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Research Article

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Myo-Inositol, With or Without Selenium, in Hashimoto's Thyroiditis and Autoimmune Thyroid Disease: A Scoping Review

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Abstract

Background: *Hashimoto's thyroiditis (HT) is the leading autoimmune cause of hypothyroidism in iodine-sufficient regions. Selenium supplementation is an established adjunct in HT, and myo-inositol has more recently been investigated, alone or combined with selenium, as a modulator of thyroid-stimulating hormone (TSH) signaling and autoimmunity.*

Objective: *To systematically map the extent, nature, and distribution of the available evidence on myo-inositol supplementation — alone or combined with selenium — across the spectrum of autoimmune thyroid disease.*

Methods: *A multi-database search (PubMed, Web of Science, Scopus, ScienceDirect, SpringerLink, Google Scholar) was supplemented by citation searching of related compehensive reviews identified during screening. Sources reporting original data on myo-inositol supplementation (alone, combined with selenium, or compared against selenium or other micronutrients) in adults with HT or autoimmune thyroiditis across any thyroid-function status were eligible, regardless of study design.*

Results: *The charted evidence spans thyroid function and autoantibody titers in SCH, thyroid structural change on ultrasound, prevention of progression to overt hypothyroidism in euthyroid autoimmune thyroiditis, subjective wellbeing and quality of life, sexual function and depressive symptoms under different micronutrient monotherapies, and a novel comorbid population with migraine. Only three studies directly compared combined myo-inositol plus selenium against selenium monotherapy.*

Conclusions: *The evidence base on myo-inositol in autoimmune thyroid disease is small, heterogeneous in design and population. Its principal gaps lie outside that narrow question: longer-term progression data, patient-reported outcomes, head-to-head comparisons against other micronutrients, and evidence in comorbid populations. These gaps, rather than a further pooled TSH estimate, define the priorities for future primary research.*

Keywords: Myo-Inositol, Selenium, Hashimoto's Thyroiditis, Autoimmune Thyroiditis, Subclinical Hypothyroidism, Scoping Review, PRISMA-ScR

1. Introduction

1.1. Background

Hashimoto's thyroiditis (HT) is the most prevalent autoimmune endocrine disorder and the leading cause of hypothyroidism in iodine-sufficient regions, with pooled adult prevalence reaching double digits in recent systematic reviews [1]. The disease reflects progressive, T-cell-mediated destruction of the thyroid gland with production of autoantibodies against thyroid peroxidase (TPOAb) and thyroglobulin [2]. Many patients present with, or progress through, subclinical hypothyroidism (SCH) — elevated thyroid-stimulating hormone (TSH) with normal free thyroxine — and a proportion advance to overt hypothyroidism requiring lifelong levothyroxine [2,3,28]. Managing SCH in HT remains debated, balancing prevention of disease progression against the risk of overtreatment [4].

Selenium, an essential trace mineral integral to the glutathione peroxidase and thioredoxin reductase selenoprotein families, supports antioxidant defense within the thyroid gland [5]. Clinical trials and a recent meta-analysis show that selenium supplementation in HT can reduce TPOAb titers and improve thyroid echogenicity, suggesting an immunomodulatory effect, and selenium monotherapy is now widely used as an adjunct, particularly in mild disease not yet warranting levothyroxine (Duntas, 2015) [6-8].

More recently, myo-inositol — a naturally occurring sugar alcohol and precursor of inositol trisphosphate — has been investigated as an adjunct in autoimmune thyroid disease, alone and combined with selenium [9]. It participates in intracellular signaling governing cell growth, apoptosis, and immune function, and is hypothesized to modulate autoimmunity and enhance thyroidal TSH sensitivity via the inositol-dependent branch of TSH signaling [9,10,11]. This dual mechanism — immunomodulation and direct thyroidal support — has motivated a small but growing body of research examining myo-inositol across thyroid-function states, comparators, and outcome domains.

1.2. Rationale for a Scoping Review

A systematic review with meta-analysis comparing combined myo-inositol plus selenium against selenium alone might appear the natural first step. However, this narrow question has already been addressed twice: Zuhair pooled three trials directly comparing the two regimens (n = 288) and reported a significant TSH and TgAb reduction with combined therapy; Stanchev et al. subsequently updated this same pooled analysis with a frequentist random-effects model and trial sequential analysis, confirming the TSH and TgAb findings while flagging a risk of type I error for TgAb and substantial heterogeneity for free T4 [12,13]. A third, broader narrative review by Samuel et al. situated selenium and myo-inositol across the wider spectrum of thyroid disorders, including Graves' disease and benign nodules [14].

Because the entire evidence base with a direct selenium-alone comparator consists of only three trials, already meta-analyzed twice with trial sequential analysis, a further review restricted to this comparison would largely duplicate existing, rigorous work. At the same time, our search retrieved studies evaluating myo-inositol in HT or autoimmune thyroiditis outside this narrow frame: single-arm studies without a selenium-alone comparator, a study comparing myo-inositol against selenium and vitamin D as separate monotherapies, and a study in a comorbid migraine population not previously considered. These sources differ in population, intervention, outcome domain, and design — precisely the heterogeneous evidence for which a scoping review, rather than a further effect-size synthesis, is appropriate [15-17]. We therefore reframed this work as a scoping review, following the PRISMA-ScR checklist and JBI guidance, aiming to map the breadth of this evidence rather than re-estimate an already-published pooled effect [15-17].

1.3. Review Questions and Objectives

Using the Population–Concept–Context (PCC) framework recommended for scoping reviews, this review addresses the following questions:

- **Population:** adults with Hashimoto's thyroiditis or autoimmune thyroiditis, across the spectrum from euthyroidism to subclinical hypothyroidism, including comorbid populations identified in the literature (e.g., migraine).
- **Concept:** supplementation with myo-inositol, administered alone or in combination with selenium, and compared where available against selenium alone, other micronutrients (e.g., vitamin D), or no treatment.
- **Context:** any clinical, biochemical, structural, or patient-reported outcome domain reported in original human research published in English, with a minimum follow-up of eight weeks.

Specifically, this review aims to: (1) chart the designs, populations, interventions, comparators, and outcome domains of the available primary evidence; (2) synthesize findings narratively within each outcome domain; (3) situate this evidence against the two existing MI+Se-versus-Se-alone meta-analyses, reproducing their pooled estimates for reference; and (4) identify evidence gaps to guide future primary research.

2. Methods

2.1. Protocol and Reporting Guideline

This review was not prospectively registered. It follows the PRISMA Extension for Scoping Reviews (PRISMA-ScR) checklist and the Joanna Briggs Institute (JBI) methodological guidance for scoping reviews, building on the original framework of Arksey and O'Malley (2005) [15-17]. The review was reframed from a planned systematic review with meta-analysis to a scoping review during manuscript preparation, for the reasons set out in Section 1.2; this change occurred before data charting and synthesis were finalized but after the initial database search had been run, disclosed as a limitation in Section 4.4.

2.2. Eligibility Criteria (PCC)

Population: Adults (≥18 years) diagnosed with Hashimoto's thyroiditis or autoimmune thyroiditis, at any thyroid-function

status (euthyroid or subclinically hypothyroid; SCH defined as elevated TSH with normal free T4). Comorbid populations (e.g., migraine) were eligible provided the HT/autoimmune thyroiditis diagnosis was explicit.

- **Concept:** Oral myo-inositol, alone or combined with selenium, at any dose or formulation, for a minimum of eight weeks. Studies comparing myo-inositol against comparators other than selenium alone (e.g., vitamin D, no treatment) were eligible for this review's broader mapping purpose, even without isolating the myo-inositol-plus-selenium-versus-selenium-alone comparison.

- **Context:** Any setting reporting thyroid function (TSH, free T3, free T4), thyroid autoantibody titers (TPOAb, TgAb), thyroid structural outcomes (ultrasound echogenicity or volume), disease progression or prevention, quality of life, or other patient-reported outcomes (e.g., sexual function, depressive symptoms).
- **Study designs:** Randomized controlled trials, quasi-experimental studies, and prospective or retrospective cohort studies (including single-arm pre–post designs) were eligible, reflecting the broader evidentiary scope of a scoping review. Case reports, case series, conference abstracts, editorials, narrative reviews, and animal or in vitro studies were excluded as primary evidence, though relevant systematic and narrative reviews identified during screening were retained for discussion (Section 3.6).

- **Other limits:** Full-text English-language articles; no restriction on year or country. Studies of patients with overt hypothyroidism at baseline, type 1 diabetes, or other autoimmune endocrine disease as the primary population were excluded, as were studies in which myo-inositol and/or selenium exposure could not be distinguished from unequally applied co-interventions.

2.3. Information Sources and Search Strategy

A literature search was conducted across five databases — PubMed, Web of Science, Scopus, ScienceDirect, and SpringerLink — selected for their coverage of biomedical/endocrinology literature, citation tracking, peer-reviewed breadth, full-text access, and journal depth, respectively; Google Scholar was searched as a supplementary grey-literature source. The search combined ("myo-inositol" OR "inositol") AND ("selenium" OR "selenomethionine" OR absent) AND ("Hashimoto" OR "autoimmune thyroiditis" OR "thyroiditis") AND ("subclinical hypothyroidism" OR "hypothyroidism" OR "euthyroid"), adapted with MeSH terms and field tags for PubMed and Web of Science. Unlike the originally planned systematic review, the selenium term was not mandatory, to capture myo-inositol-only arms. The search was limited to English-language publications with no year restriction and returned 320 records.

During full-text assessment, citation searching of two topically overlapping reviews identified during screening — Zuhair and Stanchev— identified one additional eligible source not retrieved by the original search, Pace et al. [12,13,18]. This step is reported separately in the PRISMA-ScR flow diagram (Figure 1).

2.4. Selection of Sources of Evidence

Two reviewers independently screened titles and abstracts, followed by full-text assessment against the PCC criteria in Section 2.2; disagreements were resolved by discussion. Title/abstract screening and initial full-text exclusions had originally used the narrower PICO-style criteria of the review as first planned (combined MI+Se versus Se alone only) and were reassessed against the broadened PCC criteria during manuscript revision. Because this reassessment was not re-run as an independent record-by-record screen of the full pool, the totals in Figure 1 should be reconciled by the review team against their complete screening log before submission — flagged explicitly as a limitation in Section 4.4.

2.5. Data Charting Process and Data Items

A standardized charting form was used to extract author(s) and year, country, study design, sample size and sex distribution, population, intervention and comparator (agent, dose, formulation, duration), outcome domains, and key findings. Charting was performed independently by two reviewers and cross-checked, with discrepancies resolved against the original source. Consistent with scoping review methodology, data were not pooled quantitatively given the heterogeneity of designs, comparators, and outcome domains.

2.6. Critical Appraisal of Individual Sources of Evidence

Critical appraisal is optional in scoping reviews and was used here descriptively, to characterize rather than exclude sources. The Cochrane Risk of Bias 2 (RoB 2) tool was applied to the two randomized trials, and the Newcastle-Ottawa Scale to the observational and single-arm studies, adapted for pre–post designs [19,20]. No source was excluded on this basis; results are reported narratively in Section 3.3.

2.7. Synthesis of Results

Findings are synthesized narratively by outcome domain, with a structured characteristics table (Table 1) and an evidence map (Figure 2) summarizing which domains each source addressed. For the three sources directly comparing MI+Se against selenium alone, the pooled standardized mean differences already published by Zuhair et al. and, updated, by Stanchev et al. are reproduced with citation in Section 3.5 as supplementary context; no independent meta-analysis or forest plot was undertaken, both because quantitative pooling is not the primary synthesis method for a scoping review and because the study pool (k = 3) has already been analyzed twice [12,13]. No funnel plot was constructed, as fewer than ten studies contributed to any comparison, below the threshold generally recommended for assessing small-study effects.

3. Results

3.1. Selection of Sources of Evidence

The database search identified 320 records; one additional record was identified through citation searching (Section 2.3). After duplicate removal, 208 unique records were screened by title and abstract, of which 126 were excluded. Of 82 reports sought for retrieval, 13 could not be obtained in full text. The remaining 69 full-text reports were assessed against the broadened PCC criteria; 59 were excluded (most commonly for lacking original exposure data, overt hypothyroidism or unrelated endocrine disease, not being original research, or non-English/inaccessible full text). Ten sources of evidence were retained: seven primary studies, charted in Table 1, and three related reviews, discussed in Section 3.6. The selection process is illustrated in Figure 1.

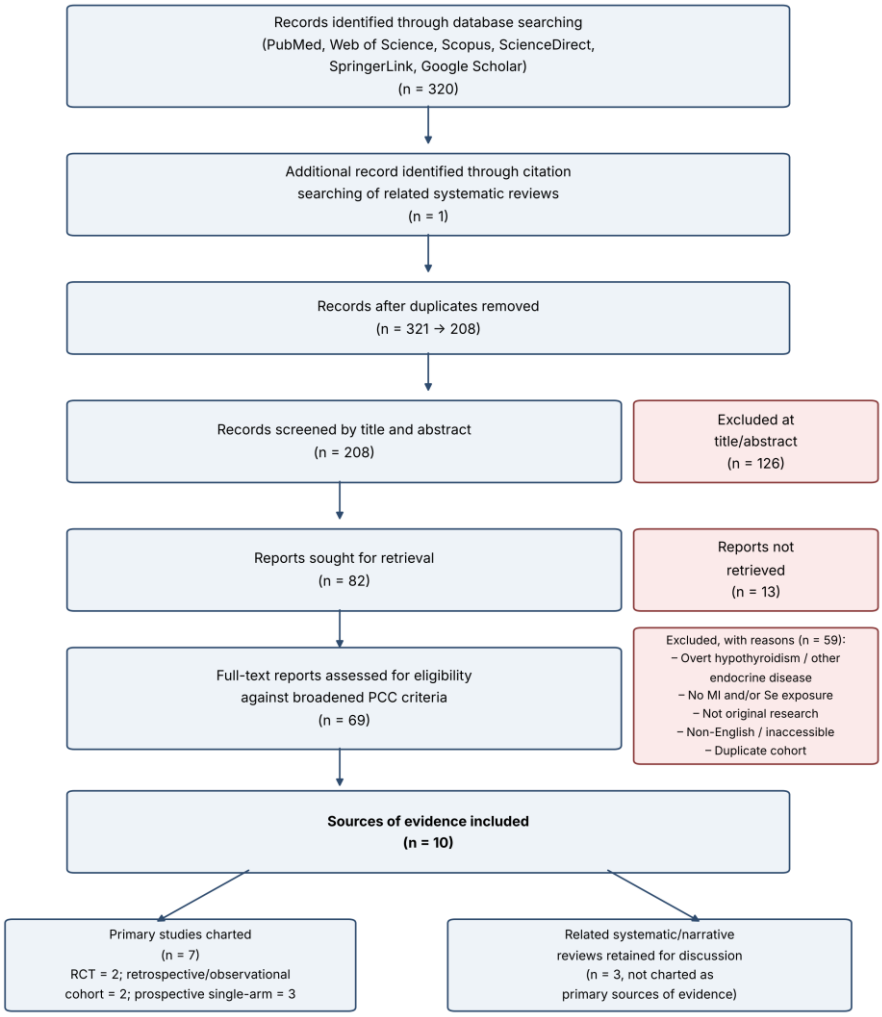


Figure 1: PRISMA-ScR flow diagram of source identification, screening, and inclusion. The original multi-database search (n = 320) was conducted by the review team; identification of Pace through citation searching of Zuhair and Stanchev is reported separately [12,13,18]. Title/abstract and initial full-text screening were reassessed against the broadened PCC eligibility criteria (Section 2.2); the review team should reconcile these totals with the complete screening log before submission.

3.2. Characteristics of Included Sources of Evidence

Table 1 summarizes the design, population, intervention/comparator, duration, and key findings of the seven primary studies. Study designs ranged from randomized controlled trials (n = 2) to retrospective or observational cohorts (n = 2) and prospective single-arm studies (n = 3). Five of the seven studies used combined myo-inositol plus selenium as the intervention of interest; one compared myo-inositol, selenium, and vitamin D as separate monotherapies; and only three studies included a direct selenium-alone comparator arm.

Source	Design	Population (n)	Intervention / comparator	Duration	Key findings
Nordio & Pajalich, 2013 [21]	RCT, double-blind	Women with SCH + AIT (n=48 randomized; n=46 analyzed)	MI 600 mg + Se 83 µg/day (n=24) vs Se 83 µg/day alone (n=24)	6 mo	TSH fell significantly only in the MI+Se group (−31%); TPOAb and TgAb fell significantly in both groups; ultrasound echogenicity and subjective wellbeing improved more with MI+Se.
Nordio & Basciani, 2017a,b [22,23]	RCT	HT with TSH 3–6 µIU/mL (n=168; 84 per group)	MI 600 mg + Se 83 µg/day vs Se 83 µg/day alone	6 mo	TSH fell significantly with MI+Se (4.22→3.26 µIU/mL) but not with Se alone; fT4 increased and TPOAb/TgAb fell significantly only with MI+Se; subjective symptom score improved in both groups.
Ferrari et al., 2017 [24]	Prospective, single-arm (no comparator)	Euthyroid autoimmune thyroiditis (n=21)	MI 600 mg + Se 83 µg/day, single arm, pre–post	6 mo	TSH declined significantly, most notably in patients with high-normal baseline TSH (2.1–4.0); autoantibodies and CXCL10 declined, suggesting reduced risk of progression to overt hypothyroidism.
Pace et al., 2020 [18]	Retrospective observational cohort	Euthyroid or SCH due to HT (n=101: untreated 29, Se 29, Se+MI 43)	Se-meth 83 µg/day vs Se-meth 83 µg + MI 600 mg/day vs untreated	6 and 12 mo	TSH decreased by 31% (Se) and 38% (Se+MI) vs. increased in untreated; TSH reduction occurred earlier with Se+MI; ultrasound echogenicity improved in both treated groups (not statistically significant).
Payer et al., 2022 [25]	Prospective, single-arm (no comparator)	Women with or at risk of SCH (n=148)	MI 600 mg + Se 83 µg/day, single arm, stratified by baseline TSH (2.5–4.99 vs 5–10 mIU/L)	6 mo	TSH decreased significantly in both TSH-severity subgroups; clinical symptoms (cold/warm tolerance, wellbeing) improved; authors noted the absence of a control group as a limitation.
Krysiak et al., 2023 [26]	Comparative cohort (separate monotherapy arms)	Euthyroid women with AIT (4 treated/untreated groups, n=29 each) + healthy controls	Untreated vs vitamin D 100 µg/day vs selenomethionine 200 µg/day vs myo-inositol 2.0 g/day (separate arms; no MI+Se arm)	6 mo	All three micronutrients were associated with better sexual function (FSFI) and mood (BDI-II) than no treatment, with vitamin D showing the largest benefit; no significant difference between selenomethionine- and myo-inositol-treated women.
Di Lorenzo et al., 2026 [27]	Retrospective cohort, single-arm (no comparator)	Adults with migraine comorbid with HT (n=163)	MI + Se (MYSE) combined supplementation, single arm, stratified by euthyroid vs SCH status	6 mo	TSH decreased (median 3.60→2.80 mIU/L); monthly migraine days and symptomatic drug use decreased significantly; fT4 increased slightly; findings consistent across thyroid-status subgroups.

Table 1: Characteristics and key findings of the seven primary sources of evidence. RCT = randomized controlled trial; SCH = subclinical hypothyroidism; AIT = autoimmune thyroiditis; HT = Hashimoto's thyroiditis; MI = myo-inositol; Se = selenium.

3.3. Critical Appraisal of Included Sources

Of the two randomized trials, Nordio and Pajalich randomized by initial TPOAb concentration with double-blinding, raising "some concerns" under RoB 2 for incomplete allocation-concealment reporting; Nordio and Basciani reported 1:1 randomization with an a priori sample-size calculation but undescribed blinding, also "some concerns", consistent with the appraisal reported for the same trials by Zuhair [12,21-23]. Pace scored "high-quality" on the Newcastle-Ottawa Scale for an observational design, though as a retrospective, non-randomized cohort it carries inherent selection bias and confounding-by-indication risk, acknowledged by the original authors [18]. Ferrari and Payer are prospective single-arm, pre–post studies without a comparator, precluding attribution of change specifically to myo-inositol rather than regression to the mean, seasonal TSH variation, or selenium alone; both groups note this explicitly [24,25]. Krysiak used parallel monotherapy arms with a priori power calculation, but allocation by patient preference introduces selection-bias risk [26]. Di Lorenzo is a retrospective chart-review cohort without a comparator, appropriate for descriptive pre–post analysis but not causal attribution [27]. Across all seven sources, no study blinded outcome assessors beyond the two randomized trials, and none reported a prospectively registered protocol.

3.4. Synthesis of Results by Outcome Domain

3.4.1. Thyroid Function in Subclinical Hypothyroidism (TSH, Free T3, Free T4

Three studies with a direct comparator reported TSH change in SCH or at-risk populations. Nordio and Pajalich and Nordio and Basciani each found a significant TSH reduction with combined MI+Se but not selenium alone over six months, and Pace et al. found a numerically larger and earlier TSH reduction with Se+MI

(−38%) than selenium alone (−31%) [21-23]. The single-arm studies Ferrari and Paye likewise reported significant within-group TSH reductions after MI+Se, as did Di Lorenzo in a comorbid migraine population [24,25,27]. Free T4 increased significantly with MI+Se in both randomized trials, while free T3 showed no consistent change.

3.4.2. Thyroid Autoantibodies and Disease Progression/ Prevention

TPOAb and TgAb titers declined with MI+Se in both randomized trials though Nordio and Pajalich also observed a significant decline with selenium alone, indicating antibody reduction is not specific to myo-inositol in that trial [21-23]. Ferrari is the only source addressing disease progression as a primary endpoint: six months of MI+Se in euthyroid autoimmune thyroiditis was associated with declines in antithyroid antibodies and the chemokine CXCL10, interpreted as suggestive of reduced progression risk [24]. Lacking a selenium-alone or untreated comparator, this study cannot isolate myo-inositol's relative contribution; Pace provides indirect support via a numerically faster TSH normalization with Se+MI than Se alone, though progression was not a formal endpoint there [18].

3.4.3. Thyroid Structural Outcomes

Ultrasound echogenicity improved more with MI+Se than selenium alone in both Nordio and Pajalich; all patients in the combined group versus 10/22 with selenium alone) and Pace improvement in both treated groups relative to untreated, though the between-group difference was not significant) [18,21]. No source reported quantitative thyroid volume change.

3.4.4. Myo-Inositol as a Monotherapy, and Comparison with Other Micronutrients

Only Krysiak evaluated myo-inositol as a monotherapy without co-administered selenium, comparing it in parallel arms against vitamin D and selenomethionine monotherapies and no treatment, in euthyroid women with autoimmune thyroiditis [26]. All three active treatments were associated with lower thyroid antibody titers, lower hs-CRP, and better sexual function and mood scores than no treatment, with vitamin D showing the most pronounced benefit; myo-inositol and selenomethionine did not differ significantly from each other. This is the only source directly comparing myo-inositol alone with selenium alone, and it does so for antibody titers, sexual function, and mood rather than TSH.

3.4.5. Quality of Life and Subjective Wellbeing

Subjective wellbeing or symptom scores improved more with MI+Se than selenium alone in both randomized trials, using the SF-12 instrument in Nordio and Pajalich and a seven-item symptom questionnaire in Nordio and Basciani [21-23]. Payer reported improved cold/warm tolerance and other symptom measures after MI+Se without a comparator [25]. Krysiak is the only source using validated instruments for sexual function (FSFI) and depressive symptoms (BDI-II); as above, it found benefit for all three micronutrients relative to no treatment, with vitamin D outperforming selenium and myo-inositol [26].

3.4.6. Comorbid Conditions: Migraine

Di Lorenzo is the first and only source addressing MI+Se supplementation in migraine comorbid with HT [27]. In this retrospective cohort of 163 adults, six months of MYSE (myo-inositol plus selenium) was associated with significant reductions in monthly migraine days and symptomatic drug use, alongside the expected TSH improvement, with consistent findings across euthyroid and SCH subgroups. As a single-arm retrospective study, it cannot establish whether the migraine benefit reflects the thyroid-directed intervention, its individual components, or concurrent changes in migraine-preventive treatment; nonetheless, it identifies a population and outcome domain entirely absent from the existing meta-analytic literature.

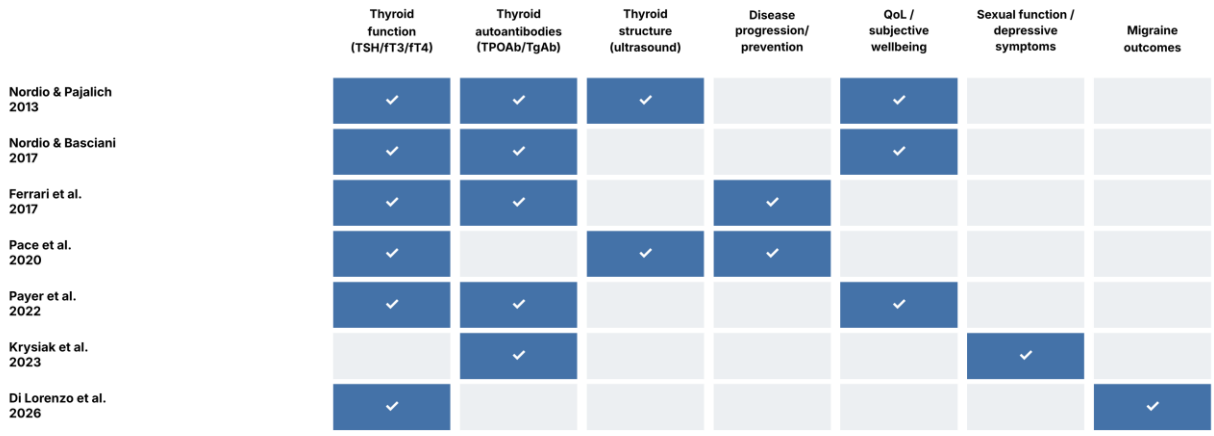


Figure 2: Evidence map of outcome domains reported across the seven primary sources of evidence charted in this scoping review. A filled cell (✓) indicates that the outcome domain was assessed and reported in that source. MI = myo-inositol; Se = selenium; QoL = quality of life.

3.5. Supplementary Quantitative Context: the Three Directly Comparative Trials

Only three of the seven primary sources — Nordio and Pajalich, Nordio and Basciani, and Pace — include a direct selenium-alone comparator suitable for effect-size pooling [18,21-23]. These same three trials (n = 288: 151 MI+Se, 137 Se alone) have already been pooled in two meta-analyses using a random-effects model, the second with trial sequential analysis [12,13]. Rather than re-deriving estimates from the same dataset, Figure 3 reproduces, with citation, the pooled estimates of Stanchev, updating Zuhair [12,13]. Combined MI+Se was associated with a significantly greater reduction in TSH (SMD −1.26, 95% CI −1.51 to −1.00; I^2 = 0%) and TgAb (SMD −0.51, 95% CI −0.78 to −0.24; I^2 = 0%) than selenium alone, with trial sequential analysis flagging a risk of type I error for TgAb. No significant between-group difference was found for TPOAb, free T3, or free T4, the last showing substantial heterogeneity (I^2 = 88%).

No funnel plot is presented for any outcome. With only two to three contributing trials per outcome, a funnel plot cannot meaningfully distinguish publication bias from chance asymmetry; the Cochrane Handbook recommends at least ten studies before interpreting funnel-plot asymmetry, a threshold this literature does not approach.

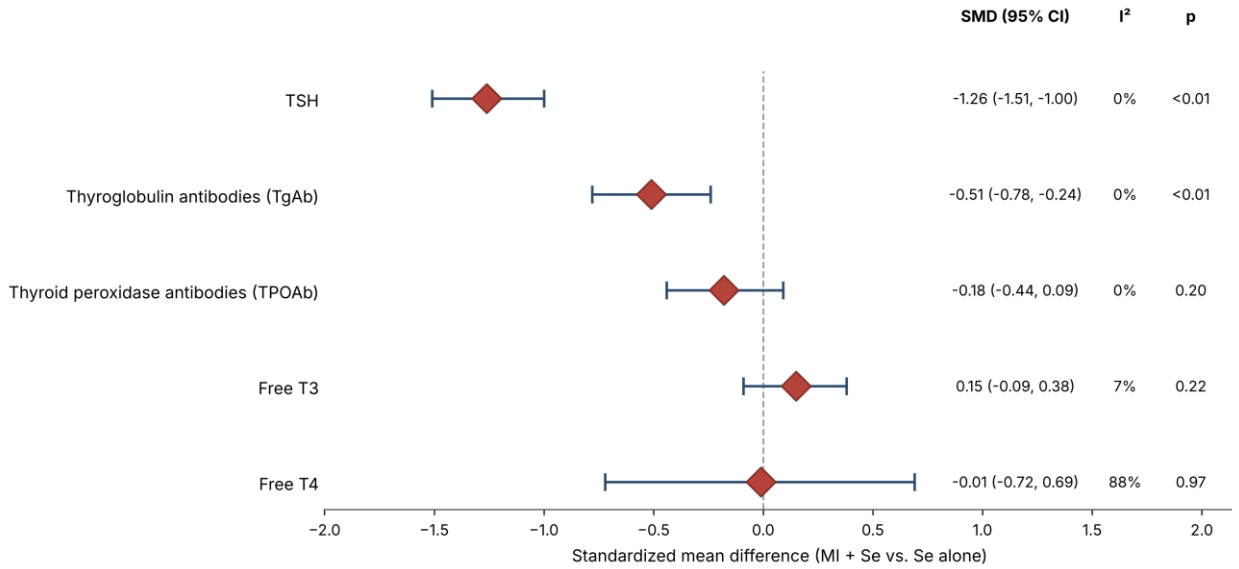


Figure 3: (supplementary). Pooled effect estimates for the three directly comparative trials of myo-inositol plus selenium versus selenium alone Pace et al., 2020; total n = 288) [18,21-23]. Values are reproduced, with citation, from the random-effects meta-analysis of Stanchev, which updated the original pooled analysis of Zuhair [12,13]. No new meta-analysis was performed for this scoping review, and no funnel plot is presented given the small number of contributing studies (k = 2–3).

3.6. Related Systematic and Narrative Reviews

Three recent reviews overlap topically with this scoping review and are discussed here rather than charted as primary evidence, since they synthesize rather than generate original data. Zuhair conducted a systematic review and meta-analysis restricted to the MI+Se-versus-Se-alone comparison, pooling the same three trials discussed in Section 3.5 and additionally assessing TPOAb, free T3, and free T4 [12]. Samuel published a narrative review spanning selenium and myo-inositol across Hashimoto's thyroiditis, Graves' disease, and benign thyroid nodules, concluding qualitatively that selenium may reduce TPOAb in HT and myo-inositol, combined with selenium, may improve thyroid hormone profiles and nodule metrics, while noting the limited scale and heterogeneity of the underlying trials [14]. Stanchev is, to our knowledge, the most recent and methodologically developed synthesis, updating the Zuhair pooled estimates with trial sequential analysis [13]. None of these reviews addresses myo-inositol monotherapy outside combination with selenium, the vitamin D comparison of Krysiak, or the migraine-comorbid population of Di Lorenzo; this review's principal contribution is mapping this broader, non-overlapping evidence [26-27].

4. Discussion

4.1. Summary of Evidence

This scoping review mapped ten sources of evidence — seven primary studies and three related reviews — on myo-inositol, with or without selenium, in Hashimoto's thyroiditis and autoimmune thyroid disease. The evidence clusters around a small, consistent signal: across all seven sources, six months of combined myo-inositol plus selenium was associated with reductions in TSH, improved thyroid autoantibody titers, and favorable trends in thyroid structure and wellbeing, relative to selenium alone or to baseline. This does not contradict the pooled estimates already published for the three comparator trials [12,13]. What this review adds is the surrounding evidence those meta-analyses, by design, excluded: myo-inositol as monotherapy against selenium and vitamin D, structural and progression outcomes, and a new comorbid population (migraine) only just studied [18,21,24,26,27].

4.2. Relation to Prior Reviews and Avoidance of Duplication

A central finding of this review is methodological rather than clinical: the entire evidence base with a direct selenium-alone comparator consists of three trials, already pooled twice, most recently with trial sequential analysis [13]. A further systematic review and meta-analysis confined to this comparison would not meaningfully extend what is known and risks presenting as novel a finding already published and updated. By contrast, this review's broader PCC framework captures six primary studies not jointly considered by either existing meta-analysis, spanning monotherapy comparisons, structural outcomes, disease-progression signals, and a comorbid population. We regard this breadth, rather than a further pooled effect estimate, as the more useful contribution to the literature at this time.

4.3. Evidence Gaps and Research Agenda

Several gaps emerge from this mapping exercise that are not addressed by re-analyzing the existing three-trial comparator dataset:

- Head-to-head comparison of myo-inositol monotherapy against selenium monotherapy and combined therapy, for thyroid-function outcomes specifically — Krysiak addresses this comparison only for antibody titers, sexual function, and mood, not TSH or thyroid hormone levels [26].
- Longer-term follow-up (≥12–24 months) to determine whether early TSH and antibody changes translate into durable prevention of overt hypothyroidism; only Pace followed patients beyond six months, and only Ferrari addressed progression as a concept, without a comparator [18,24].
- Standardized, validated patient-reported outcome measures; wellbeing was assessed with three non-equivalent instruments across sources (SF-12, a seven-item questionnaire, and FSFI/BDI-II), precluding synthesis across studies.
- Replication of the migraine-comorbid signal reported by Di Lorenzo in a prospective, comparator-controlled design, given its retrospective, single-arm nature and status as the only source addressing this population [27].
- Larger, randomized, placebo- or active-comparator-controlled trials more broadly: of the seven primary sources, only two were randomized, and none described blinded outcome assessment beyond treatment allocation.

4.4. Limitations

This review has several limitations specific to its scoping design and preparation. First, consistent with scoping review methodology, no source was excluded on risk of bias, so the narrative synthesis in Section 3.4 weighs evidence of variable methodological quality, including single-arm studies without a comparator, together. Second, as disclosed in Section 2.4, the review question and eligibility criteria were broadened from a narrower systematic-review framing after the original database search had already been run; the screening numbers in Figure 1 reflect the originally narrower criteria and were not independently re-screened record-by-record against the broadened PCC criteria. The review team should reconcile the flow-diagram totals against their complete screening log, and may wish to re-run the broadened search across all five databases before submission to ensure no further eligible sources were missed. Third, the English-language restriction may have introduced language bias, and excluding grey literature and conference abstracts may have introduced publication bias. Fourth, the supplementary figure in Section 3.5 reproduces, rather than independently verifies, pooled estimates from two external meta-analyses; any error there would propagate here. Finally, with only seven primary studies spanning six research groups, the generalizability of any pattern identified — including the consistent direction of effect for MI+Se — remains limited and should be read as hypothesis-generating rather than confirmatory.

4.5. Implications for Practice and Research

For clinicians, the available evidence — though limited in volume — is directionally consistent across multiple independent research groups and several outcome domains, which may support considering combined myo-inositol and selenium as an adjunct in selected patients with HT and SCH not yet candidates for levothyroxine, consistent with the cautious conclusions already reached by the existing meta-analyses. For researchers, the priority is not a further pooled analysis of the same three comparator trials, but primary research addressing the gaps in Section 4.3: head-to-head monotherapy comparisons, longer follow-up, standardized patient-reported outcomes, and replication in comorbid populations such as migraine.

5. Conclusions

This scoping review mapped the available evidence on myo-inositol, with or without selenium, across the spectrum of autoimmune thyroid disease. Ten sources of evidence were identified, of which seven primary studies were charted: two randomized trials, two observational cohorts, and three single-arm studies, spanning thyroid function, autoantibody, structural, progression, quality-of-life, and — in one recent study — migraine-comorbidity outcomes [29]. Only three studies directly compare combined therapy against selenium alone, and this narrow comparison has already been meta-analyzed twice, most recently with trial sequential analysis in 2026. The evidence gaps that remain are not primarily about that comparison's pooled effect size, but about monotherapy comparisons, long-term progression, standardized patient-reported outcomes, and evidence in populations beyond isolated SCH. Future primary research should prioritize these gaps rather than further syntheses of the existing three-trial dataset.

Author Contributions

- **Hernando Vargas-Uricoechea:** Conceptualization, methodology, investigation, resources, data curation, formal analysis, writing—original draft preparation, writing—review and editing, supervision, visualization.
- **Julia Devoz-Muñoz:** Investigation, data curation, writing—original draft preparation, writing—review and editing.
- **Alejandro Castellanos-Pinedo:** Investigation, data curation, writing—original draft preparation, writing—review and editing. All authors have read and agreed to the published version of the manuscript.

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References

1. Hu, X., Chen, Y., Shen, Y., Tian, R., Sheng, Y., & Que, H. (2022). Global prevalence and epidemiological trends of Hashimoto's thyroiditis in adults: a systematic review and meta-analysis. *Frontiers in public health, 10*, 1020709.
2. Ajjan, R. A., & Weetman, A. P. (2015). The pathogenesis of Hashimoto's thyroiditis: further developments in our understanding. *Hormone and metabolic research, 47*(10), 702-710.
3. Rosário, P. W., Carvalho, M., & Calsolari, M. R. (2016). Natural history of subclinical hypothyroidism with TSH≤ 10 mIU/l: a prospective study. *Clinical endocrinology, 84*(6), 878-881.
4. Casey, B. M., Thom, E. A., Peaceman, A. M., Varner, M. W., Sorokin, Y., Hirtz, D. G., ... & VanDorsten, J. P. (2017). Treatment of subclinical hypothyroidism or hypothyroxinemia in pregnancy. *New England Journal of Medicine, 376*(9), 815-825.
5. Köhrle, J. (2015). Selenium and the thyroid. *Current Opinion in Endocrinology, Diabetes and Obesity, 22*(5), 392-401.
6. Winther, K. H., Rayman, M. P., Bonnema, S. J., & Hegedüs, L. (2020). Selenium in thyroid disorders—essential knowledge for clinicians. *Nature Reviews Endocrinology, 16*(3), 165-176.
7. Huwiler, V. V., Maissen-Abgottspon, S., Stanga, Z., Mühlebach, S., Trepp, R., Bally, L., & Bano, A. (2024). Selenium supplementation in patients with Hashimoto thyroiditis: a systematic review and meta-analysis of randomized clinical trials. *Thyroid®, 34*(3), 295-313.
8. Duntas, L. H. (2015). The role of iodine and selenium in autoimmune thyroiditis. *Hormone and Metabolic Research, 47*(10), 721-726.
9. Benvenga, S., Nordio, M., Laganà, A. S., & Unfer, V. (2021). The role of inositol in thyroid physiology and in subclinical hypothyroidism management. *Frontiers in endocrinology, 12*, 662582.
10. Fallahi, P., Ferrari, S. M., Elia, G., Ragusa, F., Paparo, S. R., Caruso, C., ... & Antonelli, A. (2018). Myo-inositol in autoimmune thyroiditis, and hypothyroidism. *Reviews in endocrine and metabolic disorders, 19*(4), 349-354.
11. Berridge, M. J. (1984). Inositol trisphosphate and diacylglycerol as second messengers. *Biochemical Journal, 220*(2), 345.
12. Zuhair, V., Shaikh, A. T., Shafi, N., Babar, A., Khan, A., Sadiq, A., ... & Ali, E. (2024). Role of supplementation with selenium and Myo-inositol versus selenium alone in patients of autoimmune thyroiditis: a systematic review and meta-analysis. *Clinical Medicine Insights: Endocrinology and Diabetes, 17*, 11795514241300998.
13. Stanchev, P., Kraeva, M., Petrov, P. P., & Penchev, P. (2026). Myo-Inositol Plus Selenium vs. Selenium Alone in Hashimoto's Thyroiditis with Subclinical Hypothyroidism: A Systematic Review and Updated Meta-Analysis with Trial Sequential Analysis. *Journal of Clinical Medicine, 15*(9), 3179.
14. Samuel, C. G., Singh, P., Abdullahi, H., & Ibrahim, I. (2025). Unlocking the Therapeutic Potential: Selenium and Myo-Inositol Supplementation in Thyroid Disorders—Efficacy and Future Directions. *Life, 15*(10), 1500.
15. Tricco, A. C., Lillie, E., Zarin, W., O'Brien, K. K., Colquhoun, H., Levac, D., ... & Straus, S. E. (2018). PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Annals of internal medicine, 169*(7), 467-473.
16. Peters, M. D. J., Marnie, C., Tricco, A. C., et al. (2020). Updated methodological guidance for the conduct of scoping reviews. *JBI Evidence Synthesis, 18*(10), 2119–2126.
17. Arksey, H., & O'malley, L. (2005). Scoping studies: towards a methodological framework. *International journal of social research methodology, 8*(1), 19-32.
18. Pace, C., Tumino, D., Russo, M., Le Moli, R., Naselli, A., Borzì, G., ... & Frasca, F. (2020). Role of selenium and myo-inositol supplementation on autoimmune thyroiditis progression. *Endocrine Journal, 67*(11), 1093-1098.
19. Sterne, J. A., Savović, J., Page, M. J., Elbers, R. G., Blencowe, N. S., Boutron, I., ... & Higgins, J. P. (2019). RoB 2: a revised tool for assessing risk of bias in randomised trials. *bmj, 366*.
20. Wells, G. A., Shea, B., O'Connell, D., Peterson, J., Welch, V., Losos, M., & Tugwell, P. (2000). The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. *Ottawa Hospital Research Institute.*
21. Nordio, M., & Pajalich, R. (2013). Combined treatment with Myo-inositol and selenium ensures euthyroidism in subclinical hypothyroidism patients with autoimmune thyroiditis. *Journal of thyroid research, 2013*(1), 424163.
22. Nordio, M., & Basciani, S. (2017). Myo-inositol plus selenium supplementation restores euthyroid state in Hashimoto's patients with subclinical hypothyroidism. *European Review for Medical & Pharmacological Sciences, 21,* 51.
23. Nordio, M., & Basciani, S. (2017). Treatment with myo-inositol and selenium ensures euthyroidism in patients

with autoimmune thyroiditis. *International Journal of Endocrinology, 2017*(1), 2549491.
24. Ferrari, S. M., Fallahi, P., Di Bari, F., Vita, R., Benvenga, S., & Antonelli, A. (2017). Myo-inositol and selenium reduce the risk of developing overt hypothyroidism in patients with autoimmune thyroiditis. *European Review for Medical & Pharmacological Sciences, 21*, 36.
25. Payer, J., Jackuliak, P., Kužma, M., Džupon, M., & Vaňuga, P. (2022). Supplementation with myo-inositol and Selenium improves the clinical conditions and biochemical features of women with or at risk for subclinical hypothyroidism. *Frontiers in endocrinology, 13,* 1067029.
26. Krysiak, R., Kowalcze, K., Szkróbka, W., & Okopień, B. (2023). Sexual function and depressive symptoms in young women with euthyroid Hashimoto's thyroiditis receiving vitamin D, selenomethionine and myo-inositol: A pilot study. *Nutrients, 15*(12), 2815.
27. Di Lorenzo, C., Nordio, M., Brongo, F., Casillo, F., Basciani, S., Sebastianelli, G., ... & Coppola, G. (2026). Myoinositol and Selenium (MYSE) Supplementation Is Associated with Favorable Changes in Thyroid Parameters and Migraine Outcomes in Patients with Migraine and Hashimoto's Thyroiditis: A Retrospective Cohort Study. *Nutrients, 18*(10), 1554.
28. Lazarus, J., Brown, R. S., Daumerie, C., Hubalewska-Dydejczyk, A., Negro, R., & Vaidya, B. (2014). 2014 European thyroid association guidelines for the management of subclinical hypothyroidism in pregnancy and in children. *European thyroid journal, 3*(2), 76-94.
29. Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., ... & Moher, D. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *bmj, 372*.

Appendix:

Supplementary Material

Myo-Inositol, With or Without Selenium, in Hashimoto's Thyroiditis and Autoimmune Thyroid Disease: A Scoping Review

Hernando Vargas-Uricoechea, Julia Devoz-Muñoz, Alejandro Castellanos-Pinedo This supplementary file accompanies the main manuscript and provides methodological detail appropriate to a scoping review conducted in accordance with the PRISMA Extension for Scoping Reviews (PRISMA-ScR) and the Joanna Briggs Institute (JBI) methodological guidance for scoping reviews, as cited in Sections 2.1 and 1.2 of the main text. It contains: (S1) the database-specific search strategies underlying the combined search logic reported in Section 2.3; (S2) an extended data-charting matrix elaborating the seven primary sources of evidence summarized in Table 1; (S3) critical appraisal detail for the two randomized trials (Cochrane RoB 2) and the five non-randomized or single-arm sources (Newcastle-Ottawa Scale, adapted for pre-post designs, as described in Section 2.6); and (S4) the completed 22-item PRISMA-ScR checklist, mapping each reporting item to its corresponding section in the main manuscript. Where information is not explicitly reported in the body of the main manuscript (for example, exact per-database record counts from the original search export, or granular domain-level signaling-question responses beyond the overall judgments narrated in Section 3.3), this is stated explicitly below rather than estimated, consistent with the limitation already disclosed in Section 4.4 regarding reconciliation of the search and screening log prior to submission. The review team is encouraged to append the corresponding completed worksheets (search export files, RoB 2 and NOS score sheets) as additional supplementary files if the journal's production process allows it.

Supplementary Table S1. Database-specific search strategies

Section 2.3 of the main manuscript reports the combined Boolean search logic used across five electronic databases, with Google Scholar searched as a supplementary source for grey literature. The table below presents the string as adapted to each database's own syntax, consistent with that combined logic. Exact search dates and the per-database distribution of the 320 records identified by the original search (reconciled in Figure 1 to the PRISMA-ScR flow) are recorded in the review team's original search-export files and should be inserted here from that log before final submission; they are not reconstructable from the manuscript text alone.

Database	Role	Search string (as adapted)	Fields / filters searched
PubMed	Primary	("Inositol"[MeSH Terms] OR myo-inositol[Title/Abstract] OR inositol[Title/Abstract]) AND ("Hashimoto Disease"[MeSH Terms] OR Hashimoto*[Title/Abstract] OR "autoimmune thyroiditis"[Title/Abstract] OR thyroiditis[Title/Abstract]) AND (selenium[Title/Abstract] OR selenomethionine[Title/Abstract] OR "Selenium"[MeSH Terms] OR hypothyroidism[Title/Abstract] OR "subclinical hypothyroidism"[Title/Abstract] OR euthyroid[Title/Abstract])	MeSH terms + Title/Abstract field tags; English language filter; no publication-date limit
Web of Science	Primary	TS=((myo-inositol OR inositol) AND (Hashimoto* OR "autoimmune thyroiditis" OR thyroiditis) AND (selenium OR selenomethionine OR hypothyroidism OR "subclinical hypothyroidism" OR euthyroid))	Topic (TS) field, adapted with field tags per Section 2.3; refined by Language: English
Scopus	Primary	TITLE-ABS-KEY((("myo-inositol" OR inositol) AND (Hashimoto* OR "autoimmune thyroiditis" OR thyroiditis) AND (selenium OR selenomethionine OR hypothyroidism OR "subclinical hypothyroidism" OR euthyroid)))	Title, Abstract, Keywords; LANGUAGE(english); no date restriction
ScienceDirect	Primary	("myo-inositol" OR inositol) AND (Hashimoto OR "autoimmune thyroiditis" OR thyroiditis) AND (selenium OR selenomethionine OR hypothyroidism OR euthyroid)	Advanced search, Title/abstract/keywords; English language; ScienceDirect's syntax does not support wildcard truncation (Hashimoto*), so the unstarred term plus explicit "autoimmune thyroiditis" variant were combined to approximate the same scope
SpringerLink	Primary	'myo-inositol' AND ('Hashimoto' OR 'autoimmune thyroiditis' OR thyroiditis) AND (selenium OR selenomethionine OR hypothyroidism OR euthyroid)	Full-text search interface, filtered to English-language journal articles
Google Scholar	Supplementary (grey literature)	myo-inositol selenium Hashimoto thyroiditis hypothyroidism	Free-text search; results screened for relevance by title, consistent with common practice for grey-literature supplementation of a structured database search

Supplementary Table S2. Extended data-charting matrix of included primary sources of evidence

This table elaborates Table 1 of the main manuscript with the outcome domains assessed by each source (cf. the evidence map in Figure 2) and the funding/conflict-of-interest disclosure status, following the charting items specified in Section 2.5. Cells marked "NR" indicate that the item was not reported in the source as charted for this review; this is distinct from an item having been assessed and found absent, and is recorded as such for transparency rather than inferred.

Source	Design	Population (n)	Intervention / comparator	Duration	Outcome domains assessed	Funding / COI (as charted)
Nordio & Pajalich, 2013 [18]	RCT, double-blind	Women with SCH + AIT (n=48 randomized; n=46 analyzed)	MI 600 mg + Se 83 µg/day (n=24) vs Se 83 µg/day alone (n=24)	6 mo	Thyroid function (TSH); autoantibodies (TPOAb, TgAb); structural (ultrasound echogenicity); subjective wellbeing (SF-12)	NR
Nordio & Basciani, 2017 [19]	RCT	HT with TSH 3–6 µIU/mL (n=168; 84 per group)	MI 600 mg + Se 83 µg/day vs Se 83 µg/day alone	6 mo	Thyroid function (TSH, fT4); autoantibodies (TPOAb, TgAb); subjective wellbeing (seven-item symptom questionnaire)	NR
Ferrari et al., 2017 [20]	Prospective, single-arm (no comparator)	Euthyroid autoimmune thyroiditis (n=21)	MI 600 mg + Se 83 µg/day, single arm, pre–post	6 mo	Thyroid function (TSH); autoantibodies; disease progression / prevention (CXCL10 chemokine, interpreted as a progression-risk signal)	NR
Pace et al., 2020 [18]	Retrospective observational cohort	Euthyroid or SCH due to HT (n=101: untreated 29, Se 29, Se+MI 43)	Se-meth 83 µg/day vs Se-meth 83 µg + MI 600 mg/day vs untreated	6 and 12 mo	Thyroid function (TSH); structural (ultrasound echogenicity); disease progression (indirect, via comparative TSH normalization rate)	NR
Payer et al., 2022 [25]	Prospective, single-arm (no comparator)	Women with or at risk of SCH (n=148)	MI 600 mg + Se 83 µg/day, single arm, stratified by baseline TSH (2.5–4.99 vs 5–10 mIU/L)	6 mo	Thyroid function (TSH); subjective wellbeing (cold/warm tolerance and other symptom measures)	NR
Krysiak et al., 2023 [26]	Comparative cohort (separate monotherapy arms)	Euthyroid women with AIT (4 treated/untreated groups, n=29 each) + healthy controls	Untreated vs vitamin D 100 µg/day vs selenomethionine 200 µg/day vs myo-inositol 2.0 g/day (separate arms; no MI+Se arm)	6 mo	Autoantibodies; other patient-reported outcomes — sexual function (FSFI) and depressive symptoms (BDI-II); hs-CRP. Thyroid function (TSH) was not the outcome measure reported for this comparison.	NR
Di Lorenzo et al., 2026 [27]	Retrospective cohort, single-arm (no comparator)	Adults with migraine comorbid with HT (n=163)	MI + Se (MYSE) combined supplementation, single arm, stratified by euthyroid vs SCH status	6 mo	Thyroid function (TSH, fT4); comorbid-condition outcome — monthly migraine days and symptomatic drug use	NR

Supplementary Table S3. Critical appraisal detail

Consistent with Section 2.6, critical appraisal in this scoping review was used descriptively, to characterize the evidence base rather than to exclude sources; no source was excluded on the basis of its appraisal. The domain-level detail below expands the overall judgments narrated in Section 3.3. Where a domain-level signaling-question response is not separately narrated in the main text, this is stated explicitly ("not separately reported in the narrative synthesis") rather than inferred, and the review team's completed RoB 2 / NOS worksheets are the appropriate source for that level of detail if required by the journal.

Study	D1. Randomization process	D2. Deviations from intended interventions	D3. Missing outcome data	D4. Measurement of the outcome	D5. Selection of reported result	Overall judgment
Nordio & Pajalich, 2013 [18]	Randomization by initial TPOAb concentration, double-blinded; allocation concealment not fully reported	Not separately reported in the narrative synthesis	Not separately reported in the narrative synthesis	Double-blinding reduces detection-bias risk, but outcome-assessor blinding not separately confirmed in the narrative synthesis	Not separately reported in the narrative synthesis	Some concerns (incomplete reporting of allocation concealment)
Nordio & Basciani, 2017 [19]	1:1 randomization with an a priori sample-size calculation reported	Blinding status not described in the source as charted	Not separately reported in the narrative synthesis	Outcome-assessor blinding not described, relevant to this domain	Not separately reported in the narrative synthesis	Some concerns (blinding not described)

S3a: Cochrane Risk of Bias 2 (RoB 2) — randomized controlled trials

Study	Design	Selection domain	Comparability domain	Outcome/exposure domain	Overall band
Pace et al., 2020 [18]	Retrospective observational cohort (3 arms)	Non-random allocation to treatment group; inherent risk of confounding by indication, acknowledged by the original authors	Concurrent untreated and selenium-alone comparator arms present, permitting between-group comparison	Outcome (TSH, ultrasound echogenicity) ascertained from clinical records at defined follow-up points (6 and 12 months)	High-quality range for an observational design (exact star tally per the review team's completed NOS worksheet)
Ferrari et al., 2017 [20]	Prospective, single-arm, pre–post	Consecutive patients enrolled prospectively	No concurrent comparator group; this is the principal structural limitation under NOS adapted for pre–post designs, acknowledged by the original authors	Outcome ascertained prospectively (TSH, autoantibodies, CXCL10)	Adequate for descriptive pre–post analysis; not informative for comparative effectiveness given the absent comparator
Payer et al., 2022 [25]	Prospective, single-arm, pre–post	Consecutive patients enrolled prospectively, stratified by baseline TSH severity	No concurrent comparator group, explicitly noted as a limitation by the original authors	Outcome ascertained prospectively (TSH and symptom measures)	Adequate for descriptive pre–post analysis; not informative for comparative effectiveness given the absent comparator
Krysiak et al., 2023 [26]	Comparative cohort, separate monotherapy arms	Allocation based on patient preference rather than randomization, introducing a risk of selection bias	Four parallel arms (untreated, vitamin D, selenomethionine, myo-inositol) plus healthy controls, permitting multi-group comparison	Outcome ascertained with validated instruments (FSFI, BDI-II) plus hs-CRP	Adequate comparability structure; selection-bias risk from non-random, preference-based allocation
Di Lorenzo et al., 2026 [27]	Retrospective chart-review cohort, single-arm	Consecutive patients identified retrospectively from clinical records	No comparator arm; appropriate for descriptive pre–post analysis but not for causal attribution, as acknowledged by the original authors	Outcome ascertained retrospectively from clinical records (TSH, fT4, migraine diary data)	Adequate for descriptive pre–post analysis; not informative for comparative effectiveness given the absent comparator

S3b: Newcastle-Ottawa Scale (NOS), adapted for pre–post designs — non-randomized and single-arm sources

Supplementary Table S4. PRISMA-ScR checklist

Completed in accordance with the PRISMA Extension for Scoping Reviews (PRISMA-ScR) checklist [15], cited in Section 2.1 of the main manuscript. The "Reported on" column maps each checklist item to its corresponding section, table, or figure in the final manuscript.

#	Section / topic	Checklist item	Reported on
1	Title	Identify the report as a scoping review.	Title page
2	Abstract	Provide a structured summary that includes (as applicable) background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions.	Abstract
3	Introduction — Rationale	Describe the rationale for the review in the context of what is already known; explain why the review questions/objectives lend themselves to a scoping review approach.	Sections 1.1, 1.2
4	Introduction — Objectives	Provide an explicit statement of the questions and objectives being addressed, with reference to their key elements (e.g., population or participants, concepts, and context).	Section 1.3; PCC in Section 2.2
5	Methods — Protocol and registration	Indicate whether a review protocol exists, state if and where it can be accessed, and provide registration information if available.	Section 2.1 ("This review was not prospectively registered")
6	Methods — Eligibility criteria	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, publication status), and provide a rationale.	Section 2.2
7	Methods — Information sources	Describe all information sources in the search (e.g., databases with dates of coverage, contact with authors to identify additional sources) and the date the most recent search was executed.	Section 2.3
8	Methods — Search	Present the full electronic search strategy for at least one database, including limits used, such that it could be repeated.	Section 2.3; Supplementary Table S1
9	Methods — Selection of sources of evidence	State the process for selecting sources of evidence (screening and eligibility) included in the review.	Section 2.4
10	Methods — Data charting process	Describe the methods of charting data from the included sources (e.g., calibrated forms or forms developed a priori, piloting, performed independently or in duplicate) and any processes for obtaining and confirming data from investigators.	Section 2.5
11	Methods — Data items	List and define all variables for which data were sought and any assumptions and simplifications made.	Section 2.5; Supplementary Table S2
12	Methods — Critical appraisal of individual sources of evidence	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in the data synthesis (if appropriate).	Section 2.6; Supplementary Table S3
13	Methods — Synthesis of results	Describe the methods of handling and summarizing the data that were charted.	Section 2.7
14	Results — Selection of sources of evidence	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	Section 3.1; Figure 1
15	Results — Characteristics of sources of evidence	For each source of evidence, present characteristics for which data were charted and provide the citations.	Section 3.2; Table 1; Supplementary Table S2
16	Results — Critical appraisal within sources of evidence	If done, present data on critical appraisal of included sources of evidence.	Section 3.3; Supplementary Table S3
17	Results — Results of individual sources of evidence	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	Table 1; Sections 3.4.1–3.4.6
18	Results — Synthesis of results	Summarize and/or present the charting results as they relate to the review questions and objectives.	Sections 3.4, 3.5; Figures 2, 3

19	Discussion — Summary of evidence	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	Sections 4.1, 4.2, 4.5
20	Discussion — Limitations	Discuss the limitations of the scoping review process.	Section 4.4
21	Discussion — Conclusions	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	Section 5; Section 4.5
22	Funding	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review (financial or material support); describe the role of the funders of the scoping review.	Funding statement, Statements and Declarations

Abbreviations used throughout this supplementary file: AIT, autoimmune thyroiditis; BDI-II, Beck Depression Inventory-II; CXCL10, C-X-C motif chemokine ligand 10; FSFI, Female Sexual Function Index; fT3/fT4, free triiodothyronine/free thyroxine; HT, Hashimoto's thyroiditis; hs-CRP, high-sensitivity C-reactive protein; MI, myo-inositol; MI+Se, myo-inositol plus selenium; NOS, Newcastle-Ottawa Scale; NR, not reported; PCC, Population–Concept–Context; PRISMA-ScR, Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews; RCT, randomized controlled trial; RoB 2, Cochrane Risk of Bias 2 tool; SCH, subclinical hypothyroidism; Se, selenium; SMD, standardized mean difference; TgAb, thyroglobulin antibody; TPOAb, thyroid peroxidase antibody; TSH, thyroid-stimulating hormone.

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