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ISSUE 6: MARCH 2025
THYROID HEALTH

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WELCOME

Clare Grundel
Managing Editor

TO KICK OFF 2025, WE FOCUS ON THE THYROID

The thyroid is a gland with major physiological roles throughout our lifespan, in terms of growth, development and metabolism. Dysfunction of the thyroid has far-reaching impacts, from energy, weight, mental health, digestion and more. Nutrition and key nutrients have a role to play in thyroid health.

We open this edition with a feature article from the NED Editorial Board and Expert Review Panel. Masterminded by the NED Board, Editor Dr Jessica Rigutto lead a team of NED reviewers to answer key questions related to the thyroid, nutrition and lifestyle medicine. Backed by research, it provides a high-level overview of the science on this topic. With many thanks to Jessica for being the front runner in what will become a series of 'key question' papers from NED and with a special mention to Chloe Steele for stepping in with drafting and editorial comment.

The feature is followed by a series of expert reviews on newly released science, which provide summary overviews of an article and clinical takeaways for you to apply to your own decision making with clients.

Looking forward, we are planning and anticipating some lively nutrition and lifestyle medicine debate at the 2025 NED Science Forum on 13 May at The Royal Society of Medicine in London. Over 4 hours of presentation, debate and networking with industry leaders, peers and sponsors. Topics include The Battle of the Polyphenols and The Art and Science of Nutritional Therapy and Lifestyle Medicine. With presentations from Professor Justin Roberts, Tanya Borowski, Ben Brown and others. We expect tickets to sell fast. Grab yours here now.

The **British Association of Nutrition and Lifestyle Medicine (BANT)** is a professional membership body for nutrition practitioners, trained in nutrition sciences and the delivery of personalised nutrition services. BANT members are reading and interpreting nutrition and lifestyle sciences such as that found in this NED Journal on a routine basis to inform their clinical decision making. You can find the BANT member practitioner listing **here**.

The **Nutrition Evidence Database** is one of the ways that BANT contributes to the evidence-based practice of precision nutrition. BANT is delighted to make this resource open access for all and encourages all healthcare practitioners interested in personalised healthcare to make use of the resource on a regular basis. You can subscribe to receive monthly NED alerts **here**.

Read previous copies of the NED Journal **here** which BANT produces and makes available open access to all. BANT aims to bring good nutrition and lifestyle sciences to the forefront of healthcare and is able to do this through its ambition, careful management and the support of sponsors and advertisers. Thanks to the organisations who have supported this edition - **VitOrtho.**

Give your thyroid some love - read on.

IN THIS ISSUE

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EDITOR

Dr Jessica Rigutto, MPharm, MPH, Dr. sc. ETH Zurich, DipION, MBANT - NED Editor

Dr Jessica Rigutto is specialized in micronutrient nutrition and nutrition methodology meta-research. With a focus on vulnerable groups including children and women, Jessica uses individual- and population-level data to construct evidence-based nutrient profiles that inform intervention design and advise public health policy. Jessica also leads international initiatives to support and promote standards in the science of nutrition for improved translation of nutrition research findings. She teaches across diverse topics in human nutrition at under- and graduate level, as well as on nutrition research procedures and scientific integrity, and is a sought-after speaker on these subjects externally. .

She has contributed to policy guidance for WHO, UNICEF and the OECD and is widely published in the peer-reviewed, scientific press. Alumnus of the European Nutrition Leadership Platform, she is the current director of the Advanced Seminar. Jessica holds a Doctor of Science in human nutrition from ETH Zürich, Switzerland, as well as master's degrees in international public health and pharmacy. She is a registered nutritionist with BANT and a Kharrazian Institute Certified Functional Medicine Health ConsultantTM

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MEET THE NED EXPERT REVIEWERS

Our Expert Reviewers work within the nutrition industry in academia, research, clinical practice and wider healthcare, and provide unique and invaluable insights on the latest nutrition research to enable practitioners to apply the science to clinical practice.

Knowledge sharing is a key strategic pillar for the NED editorial team. Not only do the expert reviews get directly published on the NED database, they are further communicated via a series of monthly resources and across our BANT social media channels reaching in excess of 25,000 practitioners and followers.

EXPERT REVIEWERS IN THIS ISSUE

(In order of appearance)

Wilma Kirsten MSc

Wilma has been in clinical practice since 2005. The topic for her MSc dissertation project was “The impact of Coenzyme Q10 deficiency in late-onset Alzheimer’s disease in patients who use cholesterol lowering medication”. She furthermore obtained two honours science degrees, one in Nutritional Therapy and the other in Molecular Cell Biology and Health Sciences. Wilma specialises in digestive disorders (IBS and IBD), female hormonal well-being (PMS and menopause), and mental health. She has successfully helped hundreds of patients address symptoms of ill health in her clinic. Wilma is furthermore the author of the popular science book, “Ideal Plate Composition - Choose Food to Help You Be Your Best Self”.

Chloe Steele MSc

Chloe has an MSc in Personalised Nutrition from the University of Middlesex, and specialises in cardiovascular disease, type 2 diabetes, and anxiety. Chloe started her career at BANT as a member of the Nutrition Evidence Database research team and now has over 5 years experience of research and writing. She has worked in several countries, and is currently in Australia, where she worked for Nutrition Australia and is currently the principal nutritionist for Heart Research Australia. She has published two papers in the Nutrition Medicine Journal, on gut microbiota and collagen. Chloe is a member of BANT and the Nutrition Society of Australia and sits on the editorial board for the Nutrition Medicine Institute in the UK.

Kirsty Baxter MSc

Kirsty is a BANT and Registered Nutritional Therapy Practitioner, who has been in practice since 2016, with a Master of Science in Nutrition (Advanced Research and Practice) and research project on the nutritional therapy approach to harnessing psychological aspects of obesity weight loss. from London South Bank University. She works collaboratively with a wide range of GPs and doctors, giving presentations to support awareness around the nutritional intervention for metabolic conditions.

Miranda Harris MSc

Miranda is a member of BANT and a CNHC Registered Nutritional Therapy Practitioner with over 10 years clinical experience, specialising in endurance sport. She is a senior lecturer (SFHEA) focusing on research methods, dissertation supervision and sports nutrition on the Nutrition and Lifestyle Medicine MSc course at the University of Worcester. She has recently published in the European Journal of Integrated Medicine and the Journal of Nutrition and Health and is working towards a PhD by publication. She is a keen triathlete training for Ironman.

Nicky Ester MSc

Nicky received her Masters in Nutrition from University College Cork in Ireland. She also has a diploma in nutritional medicine and has trained as Natural Chef. She brings with her over 20 years' experience of working within the Health and Wellbeing sector, 10 years of which were spent in her own private clinical practice. Throughout her career she has given lectures to help increase the awareness of nutrition and its importance in relation to optimal health and well-being. She is passionate about empowering individuals to understand the role they play in their health in order to create meaningful and lasting change.

Daniel Quinones MSc

Daniel Quinones is a BANT and CNHC Registered Nutritional Therapist. He obtained his nutritional therapy diploma from the College of Naturopathic Medicine and MSc in Personalised Nutrition from CNELM, Middlesex University. Daniel contributes to Nutrition Evidence through his clinical experience working with weight loss clients and research into the drivers of obesity.

Georgie Murphy MSc

Georgie is a Registered Nutritional Therapist and BANT member. She studied Nutritional Therapy at the College of Naturopathic Medicine in London. Prior to this she completed her MSc in Nutrition at King's College London and BSc in Biomedical Science from University College Dublin. Georgie brings experience working as the Head of Nutrition at a personalised nutrition start-up. As well this she has experience in supplement development, clinical research, biotech and early-stage clinical trials. Her passion and areas of specialism include gut health and how it affects skin health.

Anna Papoutsa MSc

Anna is a Registered Nutritional Therapy Practitioner and a member of BANT, holding an MSc in Personalised Nutrition and a PGCert in Higher Education. Her dissertation delved into the intricate relationship between dietary refined carbohydrates and the onset of gout in overweight individuals, highlighting a beneficial role of magnesium in managing hyperuricaemia. Anna is dedicated to supporting clients in optimising their health, with a particular focus on cardio-metabolic and immune function disorders. Committed to staying at the forefront of nutritional science and technology, Anna integrates AI-driven tools and laboratory assessment insights into her practice to offer advanced, data-driven nutritional recommendations and support. Beyond her clinical work, she teaches and lectures at the Centre for Nutrition Education & Lifestyle Management (CNELM), where she leads BSc and MSc modules.

Ana-Paula Agrela MSc

Ana is a Nutrition Consultant, and Health Coach who graduated with a BSc. (Hons) in Nutritional Science from Middlesex University and holds a Health Coaching certificate from Zest for Life. She completed her Master's degree in Holistic Health and Nutritional Education through Hawthorn University in the United States. Ana has over 20 years' experience in researching and developing health supplements for the nutraceutical industry. She also offers group education programs and private consultations to help clients make healthier food choices and lifestyle habits.

Gail Brady MSc

Gail is a Registered Nutritional Therapy Practitioner RCNHC MBANT. She qualified is 2013 from The Institute for Optimum Nutrition in London and has since furthered her studies and completed a Master's of Science (MSc) degree in Advanced Nutrition (Research and Practice). The topic for her MSc dissertation project was menopause and potential diet and lifestyle interventions that my help to prevent weight gain. In clinical practice, Gail specialises in female health and works 1:1 with clients using a Functional Medicine framework. She also runs an online course providing a tool kit for managing perimenopause and menopause.

Carol Granger DProf

Carol is a Registered Nutritional Therapist and microbiologist. She completed research for a professional doctorate at the University of Westminster on the practice of nutritional therapy for people affected by cancer. She is a chartered biologist with a degree in biochemistry and a Master's in microbiology and brings to Nutrition Evidence her experience from a health and life sciences career over 30 years, and a personal commitment to evidence-based practice, professional regulation and inter-professional collaboration. Carol is co-chair of the Research Council for Complementary Medicine (RCCM), a director of the British Society for Integrative Oncology, and participates in the National Institute for Health Research Collaboration on nutrition and cancer.

Karin Elgar PhD

Following the completion of a PhD in Physiology and a career in the pharmaceutical industry, Karin graduated as a nutritional therapist from the Institute of Optimum Nutrition in 2004. She has since been practicing in the Greater Manchester area, specialising in women's health and autoimmunity. Karin has written a number of literature reviews and carried out a variety of research and editing projects. She has also delivered CPD seminars and webinars on various topics.

THE THYROID: CONSIDERATIONS FOR NUTRITIONAL THERAPY AND PERSONALISED LIFESTYLE SUPPORT

Authors: Chloe Steele[1], Ana-Paula Agrela[2], Gail Brady[3], Nicky Ester[4], Anna Papoutsa Shue[5], Jessica Rigutto[6]*

Abstract

The thyroid gland has major physiological roles in growth, development and metabolism, from conception to older age. Thyroid function is associated with some of the major causes of morbidity and mortality globally, and dysfunction of the thyroid gland can impact daily quality of life through its effects on energy, muscle strength, body weight, bowel frequency, heart rate, mental health, and temperature regulation. Such symptoms may be frequently seen in individuals presenting with suboptimal thyroid function in nutritional therapy practice. Various nutrients such as iodine, iron, selenium, vitamin A, zinc, vitamin D, and magnesium are influential to thyroid function and personalised lifestyle choices adapted to the individual may help provide additional support. The aim of this review is to describe the research surrounding the relationship of these factors to thyroid function and thereby support evidence-based therapeutic decision-making in clinic.

Introduction

The thyroid is an important endocrine gland situated at the front of the throat. Its main function is to produce hormones required for growth, development and metabolism, namely triiodothyronine (T3), and tetraiodothyronine (thyroxine, T4). In response to existing circulating concentrations of T3 and T4, hormones from the hypothalamus and pituitary gland control the amount of these hormones produced by the thyroid (1). This feedback loop is known as the hypothalamus-pituitary-thyroid axis (HPT). A poorly functioning thyroid gland or problems HPT axis signalling can be involved in the development of many diseases and are associated with three of the top ten global causes of death: heart disease, Alzheimer's disease and diabetes (2–4). Disrupted lipid metabolism, metabolic syndrome, and hyperglycaemia may all be involved in the pathogenesis (5,6). Practitioners should therefore consider thyroid function when seeing individuals with these conditions, as well as individuals who have classic thyroidal symptoms such as tiredness, weakness, weight gain or difficulty losing weight, muscle aches, constipation, slow heart rate, anxiety, and sensitivity to cold.

Lifestyle factors such as diet, sleep, exercise, stress, and environmental toxins may affect thyroid function (7). Practitioners should consider the role of nutrient deficiencies and excesses in thyroid health. It has long been recognised that several minerals and vitamins are essential to thyroid function and hormone production, including iodine, selenium (Se), iron (Fe), and vitamin A (VA), as well as the enzyme co-factors Zn and magnesium (Mg) (8). As a result, individuals with nutrient deficiencies may be at risk of poor thyroid health.

Whilst it is often assumed that nutrient deficiencies are uniquely associated with low- and middle-income countries, it is interesting to note that deficiencies are emerging amongst high income countries too. For example, in a 2021 review of data from the United Kingdom, pregnant women over the period 1991 to 2014 showed that in no survey year were iodine intakes sufficient to cover the additional needs of pregnancy (9).

Undiagnosed thyroid disorders could possibly occur in as much as 4-7% of the UK and European population and metabolic disorders are increasing (10–13). Nutrient imbalances and lifestyle choices may be contributing to modifiable risk factors influencing thyroid disorders.

This narrative review therefore seeks to provide a useful overview of the literature and support decision-making by nutrition practitioners in their recommendations for this growing number of individuals.

1. What is the role of iodine in thyroid health?

The thyroid gland, which stores 70-80% of the body's iodine (1), uses it to synthesise the thyroid hormones T4 and a smaller amount of T3, with most T3, as the active form, being produced through the peripheral conversion of T4 at the site of action. Thyroid hormone (TH) is crucial for cellular energy production, oxygen consumption, neural development and reproductive function (14). Iodine deficiency is linked to a number of disorders including goitre, hypothyroidism, mental retardation historically known as cretinism, cognitive impairment, and reproductive issues (1); while iodine excess may contribute to goitre, development of iodine-induced hyperthyroidism, overt hypothyroidism and most of the other iodine deficiency disorders through its inhibition of TH production (15), and, rarely, acute toxicity (1,16). Both deficiency and excess may contribute to thyroid autoimmunity and influence thyroid cancer risk (17-20).

Iodine deficiency may affect fertility (19) and is linked to thyroid disorders in children, including goitre and hypothyroidism, as well as increased risk of infant mortality (20). Even in adults, insufficient iodine intake can cause reduced T4 and T3 synthesis and elevated thyroid-stimulating hormone (TSH) (hypothyroidism). This can result in goitre as the thyroid tissue enlarges to compensate for low hormone concentrations; an adaptation aimed at maximising iodine uptake and hormone production (21).

Temporary exposure to excess iodide (the ionic form of iodine, I-) inhibits TH synthesis through a phenomenon known as the Wolff-Chaikoff effect. This acts by downregulating the sodium/iodide symporter when plasma iodide exceeds a critical threshold, thereby protecting against hormone overproduction (22).

As circulating iodide returns to normal, "escape" from the Wolff-Chaikoff effect occurs and hormone production is resumed. However, failure to escape due to impaired symporter function or continued exposure over tolerable limits can result in sustained inhibition of hormone synthesis and subsequent risk of hypothyroidism (22).

Thyroid autoimmune diseases, such as Hashimoto's thyroiditis and Graves' disease (GD), involve the elevation of antibodies to self-proteins in the thyroid gland (23). In the case of Hashimoto's thyroiditis, antibodies to thyroid peroxidase (TPO) and thyroglobulin (Tg) target the body's own TPO enzyme and Tg protein (23). This leads to immune-mediated destruction of thyroid cells, impaired hormone production and hypothyroidism. In the case of GD, thyroid-stimulating immunoglobulins or TSH receptor antibodies (TRAb) bind to and activate the TSH receptor, leading to excessive TH production and hyperthyroidism (23).

Excess iodine intake, especially by people previously exposed to iodine deficiency, has been linked to increased TPO and Tg antibodies, which damage thyroid cells and impair hormone production especially in sensitive populations, such as children and pregnant women (15,24).

In iodine-deficient regions (e.g. deficient soil or lack of seafood consumption), low dietary iodine reduces TH production, prompting the body to lower its TSH baseline to prevent thyroid overstimulation, which over time, could lead to goitre and autonomously-functioning nodules (25). This adaptation increases the risk of iodine-induced hyperthyroidism if iodine intake suddenly rises, even to normal intakes.

According to the World Health Organisation (WHO), populations with a median urinary iodine concentration (UIC) between 100–299 µg/L are considered iodine-sufficient (26). [Note that UIC is a population-only measure and is not suitable for use in individuals (27)]. An Italian nationwide surveillance study found that iodine sufficiency with a median urinary concentration of 124 µg/L, can be achieved through iodised salt use. Compared to earlier surveillance data from 2000–2005, when the median UIC was below 100 µg/L and goitre prevalence was approximately 15%, there was a considerable reduction in both goitre prevalence and iodine

deficiency–related hyperthyroidism. However, pre-existing thyroid autoimmunity was not impacted (28). This finding emphasises that improving iodine intake through dietary interventions, such as replacing regular salt with iodised salt, can measurably reduce the risk of iodine deficiency disorders in populations. However, this strategy may not impact established autoimmune thyroid conditions underscoring the need for personalised nutritional interventions that address both deficiency and the complex management of autoimmunity.

Since iodine is essential for TH synthesis and its deficiency can lead to iodine-related disorders, supplementation may be essential for individuals in iodine-deficient regions or in countries with no iodised salt policy, individuals who exclude food sources of iodine from their diet (such as dairy, seafood and eggs) and those with increased physiological needs, such as pregnant or lactating women. Supplementation should be approached cautiously, as the balance between deficiency and excess is key. The recommended daily intake for adults is 150 µg/L, increasing to 250 µg/L during pregnancy and lactation to cover additional requirements (29).

An experimental balance study by Yang et al. (2020) of a Chinese population of young adults (n=60) found a higher physiological need for additional iodine storage in women than in men (30). It was suggested that this could be due to hormonal and metabolic factors unique to women such as the influence of oestrogens on iodine metabolism and the anticipation of higher TH demands during pregnancy and lactation. This finding underscores the importance of sex-specific dietary recommendations. For women, particularly those of reproductive age, ensuring sufficient iodine intake is essential not only for maintaining optimal thyroid function but also for supporting maternal and foetal health during pregnancy and lactation. Furthermore, iodine sufficiency prior to and during pregnancy has been associated with improved cognitive abilities in children. A randomised control trial (RCT) found that children of n=1220 mothers with pre-pregnancy access to iodised salt scored higher on cognitive tests (effect size d = 0.17; ~4 IQ points; 95% CI 0.0, 1.3; p=0.01) (31). This underscores the importance of assessing iodine intake as part of care for women looking to become pregnant or prenatal care, especially in populations at risk for deficiency.

2. How does Iron impact thyroid function?

Fe deficiency has been associated with thyroid dysfunction, most commonly hypothyroxinaemia and subclinical hypothyroidism (SCH) (32). Fe is a key component of TPO, a haemoprotein and enzyme involved in the biosynthesis of TH. TPO catalyses two essential reactions: the iodination of Tg, a precursor protein for TH, and the coupling of iodotyrosine residues to produce T4 and T3 (8). Fe deficiency may reduce TPO activity (33), as well as negatively impact the effective use of iodine for TH synthesis (34) and the conversion of free T4 (FT4) to free T3 (FT3) (35). In a pooled analysis of individual patient data (n=42,162) it was found that patients with thyroid dysfunction were more likely to have anaemia (36).

The restoration of serum ferritin (SF), a biomarker for stored Fe, has been shown through oral bioavailable Fe supplements in humans, to normalise production of TH (37). However, scientific research is inconclusive, and a combination of physiological mechanisms may be involved (32).

Fe deficiency is most frequently diagnosed in pregnant women and women of reproductive age. Demand for Fe is increased during pregnancy (35) and TH plays a fundamental role in the skeletal and neurological development of the foetus (38). For this reason, numerous scientific studies have been conducted in these populations. A systematic review and meta-analysis of eight cross-sectional studies involving pregnant women or women of reproductive age found that those with Fe deficiency had increased TSH and decreased FT4 (p=0.00001) (35). This was also seen in a study of n=209 pregnant women in their second trimester in China (39).

Similar results were also found in India in a cross-sectional study of women (n=113) in their first trimester of pregnancy (40).

Sixty-eight percent were Fe deficient. In this group, elevated TSH was found in 35% compared to 6% in the non-Fe deficient group. As serum ferritin increased, TSH declined but FT4 did not change. In n=227 Nepalese school children aged 6-12 years thyroid dysfunction was found to be predominant in those with Fe deficiency (44 %) or anaemia (35 %) (41). In a general population, a cross-sectional Spanish study of n=3846 adults without diagnosed thyroid disease, found that as serum ferritin levels decreased, FT4 and FT3 levels also declined (32). There were no changes to TSH. Subgroup analysis found that pre-menopausal females were most likely to be affected. Another systematic review and meta-analysis of 10 cross-sectional studies in adults found lower TSH (p=0.005), FT4 and FT3 (both p=0.000001) in patients with Fe deficiency, though eight out of the 10 included studies were in pregnant women, so results should be interpreted with caution (42). Despite these correlations, most studies are cross sectional and causality cannot be determined. There are also few studies in children or across general populations. More research, in particular RCTs, in these groups are needed to confirm the results as well as the mechanisms involved.

3. How does selenium influence the role of the thyroid gland?

An indicator of the role of Se in thyroid function originated with the early discovery that the thyroid gland contained surprisingly large concentrations of Se and that the body may retain Se in the thyroid even under conditions of deficiency (43).
The role of Se in thyroid health has also been indicated in observational studies showing that a low Se status is associated with poor thyroid function. One systematic review and meta-analysis of 10 case-control and cohort studies with n=2205 individuals showed that individuals with thyroid cancer had lower serum Se than healthy controls (standardised mean difference (SMD) = -1.25; 95% CI -2.07, -0.44; p=0.003) (44). Similar observations have been made in cross-sectional studies from France, Denmark, and China, with low Se levels associated with an increased risk for hypothyroidism, autoimmune thyroiditis (AIT), goitre, enlarged thyroid, thyroid nodules, and GD (45–48).

Many biomarkers are used to test for Se status. Historically glutathione peroxidases (GPx), which require Se for synthesis, have been used to determine Se levels. However, one cohort study (n=51) has shown only a weak relationship between GPx activity and Se levels (r = 0.186, p = 0.021) (49). Selenoprotein P (SeP), which is a transport protein, may be a better biomarker of Se status and has a stronger relationship with serum Se (r = 0.467; p= <0.0001) (49,50). Yet, it has been shown that serum Se may not be indicative of thyroid Se (43). However, given that Se is stored in the thyroid during times of deficiency, it could be assumed that if serum Se is continuously low then thyroid gland Se will eventually follow.

Several factors may affect Se levels. Animal products are good sources of Se and little is found in fruits and vegetables, although plants from the Brassica genus tend to accumulate Se (51). As such, vegetarians may be at risk of Se deficiency. Genetic polymorphisms may also leave individuals susceptible to low Se status. Genetic variation in the dimethylglycine dehydrogenase (DMGDH) rs921943 gene, which is involved in the metabolism of sulphur-containing amino acids, has been shown in pregnant women to be associated with Se status. Furthermore, pregnant women who carry the selenoprotein P (SEPP1) rs3877899 minor A allele are more able to maintain Se levels during pregnancy (52). However, further understanding of the role of genetic polymorphisms on Se status in the wider population are required before genetic testing is recommended.

In combination with observational data, supplementation studies would suggest Se is required for optimal thyroid health and function especially in those with autoimmune disease of the thyroid. In individuals with chronic AIT, one systematic review and meta-analysis revealed that Se supplementation (200 µg/day) for durations of 3-12 months in combination with levothyroxine (synthetic T4), improved TPO autoantibody levels (weighted mean difference (WMD) = –271; 95% CI -366 to -175; p=< 0.0001; I2 = 45%) (53).

Improvements to autoantibodies have also been seen in individuals with Hashimoto's thyroiditis given 200 µg/day Se, which was attributed to improved antioxidant activity (GPx3 SYT: 45.2 ng/ml; 95% CI 23.7, 68.4 ng/ml; vs control 24.2 ng/ml; CI = 15.3, 50.4 ng/ml; p=0.028). Supplementation also resulted in upregulated regulatory T (Treg) cells (13.19 ± 3.5 vs 11.49 ± 2.79; p=0.012), which are involved in the prevention of autoimmune disease (54).

Given the antioxidant nature of Se, supplemental research in individuals with Graves' orbitopathy (GO), which is an inflammatory, autoimmune disorder of the retro-ocular tissue as a result of GD, has also shown promising results. At doses of 100 µg twice daily for 6 months, it has been shown in one RCT that Se may be beneficial to quality of life (QoL) and may slow progression of disease (55). In this study, 159 individuals with GO were randomised to sodium selenite, pentoxifylline (600mg twice daily), which has been indicated as a potential GO treatment, or placebo. Compared to placebo, individuals on sodium selenite showed improvements to QoL (p=<0.001), slowing of disease (p=0.01), and less eye involvement (p=0.01), observations that were not observed in the pentoxifylline group. Sodium selenite was not associated with any side effects, but gastrointestinal problems were frequently seen in those taking pentoxifylline. Similar results have been seen in a five-year prospective controlled cohort study of 74 individuals with mild-moderate GO, with improvements from baseline to QoL (p=0.01) and disease state (p= <0.05) after 3-6 months' Se therapy (56). However, this study did highlight that there may be no difference to long-term outcomes of disease.

Due to its role as an antioxidant and suppression of autoantibodies, it could be hypothesised that the use of Se in all autoimmune conditions would be of benefit. However, studies on individuals with GD have shown mixed results and may be dependent on serum Se. One RCT in 38 Se deficient individuals with GD has shown that supplementation of 200 µg/day resulted in improvements to biochemical parameters such as TSH (0.05 vs. 0.02 mIU/l; p=0.04), and T4 (15 vs. 18 pmol/l; p=0.01), but had no effect on FT3 (57).

In contrast studies on Se sufficient individuals with GD have shown no improvements to symptoms or disease status (58,59).

4. How can vitamin A influence thyroid health?

Vitamin A may influence thyroid function in two ways, namely through modulation of hormones responsible for thyroid gland metabolism, and through stimulation of the production of TSH by the pituitary. Vitamin A deficiency (VAD) may be involved in the development of thyroid disorders. Hypothyroidism was observed in a cross-sectional study of individuals with obesity-associated VAD with increased TSH (p=0.037), decreased T4 (p=0.001), and a negative association with TSH (r=-0.151; p=0.006) compared to individuals with normal VA levels (60).

The involvement of VA in thyroid homeostasis may be due to its involvement in HPT signalling from the pituitary. In a 10-month double-blind RCT in n=138 iodine-deficient children who also had VAD showed that, upon supplementation of high-dose VA (200,000 IU retinyl palmitate) and iodine (salt fortification), TSH and Tg concentrations as well as goitre rate were decreased compared to children given iodised salt and placebo (p=<0.01). At baseline, increasing VAD severity was a predictor of greater thyroid volume, TSH and Tg (p=<0.001 for all). The authors hypothesised that the physiological mechanism responsible for this effect could be VA-mediated suppression of the pituitary TSHβ gene (61).

It has also been shown that vitamin A may still be important regardless of iodine status. In a double blind RCT of children in Africa with both VAD and iodine deficiency, it was shown that there was an effect of VA supplementation in children who were not given iodine co-supplementation, as TSH, Tg and thyroid volume all decreased (p=<0.05 for all). However, the supplementation of both VA and iodine was more effective at reducing circulating TSH, serum Tg and thyroid size (p=<0.001 for all) (62). It was unclear from this study how TH concentration was regulated independently of iodine levels, but again, it may be due to the actions of VA on the pituitary.

5. The relationship between zinc and thyroid health

Zinc is an essential trace mineral that influences gene expression and cellular growth and serves as a cofactor for many enzymes involved in crucial physiological processes (8). It plays an important role in TH synthesis, metabolism, and regulation (63), and deficiency may impair TH receptor function, limiting the receptors' ability to bind TH and regulate gene expression, thereby disrupting essential TH signalling pathways (8).

Zn deficiency has been linked to thyroid enlargement in children and adults. A study of 68 goitrous school children with low Zn concentrations found an inverse correlation between Zn status and thyroid size. The authors hypothesised that this may be due to Zn loss, impaired T3 action, and reduced T3 binding to its nuclear receptor (64).

Low Zn concentrations are associated with hypothyroidism, while elevated Zn intakes may be related to hyperthyroidism (65–68). In patients with normal thyroid function, Zn concentrations positively correlated with T3 concentrations (p= <0.001) (69). Zn-deficient women consuming 30mg of Zn gluconate daily for 12 weeks showed increases in serum concentrations of FT3 and FT4 (p=<0.05) (70). Given these findings, practitioners may consider assessing Zn when low FT4 concentrations are observed (63)

Research suggests that Zn is involved in enhancing levels of TH, indicating its regulatory effect on TH production (65). Zn acts as a link between T3 and its nuclear receptor in the hypothalamus to stimulate the synthesis of TRH. TRH stimulates the synthesis and release of TSH by thyrotrophs in the pituitary glands, and in turn, TSH stimulates the synthesis of TH for release into the bloodstream (68)

6. Can other nutrients impact thyroid health?

Several other nutrients may have an impact on thyroid function including vitamin D and magnesium.

Vitamin D modulates the immune system through several mechanisms.

In a systematic review and meta-analysis of observational studies, individuals with thyroid disorders had lower serum vitamin D concentrations compared with healthy controls (71). Specifically, the weighted mean difference (WMD) of serum vitamin D was lower in autoimmune thyroid diseases, excluding Graves' disease, (WMD – 3.1 ng/dl; 95% CI –5.57 to –0.66; p=0.013; I2= 99.9%), Hashimoto's thyroiditis (WMD – 6.05 ng/dl; 95% CI, – 8.35 to – 3.75; p<0.001; I2= 91.0%) and hypothyroidism patients (WMD – 13.43 ng/dl; 95% CI –26.04 to –0.81; p=0.03; I2=99.5%).

Subgroup analysis showed a significant association with Graves' disease only in individuals aged ≥40 years (WMD –8.79 ng/dl; 95% CI –15.87 to –1.72; p<0.001) (71). The lower occurrence of autoimmune conditions observed in individuals with higher serum vitamin D may be the result of the vitamin's regulatory effects on immune cells.

Thyroid autoimmune disorders have been linked to heightened T-helper (Th)-1 and Th17 responses (72) and increased levels of pro-inflammatory cytokines such as interferon gamma (IFN-γ), interleukin (IL)-17, and tumour necrosis factor alpha (TNF-α) (73).

Vitamin D has been found to suppress Th1 responses by downregulating IFN-γ and TNF-α production (74).

Vitamin D may decrease the production of cytokines such as IL-6, IL-2, and TNF-α, which are involved in the immune-mediated destruction of thyroid tissue in Hashimoto's thyroiditis, or the thyroid-stimulating antibody production of GD (74).

Vitamin D deficiency is considered a risk factor for the development of autoimmune thyroid diseases such as Hashimoto's and GD (71,75).

Magnesium is an important nutrient for the conversion of T4 to its active form, T3, in target tissues.
Mg is an essential cofactor that supports adenosine triphosphate (ATP) synthesis, overall cellular metabolism and maintains intracellular oxidative balance during energy production.

Efficient ATP production is critical for the optimal activity of deiodinase enzymes, as these enzymes require high ATP availability for the catalytic reactions needed to convert T4 into the active hormone T3 in peripheral tissues (8). Therefore, low Mg levels may impair T4-to-T3 conversion. This may contribute to the development of symptoms of thyroid dysfunction.

In a cross-sectional study of 1,257 participants that investigated the association between low serum Mg levels and thyroid disorders (76), those with severely low Mg levels (≤0.55 mmol/L) had a higher risk of anti-Tg antibody (TGAb) positivity (odds ratios [ORs]: 3.036–3.236) p=0.000), Hashimoto's thyroiditis (ORs: 2.748– 2.847 p=< 0.001), and hypothyroidism (ORs = 4.482–4.971, p=< 0.01), compared to individuals with adequate Mg levels (0.851–1.15 mmol/L).

7. Are there any modifiable lifestyle factors that can support thyroid function?

Many lifestyle factors including nutrition, sleep hygiene, stress, physical activity, gut microbiome and endocrine disruptors have been found to play a role in supporting or disrupting thyroid function (77). Understanding the effect of each of these can help practitioners to identify strategies for incorporation into a client's protocol.

Tian et al (2024) extracted data on physical activity from the US National Health And Nutrition Examination Survey (NHANES) (78). They found a non-linear relationship between thyroid health and exercise, highlighting that the effect physical activity has on thyroid health varies.

Overall, their results suggest that moderate exercise may support optimal thyroid health.

There is a direct link between stress as an environmental trigger for those susceptible to developing GD (79), such as smokers, females, individuals with a genetic susceptibility to the disease, and those with other autoimmune diseases such as type 1 diabetes and rheumatoid arthritis. To obtain a broader view of stress and its impact on thyroid health more research is needed on the HPT axis and longitudinal studies monitoring thyroid function against exposure to stress.

A cross-sectional study concluded that poor sleep quality may increase the risk of SCH (77). However, a recent systemic review (80) did not draw the same conclusion; while a correlation between sleep quality and risk of SCH was identified, it was not possible to extrapolate the casual direction of effect, i.e. whether sleep deprivation caused SCH or if the opposite was true. This data included in the review, however, were subject to high heterogeneity, which may have influenced the result. The thyroid gland is susceptible to exogenous substances or contaminants, like endocrine disruptors found in the environment and in food. These different chemicals, including bisphenol A (BPA) and phthalates found in plastics have, amongst others, been shown to cause TH fluctuations, reduce the uptake of iodine (81) and increase the risk of thyroid cancer (82).

The gut-thyroid axis refers to the interplay between the thyroid and the gut and research shows the varied role the microbiome plays in thyroid health. Dysbiosis, for example, impacts several factors related to the thyroid gland, including the absorption of key micronutrients like Se and iodine. Intestinal permeability, which can be increased by dysbiosis, has also been linked to autoimmune diseases like thyroiditis (83) and thyroid cancer (84).

8. Summary and key points

The thyroid gland is essential for metabolism and growth of the body, and it is important for practitioners to consider it when seeing individuals

with metabolic disorders such as heart disease, Alzheimer's disease, and diabetes. Several lifestyle factors can affect the function of the thyroid gland, all of which can be modified with support. Diet is particularly important to thyroid health, and as such Nutritional Therapists should take a key role in the management of individuals with or at risk of thyroid dysfunction. Thyroid function testing in individuals with metabolic disorders and accompanying thyroid dysfunction symptoms is important, given that dysfunction is underdiagnosed (10). In confirmed and borderline cases, dietary analysis is essential to understand where support can be given. Iodine, Fe, Se, VA, zinc, vitamin D, and Mg have all been shown to be involved in thyroid function.

Iodine is needed for TH synthesis, in particular T4, but it is important that intakes are carefully balanced, as both iodine deficiency and excess can lead to dysfunction. It is especially important to carefully monitor intakes in individuals who have previously been deficient, as in these individuals, even intakes slightly above optimal intake may damage thyroid gland cells. Iodine levels should be gradually increased to prevent iodine-induced hyperthyroidism. At-risk populations may require additional dietary iodine including vegans, pregnant and lactating women, those in areas with no iodised salt policy, or in regions of deficiency. Pregnant women should be advised to use iodised salt and/or regularly consume iodine-rich foods such as fish, algae, eggs and milk, to ensure adequate iodine levels for foetal brain development.

The role of Fe in thyroid gland health is currently unclear, although cross-sectional studies indicate that individuals with Fe deficiency or anaemia may also be experiencing thyroid dysfunction. This may be due to the role of Fe in TH synthesis and the conversion of T4 to T3. Women who are pre-menopausal may be particularly susceptible to thyroid dysfunction because of Fe deficiency and should be closely monitored. Fe deficiency could be addressed by increasing intakes of Fe-rich foods including meat, fish, dark green leafy vegetables, egg yolks, beans, and nuts, alongside vitamin C rich foods and using a bioavailable Fe supplement.

The thyroid gland Is a major storage centre for **Selenium** and may benefit from Its antioxidant properties. If individuals are experiencing poor thyroid function or autoimmunity, then low Se levels may be contributing, especially if seen in vegetarians. Practitioners may like to consider testing, and SeP is a reliable biomarker for serum Se levels. Dietary changes should be considered first-line, but supplementation of 200µg/day may be a good option if dietary restrictions are in place. Due care should be exercised with Se supplementation since the therapeutic window for Se is narrow, and excessive intakes can be deleterious to health (85).

Practitioners should be aware that fluctuations in **Vitamin A** may affect thyroid homeostasis and function. VA acts by regulating the action of iodine and through regulation of TSH secretion by the pituitary gland. Individuals with suboptimal thyroid function may consider testing and optimising both VA and iodine status to support rebalancing thyroid function. In lieu of a low iodine status, low VA may still need to be addressed for optimal thyroid function.

Zinc may be involved in TH regulation and balance may be essential to thyroid health. Excess may lead to hyperthyroidism and deficiency may lead to hypothyroidism and zinc levels should be considered when individuals are experiencing low TSH and T4.

Vitamin D may have a role in thyroid health through its anti-inflammatory actions and decrease the risk for autoimmune conditions such as GD and Hashimoto's thyroiditis (75,86). The Clinical Guidelines Subcommittee of The Endocrine Society recommends maintaining sufficient vitamin D intake by ensuring adequate sunlight exposure, dietary intake, or supplementation to achieve optimal serum 25(OH)D levels (87). These levels should be at least 30 ng/mL (75 nmol/L), with an ideal range of 40–60 ng/mL (100–150 nmol/L) (88).

Magnesium deficiency can result from various factors, including inadequate dietary magnesium intake, malabsorption, and excessive alcohol consumption (89). Assessment of magnesium intake and ensuring adequate magnesium intake, through diet and supplementation where needed, should be

part of the thyroid management strategy, particularly in conditions that deplete magnesium, such as excessive alcohol use.

Despite its importance in thyroid health, dietary adjustments should be accompanied with other lifestyle recommendations for optimal thyroid health. The thyroid gland affects most organ systems in the body and incorporating changes in lifestyle could be a simple yet effective way of positively influencing thyroid health. From a nutritional perspective, increasing the nutrient content of the diet with nutrients key to thyroid health can help support thyroid balance. Moderate exercise, appropriate stress management, prioritising sleep, reducing exposure to chemicals in the environment and in food, and modulating the microbiome may be key areas of focus for nutritional therapy practitioners.

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References: Pages 60 - 63

Author contributions

JR conceived of the review, provided comments to other authors, revised the final draft and is responsible for content. CS wrote the introduction, parts 3 and 4, the discussion and provided editing. APA wrote part 5, APS wrote parts 1 and 6, GB wrote part 2, NS wrote part 7. All authors reviewed and accepted the final manuscript.

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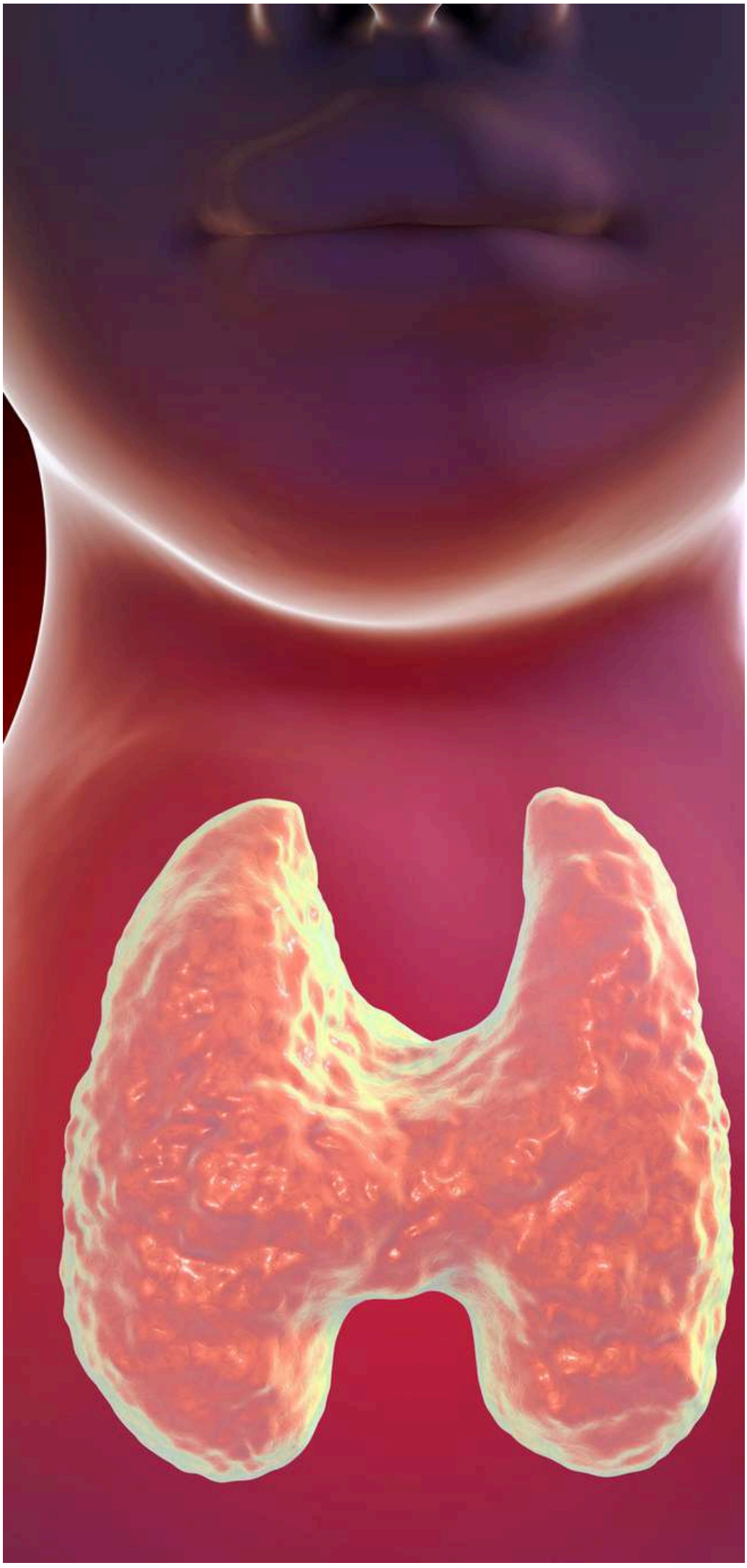
THYROID HEALTH

10 REVIEWS



PRE & PROBIOTICS & THYROID

EFFECT OF PROBIOTICS OR PREBIOTICS ON THYROID FUNCTION: A META-ANALYSIS OF EIGHT RANDOMIZED CONTROLLED TRIALS

Shu, Q ; Kang, C ; Li, J ; Hou, Z ; Xiong, M ; Wang, X ; Peng, H
PloS one. 2024;19(1):e0296733

INTRODUCTION:

- Research has highlighted the important role that the gut microbiome might play in thyroid function. As such, the potential role for probiotics and prebiotics to manipulate thyroid function has been considered. Given the inconsistencies in study findings, this systematic review aimed to assess the current consensus in the research.

METHOD:

- This systematic review was completed in accordance with the PRISMA guidelines.
- The search was performed using the following databases: MEDLINE, Scopus, Web of Science and Embase, plus a manual search and search of grey literature.
- After exclusions, eight peer-reviewed randomised controlled trials were included in the systematic review and meta analysis.
- Studies were conducted in China, Iran and Italy and included a range of different probiotic, prebiotic and synbiotic supplements at varying doses.
- The study included a heterogeneous sample of 367 participants, comprising individuals at risk of thyroid disorders, those diagnosed with thyroid disorders, individuals with obesity, and postmenopausal women.
- A number of outcome measures were considered including: free triiodothyronine (fT3), free thyroxine (fT4), thyroid stimulating hormone (TSH), and thyroid stimulating hormone receptor antibody (TRAb) levels.
- Three studies were found to have low risk of bias, with four studies raising concerns of bias and one being deemed to have a high risk of bias.

RESULTS:

- **The meta-analysis showed no significant differences (following supplementation) in a number of key hormones: thyroid stimulating hormone (TSH) (SMD: -0.01, 95% CI: −0.21, 0.20); free thyroxine (fT4) (SMD: 0.04, 95% CI: −0.29, 0.21); free triiodothyronine (FT3) (SMD: 0.45, 95% CI: −0.14, 1.03).**
- **Analysis revealed supplementation was associated with a significant reduction in thyroid stimulating hormone receptor antibody (TRAb) levels (SMD: -0.85, 95% CI: -1.54, -0.15).**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **Current evidence does not support a measurable effect of probiotic, prebiotic or symbiotic supplementation on thyroid hormone levels.**
- **There may be some benefits of these supplements for patients with Grave's disease, in terms of lowering their thyroid stimulating hormone antibody levels.**

CLINICAL PRACTICE APPLICATIONS:

- Current research evidence does not support the role of probiotics, prebiotics or synbiotics in influencing thyroid hormone levels.
- The use of probiotics, prebiotics and synbiotics may be a helpful additional strategy in managing patients with Grave's disease, where thyroid stimulating hormone receptor antibody levels are raised.

CONSIDERATIONS FOR FUTURE RESEARCH:

- Future research would benefit from focusing on individual sample groups with specific thyroid diagnoses.
- Additional studies would benefit from comparing the effects of probiotics, prebiotics and synbiotics in patients with Grave's Disease.
- Since hormone levels do not always correlate well with subjective experience of thyroid symptoms, future studies might like to consider patient-report measures of health and wellbeing.

CONCLUSIONS:

- **The meta-analysis would suggest that supplementing with probiotics, prebiotics and synbiotics has little impact on the level of thyroid hormones.**
- **Supplementing with probiotics, prebiotics and synbiotics may, however, have an impact on thyroid stimulating hormone receptor antibody levels, by reducing them.**

EXPERT REVIEWER Dr. Kate Lawrence

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

FLUORIDE AFFECTS ON THYROID

DOES FLUORIDE EXPOSURE AFFECT THYROID FUNCTION? A SYSTEMATIC REVIEW AND DOSE-RESPONSE META-ANALYSIS

Iamandii, I ; De Pasquale, L ; Giannone, ME ; Veneri, F ; Generali, L ; Consolo, U ; Birnbaum, LS ; Castenmiller, J ; Halldorsson, TI ; Filippini, T ; Vinceti, M
Environmental research. 2024;242:117759

INTRODUCTION:

Excess fluoride intake is believed to be associated with thyroid disease risk by various biochemical means. A meta-analysis of relevant articles aimed to explore the association between fluoride concentrations in water, serum and urine with thyroid disorders in both children and adults. The Population, Exposure, Comparator, Outcomes, and Study design (PECOS) was based on the statement, “What is the effect of fluoride exposure on thyroid, according to a dose-response relation in humans?”

METHODS

This systematic review was based on PubMed/MEDLINE, Web of Science, and Embase databases searches with 33 Articles meeting the inclusion criteria. This one-stage dose-response meta-analysis of original data included 45,000 participants from a predominantly Asian population (age range 6-76 years). Long-term fluoride exposure in both water and diet, and urinary or serum fluoride bio-markers, were assessed and compared to thyroid function and disease risk.

RESULTS:

- **Drinking water, urinary serum concentration or daily fluoride intake were assessed for fluoride exposure.**
- **The average range of concentrations of fluoride in drinking water was measured at 0.08 to 25.10 mg/L (median: 0.80 and interquartile range (IQR): 2.04; n=25). Urinary fluoride concentrations ranged from 0.06 to 4.57 mg/L (median: 0.82 and IQR: 1.51; n=19). Serum fluoride concentration was 0.065 ± 0.17 mg/L (range: 0.03–0.395; n=11).**
- **Comparing highest and lowest drinking water fluoride content, the relative risk (RR) for goiter in children was stated as 1.79 (95% CI: 1.18; 2.73) and 7.93 (95% CI: 1.93; 32.59) for urinary fluoride content.**
- **Goiter risk in adults for water fluoride content was 7.38 (95% CI: 1.17; 46.53) with hypothyroidism risk at 1.62 (95% CI: 1.36; 1.93).**
- **A Canadian study showed positive association with hypothyroidism and fluoride intake via beverages (OR: 1.25; 95% CI: 0.99–1.57), and drinking water fluoride content (OR: 1.65; 95% CI: 1.04–2.60), but no such association with urinary fluoride concentration.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **Fluoride is a naturally occurring mineral and is ingested via food, plants and water and primarily important for dental health.**
- **Excess intake might be due to dental products, fluoridated water, and enriched food and beverages.**
- **Suspected growth and/or neurodevelopment concerns in children necessitate assessment of fluoride concentrations in urine and/or serum.**
- **Adult hypothyroidism and goiter symptomatology may be associated with excess fluoride concentrations and similarly require investigation and careful elimination of exogenous sources.**

CLINICAL PRACTICE APPLICATIONS:

- Patients, both children and adults, with thyroid function symptomatology may benefit from fluoride urinary concentration assessment in conjunction with iodine status.
- Dietary and environmental sources of fluoride overexposure need to be carefully augmented given the role of fluoride in dental health.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Larger homogenous studies are needed to establish the role of fluoride overexposure in thyroid health outcome.
- Data assessing the dose-response relationship between fluoride exposure and thyroid disease outcome is much needed.
- The effect of fluoride on iodine concentrations needs to be investigated given the important role of the latter on thyroid function.
- Genetic factors regarding the effect of fluoride overexposure furthermore warrant assessment.

CONCLUSIONS:

The data indicates an association between fluoride exposure and thyroid disease risk. However, the authors conclude that an increase in thyroid stimulating hormone is associated only in drinking water fluoride concentrations above 2.5 mg/L.

EXPERT REVIEWER Wilma Kirsten

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

THYROID AND TYPE 2 DIABETES

PREVALENCE OF THYROID DYSFUNCTION AND ASSOCIATED FACTORS AMONG ADULT TYPE 2 DIABETES MELLITUS PATIENTS, 2000-2022: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Hadgu, R ; Worede, A ; Ambachew, S
Systematic reviews. 2024;13(1):119

INTRODUCTION:

- The thyroid gland is responsible for the production of hormones involved in growth and metabolism. Thyroid disorders (TD) are often associated with comorbidities such as type 2 diabetes mellitus (T2D). However, the pathophysiological links between these two diseases are still not fully understood.
- This systematic review and meta analysis aimed to determine the prevalence of TD in individuals with T2D and any associated factors.

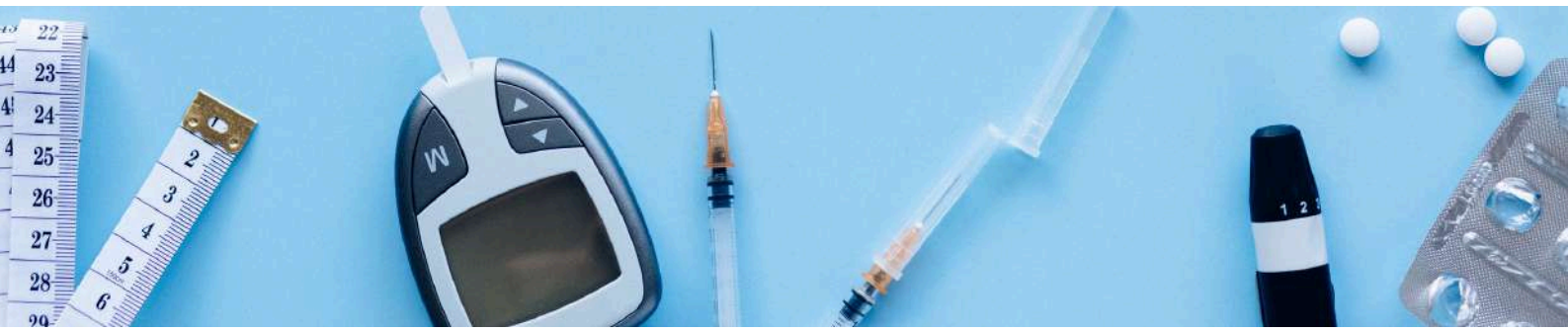
METHOD:

- Studies published between 2000 and 2022, where TD participants had been classified with hypothyroidism, hyperthyroidism, subclinical hypothyroidism, and subclinical hyperthyroidism by using laboratory measurements of TSH, T4, and T3 were included.
- Studies had to include sample size and status of TD. This data was used to analyse the pooled estimates of the prevalence of TD and associated factors among adult T2DM patients.
- 38 case-control, cross-sectional, case series, and cohort studies were included from five different continents.
- Studies involved a total of 19,803 participants.

RESULTS:

- **The pooled prevalence of TD amongst individuals with T2D was 20.24% (95% CI: 17.85, 22.64).**
- **Subclinical hypothyroidism was the most associated comorbidity with a prevalence of 11.87% .**
- **Subclinical hyperthyroidism was the least associated comorbidity with a prevalence of 2.49%.**
- **Amongst individuals with T2D and TD, nine associated factors were found. Being female, central obesity, HbA1c ≥ 7%, more than 5 years duration of diabetes mellitus, education level, diabetic neuropathy and retinopathy, family history of TD, and smoking.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE



TAKE HOME MESSAGE:

- **T2D and TD are closely linked.**
- **It is likely that T2D drives the development of TD through the suppression of the production of thyroid stimulating hormone by the pituitary gland.**
- **It is therefore important to ensure that individuals with T2D are screened for TD to ensure timely diagnosis and effective management.**
- **Lifestyle changes such as smoking cessation, exercise, and dietary changes could support thyroid function.**

CLINICAL PRACTICE APPLICATIONS:

- Individuals with T2D may also be experiencing TD.
- Practitioners may like to consider screening for TD amongst individuals with T2D.
- Women, smokers, those with uncontrolled HbA1c, and those with a family history of TD may be at a higher risk.

CONSIDERATIONS FOR FUTURE RESEARCH:

- Future research development could address causation and the mechanistic links between the two diseases.

CONCLUSIONS:

- It was concluded that the prevalence of TD amongst individuals with T2D was higher than the general population.

EXPERT REVIEWER Chloe Steele

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

THYROID FUNCTION & NAFLD

ASSOCIATION BETWEEN THYROID FUNCTION AND NONALCOHOLIC FATTY LIVER DISEASE: A DOSE-RESPONSE META-ANALYSIS

Xiang, LL ; Cao, YT ; Sun, J ; Li, RH ; Qi, F ; Zhang, YJ ; Zhang, WH ; Yan, L ; Zhou, XQ
Frontiers in endocrinology. 2024;15:1399517

INTRODUCTION:

This dose-response meta-analysis of observational studies investigated the dosage-dependent correlation between thyroid hormone (TH) levels and non-alcoholic fatty liver disease (NAFLD).

METHOD:

- The meta-analysis followed the PRISMA guidelines and was registered on PROSPERO. PubMed, Web of Science, Cochrane Library and Embase databases were searched from inception to February 2023.
- 10 studies published between 2015 and 2022 were included in the meta-analysis of 38,425 individual, with a follow-up period between 1 and 10 years. On the Newcastle-Ottawa Scale assessment all studies were of high quality.

RESULTS:

Analysis used combined risk ratios (ORs) with 95% CIs, a random effects model and a robust-error meta-regression (REMR) model to achieve an "average" dose-response relationship between thyroid hormones and NAFLD. Cochrane Q statistic and the I2 statistic evaluated heterogeneity among the studies. Key findings were as follows:

- **High levels of free triiodothyronine (FT3) were associated with a high risk of NAFLD, and a nonlinear inverse association was found between elevated free thyroxine (FT4) and incidence of NAFLD (OR=1.580, 95%CI 1.370 to 1.830, I2= 0.0%, p<0.001).**
- **High serum thyroid stimulating hormone (TSH) levels (OR=0.670, 95%CI 0.336–1.341, I2 = 96.6%, P=0.259), and high FT4 (OR=1.190, 95%CI 0.540 to 2.590, I2= 95.5%, p=0.666) were not related with NAFLD risk.**
- **For FT4 levels above 1.019 ng/ dL, every 1 ng/dL increase in FT4 lead to a 10.56% reduction in the relative risk of NAFLD (p=0.003).**
- **The result of a random-effects model looking at TSH level and liver fibrosis, suggests that the incidence of liver fibrosis is significantly higher with high TSH levels than with low TSH levels (SMD 1.320, 95%CI 0.660 to 1.970, p<0.001).**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **Thyroid hormones are closely associated with non-alcoholic fatty liver disease and play an important role in lipogenesis, beta-oxidation, cholesterol metabolism and carbohydrate metabolism.**
- **Therefore, monitoring of thyroid levels may be useful for nutrition practitioners when considering NAFLD.**

CLINICAL PRACTICE APPLICATIONS:

- Awareness or monitoring of subclinical hypothyroidism may be worth considering as a risk factor for NAFLD.
- While a nonlinear inverse association exists between elevated FT4 and incidence of NAFLD, indicators of liver fibrosis have been shown to be higher in individuals with high TSH hormone levels.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- More comprehensive prospective studies with larger samples are needed to clarify the relationship between thyroid-related hormones and NAFLD and to achieve more clinically meaningful evidence.

LIMITATIONS

- **Heterogeneity could not be explained even with subgroup analysis.**
- **As the article included a limited number of studies, the authors highlighted that the potential for "false positives" should also be recognised.**

CONCLUSIONS:

- **Despite limitations, this review provides further consideration of subclinical hypothyroidism (SH) as a risk factor for NAFLD.**

EXPERT REVIEWER Kirsty Baxter

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

SELENIUM AND COENZYME Q10

SUPPLEMENTATION WITH SELENIUM AND COENZYME Q10 IN AN ELDERLY SWEDISH POPULATION LOW IN SELENIUM - POSITIVE EFFECTS ON THYROID HORMONES, CARDIOVASCULAR MORTALITY, AND QUALITY OF LIFE.

Alehagen, U ; Alexander, J ; Aaseth, JO ; Larsson, A ; Opstad, TB
BMC medicine. 2024;22(1):191

INTRODUCTION:

- Important metabolic pathways in the cells require adequate supply of coenzyme Q10 (CoQ10) and selenoproteins for optimal functioning, however endogenous CoQ10 production decreases with age.
- Previous research reports selenium and CoQ10 supplementation reduced cardiovascular mortality (CVM) and improved health related quality of life (Hr-QoL) in the elderly with low selenium intake.
- Less focus has been on low selenium in thyroid hormone regulation and the association with CVM and Hr-QoL, therefore this study aimed to evaluate an intervention of selenium and CoQ10 on thyroid hormonal status, CVM and Hr-QoL.

METHOD:

- A randomised, placebo-controlled, double-blind 4-year study was executed with 414 participants aged between 70-88, identified with low selenium.
- 210 individuals were randomised to active intervention of selenium yeast (200µg/day) and CoQ10 (200mg/day) and 204 to placebo.
- Changes in hormone concentrations were assessed using t-tests, repeated measures of variance and ANCOVA, while CVM and Hr-QoL were evaluated with Short Form-36 (SF-36).

RESULTS:

In the supplementation group there was a significant increase in free triiodothyronine (fT3) and reverse triiodothyronine (rT3), and a significant decrease in free thyroxine (fT4) and thyroid stimulating hormone (TSH) levels compared with placebo (p=0.03 in each).

In the placebo group, TSH and fT4 above median values were correlated with increased 10-year CVM compared with mortality risk in those with TSH and fT4 below median (p<0.04 in both).

In the supplementation group there was no difference in mortality rate according to TSH and fT4 levels.

In the placebo group, TSH > and fT3 < median were correlated with a decline in items of Hr-QoL such as 'vitality', 'bodily pain' and social function' as well as 'composite physical score' compared to those with TSH < and fT3 > median over 4 years.

In the supplementation group there was no difference in Hr-QoL according to TSH and fT3 levels.

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **Low selenium was associated with elevated TSH levels and significantly increased CVM within 10 years.**
- **Supplementation with selenium and CoQ10 may be beneficial for those identified with even a mild selenium deficiency for reduced CVM and improved Hr-QoL.**

CLINICAL PRACTICE APPLICATIONS:

- In light of these findings, routine testing of thyroid hormone levels of TSH, T3 and T4 is advisable.
- Individuals with low selenium concentrations presented with significantly higher TSH levels and higher CVM compared to those with higher selenium, thus monitoring those who may be at risk of low selenium status, may be prudent.
- Supplementation with selenium may help to restore deiodinase activity and thyroid hormone balance as well as have clinical implications for reduced CVM and inflammation.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Further research is needed to explore the impact of selenium status on human physiology.
- As results are reported as hypothesis generating, future research is necessary and would benefit from a more diverse ethnicity rather than only Caucasians, as well as a broader age range. Evaluation of hypothyroidism symptoms, as well as general health symptoms and risk factors for CVM would be of interest.
- Evaluation of C-reactive protein concentration in relation to T3 levels and relationship between inflammation, oxidative stress and selenium may be helpful.

CONCLUSIONS:

- **Selenium and CoQ10 supplementation has a positive effect on thyroid hormones with reduced CVM and improved Hr-QoL in older adults.**
- **Changes in thyroid hormones may be explained by increased selenium-dependent deiodinases, important enzymes in thyroid hormone homeostasis.**

EXPERT REVIEWER Miranda Harris

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

HYPOTHYROIDISM NORMALIZATION

INCIDENCE AND DETERMINANTS OF SPONTANEOUS NORMALIZATION OF SUBCLINICAL HYPOTHYROIDISM IN OLDER ADULTS

van der Spoel, E ; van Vliet, NA ; Poortvliet, RKE ; et al.
The Journal of clinical endocrinology and metabolism. 2024;109(3):e1167-e1174

INTRODUCTION:

- As we age the incidence of subclinical hypothyroidism, defined in this study as elevated TSH 4.60-19.99mIU/L with fT4 within normal range, increases.
- The paper aims to pool data from 2 randomised clinical controlled trials to investigate incidence and determinants of spontaneous normalisation of TSH levels in older adults with subclinical hypothyroidism.

METHOD:

- The paper analyses 2 randomised, double blind, placebo-controlled parallel-group trials on the effect of levothyroxine treatment for subclinical hypothyroidism in older adults.
- One trial by TRUST recruited adults (n=2647) ≥65 years (April 2013- May 2015) from the Netherlands, Switzerland, Ireland and the United Kingdom.
- The second trial, IEMO recruited adults (n=342) ≥80 years (May 2014-May 2017) from the Netherlands and Switzerland.
- Data was pooled from 1) pretrial population and 2) in-trail placebo group.
- The pretrial cohort (baseline) (N=2335) had 2 readings of TSH taken to assess subclinical hypothyroidism, one 3 months to 3 years before trial and one at trial baseline.
- The in-trial cohort (N=361, placebo) had persistently elevated TSH confirmed pre-baseline and baseline, with a follow up TSH measurement taken 300-400 days later to assess if normalisation had occurred.

RESULTS:

- **In the pretrial, subclinical hypothyroidism (based on at least 1 elevated TSH measure) normalised without intervention, after a median follow-up of 1 year in 1419 of the 2335 participants (60.8%).**
- **In the in-trial cohort, persistent subclinical hypothyroidism normalised in 144 of 361 participants (39.9%).**
- **Normalisation was linked to lower age (OR 0.98, P=0.007 and OR 0.96, P=0.05), female sex (OR 1.39, P<0.01 and OR 1.80, P=0.05), lower trial baseline TSH (OR 1.22, P=0.01), lower screening TSH (OR 0.57, P<0.001), higher normal fT4 (OR 1.06, P=0.03) a second measurement in summer (OR 0.59, P<0.001) and absence of TPO antibodies (OR 0.36, P=0.007).**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **The paper demonstrates that subclinical hypothyroidism in older adults can resolve naturally and that this should be taken into consideration in their treatment plan.**

CLINICAL PRACTICE APPLICATIONS:

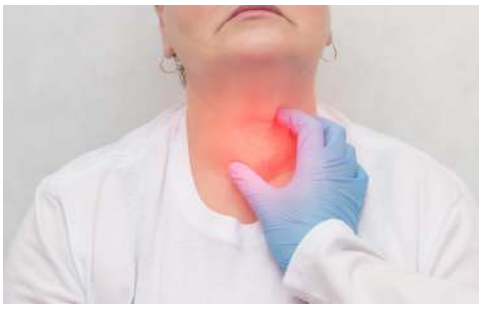
- Supporting older adults with nutritional intervention aimed to optimise thyroid function could support spontaneous TSH normalisation.
- Older adults may benefit from 2 or 3 measures of TSH to assess if spontaneous normalisation is achievable before treatment is considered.

CONSIDERATIONS FOR FUTURE RESEARCH:

- Identify if the findings can be replicated and therefore support a review of reference ranges in TSH for older adults.
- Explore why certain parameters e.g. testing in summer are associated with TSH normalisation and how these findings can be applied to improve clinical outcome.

CONCLUSIONS:

- **Subclinical hypothyroidism in older adults can normalise without medical intervention.**
- **Parameters like lower age, female sex, lower initial TSH, higher initial fT4, and summer follow-up measurements are independently associated with a higher chance of spontaneous TSH normalisation.**



EXPERT REVIEWER Nicky Ester

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

METS & THYROID DISEASES

A SYSTEMATIC REVIEW AND META-ANALYSIS INVESTIGATING THE RELATIONSHIP BETWEEN METABOLIC SYNDROME AND THE INCIDENCE OF THYROID DISEASES

Alwan, H ; Ribero, VA ; Efthimiou, O ; Del Giovane, C ; Rodondi, N ; Duntas, L
Endocrine. 2024;84(2):320-327

INTRODUCTION:

- Metabolic syndrome (MetS) increases an individual's risk of developing cardiovascular disease and type 2 diabetes. Thyroid disorders have also been linked to MetS. This systematic review and meta-analysis aimed to investigate the association between MetS, and its components, and incidence of thyroid disorders.

METHOD:

- The study adhered to the PRISMA statement.
- 4 outcomes were investigated: overt hypothyroidism, subclinical hypothyroidism, overt hyperthyroidism and subclinical hyperthyroidism.
- 8 studies were included in the qualitative synthesis.
- 7 studies were included in the quantitative synthesis (n=153, 237).

RESULTS:

- **The pooled unadjusted odds ratio (OR) for the association between MetS and incidence of overt hypothyroidism was 0.78 (0.52–1.16).**
- **Pooled unadjusted OR from 3 studies for the association between diabetes mellitus and the incidence of overt hypothyroidism was 0.83 (0.37-1.86).**
- **The pooled OR from 2 studies for the association between prediabetes and overt and subclinical hypothyroidism was 0.87 (0.50–1.52) and 1.01 (0.89–1.15), respectively.**
- **1 study reported the association between abdominal obesity and subclinical hypothyroidism (adjusted Hazard Ratio (HR): 1.07, 0.93–1.25) and overt hypothyroidism (unadjusted OR: 1.32 (0.72–2.42).**
- **2 studies assessed the association between obesity at baseline and overt (pooled RR: 3.10, 1.56–4.64) and subclinical hypothyroidism (pooled RR 1.50, 1.05–1.94).**
- **The association between hypertension and overt (Relative Risk (RR): 1.68, 1.53–1.84) and subclinical hypothyroidism (adjusted HR: 1.24, 1.04–1.48) were reported in 1 study each.**
- **1 study reported an association between hypertriglyceridemia and overt hypothyroidism (RR: 1.79, 1.15–2.79) and high total cholesterol and subclinical hypothyroidism (RR: 1.60, 1.15–2.23).**
- **1 study found an association between hypertriglyceridemia and an increased risk of subclinical hypothyroidism (adjusted HR: 1.18, 1.00–1.39).**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **Obesity is associated with an increased risk of overt and subclinical hypothyroidism.**
- **Maintaining a healthy body weight may reduce the risk of hypothyroidism.**

CLINICAL PRACTICE APPLICATIONS:

- The link between MetS and its components and thyroid disease is inconclusive.
- Obesity was shown to be associated with overt and subclinical hypothyroidism.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Obesity was found to be associated with an increased risk of overt and subclinical hypothyroidism. Further studies exploring the mechanism for obesity to disrupt thyroid hormones may inform clinical interventions and offer insights into potential preventative treatments for hypothyroidism.
- Studies investigating the impact of weight loss interventions on TSH levels in obese individuals with overt and subclinical hypothyroidism are warranted to explore the potential benefit of weight loss in the management of hypothyroidism

CONCLUSIONS:

- **MetS was not associated with overt or subclinical hypothyroidism. Obesity was positively associated with overt and subclinical hypothyroidism.**

EXPERT REVIEWER Daniel Quinones

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

BISPHENOLS EXP. & THYROID IN KIDS

MATERNAL BISPHENOLS EXPOSURE AND THYROID FUNCTION IN CHILDREN: A SYSTEMATIC REVIEW AND META-ANALYSIS

Liu, J ; Tian, M ; Qin, H ; Chen, D ; Mzava, SM ; Wang, X ; Bigambo, FM
Frontiers in endocrinology. 2024;15:1420540

INTRODUCTION:

Bisphenols (BPs), integral to plasticisers, are ubiquitous in our environment and are commonly found in urine samples, placenta, amniotic fluid, breast milk, and umbilical cords. This is suggestive that BP crosses the placental barrier leading to prenatal exposure. BP is similar structurally to thyroid hormones (TH) and may cause disturbances by interacting with TH receptors, gene expression and signalling.

METHOD:

- A systematic review and comprehensive meta-analysis of 11 prospective cohort studies including 5,363 children was conducted to investigate the effect of maternal exposure to BPs (including BPA, BPF, BPS, BPAF and TCBPA) in pregnancy on thyroid hormone levels (TSH, TT3, TT4, FT3, and FT4) in children and to explore the sex-specific effect on thyroid function. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used. Cohort studies from the United States, China, Japan, Korea, France, Spain, and the Netherlands, from 2013 to 2023 were used. Subgroup analysis was performed with 1.5 ug/g creatinine (Cr) as the threshold value to categorise the exposure groups into high and low BP exposure levels.

Results:

- **The impact of prenatal exposure to bisphenols in children (11 studies) found a statistically significant reduction in TSH levels (β = -0.013, 95% CI: -0.025, -0.001), which was more pronounced in female offspring (β = -0.020, 95% CI: -0.036, -0.005) and no significant association observed in males (β = -0.005, 95% CI: -0.024, -0.015).**
- **Analysis from 5 cohorts found that exposure to prenatal BPs was associated with an increase in TT3 levels in female offspring (β = 0.011, 95% CI: 0.001, 0.021, while no association of BP exposure on TT4 or FT4 levels was observed irrespective of sex. Exposure was related to decreased FT3 levels in all children (b = -0.011, 95% CI: -0.019, -0.003).**
- **Subgroup analysis of prenatal BPA exposure found the same effects as broader bisphenol exposure analysis i.e. a reduction in TSH, an increase in TT3 levels in girls and a decrease in TT3 levels in boys.**
- **It was found that high level of exposure to BPs (>1.5 ug/g Creatinine) significantly reduced FT3 levels (b = -0.011, 95% CI: -0.020, -0.003) in contrast to low exposure groups but no other specific exposure effects on other thyroid hormones were noted.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

Maternal exposure to BPs and single exposure to BPA were linked to reduced TSH and increased TT3 levels in female offspring. Only single BPA exposure showed reduced TT3 levels in male offspring. Measures to protect children and expectant mothers from bisphenol exposure should be considered.

CLINICAL PRACTICE APPLICATIONS:

- BPA has a low metabolism rate as reported in animal studies. Therefore, the foetus may be particularly sensitive to exposure.
- While findings have been inconsistent, their significance is still of importance as BPs may traverse the placental barrier, potentially exerting long-term effects on foetal thyroid development, function, and postnatal outcomes. Therefore maternal exposure has crucial implications.
- Since worldwide bans on the use of BPA in products in 2011, there has been a significant increase in the use of other bisphenol derivatives such as BPF and TCBPA as substitutes for BPA.
- At high concentrations BPs may intensify interference with the thyroid by increasing the binding affinity of bisphenols to thyroid hormone receptors, while at lower concentrations they may be more readily excreted by the body, reducing their accumulation in the body.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- More studies, investigating both neonatal and childhood stages, should be included in future research, including exploring exposure to other bisphenols particularly those being substituted for BPA.
- The impact of simultaneous exposure to multiple substances on TH should be taken into account in future studies as is normal in terms of environmental pollutant exposure.
- Study population diversity, including demographic characteristics and health status of pregnant women e.g. vitamin intake, may significantly influence the outcomes and should be considered.
- Methodological differences were present and therefore more studies with greater sample sizes, similar outcome measurements and similar timings and frequency of BPs measurement would be important to further strengthen these results. For example, the half-life of BPA is relatively short and a single measurement may not properly reflect exposure throughout pregnancy.

CONCLUSION:

- **Maternal exposure to bisphenols is linked to alterations in thyroid hormones in offspring, particularly in girls.**

EXPERT REVIEWER Georgie Murphy

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

THYROID & DIABETES

SUBCLINICAL THYROID DYSFUNCTION AND INCIDENT DIABETES: A SYSTEMATIC REVIEW AND AN INDIVIDUAL PARTICIPANT DATA ANALYSIS OF PROSPECTIVE COHORT STUDIES.

Alwan, H ; Villoz, F ; Feller, M ; et al.
European journal of endocrinology. 2022;(5):S35-S46

INTRODUCTION:

The study aimed to investigate if subclinical thyroid dysfunction (STD) (both hypothyroidism and hyperthyroidism) is associated with an increased risk of developing diabetes. Given the conflicting results from previous research, the study sought to clarify whether individuals with STD might be more prone to developing diabetes compared to euthyroid individuals.

METHOD:

- A systematic review and an individual participant data analysis (IPD) of multiple prospective cohort studies.
- Pooled data from 18 international cohorts with over 61,000 participants and an average follow-up of 8.2 years.
- Systematic search in Medline, Embase, and Cochrane Library (up to Feb 11, 2022).
- Participants classified as subclinical hypothyroidism (Shypo), subclinical hyperthyroidism (Shyper), or euthyroid (control).
- Incident diabetes was defined per American Diabetes Association criteria (e.g., fasting glucose ≥7.0 mmol/L, HbA1c ≥6.5%, or diabetes medication use).
- Two-stage meta-analysis: Logistic regression (age- & sex-adjusted) and random-effects model.

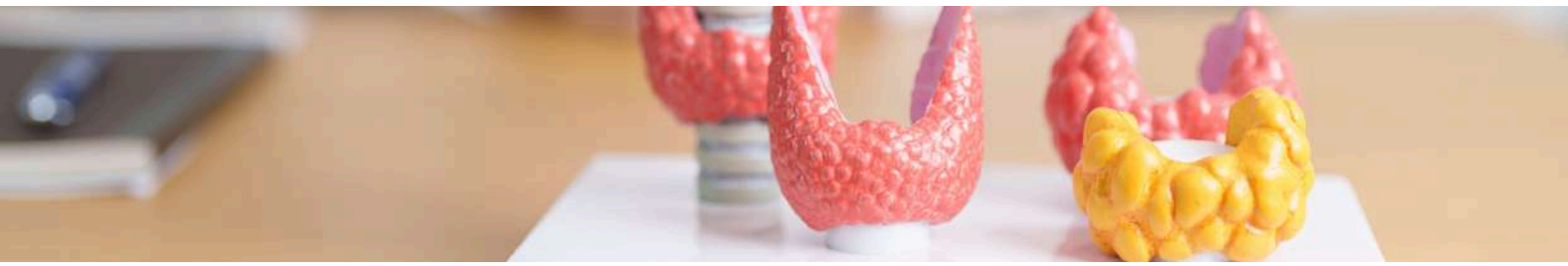
RESULTS: **Among 61,178 participants (mean age 58 years, 49% female, mean follow-up 8.2 years), 7.3% (2,910 cases) developed diabetes. Primary Outcome: Incident Diabetes:**

- **Subclinical hypothyroidism (Shypo) was not associated with increased diabetes risk (OR = 1.02, 95% CI: 0.88–1.17, I^2 = 0%);**
- **Subclinical hyperthyroidism (Shyper) showed no significant association (OR = 1.03, 95% CI: 0.82–1.30, I^2 = 0%);**
- **Time-to-event analysis confirmed these findings (HR for Shypo: 0.98, 95% CI: 0.87–1.11; HR for Shyper: 1.07, 95% CI: 0.88–1.29).**

Secondary Outcomes:

- **No association between Shypo and prediabetes (OR = 0.94, 95% CI: 0.84–1.05);**
- **Multivariable models adjusting for BMI, blood pressure, smoking, cholesterol, and glucose showed consistent results (OR = 0.97, 95% CI: 0.82–1.13);**
- **Subgroup and sensitivity analyses (age, sex, TSH levels, thyroid antibodies, excluding medication users) did not change findings.**
- **No statistically or clinically significant link between STD and diabetes risk.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE



TAKE HOME MESSAGE:

Individuals with mild thyroid abnormalities -(subclinical hypothyroidism or hyperthyroidism):

- are not at higher risk of developing diabetes compared to those with normal thyroid function;
- do not need screening for diabetes unless other reasons or risk factors (e.g., obesity, family history, high blood sugar) are present.

CLINICAL PRACTICE APPLICATIONS:

- This large systematic review found no association between STD and diabetes risk.
- Diabetes risk assessment should be based on metabolic risk factors such as BMI, glucose control, insulin sensitivity and other metabolic markers rather than thyroid status.
- Thyroid interventions may not prevent diabetes

CONSIDERATIONS FOR FUTURE RESEARCH:

- Future studies should examine whether STD influences insulin resistance or beta-cell function through detailed metabolic assessments (e.g., HOMA-IR, glucose clamp studies).
- Expanding research to assess thyroid dysfunction in relation to gut microbiota, inflammation, and metabolic syndrome components could help clarify the broader role of thyroid dysfunction in metabolic health.

CONCLUSION:

This large systematic review and IPD analysis found no significant association between STD (both hypothyroidism and hyperthyroidism) and incident diabetes. These results do not support screening or treating STD to prevent diabetes.

EXPERT REVIEWER Anna Papoutsa

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: B: Systematic reviews including RCTs of limited number)

TRE & THYROID FUNCTION

TIME-RESTRICTED EATING WITH OR WITHOUT A LOW-CARBOHYDRATE DIET IMPROVED MYOCARDIAL STATUS AND THYROID FUNCTION IN INDIVIDUALS WITH METABOLIC SYNDROME: SECONDARY ANALYSIS OF A RANDOMIZED CLINICAL TRIAL

Zheng, Y ; Wang, J ; Liu, M ; et al.
BMC medicine. 2024;22(1):362

INTRODUCTION:

- Individuals with metabolic syndrome (MetS) are at an increased risk of cardiovascular disease, type 2 diabetes and thyroid dysfunction.
- A low carbohydrate diet (LCD) and time restricted eating (TRE) may be effective dietary interventions to support weight loss and improve MetS. This randomised clinical trial aimed to identify the impact of a LCD, TRE and their combination on markers of cardiovascular health and thyroid function in individuals with MetS.

METHOD:

- 169 men and women with MetS were randomly assigned to the LCD (n=56), TRE (n=57) or the combination group (n=56) for 3 months.
- The LCD group was instructed to consume < 130g of carbohydrates daily or < 26% total energy from carbohydrates without time limitations.
- The TRE group was instructed to consume their food within an 8 hour eating window.
- Individuals in the combined group were instructed to restrict carbohydrate intake and consume their food within the 8 hour eating window.
- 135 completed the interventions. 57 who adhered to their protocol (5 days per week /3 months) were included in the per-protocol (PP) analysis.
- The outcomes investigated were lactate dehydrogenase (LDH), creatine kinase (CK), creatine kinase MB (CKMB), hydroxybutyrate dehydrogenase (HBDH), free triiodothyronine (FT3), free thyroxine (FT4), TSH, T3, T4, thyroglobulin antibodies (TgAb) and thyroid microsomal antibodies (TMAb).

RESULTS:

- **All 3 groups demonstrated reductions in LDH, CK, CKMB, and HBDH (P<0.01).**
- **FT3 decreased (P<0.001 for all) and FT4 increased (P<0.001 for all) in all three groups.**
- **TSH and T3 (P=0.011 for both) were reduced in the combination group.**
- **T4 increased in the TRE group (P=0.013).**
- **T3/T4 ratio decreased in the TRE (P=0.003) and combination (P=0.012) groups.**
- **All 3 groups experienced increases in TgAb (LCD: P=0.011, TRE: P=0.001, Combined: P=0.001) and TMAb (LCD: P=0.003, TRE: P<0.001, Combined: P<0.001) levels from baseline.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

PP RESULTS:

- **CK decreased only in the TRE (P<0.001) and combination (P=0.003) groups.**
- **TSH and T3 levels were unchanged in all three groups.**
- **The T3/T4 ratio decreased only in the TRE (P=0.020) group.**
- **TgAb (P=0.021) and TMAb (P<0.001) increased only in the TRE group.**

TAKE HOME MESSAGE:

- **LCD, TRE and their combination may help to improve myocardial and thyroid health.**
- **TRE on its own and when combined with a LCD lead to improvements in CK, TSH, T3, T4, and T3/T4 ratio.**

CLINICAL PRACTICE APPLICATIONS:

A low carbohydrate diet (< 130 g/day or < 26% total energy) and time restricted eating (16:8) and their combination may support individuals with MetS by improving myocardial health and thyroid function within a period of 3 months. Therefore, practitioners could employ strategies that align most closely with patients' lifestyle or preferences.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Individuals in the TRE group chose to reduce their carbohydrate intake by 4.6%. Further studies controlling for macronutrient intake may help to reduce the risk of bias.
- Iodine intake across the groups was not clearly defined. Analysis and controlling for micronutrient intake may help to reduce the risk of bias and better demonstrate the impact of LCD and TRE on thyroid function.
- Due to low adherence, a limited number of participants were included in the PP analysis. Further larger scale studies would help to confirm the results.
- The addition of a control group may have further demonstrated the efficacy of the interventions.

CONCLUSIONS:

- **LCD, TRE and their combination can help to improve myocardial and thyroid health. Given that no significant differences were observed between groups, it suggests that the different dietary strategies may offer potential benefits.**

EXPERT REVIEWER Daniel Quinones

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

THYROID HEALTH & SCIENCE TAKEAWAYS

NED INFOBITES & CLINICAL RESOURCES

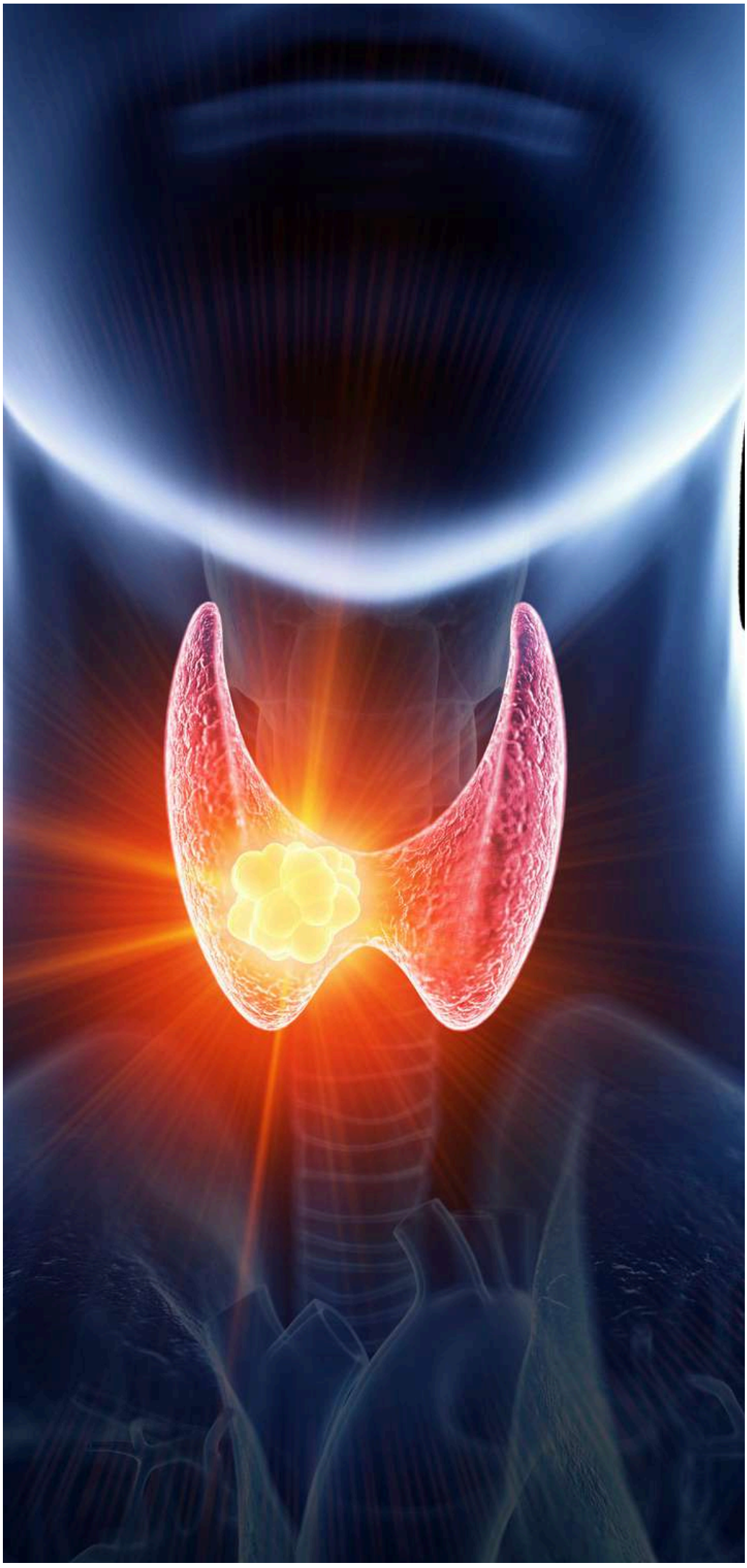
Not yet discovered our one page science summaries? Our NED InfoBites are designed to provide quick overviews of some of the latest research available on particular health issues and nutrition topics. Designed as a one-page clinical handout, the NED InfoBites unite our editorial team's pick of the research and provide a plain-language summary suitable for sharing with nutrition clients. Download the latest InfoBites on Thyroid Health here.

Additionally, BANT has developed a dedicated range of resources to support practitioners and help educate on common symptoms, biological processes, and dietary and lifestyle approaches. These are suitable to share with clients in clinical consultations and group programmes.

CLIENT-FRIENDLY GUIDES:

Providing practitioners with health resources and client-friendly educational materials to support their clinical recommendations.

HASHIMOTO'S THYROIDITIS



5 REVIEWS

NUTRITION & HASHIMOTO'S

THE INFLUENCE OF NUTRITIONAL INTERVENTION IN THE TREATMENT OF HASHIMOTO'S THYROIDITIS-A SYSTEMATIC REVIEW

Osowiecka, K ; Myszkowska-Ryciak, J
Nutrients. 2023;15(4)

INTRODUCTION:

A systematic review was conducted to investigate the impact of various nutritional interventions on anti-thyroid antibodies and thyroid hormone levels in participants with Hashimoto's thyroiditis.

METHOD:

The review followed the PRISMA checklist and PICO (population, intervention, comparative, outcome) Model. PubMed, Scopus and Web of Science databases were searched and nine studies were included. Nutritional interventions such as gluten or lactose-free diets, Nigella sativa, and iodine supplementation were examined. The primary outcomes related to thyroid function and autoimmune markers.

GLUTEN AND LACTOSE-FREE DIETS

A gluten-free diet showed a decreased TSH in levothyroxine LT4-treated patients, ($p = 0.044$). However, there was no significant effect on thyroid hormones or anti-TPO and anti-TG antibodies.

Additionally, in women with Hashimoto's disease, a gluten-free diet and vitamin D supplementation reported a decrease in thyroid antibodies anti-TPO ($p=0.0017$) and anti-TG ($p=0.0056$) and an increase in vitamin D concentrations ($p= 0.0006$) in the control group compared to the experimental group. No changes were observed in the case of TSH, fT4 and fT3 in the groups.

A lactose-free diet was reported to significantly decrease TSH after the intervention in LT4-treated patients with HT and lactose intolerance ($p < 0.05$).

WEIGHT & BMI

- **In a study where body weight, BMI, and percentage of body fat was observed, TSH, fT3, fT4, anti-TG, and anti-TPO levels showed a significant decrease in both the control and experimental groups ($p = 0.001$). Changes in body weight, BMI, and adipose tissue were reported to be positively correlated with anti-TG levels ($p = 0.001$, $p = 0.001$, and $p = 0.003$).**

SUPPLEMENTATION

- **Participants in a study group who consumed 2g of Nigella sativa, showed a significant improvement in TSH ($p = 0.02$), fT4 ($p = 0.04$), and anti-TPO ($p = 0.01$) compared to the control group.**
- **An improvement in TSH ($p = 0.02$), fT4 ($p = 0.04$), and anti-TPO ($p = 0.01$) levels were reported in a region with excessive iodine intake (>1100 mcg/day).**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **Diet, supplementation, and lifestyle factors play an important role in managing Hashimoto's thyroiditis.**
- **Tailored interventions based on individual dietary sensitivity, nutritional status and lifestyle factors are needed to optimise the effectiveness of the treatment and the patient's well-being.**

CLINICAL PRACTICE APPLICATIONS:

- For patients with Hashimoto's thyroiditis who require high doses of levothyroxine, or struggle with TSH regulation, testing for gluten and lactose intolerance may be beneficial.
- Monitoring and possibly supplementing with vitamin D might benefit patients with HT by potentially reducing antibody levels. Routine testing for vitamin D deficiency could help identify patients who may benefit from supplementation.
- Assessing HT patient's iodine levels to advise if levels are found to be higher or lower than recommended may be recommended.
- Clinicians might also consider weight management and lifestyle counselling as part of a therapeutic plan.

CONSIDERATIONS FOR FUTURE RESEARCH:

- The number of studies included in this review was small and the interventions were diverse. Further larger studies are needed to determine which type of nutritional intervention would be the most beneficial for patients with Hashimoto's thyroiditis.
- Hashimoto's thyroiditis is not a homogeneous condition, and variability between patients is high. Future studies should aim to investigate tailored treatment protocols based on individual patient characteristics to help identify specific subgroups that respond differently to interventions.
- Nutrient interventions such as iodine, selenium and iron were not addressed in the included studies. Further research is needed to determine if these nutrients may benefit individuals with Hashimoto's thyroiditis.

CONCLUSIONS:

Although previous studies have reported a positive or neutral impact on the biochemical parameters of Hashimoto's thyroiditis symptoms, this review found it challenging to present an unequivocal conclusion.

EXPERT REVIEWER Ana-Paula Agrela

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: B: Systematic reviews including RCTs of limited number

SUPPLEMENTS IN HASHIMOTO'S

DO DIETARY SUPPLEMENTS AFFECT INFLAMMATION, OXIDATIVE STRESS, AND ANTIOXIDANT STATUS IN ADULTS WITH HYPOTHYROIDISM OR HASHIMOTO'S DISEASE?-A SYSTEMATIC REVIEW OF CONTROLLED TRIAL

Kubiak, K ; Szmidt, MK ; Kaluza, J ; Zylka, A ; Sicinska, E
Antioxidants (Basel, Switzerland). 2023;12(10)

INTRODUCTION:

A comprehensive systematic review was conducted to investigate the effects of dietary supplements (DS) on inflammation, oxidative stress, and antioxidant status in adults (>18 years old) with hypothyroidism (HT) or Hashimoto's thyroiditis (AIT).

METHOD:

- The review was conducted following the PRISMA guidelines, reviewing 22 controlled trials. The primary outcomes assessed were inflammatory markers, oxidative stress, antioxidant levels, and thyroid function parameters. The supplements reviewed were primarily selenium and vitamin D, alongside others like Nigella sativa and genistein.

SELENIUM SUPPLEMENTATION:

- **Six studies indicated selenium's beneficial effects on inflammation, including decreased levels of pro-inflammatory markers. For example, Sun et al. demonstrated a significant reduction in IL-2 and TNF-α after 3 months of selenium yeast supplementation ($p = 0.001$).**
- **Selenium supplementation significantly improved antioxidant markers like glutathione peroxidase (GPx) and superoxide dismutase (SOD). In one study, GPx activity rose from 58.4 ± 23.2 to 80.2 ± 12.1 U/gHB ($p = 0.001$).**
- **Seven studies demonstrated improvements in thyroid function. For instance, Chakrabarti et al. reported a significant reduction in TSH levels after selenium supplementation, dropping from 25.8 ± 9.5 to 1.7 ± 0.7 μIU/mL ($p = 0.001$).**

VITAMIN D SUPPLEMENTATION:

- **There were no significant differences in inflammatory or thyroid function markers between intervention and control groups post-supplementation.**
- **None of the vitamin D studies assessed oxidative stress markers.**

OTHER SUPPLEMENTATION:

- **Nigella sativa demonstrated a decrease in Thyroid-stimulating hormone (TSH) levels ($p = 0.03$), as well as improvements in thyroid antibodies such as TPO-Ab ($p = 0.019$).**
- **In one study, genistein showed effects on thyroid antibodies ($p= 0.01$).**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **Selenium supplementation, especially at doses of 200 µg/day, was associated with significant reductions in thyroid-stimulating hormone (TSH) levels and improvements in markers of oxidative stress, such as glutathione peroxidase (GPx).**
- **Further research is needed to support the effects of selenium and other nutrients in patients with hypothyroidism (HT) or Hashimoto's thyroiditis (AIT).**

CLINICAL PRACTICE APPLICATIONS:

- Selenium supplementation may help reduce inflammation and improve thyroid function in patients with Hashimoto's thyroiditis and hypothyroidism.
- Clinicians could therefore consider selenium for patients with nutrition deficiencies and elevated TSH.
- Vitamin D did not seem to be effective, and further research is needed for other noted supplements.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Many of the studies were limited by small sample sizes (<50 participants) and methodological weaknesses (conducted only among women). Future research should prioritize larger, well-controlled randomised trials to better assess the efficacy of additional supplements like zinc, iodine, magnesium, and omega-3 in hypothyroidism and Hashimoto's thyroiditis.
- Understanding how supplements affect inflammation, oxidative stress, and thyroid autoimmunity at a mechanistic level is crucial. Future research should explore the biological pathways, particularly for selenium, to clarify its role in immune modulation and thyroid health.

CONCLUSIONS:

- **This review suggests that selenium supplementation may help reduce inflammation and improve thyroid function in HT/AIT patients. While vitamin D supplementation raised serum 25-hydroxy levels, it had minimal effects on inflammatory and thyroid parameters.**

EXPERT REVIEWER Ana-Paula Agrela

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: B: Systematic reviews including RCTs of limited number

VITAMIN D ON AUTOANTIBODIES

EFFECTS OF VITAMIN D SUPPLEMENTATION ON AUTOANTIBODIES AND THYROID FUNCTION IN PATIENTS WITH HASHIMOTO'S THYROIDITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Tang, J ; Shan, S ; Li, F ; Yun, P
Medicine. 2023;102(52):e36759

INTRODUCTION:

A higher prevalence of vitamin D insufficiency or deficiency has been found in people with Hashimoto's Thyroiditis (HT). This may be a contributing factor to the aetiology of HT due to vitamin D's regulatory role on the immune system. Supplementation with 25-hydroxyvitamin D (25(OH)D) may improve thyroid function and reduce thyroid antibodies, however, there is conflicting evidence. The aim of this study was to evaluate the efficacy of 25(OH)D supplementation for improving HT based on a meta-analysis of randomised controlled trials (RCTs).

METHOD:

- 12 RCTs were included with a total population of n=862. Patients were diagnosed with either HT, subclinical hypothyroidism or euthyroid.
- N=429 were allocated to treatment groups and N=423 to control groups. Treatment included calcitriol (6 studies) or vitamin D3 (1 study), alongside thyroxine treatment, or 25(OH)D exclusively if euthyroid or subclinical hypothyroid (2 studies D2, 1 study D3, 2 studies calcitriol). Control groups were given a placebo or no treatment. Study durations ranged from 12-24 weeks.
- Baseline and end of study measurements included: 25(OH)D, thyroid-stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3), anti-thyroid peroxidase antibody (TPO-Ab), and thyroglobulin antibody (TG-Ab).
- Subgroup analyses included study duration (> or < 12wk), type of 25(OH)D supplementation, baseline thyroid function (HT, Subclinical hypothyroid, euthyroid). Baseline vitamin D levels (deficient, insufficiency, indeterminant).

Results:

- **TSH levels were reduced following 25(OH)D supplementation in patients with HT (SMD =-0.167, 95% CI).**
- **Increases in FT4 (p=<0.009, SMD=0.734, 95% CI) and FT3 (p=<0.02, SMD =0.549, 95% CI) were observed in 10/12 studies in patients with HT with greater reductions in treatment durations >12 weeks (p=<0.05).**
- **A reduction in TG-Ab (assessed in 11/12 studies) compared to control groups in patients with HT (p=0.001, SMD =-0.996, 95% CI) was consistently reported in 9/12 studies.**
- **Calcitriol was more effective than naïve 25(OH)D (p=<0.001, SMD -1.522, 95% CI) for reducing TPO-Ab in HT patients. Greater reductions were observed in studies of >12 weeks in duration.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

Regular monitoring of vitamin D levels in patients with Hashimoto's Thyroiditis is recommended to prevent exacerbation of their symptoms and condition. Ideally, this should be carried out by a qualified healthcare professional.

CLINICAL PRACTICE APPLICATIONS:

- 25(OH)D supplementation for >12 weeks may lower TSH and increase FT3 and FT4 and in people with HT. However, baseline thyroid function may be a significant factor affecting the FT3 results. Treatment duration >12 weeks led to more significant increases in FT4 and FT3.
- A decrease in antibodies TPO-Ab and TG-Ab, was found regardless of baseline thyroid function. A treatment duration >12 weeks further improved TPO-Ab levels and calcitriol had a more pronounced effect (p=<0.001) compared to vitamin D2 or D3. However, the safety of calcitriol for HT requires further investigation due to an increased risk of hypercalcemia.
- Clients with hyperthyroidism or hypothyroidism may benefit from receiving 25(OH)D supplementation of 1500 to 2000 IU/d to prevent a deficiency from exacerbating their condition. Regular monitoring (serum/urine) for calcium is recommended.

CONSIDERATIONS FOR FUTURE RESEARCH:

- Further prospective studies with longer durations and larger populations are needed. These should also consider, racial diversity (10 studies were in China and 2 in Iran), somatotype variations, environmental variables, baseline thyroid function, vitamin D levels, dosage and duration of vitamin D treatment and L-4 dosage.
- Further research into the safety of calcitriol as an HT intervention are needed.

CONCLUSION:

25(OH)D Supplementation may be beneficial for improving thyroid function and modulating immune responses in people with HT. Further prospective studies with large and diverse populations are needed to confirm these results.

EXPERT REVIEWER Gail Brady

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

INFLAMMATORY INDEX & THYROID

ASSOCIATION OF DIETARY INFLAMMATORY INDEX AND THYROID FUNCTION IN PATIENTS WITH HASHIMOTO'S THYROIDITIS: AN OBSERVATIONAL CROSS-SECTIONAL MULTICENTER STUDY.

Klobučar, S ; Kenđel Jovanović, G ; Kryczyk-Kozioł, J ; et al.
Medicina (Kaunas, Lithuania). 2024;60(9)

INTRODUCTION:

- This observational study of 149 adults diagnosed with Hashimoto's thyroiditis, compared dietary inflammatory potential with clinical indicators of thyroid function and inflammation.

METHOD:

- Study group age range 19-72 years, of which 140 women and 9 men, recruited from thyroid outpatient clinics in Croatia in 2022.
- 95/149 patients were using T4 thyroid replacement (levothyroxine).
- Exclusion criteria were pregnancy and lactation, use of T3 thyroid replacement, anti-inflammatory medication or nutritional supplements. Patients with malignancies, co-morbidities affecting heart, liver or kidney, and confirmed hypothyroid function were also excluded from the analysis.
- Anthropometric data were collected to calculate BMI.
- 12-hour fasted blood was collected to measure thyroid function markers: free thyroxine (fT4), thyroid stimulating hormone (TSH) and thyroid peroxide antibodies (TPO-Ab), and inflammation as high-sensitivity C-Reactive Protein (hsCRP).
- Self-administered questionnaires collected data on demographics, smoking and exercise habits, and a 141-item food frequency questionnaire was used to calculate the Dietary Inflammatory Index (DII®).
- Statistical analyses produced categorical and continuous variables, with adjustments for potential confounders including age, gender, energy intake and physical activity.

RESULTS:

- **Mean age of 149 participants at recruitment was 47.4 years (SD+12.9), mean BMI was 28.3 (SD+5.9) kg/m2.**
- **Mean DII® score for the cohort was 0.03, with range -3.49 (least inflammatory) to 4.68.**
- **54.4% of participants had DII® scores below 0, indicating an anti-inflammatory diet.**
- **DII® values were expressed in tertiles. Protein intakes were seen to increase and omega-3 fatty acid intakes decreased with the DII® score.**
- **There were no significant differences in age, gender, smoking, BMI, education or occupation between the three DII® tertiles.**
- **Self-reported physical activity was significantly higher in participants with the least inflammatory diet.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

RESULTS CONT:

- **Thyroid function markers and inflammatory marker hsCRP were all within reference range across the three tertiles, but participants in T1, the least inflammatory diet, had significantly higher T4 levels than tertiles 2 and 3.**
- **There was an upward trend in levels of hsCRP and TSH with increasing DII® score but these did not reach statistical significance.**
- **Comparing thyroid antibody levels between DII® tertiles, those in the highest DII® tertile had twice the level of these auto-immune antibodies compared with the lowest DII® tertile, but this did not reach statistical significance.**
- **Tertile 3, with highest DII® score was the youngest group and had the lowest level of physical activity, highest BMI, highest inflammatory indicator and poorest thyroid function.**
- **Linear regression models indicated a significant association between TSH and DII® score, and with BMI versus DII®. Other associations were not significant after adjusting for confounders of age, BMI, and energy intake.**

TAKE HOME MESSAGE:

- **An anti-inflammatory diet, rich in omega-3 fatty acids, coupled with physical activity, is an appropriate evidence-informed approach for personalised nutrition advice for people diagnosed with Hashimoto's thyroiditis.**

? CLINICAL PRACTICE APPLICATIONS:

- For people living with auto-immune thyroid disease, an anti-inflammatory diet may be associated with better thyroid function
- In this setting, the DII® confirmed the association of omega-3 fatty acid intake with a less inflammatory diet.
- A Mediterranean-style diet provides anti-inflammatory nutrients.
- Physical activity may augment the effects of an anti-inflammatory diet in this group of individuals.

CONSIDERATIONS FOR FUTURE RESEARCH:

- A prospective randomised trial of Mediterranean diet versus thyroid function and thyroid antibodies may provide more evidence for this intervention.
- Thyroid replacement dosage requirements over time could be monitored as an additional metric.

EXPERT REVIEWER Carol Granger

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: C: Non-randomized trials, observational studies, narrative reviews

GLUTEN FREE DIET & THYROIDITIS

EFFECT OF GLUTEN-FREE DIET ON AUTOIMMUNE THYROIDITIS PROGRESSION IN PATIENTS WITH NO SYMPTOMS OR HISTOLOGY OF CELIAC DISEASE: A META-ANALYSIS

Piticchio, T ; Frasca, F ; Malandrino, P ; Trimboli, P ; Carrubba, N ; Tumminia, A ; Vinciguerra, F ; Frittitta, L
Frontiers in endocrinology. 2023;14:1200372

INTRODUCTION:

- Autoimmune thyroiditis or Hashimoto's disease may be caused by production of antibodies against thyroglobulin (TgAb) and thyroid peroxidase (TPOAb).
- 5% of the population have this condition and it is more prevalent in women compared to men (10:1).
- The aim of this study was to review all quantitative data on the effects of gluten free diets on anti-thyroid antibodies and thyroid hormone levels in individuals with Hashimoto's and without a diagnosis of coeliac disease (CD).

METHOD:

- MOOSE guidelines were followed.
- PubMed and Scopus were used with no restrictions on publication year. Only English-language papers were included.
- Studies included - those reporting TSH, FT4, FT3, TgAb and/or TPOAb levels before and after gluten exclusion, with coeliac disease ruled out by histology or symptoms.
- Studies excluded – participants diagnosed with CD, starting or adjusting thyroxine during the study.

RESULTS:

- **4 prospective cohort studies (2019-2022) met the inclusion criteria. All 87 participants were female aged 25 to 42. The mean time frame of gluten exclusion was 5.5 months.**
- **Quantitative analysis showed overall reduction in antibody levels after a GFD period: thyroid globulin (TgAb) - ES: −0.39 for TgAb (95% CI: −0.81 to +0.02; p = 0.06; I^2 = 46.98%); thyroid peroxidase (TPOAb) – ES: -0.40 (95% CI: −0.82 to +0.03; p = 0.07; I^2 = 47.58%).**
- **Thyroid Stimulating Hormone (TSH) showed an overall reduction after a GFD - ES: −0.35 (95% CI: −0.64 to −0.05; p = 0.02; I^2 = 0%).**
- **Free Thyroxine (FT4) showed an increase after a GFD - ES: +0.35% (95% CI: 0.06 to 0.64; p = 0.02; I^2 = 0%).**
- **FT3 levels did not have any substantial variations compared to the pre GFD levels.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **A gluten-free diet may benefit thyroid function in autoimmune thyroiditis, with trends showing reduced thyroid antibodies (TgAb, TPOAb) and improved TSH and FT4 levels. However, evidence remains limited, especially for long-term effects in non-coeliac individuals.**

CLINICAL PRACTICE APPLICATIONS:

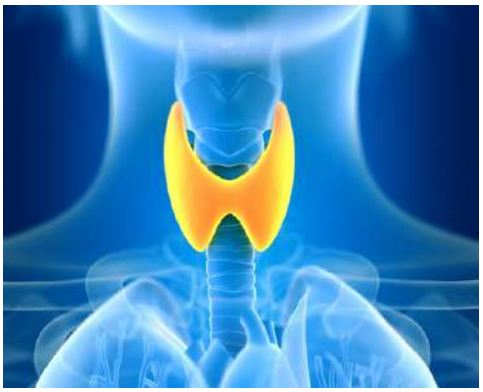
- A gluten free diet for 6 months may be trialled for individuals diagnosed with Autoimmune thyroiditis / Hashimoto's disease but that have not been diagnosed with CD.

CONSIDERATIONS FOR FUTURE RESEARCH:

- Further research is required to confirm the role of gluten in Hashimoto's management.
- The results of this paper show promising improvements in a common autoimmune condition. To further understand the impact, randomised longitudinal studies with larger cohorts and more diverse populations would help to increase data.
- Monitoring dietary adherence may gain greater understanding of the results and potential inconsistencies.

CONCLUSIONS:

- **A gluten free diet may positively impact thyroid function, particularly in those with gluten related conditions.**



EXPERT REVIEWER Nicky Ester

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

HASHIMOTO'S SCIENCE TAKEAWAYS

HASHIMOTO'S THYROIDITIS RESOURCES

BANT has developed a dedicated range of resources to complement the personalised nutrition and lifestyle advice given by practitioners in a clinical setting. These resources are open access on our website bant.org.uk and aid further comprehension of nutrition science and clinical interventions.

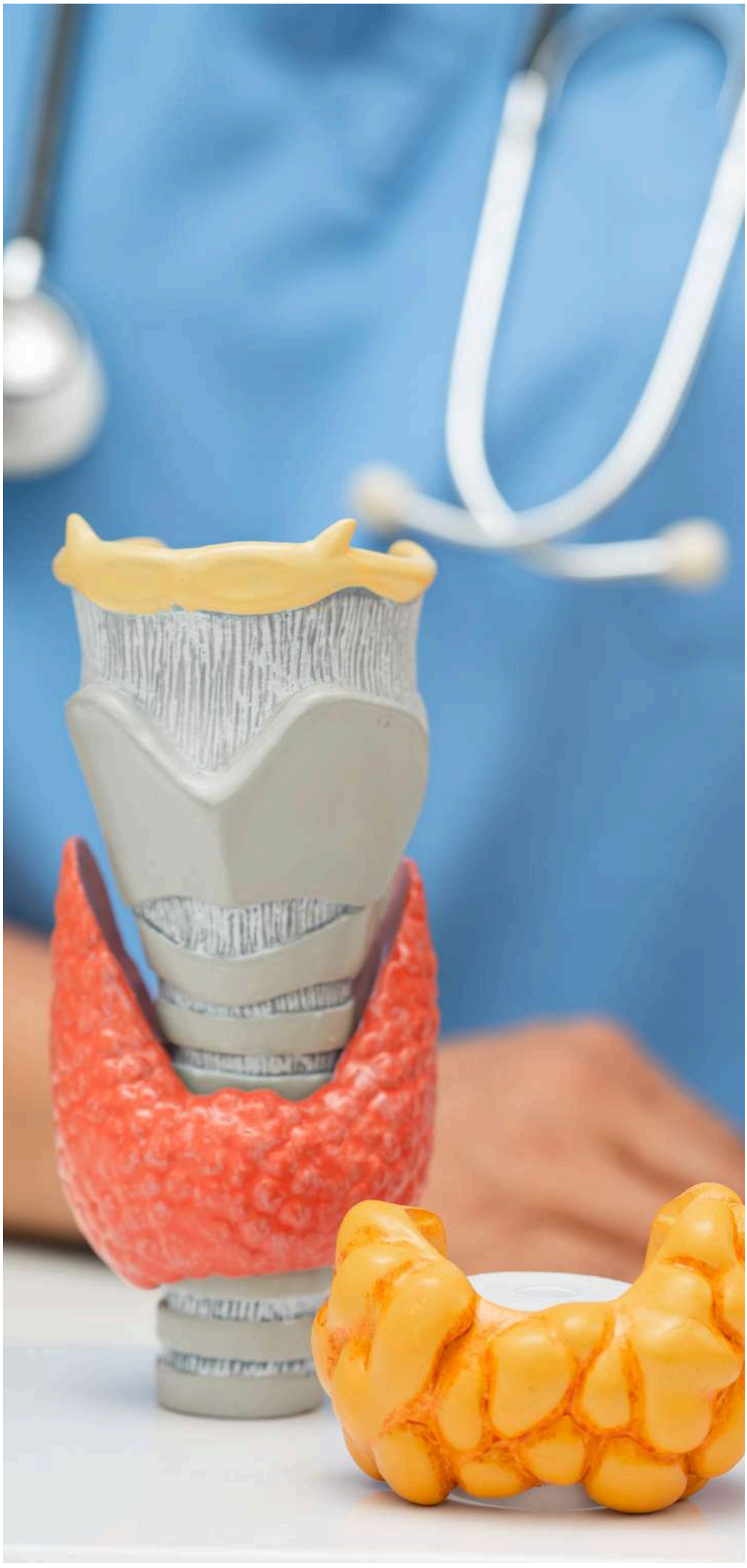
CLIENT-FRIENDLY GUIDES:

Providing practitioners with health resources to support their clinical recommendations.

Access our resources here.

GRAVES' DISEASE

2 REVIEWS



SERUM VITAMIN D AND GRAVES'

ASSOCIATION BETWEEN SERUM VITAMIN D LEVEL AND GRAVES' DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

Pang, B ; Li, L ; Liu, X ; Cao, Z ; Pang, T ; Wang, Q ; Wei, J
Nutrition journal. 2024;23(1):60

INTRODUCTION:

- Graves' Disease (GD) is an autoimmune disorder that results in an increase in the production of thyroid hormones (TH) and subsequent hyperthyroidism.
- If left untreated it can result in poor health outcomes and death.
- However, treatment can result in hypothyroidism.
- GD has been associated with low vitamin D levels. However, previous meta-analyses have used low quality papers and the association is uncertain.
- This study aimed to use high-quality peer-reviewed articles to determine the relationship between GD and vitamin D.

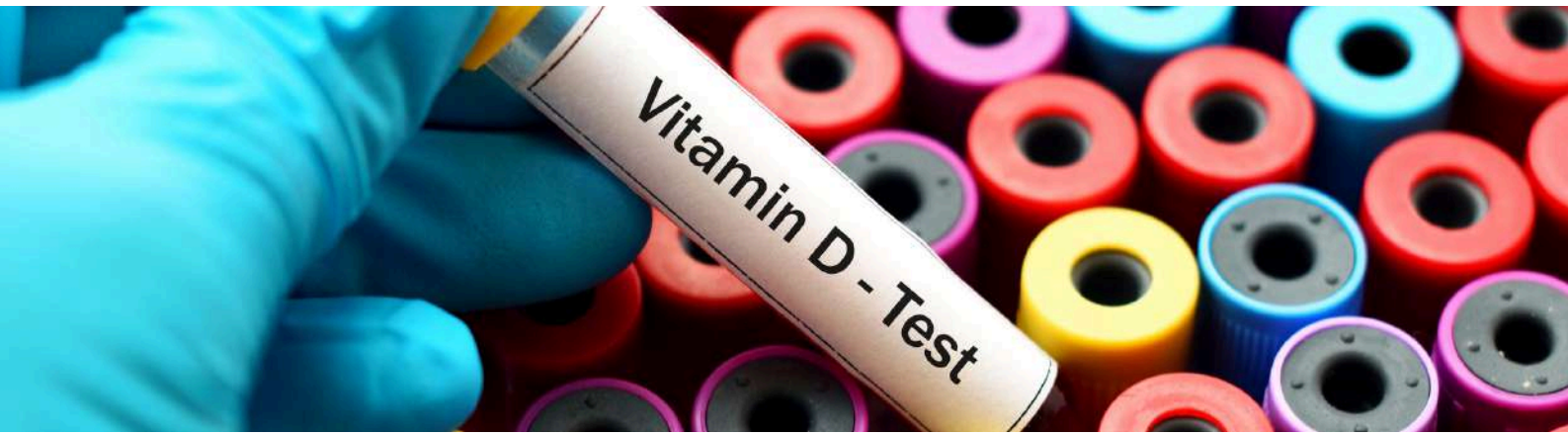
METHOD:

- This was a systematic review and meta-analysis of 12 cohort and case-control studies.
- Studies had to include a GD group and a control group for comparison.
- All studies that weren't deemed high quality were excluded.
- Studies were published between 1980 and 2020 and were mostly from China, with publications from India, USA, Sweden, Japan, Germany, and Belgium.

RESULTS:

- **The results showed that individuals with GD had low levels of vitamin D (SMD = – 0.66; 95% CI: –1.05, – 0.27; p = 0.001).**
- **There was high heterogeneity amongst the studies and this was attributed to different methods of measuring vitamin D levels, geographic location, and age.**
- **Interestingly, individuals with GD from North America did not have lower vitamin D levels, whereas those from Europe (SMD = 0.69; 95% CI: –1.30, – 0.07) and Asia (SMD = 0.75; 95% CI: –1.27, – 0.23) did.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE



TAKE HOME MESSAGE:

- **Low vitamin D levels may be a risk factor for the development of GD.**
- **However, causation needs to be determined before vitamin D can be used as a therapy for individuals with GD.**

CLINICAL PRACTICE APPLICATIONS:

- Practitioners may like to consider investigating vitamin D levels in individuals with GD.
- Those with low levels may like to consider supplementation, safe sun exposure or increasing dietary intake through oily fish, eggs, and mushrooms. However it should be acknowledged that sun exposure is challenging during the winter months in the northern hemisphere and only low levels of vitamin D are found in foods. It is therefore likely that supplementation would be more effective.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Future studies should focus on the effects of vitamin D supplementation on individuals with GD.

CONCLUSIONS:

- It was concluded that low serum vitamin D levels are a risk factor for GD.

EXPERT REVIEWER Chloe Steele

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

SELENIUM & VIT D COMBINED

ADD-ON EFFECT OF SELENIUM AND VITAMIN D COMBINED SUPPLEMENTATION IN EARLY CONTROL OF GRAVES' DISEASE HYPERTHYROIDISM DURING METHIMAZOLE TREATMENT.

Gallo, D ; Mortara, L ; Veronesi, G ; et al.
Frontiers in endocrinology. 2022;13:886451

INTRODUCTION:

- Observational studies have shown decreased levels of selenium and vitamin D in patients newly diagnosed with Graves' Disease (GD), the most common cause of hyperthyroidism.
- The aim of this study was to investigate the potential benefit of addition of selenium (Se) and vitamin D (VD) to treatment with methimazole (MMI) in GD patients with low levels of Se and VD.

METHOD:

- Single-blind, randomised controlled trial of supplementation with Se (100 mcg/day for 180 days) and VD (bolus dose dependent on VD level, followed by 7000 IU per week for the duration of the study, 270 days), alongside treatment with MMI, compared to MMI monotherapy.
- 42 Caucasian adults newly diagnosed with GD but otherwise healthy and serum Se <120 mcg/l and plasma VD <30ng/ml.
- Primary outcome: free thyroxine (T4).
- Secondary outcome variables: triiodothyronine (T3), positive TSH receptor antibody (TRAb), handgrip strength performance, systolic blood pressure, heart rate and quality of life (QoL) questionnaires, assessed by an unblinded clinician at 45, 180 and 270 days.

Results:

- **At baseline, significantly more patients in the intervention group had severe disease compared to controls. This was accounted for in the data analysis by comparing changes from baseline rather than absolute values.**
- **In the intervention group only, both serum Se and plasma VD increased significantly, both relative to baseline and to control (Increase at 45 days: Se 49.9 mcg/l (40.2;59.5) (mean/confidence interval), VD 37.8 ng/ml (32.1; 43.4)). Mean Se and VD levels were in the normal range from day 45 until the end of the study and significantly higher than in the control group (p=0.001 at 45, 180 and 270 days).**
- **T4 improved in both groups but significantly more so in the intervention group (p=0.002 at 180 days, thereafter T4 levels remained stable in both groups). QoL also improved more in the intervention group (p=0.007 at 45 days and p=0.03 at 270 days).**
- **T3, TRAb, systolic blood pressure, heart rate and hand grip strength improved in both groups with no significant difference between groups.**
- **No relevant adverse effects were observed, including no selenosis or hypercalcaemia.**

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- **Testing for Se and VD levels and appropriate supplementation to achieve sufficiency in both is recommended for patients newly diagnosed with GD.**

CLINICAL PRACTICE APPLICATIONS:

- Testing Se and VD levels in patients newly diagnosed with GD and supplementing to achieve sufficiency, where indicated, is recommended.
- Supplementing Se and VD in newly diagnosed GD patients who are insufficient in these nutrients, alongside MMI, appears to be safe.

CONSIDERATIONS FOR FUTURE RESEARCH:

- To establish whether Se and VD have a synergistic effect, larger studies with 4 groups would be of value (Se only, VD only, VD + Se, no supplementation, all in addition to standard treatment).
- Larger studies that allow for stratification by Se/VD level and/or severity of disease at baseline.

CONCLUSIONS:

- **The authors conclude that in newly diagnosed GD patients with low Se and VD levels, supplementation of Se and VD in addition to treatment with MMI supports the restoration of a euthyroid condition as well as improvement in QoL.**

EXPERT REVIEWER Karin Elgar

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

GRAVES' DISEASE SCIENCE TAKEAWAYS

GRAVES' DISEASE RESOURCES

BANT has developed a dedicated range of resources to complement the personalised nutrition and lifestyle advice given by practitioners in a clinical setting. These resources are open access on our website bant.org.uk and aid further comprehension of nutrition science and clinical interventions.

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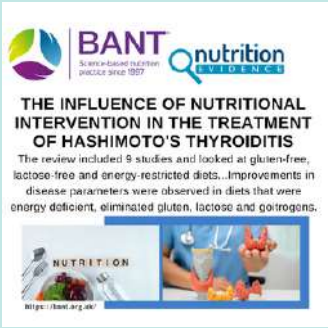

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