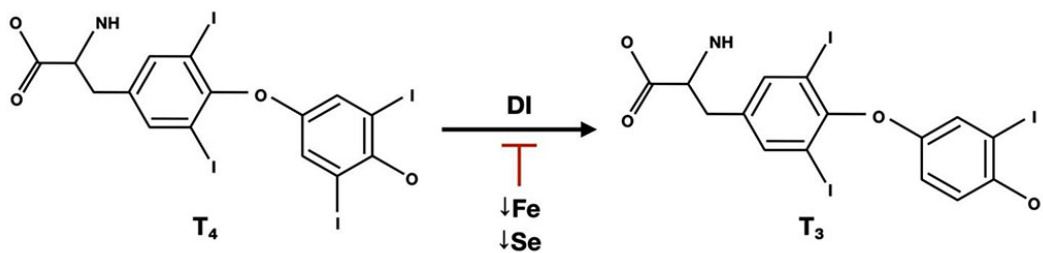


Figure 2. Impact of iron and selenium deficiency on the process of peripheral conversion in the human body cells. DI - deiodinase [14,23]

Impact of iron supplementation in hypothyroidism

We have found no prospective studies from 2016-2024, investigating the relation between iron supplementation and hypothyroidism. During a 15th international thyroid congress in Florida (2015) a work from Finland was shown, it established that iron supplementation with aim of increasing SF level above 100 µg/l may be beneficial to obtain better symptom control in patients on LT-4 therapy with proper hemoglobin concentration, although the research was conducted on a limited number of subjects, precisely 25 women [17].

Clinical presentation of hypothyroidism and anemia

Physicians must recognize that ID and hypothyroidism may present with similar clinical manifestations, such as fatigue, weakness, and concentration difficulty [11]. Moreover hypothyroidism correlates with prevalence of the anemia - in a publication from 2018 a pooled odds ratio of 1.84 was established for the risk of anemia in overt hypothyroidism [18]. It should be also stated that patients with autoimmune thyroid diseases exhibit an elevated chance of developing celiac disease, which may impair iron absorption and induce chronic inflammation in the small intestine [19].

SELENIUM

The role of selenium in the human body

Selenium is a microelement that plays a significant role in the proper development and maintenance of homeostasis in the human body. It participates in a wide variety of physiological processes, including the proper functioning of the thyroid gland and its role as an immunomodulator. Selenium has been identified as a component of selenoproteins and antioxidative enzymes. In humans, 25 selenoproteins have been characterized [20,21], from which at least 11 can be found in the thyroid gland [22].

The majority of selenoprotein family members have been classified as being involved in redox reactions. However, some are likely not enzymes themselves and require further investigation regarding their functions. The best-studied selenoproteins include glutathione peroxidases, thioredoxin reductases, iodothyronine deiodinases and methionine-R-sulfoxide reductase B1 (MSRB1). Among non-enzymatic selenoproteins, the most well-characterized in terms of immune cell function is selenoprotein K [23].

Glutathione peroxidases play a crucial role in protecting lipid membranes against oxidative stress. They catalyze the reduction of hydrogen peroxide. Iodothyronine deiodinases are involved in the activation of other thyroid hormone forms into the most active triiodothyronine (T3) (types 1 and 2) and in the inactivation of thyroxine (T4) and T3 (type 3). MSRB1 participates in the polymerization of F-actin during the innate immune response in macrophages. Other members of the selenoprotein family are involved in various functions, notably as mentioned earlier, in protection against oxidative stress and modulation of immune responses [23].

Epidemiology

According to the Food and Nutrition Board of the National Academy of Sciences (USA), the Recommended Dietary Allowance defined as average daily level of intake sufficient to meet the nutrient requirements of 97%–98% healthy individuals, for selenium is shown in the Table 1. [24].

Table 1. Food and Nutrition Board of the National Academy of Sciences recommendation for daily selenium intake [14].

Daily selenium intake	Population group
55 µg	Adults
60 µg	During pregnancy
70 µg	During lactation

As indicated by population studies, the average daily intake of selenium in European countries is 20–70 µg and in Poland 20–59 µg [20]. Its intake may widely differ between different populations because of varying concentrations of Se in the soil [25]. Due to low soil selenium, in some regions, such as Keshan in China, daily intake may be well below 20 µg per day. Such low intake has been connected with, among other conditions, Kaschin-Beck’s disease and endemic myxedematous cretinism. Although selenium seems to have some preventive influence on the development of mentioned disease, its exact role still remains uncertain [26]. Around 2 billion people worldwide may have selenium deficiency [27]. It’s been shown that excessive

intake and supplementation of selenium may also result in adverse effects such as nausea, vomiting, fever, dizziness, chest tightness, bloating, gastrointestinal problems, hair loss, and miscarriages [28]. A 300 µg per day dose of selenium taken for 5 years in a country with moderately-low Se status (Denmark) increased all-cause mortality 10 years later. The hazard ratio (95% confidence interval) for all-cause mortality comparing 300 µg per day dose of Se to placebo was 1.62 [29].

The role of selenium in the thyroid function

The crucial role of selenium proteins and compounds in synthesis of thyroid hormones, immunomodulation and protection from oxidative stress [30] are recognised as connected to hypothyroidism, especially in Hashimoto disease [31]. Selenium role in the peripheral conversion of T4 to T3 is shown in Figure 2.

Impact of selenium supplementation

According to Huwiler's et al. (2024) meta-analysis of 35 unique studies, selenium supplementation, most commonly at a dose of 200 µg, resulted in decreased TSH levels in individuals without thyroid hormone replacement therapy (THRT). Reduction of TPOAb levels was observed independently of THRT. No significant changes were found in fT4, T4, fT3, T3, TgAb, thyroid volume, interleukin (IL)-2, and IL-10. Of these 35 studies, 5 blinded studies evaluated the effect of selenium supplementation on quality of life in the population with hypothyroidism. From which two studies using the 12-item short-form health survey or unspecified questionnaire reported a higher percentage of improvement in well-being in selenium-treated patients compared with controls. The other three studies, measuring well-being with the 36-item short-form health survey questionnaire or the 12-item short-form health survey questionnaire found no significant difference in quality of life between the two groups [28].

In Larsen's et al. (2024) multicentre double-blinded randomised clinical trial, which included 412 adult patients with serum TPOAb level ≥ 100 IU/mL, supplementation of 200 µg Se in a form of Se-enriched yeast has shown no difference in Quality of life measured with ThyPRO-39 scales between selenium supplementation group and placebo group [32].

Co-supplementation with myo-inositol

Myo-inositol (MI) is a cyclic polyol with 6 hydroxyl groups. It is an important compound for the proper function of thyroid gland as it plays a role in iodine organification and thyroid hormone biosynthesis by the formation of hydrogen peroxide in thyrocytes. MI is a crucial part of the TSH signaling pathway and as such its insufficient concentration may increase the risk of the development of thyroid diseases such as hypothyroidism [33].

Recent studies also indicate that MI supplementation may have beneficial effects on thyroid function in patients with hypothyroidism. In the three studies that we analysed selenium was supplemented with the addition of MI. In all three studies equivalent to a daily dose of 600 mg MI plus 83 µg selenium was administered to the groups of patients assigned as research samples [34,35,36].

In the Payer's et al. (2022) study 148 female subjects - aged 18 to 50 - from 8 different centers of Slovakia received a combination treatment of selenium and MI for a duration of six months. They were included in the study based on TSH values, between 2.5-5 mU/l and positivity to antibodies TPOAb/TgAb, or otherwise values of TSH in the range 5-10 mU/l both with and without positivity to antibodies TPOAb/TgAb. TSH values were tested after 3 and 6 months. Significant decreases in the serum levels of TSH have been observed. In addition, a significant improvement was observed in the perception of the hypothyroidism symptoms such as, among others, level of fatigue, the perception of changes in weight, warm/cold tolerance, the perception of memory impairment over the treatment period [34].

In the Pace's et al. (2020) study 101 patients were selected based on history of treatment with selenomethionine (Se-meth) or combined Se-meth plus MI, TSH levels between 2.5 and 10 mIU/L, positive serum TgAb and/or TPOAb; USG pattern of chronic thyroiditis without the typical feature of nodular goiter. They were later divided into 3 groups. 29 untreated patients, 29 patients receiving Se-meth and 43 patients receiving Se-meth combined with MI. Each patient's blood samples were collected at the baseline and after 6 and 12 months of treatment in order to measure TSH, fT4 and fT3 serum levels. At the baseline TSH was significantly lower in the untreated group in comparison to both treated groups. After 6 months, no statistically relevant change in TSH was observed in the control group or the Se-meth group. In the Se-meth plus MI group, a considerable reduction in TSH was noted. After 12 months of treatment in the untreated group TSH level notably increased. In both treated groups there was an observed decrease in serum TSH levels. The decrease was more notable in the Se-meth plus Myo-I group. fT3 and fT4 changes were not significant in any of the observed groups [35].

In the Nordio's et al. (2017) study the supplementation of selenium was compared with the supplementation of selenium and MI combined. 168 patients with Hashimoto thyroiditis and TSH levels between 3 and 6 µIU/ml were enrolled into the study and randomized into 2 groups. The first group

received selenium and the second one - selenium combined with MI. Decreases of TSH level in the first group were noted as not significant over 6 months of treatment. In the second group a considerable decrease in serum TSH levels was reported over 6 months of treatment. There were statistically relevant differences in the TSH serum levels between the first and second group after the treatment. As a secondary result there was a notable decrease in TPOAb values in the second group and insignificant decrease in the first group. Also all patients reached improvement in the questionnaire evaluating subjective symptomatology. In the study changes in serum levels of fT4, fT3 and TgAb were not relevant in both groups [36].

ZINC

The role of zinc in the human body

Zinc is known to be one of the most important micronutrients for the functioning of the human body. It mainly plays a role in three categories: catalytic reactions, structural stability, and biological processes. It is a cofactor for more than 300 metalloenzymes, a structural component of several enzymes and a part of zinc finger proteins that work as transcription factors [37,38]. Zinc affects the immune system function, growth and wound healing [39,40]. Total concentration of zinc in an adult is 2-3 g, with the majority (90%) in skeletal muscles and bones and only about 0.5% in the blood [41]. With age the level of zinc in serum or blood plasma declines [37]. To maintain adequate levels it is necessary to provide this mineral from diet-based supplementation [42]. Zinc can be found mainly in meat, poultry, fish, liver and seafood, but also in whole grains, beans and soy products [41,43].

Epidemiology

Recommended Dietary Allowance for zinc according to the US National Academy of Medicine is shown in Table 2. [44]. Zinc deficiency is mainly caused by absence of meat in diet, excess phytates, chronic illnesses and aging. About 17% of the world population is exposed to zinc deficiency, with the highest risk in South Asia, sub-Saharan Africa and Central America [43]. Methods such as diversification of diet, fortification, biofortification and supplementation are used to cope with zinc deficiency [45].

Table 2. US National Academy of Medicine recommendations for daily zinc intake [44].

Daily zinc intake	Age in years
3 mg	1-3
4 mg	4-8
8 mg	9-13
9 mg	14-18 females
11 mg	14-18 males
8 mg	>19 females
11 mg	>19 males
11 mg	During pregnancy
12 mg	During lactation

The role of zinc in the thyroid function

Zinc influences the thyroid hormone metabolism on various levels. It takes part in the synthesis of thyrotropin-releasing hormone (TRH) in hypothalamus and the TSH in anterior pituitary gland. Zinc works as a cofactor of deiodinases type 1 and 2, which are necessary to convert T4 to metabolically more active T3. It is also involved in the structure of T3 nuclear receptors in cells, which allow T3 to work in peripheral tissues [41,46]. Although recent studies aimed to show the relation between zinc supplementation and thyroid hormone levels in human subjects, these are inconclusive. In a systematic review by Bessera et al. (2021) six clinical trials from different countries were analysed, which had assessed the effects of zinc supplementation on thyroid hormone concentrations in subjects with no thyroid disease and found no clear evidence on the relation between both [46]. In the Beserra’s (2021) case-control study researchers found no link between zinc intake, biochemical markers of zinc status, and thyroid hormone metabolism in obese

Impact of zinc supplementation

In Sivacumar’s et al. (2024) study, zinc supplementation in children and adolescents with autoimmune thyroiditis showed no impact on thyroid auto-antibodies or oxidative stress. However, unlike the control group, children receiving zinc supplements did not require an increase in their levothyroxine dosage [48]. Woźniak et al. (2021) showed that patients with hypothyroidism experience a positive improvement in their health, especially the condition of their hair thanks to supplementation of zinc [49]. In the Bessera et al. (2021) study, clinical trial was analysed, in which female subjects, with hypothyroidism and excessive weight, took 30mg per day of zinc gluconate for 6 weeks and achieved increase in fT3, no change in TSH and fT4 was reported [46].

Co-supplementation

According to Zawros et al. (2023) randomized study co-supplementation of zinc (25 mg per day) and selenium (200 µg per day) in overweight and obese people who undergo a hypocaloric diet does not affect function of thyroid hormones [50]. However, in Rabbani et al. (2021) randomized study of the effects of zinc (30 mg per day), vitamin A (25000 IU twice a week), and magnesium (250 mg per day) co-supplementation in patients with hypothyroidism during 10 week protocol, researchers found significant increase in serum fT4 and lower levels of high-sensitivity C-reactive protein (hs-CRP) [51].

Iodine

The role of iodine in the human body

Iodine can be assimilated into the human body from food, the richest products in this micronutrient are seafood, saltwater fishes and seaweed, other sources include freshwater fishes, meat, egg and dairy products. In the human digestive system iodine is reduced to iodide and subsequently absorbed in the stomach and duodenum [52]. In the thyroid gland sodium iodide symporters maintain transportation of iodide into the extracellular fluid [52], this allows 70% to 80% of iodine in the human body to be stored in the thyroid gland [14]. Iodine is a crucial micronutrient for adequate fetal development and its deficiency is associated with spontaneous abortion, higher risk of stillbirth and congenital anomalies. In neonates it may lead to endemic cretinism and infant mortality. In older children and adults it may cause impaired mental function, goitre, hypothyroidism and iodine-induced hyperthyroidism [53,54].

Epidemiology

Recommended daily intake of iodine differs from the age and increases during pregnancy and lactation (Table 3.) [55]. Due to broadly spread iodine deficiency around the world in the 20th century salt iodization was introduced in over 100 countries [56]. In 2018 it was estimated by UNICEF that 88% of the world population used iodized salt [57]. Iodine status should be monitored in all countries with the target of 90% households using iodized salt. In countries not reaching this goal, the World Health Organization (WHO) currently recommends iodine supplementation for specific groups. Oral supplementation of 250µg of iodine daily for pregnant and lactating women, 150µg for women in reproductive age and 90µg for children between 6 months and 2 years (younger children should intake an adequate dose of iodine with breast milk) is recommended [58].

Table 3. WHO/UNICEF recommendations for daily iodine intake [53].

Daily iodine intake	Age in years
90 µg	<6
120 µg	6-12
150 µg	>12
250 µg	Pregnant and lactating women

The role of iodine in the thyroid function

Iodine is the crucial subtract in the synthesis of thyroid hormones (Figure 1.). Due to the fact that most of the iodine is eliminated from the human body with urine, the easiest way to identify its deficiency or excess is to examine one's urinary iodine concentration (UIC) (Table 4.) [52].

Table 4. Criteria used to describe iodine status in children ≥6 years and adults (excluding specific norms for pregnant and lactating women) [53].

Median UIC	Iodine status
<100 µg/l	Insufficient
100-199 µg/l	Adequate
200-299 µg/l	Above adequate
≥300 µg/l	Excessive

In Weng's (2017) study, overt hypothyroidism was more prevalent in the low-iodine group (UIC <100 µg/L) than in the medium iodine group (UIC 100-299 µg/L) - this study was conducted on the healthy population i.e. with no history of thyroid diseases [59].

In the same study the authors have found that the risk of developing overt hypothyroidism was higher in the high-iodine (UIC >300 µg/L) group than in the medium-iodine group (UIC between 100 and 299 µg/L) [59] . In Katagiri's 2017 study the group with excessive iodine intake had higher risk of developing overt hypothyroidism (OR 2.78) compared to adequate iodine intake group [56]. It is important to add that both Weng's and Katagiri's publications analyse few of the same works [56,59]. Similar results had been found in other studies [60,61]. It is still not clear how excessive iodine intake may lead to hypothyroidism. Physiologically in a situation of high iodine concentration in the human body sodium-iodide symporter (NIS) activity is decreased, therefore release of thyroid hormones is suppressed for a few days, this situation is called Wolff–Chaikoff effect [56]. Dysregulation of this process may be one of the causes of prevalence of hypothyroidism observed in cited publications [56]. Also animal models have shown that high concentration of iodine might affect deiodinase function in pituitary gland and hypothalamus, which disrupt T4 to T3 conversion and thyroid negative feedback loop [61].

Impact of iodine supplementation

We haven't found studies investigating the problem of iodine deficiency and excessive intake in the population with hypothyroidism published since 2016.

DISCUSSION OF CONCLUSION

Research in endocrinology and nutraceuticals is constantly evolving. Recent clinical trials, meta-analyses, and systematic reviews provide new insights, sometimes contradicting previous findings or refining existing knowledge about the role of these micronutrients in hypothyroidism treatment. In this study, we conducted extensive research on the topic of micronutrient supplementation in hypothyroidism. This topic has been broadly explored, and in the conclusion, we aim to highlight the most important findings from this work.

However iron plays several important roles in the human body, including regulation of thyroid hormones activity, we have found only one prospective study showing benefits of iron supplementation in hypothyroidism. Importantly for physicians, iron deficiency can present with symptoms similar to hypothyroidism, making it crucial to differentiate and treat these conditions. This is particularly important because iron deficiency is a risk factor for hypothyroidism, and conversely, hypothyroidism can contribute to iron deficiency.

Selenium supplementation in hypothyroidism reduces TSH level without significantly affecting the levels of T3 and T4 hormones. The impact of selenium on quality of life is controversial, and there is still a lack of systematic studies on this topic. The addition of myo-inositol to selenium enhances its effect on lowering TSH, so their co-supplementation appears to work better than selenium supplementation alone.

Despite the strong influence of zinc on thyroid hormones metabolism and conversion, there is still a lack of definitive evidence regarding the positive effects of supplementing this element in cases of hypothyroidism.

Our study once more confirmed that both iodine deficiency and excessive iodine intake can lead to hypothyroidism. Therefore, WHO recommends that salt iodization should be continued in parallel with the need to monitor iodine status in populations. The studies cited in this work refer only to patients with no history of thyroid disease. The impact of iodine supplementation in patients with hypothyroidism remains unclear and requires further investigation.

Lastly, although there is plenty of research on the impact of microelements status on the function of thyroid, there is still a lack of prospective studies examining the clinical and biochemical benefits of microelements

REFERENCE

1. Taylor, P. N., Albrecht, D., Scholz, A., Gutierrez-Buey, G., Lazarus, J. H., Dayan, C. M., & Okosieme, O. E. (2018). Global epidemiology of hyperthyroidism and hypothyroidism. *Nature reviews Endocrinology*, 14(5), 301–316. DOI: [10.1038/nrendo.2018.18](https://doi.org/10.1038/nrendo.2018.18)
2. Kocelak, P., Mossakowska, M., Puzianowska-Kuźnicka, M., Sworczak, K., Wyszomirski, A., Handzlik, G., Stefański, A., Zdrojewski, T., & Chudek, J. (2022). Prevalence and risk factors of untreated thyroid dysfunctions in the older Caucasian adults: Results of PolSenior 2 survey. *PLoS ONE*, 17(8), e0272045. DOI: [10.1038/nrendo.2018.18](https://doi.org/10.1038/nrendo.2018.18)
3. Mendes, D., Alves, C., Silverio, N., & Marques, F. B. (2019). Prevalence of Undiagnosed Hypothyroidism in Europe: A Systematic Review and Meta-Analysis. *European Thyroid Journal*, 8(3), 130–143. DOI: [10.1159/000499751](https://doi.org/10.1159/000499751)
4. Zamwar, U. M., & Muneshwar, K. N. (2023). Epidemiology, Types, Causes, Clinical Presentation, Diagnosis, and Treatment of Hypothyroidism. *Cureus*, 15(9), e46241. DOI: [10.7759/cureus.46241](https://doi.org/10.7759/cureus.46241)
5. Almandoz, J. P., & Gharib, H. (2012). Hypothyroidism: Etiology, diagnosis, and management. *Medical Clinics of North America*, 96(2), 203–221. DOI: [10.1016/j.mcna.2012.01.005](https://doi.org/10.1016/j.mcna.2012.01.005)
6. El-Shafie K. T. (2003). Clinical presentation of hypothyroidism. *Journal of family & community medicine*, 10(1), 55–58.
7. Baldini, I., Vita, A., Mauri, M. C., Amodei, V., Carrisi, M., Bravin, S., & Cantalamessa, L. (1997). Psychopathological and cognitive features in subclinical hypothyroidism. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 21(6), 925–935. DOI: [10.1016/S0278-5846\(97\)00089-4](https://doi.org/10.1016/S0278-5846(97)00089-4)
8. Jorde, R., Waterloo, K., Storhaug, H., Nyrnes, A., Sundsfjord, J., & Jenssen, T. G. (2006). Neuropsychological Function and Symptoms in Subjects with Subclinical Hypothyroidism and the Effect of Thyroxine Treatment. *The Journal of Clinical Endocrinology & Metabolism*, 91(1), 145–153. DOI: [10.1210/jc.2005-1775](https://doi.org/10.1210/jc.2005-1775)
9. Grand view research. (2022). Europe Dietary Supplements Market Size, Share Report, 2030. Available from: https://www.grandviewresearch.com/industry-analysis/europe-dietary-supplements-market-report?fbclid=IwY2xjawIgZrdleHRuA2FlbQIxMAABHe4RzaMX25OUYpc_qT63zQkBWLuABr_nKgrMmRvGGjRWQJgkaOITtuBxA_aem_SeAZA7u8OQTSLvtxxeqkwQ [Accessed 17 February 2024]
10. Ahmed, M. H., Ghatge, M. S., & Safo, M. K. (2020). Hemoglobin: structure, function and allostery. *Sub-cellular Biochemistry/Subcellular Biochemistry*, 345–382. DOI: [10.1007/978-3-030-41769-7_14](https://doi.org/10.1007/978-3-030-41769-7_14)
11. Kassebaum, N. J., & GBD 2013 Anemia Collaborators (2016). The Global Burden of Anemia. *Hematology/oncology clinics of North America*, 30(2), 247–308. DOI: [10.1016/j.hoc.2015.11.002](https://doi.org/10.1016/j.hoc.2015.11.002)
12. Garofalo, V., Condorelli, R. A., Cannarella, R., Aversa, A., Calogero, A. E., & La Vignera, S. (2023). Relationship between Iron Deficiency and Thyroid Function: A Systematic Review and Meta-Analysis. *Nutrients*, 15(22), 4790. DOI: [10.3390/nu15224790](https://doi.org/10.3390/nu15224790)
13. Zimmermann, M. B., & Köhrle, J. (2002). The impact of iron and selenium deficiencies on iodine and thyroid metabolism: biochemistry and relevance to public health. *Thyroid*, 12(10), 867–878. DOI: [10.1089/105072502761016494](https://doi.org/10.1089/105072502761016494)
14. O'Kane, S. M., Mulhern, M. S., Pourshahidi, L. K., Strain, J. J., & Yeates, A. J. (2018). Micronutrients, iodine status and concentrations of thyroid hormones: a systematic review. *Nutrition reviews*, 76(6), 418–431. DOI: [10.1093/nutrit/nuy008](https://doi.org/10.1093/nutrit/nuy008)
15. Luo, J., Wang, X., Yuan, L., & Guo, L. (2021). Iron Deficiency, a Risk Factor of Thyroid Disorders in Reproductive-Age and Pregnant Women: A Systematic Review and Meta-Analysis. *Frontiers in endocrinology*, 12, 629831. DOI: [10.3389/fendo.2021.629831](https://doi.org/10.3389/fendo.2021.629831)
16. Zhang, H. Y., Teng, X. C., Shan, Z. Y., Wang, Z. J., Li, C. Y., Yu, X. H., Mao, J. Y., Wang, W. W., Xie, X. C., & Teng, W. P. (2019). Association between iron deficiency and prevalence of thyroid autoimmunity in pregnant and non-pregnant women of childbearing age: a cross-sectional study. *Chinese medical journal*, 132(18), 2143–2149. DOI: [10.1097/CM9.0000000000000409](https://doi.org/10.1097/CM9.0000000000000409)
17. 15TH INTERNATIONAL THYROID CONGRESS PROGRAM AND MEETING ABSTRACTS. (2015). *Thyroid : official journal of the American Thyroid Association*, 25 Suppl 1, P1–A337. DOI: [10.1089/thy.2015.29004.abstracts](https://doi.org/10.1089/thy.2015.29004.abstracts)
18. Wopereis, D. M., Du Puy, R. S., Van Heemst, D., Walsh, J. P., Bremner, A., Bakker, S. J. L., Bauer, D. C., Cappola, A. R., Ceresini, G., Degryse, J., Dullaart, R. P. F., Feller, M., Ferrucci, L., Floriani, C., Franco, O. H., Iacoviello, M., Iervasi, G., Imaizumi, M., Wouter Jukema, J., Den Elzen, W. P. J. (2018). The relation between thyroid function and anemia: A pooled analysis of individual participant data.

- Journal of Clinical Endocrinology and Metabolism*, 103(10), 3658-3667. DOI: [10.1210/jc.2018-00481](https://doi.org/10.1210/jc.2018-00481)
19. Starchl, C., Scherkl, M., & Amrein, K. (2021). Celiac Disease and the Thyroid: Highlighting the Roles of Vitamin D and Iron. *Nutrients*, 13(6), 1755. DOI: [10.3390/nu13061755](https://doi.org/10.3390/nu13061755)
20. Stuss, M., Michalska-Kasiczak, M., & Sewerynek, E. (2017). The role of selenium in thyroid gland pathophysiology. *Endokrynologia Polska*, 68(4), 440–465. DOI: [10.5603/EP.2017.0051](https://doi.org/10.5603/EP.2017.0051)
21. Kryukov, G. V., Castellano, S., Novoselov, S. V., Lobanov, A. V., Zhehtab, O., Guigo, R., & Gladyshev, V. N. (2003). Characterization of Mammalian Selenoproteomes. *Science*, 300(5624), 1439–1443. DOI: [10.1126/science.1083516](https://doi.org/10.1126/science.1083516)
22. Schmutzler, C., Mentrup, B., Schomburg, L., Hoang-Vu, C., Herzog, V., & Köhrle, J. (2007). Selenoproteins of the thyroid gland: expression, localization and possible function of glutathione peroxidase 3. *Biological Chemistry*, 388(10), 1053–1059. DOI: [10.1515/BC.2007.122](https://doi.org/10.1515/BC.2007.122)
23. Avery, J. C., & Hoffmann, P. R. (2018). Selenium, Selenoproteins, and Immunity. *Nutrients*, 10(9), 1203. DOI: [10.3390/nu10091203](https://doi.org/10.3390/nu10091203)
24. National Institutes of Health Office of Dietary Supplements. (2021). Selenium Fact Sheet for Health Professionals. Available from: <https://ods.od.nih.gov/factsheets/selenium-healthprofessional/> [Accessed 29 January 2024]
25. Winther, K. H., Rayman, M. P., Bonnema, S. J., & Hegedüs, L. (2020). Selenium in thyroid disorders — essential knowledge for clinicians. *Nature Reviews Endocrinology*, 16(3), 165–176. DOI: [10.1038/s41574-019-0311-6](https://doi.org/10.1038/s41574-019-0311-6)
26. Alexander, J., & Olsen, A. K. (2023). Selenium - a scoping review for Nordic Nutrition Recommendations 2023. *Food & nutrition research*, 67, 10.29219/fnr.v67.10320. DOI: [10.29219/fnr.v67.10320](https://doi.org/10.29219/fnr.v67.10320)
27. Köhrle, J. (2020). Selenium in Endocrinology—Selenoprotein-Related Diseases, population studies, and Epidemiological evidence. *Endocrinology*, 162(2). DOI: [10.1210/endocr/bqaa228](https://doi.org/10.1210/endocr/bqaa228)
28. Huwiler, V. V., Maissen-Abgottspon, S., Stanga, Z., Mühlebach, S., Trepp, R., Bally, L., & Bano, A. (2024). Selenium Supplementation in Patients with Hashimoto Thyroiditis: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. *Thyroid : official journal of the American Thyroid Association*, 34(3), 295–313. DOI: [10.1089/thy.2023.0556](https://doi.org/10.1089/thy.2023.0556)
29. Rayman, M. P., Winther, K. H., Pastor-Barriuso, R., Cold, F., Thvilum, M., Stranges, S., Guallar, E., & Cold, S. (2018). Effect of long-term selenium supplementation on mortality: Results from a multiple-dose, randomised controlled trial. *Free radical biology & medicine*, 127, 46–54. DOI: [10.1016/j.freeradbiomed.2018.02.015](https://doi.org/10.1016/j.freeradbiomed.2018.02.015)
30. Ruggeri, R. M., D'Ascola, A., Vicchio, T. M., Campo, S., Gianì, F., Giovino, S., Frasca, F., Cannavò, S., Campenni, A., & Trimarchi, F. (2020). Selenium exerts protective effects against oxidative stress and cell damage in human thyrocytes and fibroblasts. *Endocrine*, 68(1), 151–162. DOI: [10.1007/s12020-019-02171-w](https://doi.org/10.1007/s12020-019-02171-w)
31. Batóg, G., Dołoto, A., Bąk, E., Piątkowska-Chmiel, I., Krawiec, P., Pac-Kożuchowska, E., & Herbet, M. (2023). The interplay of oxidative stress and immune dysfunction in Hashimoto's thyroiditis and polycystic ovary syndrome: a comprehensive review. *Frontiers in immunology*, 14, 1211231. DOI: [10.3389/fimmu.2023.1211231](https://doi.org/10.3389/fimmu.2023.1211231)
32. Larsen, C., Winther, K. H., Cramon, P. K., Rasmussen, Å. K., Feldt-Rasmussen, U., Knudsen, N. J., Bjorner, J. B., Schomburg, L., Demircan, K., Chillon, T. S., Gram, J., Hansen, S. G., Brandt, F., Nygaard, B., Watt, T., Hegedus, L., & Bonnema, S. J. (2024). Selenium supplementation and placebo are equally effective in improving quality of life in patients with hypothyroidism. *European thyroid journal*, 13(1), e230175. DOI: [10.1530/ETJ-23-0175](https://doi.org/10.1530/ETJ-23-0175)
33. Paparo, S. R., Ferrari, S. M., Patrizio, A., Elia, G., Ragusa, F., Botrini, C., Balestri, E., Guarneri, F., Benvenga, S., Antonelli, A., & Fallahi, P. (2022). Myoinositol in Autoimmune Thyroiditis. *Frontiers in endocrinology*, 13, 930756. DOI: [10.3389/fendo.2022.930756](https://doi.org/10.3389/fendo.2022.930756)
34. Payer, J., Jackuliak, P., Kužma, M., Džupon, M., & Vaňuga, P. (2022). Supplementation with myo-inositol and Selenium improves the clinical conditions and biochemical features of women with or at risk for subclinical hypothyroidism. *Frontiers in endocrinology*, 13, 1067029. DOI: [10.3389/fendo.2022.1067029](https://doi.org/10.3389/fendo.2022.1067029)
35. Pace, C., Tumino, D., Russo, M., Le Moli, R., Naselli, A., Borzì, G., Malandrino, P., & Frasca, F. (2020). Role of selenium and myo-inositol supplementation on autoimmune thyroiditis progression. *Endocrine journal*, 67(11), 1093–1098. DOI: [10.1507/endocrj.EJ20-0062](https://doi.org/10.1507/endocrj.EJ20-0062)
36. Nordio, M., & Basciani, S. (2017). Myo-inositol plus selenium supplementation restores euthyroid state in Hashimoto's patients with subclinical hypothyroidism. *European review for medical and pharmacological sciences*, 21(2 Suppl), 51–59. PMID: 28724185
37. Kravchenko, V., & Zakharchenko, T. (2023). Thyroid hormones and minerals in immunocorrection of

- disorders in autoimmune thyroid diseases. *Frontiers in endocrinology*, 14, 1225494. DOI: [10.3389/fendo.2023.1225494](https://doi.org/10.3389/fendo.2023.1225494)
38. Tuerk, M. J., & Fazel, N. (2009). Zinc deficiency. *Current opinion in gastroenterology*, 25(2), 136–143. DOI: [10.1097/MOG.0b013e328321b395](https://doi.org/10.1097/MOG.0b013e328321b395)
39. Sanna, A., Firinu, D., Zavattari, P., & Valera, P. (2018). Zinc Status and Autoimmunity: A Systematic Review and Meta-Analysis. *Nutrients*, 10(1), 68. DOI: [10.3390/nu10010068](https://doi.org/10.3390/nu10010068)
40. Lin, P., Sermersheim, M., Li, H., Lee, P. H. U., Steinberg, S. M., & Ma, J. (2017). Zinc in wound healing modulation. *Nutrients*, 10(1), 16. <https://doi.org/10.3390/nu10010016>
41. Severo, J. S., Morais, J. B. S., de Freitas, T. E. C., Andrade, A. L. P., Feitosa, M. M., Fontenelle, L. C., de Oliveira, A. R. S., Cruz, K. J. C., & do Nascimento Marreiro, D. (2019). The Role of Zinc in Thyroid Hormones Metabolism. *International journal for vitamin and nutrition research*, 89(1-2), 80–88. DOI: [10.1024/0300-9831/a000262](https://doi.org/10.1024/0300-9831/a000262)
42. Stiles, L. I., Ferrao, K., & Mehta, K. J. (2024). Role of zinc in health and disease. *Clinical and Experimental Medicine*, 24(1). DOI: [10.1007/s10238-024-01302-6](https://doi.org/10.1007/s10238-024-01302-6)
43. Maxfield, L., Shukla, S., & Crane, J. S. (2019). *Zinc Deficiency*. StatPearls - NCBI Bookshelf. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK493231> [Accessed 29 January 2024]
44. Institute of Medicine (US) Panel on Micronutrients. (2001). Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. Washington (DC): National Academies Press (US). Available from: <https://www.ncbi.nlm.nih.gov/books/NBK222310/> [Accessed 29 January 2024]
45. Roohani, N., Hurrell, R., Kelishadi, R., & Schulin, R. (2013). Zinc and its importance for human health: An integrative review. *Journal of research in medical sciences : the official journal of Isfahan University of Medical Sciences*, 18(2), 144–157.
46. Beserra, J. B., Morais, J. B. S., Severo, J. S., Cruz, K. J. C., de Oliveira, A. R. S., Henriques, G. S., & do Nascimento Marreiro, D. (2021). Relation Between Zinc and Thyroid Hormones in Humans: a Systematic Review. *Biological trace element research*, 199(11), 4092–4100. DOI: [10.1007/s12011-020-02562-5](https://doi.org/10.1007/s12011-020-02562-5)
47. Beserra, J. B., Morais, J. B. S., Severo, J. S., Cruz, K. J. C., de Oliveira, A. R. S., de Oliveira, F. E., de Matos Neto, E. M., Henriques, G. S., & Marreiro, D. D. N. (2021). No association between zinc and thyroid activity in obese women. *International journal for vitamin and nutrition research*, 91(1-2), 40–47. DOI: [10.1024/0300-9831/a000600](https://doi.org/10.1024/0300-9831/a000600)
48. Sivakumar, R. R., Chinnaiiah Govindareddy, D., Sahoo, J., Bobby, Z., & Chinnakali, P. (2024). Effect of daily zinc supplementation for 12 weeks on serum thyroid auto-antibody levels in children and adolescents with autoimmune thyroiditis - a randomized controlled trial. *Journal of pediatric endocrinology & metabolism : JPEM*, 37(2), 137–143. DOI: [10.1515/jpem-2023-0165](https://doi.org/10.1515/jpem-2023-0165)
49. Woźniak, D., Drzymała, S., Przysławski, J., & Drzymała-Czyż, S. (2021). Dietary supplements in hypothyroidism. *Acta scientiarum polonorum. Technologia alimentaria*, 20(4), 375–381. DOI: [10.17306/J.AFS.0985](https://doi.org/10.17306/J.AFS.0985)
50. Zavros, A., Andreou, E., Aphamis, G., Bogdanis, G. C., Sakkas, G. K., Roupas, Z., & Giannaki, C. D. (2023). The Effects of Zinc and Selenium Co-Supplementation on Resting Metabolic Rate, Thyroid Function, Physical Fitness, and Functional Capacity in Overweight and Obese People under a Hypocaloric Diet: A Randomized, Double-Blind, and Placebo-Controlled Trial. *Nutrients*, 15(14), 3133. DOI: [10.3390/nu15143133](https://doi.org/10.3390/nu15143133)
51. Rabbani, E., Golgiri, F., Janani, L., Moradi, N., Fallah, S., Abiri, B., & Vafa, M. (2021). Randomized Study of the Effects of Zinc, Vitamin A, and Magnesium Co-supplementation on Thyroid Function, Oxidative Stress, and hs-CRP in Patients with Hypothyroidism. *Biological trace element research*, 199(11), 4074–4083. DOI: [10.1007/s12011-020-02548-3](https://doi.org/10.1007/s12011-020-02548-3)
52. Lisco, G., De Tullio, A., Triggiani, D., Zupo, R., Giagulli, V. A., De Pergola, G., Piazzolla, G., Guastamacchia, E., Sabbà, C., & Triggiani, V. (2023). Iodine Deficiency and Iodine Prophylaxis: An Overview and Update. *Nutrients*, 15(4), 1004. DOI: [10.3390/nu15041004](https://doi.org/10.3390/nu15041004)
53. World Health Organization. (2007). Assessment of iodine deficiency Disorders and Monitoring their Elimination: A Guide for Programme Managers, Third edition. Available from: https://iris.who.int/bitstream/handle/10665/43781/9789241595827_eng.pdf?sequence=1 [Accessed 29 January 2024]
54. World Health Organization. (2014). Fortification of food-grade salt with iodine for the prevention and control of iodine deficiency disorders. WHO guidelines approved by the Guidelines Review Committee. Available from: <https://www.who.int/publications/i/item/9789241507929> [Accessed 29 January 2024]
55. Rayman M. P. (2019). Multiple nutritional factors and thyroid disease, with particular reference to autoimmune thyroid disease. *The Proceedings of the Nutrition Society*, 78(1), 34–44. DOI: [10.1017/S0029665118001192](https://doi.org/10.1017/S0029665118001192)

56. Katagiri, R., Yuan, X., Kobayashi, S., & Sasaki, S. (2017). Effect of excess iodine intake on thyroid diseases in different populations: A systematic review and meta-analyses including observational studies. *PloS one*, 12(3), e0173722. DOI: [10.1371/journal.pone.0173722](https://doi.org/10.1371/journal.pone.0173722)
57. Zimmermann, M. B., & Andersson, M. (2021). GLOBAL ENDOCRINOLOGY: Global perspectives in endocrinology: coverage of iodized salt programs and iodine status in 2020. *European Journal of Endocrinology*, 185(1), R13–R21. DOI: [10.1530/EJE-21-0171](https://doi.org/10.1530/EJE-21-0171)
58. World Health Organization, UNICEF. (2007). Reaching optimal iodine nutrition in pregnant and lactating women and young children. Available from: https://cdn.who.int/media/docs/default-source/nutritionlibrary/reaching-optimal-iodine-nutrition-in-pregnant-and-lactating-women-and-young-children.pdf?sfvrsn=4f864061_2 [Accessed 29 January 2024]
59. Weng, W., Dong, M., Zhang, J., Yang, J., Zhang, B., & Zhao, X. (2017). A PRISMA-compliant systematic review and meta-analysis of the relationship between thyroid disease and different levels of iodine intake in mainland China. *Medicine*, 96(25), e7279. DOI: [10.1097/MD.00000000000007279](https://doi.org/10.1097/MD.00000000000007279)
60. Jeon, M. J., Kim, W. G., Kwon, H., Kim, M., Park, S., Oh, H. S., Han, M., Kim, T. Y., Shong, Y. K., & Kim, W. B. (2017). Excessive Iodine Intake and Thyrotropin Reference Interval: Data from the Korean National Health and Nutrition Examination Survey. *Thyroid : official journal of the American Thyroid Association*, 27(7), 967–972. DOI: [10.1089/thy.2017.0078](https://doi.org/10.1089/thy.2017.0078)
61. Shan, Z., Chen, L., Lian, X., Liu, C., Shi, B., Shi, L., Tong, N., Wang, S., Weng, J., Zhao, J., Teng, X., Yu, X., Lai, Y., Wang, W., Li, C., Mao, J., Li, Y., Fan, C., & Teng, W. (2016). Iodine Status and Prevalence of Thyroid Disorders After Introduction of Mandatory Universal Salt Iodization for 16 Years in China: A Cross-Sectional Study in 10 Cities. *Thyroid : official journal of the American Thyroid Association*, 26(8), 1125–1130. DOI: [10.1089/thy.2015.0613](https://doi.org/10.1089/thy.2015.0613)

[back](#)