

Beyond Hormone Replacement: A Systematic Review of Lifestyle, Cognition, and Psychological Well-Being in Hypothyroidism.

Abstract:

Background

Hypothyroidism is an endocrine disorder that may affect physical health, cognitive performance, emotional functioning, and health-related quality of life. Thyroid hormone replacement is the standard treatment when indicated, but some individuals continue to report fatigue, reduced concentration, memory complaints, sleep disturbance, depressive symptoms, or impaired daily functioning. Non-dietary lifestyle and behavioural factors may be associated with these outcomes, although their direction and clinical significance can be difficult to establish. A careful synthesis should distinguish observational associations from intervention effects and should consider differences in hypothyroidism classification, treatment status, and outcome measurement.

Objective

To systematically review evidence on non-dietary lifestyle and behavioural factors associated with cognitive function and psychological well-being in people with overt or subclinical hypothyroidism, and to evaluate the effects of lifestyle-based interventions on cognitive, psychological, and other patient-centred outcomes.

Methods

The review will be reported in accordance with PRISMA 2020. Searches are planned for PubMed/MEDLINE, Embase, Scopus, Web of Science Core Collection, the Cochrane Library, and PsycINFO, subject to access. Eligible studies will include observational and intervention designs involving people with diagnosed hypothyroidism and reporting cognitive, psychological, fatigue, sleep, quality-of-life, daily-functioning, or treatment-adherence outcomes. Exposures and interventions of interest include sleep, physical activity, exercise, stress-management practices, and other relevant non-dietary behaviours. Two reviewers should independently screen records and extract data. Risk of bias will be assessed using tools appropriate to each study design. Findings will be synthesised narratively; meta-analysis will be considered only where studies are sufficiently comparable.

Results

To be completed after the searches, screening, extraction, and appraisal. Report the verified numbers of records identified, duplicates removed, full-text reports assessed, studies included, participant characteristics, risk-of-bias judgements, and outcome findings. Include the completed PRISMA 2020 flow diagram. No numerical results should be inserted until they are supported by the included studies.

Conclusion

The review will clarify the extent and certainty of evidence linking non-dietary lifestyle and behavioural factors with cognitive health and psychological well-being in hypothyroidism. Conclusions will distinguish observational associations from intervention effects and will be limited to the evidence identified through the completed review.

Keywords: hypothyroidism; lifestyle; cognitive function; psychological well-being; sleep; physical activity; stress; fatigue; quality of life; systematic review; PRISMA 2020.

1. INTRODUCTION

1.1 Clinical significance and burden of hypothyroidism

Hypothyroidism is characterised by inadequate thyroid hormone production or activity relative to physiological requirements. Common causes include autoimmune thyroid disease, previous thyroid surgery or radioiodine treatment, medication effects, and disorders affecting the hypothalamic–pituitary–thyroid axis. Clinical presentation is heterogeneous: symptoms depend on the degree and duration of hormone deficiency, age, underlying aetiology, comorbidities, and whether treatment has been initiated and adequately monitored. Symptoms may include tiredness, reduced energy, cold intolerance, constipation, changes in weight, muscle discomfort, and cognitive complaints.

The burden of hypothyroidism cannot be described solely by thyroid-stimulating hormone (TSH) or free thyroxine concentrations. Clinical care also considers symptoms, function, comorbidities, treatment tolerability, and patient priorities. Some symptoms are nonspecific and may occur in people with normal thyroid function. Consequently, symptoms should be interpreted in context and should not automatically be attributed to thyroid dysfunction.

This distinction is particularly relevant to the present review. A patient-centred perspective considers whether people experience meaningful changes in cognition, emotional well-being, sleep, fatigue, and everyday function, while recognising that these outcomes may have multiple determinants.

1.2 Thyroid hormones and cognitive function

Thyroid hormones play important roles in central nervous system development and function. Cognitive domains potentially relevant to thyroid dysfunction include attention, working memory, learning, processing speed, verbal memory, and executive function. Individuals may describe forgetfulness, mental slowing, difficulty concentrating, or a subjective feeling of cognitive clouding. The prevalence, severity, and persistence of these complaints vary across clinical populations and study designs.

Cognitive outcomes must be carefully defined in a systematic review. Subjective complaints measured by questionnaires are clinically meaningful but can be influenced by mood, sleep, fatigue, and expectations. Objective neuropsychological tests assess defined cognitive domains under standardised conditions, while dementia diagnoses and global screening tools represent different constructs again. These outcomes should not be treated as interchangeable. The extraction form will record the construct, instrument, score direction, and assessment time point.

Studies may also differ according to overt versus subclinical hypothyroidism, disease duration, age, autoimmune status, treatment exposure, and biochemical control. If these groups are combined without adequate consideration, a pooled estimate may obscure clinically important differences. The review will therefore describe the population and diagnostic criteria for each study and will avoid interpreting an association with one cognitive outcome as evidence about all cognitive functioning.

Existing meta-analytic work has examined thyroid disease in relation to dementia and cognitive impairment. Such evidence provides context but does not answer every question about subjective cognitive symptoms, individual neuropsychological domains, or the effects of behavioural interventions. The present review will evaluate these outcomes according to the actual studies that meet the eligibility criteria.

1.3 Psychological well-being and emotional outcomes

Psychological well-being encompasses emotional functioning, mood, perceived stress, psychological distress, and the ability to participate in usual activities and relationships. Relevant outcomes include depressive symptoms, anxiety, perceived stress, mental health-related quality of life, and validated well-being measures. Fatigue

and low motivation may overlap with psychological symptoms, but they should be extracted as separate outcomes when the original studies distinguish them.

The relationship between hypothyroidism and psychological symptoms is multifactorial. Thyroid dysfunction may contribute to mood or cognitive symptoms in some patients, while sleep disruption, chronic illness burden, coexisting medical conditions, social factors, and psychological distress may also influence symptom reporting and daily functioning. Cross-sectional studies cannot reliably establish temporal order, and uncontrolled pre–post intervention studies cannot by themselves establish that an intervention caused an observed improvement.

A review of psychological outcomes should therefore evaluate study design, confounder adjustment, validated measurement, and the comparator used. Where several measures are reported, depression, anxiety, stress, and broader psychological well-being should be synthesised separately before any broader interpretation is attempted.

1.4 Sleep and circadian-related behaviours

Sleep is relevant to cognition and psychological health because sleep duration, continuity, and perceived quality can affect daytime alertness, attention, memory, fatigue, and mood. Sleep disturbance may coexist with hypothyroidism, but the relationship may be bidirectional and influenced by age, medications, sleep-disordered breathing, mood symptoms, pain, and other comorbidities. Sleep quality should therefore be treated as a potential exposure, outcome, or mediator according to each study's design, rather than assuming one universal direction of effect.

The review will record how sleep is measured, including validated questionnaires, sleep diaries, actigraphy, or clinical sleep assessments. It will distinguish observational comparisons of sleep quality from interventions intended to modify sleep-related behaviours. Where a study measures sleep and cognitive outcomes at the same time point, the findings will be interpreted as associations unless the design supports stronger conclusions.

1.5 Physical activity and exercise

Physical activity and structured exercise may affect general physical function, mood, sleep, energy, and quality of life. In people with hypothyroidism, exercise interventions may vary in modality, intensity, frequency, duration, supervision, and participant baseline fitness. Studies may also differ in whether participants have overt or subclinical disease and whether thyroid hormone replacement is stable.

Exercise evidence should be evaluated on the basis of patient-centred outcomes as well as biochemical measures. A change in TSH does not necessarily imply a clinically meaningful improvement in cognition or psychological well-being. The review will record intervention components, adherence, comparator conditions, follow-up, adverse events, and outcome measures. It will avoid generalising from small or methodologically limited studies to all people with hypothyroidism.

1.6 Stress, coping, and behavioural routines

Perceived stress and coping strategies may be related to sleep, mood, concentration, and the ability to maintain health-related routines. Stress-management programmes can include relaxation training, mindfulness-based approaches, structured coping skills, or other behavioural components. These approaches are not equivalent, and their effects should be assessed according to the intervention actually delivered.

Daily routines, sedentary behaviour, and treatment-related behaviours may also be relevant to functioning and well-being. Medication adherence is influenced by factors such as understanding of treatment, routines, access to care, perceived benefit, and treatment burden. Studies of adherence will be included only when the outcome is relevant to the review question and is reported for a hypothyroid population. Behavioural associations will not be interpreted as proof of causation without suitable design and analysis.

1.7 Beyond hormone replacement: clinical context

The phrase 'beyond hormone replacement' refers to examining additional dimensions of health and care, not to replacing indicated medical treatment. Thyroid hormone replacement remains central for patients for whom it is prescribed. Persistent symptoms warrant appropriate clinical evaluation, including consideration of treatment adequacy, medication use, coexisting conditions, sleep problems, and alternative explanations.

Lifestyle and behavioural strategies may be useful components of general health care, but the extent to which specific approaches improve hypothyroidism-related cognitive or psychological outcomes must be established from the evidence. The review will therefore avoid presenting lifestyle interventions as established treatments unless the included studies provide sufficiently reliable support.

1.8 Rationale, knowledge gap, and objectives

Evidence concerning cognition, sleep, physical activity, stress, psychological symptoms, and quality of life is distributed across diverse populations and study

designs. Definitions of hypothyroidism, outcome instruments, exposure measurement, and intervention delivery may differ considerably. A systematic synthesis can help clarify which relationships have been studied, the consistency and precision of reported findings, and whether intervention studies provide evidence beyond observational associations.

Before the review is registered and submitted, the review team should search for existing systematic reviews with overlapping scope and explain how this review adds value. The novelty claim should be based on that documented comparison rather than assumed.

Primary objective: To systematically evaluate evidence concerning non-dietary lifestyle and behavioural factors associated with cognitive function and psychological well-being in people with overt or subclinical hypothyroidism.

Secondary objectives are to: (1) describe cognitive and psychological outcomes reported in hypothyroidism; (2) assess associations involving sleep, physical activity, stress-related factors, and other eligible behaviours; (3) evaluate effects of lifestyle-based interventions on cognition, psychological symptoms, fatigue, and quality of life; (4) explore variation by hypothyroidism classification, treatment status, and study design; (5) assess risk of bias and certainty of evidence; and (6) identify research priorities.

2. METHODS

2.1 Review design and reporting standard

The review will use explicit eligibility criteria, systematic searches, reproducible study selection, structured data extraction, critical appraisal, and transparent synthesis. Reporting will follow the PRISMA 2020 statement and its explanation and elaboration document. PRISMA 2020 includes a 27-item checklist and flow diagram, but it is a reporting guideline rather than a complete conduct manual. Appropriate systematic-review methods will therefore be used for searching, screening, appraisal, and synthesis.

The protocol should be finalised before screening begins. Any changes to eligibility criteria, outcomes, subgroup analyses, or synthesis methods should be documented with the date and reason, and their implications should be reported.

2.2 Eligibility framework

For observational evidence, eligibility will be considered using population, exposure, comparator or reference group, outcome, and study design. For intervention studies, the corresponding elements will be population, intervention, comparator, outcome, and follow-up. The review will include studies of overt or subclinical hypothyroidism and eligible non-dietary behavioural exposures or interventions.

2.2.1 Population

Eligible studies will include participants with a diagnosis of overt or subclinical hypothyroidism based on clinical or biochemical criteria reported by the investigators. The review will extract the diagnostic definition, laboratory thresholds where available, aetiology, treatment status, and disease duration. Mixed thyroid populations will be included only if data for hypothyroidism can be separated. Congenital hypothyroidism, if included, will be described and synthesised separately where developmental and treatment differences make pooling inappropriate.

2.2.2 Exposures and interventions

Eligible exposures include sleep quality or duration, physical activity, exercise participation, sedentary behaviour, stress-related factors, stress-management practices, and relevant non-dietary health behaviours. Eligible interventions include structured exercise or activity programmes, sleep-focused behavioural interventions, stress-management programmes, and other behavioural or lifestyle approaches that report at least one prespecified outcome. Programmes with inseparable dietary components will be assessed under a rule established before screening; studies will be excluded from the relevant synthesis if the non-dietary component cannot be interpreted independently.

2.2.3 Comparators

Eligible comparators include usual care, no intervention, wait-list or attention control, an alternative intervention, baseline assessment, healthy controls, or different exposure levels. Observational studies without a formal control group may be included if they provide an eligible analytical association. The comparator and its limitations will be recorded.

2.2.4 Outcomes

Primary outcomes are cognitive function and psychological well-being. Cognitive outcomes include memory, attention, concentration, processing speed, executive function, global cognition, and clinically identified cognitive impairment.

Psychological outcomes include depression, anxiety, perceived stress, emotional functioning, and validated well-being measures. Secondary outcomes include fatigue, sleep outcomes, health-related quality of life, daily functioning, and treatment adherence. Biochemical thyroid measures may be extracted as contextual outcomes but will not replace patient-centred outcomes.

2.2.5 Study designs and publication types

Eligible quantitative designs include randomised controlled trials, non-randomised intervention studies, cohort studies, case-control studies, and analytical cross-sectional studies. Qualitative studies will be included only if a separate qualitative synthesis is planned and suitable appraisal methods are specified. Case reports, small non-analytical case series, editorials, commentaries, narrative reviews, animal studies, and laboratory-only studies will be excluded from the primary evidence synthesis. Existing systematic reviews may be used for background and citation searching but will not be counted as primary studies.

2.2.6 Language and date limits

The planned search period is from database inception to the final search date. No publication-date restriction is planned. Searches should initially be run without language restrictions where feasible. If translation or access constraints require restrictions, the exact restriction and rationale must be reported. The final manuscript should identify whether preprints, theses, conference abstracts, and other grey literature were considered.

2.3 Information sources

The planned electronic sources are PubMed/MEDLINE, Embase, Scopus, Web of Science Core Collection, the Cochrane Library, and PsycINFO, subject to access. Reference lists of included studies and relevant reviews will be examined, and forward citation searching may be undertaken. For each source, the final report must provide the date searched, full strategy, filters or limits, and records retrieved. Only databases and supplementary sources actually searched may be reported as completed.

2.4 Search strategy

The search will combine controlled vocabulary where available with free-text terms for hypothyroidism and cognitive, psychological, and non-dietary lifestyle concepts. Search terms should be adapted to the indexing and syntax of each database. The preliminary PubMed strategy below requires piloting and validation before use as the final search.

265 (("Hypothyroidism"[Mesh] OR hypothyroid*[Title/Abstract] OR "subclinical
266 hypothyroidism"[Title/Abstract] OR "Hashimoto thyroiditis"[Title/Abstract]) AND
267 ("Cognition"[Mesh] OR cognit*[Title/Abstract] OR memory[Title/Abstract] OR
268 attention[Title/Abstract] OR concentration[Title/Abstract] OR "executive
269 function"[Title/Abstract] OR "cognitive impairment"[Title/Abstract] OR "mental
270 health"[Title/Abstract] OR psycholog*[Title/Abstract] OR depress*[Title/Abstract]
271 OR anxi*[Title/Abstract] OR stress[Title/Abstract] OR fatigue[Title/Abstract] OR
272 "quality of life"[Title/Abstract] OR sleep[Title/Abstract] OR exercise[Title/Abstract]
273 OR "physical activity"[Title/Abstract] OR lifestyle[Title/Abstract] OR
274 behaviour*[Title/Abstract] OR behavior*[Title/Abstract]))

275 The strategy should be piloted to determine whether it retrieves known relevant studies
276 and whether its breadth is appropriate. A librarian or information specialist may review
277 the strategy. The full final strategy for every database, including any filters, will be
278 reproduced in the manuscript or supplement. Dietary concepts will not be used as
279 target exposure categories.

280 **2.5 Record management and deduplication**

281 All records will be imported into reference-management or systematic-review
282 software. Duplicate detection will use automated matching and manual review where
283 needed. Multiple reports describing the same underlying study will be linked to avoid
284 double counting participants or results. The software and deduplication method will be
285 named in the final report.

286 **2.6 Study selection**

287 Screening will be conducted in two stages: title and abstract screening, followed by
288 full-text assessment. Two reviewers should independently assess records against the
289 prespecified criteria. Disagreements will be resolved by discussion and, if needed, a
290 third reviewer. If the review team uses a different verification process, the manuscript
291 must describe what was actually done.

292 Full-text reports excluded after assessment will be assigned a specific reason. The
293 PRISMA flow diagram will report records identified, duplicates removed, records
294 screened, reports sought, reports not retrieved, full texts assessed, reports excluded
295 with reasons, and studies included. The unit 'report' should be distinguished from the
296 unit 'study' when several publications relate to one study.

2.7 Data collection process

A standardised extraction form will be piloted on a small number of eligible studies. Two reviewers should independently extract key data or one reviewer should extract with independent verification, with the chosen process reported transparently. Discrepancies will be resolved by consensus or third-reviewer adjudication. Authors may be contacted for missing or unclear data. Any imputation or derivation of numerical values must be justified and documented.

2.8 Data items

- Study identification: author, year, country, setting, publication type, funding, and conflicts of interest.
- Methods: design, recruitment, eligibility criteria, sample size, follow-up, statistical methods, and confounder adjustment.
- Participants: age, sex or gender as reported, hypothyroidism classification, diagnostic criteria, aetiology, disease duration, treatment status, thyroid function, and relevant comorbidities.
- Exposure/intervention: definition, measurement, intensity, frequency, duration, delivery mode, comparator, adherence, co-interventions, and adverse events.
- Outcomes: domain, instrument, scale direction, baseline and follow-up values, effect estimates, confidence intervals, P values, missing data, and analysis population.
- Interpretation: study authors' conclusions, stated limitations, and information relevant to risk of bias and synthesis.

Data will be transcribed as reported. Missing information will be labelled as not reported rather than inferred. For studies with several reports, the most complete information will be assembled at the study level and citations to companion reports retained.

2.9 Outcome prioritisation and measurement

The primary outcomes are cognitive function and psychological well-being. Cognitive outcomes will be categorised as objective performance, subjective cognitive complaints, screening measures, or clinical diagnoses. Psychological outcomes will be grouped by construct, including depression, anxiety, perceived stress, and general well-being. Secondary outcomes include fatigue, sleep, quality of life, daily functioning, and treatment adherence.

Before extraction, the team should define how multiple scales or time points will be handled. Validated instruments and prespecified primary outcomes will be prioritised

where possible. If several outcomes assess the same construct, all relevant results should be recorded and selection rules applied consistently to reduce selective reporting.

2.10 Risk-of-bias assessment

Risk of bias will be assessed with design-appropriate tools. RoB 2 may be used for randomised trials, ROBINS-I for non-randomised intervention studies, and an appropriate validated checklist such as a Joanna Briggs Institute tool for observational designs. The final tools, versions, domains, and decision rules must be stated. Two reviewers should assess independently, document supporting evidence, and resolve disagreements through discussion or third-reviewer adjudication.

Potential domains include selection processes, confounding, exposure or intervention classification, outcome measurement, missing data, deviations from intended interventions, and selective reporting. Risk-of-bias results will be presented by study and domain. They will inform interpretation and sensitivity analyses where feasible; a single summed quality score should not replace domain-based judgements.

2.11 Effect measures

For continuous outcomes measured on the same scale, mean differences with confidence intervals may be appropriate. When studies measure the same construct using different scales, standardised mean differences may be considered if their clinical interpretation is defensible. Binary outcomes may be summarised using risk ratios, odds ratios, or other appropriate measures. Observational studies may report correlation coefficients or adjusted regression estimates; these will be retained in their reported form where pooling is not justified.

Between-group estimates will generally be preferred for intervention effects over within-group pre-post changes. Adjusted observational estimates will generally be prioritised where appropriate, while the covariates included in adjustment will be documented. Estimates from fundamentally different designs or constructs will not be combined merely because they are numerically available.

2.12 Synthesis methods

The synthesis will begin with structured tables and descriptive summaries. Studies will be grouped by design, hypothyroidism classification, lifestyle domain, intervention type, and outcome. Observational associations will be synthesised separately from intervention effects. For each synthesis, the report will identify contributing studies,

populations, outcome measures, direction and magnitude of findings, precision, heterogeneity, and risk-of-bias considerations.

Meta-analysis will be undertaken only if population, exposure or intervention, comparator, outcome definition, and study design are sufficiently comparable. A random-effects model may be used when the studies are expected to estimate related but non-identical effects. Statistical heterogeneity may be assessed using I^2 and other relevant information, but the interpretation will also consider clinical and methodological differences. If quantitative pooling is inappropriate, a transparent narrative synthesis will be provided, following an explicit structure rather than counting statistically significant studies.

2.13 Subgroup and sensitivity analyses

If enough comparable studies are available, planned subgroup analyses may compare overt with subclinical hypothyroidism, treated with untreated populations, adult with paediatric populations, observational with intervention designs, and objective with subjective cognitive outcomes. Sensitivity analyses may assess whether conclusions change when studies at high risk of bias or studies with substantial methodological differences are excluded. These analyses will be performed only when justified by the data and will be identified as prespecified or exploratory.

2.14 Missing evidence and reporting bias

The review will document missing outcome data and incomplete reporting. Authors may be contacted when missing information materially affects eligibility or synthesis. Any assumptions or calculations used to derive statistics will be documented. Potential reporting bias and missing results will be considered in the interpretation. Funnel plots or statistical tests for small-study effects will be considered only where a sufficient number of comparable studies is available and the assumptions of the method are reasonable.

2.15 Certainty of evidence

Where appropriate, certainty of evidence for important outcomes will be assessed using GRADE. The assessment will consider risk of bias, inconsistency, indirectness, imprecision, and publication bias or other missing-evidence concerns. Judgements will be outcome-specific and justified. A summary-of-findings table may be produced if the evidence and review scope support it. The certainty of evidence must not be inferred from P values alone.

2.16 Protocol registration and amendments

The protocol should be finalised before formal screening and registered prospectively in PROSPERO if the review meets the registry's eligibility criteria. The registration number and protocol location will be provided only after confirmation. If no protocol was prepared or registration was not completed, this must be stated accurately. Deviations will be reported with their reasons and implications.

2.17 Ethics, funding, competing interests, and data availability

A review of published research generally does not require participant-level ethics approval, but institutional and journal requirements should be checked. Funding and the funder's role, author competing interests, and contributions must be reported accurately. The final article should state whether the search strategies, extraction form, extracted data, risk-of-bias judgements, and analysis materials are available and where they can be accessed.

3. RESULTS — TO BE COMPLETED AFTER THE REVIEW

The Results section cannot be finalised until the search and screening process has been completed. The headings below are the planned reporting structure; they are not evidence of completed results.

3.1 Study selection

[Insert actual counts for each database and supplementary source; duplicates removed; records screened; reports sought and not retrieved; full texts assessed; full-text exclusions with reasons; and final included studies. Insert the completed PRISMA 2020 flow diagram.]

3.2 Characteristics of included studies

[Summarise the study designs, countries, populations, diagnostic definitions, treatment status, exposures/interventions, comparators, outcome instruments, and follow-up. Include a study-characteristics table.]

3.3 Risk of bias

[Report study-level risk-of-bias judgements using the selected tools and describe the domains most likely to affect confidence in the findings.]

3.4 Results of individual studies

[Report outcome data and effect estimates with precision for each study, as available. Clearly distinguish adjusted from unadjusted estimates and between-group intervention effects from within-group changes.]

3.5 Results of syntheses

[Organise results by cognitive function; psychological well-being; sleep; physical activity and exercise; fatigue and quality of life; and treatment adherence or other eligible behaviours. Identify which studies contribute to each synthesis and report heterogeneity and certainty where assessed.]

3.6 Reporting bias and certainty of evidence

[Report assessments of missing results or reporting bias and the certainty of evidence for important outcomes. Explain if an assessment was not feasible.]

4. DISCUSSION

4.1 Principal findings

Once the analysis is complete, summarise the main findings in relation to the objectives. Identify the lifestyle domains with the most consistent evidence, which outcomes are supported by intervention studies, and where evidence is uncertain. Avoid implying that a behavioural factor causes an outcome when the contributing evidence is observational.

4.2 Interpretation of cognitive findings

Discuss results according to the cognitive domain, measurement method, hypothyroidism classification, treatment status, and risk of bias. Explain differences between subjective cognitive complaints and objective tests if the evidence shows divergence. Consider confounding by sleep, fatigue, psychological symptoms, comorbidities, and age where the included studies allow.

4.3 Interpretation of psychological findings

Discuss depression, anxiety, stress, emotional functioning, and mental health-related quality of life as distinct but potentially overlapping outcomes. Evaluate consistency across study designs and whether intervention effects are supported by appropriate comparators, clinically interpretable effect estimates, and adequate follow-up.

4.4 Clinical implications

If supported by the evidence, findings may inform a broader patient-centred approach to hypothyroidism care, including assessment of sleep, activity, stress, cognition, mood, and daily functioning. Any clinical implications should be proportionate to certainty and applicability. Lifestyle strategies must not be presented as replacements for indicated thyroid hormone therapy or appropriate clinical evaluation of persistent symptoms.

4.5 Strengths and limitations of the evidence

Discuss limitations demonstrated by the included studies, potentially including small samples, heterogeneous diagnostic criteria, self-reported outcomes, short follow-up, residual confounding, incomplete intervention descriptions, and inconsistent outcome measures. These should be reported only if they are actually present in the included evidence.

4.6 Strengths and limitations of the review

Potential strengths include a prespecified question, reproducible searching, transparent eligibility criteria, structured extraction, design-appropriate risk-of-bias assessment, and separation of observational and intervention evidence. Potential limitations may include inaccessible full texts, language restrictions, limited database access, heterogeneity preventing meta-analysis, and missed unpublished evidence. The final manuscript must describe only limitations that genuinely apply.

4.7 Implications for future research

Future research would benefit from consistent diagnostic definitions, clear reporting of thyroid treatment and biochemical status, adequate control of confounders, validated cognitive and psychological outcomes, and longer follow-up. Intervention studies should prespecify primary outcomes, use appropriate comparators, report adherence and adverse events, and include patient-centred measures alongside biochemical outcomes. Research should distinguish subjective cognitive symptoms from objectively measured performance and consider whether results vary by disease subtype and treatment status.

5. CONCLUSION

This review is designed to evaluate evidence on non-dietary lifestyle and behavioural factors in relation to cognition and psychological well-being in hypothyroidism. By distinguishing observational associations from intervention effects, it aims to clarify what is known, where uncertainty remains, and which outcomes require further investigation. The final conclusions must be based on verified included studies, risk-of-bias assessments, and certainty of evidence. Lifestyle approaches should be considered within comprehensive, patient-centred care and not as substitutes for clinically indicated thyroid hormone replacement.

DECLARATIONS

Protocol and registration

[Insert protocol availability and confirmed registration details, or state accurately that registration was not completed.]

Funding

[Insert the actual funding source and the funder's role, or state that no specific funding was received if confirmed.]

Competing interests

[Insert the authors' confirmed declarations.]

Author contributions

[Insert actual contributions according to the target journal's format.]

Data and materials availability

[State whether the final search strategies, screening decisions, extraction form, extracted data, risk-of-bias assessments, and analysis files are available and provide the location if shared.]

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