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Effects of gluten-free diet intervention in the treatment of Hashimoto's thyroiditis in non-celiac disease: A systematic review protocol

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Objective. Hashimoto's thyroiditis (HT) is a prevalent condition characterized by increased thyroid antibody titers (TAT) in non-celiac disease. The emergence of a gluten-free diet (GFD) as a potential treatment for reducing TAT and HT symptoms is a promising development. However, the potential benefits of gluten withdrawal in HT are not fully understood and the overall evidence is inconclusive. The aim of this review article is to present a systematic protocol for evaluating the effects of a GFD intervention in the treatment of HT in non-celiac disease.

Methods. Randomized controlled trials in adults and older people with HT and non-celiac disease following the GFD intervention compared to any gluten dietary and no dietary interventions or placebo (as long as it contains gluten) will be included. We will use Cochrane Central, Medline, Lilacs, Embase, Scopus, and Web of Science for the search. Free triiodothyronine (fT3), free thyroxine (fT4), thyroid stimulating hormone (TSH), TAT - anti-thyroid peroxidase (TPO) and anti-thyroglobulin (Tg), C-reactive protein (CRP), vitamin D, adverse effects, body weight, body mass index (BMI), diet adherence and health-related quality of life will be used as the outcomes. We will present the results in a narrative format and if possible, we will conduct a meta-analysis using a random effects model. The certainty of the evidence using the Grading of Recommendations Assessment Development and Evaluation (GRADE) will be assessed.

Conclusion. We will disseminate the results through peer-reviewed publications, social networks, and educational talks. The systematic review will provide valuable information on the effects of the GFD in the treatment of HT in non-celiac disease verifying its impact mainly on TAT.

Keywords: gluten-free diet, Hashimoto's thyroiditis, non-celiac disease, systematic review

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Hashimoto's thyroiditis (HT) is the most common organ-specific autoimmune disorder worldwide (McGrogan et al. 2008). In a recent systematic review, the general prevalence of HT in adults was 7.5%, 17.5% in women, and 6% in men. The risk of developing HT in adult women was approximately four times higher than in adult men (Hu et al. 2022) and can reach 350/100,000/year in women and 80/100,000/year in men (McGrogan et al. 2008). HT is known as a lymphocytic thyroiditis and chronic autoimmune thyroiditis and its main clinical manifestation is primary hypothyroidism; in other words, the central damage to the thyroid gland (Ralli et al. 2020; Jin et al. 2022). The HT is associated with cardiovascular disease (Jin et al. 2022) and a risk factor for developing cancer (Rahman et al. 2019). Despite its high prevalence and negative impact on patients' health and quality of life, the exact pathogenesis of HT remains elusive and treatment options often provide only partial relief (Rodziewicz et al. 2024).

Consequently, there is growing interest in exploring alternative therapeutic approaches that target the mechanisms underlying HT and its symptoms (Ralli et al. 2020; Osowiecka and Myszkowska-Ryciak 2023). In recent years, dietary interventions have gained considerable attention in managing HT symptoms due to their potential to modulate visceral hypersensitivity, gut motility, and microbiota composition (Drago et al. 2006; Ralli et al. 2020; Cayres et al. 2021; Zhao et al. 2022; Osowiecka and Myszkowska-Ryciak 2023; Stramazzo et al. 2023; Rodziewicz et al. 2024). Among these interventions, a gluten-free diet (GFD) has emerged as one currently used alternative.

Non-celiac disease, which may be present in HT, is characterized by symptoms similar to those seen in celiac disease patients after consuming gluten-containing foods (Koning 2015), but without an increase in antibodies, and may also present intestinal damage (Di Sabatino et al. 2016). Autoimmune diseases such as HT are known to have a high prevalence in individuals with non-celiac disease (Drago et al. 2006; McGrogan et al. 2008; Ihnatowicz et al. 2021; Frommer et al. 2023). However, the specific role of gluten in the pathogenesis of HT and as a trigger for its symptoms is not yet fully understood, especially in non-celiac disease patients (Effraimidis and Wiersinga 2014). While some studies have suggested potential benefits, the overall evidence is limited and inconclusive. Some authors have found that the GFD reduced thyroid antibody titers and slightly increased vitamin D levels in women with HT (Krysiak et al. 2019). However, other current evidence does not support recommending the GFD for HT patients without celiac disease (Ihnatowicz et al. 2021; Piticchio et al. 2023). Thus, the authors emphasized the importance of a balanced diet high in essential nutrients for thyroid function. For other authors, non-celiac autoimmune diseases may partially respond to the GFD, but the mechanisms are not fully understood (Lerner et al. 2022).

A possible explanation for the mechanisms of thyroid response to gluten consumption is that this protein found naturally in some cereals, especially wheat (Koning 2015), can interact with the intestinal epithelium through the C-X-C motif chemokine receptor 3 (CXCR3), promoting the release of zonulin by enterocytes allowing the passage of molecules from the intestinal epithelium towards the lamina propria. Once gliadin peptides (the central part of gluten that can cause proinflammatory reactions) have entered the lamina propria, those peptides could activate the innate immune system via toll-like receptors 2 and 4 (TLR-2 and TLR-4) inducing the release of proinflammatory cytokines such as interferon gamma-induced protein (IP-10/CXCL10) and tumor necrosis factor (TNF) (Drago et al. 2006; Effraimidis and Wiersinga 2014; Rahman et al. 2019; Lerner et al. 2022), i.e. gluten in HT patients increases the circulating levels of proinflammatory cytokines and intestinal permeability (Tovoli et al. 2015). As a result, these cytokines could cause an increase in anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-Tg) antibodies in the thyroid (Muhammad et al. 2017).

Although gluten accounts for up to 50% of the energy consumed in the developed and developing countries (Tovoli et al. 2015), the restrictions caused by removing it from the diet make this nutritional intervention challenging leading to high percentages of non-adherence. There are several reasons for this non-adherence, namely the lack of knowledge on the part of consumers and food handlers, inadequacies in labels, and lack of understanding in reading them (Ho et al. 2023), cross-contamination and high cost of gluten-free foods, lack of availability and access to these foods and unpleasant sensory characteristics (Garnweidner-Holme et al. 2020; Nikniaz et al. 2022) as well as issues of an individual and social nature (Muhammad et al. 2017). These reasons highlight the factors interfering with adherence and the need for individualized care to monitor this situation, so nutrition professionals can propose assertive, applicable interventions (Garnweidner-Holme et al. 2020).

To date, only one systematic review has attempted to explain the effect of gluten withdrawal on HT

in patients without celiac disease. The results were inconclusive for various reasons pointed out by the authors and some methodological design issues (Piticchio et al. 2023; Araujo et al. 2024). Given the conflicting results and limited high-quality studies, we will conduct a systematic review to evaluate the effectiveness of gluten withdrawal in treating HT in non-celiac individuals.

Our review will be unprecedented and unique in its methodological rigor. The specific objectives are to verify the effects of GFD on C-reactive protein, vitamin D, body weight, and body mass index (BMI) in individuals with HT and without celiac disease; to assess whether this gluten-free intervention improves the quality of life of these individuals; and to identify whether the GFD causes any adverse effects in these individuals.

Methods

Protocol and registration. The present protocol followed the reporting guidance provided in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) (Moher et al. 2016) (Supplementary Material 1, available upon request from the authors). We will conduct a systematic review following the Cochrane Handbook for Systematic Reviews (Higgins et al. 2024). The protocol for this systematic review is in the International Prospective Register of Systematic Reviews (PROSPERO, registration ID: CRD42024566034).

Eligibility criteria. The inclusion criteria for studies were established according to the PICOS framework (Table 1). The study population will consist of adults and the older people diagnosed with HT and non-celiac disease participating in a randomized controlled trial (RCT), including crossover trials, following GFD intervention. Valid comparator groups will comprise those receiving any gluten dietary intervention, no dietary intervention or placebo (as long as all contain gluten). Therefore, the research question is: Is the gluten withdrawal from the diet effective in treating HT in non-celiac disease?

Moreover, the studies reporting pregnancy or lactation, gluten-reduced diet intervention, patients with thyroidectomy, supplementation intervention, interventions with other supporting diets, multifactorial interventions, interventions that induce autoimmune thyroid diseases, patients who started HT drug therapy at the same time as GFD, patients who changed HT drug therapy during the GFD period, patients with hyperthyroidism or other endocrine disorders, will be excluded.

Intervention details. According to the eligibility criteria, to avoid confounding, the studies that have interventions with other supporting diets, such as low carbohydrate diet, mediterranean diet, hypocaloric diet, Brazilian cardio-protective diet (DICA/BR diet) or multifactorial interventions, such as lifestyle, physical exercise, use of supplements, or both will be excluded. We will exclude the diets with a low gluten content and the studies with interrupted time series and non-human studies. As for the comparison group, it may be any gluten-containing diet, such as usual/unusual diets without intervention, calculated, prescribed or managed; however, it is possible to evaluate, at least qualitatively, the gluten intake by the researchers or placebo diet, described by the authors, as long as it contains gluten. For all diets, we will consider the nutritional profile of adults and the elderly for better discussion and data analysis. The GFD is a proposed diet, in which all foods and gluten-containing products are excluded. Gluten is a protein found naturally in some cereals, especially wheat, rye, barley, spelled (red wheat), and kamut (Khorasan or Eastern wheat) (Koning 2015). It can also be added to processed foods to flavor or texture (Drago et al. 2006; Ihnatowicz et al. 2021).

Table 1
PICOS criteria for studies inclusion in the systematic review

P =	Adults and older people diagnosed with Hashimoto's thyroiditis and non-celiac disease
I =	Gluten-free diet
C =	Any gluten dietary intervention; no dietary intervention; placebo (As long as all of them contain gluten)
O =	Serum levels of
	Thyroid hormones: fT3, fT4
	TSH
	Anti-thyroid antibodies: Anti-TPO, Anti-Tg
	CRP
	Vitamin D
	and
	Adverse effects
	Anthropometric measurements: body weight, BMI
	Diet adherence
S =	Randomized controlled trial, including crossover trials

Abbreviations: Anti-Tg – anti-thyroglobulin antibodies; anti-TPO – thyroid peroxidase antibodies; BMI – body mass index; CRP – C-reactive peptide; fT3 – free triiodothyronine; fT4 – free thyroxine; PICOS: P – participants; I – intervention; C – comparator; O – outcomes; S – study; TSH – thyroid stimulating hormone.

Information sources and search strategy. We carried out a highly sensitive search strategy with the assistance of a librarian. This strategy will be carried out based on Cochrane Central, Medline (via PubMed), Lilacs (Latin American and Caribbean Health Sciences Literature in the Virtual Health Library, via Virtual Health Library), Embase (Elsevier), Scopus (Elsevier), and Web of Science (Elsevier) without language or publication period restrictions (Figure 1). We used accessible terms in combination with Boolean operators to carry out the search strategy, as shown in Table 2 and Supplementary Material 2 (available upon request from the authors). The search strategy has been tested by Peer Press (McGowan et al. 2016) (Supplementary Material 3, available upon request from the authors).

Additionally, clinical trials will be searched, whether ongoing or unpublished trials, or previous systematic reviews on the topic. We will also carry out an additional search in the gray literature (Google Scholar and ProQuest), hand-searching the reference lists of the included studies and with experts. If we need to include data, we will contact the authors by email requesting information.

The electronic database searches will be limited to keywords, titles, and abstracts. The search terms were identified and grouped from the research question's principal components (PICOS elements). If the timeframe to complete the review exceeded 12 months, we will update the search and include new studies that meet the review eligibility criteria.

Study records

Data management. A preliminary pilot test encompassing two studies according to inclusion and exclusion criteria during the initial screening of titles and abstracts will be conducted. Two investigators (E.A. and C.C-L.) will independently perform the study selection. We will import all articles from electronic searches into the Rayyan (Ouzzani et al. 2016) and delete duplicate studies. Titles, abstracts, and full-text articles will be selected and checked against the eligibility criteria for inclusion in the study independently by two reviewers (E.A. and C.C-L.). Any disagreement will be resolved through discussion or, if required, a third author will be consulted (L.DeS.). We will record he selection

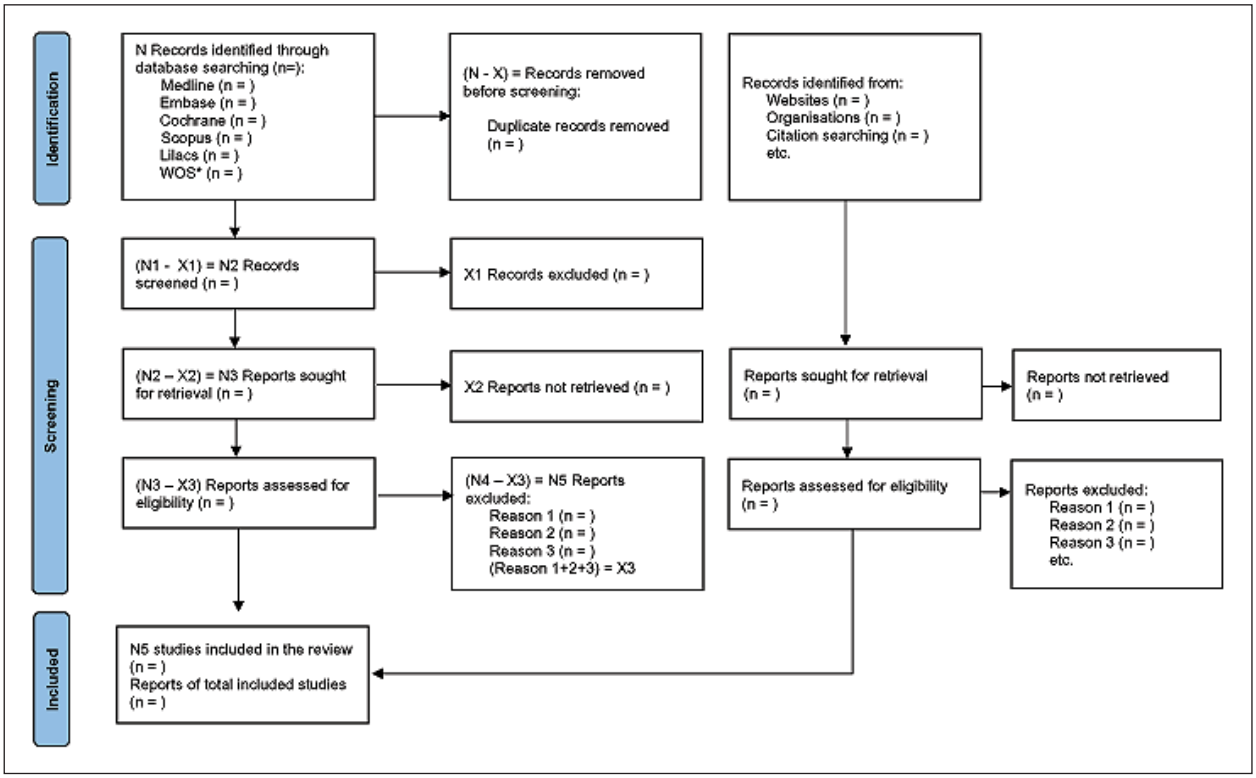

Figure 1. PRISMA flow diagram for identifying, screening and determining the eligibility and inclusion of studies and reports. Abbreviations: WOS – Web of Science (Page et al. 2021).

Table 2
Search strategy for the MEDLINE database

#1 Population*	"thyroid diseases"[MeSH Terms] OR "thyroiditis, autoimmune"[MeSH Terms] OR "Thyroiditis" [tiab] OR "Thyroid inflammation" [tiab] OR "Hashimoto" [tiab] OR "Hashimoto's thyroiditis" [tiab] OR "Hashimoto's disease" [tiab] OR "Chronic lymphocytic thyroiditis" [tiab] OR "Autoimmune thyroiditis" [tiab] OR "Thyroid Disorder" [tiab] OR "Thyroid Disorders" [tiab] OR "Thyroid Disease" [tiab] OR "Thyroid Diseases" [tiab] OR "Thyroid Autoimmunity" [tiab] OR "Autoimmune Thyroid Disease" [tiab] OR "Autoimmune Thyroid Disorders" [tiab] OR "Hashimoto's Thyroiditis" [tiab] OR "Hashimoto's Disease" [tiab] OR "Chronic Thyroiditis" [tiab] OR "Lymphocytic Thyroiditis" [tiab] OR "Autoimmune Thyroiditis" [tiab] OR "Thyroid Gland Inflammation" [tiab] OR "Thyroid Inflammatory Disease" [tiab]
#2 Intervention*	("diet, gluten free"[MeSH Terms] OR "Gluten-free"[tiab:~0] OR "Gluten deprivation"[tiab:~0] OR "Gluten restriction" [tiab] OR "Gluten withdrawal" [tiab] OR "Gluten elimination" [tiab] OR "Gluten exclusion" [tiab] OR "Gluten avoidance" [tiab] OR "Gluten removal" [tiab])
#3 Study*	((("clinical trial"[Publication Type] OR "comparative study"[Publication Type] OR ("control"[Text Word] AND "study"[Text Word]) OR "program"[Text Word] OR "epidemiologic studies"[MeSH Terms]) NOT (("animals"[MeSH Terms:noexp] NOT "humans"[MeSH Terms:noexp]) OR "comment"[Publication Type] OR "editorial"[Publication Type] OR "review"[Publication Type] OR "meta-analysis"[Publication Type] OR "case report"[Text Word] OR "consensus"[MeSH Terms] OR "guideline"[Publication Type] OR "history"[MeSH Subheading])) OR (("randomized controlled trial"[Publication Type] OR "controlled clinical trial"[Publication Type] OR "randomized"[Title/Abstract] OR "placebo"[Title/Abstract] OR "drug therapy"[MeSH Subheading] OR ("randomly"[Title/Abstract] OR "trial"[Title/Abstract] OR "groups"[Title/Abstract])) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]))))
	Search strategy: [(#1) AND (#2) AND (#3)]

From PICOS*: P – participants; I – intervention; C – comparator; O – outcomes; S= study.

process by completing a PRISMA flow diagram and 'Characteristics of excluded studies during full-text screening' will be documented (McGowan et al. 2016).

Selection process. Two independent reviewers will select the studies (E.A. and C.C-L.) in a two-phase procedure: phase 1 – title and abstract screening and phase 2 – full-text examination. Any disagreement will be resolved through discussion or, if required, a third author will be consulted (L.DeS.).

Data collection process. An initial data extraction template using Microsoft Excel will be formulated. We will conduct a preliminary pilot test with the review team comprising two studies to test the data collection instrument. If needed, we will make adjustments to the collection instrument. Two independent reviewers (E.A. and C.C-L.) will extract the data from the reviewed papers using a data extraction tool developed by the authors to capture specific details related to the PICOS structure.

Two review authors (E.A. and C.C-L.) will extract the following study characteristics and outcome data, if available: a) study information data including study design, total duration, sample size of each group, number of participants lost to follow-up/withdrawn, number of participants analyzed, number of study centers and locations, study setting, and date of study; b) participants including mean age, age range, sex, other baseline data (e.g., weight, BMI), inclusion criteria, and exclusion criteria; c) type of intervention including duration, frequency, concentration; d) type of outcomes, including primary and secondary outcomes, will be specified and collected, and time points will be reported; e) confounders including uncontrolled confounders and a list of variables authors will be included in analyses for adjusted estimates; f) methods used to control for confounders; and g) notes: funding and notable conflicts of interest of study authors.

Any disagreement will be resolved through discussion or by consulting third author. We will contact the authors for unreported outcomes and missing data through three consecutive emails, 15 days apart.

Data items/outcomes and prioritization. There is no established consensus for outcomes in the Core Outcomes Measures in Effectiveness Trials (COMET) (COMET 2010), so the outcomes chosen were based on guidelines and randomized clinical trials.

The main outcomes of the review will be: thyroid hormones (free triiodothyronine, fT3; free thyroxine, fT4), thyroid-stimulating hormone (TSH), and anti-thyroid antibodies (anti-Tg, anti-TPO) measured in the blood samples, and adverse effects described by the authors. Additional outcomes will include: anthropometric measurements (body weight, BMI) measured with scale and stadiometer, health-related quality of life assessed by validated instruments,

diet adherence described by the authors, C-reactive protein (CRP) and vitamin D measured in the blood samples.

All the parameters will be measured from a baseline before and after the nutrition intervention. The intervention duration will be considered in three periods: short duration up to three months; medium duration up to six months, and long duration over six months. The primary outcomes are essential for evaluating the thyroid function (Sakata and Miura 1987; McGowan et al. 2016; Pludowsk et al. 2022; Ulker et al. 2023). On the other hand, anthropometric measurements may be affected by removing gluten from the diet because gluten is contained in foods considered more caloric or/and inflammatory. Their exclusion can impact the qualitative/quantitative distribution of the daily diet, affecting the weight and BMI of the individuals (Ulker et al. 2023). Regarding CRP, HT is an inflammatory disease. Does removing an inflammatory agent, i.e., gluten, impact the CRP in HT patients without celiac disease (Ihnatowicz et al. 2021)? Regarding vitamin D, its absorption from food may be reduced in these patients, in addition to the critical role of this vitamin in the immune system and its anti-inflammatory properties (Ihnatowicz et al. 2021). Another factor is adherence to the diet. Evidence has shown insufficient adherence to GFD, which deserves attention. Factors such as cost, knowledge, taste, food availability, and social issues, among others, are often cited as interfering factors in the diet. In addition, some studies point to low adherence of around 36% to 96%, which can vary according to the method used to determine it (Piticchio et al. 2023).

We will consider the following features in the normal range (Pludowsk et al. 2022; Ulker et al. 2023): anti-TPO (<5.61 IU/mL), anti-Tg (<4.11 IU/mL), TSH (0.35–4.94 mIU/L), fT3 (1.58–3.91 pg/mL), fT4 (0.70–1.48 ng/dL), vitamin D (30–50 ng/mL; ≥20–<30 ng/mL = insufficient; <20 ng/mL = deficient), CRP (<0.1 mg/dL = low risk; 0.1 to 0.3 mg/dL = intermediate risk; >0.3 mg/dL = increased risk), BMI (18.5 to 24.9 kg/m² for adults; 22 to 27 kg/m² for older people. These values may vary due to the method used to measure them. If another unit of measurement is used, they will be transformed to facilitate data analysis.

Risk of bias in individual studies. We will assess the risk of bias using the Cochrane 'Risk of Bias' tool (Rob2), as outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al. 2024). This systematic review will assess the effect of the assignment to the intervention (the intention to treat, ITT, effect), so we will perform all risk of bias assessments on this effect. Two review authors (E.A. and C.C-L.) independently will assess the risk of bias of specific results of a trial according to the following domains: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data; bias in the measurement of the outcome; bias in the selection of the reported result. We will use the signaling in the RoB2 tool and rated each domain as 'low risk of bias,' 'some concerns', or 'high risk of bias.' The overall risk of bias for the result will be the least favorable assessment across the domains of bias (Higgins et al. 2024).

Data Analysis

Synthesis. First, we will perform a narrative synthesis, synthesizing the literature for each category of all relevant parameters. A meta-analysis may be conducted: we plan to summarize the effect using RRs and 95% CIs for dichotomous outcomes. For continuous outcomes collected on the same scale, we will intend to pool the effect using an MD with corresponding standard deviation (SD) and 95% CI; for continuous outcomes collected with different scales (e.g., quality of life), we plan to use an SMD with 95% CI. The data with a random effects model will be pooled. We will use a forest plot with RRs for primary and secondary outcomes. The meta-analysis using the Revman, R, and RStudio tools and the GRADE system will be performed (Higgins et al. 2024).

Dealing with the missing data. We plan to contact the study authors, investigators, or sponsors to verify key study characteristics and to obtain missing numerical outcome data, if necessary (e.g. when a study was identified as an abstract only). If this approach is not unsuccessful, we intend to input missing data using appropriate statistical methods. Where this is not possible (and the missing data are thought to introduce bias), we plan to explore the impact of including such studies in the overall assessment by conducting a sensitivity analysis. A sensitivity analysis to evaluate studies with a high risk of bias will be performed (Higgins et al. 2024).

Analysis of subgroups or subsets. We will assess a statistical heterogeneity using Cochran's Q test to determine whether heterogeneity is significant (considering a threshold value of $P<0.1$ to indicate that heterogeneity is statistically significant). In addition, Higgins' I^2 will be applied with the following interpretation: (i) 0% to 40% – may not be important; (ii) 30% to 60% – may represent moderate heterogeneity;

(iii) 50% to 90% – may represent substantial heterogeneity; and (iv) 75% to 100% – considerable heterogeneity. Additionally, we will visually inspect the forest plots for signs of heterogeneity (e.g., non-overlapping CI). If substantial heterogeneity has been identified and information is available, the subgroup analyses will be carried out according to the characteristics of the population (gender, age group) and the outcome (BMI). A random-effect meta-regression analysis, considering the potential main factors causing heterogeneity (e.g., gender, age, BMI, CRP, vitamin D concentration) will be performed (Deeks et al. 2024).

Certainty of evidence. The certainty of the evidence will be rated using the GRADE methodology approach by two independent reviewers (E.A. and C.C-L.). Disagreements will be resolved through deliberation or by a third reviewer (L.DeS.). We will use four levels to rate the quality of evidence across trials in the GRADE system: very low, low, moderate, and high. RCTs are categorized as high quality but can be downgraded due to limitations in study design, indirectness of evidence, imprecision of results, unexplained heterogeneity or inconsistency, or high probability of publication bias (Schunemann et al. 2024).

Publication bias. If there are fewer than ten studies in a meta-analysis, the publication of bias will be tested by visual inspection of funnel plots and using Egger's regression asymmetry test (Page et al. 2024).

Discussion

The evidence on the benefits of GFD needs to be more consistent. However, there is a growing trend to avoid gluten due to its supposed adverse health outcomes. Regarding TH, for example, the evidence is limited and more research is needed to prove it (Ihnatowicz et al. 2021). This protocol describes the methodology we will apply for the first robust systematic review with possible meta-analysis synthesizing the efficacy of gluten withdrawal in treating HT in non-celiac individuals.

There is a recently published meta-analysis (Piticchio et al. 2023), in which the authors have concluded that their results were insufficient "to recommend" GFD for non-celiac patients diagnosed with HT despite the positive effects of removing gluten on the thyroid (Piticchio et al. 2023). The limiting factors of this research were many: 1) small sample size due to the few databases searched, only PubMed and Scopus; 2) there was a language restriction, only to English; 3) few outcomes analyzed; 4) the study was conducted and evaluated for risk of bias according to observational studies, a tool that is not suitable for evaluating articles such as clinical trials; 5) it evaluated randomized and non-randomized clinical trials in the same way; and 6) it included a study with mixed nutritional interventions making it difficult to assess whether the effect was of GFD (Araujo et al. 2024). Therefore, a systematic review with greater methodological rigor is needed from the strategic search of the literature with high sensitivity and broad language to the use of an appropriate tool to assess the risk of bias of the selected studies and assess the certainty of the evidence found by GRADE (Schunemann et al. 2024).

The limitations of the review may include the usual limitations of systematic reviews and meta-analyses, such as publication bias, low methodological quality, and heterogeneity of the included studies. The differences among sample characteristics, dietary data, diet adherence, adverse effects, methodological quality, and the limited number of RCT studies with a risk of bias on some outcome variables can lead to inconclusive results and restrict comparisons between the included studies affecting the generalizability of the results.

The findings from this review may be helpful for research and health professionals responsible for adult and older people lifestyle surveillance and health promotion, such as nutritionists and endocrinologists. We will disseminate the results obtained through peer-reviewed publications. We will be available on a freely accessible public website, scientific health conferences of great interest in these conclusions, social networks, and educational talks. If the review findings justify a change in practice, we will draft a summary report and send it to key health professionals in the National Health Service.

Conclusion

This systematic review and possible meta-analysis will provide updated evidence of the effectiveness of gluten withdrawal in treating HT in non-celiac individuals verifying its impact mainly on the thyroid autoantibodies.

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