

Evidence on the clinical effectiveness of selected nutritional supplements prescribed in the context of naturopathic practice for preventing and/or treating injury, disease, medical conditions, or pre-clinical conditions: Overview of Reviews

## **Appendices**

Version 3 Date 27 September 2024

Prepared for National Health and Medical Research Council

Prepared by Centre for Applied Health Economics Griffith University

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# **Report Information**

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## Dates

This evidence evaluation and accompanying technical report received approval from the National Health and Medical Research Council (NHMRC) Natural Therapies Working Committee (NTWC) on 20 Nov 2024. The protocol for the evidence evaluation was approved by NTWC 15 December 2022 (PROSPERO: CRD42023410906).

## **History**

NHMRC has been engaged by the Department of Health and Aged Care (the Department) to update the evidence underpinning the 2015 Review of the Australian Government Rebate on Natural Therapies for Private Health Insurance (2015 Review) (1). The natural therapies to be reviewed are Alexander technique, aromatherapy, Bowen therapy, Buteyko, Feldenkrais, homeopathy, iridology, kinesiology, naturopathy, Pilates, reflexology, Rolfing, shiatsu, tai chi, western herbal medicine, and yoga. These therapies are among those excluded from the private health insurance rebate as of 1 April 2019.

To support NHMRC in their evidence review, the Centre for Applied Health Economics at Griffith University has been engaged to conduct an overview of the evidence of the clinical effectiveness of selected nutritional supplements prescribed in the context of naturopathic practice. This overview is designed to complement the systematic review of *"Whole system, multi-modal or single modal interventions delivered in the context of naturopathic practice, for preventing and treating health conditions"* (PROSPERO CRD42021266381), which will assess primary research as part of a review of whole system naturopathy.

This evidence evaluation was developed by the Centre for Applied Health Economics at Griffith University in conjunction with NHMRC, NTWC, and the Department of Health and Aged Care, Natural Therapy Advisory Panel (NTREAP). It describes the main body of evidence related to the clinical effectiveness of selected nutritional supplements prescribed in the context of naturopathic practice. Supplementary data are provided in Appendices A to H. All associated materials have been developed in a robust and transparent manner in accordance with relevant best practice standards.

## Funding

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## Acknowledgements

Thank you to the members of the Department's Natural Therapies Review Expert Advisory Panel and the National Health and Medical Research Council's Natural Therapies Working Committee for their advice and comments throughout the creation of this document. PRACI data was provided by Dr Amie Steel at UTS.

Membership and other details of the Panel and Committee can be found at:

www.health.gov.au/committees-and-groups/natural-therapies-review-expert-advisory-panel

www.nhmrc.gov.au/about-us/leadership-and-governance/committees/natural-therapies-workingcommittee

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# Appendix A. Searching, selection criteria and screening

This overview's protocol was approved by NHMRC's Natural Therapies Working Committee (NTWC) on 15 December 2022 (PROSPERO: CRD42023410906). Deviations from the protocol are reported in Appendix G.

The methodologies for this overview are based on those reported in the Cochrane Handbook Chapter V: Overviews of Reviews (2) and the Preferred Reporting Items for Overviews of Reviews (PRIOR) checklist (3). The final Evidence Evaluation Report is reported in line with the PRIOR checklist (3).

This evidence evaluation primarily assessed systematic reviews of randomised controlled trials (RCTs) using an Overview methodology (a systematic review of systematic reviews) (2). EndNote20 (endnote.com) and Covidence (covidence.org) were used for screening, managing citations, and data extraction. GRADEpro GDT software (gradepro.org) was used to record decisions and derive an overall assessment of the certainty of evidence for each outcome guided by GRADE methodology.

This document contains the methodological and technical details.

## A1 Search methods for identification of reviews

## A1.1 Electronic searches

Search strategies (see Appendix A2) were based on key elements of the research question (i.e. intervention, population, and study design). Individual searches were conducted for each priority population-supplement pair. In developing the proposed search strategy, relevant search strategies from Cochrane Overviews of Systematic Reviews were appraised. The following electronic databases were searched (based on guidance from NTWC and the Department of Aged Care's Natural Therapies Review Expert Advisory Panel - NTREAP), from inception until April or May 2023 (depending on the pairing):

- Epistemonikos (includes; Cochrane, PubMed, Embase, CINAHL, PsycINFO, Campbell, JBI)
- AMED (OVID)
- Emcare (OVID)
- Natural Medicines Comprehensive Database
- PROSPERO

Specifically, PROSPERO was searched for population-supplement pairs which were identified as priority, but where no systematic reviews were identified from other sources. This is to check if any relevant systematic reviews were ongoing or completed, but not yet published.

## A1.2 Search restrictions

Searches were limited to human research (by excluding articles that were tagged as "animal" and "not human", so as not to miss articles which are not specifically tagged as "human" but would still be relevant). No date, language or geographic limitations were applied when conducting the search of databases. Non-English databases were not searched, however when non-English reviews were found because of English language database searches, the process outlined in "Reviews published in languages other than English" was followed.

## A1.3 Other sources

Reference lists of all included reviews were reviewed for potential additional eligible reviews (ancestry search). The Department of Health and Aged Care invited the public and key stakeholders to provide published research evidence. Publicly submitted evidence was provided to evidence reviewers once

the protocol was finalised. Potential reviews were considered and assessed against the predetermined inclusion criteria (see Section A3). Grey literature was out of scope (including conference abstracts).

## A2 Search strategies

Condition/intervention	Search syntax
1. Anxiety (including	Epistemonikis
postnatal) andmagnesium	(title:(anxiety OR "affective disorder" OR anxiousness OR anxious) OR abstract:(anxiety
	OR "affective disorder" OR anxiousness OR anxious)) AND (title:(magnesium) OR
Conducted 29/04/2023	abstract:(magnesium))
	AMED
	(magnesium and (anxiety or anxious) and ((living and review) or (rapid and review) or
	meta^analysis or meta review or (overview and (reviews or systematic)) or (systematic
	And review))).mp. [mp=abstract, neading words, titte]
	1. exp anxiety/ or exp anxiety neurosis/ or exp generalized anxiety disorder/ or exp
	anxiety disorder/ or anxiety.mp. or exp "mixed anxiety and depression"/
	2. magnesium.mp. or exp magnesium/
	3. systematic review/ or systematic*.ti. or (systematic adj (review\$1 or overview\$1)).tw.
	or (uving and review). u. or meta analysis/ or meta analys. u. or metaanalys. u. or (overview and
	(review * or systematic)) mp. or (ranid and review) ti_or ((meta adi analy\$) or
	metaanalvs\$).tw.
	4. 1 and 2 and 3
	5. limit 4 to human
	PROSPERO
	((MeSH DESCRIPTOR Anxiety EXPLODE 1) OR (MeSH DESCRIPTOR Mood Disorders
	EXPLODE ALL TREES) OR anxiety OR "affective disorder" OR anxiousness OR anxious)
	AND ((MeSH DESCRIPTOR Magnesium EXPLODE ALL TREES) OR magnesium)
	NatMed Pro database
	1. The Food, Herbs and Supplements database was searched recursively for terms
	related to the intervention. Where such terms were identified, the accompanying
	monograph references were then searched for relevant reviews.
	2. Similarly, the Comparative Effectiveness database was searched recursively for all
	terms related to the condition. For each of these terms, where the intervention and/or
	related terms was identified as a therapy on the Comparative Effectiveness Chart, the
	accompanying monograph references were searched for relevant reviews.
2. Stress	Epistemonikos
(perceived/occupational)	(title:((title:(stress OR distress OR crisis) OR abstract:(stress OR distress OR crisis))
and magnesium	AND (title:(magnesium OR mg*) OR abstract:(magnesium OR mg*))) OR
Conducted 20/04/2022	abstract:((title:(stress OR distress OR crisis) OR abstract:(stress OR distress OR crisis))
Conducted 20/04/2023	AND (title:(magnesium OR mg*) OR abstract:(magnesium OR mg*))))
	AMED
	(magnesium and (stress or distress or crisis) and ((living and review) or (rapid and
	review) or meta*analysis or meta review or (overview and (reviews or systematic)) or
	(systematic and review))).mp. [mp=abstract, heading words, title]
L	

	Ovid Emcare <1995 to 2023 Week 15>
	<ol> <li>exp distress syndrome/ or exp physiological stress/ or stress.mp. or distress.mp. or crisis.mp.</li> <li>magnesium.mp. or exp magnesium/</li> <li>systematic review/ or systematic*.ti. or (systematic adj (review\$1 or overview\$1)).tw. or (living and review).ti. or meta analysis/ or meta analy\$.ti. or metaanaly\$.ti. or (overview adj (review or systematic)).mp. or review of review*.mp. or (overview and (review* or systematic)).mp. or (rapid and review).ti. or ((meta adj analy\$) or metaanalys\$).tw.</li> <li>1 and 2 and 3</li> <li>limit 4 to human</li> </ol>
	PROSPERO
	((MeSH DESCRIPTOR Occupational Stress EXPLODE ALL TREES) OR (MeSH DESCRIPTOR Psychological Distress EXPLODE ALL TREES) OR (MeSH DESCRIPTOR Stress, Psychological EXPLODE ALL TREEs) or stress or crisis or distress) AND ((MeSH DESCRIPTOR Magnesium EXPLODE ALL TREES) OR magnesium)
	NatMed Pro database
	1. The Food, Herbs and Supplements database was searched recursively for terms related to the intervention. Where such terms were identified, the accompanying monograph references were then searched for relevant reviews.
	2. Similarly, the Comparative Effectiveness database was searched recursively for all terms related to the condition. For each of these terms, where the intervention and/or related terms was identified as a therapy on the Comparative Effectiveness Chart, the accompanying monograph references were searched for relevant reviews.
3. Irritable bowel syndrome	Epistemonikos
and probiotics Conducted 22/05/2023	(title:(probiotic* OR synbiotic* OR symbiotic* OR lactobacill* OR bifidobacteri* OR saccharomyces OR "escherichia coli" OR bacillus OR "clostridium butyricum" OR streptococcus) OR abstract:(probiotic* OR synbiotic* OR symbiotic* OR lactobacill* OR bifidobacteri* OR saccharomyces OR "escherichia coli" OR bacillus OR "clostridium butyricum" OR streptococcus)) AND (title:("irritable bowel syndrome" OR "irritable bowel disorder" OR IBS) OR abstract:("irritable bowel syndrome" OR "irritable bowel disorder" OR IBS))
	AMED ((probiotic* or synbiotic* or symbiotic* or lactobacill* or bifidobacteri* or saccharomyces or escherichia coli or bacillus or clostridium butyricum or streptococcus) and (Irritable bowel syndrome or ibs) and ((living and review) or (rapid and review) or meta*analysis or meta review or (overview and (reviews or systematic)) or (systematic and review))).mp. [mp=abstract, heading words, title] Ovid Emcare <1995 to 2023 Week 15>
	<ol> <li>exp probiotic agent/ or probiotic*.mp. or exp synbiotic agent/ or synbiotic*.mp. or exp prebiotic agent/ or prebiotic*.mp. or symbiotic*.mp. or lactobacillus.mp. or exp lactobacillus/ or exp saccharomyces/ or saccharomyces.mp. or bifidobacteri*.mp. or exp bifidobacterium/ or escherichia coli.mp. or exp escherichia coli/ or bacillus.mp. or exp bacillus/ or clostridium butyricum.mp. or exp clostridium butyricum/ or streptococce*.mp. or exp streptococcus/</li> <li>(Irritable bowel syndrome or IBS).mp. or exp irritable colon/</li> <li>systematic review/ or systematic*.ti. or (systematic adj (review\$1 or overview\$1)).tw. or (living and review).ti. or meta analysis/ or meta analy\$.ti. or metaanaly\$.ti. or (overview adj (review or systematic)).mp. or review of review*.mp. or (overview and (review* or systematic)).mp. or (rapid and review).ti. or ((meta adj analy\$) or metaanaly\$).tw.</li> <li>1 and 2 and 3</li> <li>limit 4 to human</li> </ol>
	PROSPERO
	((MeSH DESCRIPTOR Irritable Bowel Syndrome EXPLODE ALL TREES) OR "irritable bowel" OR IBS) AND ((MeSH DESCRIPTOR Probiotics EXPLODE ALL TREES) OR probiotic* OR synbiotic* OR symbiotic* OR lactobacill* OR bifidobacteri* OR

	saccharomyces OR "escherichia coli" OR bacillus OR "clostridium butyricum" OR streptococcus)
	NatMed Pro database
	1. The Food, Herbs and Supplements database was searched recursively for terms related to the intervention. Where such terms were identified, the accompanying monograph references were then searched for relevant reviews.
	2. Similarly, the Comparative Effectiveness database was searched recursively for all terms related to the condition. For each of these terms, where the intervention and/or related terms was identified as a therapy on the Comparative Effectiveness Chart, the accompanying monograph references were searched for relevant reviews.
4. Insomnia/sleep	Epistemonikos
disorders and magnesium	(title:((title:(insomnia OR narcolepsy OR hypersomnia OR dyssomnia OR sleep OR
Conducted 04/04/3023	nightmare OR snoring OR "Nocturnal paroxysmal dystonia" OR "Restless leg syndrome" OR "periodic limb movement disorder" OR "rhythmic movement disorder" OR "hypnagogic hallucinations") OR abstract:(insomnia OR narcolepsy OR hypersomnia OR dyssomnia OR sleep OR nightmare OR snoring OR "Nocturnal paroxysmal dystonia" OR "Restless leg syndrome" OR "periodic limb movement disorder" OR "rhythmic movement disorder" OR "hypnagogic hallucinations")) AND (title:(magnesium) OR abstract:(magnesium))) OR abstract:((title:(insomnia OR narcolepsy OR hypersomnia OR dyssomnia OR sleep OR nightmare OR snoring OR "Nocturnal paroxysmal dystonia" OR dyssomnia OR sleep OR nightmare OR snoring OR "Nocturnal paroxysmal dystonia" OR dyssomnia OR sleep OR nightmare OR snoring OR "Nocturnal paroxysmal dystonia" OR "Restless leg syndrome" OR "periodic limb movement disorder" OR "rhythmic movement disorder" OR "hypnagogic hallucinations") OR abstract:(insomnia OR narcolepsy OR hypersomnia OR dyssomnia OR sleep OR nightmare OR snoring OR "Nocturnal paroxysmal dystonia" OR "Restless leg syndrome" OR "periodic limb movement disorder" OR "rhythmic movement disorder" OR "hypnagogic hallucinations")) AND (title:(magnesium) OR abstract:(magnesium))))
	AMED
	(magnesium and (insomnia or narcolepsy or hypersomnia or dyssomnia or sleep or nightmare or snoring or "Nocturnal paroxysmal dystonia" or "Restless leg syndrome" or "periodic limb movement disorder" or "rhythmic movement disorder" or "hypnagogic hallucinations") and ((living and review) or (rapid and review) or meta*analysis or meta review or (overview and (reviews or systematic)) or (systematic and review))).mp. [mp=abstract, heading words, title]
	Ovid Emcare <1995 to 2023 Week 13>
	<ol> <li>magnesium.mp. or exp magnesium</li> <li>/exp sleep deprivation/ or exp sleep disorder/ or sleep disordered breathing/ or insomnia.mp. or narcolepsy.mp. or hypersomnia.mp. or dyssomnia.mp. or sleep hypoventilation.mp. or sleep hypoxemia.mp. or nightmare.mp. or sleep enuresis.mp. or sleep bruxism.mp. or snoring.mp. or nocturnal paroxysmal dystonia.mp. or restless legs syndrome.mp. or periodic limb movement disorder.mp. or rhythmic movement disorder.mp. or sleep walking.mp. or sleep talking.mp. or sleep myoclonus.mp. or sleep hyperhidrosis.mp. or hypnagogic hallucinations.mp. or sleeplessness.mp. or sleep disorder.mp. or daytime somnolence.mp.</li> <li>systematic review/ or systematic*.ti. or (systematic adj (review\$1 or overview\$1)).tw. or (living and review).ti. or meta analysis/ or meta analy\$.ti. or metaanaly\$.ti. or (overview adj (review or systematic)).mp. or review of review*.mp. or (overview and (review* or systematic)).mp. or (rapid and review).ti. or ((meta adj analy\$) or metaanalys\$).tw.</li> <li>1 and 2 and 3</li> <li>limit 4 to human</li> </ol>
	PROSPERO
	((MeSH DESCRIPTOR Sleep Wake Disorders EXPLODE ALL TREES) OR insomnia or narcolepsy or hypersomnia or dyssomnia OR sleep hypoventilation OR sleep hypoxemia OR nightmare OR sleep enuresis OR sleep bruxism OR snoring OR Nocturnal paroxysmal dystonia OR Restless legs syndrome OR periodic limb movement disorder OR rhythmic movement disorder OR sleep walking OR sleep talking OR sleep myoclonus OR sleep hyperhidrosis OR hypnagogic hallucinations) AND ((MeSH DESCRIPTOR Magnesium EXPLODE ALL TREES) OR magnesium)

	NatMed Pro database
	1. The Food, Herbs and Supplements database was searched recursively for terms related to the intervention. Where such terms were identified, the accompanying monograph references were then searched for relevant reviews.
	2. Similarly, the Comparative Effectiveness database was searched recursively for all terms related to the condition. For each of these terms, where the intervention and/or related terms was identified as a therapy on the Comparative Effectiveness Chart, the accompanying monograph references were searched for relevant reviews.
5. Depression (including	Epistemonikos
postpartum) and omega-3 Conducted 29/04/2023	(title:((title:(depression OR depressive OR "mood disorder*" OR "affective disorder*" OR post?natal OR post?partum) OR abstract:(depression OR depressive OR "mood disorder*" OR "affective disorder*" OR post?natal OR post?partum))) OR abstract:((title:(depression OR depressive OR "mood disorder*" OR "affective disorder*" OR post?natal OR post?partum)) OR abstract:(depression OR depressive OR "mood disorder*" OR "affective disorder*" OR post?natal OR post?partum))) AND (title:((Fatty acid* OR omega-3* OR fish oil* OR linolen* OR eicosapent*enoic* OR docosapent*enoic* OR docosahex?enoic* OR hexadecatrienoic* OR stearidonic* OR eicosatetr*enoic* OR heneicosapent*enoic* OR tetracosapent*enoic* OR tetracosahex*enoic*)) OR abstract:((Fatty acid* OR omega-3* OR fish oil* OR linolen* OR eicosapent*enoic* OR docosapent*enoic* OR or fish oil* OR linolen*
	hexadecatrienoic* OR stearidonic* OR eicosatrienoic* OR eicosatetr*enoic* OR icosatrienoic* OR icosapent*enoic* OR icosatetr*enoic* OR heneicosapent*enoic* OR tetracosapent*enoic* OR tetracosahex*enoic*)))
	AMED
	(depression or depressive or affective disorder*) AND (Fatty acid* or omega-3* or fish oil* or linolen* or eicosapent*enoic* or docosapent*enoic* or docosahex?enoic* or hexadecatrienoic* or stearidonic* or eicosatrienoic* or eicosatetr*enoic* or icosatrienoic* or icosapent*enoic* or icosatetr*enoic* or heneicosapent*enoic* or tetracosapent*enoic* or tetracosahex*enoic*) AND ((systematic and review) or (living and review) or (rapid and review) or meta*analysis or meta*review or overview).mp
	Ovid Emcare <1995 to 2023 Week 16>
	1. exp fatty acid/ or fatty acid*.mp. or exp omega 3 fatty acid/ or exp fish oil/ or omega 3.mp. or exp docosahexaenoic acid/ or docosahex*.mp. or hexadecatrienoic*.mp. or exp docosapentaenoic acid/ or docosapent*.mp. or exp linolenic acid/ or linolen*.mp. or exp icosapentaenoic acid/ or icosapent*.mp. or exp icosatrienoic acid/ or icosapent*.mp. or exp icosatrienoic acid/ or icosapent*.mp. or eicosater*.mp. or eicosater*.mp. or eicosater*.mp. or eicosapent*.mp. or
	tetracosapent*.mp. or tetracosanex*.mp. 2. exp chronic depression/ or exp minor depression/ or exp "mixed anxiety and depression"/ or exp "mixed depression and dementia"/ or exp antenatal depression/ or exp agitated depression/ or exp adolescent depression/ or exp major depression/ or exp long term depression/ or depression.mp. or exp endogenous depression/ or exp postoperative depression/ or exp late life depression/ or exp reactive depression/ or exp perinatal depression/ or exp atypical depression/ or exp recurrent brief depression/ or exp depression/ or exp treatment resistant depression/ or exp postnatal depression/ or exp "mixed mania and depression"/ or exp post-stroke depression/ or exp bipolar depression/ or exp organic depression/ or depressi*.mp. or affective disorder*.mp. 3. systematic review/ or systematic*.ti. or (systematic adj (review\$1 or overview\$1)).tw. or (living and review).ti. or meta analysis/ or meta analy\$.ti. or metaanaly\$.ti. or (overview adj (review or systematic)).mp. or review of review*.mp. or (overview and (review* or systematic)).mp. or (rapid and review).ti. or ((meta adj analy\$) or metaanalys\$).tw. 4. 1 and 2 and 3 5. limit 4 to human PROSPERO
	DESCRIPTOR Depression EXPLODE ALL TREES) OR mood.tw OR (MeSH DESCRIPTOR Depression EXPLODE ALL TREES) or depression OR depressive OR affect* AND (Fatty ADJ acid* OR fish ADJ oil* OR omega-3 OR omega 3 OR icosapent* OR

	linolen* OR eicosapent* OR docosapent* OR PUFA* OR polyunsaturated OR poly- unsaturated OR hexadeca* OR steari* OR eicosatrie* OR eicosatet* OR icosapent* OR icosatet* OR icosatetr* OR heneicosa* OR tetracosapent* OR tetracosahex*))
	NatMed Pro database
	1. The Food, Herbs and Supplements database was searched recursively for terms related to the intervention. Where such terms were identified, the accompanying monograph references were then searched for relevant reviews.
	2. Similarly, the Comparative Effectiveness database was searched recursively for all terms related to the condition. For each of these terms, where the intervention and/or related terms was identified as a therapy on the Comparative Effectiveness Chart, the accompanying monograph references were searched for relevant reviews.
6. Dysmenorrhea and	Epistemonokis
Cruciferous Indoles (indole-3- carbinol, di - indolylmethane) Conducted 28/04/2023	(title:(dysmenorrhea OR (menstrua* AND disturbance*) OR (menstrua* AND disorder*) OR (menstrua* AND disease*) OR (pelvic AND pain*) OR (menstrua* AND pain*) OR (period* AND pain*)) OR abstract:(dysmenorrhea OR (menstrua* AND disturbance*) OR (menstrua* AND disorder*) OR (menstrua* AND disease*) OR (pelvic AND pain*) OR (menstrua* AND pain*) OR (period* AND pain*))) AND (title:((title:(cruciferae OR brassicacea* OR brassica* OR (cruciferous AND vegetable*) OR broccoli OR cabbage* OR cauliflower* OR (brussel AND sprout*) OR mustard OR sauerkraut OR coleslaw OR (cole AND slaw) OR collard* OR (bok AND choy) OR (turnip AND green) OR raddish* OR (indole AND carbinol) OR I3C OR di*indolylmethane) OR abstract:(cruciferae OR brassicacea* OR brassica* OR (cruciferous AND vegetable*) OR broccoli OR cabbage* OR cauliflower* OR (brussel AND sprout*) OR mustard OR sauerkraut OR coleslaw OR (and the AND carbinol) OR I3C OR di*indolylmethane) OR abstract:(cruciferae OR brassicacea* OR brassica* OR (cruciferous AND vegetable*) OR broccoli OR cabbage* OR cauliflower* OR (brussel AND sprout*) OR mustard OR sauerkraut OR coleslaw OR (cole AND carbinol) OR I3C OR di*indolylmethane) OR abstract:(cruciferae OR brassicacea* OR brassica* OR (cruciferous AND vegetable*) OR broccoli OR cabbage* OR cauliflower* OR (brussel AND sprout*) OR mustard OR sauerkraut OR coleslaw OR
	(cole AND staw) OR collard* OR (bok AND choy) OR (turnip AND green) OR raddish* OR (indole AND carbinol) OR I3C OR di*indolylmethane))) OR abstract:((title:(cruciferae OR brassicacea* OR brassica* OR (cruciferous AND vegetable*) OR broccoli OR cabbage* OR cauliflower* OR (brussel AND sprout*) OR mustard OR sauerkraut OR coleslaw OR (cole AND slaw) OR collard* OR (bok AND choy) OR (turnip AND green) OR raddish* OR (indole AND carbinol) OR I3C OR di*indolylmethane) OR abstract:(cruciferae OR brassicacea* OR brassica* OR (cruciferous AND vegetable*) OR broccoli OR cabbage* OR cauliflower* OR (brussel AND sprout*) OR mustard OR sauerkraut OR coleslaw OR (cole AND slaw) OR collard* OR (cruciferous AND vegetable*) OR broccoli OR cabbage* OR cauliflower* OR (brussel AND sprout*) OR mustard OR sauerkraut OR coleslaw OR (cole AND slaw) OR collard* OR (bok AND choy) OR (turnip AND green) OR raddish* OR (indole AND carbinol) OR I3C OR di*indolylmethane))))
	AMED
	(Dysmenorrhea or (menstrua* and disturbance*) or (menstrua* and disorder*) or (menstrua* and disease*) or (pelvic and pain*) or (menstrua* and pain*) or (period* and pain*)) AND (cruciferae or brassicacea* or brassica* or (cruciferous and vegetable*) or broccoli or cabbage* or cauliflower* or (brussel and sprout*) or mustard or sauerkraut or coleslaw or (cole and slaw) or collard* or (bok and choy) or (turnip and green) or raddish* or (indole and carbinol) or I3C or di*indolylmethane) AND ((systematic and review) or (living and review) or (rapid and review) or meta*analysis or meta*review or overview).mp

	Ovid Emcare <1995 to 2023 Week 16>
	<ol> <li>brassicaceae.mp. or exp brassicaceae/ or brassica.mp. or (cruciferae or cruciferous).mp. or cabbage*.mp. or exp celery/ or cabbage/ or exp white cabbage/ or exp cabbage/ or exp red cabbage/ or exp Chinese cabbage/ or exp Savoy cabbage/ or exp celery/ or celery.mp. or exp cauliflower/ or cauliflower*.mp. or broccoli.mp. or exp broccoli/ or exp brussels sprout/ or (brussel* and sprout*).mp. or coleslaw.mp. or cole slaw.mp. or exp bok choy/ or bok choy.mp. or exp turnip/ or turnip*.mp. or radish.mp. or exp radish/ or raddish*.mp. or indole*.mp. or exp turnip/ or turnip*.mp. or radish.mp. or exp indole derivative/ or carbinol*.mp. or exp carbinol/ or 3 indolemethanol*.mp. or exp 3 indolemethanol/ or 3,3' diindolylmethane*.mp. or exp 3,3' diindolylmethane/ or IC3.mp. or di*indolylmethane.mp.</li> <li>exp dysmenorrhea/ or exp menstruation disorder/ or dysmenorrhea.mp. or dys- menorrhea.mp. or dys-menorrhoea.mp. or (menstrua* and disorder*).mp. or (menstrua* and disturbance*).mp. or (pelvic and pain*).mp. or exp pelvic pain/ or (menstrua* and pain*).mp. or (period* and pain*).mp. or (pain* and menstrua*).mp. or (mustrua* and cramp*).mp.</li> <li>systematic review/ or systematic*.ti. or (systematic adj (review\$1 or overview\$1)).tw. or (living and review).ti. or meta analysis/ or meta analy\$.ti. or metaanaly\$.ti. or (overview adj (review or systematic)).mp. or review of review*.mp. or (overview and (review* or systematic)).mp. or (rapid and review).ti. or ((meta adj analy\$) or metaanalys\$).tw.</li> <li>1 and 2 and 3</li> <li>limit 4 to human</li> </ol>
	(dysmenorrhea OR (menstrua* AND disturbance*) OR (menstrua* AND disorder*) OR (menstrua* AND disease*) OR (pelvic AND pain*) OR (menstrua* AND pain*) OR (period* AND pain*)) AND ( cruciferae OR brassicacea* OR brassica* OR (cruciferous AND vegetable*) OR broccoli OR cabbage* OR cauliflower* OR (brussel AND sprout*) OR mustard OR sauerkraut OR coleslaw OR (cole AND slaw) OR collard* OR (bok AND choy) OR (turnip AND green) OR raddish* OR (indole AND carbinol) OR I3C OR di*indolylmethane)
	NatMed Pro database
	1. The Food, Herbs and Supplements database was searched recursively for terms related to the intervention. Where such terms were identified, the accompanying monograph references were then searched for relevant reviews.
	2. Similarly, the Comparative Effectiveness database was searched recursively for all terms related to the condition. For each of these terms, where the intervention and/or related terms was identified as a therapy on the Comparative Effectiveness Chart, the accompanying monograph references were searched for relevant reviews.
7. Premenstrual syndrome	Epistemonikis
and Cruciferous Indoles (indole-3- carbinol, di - indolylmethane) Conducted 28/04/2023	(title:((cruciferae OR brassicacea* OR brassica* OR (cruciferous AND vegetable*) OR broccoli OR cabbage* OR cauliflower* OR (brussel AND sprout*) OR mustard OR sauerkraut OR coleslaw OR (cole AND slaw) OR collard* OR (bok AND choy) OR (turnip AND green) OR raddish* OR (indole AND carbinol) OR I3C OR di*indolylmethane)) OR abstract:((cruciferae OR brassicacea* OR brassica* OR (cruciferous AND vegetable*) OR broccoli OR cabbage* OR cauliflower* OR (brussel AND sprout*) OR mustard OR sauerkraut OR coleslaw OR (cole AND slaw) OR collard* OR (bok AND choy) OR (turnip AND green) OR raddish* OR (indole AND carbinol) OR I3C OR di*indolylmethane))) AND green) OR raddish* OR (indole AND carbinol) OR I3C OR di*indolylmethane))) AND (title:(premenstrual syndrome) OR abstract:(premenstrual syndrome))
	AMED
	((premenstrual AND syndrome) OR PMS OR (premenstrual AND disorder) OR (premenstrual AND dysphoria) OR PMDD OR (premenstrual AND tension) OR PMT OR (premenstrual AND cramp*) OR (premenstrual AND pain) OR (prementrual AND symptoms)) AND (cruciferae or brassicacea* or brassica* or (cruciferous and vegetable*) or broccoli or cabbage* or cauliflower* or (brussel and sprout*) or mustard or sauerkraut or coleslaw or (cole and slaw) or collard* or (bok and choy) or (turnip and green) or raddish* or (indole and carbinol) or I3C or di*indolylmethane) AND

	((systematic and review) or (living and review) or (rapid and review) or meta*analysis or meta*review or overview).mp
	Ovid Emcare <1995 to 2023 Week 16>
	1. brassicaceae.mp. or exp brassicaceae/ or brassica.mp. or (cruciferae or cruciferous).mp. or cabbage*.mp. or exp celery/ or cabbage/ or exp white cabbage/ or
	exp cabbage/ or exp red cabbage/ or exp Chinese cabbage/ or exp Savoy cabbage/ or exp celery/ or celery.mp. or exp cauliflower/ or cauliflower*.mp. or broccoli.mp. or exp broccoli/ or exp brussels sprout/ or (brussel* and sprout*) mp. or colesiaw mp. or cole
	slaw.mp. or exp bok choy/ or bok choy.mp. or exp turnip/ or turnip*.mp. or radish.mp. or exp radish/ or raddish*.mp. or indole*.mp. or exp indole/ or indole derivative*.mp. or exp indole derivative/ or carbinol*.mp. or exp carbinol/ or 3 indolemethanol*.mp. or exp 3 indolemethanol/ or 3.3' diindolylmethane*.mp. or exp 3.3' diindolylmethane/ or
	IC3.mp. or di*indolylmethane.mp.
	2. exp premenstrual syndrome/ or (premenstrual and dysphoria).mp. or exp premenstrual syndrome/ or exp premenstrual dysphoric disorder/ or premenstrual.mp.
	or (premenstrual and syndrome).mp. or exp premenstrual syndrome/ or PMS.mp. or (premenstrual and disorder).mp. or (premenstrual and dysphoria).mp. or PMDD.mp. or (premenstrual and tension).mp. or PMT.mp. or (premenstrual and cramp*).mp. or
	(premenstrual and pain).mp. 3. systematic review/ or systematic*.ti. or (systematic adj (review\$1 or overview\$1)).tw.
	or (living and review).ti. or meta analysis/ or meta analy\$.ti. or metaanaly\$.ti. or (overview adj (review or systematic)).mp. or review of review*.mp. or (overview and (review* or systematic)).mp. or (rapid and review).ti. or ((meta adj analy\$) or
	metaanalys\$).tw. 4. 1 and 2 and 3
	5. limit 4 to human
	cabbage OR cauliflower OR (brussel adj1 sprout*) OR (mustard adj1 plant*) OR sauerkraut OR coleslaw OR (cole adj1 slaw) OR collard* OR (bok adj1 choy) OR (turnip adj1 green*) OR raddish OR indole-3-carbinol OR indole-3 carbinol OR I3C OR di?ndolylmethane AND (MeSH DESCRIPTOR Premenstrual Syndrome EXPLODE ALL
	TREES) NatMed Pro database
	1 The Food Herbs and Supplements database was searched recursively for terms
	related to the intervention. Where such terms were identified, the accompanying monograph references were then searched for relevant reviews.
	2. Similarly, the Comparative Effectiveness database was searched recursively for all
	terms related to the condition. For each of these terms, where the intervention and/or related terms was identified as a therapy on the Comparative Effectiveness Chart, the
	accompanying monograph references were searched for relevant reviews.
8. Atopic disorders (incl. Eczema/ dermatitis /	Epistemonikis
Allergic rhinitis/ allergy (incl. Hay fever)) and zinc	(title:(zinc OR zn) OR abstract:(zinc OR zn)) AND (title:(atopic OR atopy OR atopia OR hypersenitivit* OR hyper-sensitivit* OR hyper-responsiven* OR hyperresponsive* OR
Conducted 21/04/2023	AND test) OR allerg* OR asthma OR asthmat* OR wheez* OR bronchial OR bronch* OR
	rhinitis OR rhinitides OR hayfever OR (hay AND fever) OR rhinoconjunctivitis OR
	pollinosis OR pollen* OR(nasal AND obstruction) OR radioallergosorbent OR RAST OR
	anaphylactoid OR shock* OR react* OR hives OR weals OR welts OR rash OR pruriti* OR
	itch* OR (dust AND mite) OR (immun* AND dysregulation) OR immunogenicity OR
	OR atopia OR hypersenitivit* OR hyper-sensitivit* OR hyper-responsiven* OR
	hyperresponsiv* OR sensitisat* OR sensitizat* OR (skin AND prick) OR (skin AND test)
	bronchial OR bronch* OR dermatiti* OR eczem* OR neurodermatit* OR epidermal* OR
	(besnier* AND prurigo) OR rhinitis OR rhinitides OR hayfever OR (hay AND fever) OR
	radioallergosorbent OR RAST OR "immunogloblin E" OR IgE OR intradermal OR
	anaphylaxis OR anaphylactic OR anaphylactoid OR shock* OR react* OR hives OR

weals OR welts OR rash OR pruriti* OR itch* OR (dust AND mite) OR (immun* AND
dysregulation) OR immunogenicity OR intolerance* OR tolerance OR urticar* OR
angioadema))
AMED
(zing or zn) AND (stopic or stopy or stopic or hypersonitivity or hyper sonsitivity or hyper
(zinc of zin AND (atopic of atopic of atopic of hypersentium, of hyper-sensitivit, of hyper-
responsiven* or hyperresponsiv* or sensitisat* or sensitizat* or (skin and prick) or (skin
and test) or SPT or (patch and test) or allerg* or asthma or asthmat* or wheez* or
bronchial or bronch* or dermatiti* or eczem* or neurodermatit* or epidermal* or
(besnier* and prurigo) or rhinitis or rhinitides or havfeyer or (hay and feyer) or
(constructivities or pollionsis or pollen* or (pasal and obstruction) or
radioallergosorbent or RAST or "immunogloblin E" or IgE or intradermal or anaphylaxis or
anaphylactic or anaphylactoid or shock* or react* or hives or weals or welts or rash or
pruriti* or itch* or (dust and mite) or (immun* and dysregulation) or immunogenicity or
intolerance* or tolerance or urticar* or angioedema) AND ((systematic and review) or
(living and rovious) or (rapid and rovious) or matatanalysis or matatarovious or
overview).mp"
Ovid Emears <1995 to 2022 Week 17>
Ovid Efficate < 1995 to 2023 Week 172
1, exp atopic keratoconiunctivitis/ or atopic.mp. or exp atopic dermatitis/ or exp
"Severity Scoring of Atonic Dermatitis"/
2 stony mp. srove stony/
2. atopy.mp. or exp atopy/
3. atopia.mp. or exp atopy/
<ol><li>exp hypersensitivity/ or hypersensitivit*.mp.</li></ol>
5. hyperresponsive.mp.
6. hyperresponsiv*.mp.
7 sonsitiestion mp. or over sonsitization/
8. sensitisat*.ti.
9. sensitizat*.ti.
10. (skin and prick).mp.
11. (skin and test).mp
12 (patch and test) mn
12. papert and test, mp.
13. peandraitergy of periodicin allergy of latex allergy of closs allergy of hose allergy
or allergy rapid test/ or Hymenoptera venom allergy/ or allergy patient/ or IgE mediated
food allergy/ or oral allergy syndrome/ or house dust allergy/ or cobalt allergy/ or
multiple food allergy/ or nut allergy/ or nickel allergy/ or "nut and peanut allergy"/ or
allergy CLIA kit/ or cashew allergy/ or fruit allergy/ or allergy.mp, or red meat allergy/ or
milk allergy/ or egg allergy/ or page allergy/ or respiratory tract allergy/ or eye allergy/ or
The states of th
ragrance allergy or mold allergy or almond allergy or meal allergy or rungal allergy or
exp allergy/ or metal allergy/ or food allergy/ or occupational allergy/ or contact allergy/
or soy allergy/ or wheat allergy/ or allergy test/ or seafood allergy/ or dog allergy/ or
walnut allergy/ or fish allergy/ or allergy test kit/ or seed allergy/ or hazelnut allergy/ or
crustacean allergy/ or shellfish allergy/ or allergy FI ISA/ or animal allergy/ or nollen
allergy/ or rice allergy/ or sesame allergy/ or every perimental allergy/ or inegat allergy/ or
allergy/ of noe allergy/ of sesame allergy/ of experimental allergy/ of insect allergy/ of
apple allergy/ or cat allergy/ or legume allergy/
14. allergy.mp. or exp allergy/
15. exp asthma/ or exp allergic asthma/ or asthma.mp.
16. bronchial.mp.
17. eczema.mp. or exp eczema/ or exp occupational eczema/ or exp hand eczema/
18 allerg* mn
is. wheez^.mp.
20. hyper-sensitivit*.mp.
21. hyper-responsiven*.mp.
22. epidermal*.ti,ab.
23. (besnier* and prurigo).mp.
21 rhinitis mp, or eyn rhinitis/ or eyn allergic rhinitis/ or eyn perennial rhinitis/ or eyn
2 minutes inp. of exp minutes of exp attended in minutes of exp peremination in the peremination of exp
25. rhinitides.mp.
26. hayfever.mp. or exp pollen allergy/
27. (hay and fever).mp.
28. rhinoconiunctivitis.mp. or exp. rhinoconiunctivitis/
20. nollinosis mn
30. pollen antigen/ or grass pollen/ or pollen/ or pollen.mp.
31. (nasal and obstruction).mp.

	32. exp radioallergosorbent test/ or radioallergosorbent.mp. or exp immunoglobulin E/ or exp allergen/
	33. RAST.mp. 34. JøF.mp.
	35. intradermal.mp.
	36. exp skin anaphylaxis/ or exp anaphylaxis/ or anaphylaxis.mp. or exp food induced
	anaphylaxis/ or exp systemic anaphylaxis/
	37. anaphylactic.mp. or exp anaphylactic shock/
	38. anaphylactoid.mp. or exp anaphylactoid purpura/
	39. endotoxic shock/ or exp shock/ or vasodilatory shock/ or shock.mp.
	40. cumcal skin reaction/ or reaction.mp. or tocal skin reaction/
	41. nives. nip. of explanation and a second se
	43. welts.mp.
	44. exp rash/ or rash.mp. or exp allergic rash/ or exp urticarial rash/ or exp nevirapine-
	induced skin rash/
	45. pruritis.mp. or exp pruritus/
	46. itch.mp.
	47. itch*.mp.
	48. (dust and mite).mp.
	49. (Immun* and dysregulation).mp.
	50. Immunogenicity.mp. or exp immunogenicity/
	51. Intolerance mp. or evo immunological tolerance/
	53. angioedema.mp. or angioneurotic edema/
	54. exp zinc/ or zinc.mp.
	55. systematic*.ti.
	56. (systematic adj (review\$1 or overview\$1)).tw.
	57. (living and review).ti.
	58. exp meta analysis
	59. systematic review.mp. or exp "systematic review"
	60. (overview adj (review or systematic)).mp.
	61. meta analy\$.tl.
	63 review of review* mp
	64. (overview and (review* or systematic)).mp.
	65. (rapid and review).ti.
	66. ((meta adj analy\$) or metaanalys\$).tw.
	67. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or
	18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or
	34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or
	50 or 51 or 52 or 53
	68. 55 0r 56 0r 57 0r 58 0r 59 0r 60 0r 61 0r 62 0r 63 0r 64 0r 65 0r 66
	70 limit 69 to human
•	PBOSPERO
	((MeSH DESCRIPTOR Skin Diseases, Eczematous EXPLODE ALL TREES) OR (MeSH
	Allorgic Agents) OP (MoSH DESCRIPTOP Acthmo EVD) ODE ALL TREES) OR (MOSH DESCRIPTOR ANI-
	DESCRIPTOR Bronchial Hyperreactivity) OR (MeSH DESCRIPTOR Badioallergosorbent
	Test EXPLODE ALL TREES) OR (MeSH DESCRIPTOR Immunoglobulin E EXPLODE ALL
	TREES) OR (MeSH DESCRIPTOR Angioedema) OR atop* OR eczema* OR dermatiti* OR
	neurodermatitis OR hypersensitivit* OR hyper-sensitivit* OR hyperresponsiv* OR hyper-
	responsiven* OR hyperreactivity OR sensitisation OR sensitization OR (skin ADJ prick)
	OR (skin ADJ test) OR (patch ADJ test) OR (skin ADJ reaction) OR hives OR urticaria OR
	urticarial OR (dust ADJ mite) OR pruriti* OR weals OR welts OR itch* OR allerg* OR
	Wheez^ UK asthma* UK beshier* UK prurigo UK rhiniti* UK hayfever UK (hay ADJ fever)
	on polynosis On polyne On (nasal ADJ obstruction) ON anaphylact^ OK
	F) OR lot OR rhinoconjunctivitis OR rhino-conjunctivitis OR (immune AD) divergulation)
	OR immunodysregulation OR immunogenicity OR immunoinflammatory OR
	angioedema OR (angioneurotic ADJ edema) OR (angioneurotic ADJ oedema)) AND
	(((MeSH DESCRIPTOR Zinc EXPLODE ALL TREES) OR zinc or zn)

	NatMed Pro database		
	<ol> <li>The Food, Herbs and Supplements database was searched recursively for terms related to the intervention. Where such terms were identified, the accompanying monograph references were then searched for relevant reviews.</li> <li>Similarly, the Comparative Effectiveness database was searched recursively for all terms related to the condition. For each of these terms, where the intervention and/or related terms was identified as a therapy on the Comparative Effectiveness Chart, the accompanying monograph references were searched for relevant reviews.</li> </ol>		
<ul> <li>9. Fatigue (general) (incl. Myalgic encephalomyelitis/Chronic Fatigue Syndrome and antioxidants (specifically CoQ10 &amp; alpha -Lipoic acid)</li> <li>Conducted 27/04/2023</li> </ul>	Epistemonikis (title:((title:(fatigu* OR tired* OR exhaust* OR weakness OR astheni* OR neurastheni* OR weary OR weariness OR lassitude OR listless* OR apath* OR malaise OR energy OR letharg* OR myalgi* OR encephalomyelitis OR CFS) OR abstract:(fatigu* OR tired* OR exhaust* OR weakness OR astheni* OR neurastheni* OR weary OR weariness OR lassitude OR listless* OR apath* OR malaise OR energy OR letharg* OR myalgi* OR encephalomyelitis OR CFS)) AND (title:(antioxidant* OR *Q10 OR coenzyme* OR co- enzyme* OR ALA OR thioctic OR *linolenic OR lipoid) OR abstract:(antioxidant* OR *Q10 OR coenzyme* OR co-enzyme* OR ALA OR thioctic OR *linolenic OR lipoid))) OR abstract:((title:(fatigu* OR tired* OR exhaust* OR weakness OR astheni* OR neurastheni* OR weary OR weariness OR lassitude OR listless* OR apath* OR malaise OR energy OR letharg* OR myalgi* OR encephalomyelitis OR CFS) OR abstract:(fatigu* OR tired* OR exhaust* OR weakness OR astheni* OR neurastheni* OR weary OR weariness OR lassitude OR listless* OR apath* OR malaise OR energy OR letharg* OR myalgi* OR encephalomyelitis OR CFS) OR abstract:(fatigu* OR tired* OR exhaust* OR weakness OR astheni* OR neurastheni* OR weary OR weariness OR lassitude OR listless* OR apath* OR malaise OR energy OR letharg* OR myalgi* OR encephalomyelitis OR CFS)) AND (title:(antioxidant* OR *Q10 OR coenzyme* OR co-enzyme* OR ALA OR thioctic OR *linolenic OR lipoid) OR abstract:(antioxidant* OR *Q10 OR coenzyme* OR co-enzyme* OR ALA OR thioctic OR *linolenic OR lipoid) OR abstract:(antioxidant* OR *Q10 OR		
	*linolenic OR lipoid)))) AMED (antioxidant* OR *Q10 OR coenzyme* OR co-enzyme* OR ALA OR thioctic OR *linolenic OR lipoid) AND (fatigu* OR tired* OR exhaust* OR weakness OR astheni* OR neurastheni* OR weary OR weariness OR lassitude OR listless* OR apath* OR malaise OR energy OR letharg* OR myalgi* OR encephalomyelitis OR CFS) AND ((systematic and review) or (living and review) or (rapid and review) or meta*analysis or meta*review or overview).mp		
	Ovid Emcare <1995 to 2023 Week 16> 1. exp fatigue/ or exp mental fatigue/ or exp Fatigue Impact Scale/ or Fatigue.mp. or exp postviral fatigue syndrome/ or exp Fatigue Severity Scale/ or exp chronic fatigue syndrome/ or exp muscle fatigue/ or tired*.mp. or exp exhaustion/ or exhaustion.mp. or exhaut*.mp. or weakness.mp. or exp weakness/ or muscle weakness/ or asthenia.mp. or exp asthenia/ or neurasthenia.mp. or exp neurasthenia/ or neurastheni*.mp. or exp burnout/ or weary.mp. or weariness.mp. or lassitude.mp. or exp apathy/ or apath*.mp. or malaise.mp. or lethargy.mp. or exp lethargy/ or letharg*.mp. or exp myalgia/ or myalgia.mp. or myalgi*.mp. or exp encephalomyelitis/ or encephalomyelitis.mp. or Q10.mp. or exp coenzyme Q10 deficiency/ or coenzyme.mp. or exp linolenic acid/ or exp antioxidant activity/ or exp antioxidant/ or antioxidant.mp. or lipoid.mp. or coenzyme *.mp. or exp ubidecarenone/ 3. systematic review/ or systematic*.ti. or (systematic adj (review\$1 or overview\$1)).tw. or (living and review).ti. or meta analysis/ or meta analy\$.ti. or metaanaly\$.ti. or (overview adj (review or systematic)).mp. or review of review*.mp. or (overview and (review* or systematic)).mp. or (rapid and review).ti. or ((meta adj analy\$) or metaanalys\$).tw. 4. 1 and 2 and 3 5. limit 4 to human		

	PROSPERO
	((MeSH DESCRIPTOR Fatigue Syndrome, Chronic EXPLODE ALL TREES) OR MeSH DESCRIPTOR Fatigue EXPLODE ALL TREES OR fatigu* OR tired* OR exhaust* OR weakness OR astheni* OR neurastheni* OR weary OR weariness OR lassitude OR listless* OR apath* OR malaise OR energy OR letharg* OR myalgi* OR encephalomyelitis OR CFS) AND ((MeSH DESCRIPTOR Antioxidants EXPLODE ALL TREES) OR MeSH DESCRIPTOR Thioctic Acid EXPLODE ALL TREES OR MeSH DESCRIPTOR alpha-Linolenic Acid EXPLODE ALL TREES OR antioxidant* OR "coenzyme Q10" OR "co-enzyme Q10" OR ALA OR thioctic OR linolenic OR "lipoid acid" OR ubidecarenone OR coQ10* OR "alpha-lipoid" OR co-enzyme* OR coenzyme*) NatMed Pro database
	1. The Food, Herbs and Supplements database was searched recursively for terms related to the intervention. Where such terms were identified, the accompanying monograph references were then searched for relevant reviews.
	2. Similarly, the Comparative Effectiveness database was searched recursively for all terms related to the condition. For each of these terms, where the intervention and/or related terms was identified as a therapy on the Comparative Effectiveness Chart, the accompanying monograph references were searched for relevant reviews.
10. Headache/migraine	Epistemonikis
and magnesium Conducted 23/04/2023	(title:(cephalgi* OR headache* OR migraine*) OR abstract:(cephalgi* OR headache* OR migraine*)) AND (title:(magnesium OR Mg) OR abstract:(magnesium OR Mg))
	AMED
	magnesium AND (cephalgi* OR headache* OR migraine*) AND ((systematic and review) or (living and review) or (rapid and review) or meta*analysis or meta*review or overview).mp
	Ovid Emcare <1995 to 2023 Week 16>
	<ol> <li>headache.mp. or exp headache/ or exp complicated migraine/ or migraine.mp. or exp migraine/ or cephalgia.mp. or exp headache/ or headache*.mp. or migraine*.mp.</li> <li>magnesium.mp. or exp magnesium/</li> <li>systematic review/ or systematic*.ti. or (systematic adj (review\$1 or overview\$1)).tw. or (living and review).ti. or meta analysis/ or meta analy\$.ti. or metaanaly\$.ti. or (overview adj (review or systematic)).mp. or review of review*.mp. or (overview and (review* or systematic)).mp. or (rapid and review).ti. or ((meta adj analy\$) or metaanalys\$).tw.</li> <li>1 and 2 and 3</li> <li>limit 4 to human</li> </ol>
	PROSPERO
	((MeSH DESCRIPTOR Headache EXPLODE ALL TREES) OR (MeSH DESCRIPTOR Migraine Disorders EXPLODE ALL TREES) OR (MeSH DESCRIPTOR Cluster Headache EXPLODE ALL TREES) OR cephalgi* OR headache* OR migraine*) AND (magnesium OR mg OR mg*)
	NatMed Pro database
	1. The Food, Herbs and Supplements database was searched recursively for terms related to the intervention. Where such terms were identified, the accompanying monograph references were then searched for relevant reviews.
	2. Similarly, the Comparative Effectiveness database was searched recursively for all terms related to the condition. For each of these terms, where the intervention and/or related terms was identified as a therapy on the Comparative Effectiveness Chart, the accompanying monograph references were searched for relevant reviews.
11. Arthritis/osteoarthritis	Epistemonikis
and magnesium Conducted 21/04/2023	(title:((title:(Arthrit* OR polyarthriti* OR arthrochondriti* OR arthrosynovitis OR oligoarthriti* OR "joint inflammation" OR (psoria* adj3 arthropath*)) OR abstract:(Arthrit* OR polyarthriti* OR arthrochondriti* OR arthrosynovitis OR
	oligoarthriti* OR "joint inflammation" OR (psoria* adj3 arthropath*))) OR (title:(psoria* OR rheumatoid OR osteoarthr* OR osteophytosis OR spondylarthropath* OR ankylosing) OR abstract:(psoria* OR rheumatoid OR osteoarthr* OR osteophytosis OR

spondylarthropath\* OR ankylosing)) AND (title:(magnesium OR mg) OR abstract:(magnesium OR mg))) OR abstract:((title:(Arthrit\* OR polyarthriti\* OR arthrochondriti\* OR arthrosynovitis OR oligoarthriti\* OR "joint inflammation" OR (psoria\* adj3 arthropath\*)) OR abstract:(Arthrit\* OR polyarthriti\* OR arthrochondriti\* OR arthrosynovitis OR oligoarthriti\* OR "joint inflammation" OR (psoria\* adj3 arthropath\*))) OR (title:(psoria\* OR rheumatoid OR osteoarthr\* OR osteophytosis OR spondylarthropath\* OR ankylosing) OR abstract:(psoria\* OR rheumatoid OR osteoarthr\* OR osteophytosis OR spondylarthropath\* OR ankylosing)) AND (title:(magnesium OR mg) OR abstract:(magnesium OR mg))))

#### AMED

magnesium AND (arthriti\* OR polyarthr\* OR arthrochondriti\* OR arthrosynoviti\* OR oligoarthriti\* OR (joint AND inflammation) OR (arthritis AND psoriatic) OR (psoria\* AND arthropath\*) OR (psoria\* AND rheumatism) OR (arthriti\* AND psoriasis) OR rheum\* OR caplan\* OR felty\* OR (inflammatory AND arthr\*) OR gout OR osteoarthr\* OR arthritid\* OR (degenerative AND joint) OR arthros\* OR coxartheros\* OR coxarthros\* OR (malum AND coxae AND senilis) OR gonarthr\* OR spondyl\*s OR (barre AND lieou) OR (brachialgia AND paraesthetica AND nocturna) OR (neri AND barre) OR osteophyt\* OR (posterior AND cervical AND sympathetic) OR spondylarthros\* OR spondyloarthros\* OR (vertebral AND artery AND syndrome) OR periarthr\* OR sacroiliitis OR sacroiliitide\* OR sacroileitis OR spondylarthriti\* OR spondylarthropath\* OR arthropath\* OR bechterew\* OR (inflammatory AND joint) OR sacro-iliitis) AND ((systematic and review) or (living and review) or (rapid and review) or meta\*analysis or meta\*review or overview).mp

#### Ovid Emcare <1995 to 2023 Week 16>

1. arthritis.mp. or exp arthritis/ or arthriti\*.mp. or polyarthritis.mp. or exp polyarthritis/ or polyarthriti\*.mp. or arthrochondritis.mp. or arthrosynovitis.mp. or oligoarthritis.mp. or (joint and inflammation).mp. or arthropath\*.mp. or rheumatism.mp. or rheum\*.mp. or caplan\*.mp. or exp Felty syndrome/ or felty\*.mp. or gout.mp. or exp gout/ or osteoarthritis.mp. or exp osteoarthritis/ or osteoarthriti\*.mp. or arthritid\*.mp. or (degenerative and joint).mp. or arthros\*.mp. or coxarthros\*.mp. or (malum and coxae and senilis).mp. or gonarthr\*.mp. or (barre and lieou).mp. or (brachialgia and paraesthetica and nocturna).mp. or (neri and barre).mp. or osteophyte.mp. or exp osteophyte/ or spondylarthropathy.mp. or exp spondyloarthropathy/ or exp arthropathy/ or arthropathy.mp. or sacroiliitis.mp. or (posterior and cervical and sympathetic).mp. or (vertebral and artery and syndrome).mp. or exp periarthritis/ or periarthritis.mp. or sacroileitis.mp. or exp sacroiliitis/

2. magnesium.mp. or exp magnesium/

3. systematic review/ or systematic\*.ti. or (systematic adj (review\$1 or overview\$1)).tw. or (living and review).ti. or meta analysis/ or meta analy\$.ti. or metaanaly\$.ti. or (overview adj (review or systematic)).mp. or review of review\*.mp. or (overview and (review\* or systematic)).mp. or (rapid and review).ti. or ((meta adj analy\$) or metaanalys\$).tw.

4.1 and 2 and 3

5. limit 4 to human

#### PROSPERO

((MeSH DESCRIPTOR Joint Diseases EXPLODE ALL TREES) OR arthrit\* OR polyarthriti\* OR arthrochondriti\* OR arthrosynovitis OR oligoarthriti\* OR "joint inflammation" OR ankylosing OR spondylarthropath\* OR osteoarthrit\* OR rheumatoid OR osteoarthr\* OR psoria\* OR osteophytosis) AND ((MeSH DESCRIPTOR Magnesium EXPLODE ALL TREES OR magnesium OR mg\*)

NatMed Pro database

1. The Food, Herbs and Supplements database was searched recursively for terms related to the intervention. Where such terms were identified, the accompanying monograph references were then searched for relevant reviews.

2. Similarly, the Comparative Effectiveness database was searched recursively for all terms related to the condition. For each of these terms, where the intervention and/or related terms was identified as a therapy on the Comparative Effectiveness Chart, the accompanying monograph references were searched for relevant reviews.

12. Hypertension and	Epistemonikos
omega-3	/title:/Eatty.acid* OP.amora 2* OP.fish.ail* OP.linglan* OP.aicosanont*anoio* OP
Conducted 21/04/2023	(Intel) raty acid On Onega-S Or hishoft On Initiden On Concersion of the consequence of t
	AMED
	(hyperten* OR HTN OR pre-hyptertens* OR prehypertens* OR anti-hypertens* OR antihypertens* OR (blood AND pressure) OR (arterial AND pressure) OR (systolic AND pressure) OR (diastolic AND pressure) OR bp OR dbp OR sbp) AND (Fatty acid* or omega-3* or fish oil* or linolen* or eicosapent*enoic* or docosapent*enoic* or docosahex?enoic* or hexadecatrienoic* or stearidonic* or eicosatrienoic* or eicosatetr*enoic* or icosatrienoic* or icosapent*enoic* or icosatetr*enoic* or heneicosapent*enoic* or tetracosapent*enoic* or tetracosahex*enoic*) AND ((systematic and review) or (living and review) or (rapid and review) or meta*analysis or meta*review or overview).mp
	Ovid Emcare <1995 to 2023 Week 16>
	<ol> <li>exp hypertension/ or hypertens*.mp.</li> <li>high blood pressure.mp.</li> <li>exp pre hypertension/</li> <li>exp prehypertension/</li> <li>pre-hypertensi*.mp.</li> <li>pre-hypertens*.mp.</li> <li>exp blood pressure/</li> <li>exp diastolic blood pressure/</li> <li>exp systolic blood pressure/</li> <li>exp systolic blood pressure/</li> <li>exp antihypertensive agent/ or antihypertens*.mp. or anti-hypertens*.mp.</li> <li>(blood and pressure).mp.</li> <li>exp arterial pressure/ or arterial pressure.mp.</li> <li>diastolic blood pressure.mp.</li> <li>diastolic blood pressure.mp.</li> <li>fold and pressure.mp.</li> <li>fold and pressure.mp.</li> <li>gen arterial pressure.mp.</li> <li>fold astolic blood pressure.mp.</li> <li>fold astolic bl</li></ol>
	<ul> <li>23. omega*.mp.</li> <li>24. exp fish/ and exp oil/</li> <li>25. exp linolenic acid/</li> </ul>

26. linolen*.mp.
27. exp icosapentaenoic acid/
28. icosapentaen*.mp.
29. eicosapent*.mp.
30. exp docosahexaenoic acid/
31. docosahex*.mp.
32. docosapent*.mp.
33. hexadecatrienoic*.mp.
34. exp omega 3 fatty acid/
35. exp stearidonic acid/
36. stearidonic*.mp.
37. exp icosatrienoic acid/
38. eicosat*.mp.
39. Alpha-Linolenic Acid.mp.
40. Alpha-Linolen*.mp.
41. icosatetr*.mp.
42. icosapent*.mp.
43. heneicosapen?tenoic.mp.
44. heneicosapent?enoic*.mp.
45. (tetracosapent?enoic* or tetracosahex?enoic*).mp.
46. n-3 Fatty Acids.ti,ab,kw.
47. Linolenate.ti,ab,kw.
48. ('n 3' and fatty).mp. and (exp acids/ or acids.mp.)
49. (exp fish/ or fish.mp.) and (exp oil/ or oil.mp.)
50. (fatty and acids).mp. and (exp omega 3/ or omega 3.mp.)
51. systematic*.ti.
52. (systematic adj (review\$1 or overview\$1)).tw.
53. (living and review).ti.
54. exp meta analysis/
55. systematic review.mp.
56. exp "systematic review"/
57. exp "systematic review"/
58. (overview adj (review or systematic)).mp.
59. (rapid and review).ti.
60. (meta adj analy\$) or metaanaly\$\$).tw.
61. meta analy\$.ti.
62. metaanaty\$.u.
63. review of review^.mp.
64. (overview and (review $^{\circ}$ or systematic)).mp.
65. 1 0 r 2 0 r 3 0 r 4 0 r 5 0 r 6 0 r 7 0 r 8 0 r 9 0 r 10 0 r 11 0 r 12 0 r 13 0 r 14 0 r 15 0 r 16 0 r 17 0 r
60. 19 01 20 01 21 01 22 01 23 01 24 01 25 01 26 01 27 01 28 01 29 01 30 01 31 01 32 01 33 01 24 or 25 or 26 or 27 or 28 or 20 or 40 or 41 or 42 or 42 or 44 or 45 or 46 or 47 or 48 or 40 or
68. 65 and 66 and 67
69 limit 68 to human
PROSPERO
rnospeno
((MeSH DESCRIPTOR Fatty Acids, Omega-3 EXPLODE ALL TREES) OR omega-3* OR fish
oil* OR linolen* OR eicosapent*enoic* OR docosapent*enoic* OR docosahex?enoic*
OR hexadecatrienoic* OR stearidonic* OR eicosatrienoic* OR eicosatetr*enoic* OR
icosatrienoic* OR icosapent*enoic* OR icosatetr*enoic* OR heneicosapent*enoic* OR
tetracosapent*enoic* OR tetracosahex*enoic*) AND ((MeSH DESCRIPTOR
Hypertension) OR hypertens* OR HTN OR pre-hyperten* OR prehyperten* OR anti-
hypertens* OR antihypertens* OR (blood AND pressure) OR (arterial AND pressure)
OR (systolic AND pressure) OR (diastolic AND pressure) OR bp OR sbp OR dbp)
NatMed Pro database
1. The Food, Herbs and Supplements database was searched recursively for terms
related to the intervention. Where such terms were identified the accompanying
monograph references were then searched for relevant reviews
2. Similarly, the Comparative Effectiveness database was searched recursively for all
terms related to the condition. For each of these terms, where the intervention and/or

	related terms was identified as a therapy on the Comparative Effectiveness Chart, the accompanying monograph references were searched for relevant reviews.			
13. Fibromyalgia and	Epistemonikos			
magnesium	(title:(fibromyalg* OR (chronic AND pain)) OR abstract:(fibromyalg* OR (chronic AND pain))) AND (title:(magnesium OR Mg) OR abstract:(magnesium OR Mg))			
0011000100 21704/2020	AMED			
	magnesium AND (fibromyalg* OR (chronic AND pain)) AND ((systematic and review) or (living and review) or (rapid and review) or meta*analysis or meta*review or overview).mp			
	Ovid Emcare <1995 to 2023 Week 16>			
	<ol> <li>exp fibromyalgia/ or fibromyalgia.mp. </li> <li>fibromyalg*.mp. </li> <li>chronic pain.mp. or exp chronic pain/ </li> <li>(chronic adj3 pain).mp. </li> <li>magnesium.mp. or exp magnesium/ </li> <li>systematic*.ti. </li> <li>(systematic adj (review\$1 or overview\$1)).tw. </li> </ol>			
	8. (living and review).ti.			
	9. exp meta analysis/			
	11. exp "systematic review"/			
	12. (overview adj (review or systematic)).mp.			
	13. (rapid and review).ti.  14. ((meta adj analy\$) or metaanalys\$).tw.			
	15. meta analy\$.ti.			
	16. metaanaly\$.mp.			
	1 /. review of review*.mp.] 18. (overview and (review* or systematic)).mp.1			
	19. 1 or 2 or 3 or 4			
	20. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 21. 5 and 19 and 20			
	22. limit 21 to human			
	21 records identified			
	PROSPERO			
	((MeSH DESCRIPTOR Fibromyalgia EXPLODE ALL TREES) OR fibromyalg*.mp OR (MeSH DESCRIPTOR Chronic Pain EXPLODE ALL TREES) OR (chronic NEAR6 pain) OR chronic pain) AND ((MeSH DESCRIPTOR Magnesium EXPLODE ALL TREES) or magnesium)			
	NatMed Pro database			
	1. The Food, Herbs and Supplements database was searched recursively for terms related to the intervention. Where such terms were identified, the accompanying monograph references were then searched for relevant reviews.			
	2. Similarly, the Comparative Effectiveness database was searched recursively for all terms related to the condition. For each of these terms, where the intervention and/or related terms was identified as a therapy on the Comparative Effectiveness Chart, the accompanying monograph references were searched for relevant reviews.			
14. Recurrent infection/s	Epistemonikos			
(including urinary tract infections, cystitis, respiratory tract infection, otitis media in children, etc.) and zinc Conducted 23/04/2023	(title:(zinc OR zn) OR abstract:(zinc OR zn)) AND (title:((title:(infect* OR (recurr* AND infect*) OR (urin* AND infect*) OR UTI OR cystitis OR (neurogenic AND bladder) OR (vesico-uretal AND reflux) OR (vesicouretal AND reflux) OR anti-infect* antimicrobial* OR anti-microbial* OR antibiotic* OR anti-bacterial* OR antibacterial* OR (antibiotic* AND prophyla*) OR (respiratory AND infect*) OR TI* OR URTI* OR LRTI* OR (respiratory AND tract) OR (common AND cold) OR (sore AND throat) OR pharyngitis OR rhinosinusitis OR nasopharyngitis OR tonsillitis OR laryngitis OR sinusitis OR epiglottitis			
	OR laryngotracheitis OR phuemon* OR bronchiectasis OR bronchitis OR bronchiolitis OR "otitis AND media" OR (Clostridium AND difficile) OR "C. difficile" OR "c.difficile") OR abstract:(infect* OR (recurr* AND infect*) OR (urin* AND infect*) OR UTI OR cystitis OR (neurogenic AND bladder) OR (vesico-uretal AND reflux) OR (vesicouretal AND reflux)			

OR anti-infect\* antimicrobial\* OR anti-microbial\* OR antibiotic\* OR anti-bacterial\* OR antibacterial\* OR (antibiotic\* AND prophyla\*) OR (respiratory AND infect\*) OR RTI\* OR URTI\* OR LRTI\* OR (respiratory AND tract) OR (common AND cold) OR (sore AND throat) OR pharyngitis OR rhinosinusitis OR nasopharyngitis OR tonsillitis OR laryngitis OR sinusitis OR epiglottitis OR laryngotracheitis OR pnuemon\* OR bronchiectasis OR bronchitis OR bronchiolitis OR "otitis AND media" OR (Clostridium AND difficile) OR "C. difficile" OR "c.difficile"))) OR abstract:((title:(infect\* OR (recurr\* AND infect\*) OR (urin\* AND infect\*) OR UTI OR cystitis OR (neurogenic AND bladder) OR (vesico-uretal AND reflux) OR (vesicouretal AND reflux) OR anti-infect\* antimicrobial\* OR anti-microbial\* OR antibiotic\* OR anti-bacterial\* OR antibacterial\* OR (antibiotic\* AND prophyla\*) OR (respiratory AND infect\*) OR RTI\* OR URTI\* OR LRTI\* OR (respiratory AND tract) OR (common AND cold) OR (sore AND throat) OR pharyngitis OR rhinosinusitis OR nasopharyngitis OR tonsillitis OR laryngitis OR sinusitis OR epiglottitis OR laryngotracheitis OR pnuemon\* OR bronchiectasis OR bronchitis OR bronchiolitis OR "otitis AND media" OR (Clostridium AND difficile) OR "C. difficile" OR "c.difficile") OR abstract:(infect\* OR (recurr\* AND infect\*) OR (urin\* AND infect\*) OR UTI OR cystitis OR (neurogenic AND bladder) OR (vesico-uretal AND reflux) OR (vesicouretal AND reflux) OR anti-infect\* antimicrobial\* OR anti-microbial\* OR antibiotic\* OR anti-bacterial\* OR antibacterial\* OR (antibiotic\* AND prophyla\*) OR (respiratory AND infect\*) OR RTI\* OR URTI\* OR LRTI\* OR (respiratory AND tract) OR (common AND cold) OR (sore AND throat) OR pharyngitis OR rhinosinusitis OR nasopharyngitis OR tonsillitis OR laryngitis OR sinusitis OR epiglottitis OR laryngotracheitis OR pnuemon\* OR bronchiectasis OR bronchitis OR bronchiolitis OR "otitis AND media" OR (Clostridium AND difficile) OR "C. difficile" OR "c.difficile"))))

#### AMED

(zinc or zn) AND (infect\* OR (recurr\* AND infect\*) OR (urin\* AND infect\*) OR UTI OR cystitis OR (neurogenic AND bladder) OR (vesico-uretal AND reflux) OR (vesicouretal AND reflux) OR anti-infect\* antimicrobial\* OR anti-microbial\* OR antibiotic\* OR antibacterial\* OR antibacterial\* OR (antibiotic\* AND prophyla\*) OR (respiratory AND infect\*) OR RTI\* OR URTI\* OR LRTI\* OR (respiratory AND tract) OR (common AND cold) OR (sore AND throat) OR pharyngitis OR rhinosinusitis OR nasopharyngitis OR tonsillitis OR laryngitis OR sinusitis OR epiglottitis OR laryngotracheitis OR pnuemon\* OR bronchiectasis OR bronchitis OR bronchiolitis OR "otitis AND media" OR (Clostridium AND difficile) OR "C. difficile" OR "c.difficile") AND ((systematic and review) or (living and review) or (rapid and review) or meta\*analysis or meta\*review or overview).mp

	Ovid Empare <1995 to 2023 Week 175
	<ol> <li>Infect*.ti,ab, kw. or (recur* adj3 infect*).mp. or (urin* adj3 infect*).mp. or exp vesicoureteral reflux/ or exp recurrent infection/ or exp neurogenic bladder/ or exp urinary tract infection/ or (urin* and infect*).mp. or cystitis/ or cystitis.mp. or (vesico- uretal and reflux).mp. or (vesicouretal and reflux).mp. or exp antiinfective agent/ or Antibiotics/ or Antibiotic prophylaxis/ or antiinfective agent/ or antimicrobial.mp. or antimicrobial activity/ or antibacterial activity/ or anti-microbial*.mp. or antimicrobial therapy/ or antimicrobial activity/ or antimicrobial dressing/ or antimicrobial*.mp. or antibiotic associated diarrhea/ or antibiotic agent/ or antibiotic*.mp. or antibiotic therapy/ or anti-bacterial*.mp. or antibacterial*.mp. or (antibioti* and prophyla*).mp. or (respiratory and infect*).mp. or respiratory tract infection/ or common cold.mp. or common cold/ or sore throat.mp. or sore throat/ or streptococcal pharyngitis/ or pharyngitis.mp. or pharyngitis/ or viral pharyngitis/ or chronic thinosinusitis/ or rhinosinusitis.mp. or acute rhinosinusitis/ or rhinosinusitis/ or nasopharyngitis.mp. or rhinopharyngitis/ or platine tonsillitis/ or tonsillitis.mp. or chronic tonsillitis/ or por poneumonia/ or bronchiectasis.mp. or laryngotracheobronchitis/ or pneumonia.mp. or pronchiolitis.mp. or laryngotracheitis.mp. or clostridioides difficile/ or Clostridium difficile infection/ or "Clostridium difficile.mp. or clostridioides difficile/ or Clostridium difficile infection/ or "Clostridium AND difficile".mp. or pesudomembranous colisi/ or "C. difficile".mp. or anti-microbial.mp.</li> <li>exp zinc/ or zinc.mp.</li> <li>systematic review/ or systematic*.ti. or (systematic adj (review\$1 or overview\$1)).tw. or (living and review).ti. or meta analysis/ or meta analy\$.ti. or metaanaly\$.ti. or (overview adj (review or systematic*).mp. or review of review*.mp. or (overview and (review* or systematic)).mp. or (rapid and review).ti. or ((meta adj analy\$) or metaanaly\$).tw.</li> <li>1 and</li></ol>
	PROSPERO ((MeSH DESCRIPTOR Reinfection EXPLODE ALL TREES OR (recurr* AND infection) OR (urinary AND infection) OR UTI or cystitis OR (neurogenic AND bladder) OR (vesico- uretal AND reflux) OR (vesicouretal AND reflux) OR anti-infect* OR antimicrobial* OR anti-microbial* OR antibiotic* OR anti-bacterial* OR antibacterial* OR (antibiotic* AND prophyla*) OR (respiratory AND infect*) OR RTI* OR URTI* OR LRTI* OR (respiratory AND tract) OR (common AND cold) OR (sore AND throat) OR pharyngitis OR rhinosinusitis OR nasopharyngitis OR tonsillitis OR laryngitis OR sinusitis OR periglottitis OR laryngotracheitis OR pnuemon* OR bronchiectasis OR bronchitis OR bronchiolitis OR (otitis AND media) OR (Clostridium AND difficile) OR (c. difficile)) AND ((MeSH DESCRIPTOR Zinc EXPLODE ALL TREES OR (zinc or zn))
	NatMed Pro database 1. The Food, Herbs and Supplements database was searched recursively for terms related to the intervention. Where such terms were identified, the accompanying monograph references were then searched for relevant reviews.
	2. Similarly, the Comparative Effectiveness database was searched recursively for all terms related to the condition. For each of these terms, where the intervention and/or related terms was identified as a therapy on the Comparative Effectiveness Chart, the accompanying monograph references were searched for relevant reviews.
15. Type 2 diabetes and antioxidants (specifically CoQ10 & alpha -Lipoic acid) Conducted 13/05/2023	Epistemonikos (title:(diabet* OR DM OR metabolic OR (blood AND glucose) OR hyperglycaemia " OR (blood AND sugar) T2DM OR glycosylat* OR HB1AC OR NIDDM OR IDDM OR MODY OR DM2 OR glucose OR hyperglyceami* OR hyperglycem* OR (insulin AND resistance) OR insulin OR anti-hyperglyceami* OR antihyperglyceami* OR anti-hyperglyceami* OR anti- hyperglycemi* OR antihyperglyceami* OR non-insulin OR sugar) OR abstract:(diabet* OR DM OR metabolic OR (blood AND glucose) OR hyperglycaemia " OR (blood AND sugar) T2DM OR glycosylat* OR HB1AC OR NIDDM OR IDDM OR MODY OR DM2 OR glucose OR hyperglyceami* OR hyperglycem* OR (insulin AND resistance) OR insulin OR anti-hyperglyceami* OR nyperglyceami* OR anti-

	hyperglycemi* OR antihyperglyceami* OR non-insulin OR sugar)) AND (title:(antioxidant* OR *Q10 OR coenzyme* OR co-enzyme* OR ALA OR thioctic OR *linolenic OR lipoid) OR abstract:(antioxidant* OR *Q10 OR coenzyme* OR co-enzyme* OR ALA OR thioctic OR *linolenic OR lipoid))
-	AMED
	(Diabetes Mellitus, Type 2/ or Metabolic syndrome/ or T2DM or dm2 or diabet* or MODY or NIDDM or T2DM or IDDM or "DM 1" or "DM 2" or metabolic or (blood and glucose) or hyperglycaemia or (blood and sugar) or glycosylat* or HB1AC or glucose or hyperglyceami* or hyperglycem* or (insulin and resistance) or insulin or anti- hyperglyceami* or antihyperglyceami* or anti-hyperglyceami* or anti-hyperglyceami* or antihyperglyceami* or non-insulin or sugar) AND (antioxidant* or *Q10/ or coenzyme* or co-enzyme* or ALA or thioctic or *linolenic/ or lipoid) AND ((systematic and review) or (living and review) or (rapid and review) or meta*analysis or meta*review or overview)
-	Ovid Emcare <1995 to 2023 Week 17>
	<ol> <li>exp non insulin dependent diabetes mellitus/</li> <li>type 2 diabetes.ab,hw,kf,kw,ot,ti.</li> <li>((typ* 2 or typ* II or type 2) adj3 diabet*).ti,ab.</li> <li>(((typ* 2 or typ* II or type 2) adj3 diabet*) or (T2DM or dm2)).mp.</li> <li>(T2DM or dm2).mp.</li> </ol>
	6. diabet*.mp. 7. (MODX or NIDDM or T2DM or IDDM or DM 1 or DM 2) mp.
	<ul> <li>9. (blood adj glucose).mp.</li> <li>10. (blood adj sugar).mp.</li> </ul>
	11. hyperglycemia/
	<ul> <li>12. (nypergivcem^ or nypergicaem^).mp.</li> <li>13. glycosylated hemoglobin/ or glycosylat*.mp. or glucose blood level/</li> <li>14. insulin resistance/</li> </ul>
	15. (Insulin adj resistance).mp. 16. antidiabetic agent/ or antidiabetic activity/
	17. anti hyperglycaem*.mp.
	18. anti-hyperglyc*.mp. 19. (non-insulin and diabetes) mn
	20. (noninsulin and diabetes).mp.
	21. antioxidant activity/ or antioxidant/
	22. antioxidant*.mp. 23. ubidecarenone/
	24. coQ10*.mp.
	25. (coenzyme Q10 or co-enzyme Q10).mp.
	26. Thioctic acid.mp. or thioctic acid/
	28. ((ALA or alpha-lipoid acid or lipoid acid or linolenic) adj acid).mp.
	29. (ALA or alpha-lipoid acid or lipoid acid).mp.
	30. (linolenic adj acid).mp. 31. systematic* ti
	32. (systematic adj (review\$1 or overview\$1)).tw.
	33. (living and review).ti.
	34. exp meta analysis/ 35. systematic review mp. or exp "systematic review"/
	36. (overview adj (review or systematic)).mp.
	37. meta analy\$.ti.
	38. metaanaly\$.ti. 39. review of review* mn
	40. (overview and (review* or systematic)).mp.
	41. (rapid and review).ti.
	42. ((meta adj analy\$) or metaanalys\$).tw. 43. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or
	18 or 19 or 20
	44. 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
	45. 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 46, 43 and 44 and 45

PROSPERO
((MeSH DESCRIPTOR Diabetes Mellitus EXPLODE ALL TREES) OR (MeSH DESCRIPTOR Insulin Resistance EXPLODE ALL TREES) OR (MeSH DESCRIPTOR Hypoglycemic Agents EXPLODE ALL TREES) OR (MeSH DESCRIPTOR Hypoglycemia EXPLODE ALL TREES) OR (MeSH DESCRIPTOR Glycated Hemoglobin EXPLODE ALL TREES) OR (MeSH DESCRIPTOR Prediabetic State EXPLODE ALL TREES) OR (MeSH DESCRIPTOR Hyperglycemia EXPLODE ALL TREES) OR (MeSH DESCRIPTOR Glucose Tolerance Test EXPLODE ALL TREES) OR (MeSH DESCRIPTOR Glycemic Index EXPLODE ALL TREES) OR (MeSH DESCRIPTOR Blood Glucose Self-Monitoring EXPLODE ALL TREES) OR (MeSH DESCRIPTOR Glycemic Control EXPLODE ALL TREES) OR (MeSH DESCRIPTOR Diabetes, Gestational EXPLODE ALL TREES) OR diabet* OR type 2 diabetes mellitus OR type II diabetes mellitus OR (typ* 2 or typ* II or type 2) ADJ3 diabet*) OR MODY OR NIDDM OR T2DM OR IDDM OR (DM ADJ 1) OR (DM ADJ 2) OR (metabolic ADJ syndrome) OR (blood ADJ glucose) OR (blood ADJ sugar) OR hyperglycem* OR hyperglycem* OR hyperglyceam* OR (glycosylated ADJ hemoglobin) OR (glycosylated ADJ haemoglobin) OR (glycated ADJ hemoglobin) OR (glycated ADJ haemoglobin) OR (insulin ADJ resistance) OR (glucose ADJ intolerance) OR anti-diabet* OR anti-diabet* OR antihyperglyceam* OR antihyperglycem* OR anti-hyperglycem* OR (noninsulin ADJ diabetes) OR (non-insulin ADJ diabetes) AND ((MeSH DESCRIPTOR Antioxidants EXPLODE ALL TREES) OR (MeSH DESCRIPTOR Ubiquinone EXPLODE ALL TREES) OR (MeSH DESCRIPTOR alpha-Linolenic Acid) OR (MeSH DESCRIPTOR Thiotic Acid) OR (MeSH DESCRIPTOR alpha-Linolenic CR linolenic OR thiotic OR ubidecarenone* OR ubiquinone* OR alpha-linolenic OR linolenic OR thiotic OR
NatMed Pro database
1. The Food, Herbs and Supplements database was searched recursively for terms related to the intervention. Where such terms were identified, the accompanying monograph references were then searched for relevant reviews.
2. Similarly, the Comparative Effectiveness database was searched recursively for all terms related to the condition. For each of these terms, where the intervention and/or related terms was identified as a therapy on the Comparative Effectiveness Chart, the accompanying monograph references were searched for relevant reviews.

## A3 Criteria for considering reviews for this overview

Assessment of reviews to be included in the overview was done in two stages. Firstly, criteria for considering eligible reviews (used to assess articles at title/abstract and full text level), then additional criteria for choosing the preferred review to report evidence for each PICO. Additional criteria and the process for choosing preferred reviews is detailed in Appendix A4.5.

## A3.1 Types of reviews

Systematic reviews of randomised or quasi-randomised trials (RCTs), with or without meta-analysis, were eligible for inclusion in the overview. Reviews were only to be included if they met a set of minimum quality criteria, which were applied at both title/abstract and full-text assessment stages of screening. If it was unclear at title/abstract if a systematic review met or did not meet one of the below criteria, they were sent for full-text assessment.

The set of minimum quality criteria were informed by existing literature on overviews (4) and PRIOR reporting guidelines (3). The minimum quality criteria for inclusion in this overview were:

#### 1. Met the definition of a systematic review

Systematic reviews that did not (a) report sufficient PICO information and inclusion criteria, or (b) conduct a comprehensive search of the literature (i.e. searching more than one database) were not included. These reviews do not meet the minimum criteria to be considered 'systematic' and may not accurately summarise the body of evidence.

2. Primary studies were RCTs or quasi-RCTs

Systematic reviews including only non-randomised studies of the effects of interventions, or other study designs, were not included. If the method of randomisation of a study included within a systematic review was not specifically stated, or not considered strictly random, then the study was considered quasi-randomised. Where a systematic review includes quasi-RCTs, these were treated as RCTs (rather than NRSIs) for the purpose of risk of bias assessment and synthesis.

Eligible reviews that include a single RCT were included.

- 3. Risk of bias of the included primary studies was reported in the systematic review The systematic review needed to assess and report risk of bias or quality assessment of the primary studies.
- 4. Reported sufficient primary study characteristics for interpretation of results At minimum, all PICO elements, and a risk of bias assessment must have been reported. If other information was missing, this was dealt with via methods described in Appendix B1.1.

Deviations from the intended minimal quality criteria described in the overview protocol, but not used, are presented in Appendix G.

The intended protocol for inclusion of supplemental primary studies was not followed due to the volume of primary studies that would need to be screened, amounting to a systematic review for each population-supplement pair (see Appendix G – changes from protocol).

Where a systematic review was not identified for a priority population-supplement pair, this was noted.

#### **Publication type**

Overviews of systematic reviews were not eligible for inclusion, however, overviews identified in literature searches or submitted through the Department's public call for evidence were checked to identify any cited systematic reviews that may be eligible. As a publication type, expert opinion articles, editorials, letters, or emails were excluded.

#### **Publication date**

There were no limitations on publication date, however, systematic reviews published after the overview literature search date were not included. Systematic reviews published (or submitted to the Department) after the literature search date were to be listed in the "Reviews awaiting classification" table (Appendix C3). However, none met this criterion.

#### Language

Database searches, as well as the Department's call for evidence, did not exclude systematic reviews based on language of publication. Databases in languages other than English were not searched, however, systematic reviews in languages other than English were identified via the English-language databases. Pragmatically, potentially eligible systematic reviews did not undergo full-text translation or data extraction but, as per protocol, were documented via the process outlined in the "Reviews published in languages other than English" section (Appendix A4.3).

## A3.2 Types of participants

The overview's focus was the use of nutritional supplementation to treat certain populations/conditions regularly seen by naturopaths in Australia. This includes both (a) treatment for populations with a confirmed diagnosis of a condition, and (b) disease prevention in at-risk healthy populations (broadly defined as those who are at increased risk of becoming ill with any of the specified conditions). The definition of "at-risk" was clarified by NTWC as noted in Appendix G2 (clarification from protocol).

Reviews that examined the treatment of populations of interest with a supplement where the patient was known to have a deficiency of that supplement were excluded, as per protocol. This is because

patients with a known deficiency would need to have this diagnosed via a blood test and would seek diagnosis and treatment from a doctor. Therefore, treatment of patients with a known deficiency was deemed as not part of normal naturopathy practice in Australia.

Healthy participants (not at-risk) seeking health improvement, such as general wellbeing, fitness, aesthetic improvements, resilience and cognitive or emotional intelligence were not eligible for inclusion, as per protocol.

Reviews were often broader than the PICOs of interest for the overview (e.g., for "mental health conditions" rather than "depression"). Where systematic reviews included both eligible and ineligible PICOs, reviews were included where results could be independently determined for relevant PICOs.

## **Target conditions**

The NTWC, with advice from NTREAP, developed a ranked list of priority populations/conditions, and nutritional supplements commonly used by naturopaths to treat and/or manage these conditions. The highest priority population-supplement pairs were identified based on their relevance and importance to conditions and interventions commonly seen and reported by naturopaths and derived using TEQSA approved naturopathic curriculums, in consultation with educational providers, and data derived from an Australian PRACI survey (see Table A1 below and in the main report) (5, 6).

## A3.3 Types of interventions

Interventions were chosen alongside populations – identified as priority population-supplement pairs and ranked by NTWC (with Tier 1 being highest priority, and Tier 3 being lowest priority), with advice from NTREAP (presented in December 2021). These were developed prior to the overview protocol based on initial scoping. Following searches during the evidence evaluation, it was determined to only consider the Tier 1 combinations (15 highest priority) due to the volume of reviews. These are listed in Table A1.

Eligible interventions were those that contained either the supplement of interest alone or with other ingredients, given nutritional supplements often have co-supplementation (e.g. multivitamins). Other co-interventions likely to be prescribed in naturopathic practice (such as diet, education programs, lifestyle modification) were also considered. Nutritional supplements included in this overview contained single ingredients (e.g. a vitamin, mineral, amino acid) or a combination of ingredients. There was no limit on the type of preparation (i.e. capsule, tablet, liquid, etc.), however the nutritional supplement must be taken orally.

This overview excluded any nutritional supplement products which contained an ingredient not permitted by the Australian Register of Therapeutic Goods (ARTG) as a complementary medicine (5). Therefore, pharmaceutical ingredients and any product required to be sterile (for injection) were excluded, as these do not reflect naturopathic practice in Australia. Preparations that are administered via injection (i.e. intravenous, intramuscular, subcutaneous) were also excluded. Population-based interventions, including food fortification, were also excluded as these types of interventions are not part of naturopathy practice, but public health policy.

In contrast to the review of whole-system naturopathy, this overview did not require the treatment to be delivered by a naturopath.

	Priority population (listed in order of priority)	Priority intervention (Tier 1)	Priority intervention (Tier 2) – not considered	Priority intervention (Tier 3) – not considered
1	Anxiety (including post- natal)	Magnesium	Vitamin B and mineral complex (B6, B12, folate – individually and in combination)	N-acetylcysteine (NAC)

#### Table A1. List of target population-supplement pairs by priority tier.

2	Stress (perceived, occupational)	Magnesium	Vitamin B and mineral complex (B6, B12, folate – individually and in combination)	N-acetylcysteine (NAC)
3	Irritable bowel syndrome	Probiotics (see TGA list for specific strains)	Glutamine	Digestive enzymes (including betaine hydrochloride, papain, bromelain)
4	Insomnia/Sleeping disorders	Magnesium	5-HTP (5- hydroxytryptophan)	Palmitoylethanolamide (PEA)
5	Depression (including post-natal)	Omega-3 fatty acids	Vitamin B and mineral complex (B6, B12, folate – individually and in combination)	N-acetylcysteine (NAC)
6	Dysmenorrhea	Cruciferous Indoles (indole-3- carbinol, di- indolylmethane)	Magnesium	Vitamin B and mineral complex (B6, B12, folate – individually and in combination)
7	Premenstrual syndrome (PMS)	Cruciferous Indoles (indole-3- carbinol, di- indolylmethane)	Magnesium	Vitamin B and mineral complex (B6, B12, folate – individually and in combination)
8	Atopic disorders (including eczema, dermatitis, allergic rhinitis, allergies (e.g. hay fever))	Zinc	Prebiotics (including beta-glucan, guar gum and others listed on the TGA list)	Probiotics (see TGA list for specific strains)
9	Fatigue (general) (including myalgic encephalomyelitis (ME) and Chronic Fatigue Syndrome (CFS))	Antioxidants (specifically: CoQ10 and alpha-lipoic acid)	Vitamin B and mineral complex (B6, B12, folate – individually and in combination)	Magnesium
10	Headache and migraine	Magnesium	Vitamin B and mineral complex (B6, B12, folate – individually and in combination)	N-acetylcysteine (NAC)
11	Arthritis/Osteoarthritis	Magnesium	Omega-3 fatty acids	Vitamin D
12	Hypertension	Omega-3 fatty acids	Antioxidants (specifically: CoQ10 and alpha-lipoic acid)	Magnesium
13	Fibromyalgia	Magnesium	Omega-3 fatty acids	Vitamin D
14	Recurrent infection/s (including urinary tract infections, cystitis, respiratory tract infection, otitis media in children, etc.)	Zinc	Prebiotics (including beta-glucan, guar gum and others listed on the TGA list)	Probiotics (see TGA list for specific strains)
15	Diabetes (Type II) (including metabolic syndrome)	Antioxidants (specifically: CoQ10 and alpha-lipoic acid)	Chromium (specifically: chromium picolinate, chromium enriched brewers' yeast)	Inositol

Note: Glutathione, Vitamin B12 (including cyanocobalamin and methylcobalamin) and Vitamin C were also considered but were not identified as a priority for any of the target populations/conditions.

## A3.4 Types of comparators

Comparisons as part of the overview were presented in accordance with how they were reported in each systematic review and no new analysis was undertaken.

Comparators included were placebo, inactive control or usual care. Active comparators were not included as the overview was trying to determine the effect of chosen supplements with or without cointerventions, and not to compare against other interventions. As the protocol was somewhat unclear about whether active comparators were to be included, this has been detailed in Appendix G. Nutritional supplement co-interventions delivered with the supplement of interest were included. This is because in naturopathic practice, nutritional supplements are commonly delivered in tandem with other supplements (e.g., multivitamins).

Non-nutritional supplement co-interventions were only included if all arms of a study received the same co-interventions. However, if nutritional supplementation was delivered with another intervention so that the effects of nutritional supplementation alone could not be determined, these were excluded. This was evaluated at a systematic review, not primary study, level – so if any results for nutritional supplementation could be individually determined, the systematic review was included.

Examples of comparisons which were eligible:

- Eligible supplement VS placebo/sham/inactive control
- Eligible supplement + naturopathy co-intervention VS placebo/sham/inactive control
- Eligible supplement + naturopathy co-intervention VS naturopathy co-intervention
- Eligible supplement + non-naturopathy co-intervention VS non-naturopathy co-intervention

Examples of comparisons which were excluded:

- Eligible supplement VS another eligible supplement
- Eligible supplement VS other intervention (where considered active)
- Eligible supplement + non-naturopathy co-intervention VS placebo/sham/inactive control
- Eligible supplement VS the same supplement administered in a different way (i.e. different dose, route of administration, prescriber, formulation)

## A3.5 Types of outcomes

Prioritised outcomes aligned with reasons why patients use the intervention and/or practitioners prescribe the intervention. This includes recovery, rehabilitation, changes in disease outcomes and symptoms (including proxy surrogate clinical outcomes e.g. HbA1C, BMI, lung function tests), health-related psychological/behavioural outcomes, health-related quality of life domains, medication use or compliance with conventional medicine treatment, and disease specific prevention outcomes (e.g. smoking cessation). Patient reported experience outcomes (e.g. satisfaction), safety, quality and economic outcomes were out of scope for this overview.

Given the broad range of populations, conditions, and interventions included in the overview, outcomes were not pre-specified. As part of the overview process, an outcome prioritisation exercise (detailed below) was conducted.

There were no limits on timepoints for measurement, and short and long-term outcomes were included. The plan in the protocol was to group results according to measurement timepoints, however this was not possible due to reporting issues in the systematic reviews (see Appendix G).

#### **Outcome prioritisation exercise procedure**

Once all eligible systematic reviews were identified in full-text screening, outcomes were selected using a blinded approach with NTWC and in consultation with NTREAP (Figure A1). An outcome prioritisation spreadsheet was developed that included:

- A tab for each pre-specified priority population-supplement pair.
- For each priority population-supplement pair, a list of outcome domains and associated outcome measures reported in systematic reviews selected for full-text screening.
- In addition to outcome domains from eligible systematic reviews, outcome domains from relevant core outcome sets and relevant Cochrane reviews were included to prevent knowledge of study or review results, or other characteristics such as study design, from influencing decision-making about priority outcomes. This also helped to identify outcomes that are important but not addressed in included systematic reviews.

Critical and important outcome domains were identified by NTREAP and NTWC using the spreadsheet. This resulted in a list of up to 7 outcome domains per priority population-supplement pair that were included in the overview.

All pre-specified outcomes for the overview which were reported in an eligible systematic review (as determined from the systematic review protocol or registry entry, or, if unavailable, the Methods and Results section of the review) were recorded and presented in the Characteristics of included reviews tables (Appendix D). However, only results for preferred reviews (see Appendix B1.1) were reported in GRADE 'Summary of Findings' tables with corresponding evidence statements.

It was intended that results for all outcomes from included systematic reviews would be recorded and extracted. However, this was only completed for prioritised outcomes due to the large volume of information in the overview (many reviews with many outcomes; see Appendix G).



#### Figure A1. Summary of Process for Outcome Prioritisation (provided by NTWC)

## A4 Review selection (inclusion decision)

In the first instance, the overview aimed to assess the full breadth of eligible reviews.

## A4.1 Inclusion decisions – title/abstract screening

Records retrieved from the database and citation searches, together with any citations provided by the Department, were imported into Covidence or EndNote and duplicates were removed using automated tools within the software. Records were independently screened against the inclusion criteria by two reviewers, with any discrepancies resolved by discussion. Citations in languages other than English were tagged and managed as described in "Reviews published in languages other than English" (Appendix A4.3). Endnote 20 was used to cross-check for retractions with the Retraction Watch database. Errata and corrigenda of included reviews were also checked through the publication sites, though none were found for reviews contributing to results (preferred reviews).

## A4.2 Inclusion decisions – full-text screening

One reviewer retrieved full-text copies of potentially eligible systematic reviews, and two reviewers independently screened the reviews for inclusion. Following outcome prioritisation, additional full-text screening was undertaken, and reviews were excluded if they did not report any prioritised outcomes. Any disagreements were resolved by discussion, and/or with reference to a third reviewer. Ineligible reviews were marked with a reason for exclusion and listed in "Characteristics of excluded reviews" (Appendix C). Recorded exclusion reasons in Appendix C are the first reasons identified, noting that in some cases there may have been more pressing/relevant reason for exclusion.

We had intended to present information on the review selection process as a PRIOR flow diagram (3), however determined that a PRISMA diagram for each population-supplement pair was more informative (see Appendix G).

It was intended that if a review was the only review for a priority population/intervention relevant and did not contain the required PICO information for a decision to be made regarding eligibility, the information would be sought from the review's authors. However, this did not happen during the overview.

Eligible reviews that were not available in English were noted and managed as described below in "Reviews published in languages other than English" (Appendix A4.3).

## A4.3 Reviews published in languages other than English

Reviews published in languages other than English underwent title and abstract translation using Google translate (or an equivalent tool). Translated titles and abstracts were screened during the title/abstract screening stage and reported in the PRISMA flow diagrams.

For reviews not published in English but which were eligible for full-text review and were likely to meet the inclusion criteria, or if there was any uncertainty, the full-text report was not translated to determine the reviews' compliance with eligibility criteria. These reviews were recorded in a "Reviews awaiting classification" table (Appendix C3).

Appropriate qualifying statements were made throughout the overview to acknowledge that only evidence published in English was reviewed and included. In relevant sections of the report, potential limitations due to language bias that might influence the conclusions of the review are discussed.

## A4.4 Evidence provided through the Department's public call for evidence

Evidence provided through the Department's public call for evidence (or provided by any other key stakeholders) was assessed according to the inclusion criteria. Evidence not meeting the inclusion criteria was considered out of scope, and a rationale for exclusion was provided. Eligible reviews that have not been identified in database searches and other search processes were incorporated into the review. Details are provided in Appendix C2.

## A4.5 Selection of preferred reviews

The systematic review that provided the "best" evidence for each PICO was selected – termed "preferred" review (6). Where there were multiple reviews which reported on the same PICO, the most comprehensive and/or highest quality review based on Risk of Bias in Systematic Reviews (ROBIS) assessment was selected (6). If there were multiple systematic reviews of a given quality and comprehensiveness, we prioritised the most recent review for inclusion (based on date review was published, and, if relevant, date included primary studies were published). Risk of bias of included primary studies was not considered in the selection of preferred reviews.

Rather than implementing rigid decision rules for use of the criteria to select "preferred reviews", these were used as guiding principles for choosing the most relevant evidence (per advice from NTWC and NTREAP). Explanations for choosing the preferred review for each PICO are presented in the relevant results sections.

Key criteria considered in selection of preferred reviews was:

Criteria	Assessed by:
Comprehensive	<ul> <li>Meta-analysis preferred to systematic review.</li> <li>Highest number of included studies and/or participants in meta-analysis or</li> </ul>
	systematic review.
Highest quality	<ul> <li>Lowest risk of bias of review assessed using ROBIS.</li> </ul>
Recency	Most recent review publish date.
	<ul> <li>Most recent publish dates of included primary studies</li> </ul>
# Appendix B Methods of data collection, appraisal and reporting

# **B1** Data collection

# B1.1 Data collection process

The data extraction form finalised after the outcome prioritisation exercise was piloted on 5 systematic reviews across multiple population-supplement pairs to test practicality and reliability. During piloting, two reviewers independently extracted the data from the systematic reviews into the extraction forms to ensure consistent understanding and suitability of the forms. Completed data extraction forms were compared by a third reviewer, with any discrepancies in extractions reconciled by discussion.

Two reviewers independently extracted data from reports of included systematic reviews using data extraction forms. All information was extracted and reported in Appendix D and E as per the review, with no or minimal editing.

## Addressing overlap

All systematic reviews that met inclusion criteria, regardless of overlap, were included and recorded in "Characteristics of included reviews" tables (Appendix D). To assess which reviews addressed the same or similar questions the aim of the study and PICO were examined. The protocol listed that following inclusion decision, an assessment of the overlap across systematic reviews would be completed. However, it was determined that this was not necessary given that evidence from only the most relevant systematic review for each PICO was included (see Appendix G).

## Addressing discrepant or missing information

As only one systematic review for each PICO was presented (i.e. the most comprehensive, recent and/or highest quality), addressing discrepant data across included systematic reviews was not required.

Where there were incompletely reported results in systematic reviews (either meta-analysis or primary studies), review authors were not contacted as intended in the protocol due to the volume of reviews. Where results were not reported adequately (e.g. no effect estimates or confidence intervals, no information about inconsistency [such as a forest plot displaying effect estimates for individual studies] or no heterogeneity statistics), this was considered in GRADE assessments. Unclear or missing information may impact reported results and GRADE assessments, which is a limitation.

Retrievable results (e.g. summary statistics, effect estimates and confidence intervals) were extracted and reported from reviews (including risk of bias assessments of primary studies and sensitivity analyses). No new analysis was undertaken as part of the overview, including any independent analyses to explain inconsistency or publication bias.

Across different systematic reviews, risk of bias assessments for primary studies were performed with different tools. These were extracted as reported in the reviews using the tool or measure specified, with no independent assessments of risk of bias by overview authors.

## Inclusion of supplemental primary studies

The protocol noted that supplementary studies would be included if there was no systematic review for a population-supplement pair or if the available systematic review did not meet the minimum criteria (see Appendix A3.1). However, to appropriately cover primary studies for a populationsupplement pair would require conducting a full systematic review. Given the scope of the overview, this was not possible. This change from protocol is noted in Appendix G. Four population-supplement pairs were not covered by a relevant systematic review and therefore none of the prioritised outcomes were reported on in the overview:

- Stress (perceived, occupational) and magnesium.
- Dysmenorrhea and cruciferous indoles.
- Premenstrual syndrome (PMS) and cruciferous indoles.
- Arthritis/osteoarthritis and magnesium.

## **Requests for data**

Authors of potentially eligible systematic reviews where a full-text article could not be located were intended to be contacted through an open-ended request for data or further information. For conference abstracts, no non-published potentially relevant abstracts were found, therefore this was not completed. This change from protocol is noted in Appendix G.

# B1.2 Data items for collection

Results were presented as a descriptive summary of the included systematic reviews, rather than resynthesis of information, due to the breadth of the PICO and outcomes. Data was extracted and presented in Appendix D and E exactly as it was reported in the publications with limited formatting or wording changes.

Included reviews often also included outcomes not of interest to the overview. These outcomes were intended to be extracted as part of data collection per the protocol, but were not for practicality and given that they would not contribute to findings (see Appendix G).

The following broad characteristics of included systematic reviews were extracted:

- Author, year, review design (e.g. meta-analysis)
- Search information (number and names of databases searched, date of last search, restrictions)
- Number/type of included primary studies
- Systematic review eligibility criteria for participant characteristics
- Systematic review eligibility criteria for intervention description
- Comparator description
- Number of participants (total)
- Outcome measures
- Follow-up
- Risk of bias tool used to appraise included primary studies and their ratings
- Results (effect size, heterogeneity statistics, reported visual inspection of plots, results of any subgroup analyses or similar that might be needed to explain inconsistency)
- PICO characteristics of primary studies contributing data for each result
- Risk of bias of primary studies contributing data (only for "preferred reviews")
- Funding sources
- Ethics information

Study characteristics and results are presented in Appendix D and E.

If only a subset of the data within the included systematic reviews was relevant (i.e. if a systematic review reported multiple PICOs but only one is of interest for the overview), results for the relevant PICO only were extracted.

# B2 Data analysis and synthesis

# B2.1 Data synthesis

'Summary of Findings' tables were used to report and present data for up to 7 critical and important outcome domains prioritised for each priority population-supplement pair, guided by the GRADE framework. In reporting results, the PRIOR checklist was used as a guide (3).

Results from preferred reviews were reported without reanalysis. Quantitative results were presented where available, and results were summarised narratively for each PICO as part of each populationsupplement pair in the 'Summary of Findings' tables in the main report. Detailed results as extracted from all eligible reviews were reported in Appendix D and E. Data was extracted in the format and language as provided in each systematic review. Data was transformed minimally for presentation and summary in the overview.

The procedure for dealing with missing data is described in Appendix B1.1. If insufficient summary statistics were provided in selected systematic reviews, this was noted and considered in ROBIS assessments and GRADE evaluations. Implications for the potential for missing data were also considered when interpreting the evidence and limitations are discussed in Section 5.6. Where there was no quantitative synthesis or summary statistics/effect sizes, but results were still relevant to the outcome, these were recorded and presented narratively.

Thresholds for interpretation of effect estimates and confidence intervals were determined for each outcome based on a minimal clinically important difference (MCID). While it was originally reported in the protocol that statistical significance would also be considered, this was not done as Cochrane guidance strongly recommends against interpretation based on statistical significance and it is incompatible with GRADE. As MCIDs are different for different outcomes, the interpretation of effect estimates were based on what was included in the outcome prioritisation exercise. MCIDs were derived firstly from what was used in the review, and if not specified, then from published estimates in the literature. References and explanations are included in footnotes Summary of Findings tables.

## **B2.2** Investigations of heterogeneity

## **Clinical heterogeneity**

Clinical heterogeneity (termed non-statistical heterogeneity in the protocol) between systematic reviews (i.e. differences in PICO) was assessed by evaluating the inclusion criteria of each systematic review. This was completed to understand directness of the evidence to the PICO of interest, and hence was incorporated in GRADE assessments of the indirectness domain.

## Statistical heterogeneity

Statistical heterogeneity for each outcome was extracted where available and incorporated into interpretation of GRADE. Presence of subgroup analysis for each systematic review was assessed, and whether planned *a priori*. Reanalysis of subgroups was not undertaken per overview procedures.

## Sensitivity analysis

Given reanalysis of data was not undertaken, the robustness of results for each PICO was considered by inclusion and presentation of any relevant sensitivity analyses within the original review.

# **B3** Risk of bias of evidence in included reviews

## B3.1 Assessment of risk of bias of systematic reviews

The Risk of Bias in Systematic Reviews (ROBIS) tool was used to assess the risk of bias of included systematic reviews (6). This was done by reading and considering the entire article as published,

rather than referring only to extracted information. A ROBIS template form was used for assessments, with all signalling questions completed, and rationale and evidence to support judgements for items for which there are concerns. The three questions described in ROBIS were used to arrive at a final risk of bias judgement. ROBIS assessments (including responses to signalling questions) are provided in Appendix F. We did not provide narrative domain or overall summary judgements for systematic reviews as intended due to the volume of work.

An assessment of systematic review quality was completed by one reviewer, with another reviewer independently checking and confirming assessments made (7). Disagreements were resolved by discussion, with reference to a third reviewer if necessary. An overall risk of bias judgement for each systematic review is presented in the main report and Appendix F.

# B3.2 Assessment of risk of bias of primary studies included in systematic reviews

For all included reviews, the tool used to assess risk of bias of the included studies extracted and reported in Characteristics of Included Reviews (Appendix D).

For preferred reviews, a summary of the quality or risk of bias assessment for each outcome is presented in Appendix E. It was intended that all included reviews would have risk of bias information extracted and reported, however this was not completed for pragmatism with the size of the overview and given that the information would not contribute to evidence evaluation. Risk of bias of primary studies was, however, considered in ROBIS assessments by reading and considering the full paper for all included reviews.

We note that the ability to report risk of bias information for each outcome is limited by the information availability in the included reviews, as is the weight of studies at high risk of bias in the analysis and results of any sensitivity analyses.

It was intended that where risk of bias was not reported in primary studies, an independent assessment of the risk of bias would be conducted. However, this was not necessary given the minimum quality criteria specified risk of bias assessment as required for inclusion of a review (noted in Appendix G).

Any concerns about risk of bias in the primary studies are addressed in the GRADE assessment. As noted above, collecting data about the weight of studies at high risk of bias contribute to the analysis and/or results of sensitivity analysis can be important inputs to the GRADE assessments.

# B3.3 Risk of reporting bias

Risk of reporting bias for each outcome in each priority population-supplement pair was assessed as part of GRADE assessments.

## Systematic reviews

For each outcome in each priority population-supplement pair, the assessments for publication and reporting biases completed by systematic review authors were considered. If systematic review authors did not assess for publication or reporting biases, this was noted in the GRADE assessment in footnotes of 'Summary of Findings' tables. As well, it was considered whether systematic review authors reported on pre-specified outcomes (from protocols or registers) along with rationale for any changes, and whether these may impact selective reporting.

## **Primary studies**

Reporting bias may arise from missing results in a summary of synthesis. Due to the scope of this overview (i.e. the number of priority population-supplement pairs and outcomes, and therefore the number of primary studies), missing data from primary studies was not sought (either by reviewing corresponding primary studies or by contacting systematic review authors for missing information or clarification). However, potential missing information from primary studies was considered in the GRADE assessment and reported in 'Summary of Findings' tables.

## Supplemental primary studies

As noted above and in Appendix G, supplementary primary studies were not sought or assessed.

# B3.4 Addressing risk of bias

### At the systematic review level

Risk of bias of the systematic review was a key criterion in choosing contributing evidence (preferred review) for each PICO. Where there were concerns related to the risk of bias of a systematic review contributing data to the synthesis, this was noted and considered in synthesis of findings in the main report. If there were concerns, it was planned that data across systematic reviews would be cross-checked, however this was not required.

#### At the primary study level

Risk of bias at the primary study level was extracted from systematic reviews at a summary level for outcomes for preferred reviews. Independent risk of bias assessments for primary studies were not undertaken due to the volume of evidence. Risk of bias of the contributing evidence was considered in GRADE assessments.

## B3.5 Subgroup analyses

Relevant subgroup analyses conducted as part of the included systematic reviews were extracted and reported in Appendix E. These were considered in GRADE assessments.

No reanalysis was undertaken to explore potential sources of inconsistency. This was a deviation from the protocol and is noted in Appendix G.

# **B4** Certainty of the evidence

The GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach was used to assess the certainty of the body of evidence for each outcome (8). For consistency and to provide an independent interpretation of the information, GRADE assessments were completed for all outcomes included in the Summary of Findings tables as part of this overview regardless of whether they were completed as part of included systematic reviews.

GRADE assessments presented in the included systematic reviews were not extracted given reassessments were completed, though if GRADE was conducted this was noted in data extraction.

The GRADE framework is used to determine the certainty of the evidence based on consideration of five factors (9). An explanation is provided as footnotes in the 'Summary of Findings' table to support each GRADE assessment. Specifically, decisions and explanations reflect:

#### Risk of bias, considering:

 Risk of bias of contributing primary studies per assessment by review authors.
 Generally, "some" or "low" risk of bias concerns for most primary studies did not warrant downgrading, however this was assessed on a case-by-case basis.

**Inconsistency**, considering:

- $\circ$  The measures used to judge inconsistency (l<sup>2</sup>, Chl<sup>2</sup>, Tau).
- The overlap of confidence intervals, and similarity of point estimates across included primary studies. In reference to the MCID, whether the upper and lower CI bounds would have similar or different inferences of effect.
- Whether heterogeneity was explained by subgroup analyses by PICO, and reasons for potential heterogeneity.

Imprecision, considering:

• Whether the confidence interval crossed the thresholds for an important difference in relation to a minimal clinically important threshold (i.e. if CI is compatible with

appreciable benefit and little or no difference suggesting serious imprecision, appreciable benefit and appreciable harm suggesting very serious imprecision).

• Based on updated GRADE guidance, optimal information size (OIS) was considered if thresholds were not available, or the effect is large, the CI does not overlap with the threshold(s) of interest and the results may be considered by the overview authors as implausible (10).

Indirectness, considering:

• How closely the research questions of the primary studies address the overview PICO. Publication bias, considering (see Appendix B3.3):

- Whether there is evidence of publication and reporting bias.
- Whether systematic review authors reported on pre-specified outcomes (from protocols or registers) along with rationale for any changes, and whether these may impact selective reporting.

Given that some of the included and preferred reviews did not present effect sizes (i.e. did not use meta-analysis or used narrative synthesis), guidance for rating the certainty of evidence in the absence of a single estimate of effect was used (11).

Using the GRADE assessment approach, certainty is rated as:

High  $(\bigoplus \bigoplus \bigoplus)$ : the authors have a lot of confidence that the true effect is similar to the estimated effect.

Moderate  $(\bigoplus \bigoplus \bigoplus \bigcirc)$ : the true effect is probably close to the estimated effect.

Low  $(\bigoplus \bigoplus \bigcirc \bigcirc)$ : the true effect may be very different from the estimated effect.

Very low  $(\bigoplus \bigcirc \bigcirc \bigcirc)$ : the true effect is probably markedly different from the estimated effect.

Results will be downgraded based on whether they meet certain criteria, to reach a final assessment of the certainty of the body of evidence (high, moderate, low, or very low).

Information required for full GRADE assessment was only extracted from preferred reviews, and not all included reviews both for pragmatism and because the information would not have contributed to the evidence review for non-preferred reviews.

## B4.1 'Summary of Findings' tables and evidence statements

Findings were reported in Summary of Findings tables in the Evidence Evaluation Report. These included all reported results on clinical effectiveness, grouped by condition of interest and/or comparator. The Summary of Findings tables provide a synthesis of the body of evidence, key results, and a summary judgment about the certainty of the underlying evidence for each outcome. Absolute effects and relative effects were extracted if available; in GRADE assessments, absolute effects were preferred for interpretation of dichotomous outcomes.

As part of the Summary of Findings table, an evidence statement pertaining to each outcome is included, guided by GRADE information on writing informative statements (12). Evidence statements are guided by the following format: The use of [nutritional supplement] in [population] [probably, may, results] in [little to no effect, reduce, increase, promote etc.] on [outcome] compared with [placebo or no intervention]. A table of selected statements based on the size of effect and certainty in evidence used to guide evidence statements in the Evidence Evaluation Report are listed below.

Size of the effect estimate	Suggested statements *
HIGH Certainty of the evidence	
Large effect	X results in a large reduction/increase in outcome
Moderate effect	X reduces/increases outcome
Small important effect	X reduces/increases outcome slightly

Size of the effect estimate	Suggested statements *
Trivial, small unimportant effect or no effect	X results in little to no difference in outcome
MODERATE Certainty of the evidence	
Large effect	X probably results in a large reduction/increase in outcome
Moderate effect	X probably reduces/increases outcome
Small important effect	X probably results in a slight reduction/increase in outcome
Trivial, small unimportant effect or no effect	X probably results in little to no difference in outcome
LOW Certainty of the evidence	
Large effect	X may result in a large reduction/increase in outcome
Moderate effect	X may result in a reduction/increase in outcome
Small important effect	X may result in a slight reduction/increase in outcome
Trivial, small unimportant effect or no effect	X may result in little to no difference in outcome
VERY LOW Certainty of the evidence	·
Any effect	The evidence is very uncertain about the effect of X on outcome

Source: selected statements from Santesso et al. (2020) (12).

\* Replace X with intervention, replace 'reduce/increase' with direction of effect, replace 'outcome' with name of outcome, include 'when compared with Y' when needed)

# Appendix C Citation details of reviews assessed at full text but not included

Reports may have been excluded for more than one reason. The reported exclusion reason in tables is the first one identified by one review author during screening.

# C1 Citation details of reviews from search results excluded (not eligible)

Table C-1. Excluded reviews,	reason for exclusion -	- anxiety (includin	g post-natal), ma	agnesium (n=6).
,			<b>S I I I I</b>	

Title	Authors	Year	Journal	Volume	Issue	Pages	Exclusion reason
Nutritional and herbal supplements for anxiety and anxiety-related disorders: Systematic review	Lakhan, S. E.; Vieira, K. F.	2010	Nutrition journal	9	1	42	Does not meet minimum criteria for systematic review
Complementary medicine, exercise, meditation, diet, and lifestyle modification for anxiety disorders: A review of current evidence	Sarris, J.; Moylan, S.; Camfield, D. A.; Pase, M. P.; Mischoulon, D.; Berk, M.; Jacka, F. N.; Schweitzer, I.	2012	Evidence-based Complementary and Alternative Medicine	2012	-	809653	Does not meet minimum criteria for systematic review
The Role and the Effect of Magnesium in Mental Disorders: A Systematic Review	Botturi, A.; Ciappolino, V.; Delvecchio, G.; Boscutti, A.; Viscardi, B.; Brambilla, P.	2020	Nutrients	12	6	1661	Does not meet minimum criteria for systematic review
The effects of magnesium supplementation on subjective stress and anxiety: A systematic review	Boyle, N.; Lawton, C.; Dye, L.	2017	Nutrients	9	5	429	Does not meet minimum criteria for systematic review
The impact of essential fatty acid, B vitamins, vitamin C, magnesium and zinc supplementation on stress levels in women: a systematic review	McCabe, D.; Lisy, K.; Lockwood, C.; Colbeck, M.	2017	JBI database of systematic reviews and implementation reports	15	2	402-453	Wrong patient population
Protective role of antioxidant supplementation for depression and anxiety: A meta-analysis of randomized clinical trials	Wang, H.; Jin, M.; Xie, M.; Yang, Y.; Xue, F.; Li, W.; Zhang, M.; Li, Z.; Li, X.; Jia, N.; Liu, Y.; Cui, X.; Hu, G.; Dong, L.; Wang, G.; Yu, Q.	2022	Journal of Affective Disorders	323	-	264-279	Wrong outcomes

#### Table C-2. Excluded reviews, reason for exclusion – stress (perceived, occupational), magnesium (n=3).

Title	Authors	Year	Journal	Volume	Issue	Pages	Exclusion reason
The Effects of Magnesium Supplementation on Subjective Anxiety and Stress-A Systematic Review	Boyle, N. B.; Lawton, C.; Dye, L.	2017	Nutrients	9	5	429-450	Does not meet minimum criteria for systematic review
The impact of essential fatty acid, B vitamins, vitamin C, magnesium and zinc supplementation on stress levels in women: a systematic review	McCabe, D.; Lisy, K.; Lockwood, C.; Colbeck, M.	2017	JBI database of systematic reviews and implementation reports	15	2	402-453	Wrong patient population - did not meet the criteria for "at risk"
The efficacy and safety of nutritional supplements in the treatment of mental disorders: a systematic synthesis	Firth, J.	NR	NR	NR	NR	NR	Wrong patient population

and evaluation of evidence from meta-analyses of				
randomized trials				

## Table C-3. Excluded reviews, reason for exclusion – IBS/probiotics.

Title	Authors	Year	Journal	Volume	Issue	Pages	Exclusion reason
The utility of probiotics in the treatment of irritable bowel syndrome: a systematic review	Brenner, D. M.; Moeller, M. J.; Chey, W. D.; Schoenfeld, P. S.	2009	The American journal of gastroenterology	104	4	1033-49	Does not meet minimum criteria for systematic review
Review article: probiotics for the treatment of irritable bowel syndromefocus on lactic acid bacteria	Clarke, G.; Cryan, J. F.; Dinan, T. G.; Quigley, E. M.	2012	Alimentary pharmacology & therapeutics	35	4	403-13	Does not meet minimum criteria for systematic review
Bifidobacterium longum W11: Uniqueness and individual or combined clinical use in association with rifaximin	Di Pierro, F.; Pane, M.	2021	Clin. Nutr. ESPEN	42	-	15-21	Does not meet minimum criteria for systematic review
Effectiveness of probiotics in irritable bowel syndrome: Updated systematic review with meta-analysis	Didari, T.; Mozaffari, S.; Nikfar, S.; Abdollahi, M.	2015	World journal of gastroenterology	21	10	3072-84	Does not meet minimum criteria for systematic review
Do probiotic or synbiotic preparations alleviate symptoms associated with constipation or irritable bowel syndrome?	Eddins, C.; Gray, M.	2007	Journal of Wound, Ostomy & Continence Nursing	34	6	615-624	Does not meet minimum criteria for systematic review
Systematic review: probiotics in the management of lower gastrointestinal symptoms in clinical practice an evidence-based international guide	Hungin, A. P.; Mulligan, C.; Pot, B.; Whorwell, P.; Agréus, L.; Fracasso, P.; Lionis, C.; Mendive, J.; Philippart de Foy, J. M.; Rubin, G.; Winchester, C.; de Wit, N.; European Society for Primary Care, Gastroenterology	2013	Alimentary pharmacology & therapeutics	38	8	864-86	Does not meet minimum criteria for systematic review
Probiotic therapy of the irritable bowel syndrome: A systematic review but not a meta-analysis	Mazurak, N.; Broelz, E.; Storr, M.; Enck, P.	2015	Neurogastroenterology and Motility	21	4	471-85	Does not meet minimum criteria for systematic review
Evaluating the Efficacy of Probiotics in IBS Treatment Using a Systematic Review of Clinical Trials and Multi- Criteria Decision Analysis	Ceccherini, C.; Daniotti, S.; Bearzi, C.; Re, I.	2022	Nutrients	14	13	2689	Comparison of different probiotic strains only
Systematic review with meta-analysis: the efficacy of prebiotics, probiotics, synbiotics and antibiotics in irritable bowel syndrome	Ford, A. C.; Harris, L. A.; Lacy, B. E.; Quigley, E. M. M.; Moayyedi, P.	2018	Alimentary pharmacology & therapeutics	48	10	1044- 1060	Comparison of different probiotic strains only
Low FODMAP Diet and Probiotics in Irritable Bowel Syndrome: A Systematic Review With Network Meta- analysis	Xie, C. R.; Tang, B.; Shi, Y. Z.; Peng, W. Y.; Ye, K.; Tao, Q. F.; Yu, S. G.; Zheng, H.; Chen, M.	2022	Frontiers in pharmacology	13	-	853011	Comparison of different probiotic strains only
Effects of probiotic type, dose and treatment duration on irritable bowel syndrome diagnosed by Rome III criteria: a meta-analysis	Zhang, Y.; Li, L.; Guo, C.; Mu, D.; Feng, B.; Zuo, X.; Li, Y.	2016	BMC gastroenterology	16	1	62	Comparison of different probiotic strains only
Outcome-Specific Efficacy of Different Probiotic Strains and Mixtures in Irritable Bowel Syndrome: A Systematic Review and Network Meta-Analysis	Xie, Peiwei ; Luo, Mei ; Deng, Xuehong ; Fan, Jiahui ; Xiong, Lishou	2023	Nutrients	15	17	3856	Comparison of different probiotic strains only
Chinese herbal medicine versus probiotics for irritable bowel syndrome: A systematic review and meta-analysis of randomized controlled trials	Bu, F. L.; Chen, R. L.; Lin, Z. Y.; Cao, H. J.; Robinson, N.; Liang, N.; Liu, J. P.	2020	European Journal of Integrative Medicine	38	-	101177	Wrong comparator

Pharmacologic Treatment in Functional Abdominal Pain Disorders in Children: A Systematic Review	Rexwinkel, Robyn; de Bruijn, Clara M. A.; Gordon, Morris; Benninga, Marc A.; Tabbers, Merit M.	2021	Pediatrics	147	6	e202004 2101	Wrong intervention
Western herbal medicines in the treatment of irritable bowel syndrome: A systematic review and meta-analysis	Hawrelak, Jason A.; Wohlmuth, Hans; Pattinson, Martina; Myers, Stephen P.; Goldenberg, Joshua Z.; Harnett, Joanna; Cooley, Kieran; Van De Venter, Claudine; Reid, Rebecca; Whitten, Dawn L.	2020	Complementary Therapies in Medicine	48	-	102233	Wrong intervention
Therapeutic effects of lactobacillus in treating irritable bowel syndrome: A meta-analysis	Tiequn, B.; Guanqun, C.; Shuo, Z.	2015	Internal Medicine	54	3	243-249	Wrong outcomes
Probiotics for management of functional abdominal pain disorders in children	Wallace, C.; Gordon, M.; Sinopoulou, V.; Akobeng, A. K.	2023	Cochrane database of systematic reviews	2	2	CD0128 49	Wrong patient population
Meta-analysis of the efficacy of probiotics to treat diarrhea	Wang, F.; Zhao, T.; Wang, W.; Dai, Q.; Ma, X.	2022	Medicine	101	38	e30880	Wrong patient population
Effectiveness of Probiotics in Children With Functional Abdominal Pain Disorders and Functional Constipation: A Systematic Review	Wegh, C. A. M.; Benninga, M. A.; Tabbers, M. M.	2018	Journal of clinical gastroenterology	52 Suppl 1	-	S10-S26	Wrong patient population
The effect of probiotics on functional constipation in adults: a systematic review and meta-analysis of randomized controlled trials	Dimidi, E.; Christodoulides, S.; Fragkos, K. C.; Scott, S. M.; Whelan, K.	2014	Am J Clin Nutr	100	4	1075-84	Wrong patient population
Use of probiotics in the treatment of functional abdominal pain in children-systematic review and meta-analysis	Trivifá, I.; Niseteo, T.; Jadre≈ºin, O.; Hojsak, I.	2021	Eur J Pediatr	180	2	339-351	Wrong patient population
Effectiveness of probiotics in irritable bowel syndrome: Methodological quality of meta-analyses and systematic reviews	Jia, Y.; Guo, L. M.; Yang, S. Y.; Wu, Q.; Meng, F. J.	2019	Frontiers of Nursing	6	2	115-121	Wrong study design
British Dietetic Association systematic review and evidence-based practice guidelines for the dietary management of irritable bowel syndrome in adults (2016 update)	McKenzie, Y. A.; Bowyer, R. K.; Leach, H.; Gulia, P.; Horobin, J.; O'Sullivan, N. A.; Pettitt, C.; Reeves, L. B.; Seamark, L.; Williams, M.; Thompson, J.; Lomer, M. C.	2016	Journal of human nutrition and dietetics : the official journal of the British Dietetic Association	29	5	549-575	Wrong study design
An integrative review of dietetic and naturopathic approaches to functional bowel disorders	Grace, Sandra; Barnes, Larisa; Reilly, Wayne; Vlass, Ann; de Permentier, Patrick	2018	Complementary Therapies in Medicine	41	-	67-80	Wrong study design
Probiotics in Irritable Bowel Syndrome: An Up-to-Date Systematic Review	Dale, H. F.; Rasmussen, S. H.; Asiller, ÖÖ; Lied, G. A.	2019	Nutrients	11	9	2048	Does not meet minimum criteria for systematic review

## Table C-4. Excluded reviews, reason for exclusion – insomnia/sleeping disorders, magnesium.

Title	Authors	Year	Journal	Volume	Issue	Pages	Exclusion reason
Pharmacological treatment of insomnia in alcohol recovery: A systematic review	Kolla, B. P.; Mansukhani, M. P.; Schneekloth, T.	2011	Alcohol and Alcoholism	46	5	578-585	Does not meet minimum criteria for systematic review

Nutritional and herbal supplements for anxiety and anxiety- related disorders: Systematic review	Lakhan, S. E.; Vieira, K. F.	2010	Nutrition journal	9	1	42	Wrong patient population
Magnesium supplementation for the treatment of restless legs syndrome and periodic limb movement disorder: A systematic review	Marshall, N. S.; Serinel, Y.; Killick, R.; Child, J. M.; Raisin, I.; Berry, C. M.; Lallukka, T.; Wassing, R.; Lee, R. W.; Ratnavadivel, R.; Vedam, H.; Grunstein, R.; Wong, K. K.; Hoyos, C. M.; Cayanan, E. A.; Comas, M.; Chapman, J. L.; Yee, B. J.	2019	Sleep medicine reviews	48	-	101218	Wrong outcomes
Serum Magnesium Levels in Patients with Obstructive Sleep Apnoea: A Systematic Review and Meta-Analysis	Al Wadee, Z.; Ooi, S. L.; Pak, S. C.	2022	Biomedicines	10	9	2273	Wrong intervention
The Role of Magnesium in Sleep Health: a Systematic Review of Available Literature	Arab, A.; Rafie, N.; Amani, R.; Shirani, F.	2022	Biological trace element research	201	1	121-128	Wrong patient population
Effect of magnesium therapy on nocturnal leg cramps: a systematic review of randomized controlled trials with meta- analysis using simulations	Sebo, P.; Cerutti, B.; Haller, D. M.	2014	Family Practice	31	1	Jul-19	Wrong outcomes

# Table C-5. Excluded reviews, reason for exclusion – depression, omega-3 fatty acids.

Title	Authors	Year	Journal	Volume	Issue	Pages	Exclusion reason
A systematic review to investigate the effects of Omega-3 supplementation on depression scores among perinatal women	Franciskos, Arsenyadis	2019	PROSPERO	CRD42019 146925	-	-	Discontinued study
A meta-analytic review of double-blind, placebo-controlled trials of antidepressant efficacy of omega-3 fatty acids	Lin, P. Y.; Su, K. P.	2007	The Journal of clinical psychiatry	68	7	1056-61	Does not meet minimum criteria for systematic review
Complementary and alternative medicine in the treatment of anxiety and depression	Van Der Watt, G.; Laugharne, J.; Janca, A.	2008	Current Opinion in Psychiatry	21	1	37-42	Does not meet minimum criteria for systematic review
Complementary health approaches for postpartum depression: A systematic review	McCloskey, R. J.; Reno, R.	2019	Social Work in Mental Health	17	1	106-128	Does not meet minimum criteria for systematic review
Effectiveness and tolerance of anti-inflammatory drugs' add-on therapy in major mental disorders: a systematic qualitative review	Fond, G.; Hamdani, N.; Kapczinski, F.; Boukouaci, W.; Drancourt, N.; Dargel, A.; Oliveira, J.; Le Guen, E.; Marlinge, E.; Tamouza, R.; Leboyer, M.	2014	Acta psychiatrica Scandinavica	129	3	163-79	Does not meet minimum criteria for systematic review
Effectiveness of complementary and self-help treatments for depression in children and adolescents	Jorm AF; Allen NB; O'Donnell CP; Parslow RA; Purcell R; Morgan AJ	2006	Medical Journal of Australia	185	7	368-72	Does not meet minimum criteria for systematic review
Effects of low doses of polyunsaturated Fatty acids on the attention deficit/hyperactivity disorder of children: a systematic review	Grassmann, V.; Santos-Galduróz, R. F.; Galduróz, J. C.	2013	Current neuropharmacology	11	2	186-96	Does not meet minimum criteria for systematic review
Effects of omega 3 fatty acids supplementation in behavior and non-neurodegenerative neuropsychiatric disorders	Ortega, R. M.; Rodríguez-Rodríguez, E.; López-Sobaler, A. M.	2012	The British journal of nutrition	107 Suppl 2	SUPPL . 2	S261-70	Does not meet minimum criteria for systematic review

Long chain omega-3 polyunsaturated fatty acids in the treatment of psychiatric illnesses in children and adolescents	Clayton, Edward H.; Hanstock, Tanya L.; Garg, Manohar L.; Hazell, Philip L.	2007	Acta Neuropsychiatrica	19	2	92-103	Does not meet minimum criteria for systematic review
Maternal omega-3 fatty acid supplementation and risk for perinatal maternal depression	Wojcicki, J. M.; Heyman, M. B.	2011	Journal of Maternal- Fetal and Neonatal Medicine	24	5	680-686	Does not meet minimum criteria for systematic review
Meta-analysis of the effects of eicosapentaenoic acid (EPA) in clinical trials in depression	Sublette, M. E.; Ellis, S. P.; Geant, A. L.; Mann, J. J.	2011	The Journal of clinical psychiatry	72	12	1577-84	Does not meet minimum criteria for systematic review
Mood disorders and complementary and alternative medicine: a literature review	Qureshi, N. A.; Al-Bedah, A. M.	2013	Neuropsychiatric Disease and Treatment	9		639-58	Does not meet minimum criteria for systematic review
N-3 Polyunsatured Fatty Acids in Menopausal Transition: A Systematic Review of Depressive and Cognitive Disorders with Accompanying Vasomotor Symptoms	Ciappolino, V.; Mazzocchi, A.; Enrico, P.; Syrén, M. L.; Delvecchio, G.; Agostoni, C.; Brambilla, P.	2018	International journal of molecular sciences	19	7	1849	Does not meet minimum criteria for systematic review
n-3 PUFA Improve Emotion and Cognition during Menopause: A Systematic Review	Decandia, D.; Landolfo, E.; Sacchetti, S.; Gelfo, F.; Petrosini, L.; Cutuli, D.	2022	Nutrients	14	9	1892	Does not meet minimum criteria for systematic review
Nutrition and depression: A review of the evidence	Harbottle, L.; Schonfelder, N.	2008	Journal of Mental Health	17	6	576-587	Does not meet minimum criteria for systematic review
Nutritional and herbal supplements for anxiety and anxiety- related disorders: Systematic review	Lakhan, S. E.; Vieira, K. F.	2010	Nutrition journal	9	1	42	Does not meet minimum criteria for systematic review
Oiling the brain: a review of randomized controlled trials of omega-3 fatty acids in psychopathology across the lifespan	Sinn, N.; Milte, C.; Howe, P. R.	2010	Nutrients	2	2	128-70	Does not meet minimum criteria for systematic review
Omega-3 and omega-6 polyunsaturated fatty acids in bipolar disorder: A review of biomarker and treatment studies	Saunders, E. F. H.; Ramsden, C. E.; Sherazy, M. S.; Gelenberg, A. J.; Davis, J. M.; Rapoport, S. I.	2016	Journal of Clinical Psychiatry	77	10	e1301- e1308	Does not meet minimum criteria for systematic review
Omega-3 Fatty acids as Monotherapy in Treating Depression in Pregnant Women: a Meta- Analysis of Randomized Controlled Trials	Wei-Hong, L.; Cheng-Gui, Z.; Peng-Fei, G.; Heng, L.; Jian-Fang, Y.	2017	Iranian journal of pharmaceutical research	16	4	1593- 1599	Does not meet minimum criteria for systematic review
Omega-3 polyunsaturated fatty acids and depression: a review of the evidence and a methodological critique	Sontrop, J.; Campbell, M. K.	2006	Prev Med	42	1	Apr-13	Does not meet minimum criteria for systematic review
Perinatal nutrition interventions and post-partum depressive symptoms	Gould, Jacqueline F.; Best, Karen; Makrides, Maria	2017	Journal of Affective Disorders	224		2-Sep	Does not meet minimum criteria for systematic review
Pharmacotherapy of borderline personality disorder: a systematic review for publication purpose	Bellino, S.; Rinaldi, C.; Bozzatello, P.; Bogetto, F.	2011	Current medicinal chemistry	18	22	3322-9	Does not meet minimum criteria for systematic review
Polyunsaturated Fatty Acids: What is Their Role in Treatment of Psychiatric Disorders?	Bozzatello, P.; Rocca, P.; Mantelli, E.; Bellino, S.	2019	International journal of molecular sciences	20	21	5257	Does not meet minimum criteria for systematic review
Self-help interventions for depressive disorders and depressive symptoms: a systematic review	Morgan, A. J.; Jorm, A. F.	2008	Annals of general psychiatry	7	-	13	Does not meet minimum criteria for systematic review
Taking the fuel out of the fire: Evidence for the use of anti- inflammatory agents in the treatment of bipolar disorders	Ayorech, Z.; Tracy, D. K.; Baumeister, D.; Giaroli, G.	2015	Journal of Affective Disorders	174	-	467-478	Does not meet minimum criteria for systematic review

The role of n-3 polyunsaturated fatty acids (n-3PUFAs) in affective disorders	Ciappolino, Valentina; Delvecchio, Giuseppe; Agostoni, Carlo; Mazzocchi, Alessandra; Altamura, Alfredo Carlo; Brambilla, Paolo	2017	Journal of Affective Disorders	224	-	32-47	Does not meet minimum criteria for systematic review
Updated systematic review and meta-analysis of the effects of n-3 long-chain polyunsaturated fatty acids on depressed mood	Appleton, K. M.; Rogers, P. J.; Ness, A. R.	2010	American Journal of Clinical Nutrition	91	3	757-770	Does not meet minimum criteria for systematic review
What is the effectiveness of the use of polyunsaturated fatty acid omega-3 in the treatment of depression?	Rocha Araujo, D. M.; Vilarim, M. M.; Nardi, A. E.	2010	Expert review of neurotherapeutics	10	7	1117-29	Does not meet minimum criteria for systematic review
A systematic review to investigate the effects of Omega-3 supplementation on depression scores in adults with cardiometabolic disease	Franciskos Arsenyadis, Emma Redman Ehtasham Ahmad	2022	Nutrients	14	9	1827	Population does not meet at- risk definition
Early pharmacological interventions for universal prevention of post-traumatic stress disorder (PTSD)	Bertolini, F.; Robertson, L.; Bisson, J. I.; Meader, N.; Churchill, R.; Ostuzzi, G.; Stein, D. J.; Williams, T.; Barbui, C.	2022	The Cochrane database of systematic reviews	2	2	CD0134 43	Population does not meet at- risk definition
A systematic review of the evidence for the treatment of acute depression in bipolar I disorder	Cerullo, M. A.; Strakowski, S. M.	2013	CNS Spectrums	18	4	199-208	Wrong comparator
Comparative Benefits and Harms of Complementary and Alternative Medicine Therapies for Initial Treatment of Major Depressive Disorder: Systematic Review and Meta- Analysis	Asher, G. N.; Gartlehner, G.; Gaynes, B. N.; Amick, H. R.; Forneris, C.; Morgan, L. C.; Coker- Schwimmer, E.; Boland, E.; Lux, L. J.; Gaylord, S.; Bann, C.; Pierl, C. B.; Lohr, K. N.	2017	Journal of alternative and complementary medicine	23	12	907-919	Wrong comparator
Nonpharmacologic versus pharmacologic treatment of adult patients, with major depressive disorder: A clinical practice guideline from the, American College of Physicians	Qaseem A; Barry MJ; Kansagara D	2016	Annals of Internal Medicine	164	5	350-9	Wrong comparator
A Systematic Review of Nutraceuticals for the Treatment of Bipolar Disorder: Une revue systématique des nutraceutiques pour le traitement du trouble bipolaire	Ashton, M. M.; Kavanagh, B. E.; Marx, W.; Berk, M.; Sarris, J.; Ng, C. H.; Hopwood, M.; Williams, L. J.; Dean, O. M.	2020	Canadian journal of psychiatry	66	3	262-273	Wrong intervention
An evidence synthesis to evaluate the clinical effectiveness and cost-effectiveness of interventions to prevent postnatal depression	Morrell, C. J., Sutcliffe, P., Booth, A., Stevens, J., Scope, A., Stevenson, M., Harvey, R., Bessey, A., Cantrell, A., Dennis, C. L., Ren, S., Ragonesi, M., Barkham, M., Churchill, D., Henshaw, C., Newstead, J., Slade, P., Spiby, H., & Stewart- Brown, S.	2016	Health Technol Assess	20	37	1-414	Wrong intervention
Anti-inflammatory agents in the treatment of bipolar depression: a systematic review and meta-analysis	Rosenblat, J. D.; Kakar, R.; Berk, M.; Kessing, L. V.; Vinberg, M.; Baune, B. T.; Mansur, R. B.; Brietzke, E.; Goldstein, B. I.; McIntyre, R. S.	2016	Bipolar disorders	18	2	89-101	Wrong intervention
Comparative Efficacy and Acceptability of Anti- inflammatory Agents on Major Depressive Disorder: A Network Meta-Analysis	Hang, X.; Zhang, Y.; Li, J.; Li, Z.; Zhang, Y.; Ye, X.; Tang, Q.; Sun, W.	2021	Frontiers in pharmacology	12		691200	Wrong intervention
Dietary polyunsaturated fat for prevention and treatment of depression and anxiety	Sarah Hanson, Priti Biswas Oluseyi Jimoh Alex O'Brien Lee Hooper Asmaa Abdelhamid Katherine Deane	2017	PROSPERO	CRD42017 056092	-	-	Wrong intervention – Omega- 3 outcomes not reported separately

Effects of long-chain omega-3 polyunsaturated fatty acids on reducing anxiety and/or depression in adults: a systematic review and meta-analysis of randomised control trials	Simon Dyall, Leigh Gibson Christos Kelaiditis	2020	PROSPERO	CRD42020 194402	-	-	Wrong patient population – some of the population was healthy; unable to determine results for condition or at-risk group only
Effects of n-3 Polyunsaturated Fatty Acid Supplementation in the Prevention and Treatment of Depressive Disorders-A Systematic Review and Meta-Analysis	Wolters, M.; von der Haar, A.; Baalmann, A. K.; Wellbrock, M.; Heise, T. L.; Rach, S.	2021	Nutrients	13	4	1070	Wrong intervention - Omega- 3 outcomes not reported separately (omega-3 plus non-naturopathy invention e.g., stress management; omega-3 plus pharmacotherapy)
Efficacy of omega-3 fatty acid supplementation on improvement of bipolar symptoms: a systematic review	Turnbull, T.; Cullen-Drill, M.; Smaldone, A.	2008	Archives of psychiatric nursing	22	5	305-11	Wrong intervention - Omega- 3 outcomes not reported separately (omega-3 plus pharmacotherapy)
High-dose omega-3 polyunsaturated fatty acid supplementation might be more superior than low-dose for major depressive disorder in early therapy period: a network meta-analysis	Luo, X. D.; Feng, J. S.; Yang, Z.; Huang, Q. T.; Lin, J. D.; Yang, B.; Su, K. P.; Pan, J. Y.	2020	BMC psychiatry	20	1	248	Wrong comparator
Nutritional aspects of depression in adolescents - A systematic review	Khanna, P.; Chattu, V. K.; Aeri, B. T.	2019	International Journal of Preventive Medicine	10	1	1-Sep	Wrong intervention
Omega-3 fatty acids for bipolar disorder	Montgomery, P.; Richardson, A. J.	2008	Cochrane Database of Systematic Reviews	-	2	CD0051 69	Wrong intervention - Omega- 3 outcomes not reported separately (omega-3 plus pharmacotherapy)
Role of omega-3 fatty acids in the treatment of depressive disorders: A comprehensive meta-analysis of randomized clinical trials	Grosso, G.; Pajak, A.; Marventano, S.; Castellano, S.; Galvano, F.; Bucolo, C.; Drago, F.; Caraci, F.	2014	PloS one	9	5	e96905	Wrong intervention - unable to separate effects for any study of eligible supplement v placebo/sham from studies with eligible supplement + non-naturopathy co- intervention VS placebo/sham
The effect of adjunctive nutraceuticals in bipolar disorder: A systematic review of randomized placebo-controlled trials	Fusar-Poli, L.; Surace, T.; Vanella, A.; Meo, V.; Patania, F.; Furnari, R.; Signorelli, M. S.; Aguglia, E.	2019	Journal of Affective Disorders	252	-	334-349	Wrong intervention
Effects of omega-3 polyunsaturated fatty acids supplements on psychopathology and metabolic parameters in schizophrenia: A meta-analysis of randomized controlled trials	Goh, K. K.; Chen, C. Y.; Chen, C. H.; Lu, M. L.	2021	Journal of psychopharmacology (Oxford, England)	35	3	2.6988E +14	Wrong outcomes

Non-specific effect of omega-3 fatty acid supplementation on autistic spectrum disorder: systematic review and meta- analysis	de Andrade Wobido, K.; de Sü Barreto da Cunha, M.; Miranda, S. S.; da Mota Santana, J.; da Silva, D. C. G.; Pereira, M.	2022	Nutritional neuroscience	25	9	1995- 2007	Wrong outcomes
Nutritional Interventions and Cognitive-related Outcomes in Patients with Late-life Cognitive Disorders: A Systematic Review	Solfrizzi, V.; Agosti, P.; Lozupone, M.; Custodero, C.; Schilardi, A.; Valiani, V.; Santamato, A.; Sardone, R.; Dibello, V.; Di Lena, L.; Stallone, R.; Ranieri, M.; Bellomo, A.; Greco, A.; Daniele, A.; Seripa, D.; Sabbà, C.; Logroscino, G.; Panza, F.	2018	Neuroscience and biobehavioral reviews	95	-	480-498	Wrong outcomes
Omega-3 polyunsaturated fatty acid supplementation and cognition: A systematic review and meta-analysis	Cooper, R. E.; Tye, C.; Kuntsi, J.; Vassos, E.; Asherson, P.	2015	Journal of psychopharmacology (Oxford, England)	29	7	753-763	Wrong outcomes
Supplementation of omega 3 fatty acids may improve hyperactivity, lethargy, and stereotypy in children with autism spectrum disorders: A meta-analysis of randomized controlled trials	Cheng, Y. S.; Tseng, P. T.; Chen, Y. W.; Stubbs, B.; Yang, W. C.; Chen, T. Y.; Wu, C. K.; Lin, P. Y.	2017	Neuropsychiatric Disease and Treatment	13	-	2531- 2543	Wrong outcomes
The effect of omega-3 polyunsaturated fatty acid supplementation on emotional dysregulation, oppositional behaviour and conduct problems in ADHD: A systematic review and meta-analysis	Cooper, R. E.; Tye, C.; Kuntsi, J.; Vassos, E.; Asherson, P.	2016	Journal of Affective Disorders	190	-	474-482	Wrong outcomes
Treatment of neurocognitive symptoms in unipolar depression: A systematic review and future perspectives	Salagre, E.; Sole, B.; Tomioka, Y.; Fernandes, B. S.; Hidalgo-Mazzei, D.; Garriga, M.; Jimenez, E.; Sanchez-Moreno, J.; Vieta, E.; Grande, I.	2017	Journal of Affective Disorders	221	-	205-221	Wrong outcomes
A Systematic Review of Effectiveness of Omega-3 Fatty Acid Supplementation on Symptoms, Social Functions, and Neurobiological Variables in Schizophrenia	Hsu, M. C.; Ouyang, W. C.	2021	Biological Research for Nursing	23	4	723-737	Wrong patient population
Adjunctive Nutraceuticals for Depression: A Systematic Review and Meta-Analyses	Sarris, Jerome; Murphy, Jenifer; Mischoulon, David; Papakostas, George I.; Fava, Maurizio; Berk, Michael; Ng, Chee H.	2016	American Journal of Psychiatry	173	6	575-587	Wrong intervention
Adjunctive nutrients in first-episode psychosis: A systematic review of efficacy, tolerability and neurobiological mechanisms	Firth, J.; Rosenbaum, S.; Ward, P. B.; Curtis, J.; Teasdale, S. B.; Yung, A. R.; Sarris, J.	2018	Early Intervention in Psychiatry	12	5	774-783	Wrong patient population
Early interventions to prevent psychosis: systematic review and meta-analysis	Stafford, M. R.; Jackson, H.; Mayo-Wilson, E.; Morrison, A. P.; Kendall, T.	2013	BMJ (Clinical research ed.)	346	7892	f185	Wrong patient population
Efficacy and safety of anti-inflammatory agents in treatment of psychotic disorders - a comprehensive systematic review and meta-analysis	Jeppesen, R.; Christensen, R. H. B.; Pedersen, E. M. J.; Nordentoft, M.; Hjorthøj, C.; Köhler- Forsberg, O.; Benros, M. E.	2020	Brain, behavior, and immunity	90	-	364-380	Wrong patient population
Efficacy and safety of polyunsaturated fatty acids supplementation in the treatment of attention deficit hyperactivity disorder (Adhd) in children and adolescents: A systematic review and meta-analysis of clinical trials	Handel, M. N.; Rohde, J. F.; Bandak, E.; Handel, M. N.; Rohde, J. F.; Bandak, E.; Birkefoss, K.; Tendal, B.; Callesen, H. E.; Rimestad, M. L.; Lemcke, S.	2021	Nutrients	13	4	1226	Wrong patient population

Impact of polyunsaturated fatty acids on patient-important outcomes in children and adolescents with autism spectrum disorder: a systematic review	De Crescenzo, F.; D'Alò, G. L.; Morgano, G. P.; Minozzi, S.; Mitrova, Z.; Saulle, R.; Cruciani, F.; Fulceri, F.; Davoli, M.; Scattoni, M. L.; Nardocci, F.; Sch√onemann, H. J.; Amato, L.; Isaca guideline working group	2020	Health and quality of life outcomes	18	1	28	Wrong patient population
Marine Omega-3 Fatty Acid Supplementation for Borderline Personality Disorder: A Meta-Analysis	Karaszewska, D. M.; Ingenhoven, T.; Mocking, R. J. T.	2021	The Journal of clinical psychiatry	82	3	-	Wrong patient population
Omega-3 Fatty Acid Dietary Supplements Consumed During Pregnancy and Lactation and Child Neurodevelopment: A Systematic Review	Nevins, J. E. H.; Donovan, S. M.; Snetselaar, L.; Dewey, K. G.; Novotny, R.; Stang, J.; Taveras, E. M.; Kleinman, R. E.; Bailey, R. L.; Raghavan, R.; Scinto-Madonich, S. R.; Venkatramanan, S.; Butera, G.; Terry, N.; Altman, J.; Adler, M.; Obbagy, J. E.; Stoody, E. E.; de Jesus, J.	2021	The Journal of nutrition	151	11	3483- 3494	Wrong patient population
Pharmacological interventions for borderline personality disorder	Stoffers-Winterling JM, Storebø OJ, Völlm BA, Mattivi JT, Nielsen SS, Kielsholm ML, Faltinsen EG, Simonsen E, Lieb K.	2010	Cochrane database of systematic reviews (Online)	-	6	CD0056 53	Wrong patient population
Pharmacotherapy for borderline personality disorder: Cochrane systematic review of randomised trials	Lieb K, Völlm B, Rücker G, Timmer A, Stoffers JM.	2010	The British journal of psychiatry : the journal of mental science	196	1	4-12	Wrong patient population
Polyunsaturated fatty acids (PUFA) for attention deficit hyperactivity disorder (ADHD) in children and adolescents	Gillies, D.; Leach, M. J.; Perez Algorta, G.	2023	The Cochrane database of systematic reviews	4	4	CD0079 86	Wrong patient population
The association between nonpharmacological interventions and quality of life in children with attention deficit hyperactivity disorder: A systematic review	Jensen, M. L.; Vamosi, M.	2022	Journal of child and adolescent psychiatric nursing : official publication of the Association of Child and Adolescent Psychiatric Nurses, Inc	36	2	114-123	Wrong patient population
The effectiveness of omega-3 fatty acids in reducing symptoms of attention deficit hyperactivity disorder	Abdullah M, Jowett B, Whittaker PJ, Patterson L.	2019	Journal of Psychiatric Research	110	-	64-73	Wrong patient population
The efficacy of n-3 fatty acids DHA and EPA (fish oil) for perinatal depression	Jans, L. A. W.; Giltay, E. J.; Willem Van Der Does, A. J.	2010	British Journal of Nutrition	104	11	1577- 1585	Wrong patient population
The Role of Omega-3 Fatty Acids in Developmental Psychopathology: A Systematic Review on Early Psychosis, Autism, and ADHD	Agostoni, C.; Nobile, M.; Ciappolino, V.; Delvecchio, G.; Tesei, A.; Turolo, S.; Crippa, A.; Mazzocchi, A.; Altamura, C. A.; Brambilla, P.	2017	International journal of molecular sciences	18	12		Wrong patient population
Anti-Inflammatory Treatment Efficacy in Major Depressive Disorder: A Systematic Review of Meta-Analyses	Simon, M. S.; Arteaga-Henríquez, G.; Fouad Algendy, A.; Siepmann, T.; Illigens, B. M. W.	2023	Neuropsychiatric Disease and Treatment	19	-	1-25	Wrong study type
Clinical guidelines for the prescription of adjunctive drugs to optimize the benefit/risk ratio of antipsychotics in schizophrenia: a meta-review with GRADE recommendations	Fond G, Mallet J, Urbach M, Benros ME, Berk M, Billeci M, Boyer L, Correll CU, Fornaro M, Kulkarni J, Leboyer M, Llorca PM, Misdrahi D, Rey R, Schürhoff F, Solmi M, Sommer IEC, Stahl SM, Pignon B, Berna F.	2023	BMJ Ment Health	26	1	e300771	Wrong study type

Dietary n-3 PUFA, fish consumption and depression: A systematic review and meta-analysis of observational studies	Grosso, G.; Micek, A.; Marventano, S.; Castellano, S.; Mistretta, A.; Pajak, A.; Galvano, F.	2016	Journal of Affective Disorders	205		269-281	Wrong study type
Early pharmacological interventions for preventing post- traumatic stress disorder (PTSD): a network meta-analysis [Cochrane protocol]	Bertolini F, Robertson L, Ostuzzi G, Meader N, Bisson JI, Churchill R, Barbui C.	2019	<u>Cochrane Database</u> Syst Rev	10	-	CD0134 43	Wrong study type
Eicosapentaenoic acid appears to be the key omega-3 fatty acid component associated with efficacy in major depressive disorder: a critique of Bloch and Hannestad and updated meta-analysis	Martins, J. G.; Bentsen, H.; Puri, B. K.	2012	Molecular psychiatry	17	12	1144-9; discussi on 1163- 7	Wrong study type
Evidence of the Importance of Dietary Habits Regarding Depressive Symptoms and Depression	Ljungberg, T.; Bondza, E.; Lethin, C.	2020	International journal of environmental research and public health	17	5	1616	Wrong study type
Nonpharmacological Versus Pharmacological Treatments for Adult Patients With Major Depressive Disorder - An Update of the 2014 Comparative Effectiveness Review	Gartlehner G, Gaynes BN, Amick HR, Asher G, Morgan LC, Coker-Schwimmer E, Forneris C, Boland E, Lux LJ, Gaylord S, Bann C, Pierl CB, Lohr KN.	2015	AHRQ Comparative Effectiveness Reviews.	15	16	EHC031- EF	Wrong study type
Omega-3 fatty acids for treating residual depressive symptoms in adult patients with bipolar disorder: A systematic review and meta-analysis of double-blind randomized, placebo-controlled trials	Kishi, T.; Sakuma, K.; Okuya, M.; Ikeda, M.; Iwata, N.	2021	Bipolar disorders	23	7	730-731	Wrong study type
Supplementation with Omega-3 Fatty Acids in Psychiatric Disorders: A Review of Literature Data	Bozzatello, P.; Brignolo, E.; De Grandi, E.; Bellino, S.	2016	Journal of clinical medicine	5	8	67	Wrong study type
The health benefits of omega-3 polyunsaturated fatty acids: A review of the evidence	Ruxton, C. H. S.; Reed, S. C.; Simpson, J. A.; Millington, K. J.	2007	Journal of Human Nutrition and Dietetics	20	3	275-285	Wrong study type
Trim the fat: the role of omega-3 fatty acids in psychopharmacology	Nasir, M.; Bloch, M. H.	2019	Therapeutic Advances in Psychopharmacology	9	-	2045125 3198697 91	Wrong study type
Unsaturated Fatty Acids in Mental Disorders: An Umbrella Review of Meta-Analyses	Gao, X.; Su, X.; Han, X.; Wen, H.; Cheng, C.; Zhang, S.; Li, W.; Cai, J.; Zheng, L.; Ma, J.; Liao, M.; Ni, W.; Liu, T.; Liu, D.; Ma, W.; Han, S.; Zhu, S.; Ye, Y.; Zeng, F. F.	2022	Advances in Nutrition	13	6	2217- 2236	Wrong study type

## Table C-6. Excluded reviews, reason for exclusion – Dysmenorrhea, cruciferous indoles (indole-3-carbinol, di-indolylmethane).

Title	Authors	Year	Journal	Volume	Issue	Pages	Exclusion reason
Nutritional Supplements and Complementary Therapies in Polycystic Ovary Syndrome	Alesi, S.; Ee, C.; Moran, L. J.; Rao, V.; Mousa, A.	2022	Advances in Nutrition	13	4	1243- 1266	Does not meet minimum criteria for systematic review

Chinese herbal medicine for primary dysmenorrhoea	Zhu, X.; Proctor, M.; Bensoussan, A.; Wu, E.;	2008	Cochrane Database of	16	2	CD005288	Wrong intervention
	Smith, C. A.		Systematic Reviews				

### Table C-7. Excluded reviews, reason for exclusion – PMS, cruciferous indoles (indole-3-carbinol, di-indolylmethane).

Title	Authors	Year	Journal	Volume	Issue	Pages	Exclusion reason
Nutritional and herbal supplements for anxiety and anxiety- related disorders: Systematic review	Lakhan, S. E.; Vieira, K. F.	2010	Nutrition journal	9	1	42	Wrong intervention
A Comprehensive Review of Treatment Options for Premenstrual Syndrome and Premenstrual Dysphoric Disorder	Maharaj, S.; Trevino, K.	2015	Journal of Psychiatric Practice	21	5	334-350	Wrong intervention

## Table C-8. Excluded reviews, reason for exclusion – Atopic disorders (including eczema, dermatitis, allergic rhinitis, allergies), zinc).

Title	Authors	Year	Journal	Volume	Issue	Pages	Exclusion reason
Micronutrients in Atopic Dermatitis: A Systematic Review	Vaughn, A. R.; Foolad, N.; Maarouf, M.; Tran, K. A.; Shi, V. Y.	2019	J Altern Complement Med	25	6	567-577	Does not meet minimum criteria for systematic review
Clinical practice guidelines for the prevention and treatment of acute and late radiation reactions from the MASCC Skin Toxicity Study Group	Wong, R. K. S.; Bensadoun, R. J.; Boers-Doets, C. B.; Bryce, J.; Chan, A.; Epstein, J. B.; Eaby-Sandy, B.; Lacouture, M. E.	2013	Support Care Cancer	21	10	2933-2948	Wrong patient population
Counteracting side effects of combined oral contraceptives through the administration of specific micronutrients	Basciani, S.; Porcaro, G.	2022	Eur Rev Med Pharmacol Sci	26	13	4846-4862	Wrong patient population
Maternal nutrition during pregnancy and risk of asthma, wheeze and atopic diseases during childhood: a systematic review and meta-analysis	Beckhaus, A. A.; Garcia-Marcos, L.; Forno, E.; Pacheco-Gonzalez, R. M.; Celedón, J. C.; Castro-Rodriguez, J. A.	2015	Allergy	70	12	1588-604	Wrong patient population
Prevention and treatment of acute radiation-induced skin reactions: a systematic review and meta-analysis of randomized controlled trials	Chan, R. J.; Webster, J.; Chung, B.; Marquart, L.; Ahmed, M.; Garantziotis, S.	2014	BMC Cancer volume	14	1	53	Wrong patient population
Serum zinc level and children`s asthma: A systematic and meta-analysis review article	Ghaffari, J.; Alizadeh-Navaei, R.; Dabaghzadeh, A.; Ghaffari, N.	2021	Caspian J Intern Med	12	3	236-242	Does not meet minimum criteria for systematic review
Zinc as a complementary treatment for cancer patients: a systematic review	Hoppe C, Kutschan S, Dörfler J, Büntzel J, Büntzel J, Huebner J.	2021	Clin Exp Med	21	2	297-313	Wrong patient population
Nutrients and foods for the primary prevention of asthma and allergy: systematic review and meta-analysis	Nurmatov, U.; Devereux, G.; Sheikh, A.	2011	J Allergy Clin Immunol	127	3	724-33.e1-30	Wrong patient population
An evidence-based review of systemic treatments for itch	Pongcharoen, P.; Fleischer, A. B.	2016	Eur J Pain	20	1	24-31	Wrong patient population

Use of Fatty Acids, Vitamins and Minerals, and Probiotics in Alleviating Symptoms of Atopic Dermatitis: A Systematic Review	Labib A, Golpanian RS, Aickara D, Smith P, Yosipovitch G.	2023	Pediatr Dermatol	40	1	44-49	Wrong comparator
A meta-analytic review of pharmaceutical and non- pharmaceutical therapies for diaper dermatitis in infants	Fahad A. Alamri, Samar Amer Faten A. Alradini Shaker Alomary Ahmed A. Alahmari Yasir S. Almuzaini Safa Boujemaa	2023	PROSPERO	-	-	CRD42023393866	Wrong patient population
A systematic review of methods to minimise skin reactions (radiation dermatitis) in patients undergoing external beam photon, electron and proton beam radiotherapy	Heidi Probst, Gemma Burke Sara Faithfull	2019	PROSPERO	-	-	CRD42019148161	Wrong patient population
Treatment strategies for Infant Diaper Dermatitis- A Systematic Review and Network Meta-analysis	Rajendra Prasad Anne, Abhishek Aaradhya Vinay Keshavmurthy Nishant Jaiswal	NR	NR	NR	NR	NR	Wrong patient population
Blended interventions to reduce the disease burden of COPD and asthma patients: a systematic review	Xiaoyue Song, Niels Chavannes Rianne Kleij Robbert Gobbens Cynthia Hallensleben Weihong Zhang Zongliang Jiang	2021	J Med Internet Res	23	3	e24602	Wrong intervention
Association Between Circulating Zinc and Risk for Childhood Asthma and Wheezing: A Meta-analysis on 21 Articles and 2205 Children	Xue, Mei; Wang, Qiong; Pang, Bo; Zhang, Xiaoqian; Zhang, Yicheng; Deng, Xiangling; Zhang, Zhixin; Niu, Wenquan	2024	Biol Trace Elem Res	202	2	442-453	Wrong study design

## Table C-9. Excluded reviews, reason for exclusion – fatigue/antioxidants.

Title	Authors	Year	Journal	Volume	Issue	Pages	Exclusion reason
Efficacy of interventions for improving health in patients with multiple sclerosis on insomnia symptoms and sleep quality: A systematic review of randomized controlled trials	Bacaro, V.; Buonanno, C.; Mancini, F.; Baglioni, C.	2021	Journal of Behavioral and Cognitive Therapy	31	2	137-145	Wrong intervention
Antioxidant Supplements and Breast Cancer: A Systematic Review and Meta-Analysis	Moradi-Joo, Mohammad; Heidari, Saeed; Seyed- Nezhad, Maryam; Akbari, Mohammad Esmaeil; Moosavi, Ahmad; Davoodi, Sayed Hossein	2018	International Journal of Cancer Management	11	4	1-11	Wrong intervention
Effects of coenzyme Q10 on statin-induced myopathy: A meta-analysis of randomized controlled trials	Banach, M.; Serban, C.; Sahebkar, A.; Ursoniu, S.; Rysz, J.; Muntner, P.; Toth, P. P.; Jones, S. R.; Rizzo, M.; Glasser, S. P.; Lip, G. Y. H.; Dragan, S.; Mikhailidis, D. P.	2015	Mayo Clinic proceedings	90	1	24-34	Wrong outcomes
Impact of Dietary Antioxidants on Sport Performance: A Review	Braakhuis, A. J.; Hopkins, W. G.	2015	Sports Medicine	45	7	939-955	Wrong patient population
Nutrition and diet in the clinical management of multiple sclerosis	Payne, A.	2001	Journal of Human Nutrition and Dietetics	14	5	349-357	Does not meet minimum criteria for systematic review

Effects of coenzyme Q10 on statin-induced myopathy: An updated meta-analysis of randomized controlled trials	Qu, H.; Guo, M.; Chai, H.; Wang, W. T.; Ga, Z. Y.; Shi, D. Z.	2018	Journal of the American Heart Association	7	19	e009835	Wrong outcomes
Recent Developments in the Role of Coenzyme Q10 for Coronary Heart Disease: a Systematic Review	Ayers, J.; Cook, J.; Koenig, R. A.; Sisson, E. M.; Dixon, D. L.	2018	Current atherosclerosis reports	20	6	29	Does not meet minimum criteria for systematic review
Effect of Antioxidant Supplementation on Markers of Oxidative Stress and Muscle Damage after Strength Exercise: A Systematic Review	Canals-Garzón, C.; Guisado-Barrilao, R.; Martínez-García, D.; Chirosa-Ríos, I. J.; Jerez-Mayorga, D.; Guisado-Requena, I. M.	2022	International journal of environmental research and public health	19	3	1803	Wrong patient population
Effect of Coenzyme Q10 on statin-associated myalgia and adherence to statin therapy: A systematic review and meta- analysis	Kennedy, C.; Koller, Y.; Surkova, E.	2020	Atherosclerosis	299	-	1-8	Wrong outcomes
Dietary Interventions in the Management of Fibromyalgia: A Systematic Review and Best-Evidence Synthesis	Lowry, E.; Marley, J.; McVeigh, J. G.; McSorley, E.; Allsopp, P.; Kerr, D.	2020	Nutrients	12	9	2664	Wrong outcomes
Antioxidants for Treatment of Duchenne Muscular Dystrophy: A Systematic Review and Meta-Analysis	Ren, S.; Yao, C.; Liu, Y.; Feng, G.; Dong, X.; Gao, B.; Qian, S.	2022	European neurology	85	5	377-388	Does not meet minimum criteria for systematic review
An umbrella review evaluating the effects of dietary interventions on disease progression in persons living with multiple sclerosis	Abbey Tredinnick, Yasmine Probst	2020	Advances in Nutrition	11	3	-	Wrong study design
Antioxidant Micronutrients and Essential Fatty Acids Supplementation on Cystic Fibrosis Outcomes: A Systematic Review	Simon, Miriam Isabel Souza dos Santos; Dalle Molle, Roberta; Silva, Fl√°via Moraes; Rodrigues, Thais Wabner; Feldmann, Marceli; Forte, Gabriele Carra; Marostica, Paulo José Cauduro	2020	Journal of the Academy of Nutrition and Dietetics	120	6	1016-1033.e1	Wrong outcomes
Effect of coenzyme q10 supplementation on fatigue: a systematic review of interventional studiesa	arman, arab	2018	PROSPERO	-	-	CRD42018096638	Wrong patient population

# Table C-10. Excluded reviews, reason for exclusion – Headache and migraine, magnesium.

Title	Authors	Year	Journal	Volume	Issue	Pages	Exclusion reason
Evidence-based guideline update: NSAIDs and other complementary treatments for episodic migraine prevention in adults Report of the quality standards subcommittee of the american academy of neurology and the American headache society	Holland, S.; Silberstein, S. D.; Freitag, F.; Dodick, D. W.; Argoff, C.; Ashman, E.	2012	Neurology	78	17	1346- 1353	Does not meet minimum criteria for systematic review
The acute treatment of migraine in adults: The american headache society evidence assessment of migraine pharmacotherapies	Marmura, M. J.; Silberstein, S. D.; Schwedt, T. J.	2015	Headache	55	1	3-20	Wrong intervention

Management of primary headaches during pregnancy, postpartum, and breastfeeding: A systematic review	Saldanha, I. J.; Cao, W.; Bhuma, M. R.; Konnyu, K. J.; Adam, G. P.; Mehta, S.; Zullo, A. R.; Chen, K. K.; Roth, J. L.; Balk, E. M.	2021	Headache	61	1	11-43	Wrong outcomes
Acute Treatments for Episodic Migraine	Singh, R. B. H.; VanderPluym, J. H.; Morrow, A. S.; Urtecho, M.; Nayfeh, T.; Roldan, V. D. T.; Farah, M. H.; Hasan, B.; Saadi, S.; Shah, S.; Abd-Rabu, R.; Daraz, L.; Prokop, L. J.; Murad, M. H.; Wang, Z.	2020	AHRQ Comparative Effectiveness Reviews	239	-	-	Wrong intervention
Complementary and integrative medicine in the management of headache	Millstine, D.; Chen, C. Y.; Bauer, B.	2017	BMJ (Online)	357		j1805	Wrong study type
Should magnesium sulfate be administered to women with mild pre-eclampsia? A systematic review of published reports on eclampsia	Berhan, Y.; Berhan, A.	2015	The journal of obstetrics and gynaecology research	41	6	831-42	Does not meet minimum criteria for systematic review
The Efficacy of Herbal Supplements and Nutraceuticals for Prevention of Migraine: Can They Help?	Kaur, K.; Hernandez, V.; Al Hajaj, S. W.; Ebrahim, A. M.; Razack, M.; ElSharief, M. W.; Dragas, D.	2021	Cureus	13	5	e14868	Does not meet minimum criteria for systematic review
Menstrual Migraine and Treatment Options: Review	Maasumi, K.; Tepper, S. J.; Kriegler, J. S.	2017	Headache	57	2	194-208	Does not meet minimum criteria for systematic review
Evidence for efficacy of acute treatment of episodic tension- type headache: methodological critique of randomised trials for oral treatments	Moore, R. A.; Derry, S.; Wiffen, P. J.; Straube, S.; Bendtsen, L.	2014	Pain	155	11	2220-8	Wrong intervention
The role of nutrients in the pathogenesis and treatment of migraine headaches: Review	Nattagh-Eshtivani, E.; Sani, M. A.; Dahri, M.; Ghalichi, F.; Ghavami, A.; Arjang, P.; Tarighat- Esfanjani, A.	2018	Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie	102		317-325	Does not meet minimum criteria for systematic review
Acute Treatment Therapies for Pediatric Migraine: A Qualitative Systematic Review	Patniyot, I. R.; Gelfand, A. A.	2016	Headache	56	1	49-70	Does not meet minimum criteria for systematic review
Acute Migraine Treatment in Emergency Settings	Sumamo Schellenberg, E.; Dryden, D. M.; Pasichnyk, D.; Ha, C.; Vandermeer, B.; Friedman, B. W.; Colman, I.; Rowe, B. H.	2012	AHRQ Comparative Effectiveness Reviews	12	13	EHC142- EF	Wrong patient population
Pharmacological interventions for acute attacks of vestibular migraine	Webster, K. E.; Dor, A.; Galbraith, K.; Haj Kassem, L.; Harrington-Benton, N. A.; Judd, O.; Kaski, D.; Maarsingh, O. R.; MacKeith, S.; Ray, J.; Van Vugt, V. A.; Burton, M. J.	2023	The Cochrane database of systematic reviews	4	4	CD015322	Wrong intervention
Complementary and Integrative Medicine for Episodic Migraine: an Update of Evidence from the Last 3 Years	Wells, R. E.; Beuthin, J.; Granetzke, L.	2019	Current pain and headache reports	23	2	10	Does not meet minimum criteria for systematic review
Complementary and Integrative Medicines as Prophylactic Agents for Pediatric Migraine: A Narrative Literature Review	Yamanaka, G.; Kanou, K.; Takamatsu, T.; Takeshita, M.; Morichi, S.; Suzuki, S.; Ishida, Y.; Watanabe, Y.; Go, S.; Oana, S.; Kawashima, H.	2021	Journal of clinical medicine	10	1	Jan-16	Does not meet minimum criteria for systematic review

The effectiveness of essential fatty acid, B vitamin, Vitamin	McCabe D, Colbeck M.	2015	JBI Database	13	7	104-18	Wrong patient population
C, magnesium and zinc supplementation for managing			System Rev				
stress in women: a systematic review protocol			Implement Rep				

## Table C-11. Excluded reviews, reason for exclusion – Arthritis/Osteoarthritis, Magnesium.

Title	Authors	Year	Journal	Volume	Issue	Pages	Exclusion reason
Systemic drug treatment for chronic musculoskeletal pain	Moulin, D. E.	2001	The Clinical journal of pain	17	4 Suppl	S86-93	Wrong patient population
Magnesium therapy in the treatment of chronic pain: a systematic review	Evan Oliver Matthews, Matthew Bryant, Aman Ahuja, Akhilesh Tiwari	2020	PROSPERO	CRD42020 164342	-	-	Wrong patient population

## Table C-12. Excluded reviews, reason for exclusion – hypertension, omega-3 fatty acids.

Title	Authors	Year	Journal	Volume	Issue	Pages	Exclusion reason
Omega-3 fatty acids and blood pressure	Cabo, J.; Alonso, R.; Mata, P.	2012	British Journal of Nutrition	107	SUPPL. 2	S195- S200	Does not meet minimum criteria for systematic review
Effect of omega-3 fish oil on cardiovascular risk in diabetes	McEwen, B.; Morel-Kopp, M. C.; Tofler, G.; Ward, C.	2010	The Diabetes educator	36	4	565-84	Does not meet minimum criteria for systematic review
Does fish oil lower blood pressure? A meta-analysis of controlled trials	Morris, M. C.; Sacks, F.; Rosner, B.	1993	Circulation	88	2	523-33	Does not meet minimum criteria for systematic review
Omega 3 fatty acids in cardiovascular disease risk factors: An updated systematic review of randomised clinical trials	Rangel-Huerta, O. D.; Gil, A.	2018	Clinical nutrition (Edinburgh, Scotland)	37	1	72-77	Does not meet minimum criteria for systematic review
Effects of monounsaturated fatty acids on cardiovascular risk factors: A systematic review and meta-analysis	Schwingshackl, L.; Strasser, B.; Hoffmann, G.	2011	Annals of Nutrition and Metabolism	59	2-4	176-186	Wrong intervention
Polyunsaturated fatty acids for the primary and secondary prevention of cardiovascular disease	Abdelhamid, A. S.; Martin, N.; Bridges, C.; Brainard, J. S.; Wang, X.; Brown, T. J.; Hanson, S.; Jimoh, O. F.; Ajabnoor, S. M.; Deane, K. H.; Song, F.; Hooper, L.	2018	The Cochrane database of systematic reviews	7	7	CD0123 45	Wrong intervention
Scientific evidence of the association between oral intake of OMEGA-3 and OMEGA-6 fatty acids and the metabolic syndrome in adolescents: A systematic review	Tureck, C.; Barboza, B. P.; Bricarello, L. P.; Retondario, A.; Alves, M. A.; de Moura Souza, A.; Fernandes, R.; de Vasconcelos, F. A. G.	2022	Nutrition, metabolism, and cardiovascular diseases: NMCD	32	12	2689- 2704	Wrong intervention
Omega-3 fatty acids for the primary and secondary prevention of cardiovascular disease	Abdelhamid, A. S.; Brown, T. J.; Brainard, J. S.; Biswas, P.; Thorpe, G. C.; Moore, H. J.; Deane, K. H.; Summerbell, C. D.; Worthington, H. V.; Song, F.; Hooper, L.	2020	The Cochrane database of systematic reviews	3	3	CD0031 77	Wrong intervention

Omega-3 Fatty Acids and Cardiovascular Disease: An Updated Systematic Review	Balk, E. M.; Adams, G. P.; Langberg, V.; Halladay, C.; Chung, M.; Lin, L.; Robertson, S.; Yip, A.; Steele, D.; Smith, B. T.; Lau, J.; Lichtenstein, A. H.; Trikalinos, T. A.	2016	Evidence report/technology assessment	-	223	1-1252	Wrong intervention
Scientific evidence on dietary intake/supplementation of omega-3 and 6 fatty acids and metabolic syndrome in adolescents: a systematic review	Tureck, C.; Barboza, B. P.; Bricarello, L. P.; Retondario, A.; Alves, M. A.; de Moura Souza, A.; Fernandes, R.; de Vasconcelos, F. A. G.	2022	Nutrition, metabolism, and cardiovascular diseases : NMCD	32	12	2689- 2704	Wrong intervention
Omega-3 supplementation in the treatment of overweight and obese children and adolescents: A systematic review	Curioni, C. C.; Alves, N. N. R.; Zago, L.	2019	Journal of Functional Foods	52	-	340-347	Wrong intervention
Omega-3 polyunsaturated fatty acids favourably modulate cardiometabolic biomarkers in type 2 diabetes: a meta- analysis and meta-regression of randomized controlled trials	O'Mahoney, L. L.; Matu, J.; Price, O. J.; Birch, K. M.; Ajjan, R. A.; Farrar, D.; Tapp, R.; West, D. J.; Deighton, K.; Campbell, M. D.	2018	Cardiovascular diabetology	17	1	98	Wrong intervention
Omega-3 Polyunsaturated Fatty Acids Intake and Blood Pressure: A Dose-Response Meta-Analysis of Randomized Controlled Trials	Zhang, X.; Ritonja, J. A.; Zhou, N.; Chen, B. E.; Li, X.	2022	Journal of the American Heart Association	11	11	e025071	Wrong intervention
Effect of supplementation of women in high-risk pregnancies with long-chain polyunsaturated fatty acids on pregnancy outcomes and growth measures at birth: a meta- analysis of randomized controlled trials	Horvath, A.; Koletzko, B.; Szajewska, H.	2007	The British journal of nutrition	98	2	253-9	Wrong outcomes
Fish Oil Supplementation does not Reduce Risks of Gestational Diabetes Mellitus, Pregnancy-Induced Hypertension, or Pre-Eclampsia: A Meta-Analysis of Randomized Controlled Trials	Chen, B.; Ji, X.; Zhang, L.; Hou, Z.; Li, C.; Tong, Y.	2015	Med Sci Monit	21	-	2322-30	Wrong outcomes
Omega-3 Fatty Acids and Maternal and Child Health: An Updated Systematic Review	Newberry, S. J.; Chung, M.; Booth, M.; Maglione, M. A.; Tang, A. M.; O'Hanlon, C. E.; Wang, D. D.; Okunogbe, A.; Huang, C.; Motala, A.; Trimmer, M.; Dudley, W.; Shanman, R.; Coker, T. R.; Shekelle, P. G.	2016	Evidence report/technology assessment	-	224	1-826	Wrong outcomes
Efficacy of n-3 fatty acids supplementation on the prevention of pregnancy induced-hypertension or preeclampsia: A systematic review and meta-analysis	Bakouei, F.; Delavar, M. A.; Mashayekh-Amiri, S.; Esmailzadeh, S.; Taheri, Z.	2020	Taiwanese journal of obstetrics & gynecology	59	1	8-15	Wrong outcomes
Impact of n-3 polyunsaturated fatty acid intake in pregnancy on maternal health and birth outcomes: systematic review and meta-analysis from randomized controlled trails	Abdelrahman, M. A.; Osama, H.; Saeed, H.; Madney, Y. M.; Harb, H. S.; Abdelrahim, M. E. A.	2022	Archives of gynecology and obstetrics	307	1	249-262	Wrong outcomes
Effect of diet- and lifestyle-based metabolic risk-modifying interventions on preeclampsia: a meta-analysis	Allen, R.; Rogozinska, E.; Sivarajasingam, P.; Khan, K. S.; Thangaratinam, S.	2014	Acta obstetricia et gynecologica Scandinavica	93	10	973-85	Wrong outcomes
Effects of n-3 polyunsaturated fatty acid supplementation on pregnancy outcomes: a systematic review and meta- analysis	Hao, Y.; Sun, X.; Wen, N.; Song, D.; Li, H.	2022	Archives of medical science : AMS	18	4	890-899	Wrong outcomes

Omega-3 long chain polyunsaturated fatty acids to prevent preterm birth : A systematic review and meta-analysis	Saccone, G.; Berghella, V.	2015	Obstetrics and gynecology	125	3	663-672	Wrong outcomes
Effect of n-3 long-chain polyunsaturated fatty acid intake during pregnancy on maternal, infant, and child health outcomes: a systematic review	lmhoff-Kunsch, B.; Briggs, V.; Goldenberg, T.; Ramakrishnan, U.	2012	Paediatric and perinatal epidemiology	26 Suppl 1	SUPPL. 1	91-107	Wrong outcomes
The effects of omega-3 fatty acids on diabetic nephropathy: A meta-analysis of randomized controlled trials	Chewcharat, A.; Chewcharat, P.; Rutirapong, A.; Papatheodorou, S.	2020	PloS one	15	2	e022831 5	Wrong patient population
Association of polyunsaturated fatty acids with improved heart rate variability and cardiovascular events in patients with end-stage renal disease receiving maintenance dialysis: a systematic review and meta-analysis of randomized controlled trials	Chou, C. L.; Chen, J. S.; Kang, Y. N.; Chen, Y. J.; Fang, T. C.	2021	Food & function	12	17	8090- 8099	Wrong patient population
Effect of omega-3 fatty acids supplementation on cardio- metabolic and oxidative stress parameters in patients with chronic kidney disease: a systematic review and meta- analysis	Fazelian, S.; Moradi, F.; Agah, S.; Hoseini, A.; Heydari, H.; Morvaridzadeh, M.; Omidi, A.; Pizarro, A. B.; Ghafouri, A.; Heshmati, J.	2021	BMC nephrology	22	1	160	Wrong patient population
Meta-analysis of the effects of n-3 polyunsaturated fatty acids on haematological and thrombogenic factors in type 2 diabetes	Hartweg, J.; Farmer, A. J.; Holman, R. R.; Neil, H. A.	2007	Diabetologia	50	2	250-8	Wrong patient population
Potential impact of omega-3 treatment on cardiovascular disease in type 2 diabetes	Hartweg, J.; Farmer, A. J.; Holman, R. R.; Neil, A.	2009	Current opinion in lipidology	20	1	30-Aug	Wrong patient population
Effects of Omega-3 Fatty Acids Supplementation on Serum Lipid Profile and Blood Pressure in Patients with Metabolic Syndrome: A Systematic Review and Meta-Analysis of Randomized Controlled Trials	Liu, Y. X.; Yu, J. H.; Sun, J. H.; Ma, W. Q.; Wang, J. J.; Sun, G. J.	2023	Foods (Basel, Switzerland)	12	4		Wrong patient population
Omega-3, omega-6, and total dietary polyunsaturated fat for treatment of atherosclerotic cardiovascular disease: a systematic review and meta-analysis	Luo, S., Hou, H., Wang, Y., Li, Y., Zhang, L., Zhang, H., Jin, Q., Wu, G., & Wang, X	2023	Food & function	15	3	1208– 1222	Wrong patient population
Omega-3 Polyunsaturated Fatty Acid Supplementation in Patients with Lower Extremity Arterial Disease	Su, M. I.; Cheng, Y. C.; Huang, Y. C.; Liu, C. W.	2021	Journal of the American College of Nutrition	41	4	383-391	Wrong patient population
The Differential Effects of Eicosapentaenoic Acid and Docosahexaenoic Acid on Cardiometabolic Risk Factors: A Systematic Review	Innes, J. K.; Calder, P. C.	2018	International journal of molecular sciences	19	2	532	Wrong patient population
Eicosapentaenoic acid and docosahexaenoic acid containing supplements modulate risk factors for cardiovascular disease: a meta-analysis of randomised placebo-control human clinical trials	AbuMweis, S.; Jew, S.; Tayyem, R.; Agraib, L.	2018	Journal of Human Nutrition and Dietetics	31	1	67-84	Wrong patient population
The impact of omega-3 fatty acid supplementation on glycemic control in patients with gestational diabetes: a	Gao, Li; Lin, Liyuan; Shan, Nan; Ren, Chun-Yan; Long, Xin; Sun, Yu-Han; Wang, Lan	2020	The journal of maternal-fetal & neonatal medicine	33	10	1767- 1773	Wrong patient population

systematic review and meta-analysis of randomized controlled studies.							
Does supplementation of diet with 'fish oil' reduce blood pressure? A meta-analysis of controlled clinical trials	Appel, L. J.; Miller, E. R.; Seidler, A. J.; Whelton, P. K.	1993	Archives of internal medicine	153	12	1429-38	Wrong patient population
Long-chain omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid and blood pressure: a meta-analysis of randomized controlled trials	Miller, P. E.; Van Elswyk, M.; Alexander, D. D.	2014	American journal of hypertension	27	7	885-96	Wrong patient population
Effect of alpha linolenic acid on cardiovascular risk markers: A systematic review	Wendland, E.; Farmer, A.; Glasziou, P.; Neil, A.	2006	Heart	92	2	166-169	Wrong patient population
Dietetic guidelines on food and nutrition in the secondary prevention of cardiovascular disease - Evidence from systematic reviews of randomized controlled trials (second update, January 2006)	Mead, A.; Atkinson, G.; Albin, D.; Alphey, D.; Baic, S.; Boyd, O.; Cadigan, L.; Clutton, L.; Craig, L.; Flanagan, C.; Greene, P.; Griffiths, E.; Lee, N. J.; Li, M.; McKechnie, L.; Ottaway, J.; Paterson, K.; Perrin, L.; Rigby, P.; Stone, D.; Vine, R.; Whitehead, J.; Wray, L.; Hooper, L.	2006	Journal of Human Nutrition and Dietetics	19	6	401-419	Wrong study type
Fish consumption in multiple health outcomes: an umbrella review of meta-analyses of observational and clinical studies	Zhao, H.; Wang, M.; Peng, X.; Zhong, L.; Liu, X.; Shi, Y.; Li, Y.; Chen, Y.; Tang, S.	2023	Annals of translational medicine	11	3	152	Wrong study type
Omega-3 fatty acid supplementation and major cardiovascular outcomes: an umbrella review and meta- analyses of observational studies and randomized controlled trials	Choi H, Kim JY, Lee KH, Kim JS, Lee JY, Choi EK, Seong HJ, Kim G, Park H, Jung E, Hong SH, Kronbichler A, Eisenhut M, Koyanagi A, Jacob L, Yon DK, Lee SW, Kim MS, Kostev K, Shin JI, Yang JW, Smith L.	2021	Eur Rev Med Pharmacol Sci	25	4	2079- 2092	Wrong study type
The beneficial effects of omega-3 polyunsaturated fatty acids on controlling blood pressure: An umbrella meta- analysis	Musazadeh, V.; Kavyani, Z.; Naghshbandi, B.; Dehghan, P.; Vajdi, M.	2022	Frontiers in nutrition	9		985451	Wrong study type
The effects of nutrition interventions on adverse perinatal outcomes: an umbrella reviews of systematic review and meta-analysis	Xiyuan Deng, Yongxiu Yang Kehu Yang Bei Pan Qingmei Sun Xiaojuan Lin	2023	PROSPERO	CRD42023 418843	-	-	Wrong study type
Effect of omega-3 fatty acids and cardiometabolic outcomes: an umbrella review of meta-analysis	Javad Heshmati, Mahdi Sepidarkish	2021	PROSPERO	CRD42021 258098	-	-	Wrong study type
Is omega 3, omega 6, or a-linolenic acid worth taking? Umbrella review with the quantitative synthesis of randomized controlled trials for cardiovascular and non- cardiovascular outcomes	Min Seo Kim, Hye Chang Rhim	2020	PROSPERO	CRD42020 176539	-	-	Wrong study type
The effect of omega-3 fatty acids supplementation on blood pressure in adults: an umbrella of meta-analysis	parvin dehghan, Vali Musazadeh	2022	PROSPERO	CRD42022 311888	-	-	Wrong study type

#### Table C-13. Excluded reviews, reason for exclusion – fibromyalgia, magnesium.

Title	Authors	Year	Journal	Volume	Issue	Pages	Exclusion reason
Efficacy and safety of magnesium for the management of chronic pain in adults: A systematic review	Park, R.; Ho, A. M. H.; Pickering, G.; Arendt- Nielsen, L.; Mohiuddin, M.; Gilron, I.	2020	Anesthesia and analgesia	131	3	764-775	Wrong patient population
Evidence-Based role of nutrients and antioxidants for chronic pain management in musculoskeletal frailty and sarcopenia in aging	Perna, S.; Alalwan, T. A.; Al-Thawadi, S.; Negro, M.; Parimbelli, M.; Cerullo, G.; Gasparri, C.; Guerriero, F.; Infantino, V.; Diana, M.; D'Antona, G.; Rondanelli, M.	2020	Geriatrics (Switzerland)	5	1	16	Wrong patient population
A Systematic Review and Mixed Treatment Comparison of the Efficacy of Pharmacological Treatments for Fibromyalgia	Choy, E.; Marshall, D.; Gabriel, Z. L.; Mitchell, S. A.; Gylee, E.; Dakin, H. A.	2011	Seminars in arthritis and rheumatism	41	3	335- 45.e6	Wrong intervention
Do nutritional factors interact with chronic musculoskeletal pain? A systematic review	Elma, O.; Yilmaz, S. T.; Coppieters, I.; Nijs, J.; Malfliet, A.; Deliens, T.; Deliens, T.; Clarys, P.; Coppieters, I.; Nijs, J.; Malfliet, A.; Coppieters, I.	2020	J. Clin. Med.	9	3	702	Wrong intervention
Systemic drug treatment for chronic musculoskeletal pain	Moulin, D. E.	2001	The Clinical journal of pain	17	4 Suppl	S86-93	Does not meet minimum criteria for systematic review

## Table C-14. Excluded reviews, reason for exclusion – recurrent infection/s, zinc.

Title	Authors	Year	Journal	Volume	Issue	Pages	Exclusion reason
Zinc for the prevention and treatment of SARS-CoV-2 and other acute viral respiratory infections: a rapid review	Arentz, S.; Hunter, J.; Yang, G.; Beardsley, J.; Myers, S. P.; Goldenberg, J.; Beardsley, J.; Myers, S. P.; Mertz, D.; Leeder, S.	2020	Advances in Integrative Medicine	7	4	252-260	Does not meet minimum criteria for systematic review
Use of topical zinc to prevent recurrent herpes simplex infection: review of literature and suggested protocols	Eby, G. A.; Halcomb, W. W.	1985	Med Hypotheses	17	2	157-65	Does not meet minimum criteria for systematic review
Nutritional factors in the pathogenesis of ear disease in children: a systematic review	Elemraid, M. A.; Mackenzie, I. J.; Fraser, W. D.; Brabin, B. J.	2009	Annals of tropical paediatrics	29	2	85-99	Does not meet minimum criteria for systematic review
The effect of therapeutic zinc supplementation among young children with selected infections: a review of the evidence	Haider, B. A.; Bhutta, Z. A.	2009	Food and Nutrition Bulletin	30	1 Suppl	S41-59	Does not meet minimum criteria for systematic review
Zinc supplementation in young children: A review of the literature focusing on diarrhoea prevention and treatment	Liberato, S. C.; Singh, G.; Mulholland, K.	2015	Clinical Nutrition	34	2	181-188	Does not meet minimum criteria for systematic review
Acute respiratory infection and pneumonia in India: a systematic review of literature for advocacy and action: UNICEF-PHFI series on newborn and child health, India	Mathew, J. L.; Patwari, A. K.; Gupta, P.; Shah, D.; Gera, T.; Gogia, S.; Mohan, P.; Panda, R.; Menon, S.	2011	Indian pediatrics	48	3	191-218	Does not meet minimum criteria for systematic review
Potential Role of Vitamins A, B, C, D and E in TB Treatment and Prevention: A Narrative Review	Patti, G.; Pellegrino, C.; Ricciardi, A.; Novara, R.; Cotugno, S.; Papagni, R.; Guido, G.; Totaro, V.; De Iaco, G.; Romanelli, F.; Stolfa, S.; Minardi, M. L.;	2021	Antibiotics (Basel, Switzerland)	10	11	1354	Does not meet minimum criteria for systematic review

	Ronga, L.; Fato, I.; Lattanzio, R.; Bavaro, D. F.; Gualano, G.; Sarmati, L.; Saracino, A.; Palmieri, F.; Di Gennaro, F.						
Preventive zinc supplementation among infants, preschoolers, and older prepubertal children	Brown, K. H.; Peerson, J. M.; Baker, S. K.; Hess, S. Y.; Brown, Kenneth H.; Peerson, Janet M.; Baker, Shawn K.; Hess, Sonja Y.	2009	Food & Nutrition Bulletin	30	1 Suppl	Dec-40	Does not meet minimum criteria for systematic review
A meta-analysis of the effects of oral zinc in the treatment of acute and persistent diarrhea	Lukacik, M.; Thomas, R. L.; Aranda, J. V.	2008	Pediatrics	121	2	326-36	Does not meet minimum criteria for systematic review
A systematic review and meta-analysis of multiple micronutrient supplementation for the prevention and treatment of ARTIs, and implications for COVID-19	Azza Sarfraz, Zouina Sarfraz Huma Ashraf Muzna Sarfraz Roshaan Ahmad	2022	Pak J Med Sci	38	4	-	Wrong intervention
Zinc Supplementation and the Prevention and Treatment of Sepsis in Young Infants: A Systematic Review and Meta- Analysis	Irfan, O.; Black, R. E.; Lassi, Z. S.; Bhutta, Z. A.	2022	Neonatology	119	2	164–175	Wrong patient population
Zinc supplementation for the prevention of pneumonia in children aged 2 months to 59 months	Lassi, Zohra S.; Moin, Anoosh; Bhutta, Zulfiqar A.	2016	Cochrane Database of Systematic Reviews	12		CD0059 78	Wrong patient population
Zinc to treat diarrhoea in children under the age of five in Africa	Melanie Ekani, Chris Caroll Charles Beck	2012	PROSPERO	CRD42012 002794	-	-	Wrong patient population
Complementary and alternative medicine for prevention and treatment of the common cold	Nahas, R.; Balla, A.	2011	Canadian Family Physician	57	1	31-36	Wrong patient population
The effect of zinc supplements in preventing and treating infections in older adults: protocol for a systematic review	Pernille Holm Ellegaard, Hanne Nygaard Rikke Stefan Kamper Charlotte Suetta Cecilia Lund	2023	PROSPERO	CRD42023 425505	-	-	Wrong patient population
Could nutrition modulate COVID-19 susceptibility and severity of disease? A systematic review	Philip Thomas, James; Zakary, Ali; Andrew, E. Armitage; Ana, Bonell; Carla, Cerami; Hal, Drakesmith; Modou, Jobe; Kerry, S. Jones; Zara, Liew; Sophie, E. Moore; Fernanda, Morales- Berstein; Helen, Nabwera; Behzad, Nadjm; Sant- Rayn, Pasricha; Pauline, Scheelbeek; Matt, J. Silver; Megan, R. Teh; Andrew, M. Prentice; Asher, Brenner; Yair, E. Lewis; Eran, Friedler; Yael, Gilboa; Sara, Sabach; Yuval, Alfiya; Uta, Cheruti; Nadav, Davidovitch; Natalya, Bilenko; Jacob, Moran-Gilad; Yakir, Berchenko; Itay, Bar-Or; Ariel, Kushmaro; Timothy, Spector; Claire, J. Steves	2020	PRSOPERO	CRD42020 186194	-	-	Wrong patient population
A systematic review of multivitamin and multimineral supplementation for infection	Stephen, A. I.; Avenell, A.	2006	Journal of Human Nutrition and Dietetics	19	3	179-190	Wrong patient population
Role of zinc administration in prevention of childhood diarrhea and respiratory illnesses: A meta-analysis	Aggarwal, R.; Sentz, J.; Miller, M. A.	2007	Pediatrics	119	6	1120- 1130	Wrong patient population

Zinc and selenium supplementation in COVID-19 prevention and treatment: a systematic review of the experimental studies	Balboni, E.; Zagnoli, F.; Filippini, T.; Fairweather- Tait, S. J.; Vinceti, M.	2022	Journal of trace elements in medicine and biology : organ of the Society for Minerals and Trace Elements (GMS)	71		126956	Wrong patient population
Effect of Zinc and vitamin A supplementation on tuberculosis treatment outcomes and clinical responses: a systematic review and meta-analysis	Wagnew F, Alene KA, Eshetie S, Wingfield T, Kelly M, Gray D	2022	BMJ Glob Health	7	9	e008625	Wrong patient population
Zinc for the prevention or treatment of acute viral respiratory tract infections in adults: a rapid systematic review and meta-analysis of randomised controlled trials	Hunter, J.; Arentz, S.; Goldenberg, J.; Yang, G.; Beardsley, J.; Myers, S. P.; Mertz, D.; Leeder, S.	2021	BMJ open	11	11	e047474	Wrong patient population
Benefits and risks of zinc for adults during covid-19: rapid systematic review and meta-analysis of randomised controlled trials	Jennifer, Hunter; Susan, Arentz; Joshua, Goldenberg; Dominik, Mertz; Guoyan, Yang; Jennifer, Beardsley; Stephen, P. Myers; Stephen, Leeder	2020	medRxiv	-	-	-	Wrong patient population
Interventions for High-Burden Infectious Diseases in Children and Adolescents: A Meta-analysis	Khan, D. S. A.; Naseem, R.; Salam, R. A.; Lassi, Z. S.; Das, J. K.; Bhutta, Z. A.	2022	Pediatrics	149	Suppl 5	-	Wrong patient population
Zinc supplementation for the promotion of growth and prevention of infections in infants less than six months of age	Lassi, Z. S.; Kurji, J.; Oliveira, C. S. D.; Moin, A.; Bhutta, Z. A.	2020	Cochrane Database of Systematic Reviews	2020	4	CD0102 05	Wrong patient population
Preventive zinc supplementation for children, and the effect of additional iron: A systematic review and meta-analysis	Mayo-Wilson, E.; Imdad, A.; Junior, J.; Dean, S.; Bhutta, Z. A.	2014	BMJ open	4	6	e004647	Wrong patient population
Therapeutic value of zinc supplementation in acute and persistent diarrhea: A systematic review	Patel, A.; Mamtani, M.; Dibley, M. J.; Badhoniya, N.; Kulkarni, H.	2010	PloS one	5	4	e10386	Wrong patient population
What zinc supplementation does and does not achieve in diarrhea prevention: a systematic review and meta-analysis	Patel, Archana B.; Mamtani, Manju; Badhoniya, Neetu; Kulkarni, Hemant	2011	BMC infectious diseases	11	1	122	Wrong patient population
Zinc supplementation for the prevention of acute lower respiratory infection in children in developing countries: meta-analysis and meta-regression of randomized trials	Roth, D. E.; Richard, S. A.; Black, R. E.	2010	International journal of epidemiology	39	3	795-808	Wrong patient population
Oral zinc for arterial and venous leg ulcers	Ewan, A. J. Wilkinson	2014	Cochrane Database of Systematic Reviews	9	9	CD0012 73	Wrong patient population
Zinc supplementation as an adjunct to standard therapy in childhood nephrotic syndrome - a systematic review	Bhatt, G. C.; Jain, S.; Das, R. R.	2016	World journal of clinical pediatrics	5	4	383-390	Wrong patient population
Nutrient supplementation for prevention of viral respiratory tract infections in healthy subjects: a systematic review and meta-analysis	Vlieg-Boerstra, B.; de Jong, N.; Meyer, R.; Agostoni, C.; De Cosmi, V.; Grimshaw, K.; Milani, G. P.; Muraro, A.; Oude Elberink, H.; Pali-Schöll, I.; Roduit, C.; Sasaki, M.; Skypala, I.; Solokowska,	2022	Allergy	77	5	1373- 1388	Wrong patient population

# Table C-15. Excluded reviews, reason for exclusion – Diabetes (Type II) (including metabolic syndrome), Antioxidants (specifically CoQ10 and ALA).

Title	Authors	Year	Journal	Volume	Issue	Pages	Exclusion reason
Nutritional supplementation for type 2 diabetes: A systematic review	Bartlett, H. E.; Eperjesi, F.	2008	Ophthalmic and Physiological Optics	28	6	503-523	Does not meet minimum criteria for systematic review
Role of Oral Antioxidant Supplementation in the Current Management of Diabetic Retinopathy	Alfonso-Muñoz, E. A.; Burggraaf-Sánchez de Las Matas, R.; Mataix Boronat, J.; Molina Martín, J. C.; Desco, C.	2021	International journal of molecular sciences	22	8		Does not meet minimum criteria for systematic review
Critical appraisal of the use of alpha lipoic acid (thioctic acid) in the treatment of symptomatic diabetic polyneuropathy	McIlduff, C. E.; Rutkove, S. B.	2011	Therapeutics and clinical risk management	7		377-85	Does not meet minimum criteria for systematic review
Effect of Coenzyme Q10 Supplementation on Diabetes Biomarkers: a Systematic Review and Meta-analysis of Randomized Controlled Clinical Trials	Moradi, Maedeh; Haghighatdoost, Fahimeh; Feizi, Awat; Azadbakht, Leila	2016	Archives of Iranian Medicine (AIM)	19	8	588-596	Does not meet minimum criteria for systematic review
A Case for Alpha-Lipoic Acid as an Alternative Treatment for Diabetic Polyneuropathy	Nguyen, N.; Takemoto, J. K.	2018	Journal of pharmacy & pharmaceutical sciences : a publication of the Canadian Society for Pharmaceutical Sciences, Societe canadienne des sciences pharmaceutiques	21	1s	177s- 191s	Does not meet minimum criteria for systematic review
Dietary supplements and glycemic control in patients with type 2 diabetes: a systematic review and meta-analysis	Georg Hoffmann, Melanie Lehner Lukas Schwingshackl	2017	PROSPERO	CRD42017 076434	-	-	Wrong intervention
Effect of Alpha-Lipoic Acid in the Treatment of Diabetic Neuropathy: A Systematic Review	Abubaker, S. A.; Alonazy, A. M.; Abdulrahman, A.	2022	Cureus	14	6	e25750	Wrong intervention
Efficacy of Alpha-lipoic Acid in The Management of Diabetes Mellitus: A Systematic Review and Meta-analysis	Ebada, M. A.; Fayed, N.; Fayed, L.; Alkanj, S.; Abdelkarim, A.; Farwati, H.; Hanafy, A.; Negida, A.; Ebada, M.; Noser, Y.	2019	Iranian journal of pharmaceutical research : IJPR	18	4	2144- 2156	Wrong intervention
Effects of coenzyme Q10 supplementation on lipid profile: A systematic review and meta-analysis	Arash karimi, Mahdi Vajdi	2022	PROSPERO	CRD42022 350490	-	-	Wrong outcomes

Effect of coenzyme Q10 supplementation on C-reactive protein: a systematic review and meta-analysis of randomized controlled trials	Mohsen Mohammadi Sartang, Zohreh Mazloom	2016	PROSPERO	CRD42016 043073	-	-	Wrong outcomes
The effects of alpha-lipoic acid supplementation on inflammatory markers among patients with metabolic syndrome and related disorders: A systematic review and meta-analysis of randomized controlled trials	Akbari, M.; Ostadmohammadi, V.; Tabrizi, R.; Mobini, M.; Lankarani, K. B.; Moosazadeh, M.; Heydari, S. T.; Chamani, M.; Kolahdooz, F.; Asemi, Z.	2018	Nutrition and Metabolism	15	1	39	Wrong outcomes
Coenzyme Q10 Supplementation Improves Adipokine Levels and Alleviates Inflammation and Lipid Peroxidation in Conditions of Metabolic Syndrome: A Meta-Analysis of Randomized Controlled Trials	Dludla, P. V.; Orlando, P.; Silvestri, S.; Marcheggiani, F.; Cirilli, I.; Nyambuya, T. M.; Mxinwa, V.; Mokgalaboni, K.; Nkambule, B. B.; Johnson, R.; Mazibuko-Mbeje, S. E.; Muller, C. J. F.; Louw, J.; Tiano, L.	2020	International journal of molecular sciences	21	9	3247	Wrong outcomes
Antioxidant for treatment of diabetic nephropathy: A systematic review and meta-analysis	Kandhare, A. D.; Mukherjee, A.; Bodhankar, S. L.	2017	Chemico- biological interactions	278		212-221	Wrong outcomes
The effects of coenzyme Q10 supplementation on lipid profiles among patients with metabolic diseases: a systematic review and meta-analysis of randomized controlled trials	Sharifi, N.; Tabrizi, R.; Moosazadeh, M.; Mirhosseini, N.; Lankarani, K. B.; Akbari, M.; Chamani, M.; Kolahdooz, F.; Asemi, Z.	2018	Current pharmaceutical design	24	23	2729- 2742	Wrong outcomes
Effects of Alpha-lipoic Acid Supplementation on Human Diabetic Nephropathy: A Systematic Review and Meta- analysis	Vakali, E.; Rigopoulos, D.; Carrillo, A. E.; Flouris, A. D.; Dinas, P. C.	2022	Curr Diabetes Rev	18	6	e140921 196457	Wrong outcomes
The effect of CoenzymeQ10 supplementation on circulating adipokine levels in adults: a systematic review and meta- analysis of controlled clinical trials	Amin Salehi-Abargouei, Fatemeh Moghtaderi Roya Sakhaei Sadegh Zarei	2018	PROSPERO	CRD42018 087959	-	-	Wrong patient population
Evaluating the Lipid-Lowering Effects of alpha-lipoic Acid Supplementation: A Systematic Review	Erickson, N.; Zafron, M.; Harding, S. V.; Marinangeli, C. P. F.; Rideout, T. C.	2020	Journal of Dietary Supplements	17	6	753-767	Wrong patient population
An updated systematic review and dose-response meta- analysis of the effects of alpha-lipoic acid supplementation on glycemic markers in adults	Mahmoudi-Nezhad, M.; Vajdi, M.; Farhangi, M. A.	2021	Nutrition	82		111041	Wrong patient population
A meta-analysis of randomized and placebo-controlled clinical trials suggests that coenzyme Q10 at low dose improves glucose and HbA1c levels	Stojanovic, M.; Radenkovic, M.	2017	Nutrition Research	38		1-Dec	Wrong patient population
Effects of coenzyme Q10 supplementation on metabolic profile in diabetes: a systematic review and meta-analysis	Suksomboon, N.; Poolsup, N.; Juanak, N.	2015	Journal of clinical pharmacy and therapeutics	40	4	413-418	Wrong patient population
The Effects of Coenzyme Q10 Supplementation on Blood Pressures Among Patients with Metabolic Diseases: A Systematic Review and Meta-analysis of Randomized Controlled Trials	Tabrizi, R.; Akbari, M.; Sharifi, N.; Lankarani, K. B.; Moosazadeh, M.; Kolahdooz, F.; Taghizadeh, M.; Asemi, Z.	2018	High blood pressure & cardiovascular prevention: the official journal of the Italian Society of Hypertension	25	1	41-50	Wrong patient population

Effects of coenzyme Q10 intervention on diabetic kidney disease: A systematic review and meta-analysis	Zhang, X.; Shi, Z.; Liu, Q.; Quan, H.; Cheng, X.	2019	Medicine	98	24	e15850	Wrong patient population
Dose-Response Effect of Coenzyme Q10 Supplementation on Blood Pressure among Patients with Cardiometabolic Disorders: A Grading of Recommendations Assessment, Development, and Evaluation (GRADE)-Assessed Systematic Review and Meta-Analysis of Randomized Controlled Trials	Zhao, D.; Liang, Y.; Dai, S.; Hou, S.; Liu, Z.; Liu, M.; Dong, X.; Zhan, Y.; Tian, Z.; Yang, Y.	2022	Advances in Nutrition	13	6	2180- 2194	Wrong patient population
Dietary antioxidative supplements and diabetic retinopathy; a systematic review	Tabatabaei-Malazy, O.; Ardeshirlarijani, E.; Namazi, N.; Nikfar, S.; Jalili, R. B.; Larijani, B.	2019	Journal of diabetes and metabolic disorders	18	2	705-716	Wrong study design

# C2 Citation details of evidence provided through the Department's public call for evidence.

This appendix documents the studies that were provided through the Department's public call for evidence for an overview on the effect of selected population-supplement pairs prioritised based on a naturopathic context.

The table is ordered by population-supplement pairing, then alphabetically.

#### Table C-16. Evidence provided through the Department's public call for evidence.

Relevant population- supplement pair	Author/s	Publicat ion year	Title of article	Name of journal or other source	Volume and issue number	Page numbers	Digital Object Identifier	Inclusion result	Exclusion reason
2	McCabe D, Lisy K, Lockwood C, Colbeck M.	2017	The impact of essential fatty acid, B vitamins, vitamin C, magnesium and zinc supplementation on stress levels in women: a systematic review.	JBI Database System Rev Implement Rep	15(2)	402-453	10.11124/JBISRIR- 2016-002965	Excluded	Duplicate citation (already identified in search)
3	Grace S, Barnes L, Reilly W, Vlass A, de Permentier P.	2018	An integrative review of dietetic and naturopathic approaches to functional bowel disorders.	Complementary Therapies in Medicine	41	67-80	http://dx.doi.org.ezpr oxy1.library.usyd.ed u.au/10.1016/j.ctim. 2018.09.004Abs	Excluded	Duplicate citation (already identified in search)
3	Hawrelak, J. A., Wohlmuth, H., Pattinson, M., Myers, S. P., Goldenberg, J. Z., Harnett, J., and Whitten, D. L.	2019	Western Herbal Medicines in the Treatment of Irritable Bowel Syndrome: A Systematic Review and Meta-analysis.	Complementary Therapies in Medicine	48		doi.org/10.1016/j.cti m.2019.102233	Excluded	Duplicate citation (already identified in search)
5	Bae JH, Kim G.	2018	Systematic review and meta-analysis of omega-3- fatty acids in elderly patients with depression.	Nutrition Research	1(50)	1-Sep	N/A	Included	N/A

5	Grosso G, Micek A, Marventano S, Castellano S, Mistretta A, Pajak A, Galvano F.	2016	Dietary n-3 PUFA, fish consumption and depression: A systematic review and meta- analysis of observational studies.	Journal of affective disorders	15(205)	269-281	10.1016/j.jad.2016.0 8.011	Excluded	Duplicate citation (already identified in search)
5	Grosso G, Pajak A, Marventano S, Castellano S, Galvano F, Bucolo C, Drago F, Caraci F.	2014	Role of omega-3 fatty acids in the treatment of depressive disorders: a comprehensive meta- analysis of randomized clinical trials.	PloS One	9(5)	96905	N/A	Excluded	Duplicate citation (already identified in search)
5	Lin PY, Chang CH, Chong MF, Chen H, Su KP.	2017	Polyunsaturated fatty acids in perinatal depression: a systematic review and meta-analysis.	Biological psychiatry	82(8)	560-569	N/A	Excluded	Wrong intervention
5	Liu Wei-Hong, Zhang Cheng-Gui, Gao Peng-Fei, Liu Heng, Yang Jian-Fang.	2017	Omega-3 Fatty acids as Monotherapy in Treating Depression in Pregnant Women: A Meta-Analysis of Randomized Controlled Trials.	Iranian Journal of Pharmaceutical Research	16(4)	1593–1599	N/A	Excluded	Duplicate citation (already identified in search)
5	Mocking RJ, Harmsen I, Assies J, Koeter MW, Ruhé H, Schene AH.	2016	Meta-analysis and meta-regression of omega-3 polyunsaturated fatty acid supplementation for major depressive disorder.	Translational psychiatry	6(3)	756	10.1038/tp.2016.29	Excluded	Duplicate citation (already identified in search)
5	Sarris J, Murphy J, Mischoulon D, Papakostas GI, Fava M, Berk M, Ng CH.	2016	Adjunctive nutraceuticals for depression: a systematic review and meta-analyses.	American Journal of Psychiatry	173(6)	575-587	N/A	Excluded	Wrong intervention (supplement provided as adjunct therapy only)
5	Veronese N, Stubbs B, Solmi M, Ajnakina O, Carvalho AF, Maggi S.	2018	Acetyl-l-carnitine supplementation and the treatment of depressive symptoms: A systematic review and meta-analysis.	Psychosomatic medicine	80(2)	154-159	N/A	Excluded	Wrong intervention
5	Yuhua Liao, Bo Xie, Huimin Zhang, Qian He, Lan Guo, M. Subramaniapillai, et al.	2019	Efficacy of omega-3 PUFAs in depression: A meta- analysis.	Translational Psychiatry	1	1	N/A	Excluded	Duplicate citation (already identified in search)
6	Arentz S, Smith CA, Abbott J, Bensoussan A.	2017	Nutritional supplements and herbal medicines for women with polycystic ovary syndrome; a systematic review and meta-analysis.	BMC complementary and alternative medicine	17:500		ISSN: 1472-6882	Excluded	Wrong patient population
10	Hsiao-Yean Chiu, Tu-Hsueh Yeh, Yin-Cheng Huang, Pin-Yuan Chen.	2016	Effects of Intravenous and Oral Magnesium on Reducing Migraine: A Meta-analysis of Randomized Controlled Trials.	Pain Physician	19	97-112	N/A	Excluded	Duplicate citation (already identified in search)
11	Abdulrazaq M, Innes JK, Calder PC.	2017	Effect of $\omega$ -3 polyunsaturated fatty acids on arthritic pain: A systematic review.	Nutrition	39	57-66	N/A	Excluded	Duplicate citation (already

									identified in search)
12	AbuMweis S, Jew S, Tayyem R, Agraib L.	2018	Eicosapentaenoic acid and docosahexaenoic acid containing supplements modulate risk factors for cardiovascular disease: a meta-analysis of randomised placebo-control human clinical trials.	Journal of human nutrition and dietetics	31(1)	67-84	N/A	Excluded	Wrong patient population
12	Becic T, Studenik C.	2018	Effects of Omega-3 Supplementation on Adipocytokines in Prediabetes and Type 2 Diabetes Mellitus: Systematic Review and Meta- Analysis of Randomized Controlled Trials.	Diabetes & Metabolism Journal	2	101	N/A	Excluded	Wrong outcomes
12	Farimani AR, Hariri M, Azimi- Nezhad M, Borji A, Zarei S, Hooshmand E.	2018	The effect of n-3 PUFAs on circulating adiponectin and leptin in patients with type 2 diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials.	Acta Diabetologica	55(7)	641–652	N/A	Excluded	Wrong outcomes
12	Gao L, Lin L, Shan N, Ren C-Y, Long X, Sun Y-H, et al.	2018	The impact of omega-3 fatty acid supplementation on glycemic control in patients with gestational diabetes: a systematic review and meta-analysis of randomized controlled studies.	The Journal Of Maternal-Fetal & Neonatal Medicine: The Official Journal Of The European Association Of Perinatal Medicine, The Federation Of Asia And Oceania Perinatal Societies, The International Society Of Perinatal Obstetricians.	29	1–7	N/A	Excluded	Wrong patient population
12	Guo X-F, Li K-L, Li J-M, Li D.	2019	Effects of EPA and DHA on blood pressure and inflammatory factors: a meta-analysis of randomized controlled trials.	Critical Reviews In Food Science And Nutrition	4	1–14	N/A	Excluded	Duplicate citation (already identified in search)
12	Innes J, Calder P.	2018	The differential effects of eicosapentaenoic acid and docosahexaenoic acid on cardiometabolic risk factors: a systematic review.	International journal of molecular sciences	19(2)	532	N/A	Excluded	Duplicate citation (already identified in search)
12	Leslie MA, Cohen DJ, Liddle DM, Robinson LE, Ma DW.	2015	A review of the effect of omega-3 polyunsaturated fatty acids on blood triacylglycerol levels in normolipidemic and borderline hyperlipidemic individuals.	Lipids in health and disease	14(1)	53	N/A	Excluded	Wrong outcomes
12	Miller E, Van Elswyk M, Alexander D.	2014	Long-chain omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid and blood	American journal of hypertension	27(7)	885-896	N/A	Excluded	Duplicate citation (already

			pressure: a meta-analysis of randomized controlled trials.						identified in search)
12	O'Mahoney LL, Matu J, Price OJ, Birch KM, Ajjan RA, Farrar D, Tapp R, West DJ, Deighton K, Campbell MD.	2018	Omega-3 polyunsaturated fatty acids favourably modulate cardiometabolic biomarkers in type 2 diabetes: a meta-analysis and meta-regression of randomized controlled trials.	Cardiovascular diabetology	17(1)	98	N/A	Excluded	Duplicate citation (already identified in search)
12	Rangel-Huerta OD, Gil A.	2018	Omega 3 fatty acids in cardiovascular disease risk factors: an updated systematic review of randomised clinical trials.	Clinical Nutrition	37(1)	72-77	N/A	Excluded	Duplicate citation (already identified in search)
14	Hu, X. Y., Wu, R. H., Logue, M., Blondel, C., Lai, L. Y. W., Stuart, B., Flower, A., Fei, Y. T., Moore, M., Shepherd, J., Liu, J. P. and Lewith, G	2017	Andrographis paniculata for symptomatic relief of acute respiratory tract infections in adults and children: A systematic review and meta-analysis	PLoS One	12(8)	e0181780	ISSN: 1932-6203 DOI: 10.1371/journal.pon e.0181780 PMCID: PMC5544222 Accession Number: 28783743	Excluded	Wrong intervention
15	Bolignano,D, Cernaro, V,Gembillo,G., Baggetta, R, Buemi, M, and D'Arrigo, G.	2017	Antioxidant agents for delaying diabetic kidney disease progression: A systematic review and meta-analysis	Plos One	12(6)	e0178699- e0178699	ISSN: 1932-6203 DOI: 10.1371/journal.pon e.0178699	Excluded	Duplicate citation (already identified in search)
15	Dludla PV, Dias SC, Obonye N, Johnson R, Louw J, Nkambule BB.	2018	A systematic review on the protective effect of N- acetyl cysteine against diabetes-associated cardiovascular complications.	American Journal of Cardiovascular Drugs	18(4)	283-298	N/A	Excluded	Duplicate citation (already identified in search)
15	Dludla PV, Nkambule BB, Dias SC, Johnson R.	2017	Cardioprotective potential of N-acetyl cysteine against hyperglycaemia-induced oxidative damage: a protocol for a systematic review.	Syst Rev	6(1)	96	10.1186/s13643- 017-0493-8	Excluded	Wrong intervention
-	Adams JB, Baral M, Geis E, et al	2009	Safety and efficacy of oral DMSA therapy for children with autism spectrum disorders: part Amedical results	BMC Clinical Pharmacology	9	16		Excluded	Not a systematic review
-	Adams JB, Baral M, Geis E, et al	2009	Safety and efficacy of oral DMSA therapy for children with autism spectrum disorders: Part B - Behavioral results	BMC Clinical Pharmacology	9	17		Excluded	Not a systematic review
-	Akbari M, Tabrizi R, Lankarani KB, Heydari ST, Karamali M, Kashanian M et al.	2018	The effects of folate supplementation on diabetes biomarkers among patients with metabolic diseases: a systematic review and meta-analysis of randomized controlled trials.	Horm Metab Res	50(2)	93-105	10.1055/s-0043- 125148	Excluded	Wrong intervention
-	Akison LK, Kuo J, Reid N, Boyd RN, Moritz KM.	2018	Effect of choline supplementation on neurological, cognitive, and behavioral outcomes in offspring arising from alcohol exposure during	Alcohol Clin Exp Res	42(9)	1591-1611	10.1111/acer.13817	Excluded	Wrong intervention

			development: a quantitative systematic review of clinical and preclinical studies.						
-	Alfaddagh A, Elajami TK, Ashfaque H, Saleh M, Bistrian BR, Welty FK.	2017	Effect of eicosapentaenoic and docosahexaenoic acids added to statin therapy on coronary artery plaque in patients with coronary artery disease: a randomized clinical trial.	J Am Heart Assoc	6(12)	6981	10.1161/JAHA.117.0 06981	Excluded	Not a systematic review
-	Ali A, Katz DL, Njike VY, et al	2011	Effect of fruit and vegetable concentrates on endothelial function in metabolic syndrome: a randomized controlled trial	Nutrition Journal	10(1)	72		Excluded	Not a systematic review
-	Ali A, Ma Y, Reynolds J, et al	2011	Chromium effects on glucose tolerance and insulin sensitivity in persons at risk for diabetes mellitus	Endocrine Practice	17(1)	16-25		Excluded	Rationale for TBD/exclusion
-	Ali A, Ma Y, Reynolds J, et al.	2011	Chromium picolinate for the prevention of type 2 diabetes	Treatment strategies Diabetes	3(1)	34		Excluded	Not a systematic review
-	Ali A, Weiss TR, McKee D, et al	2017	Efficacy of individualised diets in patients with irritable bowel syndrome: a randomised controlled trial	BMJ Open Gastroenterology	4(1)	E000164		Excluded	Not a systematic review
-	Allen J, Bradley RD	2011	Effects of oral glutathione supplementation on systemic oxidative stress biomarkers in human volunteers	Journal of Alternative & Complementary Medicine	17(9)	827-33		Excluded	Not a systematic review
-	Amini, L., Mojab, F., Jahanfar, S., Sepidarkish, M., Raoofi, Z., & Maleki-Hajiagha, A	2020	Efficacy of Salvia officinalis extract on the prevention of insulin resistance in euglycemic patients with polycystic ovary syndrome: A double-blinded placebo-controlled clinical trial.	Complementary Therapies in Medicine	48	102245	ISSN: 0965-2299	Excluded	Not a systematic review
-	Apaydin, E. A., Maher, A. R., Shanman, R., Booth, M. S., Miles, J. N., Sorbero, M. E. and Hempel, S.	2016	A systematic review of St. John's wort for major depressive disorder	Systematic Reviews	5(1)	148	10.1186/s13643- 016-0325-2	Excluded	Wrong intervention
-	Arankalle D, Wardle J, Nair PM	2016	Alternate hot and cold application in the management of heel pain: a pilot study	The Foot	29	25-Aug		Excluded	Not a systematic review
-	Arentz S, Smith CA, Abbott J, et al	2017	Combined lifestyle and herbal medicine in overweight women with polycystic ovary syndrome (PCOS): a randomized controlled trial	Phytotherapy Research	31(9)	1330-40		Excluded	Not a systematic review
-	Arentz, S; Smith,C.A., Abbott,J., Fahey,P., Cheema,BS. and Bensoussan, A.	2017	Combined lifestyle and herbal medicine in overweight women with polycystic ovary syndrome (PCOS): A randomized controlled trial	Phytotherapy research	31 (9)	1330-1340	ISSN: 0951-418X	Excluded	Not a systematic review
-	Asevedo E, Mendes AC, Berk M, Brietzke E.	2014	Systematic review of N-acetylcysteine in the treatment of addictions.	Braz J Psychiatry	36(2)	168-175	N/A	Excluded	Wrong patient population

-	Askari G, Nasiri M, Mozaffari- Khosravi H, Rezaie M, Bagheri- Bidakhavidi M, Sadeghi O.	2017	The effects of folic acid and pyridoxine supplementation on characteristics of migraine attacks in migraine patients with aura: A double- blind, randomized placebo-controlled, clinical trial.	Nutrition	38	74-79	10.1016/j.nut.2017.0 1.007	Excluded	Not a systematic review
-	Aucoin M, Cooley K, Anand L, et al.	2018	Adjunctive vitamin D in the treatment of non- remitted depression: lessons from a failed clinical trial	Complementary Therapies in Medicine	36	38-45		Excluded	Not a systematic review
-	Aycinena AC, Valdovinos C, Crew KD, et al	2017	Barriers to recruitment and adherence in a randomized controlled diet and exercise weight loss intervention among minority breast cancer survivors	Journal of Immigrant and Minority Health	19(1)	120-9		Excluded	Not a systematic review
-	Aycinena AC, Valdovinos C, Crew KD, et al.	2017	Barriers to recruitment and adherence in a randomized controlled diet and exercise weight loss intervention among minority breast cancer survivors	Journal of Immigrant and Minority Health	19(1)	120-9		Excluded	Not a systematic review
-	Balercia G, Buldreghini E, Vignini A, Tiano L, Paggi F, Amoroso S, Ricciardo-Lamonica G, Boscaro M, Lenzi A, Littarru, GP.	2009	Coenzyme Q10 treatment in infertile men with idiopathic asthenozoospermia: a placebo-controlled, double-blind randomized trial.	Fertility and Sterility.	91(5)	1785-92.	ISSN: 0015-0282	Excluded	Not a systematic review
-	Balercia, G.,F.Regoli, T. Armeni, A.Koverech,F.Mantero and M. Boscaro	2005	Placebo-controlled double-blind randomized trial on the use of L-carnitine, L-acetylcarnitine, or combined L-carnitine and L-acetylcarnitine in men with idiopathic asthenozoospermia.	Fertility and sterility	84(3)	662-671	ISSN: 0015-0282	Excluded	Not a systematic review
-	Balfour L, Spaans JN, Fergusson D, et al	2014	Micronutrient deficiency and treatment adherence in a randomized controlled trial of micronutrient supplementation in ART-naïve persons with HIV	PloS One	9(1)	e85607		Excluded	Not a systematic review
-	Banerjee B, Vadiraj H, Ram A, et al.	2007	Effects of an integrated yoga program in modulating psychological stress and radiation- induced genotoxic stress in breast cancer patients undergoing radiotherapy	Integrative Cancer Therapies	6(3)	242-50		Excluded	Not a systematic review
-	Barber GA, Weller CD, Gibson SJ.	2018	Effects and associations of nutrition in patients with venous leg ulcers: a systematic review.	Journal of advanced nursing	74(4)	774-787	N/A	Excluded	Wrong patient population
-	Bares JM, Berger J, Nelson JE, et al	2008	Silybin treatment is associated with reduction in serum ferritin in patients with chronic hepatitis C	Journal of Clinical Gastroenterology	42(8)	937-44		Excluded	Not a systematic review
-	Barnes, L., Barclay, L., McCaffery, K., & Aslani, P	2018	Complementary medicine products used in pregnancy and lactation and an examination of the information sources accessed pertaining to maternal health literacy: a systematic review of qualitative studies	BMC- Complementary and alternative medicine	18(1)	229	10.1186/s12906- 018-2283-9	Excluded	Wrong patient population
-	Barrie SA, Wright JV, Pizzorno JE, et al	1987	Comparative absorption of zinc picolinate, zinc citrate and zinc gluconate in humans	Agents and actions	21(1-2)	223-8		Excluded	Not a systematic review
-	Bayes J, Agrawal N, Schloss J.	2019	A pilot trial examining the absorption of oral forms of folate supplementation in a healthy population: a randomised control trial	Advances in Integrative Medicine	6(2)	51-57		Excluded	Not a systematic review
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-	Bayes, J, Agrawal, N, Schloss, J	2019	The Bioavailability of Various Oral Forms of Folate Supplementation in Healthy Populations and Animal Models: A Systematic Review	Journal of Alternative and Complementary Medicine	25(2)	169-180	10.1089/acm.2018.0 086	Excluded	Wrong patient population
-	Bayes, J, Agrawal, N, Schloss, J	2019	The Bioavailability of Various Oral Forms of Folate Supplementation in Healthy Populations and Animal Models: A Systematic Review	Journal of Alternative and Complementary Medicine	25(2)	169-180	10.1089/acm.2018.0 086	Excluded	Wrong patient population
-	Berardi JM, Logan AC, Rao AV	2008	Plant based dietary supplement increases urinary pH	Journal of the International Society of Sports Nutrition	5(1)	20-Jul		Excluded	Not a systematic review
-	Bertinato J, Simpson JR, Sherrard L, et al	2013	Zinc supplementation does not alter sensitive biomarkers of copper status in healthy boys	Journal of Nutrition	143(3)	284-9		Excluded	Not a systematic review
-	Bisgaard H, Stokholm J, Chawes BL, Vissing NH, Bjarnadóttir E, Schoos AM, et al.	2016	Fish oil-derived fatty acids in pregnancy and wheeze and asthma in offspring.	N Engl J Med	5(26)	2530-2539	10.1056/NEJMoa150 3734	Excluded	Not a systematic review
-	Bishop SK, Erdrich S, Karunasinghe N, et al.	2015	An investigation into the association between DNA damage and dietary fatty acid in men with prostate cancer	Nutrients	7(1)	405-22		Excluded	Not a systematic review
-	Bradbury J, Myers SP, Meyer B, et al	2017	Chronic psychological stress was not ameliorated by omega-3 eicosapentaenoic acid (EPA)	Frontiers in pharmacology	8	551		Excluded	Not a systematic review
-	Bradbury J, Myers SP, Oliver C	2004	An adaptogenic role for omega-3 fatty acids in stress; a randomised placebo controlled double blind intervention study (pilot) [ISRCTN22569553]	Nutrition Journal	3(1)	20		Excluded	Not a systematic review
-	Bradley R, Sherman KJ, Catz S, et al	2012	Adjunctive naturopathic care for type 2 diabetes: patient-reported and clinical outcomes after one year	BMC Complementary and Alternative Medicine	12(1)	44		Excluded	Not a systematic review
-	Bradley, Ryan; Harnett, Joanna; Cooley, Kieran; McIntyre, Erica; Goldenberg, Joshua; Adams, Jon	2019	Naturopathy as a Model of Prevention-Oriented, Patient-Centered Primary Care: A Disruptive Innovation in Health Care	55(9	Medicin a		mdpi.com/1010- 660X/55/9/603/htm#	Excluded	Article does not examine clinical studies of health outcomes of any elements of naturopathy.
-	Buhling, K. J., A. Schumacher, C. zu Eulenburg and E. Laakmann	2019	Influence of oral vitamin and mineral supplementation on male infertility: a meta- analysis and systematic review.	Reproductive biomedicine online.	Electroni c journal	Electronic	ISSN: 1472-6483	Excluded	Wrong patient population

-	Burr NE, Hull MA, Subramanian V.	2017	Folic acid supplementation may reduce colorectal cancer risk in patients with inflammatory bowel disease.	Journal of clinical gastroenterology	51 (3)	247-253	N/A	Excluded	Not a systematic review
-	Calabrese C, Berman SH, Babish JG, et al.	2000	A phase I trial of andrographolide in HIV positive patients and normal volunteers.	Phytotherapy Research	14(5)	333-8		Excluded	Not a systematic review
-	Calabrese C, Gregory WL, Leo M, et al	2008	Effects of a standardized Bacopa monnieri extract on cognitive performance, anxiety, and depression in the elderly: a randomized, double- blind, placebo-controlled trial	Journal of Alternative & Complementary Medicine	14(6)	707-13		Excluded	Not a systematic review
-	Calabrese C, Myer S, Munson S, et al	1999	A cross-over study of the effect of a single oral feeding of medium chain triglyceride oil vs. canola oil on post-ingestion plasma triglyceride levels in healthy men	Alternative Medicine Review	4(1)	23-Aug		Excluded	Not a systematic review
-	Camfield DA, Wetherell MA, Scholey AB, et al	2013	The effects of multivitamin supplementation on diurnal cortisol secretion and perceived stress	Nutrients	5(11)	4429-50		Excluded	Not a systematic review
-	Canhada S, Castro K, Perry IS, Luft VC.	2018	Omega-3 fatty acids' supplementation in Alzheimer's disease: A systematic review.	Nutritional neuroscience	21(8)	529-538	N/A	Excluded	Wrong patient population
-	Casanova MA, Medeiros F, Trindade M, Cohen C, Oigman W, Neves MF.	2017	Omega-3 fatty acids supplementation improves endothelial function and arterial stiffness in hypertensive patients with hypertriglyceridemia and high cardiovascular risk.	J Am Soc Hypertens	11(1)	Oct-19	10.1016/j.jash.2016. 10.004	Excluded	Not a systematic review
-	Caudill MA, Strupp BJ, Muscalu L, Nevins JEH, Canfield RL.	2018	Maternal choline supplementation during the third trimester of pregnancy improves infant information processing speed: a randomized, double-blind, controlled feeding study.	FASEB J	32 (4)	2172-2180	10.1096/fj.20170069 2RR	Excluded	Not a systematic review
-	Cazzola M, Calzetta L, Page C, Jardim J, Chuchalin AG, Rogliani P et al.	2015	Influence of N-acetylcysteine on chronic bronchitis or COPD exacerbations: a meta-analysis.	Eur Respir Rev	24(137)	451-461	10.1183/16000617.0 0002215	Excluded	Wrong intervention
-	Chandan, S., Mohan, B. P., Chandan, O. C., Ahmad, R., Challa, A., Tummala, H., and Adler, D. G.	2020	Curcumin use in ulcerative colitis: is it ready for prime time? A systematic review and meta- analysis of clinical trials.	Annals of Gastroenterology	33(1)	53	PMCID: PMC6928475 PMID: 31892798	Excluded	Wrong patient population
-	Chang JP, Su KP, Mondelli V, Pariante CM.	2018	Omega-3 polyunsaturated fatty acids in youths with attention deficit hyperactivity disorder: a systematic review and meta-analysis of clinical trials and biological studies.	Neuropsychophar macology	43(3)	534	10.1038/npp.2017.1 60	Excluded	Wrong patient population
-	Chen AC, Martin AJ, Choy B, Fernández-Peñas P, Dalziell RA, McKenzie CA et al.	2015	A phase 3 randomized trial of nicotinamide for skin-cancer chemoprevention.	N Engl J Med	373 (17)	1618-1626	10.1056/NEJMoa150 6197	Excluded	Not a systematic review
-	Chen H, Liu S, Ji L, Wu T, Ji Y, Zhou Y, et al.	2016	Folic acid supplementation mitigates Alzheimer's disease by reducing inflammation: a randomized controlled trial.	Mediators of Inflammation Epub	5912146	N/A	10.1155/2016/59121 46	Excluded	Not a systematic review

-	Chen LH, Wang YF, Xu QH, Chen SS.	2018	Omega-3 fatty acids as a treatment for non- alcoholic fatty liver disease in children: A systematic review and meta-analysis of randomized controlled trials.	Clinical Nutrition	37(2)	516-521	N/A	Excluded	Wrong patient population
-	Cheng YS, Tseng PT, Chen YW, Stubbs B, Yang WC, Chen TY, Wu CK, Lin PY.	2017	Supplementation of omega 3 fatty acids may improve hyperactivity, lethargy, and stereotypy in children with autism spectrum disorders: A meta- analysis of randomized controlled trials.	Neuropsychiatric disease and treatment	13	2531	N/A	Excluded	Wrong patient population
-	Cheraghi E, Mehranjani MS, Shariatzadeh MA, Esfahani MH, Ebrahimi Z.	2016	N-Acetylcysteine improves oocyte and embryo quality in polycystic ovary syndrome patients undergoing intracytoplasmic sperm injection: an alternative to metformin.	Reprod Fertil Dev	28(6)	723-731	10.1071/RD14182	Excluded	Not a systematic review
-	Cheras PA, Myers SP, Paul-Brent PA, et al	2010	Randomized double-blind placebo-controlled trial on the potential modes of action of SheaFlex70 in osteoarthritis	Phytotherapy Research	24 (8)	1126-31		Excluded	Not a systematic review
-	Childs J, Higgins D, Parker S, et al	2012	Abstract OT3-1-02: Phase II randomized study of combination immunotherapy with or without Polysaccharide Krestin (PSK®) concurrently with a HER2 ICD peptide-based vaccine and trastuzumab in patients with stage IV breast cancer	Cancer Research	72(4)	OT3-1-02		Excluded	Not a systematic review
-	Citronberg J, Bostick R, Ahearn T, et al	2013	Effects of ginger supplementation on cell-cycle biomarkers in the normal-appearing colonic mucosa of patients at increased risk for colorectal cancer: results from a pilot, randomized, and controlled trial	Cancer Prevention Research	6(4)	271		Excluded	Not a systematic review
-	Citronberg J, Bostick RM, Ruffin M, et al	2012	Ginger supplementation and the expression of BAX in the normal-appearing colorectal mucosa of sporadic colorectal adenoma patients: results from a pilot randomized, controlled trial	Pharm Biol	50(5)	629-30		Excluded	Not a systematic review
-	Cohen AJ, Richardson CR, Heisler M, et al.	2017	Increasing use of a healthy food incentive: a waiting room intervention among low-income patients	American Journal of Preventive Medicine	52(2)	154-62		Excluded	Not a systematic review
-	Cooley K, Szczurko O et al.	2009	Naturopathic Care for Anxiety: A randomised controlled study	PLoS One Journal	4(8)	1-Oct	10.1371/journal.pon e.0006628	Excluded	Not a systematic review
-	Cooley K, Szczurko O, Perri D, et al	2009	Naturopathic care for anxiety: a randomized controlled trial ISRCTN78958974	PLoS One	4(8)	e6628		Excluded	Not a systematic review
-	Cooley K, Szczurko O, Perri D, Mills EJ, Bernhardt B, et. al	2009	Naturopathic Care for Anxiety: A Randomized Controlled Trial ISRCTN78958974.	PLoS One	4(8)	e6628	doi:10.1371/journal. pone.0006628	Excluded	Not a systematic review

-	Cooley K, Szczurko O, Perri D, Mills EJ, Bernhardt B, Zhou Q, Seely D.	2009	Naturopathic care for anxiety: a randomized controlled trial	PloS One	4(8)	6628	10.1371/journal.pon e.0006628	Excluded	Not a systematic review
-	Cooley, K, Szczurko, O, Perri, D, Mills, EJ, Bernhardt, B, Zhou, Q and Seely, D	2009	Naturopathic care for anxiety: a randomized controlled trial ISRCTN78958974	PLoS One	4 (8)	e6628	ISSN: 1932-6203	Excluded	Not a systematic review
-	Coulson S, Butt H, Vecchio P, et al.	2013	Green-lipped mussel extract (Perna canaliculus) and glucosamine sulphate in patients with knee osteoarthritis: therapeutic efficacy and effects on gastrointestinal microbiota profiles	Inflammopharmac ology	21(1)	79-90		Excluded	Not a systematic review
-	Coulson S, Vecchio P, Gramotnev H, et al.	2012	Green-lipped mussel (Perna canaliculus) extract efficacy in knee osteoarthritis and improvement in gastrointestinal dysfunction: a pilot study	Inflammopharmac ology	20(2)	71-6		Excluded	Not a systematic review
-	Couto JP, Moreira R.	2018	Oral N-acetylcysteine in the treatment of obsessive-compulsive disorder: a systematic review of the clinical evidence.	Prog Neuropsychophar macol Biol Psychiatry	86	245-254	10.1016/j.pnpbp.201 8.06.005	Excluded	Wrong patient population
-	Cramer H, Lauche R, Hohmann C, et al.	2013	Randomized-controlled trial comparing yoga and home-based exercise for chronic neck pain.	Clin J Pain	29(3)	216-23		Excluded	Not a systematic review
-	Crew K, Ho K, Brown P, et al.	2015	Effects of a green tea extract, Polyphenon E, on systemic biomarkers of growth factor signalling in women with hormone receptor-negative breast cancer	Journal of Human Nutrition and Dietetics	28(3)	272-82		Excluded	Not a systematic review
-	Crew KD, Brown P, Greenlee H, et al.	2012	Phase IB randomized, double-blinded, placebo- controlled, dose escalation study of polyphenon E in women with hormone receptor-negative breast cancer	Cancer Prevention Research	5(9)	1144-54		Excluded	Not a systematic review
-	Crookes DM, Shelton RC, Tehranifar P, et al	2016	Social networks and social support for healthy eating among Latina breast cancer survivors: implications for social and behavioral interventions	Journal of Cancer Survivorship	10(2)	291-301		Excluded	Not a systematic review
-	de Bock, M, Derraik, JGB, Brennan, CM, Biggs, JB, Morgan, PE, Hodgkinson, SC, Hofman, PL and Cutfield, WS	2013	Olive (Olea europaea L.) leaf polyphenols improve insulin sensitivity in middle-aged overweight men: a randomized, placebo-controlled, crossover trial	PloS one	8(3)	e57622	ISSN: 1932-6203	Excluded	Not a systematic review
-	Delgado-Cruzata L, Zhang W, McDonald JA, et al	2015	Dietary modifications, weight loss, and changes in metabolic markers affect global DNA methylation in Hispanic, African American, and Afro- Caribbean breast cancer survivors	The Journal of Nutrition	145(4)	783-90		Excluded	Not a systematic review
-	Ding Y, Li Y, Wen A.	2015	Effect of niacin on lipids and glucose in patients with type 2 diabetes: a meta-analysis of randomized, controlled clinical trials.	Clinical Nutrition	5	838	10.1016/j.clnu.2014. 09.019	Excluded	Wrong intervention

-	Dinicola S, De Grazia S, Carlomagno G, Pintucci JP.	2014	N-acetylcysteine as powerful molecule to destroy bacterial biofilms. A systematic review.	Eur Rev Med Pharmacol Sci	18(19)	2942-2948	N/A	Excluded	Wrong patient population
-	Dobos G, Overhamm T, Büssing A, et al.	2014	Effects of a mindfulness-based day-care clinic in cancer survivors	Journal of Alternative & Complementary Medicine	20(5)	A53		Excluded	Not a systematic review
-	Duailibi MS, Cordeiro Q, Brietzke E, Ribeiro M, LaRowe S, Berk M, Trevizol AP.	2017	N-acetylcysteine in the treatment of craving in substance use disorders: Systematic review and meta-analysis.	The American journal on addictions	26(7)	660-666	N/A	Excluded	Wrong patient population
-	Ducrotté, P, Sawant, P, Jayanthi, V.	2012	Clinical trial: Lactobacillus plantarum 299v (DSM 9843) improves symptoms of irritable bowel syndrome	World Journal of Gastroenterology	18 (30)	4012-4018	10.374.8/wjg.v18.40 12	Excluded	Not a systematic review
-	Dugoua J, Perri D, Seely D, et al.	2012	The anti-diabetic and cholesterol-lowering effects of common and cassia cinnamon (Cinnamomum verum and C. aromaticum): a randomized controlled trial	BMC Complementary and Alternative Medicine	12(1)	P179		Excluded	Not a systematic review
-	Erdrich S, Bishop KS, Karunasinghe N, et al.	2015	A pilot study to investigate if New Zealand men with prostate cancer benefit from a Mediterranean-style diet.	PeerJ	3	E1080		Excluded	Not a systematic review
-	Faridi Z, Njike VY, Dutta S, et al	2008	Acute dark chocolate and cocoa ingestion and endothelial function: a randomized controlled crossover trial	The American Journal of Clinical Nutrition	88(1)	58-63		Excluded	Not a systematic review
-	Feathers A, Aycinena AC, Lovasi GS, et al	2015	Food environments are relevant to recruitment and adherence in dietary modification trials	Nutrition Research	35(6)	480-8		Excluded	Not a systematic review
-	Feathers A, Aycinena AC, Lovasi GS, et al.	2015	Food environments are relevant to recruitment and adherence in dietary modification trials.	Nutrition Research	35(6)	480-8		Excluded	Not a systematic review
-	Fen F, Zhang J, Wang Z, Wu Q, Zhou X.	2019	Efficacy and safety of N-acetylcysteine therapy for idiopathic pulmonary fibrosis: An updated systematic review and meta-analysis.	Experimental and Therapeutic Medicine	18(1)	802-816	N/A	Excluded	Wrong patient population
-	Fernandes BS, Dean OM, Dodd S, Malhi GS, Berk M.	2016	N-Acetylcysteine in depressive symptoms and functionality: a systematic review and meta- analysis.	J Clin Psychiatry	77(4)	457-466	10.4088/JCP.15r099 84	Excluded	Wrong intervention
-	Fernandez-Pareja A, Hernandez- Blanco E, Perez-Maceda JM, Rubio VJ, Palazuelos JH, Dalmau JM.	2007	Prevention of Osteoporosis Four-Year Follow-Up of a Cohort of Postmenopausal Women Treated with an Ossein-Hydroxyapatite Compound.	Clin Drug Invest	27(4)	227-232	N/A	Excluded	Not a systematic review
-	Finnell J, Bradley R, Bulayeva N, et al	2014	Vitamin D sufficiency status may effect circulating levels of the anti-aging protein klotho.	Journal of Alternative & Complementary Medicine	20(5)	A90-1		Excluded	Not a systematic review

-	Firth J, Stubbs B, Sarris J, Rosenbaum S, Teasdale S, Berk M, Yung AR.	2017	The effects of vitamin and mineral supplementation on symptoms of schizophrenia: a systematic review and meta-analysis.	Psychological medicine	47(9)	1515-1527		Excluded	Wrong patient population
-	Fleming S, Gutknecht NC	2010	Naturopathic and Primary Care Practice	Primary Care	37(1)	119-36	10.1016/j.pop.2009. 09.002	Excluded	Not a systematic review
-	Fowdar K, Chen H, He Z, Zhang J, Zhong X, Zhang J, Li M, Bai J.	2017	The effect of N-acetylcysteine on exacerbations of chronic obstructive pulmonary disease: A meta- analysis and systematic review.	Heart & Lung	46(2)	120-128	N/A	Excluded	Wrong patient population
-	Fruzzetti F, Perini D, Russo M, Bucci F, Gadducci A.	2017	Comparison of two insulin sensitizers, metformin and myo-inositol, in women with polycystic ovary syndrome (PCOS).	Gynecol Endocrinol	33(1)	39-42	10.1080/09513590.2 016.1236078	Excluded	Not a systematic review
-	Galvez I, Torres-Piles S	2018	Baleneotherapy, Immune System, and Stress Response: A Hormetic Strategy?	International Journal of Molecular Science	19(6)	1687	10.3390/ijms190616 87	Excluded	Not a systematic review
-	Gao H, Geng T, Huang T, Zhao Q.	2017	Fish oil supplementation and insulin sensitivity: a systematic review and meta-analysis.	Lipids in health and disease	16(1)	131	10.1186/s12944- 017-0528-0	Excluded	Not a priority population- supplement pair
-	Goldenberg J, Ward L, Day A, and Coole K	2019	Naturopathic Approaches to Irritable Bowel Syndrome—A Delphi Study	The Journal of Alternative and Complementary Medicine	25 (2)	227-233	doi.org/10.1089/acm .2018.0255	Excluded	Not a systematic review
-	Goldenberg, J, Ward, L, Day, A, Cooley, K	2019	Naturopathic Approaches to Irritable Bowel Syndrome—A Delphi Study	Journal of Alternative and Complementary Medicine	25(2)	227–233	10.1089/acm.2018.0 255	Excluded	Not a systematic review
-	Goldenberg, JZ, Ward, L, Day, A & Cooley, K	2019	Naturopathic Approaches to Irritable Bowel Syndrome—A Delphi Study	Journal of Alternative & Complementary Medicine	25(2)	227-233	10.1089/acm.2018.0 255	Excluded	Not a systematic review
-	Govindaraj R, Naik S, Manjunath N, et al.	2018	Add-on yoga therapy for social cognition in schizophrenia: a pilot study	International Journal of Yoga	11(3)	242		Excluded	Not a systematic review
-	Greenlee H, Atkinson C, Stanczyk FZ, et al.	2007	A pilot and feasibility study on the effects of naturopathic botanical and dietary interventions on sex steroid hormone metabolism in premenopausal women	Cancer Epidemiol Biomarkers Prev	16(8)	1601-9		Excluded	Not a systematic review
-	Greenlee H, Crew KD, Shao T, et al	2013	Phase II study of glucosamine with chondroitin on aromatase inhibitor-associated joint symptoms in women with breast cancer	Supportive Care in Cancer	21(4)	1077-87		Excluded	Not a systematic review
-	Greenlee H, Gaffney AO, Aycinena AC, et al	2015	; Cocinar Para Su Salud!: randomized controlled trial of a culturally based dietary intervention among Hispanic breast cancer survivors.	Journal of the Academy of Nutrition and Dietetics	115(5)	S42-56		Excluded	Not a systematic review

-	Greenlee H, Gaffney AO, Aycinena AC, et al.	2016	Long-term diet and biomarker changes after a short-term intervention among Hispanic breast cancer survivors: The; Cocinar Para Su Salud! randomized controlled trial.	Cancer Epidemiol Biomarkers Prev	25(11)	1491-502		Excluded	Not a systematic review
-	Greenlee H, Molmenti CLS, Crew KD, et al.	2016	Survivorship care plans and adherence to lifestyle recommendations among breast cancer survivors	Journal of Cancer Survivorship	10(6)	956-63		Excluded	Not a systematic review
-	Greenlee HA, Crew KD, Mata JM, et al.	2013	A pilot randomized controlled trial of a commercial diet and exercise weight loss program in minority breast cancer survivors	Obesity	21(1)	65-76		Excluded	Not a systematic review
-	Greenlee, H., C. Atkinson, F. Z. Stanczyk and J. W. Lampe	2007	A pilot and feasibility study on the effects of naturopathic botanical and dietary interventions on sex steroid hormone metabolism in premenopausal women.	Cancer Epidemiology and Prevention Biomarkers	16 (8)	1601- 1609.	ISSN: 1055-9965	Excluded	Not a systematic review
-	Guerrero-Romero, F et al.	2014	Oral Magnesium supplementation improves insulin sensitivity in non-diabetic subjects with insulin resistance. A double-blind placebo- controlled randomized trial.	Diabetes & Metabolism.	30 (3)	253–258	N/A	Excluded	Not a systematic review
-	Gunawan M, Braun L, Esmore D, et al	2009	Integrative wellness program for cardiac surgery patients: implementation and evaluation	Heart, Lung and Circulation	18	S259		Excluded	Not a systematic review
-	Guo X, Guo S, Miao Z, Li Z, Zhang H.	2018	Myo-inositol lowers the risk of developing gestational diabetic mellitus in pregnancies: A systematic review and meta-analysis of randomized controlled trials with trial sequential analysis.	J Diabetes Complications	32(3)	342-348	10.1016/j.jdiacomp. 2017.07.007	Excluded	Wrong intervention
-	Guo XF, Yang B, Tang J, Li D.	2018	Fatty acid and non-alcoholic fatty liver disease: meta-analyses of case-control and randomized controlled trials.	Clinical Nutrition	37(1)	113-122	10.1016/j.clnu.2017. 01.003	Excluded	Wrong patient population
-	Haghiac M, Yang XH, Presley L, Smith S, Dettelback S, Minium J, et al.	2015	Dietary omega-3 fatty acid supplementation reduces inflammation in obese pregnant women: a randomized double-blind controlled clinical trial.	PLoS One	10(9)	e0137309	10.1371/journal.pon e.0137309	Excluded	Not a systematic review
-	Hall,S.D, Wang, Zaiqi, Huang, Shiew-Mei, et al.	2003	The interaction between St John's wort and an oral contraceptive	Clinical Pharmacology & Therapeutics	74(6)	525-535	ISSN: 0009-9236	Excluded	Wrong intervention
-	Hansen S, Strøm M, Maslova E, Dahl R, Hoffmann HJ, Rytter D, et al.	2017	Fish oil supplementation during pregnancy and allergic respiratory disease in the adult offspring.	J Allergy Clin Immunol	139(1)	104-111	10.1016/j.jaci.2016.0 2.042	Excluded	Wrong patient population
-	Harnett J, Myers SP, Rolfe M	2016	Probiotics and the microbiome in celiac disease: a randomised controlled trial	Evidence-Based Complementary and Alternative Medicine	2016	Jan-16		Excluded	Not a systematic review

-	Harvey C, Schofield GM, Williden M, et al.	2018	The effect of medium chain triglycerides on time to nutritional ketosis and symptoms of keto- induction in healthy adults: a randomised controlled clinical trial	Journal of Nutrition and Metabolism	2018	1-Sep		Excluded	Not a systematic review
-	Hawrelak JA, Myers SP	2010	Effects of two natural medicine formulations on irritable bowel syndrome symptoms: a pilot study	Journal of Alternative & Complementary Medicine	16(10)	1065-71		Excluded	Not a systematic review
-	Hendren RL, James SJ, Widjaja F, Lawton B, Rosenblatt A, Bent S.	2016	Randomized, Placebo-Controlled Trial of Methyl B12 for Children with Autism.	J Child Adolesc Psychopharmacol	26 (9)	774-783	N/A	Excluded	Not a systematic review
-	Herman PM, Szczurko O, Cooley K, et al	2008	Cost-effectiveness of naturopathic care for chronic low back pain	Alternative Therapies in Health & Medicine	14 (2)			Excluded	Not a systematic review
-	Herman PM, Szczurko O, Cooley K, et al	2014	A naturopathic approach to the prevention of cardiovascular disease: cost-effectiveness analysis of a pragmatic multi-worksite randomized clinical trial	Journal of Occupational and Environmental Medicine	56(2)	171		Excluded	Not a systematic review
-	Herman PM, Szczurko O, Cooley K, Seely D.	2014	A naturopathic approach to the prevention of cardiovascular disease: cost-effectiveness analysis of a pragmatic multi-worksite randomized clinical trial	Journal of Occupational and Environmental Medicine	56(2)	171-176	10.1097/JOM.000000 0000000066	Excluded	Not a systematic review
-	Heron S, Yarnell E.	2001	The safety of low-dose Larrea tridentata (DC) Coville (creosote bush or chaparral): a retrospective clinical study	Journal of Alternative & Complementary Medicine	7(2)	175-85		Excluded	Not a systematic review
-	Hershman DL, Unger JM, Crew KD, et al	2013	Randomized double-blind placebo-controlled trial of acetyl-L-carnitine for the prevention of taxane- induced neuropathy in women undergoing adjuvant breast cancer therapy	Journal of Clinical Oncology	31(20)	2627-33		Excluded	Not a systematic review
-	Hershman DL, Unger JM, Crew KD, et al	2015	Randomized multicenter placebo-controlled trial of omega-3 fatty acids for the control of aromatase inhibitor–induced musculoskeletal pain: SWOG S0927	Journal of Clinical Oncology	33(17)	1910-17		Excluded	Not a systematic review
-	Hershman DL, Unger JM, Crew KD, et al	2018	Two-year trends of taxane-induced neuropathy in women enrolled in a randomized trial of acetyl-l-carnitine (SWOG S0715)	Journal of Clinical Oncology	35(Suppl 15)			Excluded	Not a systematic review
-	Hershman DL, Unger JM, Crew KD, et al.	2018	Two-year trends of taxane-induced neuropathy in women enrolled in a randomized trial of acetyl-l-carnitine (SWOG S0715).	J Natl Cancer Inst	110(6)	669-76		Excluded	Not a systematic review
-	Houghton, Christine A	2019	Sulforaphane: Its "Coming of Age" as a Clinically Relevant Nutraceutical in the Prevention and Treatment of Chronic Disease	Oxidative Medicine and Cellular Longevity	2019	46388	doi.org/10.1155/201 9/2716870	Excluded	Not a systematic review

-	Irani M, Amirian M, Sadeghi R, Le Lez J, Roudsari RL.	2017	The effect of folate and folate plus zinc supplementation on endocrine parameters and sperm characteristics in sub-fertile men: a systematic review and meta-analysis.	Urology journal	14(5)	4069-4078	N/A	Excluded	Wrong intervention
-	Jamilian M, Samimi M, Ebrahimi FA, Hashemi T, Taghizadeh M, Razavi M, et al.	2017	The effects of vitamin D and omega-3 fatty acid co-supplementation on glycemic control and lipid concentrations in patients with gestational diabetes.	J Clin Lipidol	11(2)	459-468	10.1016/j.jacl.2017.0 1.011	Excluded	Not a systematic review
-	Jang H, Park K.	2019	Omega-3 and omega-6 polyunsaturated fatty acids and metabolic syndrome: A systematic review and meta-analysis.	Clinical Nutrition	N/A	N/A	N/A	Excluded	Not a priority population- supplement pair
-	Javanmanesh, Kashanian, Rahimi, Sheikhansari.	2016	A comparison between the effects of metformin and N-acetyl cysteine (NAC) on some metabolic and endocrine characteristics of women with polycystic ovary syndrome.	Gynecol Endocrinol	32(4)	285-289	10.3109/09513590.2 015.1115974	Excluded	Not a systematic review
-	Jayedi A, Zargar MS.	2018	Intake of vitamin B6, folate, and vitamin B12 and risk of coronary heart disease: A systematic review and dose-response meta-analysis of prospective cohort studies.	Critical reviews in food science and nutrition	1	1	N/A	Excluded	Wrong intervention
-	Jiang DQ, Zhao SH, Li MX, Jiang LL, Wang Y, Wang Y.	2018	Prostaglandin E1 plus methylcobalamin combination therapy versus prostaglandin E1 monotherapy for patients with diabetic peripheral neuropathy: A meta-analysis of randomized controlled trials.	Medicine	97(44)	N/A	N/A	Excluded	Wrong intervention
-	Jiang Y, Turgeon DK, Wright BD, et al	2013	Effect of ginger root on cyclooxygenase-1 and 15- hydroxyprostaglandin dehydrogenase expression in colonic mucosa of humans at normal and increased risk of colorectal cancer	Eur J Cancer Prev	22(5)	455		Excluded	Not a systematic review
-	Jolfaie NR, Mirzaie S, Ghiasvand R, Askari G, Miraghajani M.	2015	The effect of glutamine intake on complications of colorectal and colon cancer treatment: A systematic review.	J Res Med Sci	20(9)	910-918	10.4103/1735- 1995.170634	Excluded	Wrong intervention
-	Joseph B, Nair PM, Nanda A	2015	Effects of naturopathy and yoga intervention on CD4 count of the individuals receiving antiretroviral therapy-report from a human immunodeficiency virus sanatorium, Pune	International Journal of Yoga	8(2)	122		Excluded	Not a systematic review
-	Jung JY, Kwon HH, Hong JS, Yoon JY, Park MS, Jang MY et al.	2014	Effect of dietary supplementation with omega-3 fatty acid and gamma-linolenic acid on acne vulgaris: a randomised, double-blind, controlled trial.	Acta Derm Venereol	94(5)	521-525	10.2340/00015555- 1802	Excluded	Not a systematic review
-	Kamenova P.	2006	Improvement of insulin sensitivity in patients with type 2 diabetes mellitus after oral administration of alpha-lipoic acid.	Hormones (Athens)	5	251–258	N/A	Excluded	Not a systematic review

-	Kar S, Wong M, Rogozinska E, Thangaratinam S.	2016	Effects of omega-3 fatty acids in prevention of early preterm delivery: a systematic review and meta-analysis of randomized studies.	European Journal of Obstetrics & Gynecology and Reproductive Biology	198	40-46	10.1016/j.ejogrb.201 5.11.033	Excluded	Wrong patient population
-	Kastelein JJ, Maki KC, Susekov A, Ezhov M, Nordestgaard BG, Machielse BN, et al.	2014	Omega-3 free fatty acids for the treatment of severe hypertriglyceridemia: the Epanova for Lowering Very high triglycerides (EVOLVE) trial.	J Clin Lipidol	8(1)	94-106	10.1016/j.jacl.2013.1 0.003	Excluded	Not a systematic review
-	Kazaks AG, Uriu-Adams JY, Albertson TE, Shenoy S, Stern JS	2010	Effect of Oral Magnesium Supplementation on Measures of Airway Resistance and Subjective Assessment of Asthma Control and Quality of Life in Men and Women with Mild to Moderate Asthma: A Randomized Placebo Controlled Trial.	Journal of Asthma	47 (1)	83-92	N/A	Excluded	Not a systematic review
-	Kean JD, Sarris J, Scholey A, et al	2017	Reduced inattention and hyperactivity and improved cognition after marine oil extract (PCSO-524®) supplementation in children and adolescents with clinical and subclinical symptoms of attention-deficit hyperactivity disorder (ADHD): a randomised, double-b	Psychopharmacol ogy	234(3)	403-20		Excluded	Not a systematic review
-	Kennedy DA, Lewis E, Cooley K, et al.	2014	An exploratory comparative investigation of Food Allergy/Sensitivity Testing in IBS (The FAST Study): a comparison between various laboratory methods and an elimination diet	Advances in Integrative Medicine	1(3)	124-30		Excluded	Not a systematic review
-	Kessopoulou, E., H. J. Powers, K. K. Sharma, M. J. Pearson, J. M. Russell, I. D. Cooke and C. L. Barratt	1995	A double-blind randomized placebo cross-over controlled trial using the antioxidant vitamin E to treat reactive oxygen species associated male infertility.	Fertility and sterility	64(4):	825-831	ISSN: 0015-0282	Excluded	Not a systematic review
-	Kim CH, Han KA, Yu J, Lee SH, Jeon HK, Kim SH, et al.	2018	Efficacy and safety of adding omega-3 fatty acids in statin-treated patients with residual hypertriglyceridemia: ROMANTIC (Rosuvastatin- OMAcor in residual hyperTriglyceridemia), a randomized, double-blind, and placebo- controlled trial.	Clin Ther	40(1)	83-94	10.1016/j.clinthera.2 017.11.007	Excluded	Not a systematic review
-	Kim LS, Hilli L, Orlowski J, et al	2006	Efficacy of probiotics and nutrients in functional gastrointestinal disorders: a preliminary clinical trial	Digestive Diseases and Sciences	51(12)	2134-44		Excluded	Not a systematic review
-	Kim LS, Hilli L, Orlowski J, et al.	2006	Efficacy of probiotics and nutrients in functional gastrointestinal disorders: a preliminary clinical trial	Digestive Diseases and Sciences	51(12	2134-44		Excluded	Not a systematic review
-	Kisan R, Sujan M, Adoor M, et al.	2014	Effect of yoga on migraine: A comprehensive study using clinical profile and cardiac autonomic functions.	International Journal of Yoga	7(2)	126		Excluded	Not a systematic review

-	Koutoubi S, Heiselmann PR, Murdoch S, et al	2008	Changes in consumer knowledge and behavioral intention toward genetically engineered (GE) foods	FASEB J	22 (1Suppl)	681.9-81.9		Excluded	Not a systematic review
-	Krishnamurthy MN, Telles S	2007	Assessing depression following two ancient Indian interventions: effects of yoga and ayurveda on older adults in a residential home	J Gerontol Nurs	33(2)	17-23		Excluded	Not a systematic review
-	Kristensen S, Schmidt EB, Schlemmer A, Rasmussen C, Johansen MB, Christensen JH.	2018	Beneficial effect of n-3 polyunsaturated fatty acids on inflammation and analgesic use in psoriatic arthritis: a randomized, double blind, placebo-controlled trial.	Scand J Rheumatol	47(1)	27-36	10.1080/03009742.2 017.1287304	Excluded	Not a systematic review
-	Laganà AS, Vitagliano A, Noventa M, Ambrosini G, D'Anna R.	2018	Myo-inositol supplementation reduces the amount of gonadotropins and length of ovarian stimulation in women undergoing IVF: a systematic review and meta-analysis of randomized controlled trials.	Arch Gynecol Obstet	298(4)	675-684	10.1007/s00404- 018-4861-y	Excluded	Wrong intervention
-	Lakhan, S. E., Ford, C. T. and Tepper, D	2015	Zingiberaceae extracts for pain: a systematic review and meta-analysis	Journal of Nutrition	14	50	ISSN: 1475-2891 DOI: 10.1186/s12937- 015-0038-8 PMCID: PMC4436156 Accession Number: 25972154	Excluded	Wrong intervention
-	Langhurst J, Musial F et al.	2009	Efficacy of Hydrotherapy in Fibromyalgia syndrome- a meta-analysis of randomized controlled clinical trials	Rheumatology (Oxford)	48(9)	1156-1159	10.1093/rheumatolo gy/kep182	Excluded	Wrong intervention
-	Lauche R, Stumpe C, Fehr J, et al.	2016	The effects of tai chi and neck exercises in the treatment of chronic nonspecific neck pain: a randomized controlled trial	The Journal of Pain	17(9)	101-27		Excluded	Not a systematic review
-	Laviano A, Molfino A, Lacaria MT, Canelli A, De Leo S, Preziosa I, et al.	2014	Glutamine supplementation favors weight loss in nondieting obese female patients. A pilot study.	Eur J Clin Nutr	68(11)	1264-1266	10.1038/ejcn.2014.1 84	Excluded	Not a systematic review
-	Leach MJ, Pincombe J, Foster G	2006	Clinical efficacy of horsechestnut seed extract in the treatment of venous ulceration	Journal of Wound Care	15(4)	159-67		Excluded	Not a systematic review
-	Leech, B, Schloss, J & Steel, A	2018	Investigation into complementary and integrative medicine practitioners' clinical experience of intestinal permeability: A cross-sectional survey.	Complementary therapies in clinical practice	31	200-209	doi.org/10.1016/j.ctc p.2018.02.014	Excluded	Not a systematic review
-	Lenzi, A., P. Sgro, P. Salacone, D. Paoli, B. Gilio, F. Lombardo, M. Santulli, A. Agarwal and L. Gandini	2004	A placebo-controlled double-blind randomized trial of the use of combined l-carnitine and l- acetyl-carnitine treatment in men with asthenozoospermia.:.	Fertility and sterility	81(6)	1578-1584	ISSN: 0015-0282	Excluded	Not a systematic review

-	Leombruni P, Miniotti M, Colonna F, Sica C, Castelli L, Bruzzone M, et al.	2015	A randomised controlled trial comparing duloxetine and acetyl L-carnitine in fibromyalgic patients: preliminary data.	Clin Exp Rheumatol	33(1 Suppl 88)	S82-85	N/A	Excluded	Not a systematic review
-	Leung HW, Chan AL.	2016	Glutamine in alleviation of radiation-induced severe oral mucositis: a meta-analysis.	Nutr Cancer	68(5)	734-742	10.1080/01635581.2 016.1159700	Excluded	Wrong intervention
-	Li S, Chen X, Li Q, Du J, Liu Z, Peng Y, et al.	2016	Effects of acetyl-L-carnitine and methylcobalamin for diabetic peripheral neuropathy: A multicenter, randomized, double-blind, controlled trial.	J Diabetes Investig	7(5)	777-785	10.1111/jdi.12493	Excluded	Not a systematic review
-	Li S, Li Q, Li Y, Li L, Tian H, Sun X.	2015	Acetyl-L-carnitine in the treatment of peripheral neuropathic pain: a systematic review and meta- analysis of randomized controlled trials.	PLoS One	10(3)	119479	10.1371/journal.pon e.0119479	Excluded	Wrong intervention
-	Lubna Fatima, Arshiya Sultana	2017	Efficacy of <i>Tribulus terrestris</i> L. (fruits) in menopausal transition symptoms: A randomized placebo controlled study	Advances in Integrative Medicine	4 (2)	56-65	doi.org/10.1016/j.ai med.2017.10.003	Excluded	Not a systematic review
-	MacRedmond R, Singhera G, Attridge S, Bahzad M, Fava C, Lai Y, Hallstrand TS, Dorscheid DR.	2010	Conjugated linoleic acid improves airway hyper- reactivity in overweight mild asthmatics.	Clinical & Experimental Allergy	40	1071–1078	10.1111/j.1365- 2222.2010.03531.x	Excluded	Not a systematic review
-	Magge S, Lembo A.	2011	Complementary and Alternative Medicine for the Irritable Bowel Syndrome	Gastroenterology Clinics	40 (1)	245–253	N/A	Excluded	Not a systematic review
-	Maghsoumi-Norouzabad L, Mansoori A, Abed R, Shishehbor F.	2018	Effects of omega-3 fatty acids on the frequency, severity, and duration of migraine attacks: a systematic review and meta-analysis of randomized controlled trials.	Nutritional neuroscience	21(9)	614-623	10.1080/1028415X.2 017.1344371	Excluded	Not a priority population- supplement pair
-	Manjunath N, Telles S	2003	Effects of sirsasana (headstand) practice on autonomic and respiratory variables	Indian Journal of Physiology and Pharmacology	47(1)	34-42		Excluded	Not a systematic review
-	Manjunath N, Telles S	2001	Improved performance in the Tower of London test following yoga	Indian Journal of Physiology and Pharmacology	45(3)	351-4		Excluded	Not a systematic review
-	Manjunath N, Telles S	1999	Improvement in visual perceptual sensitivity in children following yoga training	Journal of Indian Psychology	17(2)	41-5		Excluded	Not a systematic review
-	Manjunath N, Telles S	1999	Factors influencing changes in tweezer dexterity scores following yoga training	Indian Journal of Physiology and Pharmacology	43	225-9		Excluded	Not a systematic review
-	Marchioli R, Barzi F, Bomba E, Ch ieffo C, Di Gregorio D, Di Mascio R, Franzosi MG, Geraci E,Levantesi G, Maggioni AP, Mantini L, Marfisi RM, Mastrogiuseppe G, Mininni N, Nic olosi GL, Santini M, Schweiger C,	2002	GISSI-Prevenzione Investigators. Early protection against sudden death by n-3 polyunsaturated fatty acids after myocardial infarction: time-course analysis of the results of the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI)-Prevenzione.	Circulation	105	1897–1903	N/A	Excluded	Not a systematic review

	Tavazzi L, Tognoni G, Tucci C, Val agussa F.								
-	Maroon JC, Boost JW.	2006	Omega 3 (fish oil) fatty acids as an anti- inflammatory: an alternative to non-steroidal anti- inflammatory drugs for discogenic pain.	Surgical Neurology	65	326-331	N/A	Excluded	Not a systematic review
-	Mazahery H, Stonehouse W, Delshad M, Kruger M, Conlon C, Beck K, von Hurst P.	2017	Relationship between long chain n-3 polyunsaturated fatty acids and autism spectrum disorder: systematic review and meta-analysis of case-control and randomised controlled trials.	Nutrients	9(2)	155	N/A	Excluded	Wrong patient population
-	McCrory M, Roberts S, Gehrke M, et al	2008	Dietary variety increases ad-libitum energy intake more than does dietary fat: a 13-day randomized feeding trial	Obesity	16	S231-32		Excluded	Not a systematic review
-	McCrory M, Roberts S, Gehrke M, et al	2008	Dietary variety increases ad-libitum energy intake more than does dietary fat: a 13-day randomized feeding trial	Obesity	16	S231-32		Excluded	Not a systematic review
-	McCrory MA, Gehrke MM, Eldridge GC, et al.	2006	Taste preferences: biobehavioural and nutrient correlates	FASEB J	20(4)	A175-75		Excluded	Not a systematic review
-	McDermott KA, Rao MR, Nagarathna R, et al.	2014	A yoga intervention for type 2 diabetes risk reduction: a pilot randomized controlled trial.	BMC Complementary and Alternative Medicine	14(1)	212		Excluded	Not a systematic review
-	McDougall J, Thomas LE, McDougall C, et al	2014	Effects of 7 days on an ad libitum low-fat vegan diet: the McDougall Program cohort	Nutrition Journal	13(1)	99		Excluded	Wrong intervention
-	McEwen BJ, Morel-Kopp M-C, Chen W, et al	2013	Effects of omega-3 polyunsaturated fatty acids on platelet function in healthy subjects and subjects with cardiovascular disease	Semin Thromb Hemost	39(01)	25-32		Excluded	Wrong patient population
-	McEwen BJ, Morel-Kopp M-C, Tofler GH, et al	2015	The effect of omega-3 polyunsaturated fatty acids on fibrin and thrombin generation in healthy subjects and subjects with cardiovascular disease	Semin Thromb Hemost	41(3)	315-22		Excluded	Wrong outcomes
-	McEwen BJ, Morel-Kopp MC, Tofler GH, Ward CM.	2015	The effect of omega-3 polyunsaturated fatty acids on fibrin and thrombin generation in healthy subjects and subjects with cardiovascular disease.	Seminars in thrombosis and hemostasis	41(3)	315-322	N/A	Excluded	Wrong outcomes
-	Mehdi Bahreini, Amir-Hossein Ramezani, Farideh Shishehbor, Anahita Mansoori.	2018	The effect of omega-3 on circulating adiponectin in adults with type 2 diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials.	Canadian Journal of Diabetes	42(5)	553–559	N/A	Excluded	Not a priority population- supplement pair
-	Menon R, Cribb L, Murphy J, et al	2017	Mitochondrial modifying nutrients in treating chronic fatigue syndrome: a 16-week open-label pilot study	Advances in Integrative Medicine	4(3)	109-14		Excluded	Not a systematic review

-	Mickleborough TD, Lindley MR, Ionescu AA, Fly AD.	2006	Protective effect of fish oil supplementation on exercise-induced bronchoconstriction in asthma.	Chest	129	39-49	10.1378/chest.129.1 .39	Excluded	Not a systematic review
-	Middleton P, Gomersall JC, Gould JF, Shepherd E, Olsen SF, Makrides M.	2018	Omega-3 fatty acid addition during pregnancy.	Cochrane Database of Systematic Reviews	11	N/A	N/A	Excluded	Wrong patient population
-	Milliman WB, Lamson DW, Brignall MS	2000	Hepatitis C: a retrospective study, literature review, and naturopathic protocol	Alternative Medicine Review	5(4)	355		Excluded	Wrong patient population
-	Mills E, Prousky J, Raskin G, et al	2003	The safety of over-the-counter niacin. A randomized placebo-controlled trial [ISRCTN18054903]	BMC Clinical Pharmacology	3(1)	4		Excluded	Not a systematic review
-	Miranti EH, Stolzenberg-Solomon R, Weinstein SJ, Selhub J, Mannisto S, Taylor PR, et al.	2017	Low vitamin B12 increases risk of gastric cancer: a prospective study of one-carbon metabolism nutrients and risk of upper gastrointestinal tract cancer.	Int J Cancer [Internet].	141 (6)	1120-1129	N/A	Excluded	Not a systematic review
-	Mirmasoumi G, Fazilati M, Foroozanfard F, Vahedpoor Z, Mahmoodi S, Taghizadeh M, et al.	2018	The effects of flaxseed oil omega-3 fatty acids supplementation on metabolic status of patients with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial.	Exp Clin Endocrinol Diabetes	126(4)	222-228	10.1055/s-0043- 119751	Excluded	Not a systematic review
-	Mischley LK, Conley KE, Shankland EG, et al	2016	Central nervous system uptake of intranasal glutathione in Parkinson's disease	NPJ Parkinson's Disease	2	1-Jun		Excluded	Not a systematic review
-	Mischley LK, Lau RC, Shankland EG, et al	2017	Phase IIb study of intranasal glutathione in Parkinson's disease	Journal of Parkinson's Disease	7(2)	289-99		Excluded	Not a systematic review
-	Moran LJ, Tsagareli V, Noakes M, Norman R.	2016	Altered preconception fatty acid intake is associated with improved pregnancy rates in overweight and obese women undertaking in vitro fertilisation.	Nutrients	8(1)	E10	10.3390/nu8010010	Excluded	Not a systematic review
-	Mortensen SA, Rosenfeldt E, Kumar A, Dolliner P, Eilipiak KJ, Pella D, Alehagen U, Steurer G, Littarru GP. Q-SYMBIO Study Investigators.	2014	The effect of coenzyme Q10 on morbidity and mortality in chronic heart failure: results from Q- SYMBIO: a randomized double-blind trial.	JACC. Heart failure	2 (6)	641-649	N/A	Excluded	Not a systematic review
-	Mozaffari H, Daneshzad E, Larijani B, Bellissimo N, Azadbakht L.	2019	Dietary intake of fish, n-3 polyunsaturated fatty acids, and risk of inflammatory bowel disease: a systematic review and meta-analysis of observational studies.	European Journal Of Nutrition	N/A	Jan-17	N/A	Excluded	Wrong patient population
-	Mukai T, Kishi T, Matsuda Y, Iwata N.	2014	A meta-analysis of inositol for depression and anxiety disorders.	Hum Psychopharmacol	29(1)	55-63	10.1002/hup.2369	Excluded	Wrong intervention
-	<u>Myers SP,</u> <u>Vigar V.</u>	2019	The State of the Evidence for Whole-System, Multi-Modality Naturopathic Medicine: A Systematic Scoping Review	Journal of Alternative and	25(2)	141-168	10.1089/acm.2018.0 340	Excluded	Not a priority population- supplement pair

				Complementary Medicine					
-	Myers SP, Mulder AM, Baker DG, et al.	2016	Effects of fucoidan from Fucus vesiculosus in reducing symptoms of osteoarthritis: a randomized placebo-controlled trial	Biologics : targets & therapy	10	81-8		Excluded	Not a systematic review
-	Myers SP, O'Connor J, Fitton JH, et al	2011	A combined phase I and II open-label study on the immunomodulatory effects of seaweed extract nutrient complex	Biologics : targets & therapy	4	33-44		Excluded	Not a systematic review
-	Myers SP, O'Connor J, Fitton JH, et al	2010	A combined phase I and II open label study on the effects of a seaweed extract nutrient complex on osteoarthritis	Biologics : targets & therapy	4	33-44		Excluded	Not a systematic review
-	Myers SP, Stevenson L, Cheras PA, et al.	2010	A forced titration study of the antioxidant and immunomodulatory effects of Ambrotose AO supplement.	BMC Complementary and Alternative Medicine	10	16		Excluded	Not a systematic review
-	Myers, S. P, Viga, V	2019	The State of the Evidence for Whole-System, Multi-Modality Naturopathic Medicine: A Systematic Scoping Review	Journal of Alternative and Complementary Medicine	25(2)	141-168	10.1089/acm.2018.0 340	Excluded	Not a priority population- supplement pair
-	Myers, S. P, Viga, V	2019	The State of the Evidence for Whole-System, Multi-Modality Naturopathic Medicine: A Systematic Scoping Review	Journal of Alternative and Complementary Medicine	25(2)	141-168	10.1089/acm.2018.0 340	Excluded	Not a priority population- supplement pair
-	Myers, S. P. and V. Vigar	2019	The state of the evidence for whole-system, multi- modality naturopathic medicine: a systematic scoping review.	Journal of Alternative & Complementary Medicine	25(2):	141		Excluded	Not a priority population- supplement pair
-	Myers, S. P. and Vigar V.	2019	The State of Evidence for Whole-System, Multi- Modality Naturopathic Medicine: A Systematic Scoping Review	The Journal of Alternative and Complementary Medicine	25 (2)	141 - 168	DOI: 10.1089/acm.2018.0 340	Excluded	Not a priority population- supplement pair
-	Myers, S. P., Viga, V.	2019	The State of the Evidence for Whole-System, Multi-Modality Naturopathic Medicine: A Systematic Scoping Review	Journal of Alternative and Complementary Medicine	25(2)	141-168	10.1089/acm.2018.0 340	Excluded	Not a priority population- supplement pair
-	Myers, SP & Vigar, V	2019	The State of the Evidence for Whole-System, Multi-Modality Naturopathic Medicine: A Systematic Scoping Review'	Journal of Alternative & Complementary Medicine	25(2)	141-168	10.1089/acm.2018.0 340	Excluded	Not a priority population- supplement pair
-	Myers, Stephen; Vigar, Vanessa	2019	The State of the Evidence for Whole-System, Multi-Modality Naturopathic Medicine: A Systematic Scoping Review	The journal of alternative and complementary medicine	25 (2)	141-168	DOI: 10.1089/acm.2018.0 340	Excluded	Not a priority population- supplement pair

-	Nagashree RS, Manjunath N, Indu M, et al	2017	Effect of a diet enriched with fresh coconut saturated fats on plasma lipids and erythrocyte fatty acid composition in normal adults	Journal of the American College of Nutrition	36(5)	330-4		Excluded	Not a systematic review
-	Nagasukeerthi P, Mooventhan A, Manjunath N	2017	Short-term effect of add on bell pepper (Capsicum annuum var. grossum) juice with integrated approach of yoga therapy on blood glucose levels and cardiovascular functions in patients with type 2 diabetes mellitus: a randomized controlled study	Complementary Therapies in Medicine	34	42-5		Excluded	Not a systematic review
-	Nagasukeerthi P, Mooventhan A, Manjunath N	2017	Short-term effect of add on bell pepper (Capsicum annuum var. grossum) juice with integrated approach of yoga therapy on blood glucose levels and cardiovascular functions in patients with type 2 diabetes mellitus: a randomized controlled study	Complementary Therapies in Medicine	34	42-5		Excluded	Not a systematic review
-	Nalgirkar SP, Vinchurkar SA, Saoji AA, et al.	2018	Yoga as a therapeutic intervention in the management of dysfunctional uterine bleeding: a controlled pilot study	Journal of Mid-Life Health	9(1)	Aug-13		Excluded	Not a systematic review
-	Nandakumar B, Kadam A, Srikanth H, et al	2012	Naturopathy and yoga based life style intervention for cardiovascular risk reduction in patients with cardiovascular risk factors: a pilot study	BMC Complementary and Alternative Medicine	12(Suppl 1)	P106		Excluded	Not a systematic review
-	Nandini B, Mooventhan A, Manjunath N.	2018	Add-on effect of hot sand fomentation to yoga on pain, disability, and quality of life in chronic neck pain patients.	Explore (New York, NY)	14(5)	373-8		Excluded	Not a systematic review
-	Naveen G, Rao M, Vishal V, et al.	2013	Development and feasibility of yoga therapy module for out-patients with depression in India	Indian Journal of Psychiatry	55(Suppl 3)	S350		Excluded	Not a systematic review
-	Nesic J, Duka T.	2014	Effects of stress and dietary tryptophan enhancement on craving for alcohol in binge and non-binge heavy drinkers.	Behav Pharmacol	25(5-6)	503-517	10.1097/FBP.000000 0000000067	Excluded	Not a systematic review
-	Neuendorf R, Corn J, Hanes D, Bradley R.	2019	Impact of Food Immunoglobulin G-Based Elimination Diet on Subsequent Food Immunoglobulin G and Quality of Life in Overweight/Obese Adults	Journal of Alternative and Complementary Medicine	25(2)	241-248	10.1089/acm.2018.0 310	Excluded	Not a systematic review
-	Neuendorf R, Corn J, Hanes D, et al	2019	Impact of food immunoglobulin G-based elimination diet on subsequent food immunoglobulin G and quality of life in overweight/obese adults	Journal of Alternative & Complementary Medicine	25(2)	241-8		Excluded	Not a systematic review
-	Neuendorf, R, Corn, J, Hanes, D, Bradley, R	2019	Impact of Food Immunoglobulin G-Based Elimination Diet on Subsequent Food Immunoglobulin G and Quality of Life in Overweight/Obese Adults	Journal of Alternative and Complementary Medicine	25(2)	241–248	10.1089/acm.2018.0 310	Excluded	Not a systematic review

-	Neuendorf, R, Corn, J, Hanes, D, Bradley, R	2019	Impact of Food Immunoglobulin G-Based Elimination Diet on Subsequent Food Immunoglobulin G and Quality of Life in Overweight/Obese Adults	Journal of Alternative and Complementary Medicine	25(2)	241–248	10.1089/acm.2018.0 310	Excluded	Not a systematic review
-	Newton KM, Reed SD, LaCroix AZ, et al	2006	Treatment of vasomotor symptoms of menopause with black cohosh, multibotanicals, soy, hormone therapy, or placebo: a randomized trial	Annals of Internal Medicine	145	869-79		Excluded	Not a systematic review
-	Newton KM, Reed SD, LaCroix AZ, et al.	2006	Treatment of vasomotor symptoms of menopause with black cohosh, multibotanicals, soy, hormone therapy, or placebo: a randomized trial	Annals of Internal Medicine	145	869-79		Excluded	Not a systematic review
-	Niedzielin K, Kordecki H, Birkenfeld B.	2001	A controlled, double-blind, randomized study on the efficacy of Lactobacillus plantarum 299V in patients with irritable bowel syndrome	Eur J Gastroenterol Hepatol	13	1143-1147	N/A	Excluded	Not a systematic review
-	Nocito Echevarria MA, Andrade Reis T, Ruffo Capatti G, Siciliano Soares V, da Silveira DX, Fidalgo TM.	2017	N-acetylcysteine for treating cocaine addiction - A systematic review.	Psychiatry Res	251	197-203	10.1016/j.psychres.2 017.02.024	Excluded	Wrong patient population
-	Nouri, K., K. Walch, A. Weghofer, M. Imhof, C. Egarter and J. Ott	2017	The impact of a standardized oral multinutrient supplementation on embryo quality in in vitro fertilization/intracytoplasmic sperm injection: a prospective randomized trial.	Gynecologic and obstetric investigation	82(1)	41852	ISSN: 0378-7346	Excluded	Not a systematic review
-	Oates L, Cohen M, Braun L, et al	2014	Reduction in urinary organophosphate pesticide metabolites in adults after a week-long organic diet	Environmental Research	132	105-11		Excluded	Not a systematic review
-	Oberg EB, Bradley et al.	2015	Estimated Effects of Whole System Naturopathic Medicine in Select Chronic Disease Conditions: A systematic review	Alternative and Integrative Medicine	Vol 4	192	10.4172/2327- 5162.1000192	Excluded	Not a priority population- supplement pair
-	Oberg EB, Bradley RD, Allen J, et al	2011	Evaluation of a naturopathic nutrition program for type 2 diabetes	Complementary Therapies in Clinical Practice	17(3)	157-61		Excluded	Not a systematic review
-	Oliver G, Dean O, Camfield D, Blair- West S, Ng C, Berk M, Sarris J.	2015	N-acetyl cysteine in the treatment of obsessive compulsive and related disorders: a systematic review.	Clinical Psychopharmacol ogy and Neuroscience	13(1)	12	N/A	Excluded	Wrong patient population
-	Özturan A, Arslan S, Kocaadam B, Elibol E, İmamoğlu İ, Karadağ MG.	2019	Effect of inositol and its derivatives on diabetes: a systematic review.	Crit Rev Food Sci Nutr	59(7)	1124-1136	10.1080/10408398.2 017.1392926	Excluded	Wrong intervention
-	P M Herman, O Szczurko, K Cooley, E J Mills	2008	Cost-effectiveness of naturopathic care for chronic low back pain	Alternative therapies in health and medicine	14 (2)	32-39		Excluded	Not a systematic review

-	Pan Y, Liu Y, Guo H, Jabir MS, Liu X, Cui W, Li D.	2017	Associations between folate and vitamin B12 levels and inflammatory bowel disease: A meta- analysis	Nutrients	9 (4)	382	N/A	Excluded	Wrong patient population
-	Papanikolopoulou A, Syrigos KN, Drakoulis N.	2015	The role of glutamine supplementation in thoracic and upper aerodigestive malignancies.	Nutr Cancer	67(2)	231-237	10.1080/01635581.2 015.990572	Excluded	Wrong intervention
-	Paydary K, Akamaloo A, Ahmadipour A, Pishgar F, Emamzadehfard S, Akhondzadeh S.	2016	N-acetylcysteine augmentation therapy for moderate-to-severe obsessive-compulsive disorder: randomized, double-blind, placebo- controlled trial.	J Clin Pharm Ther	41(2)	214-219	10.1111/jcpt.12370	Excluded	Not a systematic review
-	Perlman AI, Lebow DG, Raphael K, et al	2013	A point-of-sale communications campaign to provide consumers safety information on drug– dietary supplement interactions: a pilot study	Health Communication	28(7)	729-39		Excluded	Not a systematic review
-	Pipingas A, Camfield D, Stough C, et al	2013	The effects of multivitamin supplementation on mood and general well-being in healthy young adults. A laboratory and at-home mobile phone assessment	Appetite	69	123-36		Excluded	Not a systematic review
-	Pipingas A, Camfield DA, Stough C, et al	2014	Effects of multivitamin, mineral and herbal supplement on cognition in younger adults and the contribution of B group vitamins	Human Psychopharmacol ogy: Clinical and Experimental	29(1)	73-82		Excluded	Not a systematic review
-	PM Herman, O Szczurko, K Cooley, D Seely	2014	A naturopathic approach to the prevention of cardiovascular disease: cost-effectiveness analysis of a pragmatic multi- worksite randomized clinical trial	Journal of occupational and environmental medicine	56 (2)	171-176	doi.org/10.1097/JOM .0000000000000066	Excluded	Not a systematic review
-	Pundir J, Psaroudakis D, Savnur P, Bhide P, Sabatini L, Teede H et al.	2018	Inositol treatment of anovulation in women with polycystic ovary syndrome: a meta-analysis of randomised trials.	BJOG	125(3)	299-308	10.1111/1471- 0528.14754	Excluded	Wrong intervention
-	Qiang Y, Li Q, Xin Y, Fang X, Tian Y, Ma J, Wang J, Wang Q, Zhang R, Wang J, Wang F.	2018	Intake of dietary one-carbon metabolism-related b vitamins and the risk of esophageal cancer: A dose-response meta-analysis.	Nutrients	10(7)	835	N/A	Excluded	Wrong intervention
-	Quinn JF, Raman R, Thomas RG, et al	2010	Docosahexaenoic acid supplementation and cognitive decline in Alzheimer disease: a randomized trial	JAMA	304(17)	1903-11		Excluded	Not a systematic review
-	Raghavendra R, Nagarathna R, Nagendra H, et al.	2007	Effects of an integrated yoga programme on chemotherapy-induced nausea and emesis in breast cancer patients	European Journal of Cancer Care	16(6)	462-74		Excluded	Not a systematic review
-	Raghavendra RM, Vadiraja H, Nagarathna R, et al	2009	Effects of a yoga program on cortisol rhythm and mood states in early breast cancer patients undergoing adjuvant radiotherapy: a randomized controlled trial	Integrative Cancer Therapies	8(1)	37-46		Excluded	Not a systematic review

-	Rajaei E, Mowla K, Ghorbani A, Bahadoram S, Bahadoram M, Dargahi-Malamir M.	2015	The effect of omega-3 fatty acids in patients with active rheumatoid arthritis receiving DMARDS therapy: double-blind randomized controlled trial.	Glob J Health Sci	8(7)	18-25	10.5539/gjhs.v8n7p1 8	Excluded	Not a systematic review
-	Rao AV, Bested AC, Beaulne TM, et al.	2009	A randomized, double-blind, placebo-controlled pilot study of a probiotic in emotional symptoms of chronic fatigue syndrome	Gut Pathogens	1(1)	1-Jun		Excluded	Not a systematic review
-	Rao MR, Raghuram N, Nagendra H, et al	2009	Anxiolytic effects of a yoga program in early breast cancer patients undergoing conventional treatment: a randomized controlled trial	Complementary Therapies in Medicine	17(1)	1-Aug		Excluded	Not a systematic review
-	Rao RM, Raghuram N, Nagendra H, et al	2017	Effects of an integrated yoga program on self- reported depression scores in breast cancer patients undergoing conventional treatment: a randomized controlled trial	Indian Journal of Palliative Care	21(2)	174		Excluded	Not a systematic review
-	Rao RM, Raghuram N, Nagendra HR, et al.	2017	Effects of a yoga program on mood states, quality of life, and toxicity in breast cancer patients receiving conventional treatment: a randomized controlled trial	Indian Journal of Palliative Care	23(3)	247		Excluded	Not a systematic review
-	Rao RM, Vadiraja H, Nagaratna R, et al.	2017	Effect of yoga on sleep quality and neuroendocrine immune response in metastatic breast cancer patients	Indian Journal of Palliative Care	23(3)	253		Excluded	Not a systematic review
-	Ratnakumari ME, Manavalan N, Sathyanath D, et al	2018	Study to evaluate the changes in polycystic ovarian morphology after naturopathic and yogic interventions	International Journal of Yoga	11(2)	139-47		Excluded	Not a systematic review
-	Reid, R, Steel, A, Wardle, J. Adams, J	2019	Naturopathic Medicine for the Management of Endometriosis, Dysmenorrhea, and Menorrhagia: A Content Analysis	Journal of Alternative and Complementary Medicine	25(2)	202–226	10.1089/acm.2018.0 305	Excluded	Not a systematic review
-	Reid, R, Steel, A, Wardle, J. Adams, J	2019	Naturopathic Medicine for the Management of Endometriosis, Dysmenorrhea, and Menorrhagia: A Content Analysis	Journal of Alternative and Complementary Medicine	25(2)	202–226	10.1089/acm.2018.0 305	Excluded	Not a systematic review
-	Richardson J, Lee H, Koch P, et al	2013	Mediators of dietary change among hispanic breast cancer survivors in a culturally-based dietary intervention	Journal of Nutrition Education and Behavior	45(4)	S64		Excluded	Not a systematic review
-	Ritenbaugh C, Hammerschlag R, Calabrese C, et al.	2008	A pilot whole systems clinical trial of traditional Chinese medicine and naturopathic medicine for the treatment of temporomandibular disorders	Journal of Alternative & Complementary Medicine	14(5)	475-87		Excluded	Not a systematic review
-	Ritenbaugh, C, et al	2008	A Pilot Whole Systems Clinical Trial of Traditional Chinese Medicine and Naturopathic Medicine for the Treatment of Temporomandibular Disorders	The Journal of Alternative and Complementary Medicine	14 (5)	475-87	https://doi.org/10.10 89/acm.2007.0738	Excluded	Not a systematic review

-	Roffman JL, Petruzzi LJ, Tanner AS, Brown HE, Eryilmaz H, Ho NF, et al.	2018	Biochemical, physiological and clinical effects of L-methylfolate in schizophrenia: a randomized controlled trial.	Mol Psychiatry	23 (2)	316-322	10.1038/mp.2017.41	Excluded	Not a systematic review
-	Romeyke T, Nöhammer E, Scheuer HC, Stummer H	2017	Integration of naturopathic medicine into acute inpatient care: An approach for patient-centred medicine under diagnosis-related groups	Complement Ther Clin Pract	28	42979	doi:10.1016/j.ctcp.2 017.04.004	Excluded	Not a systematic review
-	Ross C, Herman PM, Rocklin O, et al	2008	Evaluation of integrative medicine supplements for mitigation of chronic insomnia and constipation in an inpatient eating disorders setting	Explore: The Journal of Science and Healing	4(5)	315-20		Excluded	Not a systematic review
-	Ryan JJ, Hanes DA, Corroon J, et al	2018	Prospective safety evaluation of a cardiovascular health dietary supplement in adults with prehypertension and stage I hypertension	Journal of Alternative & Complementary Medicine	25(2)	249-256		Excluded	Not a systematic review
-	Ryan, J, Hanes, D, Corroon, J, Taylor, J, Bradley, R	2019	Prospective Safety Evaluation of a Cardiovascular Health Dietary Supplement in Adults with Prehypertension and Stage I Hypertension	Journal of Alternative and Complementary Medicine	25(2)	249–256	10.1089/acm.2018.0 311	Excluded	Not a systematic review
-	Ryan, J, Hanes, D, Corroon, J, Taylor, J, Bradley, R	2019	Prospective Safety Evaluation of a Cardiovascular Health Dietary Supplement in Adults with Prehypertension and Stage I Hypertension	Journal of Alternative and Complementary Medicine	25(2)	249–256	10.1089/acm.2018.0 311	Excluded	Not a systematic review
-	Sahebkar A, Reiner Ž, Simental- Mendía LE, Ferretti G, Cicero AFG.	2016	Effect of extended-release niacin on plasma lipoprotein(a) levels: a systematic review and meta-analysis of randomized placebo-controlled trials.	Metabolism	65(11)	1664-1678		Excluded	Wrong intervention
-	Salazar L, Higgins D, Childs J, et al	2016	Abstract P2-11-03: Phase I/II randomized study of combination immunotherapy with or without polysaccharide krestin (PSK) concurrently with a HER2 ICD peptide-based vaccine in patients with stage IV breast cancer receiving HER2-targeted monoclonal antibody therapy	Cancer Research	76(4 Suppl)	P2-11-03		Excluded	Not a systematic review
-	Salmond SJ, George J, Strasser SI, et al.	2019	Hep573 Study: A randomised, double-blind, placebo controlled trial of silymarin alone and combined with antioxidants to improve liver function and quality of life in people with chronic hepatitis C.	Aust Journal of Herbal & Naturopathic Medicine (AJHNM)	31 (2)	64-76	10.33235/ajhnm.31. 2.64-76	Excluded	Not a systematic review
-	Salmond, S., et al	2018	Hep573 Study: A randomised, double-blind, placebo-controlled trial of silymarin alone and combined with antioxidants to improve liver function and quality of life in people with chronic hepatitis C	Australian Journal of Herbal and Naturopathic Medicine, Vol. 30, No. 1, 2018: 12-24	30, No. 1	45627	-	Excluded	Not a systematic review

-	Salmond, SJ, George, J, Strasser, SI, Byth, K, Rawlinson, B, Mori, TA, Croft, KD, Adams, LA and Batey, RG	2018	Hep573 Study: A randomised, double-blind, placebo controlled trial of silymarin alone and combined with antioxidants to improve liver function and quality of life in people with chronic hepatitis C	Australian Journal of Herbal Medicine	30(1)	45992	ISSN: 2200-3886	Excluded	Not a systematic review
-	Santamaria A, Di Benedetto A, Petrella E, Pintaudi B, Corrado F, D'Anna R, et al.	2016	Myo-inositol may prevent gestational diabetes onset in overweight women: a randomized, controlled trial.	J Matern Fetal Neonatal Med	29 (19)	3234-3237	10.3109/14767058.2 015.1121478	Excluded	Not a systematic review
-	Saper RB, Lemaster C, Delitto A, et al.	2017	Yoga, physical therapy, or education for chronic low back pain: a randomized noninferiority trial	Annals of Internal Medicine	167(2)	85-94		Excluded	Not a systematic review
-	Sarris J, Adams J, Kavanagh DJ.	2010	An explorative qualitative analysis of participants' experience of using kava versus placebo in an RCT	Australian Journal of Medical Herbalism	22(1)	12-Jun		Excluded	Not a systematic review
-	Sarris J, Byrne GJ, Bousman C, et al.	2018	Adjunctive S-adenosylmethionine (SAMe) in treating non-remittent major depressive disorder: An 8-week double-blind, randomized, controlled trial	Neuropsychophar macology	28(10)	1126-36		Excluded	Not a systematic review
-	Sarris J, Byrne GJ, Cribb L, et al.	2018	L-Theanine in the adjunctive treatment of generalised anxiety disorder: a double-blind, randomised, placebo-controlled trial	Journal of Psychiatric Research	110	31-37		Excluded	Not a systematic review
-	Sarris J, Byrne GJ, Stough C, et al.	2019	Nutraceuticals for major depressive disorder- more is not merrier: an 8-week double-blind, randomised, controlled trial	Journal of Affective Disorders	245	1007-15		Excluded	Not a systematic review
-	Sarris J, Cox KH, Camfield DA, et al	2012	Participant experiences from chronic administration of a multivitamin versus placebo on subjective health and wellbeing: a double- blind qualitative analysis of a randomised controlled trial	Nutrition Journal	11(1)	110		Excluded	Not a systematic review
-	Sarris J, Fava M, Schweitzer I, et al.	2012	St John's wort (Hypericum perforatum) versus sertraline and placebo in major depressive disorder: continuation data from a 26-week RCT	Pharmacopsychiat ry	45(07)	275-8		Excluded	Not a systematic review
-	Sarris J, Kavanagh D, Byrne G, et al.	2009	The Kava Anxiety Depression Spectrum Study (KADSS): a randomized, placebo-controlled crossover trial using an aqueous extract of Piper methysticum	Psychopharmacol ogy	205(3)	399-407		Excluded	Not a systematic review
-	Sarris J, Kavanagh DJ, Adams J, et al.	2009	Kava Anxiety Depression Spectrum Study (KADSS): a mixed methods RCT using an aqueous extract of Piper methysticum	Complementary Therapies in Medicine	17(3)	176-8		Excluded	Not a systematic review
-	Sarris J, Kavanagh DJ, Deed G, et al	2009	St. John's wort and Kava in treating major depressive disorder with comorbid anxiety: a randomised double-blind placebo-controlled pilot trial	Human Psychopharmacol ogy: Clinical and Experimental	24(1)	41-8		Excluded	Not a systematic review

-	Sarris J, Laporte E, Scholey A, et al.	2014	Does a medicinal dose of kava impair driving? A randomized, placebo-controlled, double-blind study.	Human Psychopharmacol ogy: Clinical and Experimental	29(1)	73-82		Excluded	Not a systematic review
-	Sarris J, Oliver G, Camfield DA, et al	2016	Participant characteristics as modifiers of response to N-acetyl cysteine (NAC) in obsessive-compulsive disorder	Clinical Psychological Science	4(6)	1104-11		Excluded	Not a systematic review
-	Sarris J, Papakostas GI, Vitolo O, et al	2014	S-adenosyl methionine (SAMe) versus escitalopram and placebo in major depression RCT: efficacy and effects of histamine and carnitine as moderators of response	Journal of Affective Disorders	164	76-81		Excluded	Not a systematic review
-	Sarris J, Scholey A, Schweitzer I, et al.	2012	The acute effects of kava and oxazepam on anxiety, mood, neurocognition; and genetic correlates: a randomized, placebo-controlled, double-blind study	Human Psychopharmacol ogy: Clinical and Experimental	27(3)	262-9		Excluded	Not a systematic review
-	Sarris J, Stough C, Bousman CA, et al.	2013	Kava in the treatment of generalized anxiety disorder: a double-blind, randomized, placebo-controlled study	Journal of Clinical Psychopharmacol ogy	33(5)	643-8		Excluded	Not a systematic review
-	Sarris J, Stough C, Teschke R, et al.	2013	Kava for the treatment of generalized anxiety disorder RCT: analysis of adverse reactions, liver function, addiction, and sexual effects	Phytotherapy Research	27(11)	1723-8		Excluded	Not a systematic review
-	Satish V, Rao RM, Manjunath NK, et al	2018	Yoga versus physical exercise for cardio- respiratory fitness in adolescent school children: a randomized controlled trial	International Journal of Adolescent Medicine and Health			doi: 10.1515/ijamh- 2017-0154	Excluded	Not a systematic review
-	Saunders PR, Smith F, Schusky RW	2007	Echinacea purpurea L. in children: safety, tolerability, compliance, and clinical effectiveness in upper respiratory tract infections	Canadian Journal of Physiology and Pharmacology	85(11)	1195-9		Excluded	Not a systematic review
-	Sayles C, Hickerson SC, Bhat RR, Hall J, Garey KW, Trivedi MV.	2016	Oral glutamine in preventing treatment-related mucositis in adult patients with cancer: a systematic review.	Nutr Clin Pract	31(2)	171-179	10.1177/0884533615 611857	Excluded	Wrong intervention
-	Schloss J, McIntyre E, Steel A, et al.	2019	Lessons from Outside and Within: Exploring Advancements in Methodology for Naturopathic Medicine Clinical Research.	Journal of Alternative and Complementary Medicine	25(2)	135-140	10.1089/acm.2018.0 403	Excluded	Wrong outcomes
-	Schloss J, McIntyre E, Steel A, et al.	2019	Lessons from Outside and Within: Exploring Advancements in Methodology for Naturopathic Medicine Clinical Research.	Australian Journal of Herbal & Naturopathic Medicine	25(2)	135-140	10.1089/acm.2018.0 403	Excluded	Wrong outcomes
-	Schloss J, McIntyre E, Steel A, et al.	2019	Lessons from Outside and Within: Exploring Advancements in Methodology for Naturopathic Medicine Clinical Research.	Journal of Alternative and	25(2)	135-140	10.1089/acm.2018.0 403	Excluded	Wrong outcomes

				Complementary Medicine					
-	Schloss JM, Colosimo M, Airey C, et al	2017	A randomised, placebo-controlled trial assessing the efficacy of an oral B group vitamin in preventing the development of chemotherapy- induced peripheral neuropathy (CIPN)	Supportive Care in Cancer	25(1)	195-204		Excluded	Not a systematic review
-	Schloss JM, Colosimo M, Airey C, et al	2015	Pilot trial assessing the efficacy and safety of a supplemental B vitamin complex to reduce the onset and severity of chemotherapy-induced peripheral neuropathy	Journal of Clinical Oncology	33(15Su ppl)	9604		Excluded	Not a systematic review
-	Schmidt M, Thomsen M, Schmidt U	2012	Suitability of ivy extract for the treatment of paediatric cough	Phytotherapy Research	26(12)	1942-7		Excluded	Not a systematic review
-	Schoenthaler SJ, Bier ID	2000	The effect of vitamin-mineral supplementation on juvenile delinquincy among American schoolchildren: a randomized, double-blind placebo-controlled trial	Journal of Alternative & Complementary Medicine	6(1)	Jul-17		Excluded	Not a systematic review
-	Schoenthaler SJ, Bier ID, Young K, et al	2000	The effect of vitamin-mineral supplementation on the intelligence of American schoolchildren: a randomized, double-blind placebo-controlled trial	Journal of Alternative & Complementary Medicine	6(1)	19-29		Excluded	Not a systematic review
-	Scholey A, Benson S, Gibbs A, et al.	2017	Exploring the effect of Lactium™ and Zizyphus Complex on sleep quality: a double-blind, randomized placebo-controlled trial	Nutrients	9(2)	154		Excluded	Not a systematic review
-	Schumann D, Langhorst J, Dobos G, et al.	2018	Randomised clinical trial: yoga vs a low-FODMAP diet in patients with irritable bowel syndrome	Alimentary Pharmacology & Therapeutics	47(2)	203-11		Excluded	Not a systematic review
-	Scott, R., A. MacPherson, R. Yates, B. Hussain and J. Dixon	1998	The effect of oral selenium supplementation on human sperm motility.	British journal of urology	82(1)	76-80	ISSN: 0007-1331	Excluded	Not a systematic review
-	Seely D, Singh R	2007	Adaptogenic potential of a polyherbal natural health product: report on a longitudinal clinical trial	Evidence-Based Complementary and Alternative Medicine	4(3)	375-80		Excluded	Not a systematic review
-	Seely D, Szczurko O, Cooley K, et al	2013	Naturopathic medicine for the prevention of cardiovascular disease: a randomized clinical trial	Canadian Medical Association Journal	185 (9)	E409-16		Excluded	Not a systematic review
-	Seely D, Szczurko O, Cooley K, Fritz H, Aberdour S, Herrington C, Herman P, Rouchotas P, Lescheid D, Bradley R, Gignac T, Bernhardt B, Zhou Q, Guyatt G.	2013	Naturopathic medicine for the prevention of cardiovascular disease: a randomized clinical trial	Canadian Medical Association Journal	185(9)	409-416	10.1503/cmaj.12056 7	Excluded	Not a systematic review

-	Seely D, Szczurko O, Kieran C, Fritz H, Herman P, Bradley R, Aberdour S, Herrington C, Rouchotas P, Lescheid D, Gignac T, Bernhardt B, Zhou Q, Guyatt G	2012	Naturopathic medicine for the prevention of cardiovascular disease: a pragmatic randomized clinical trial	BMC complementary and alternative medicine	12			Excluded	Not a systematic review
-	Selvakumar G, Shathirapathiy G, Jainraj R, et al.	2017	Immediate effect of bitter gourd, ash gourd, Knol- khol juices on blood sugar levels of patients with type 2 diabetes mellitus: a pilot study	Journal of Traditional and Complementary Medicine	7(4)	526-31		Excluded	Not a systematic review
-	Senftleber N, Nielsen S, Andersen J, Bliddal H, Tarp S, Lauritzen L, Furst D, Suarez- Almazor M, Lyddiatt A, Christensen R.	2017	Marine oil supplements for arthritis pain: a systematic review and meta-analysis of randomized trials.	Nutrients	9(1)	42	N/A	Excluded	Not a priority population- supplement pair
-	Shetty P, Mooventhan A, Nagendra HR	2016	Does short-term lemon honey juice fasting have effect on lipid profile and body composition in healthy individuals?	Journal of Ayurveda and Integrative Medicine	7(1)	11-Mar		Excluded	Wrong patient population
-	Shetty S, Subramanya P, Moorthy VK.	2018	Effect of yoga on flexibility and psychomotor performance in college-going healthy individuals.	International Journal of Yoga- Philosophy, Psychology and Parapsychology	6(1)	51		Excluded	Not a systematic review
-	Shi Z, Richardson JM, Aycinena AC, et al.	2018	Psychosocial mediators of dietary change among Hispanic/Latina breast cancer survivors in a culturally-tailored dietary intervention	Psycho-oncology	27(9)	2220-8		Excluded	Not a systematic review
-	Shim, Bongseok & Jeong, Hyewon & Lee, Sara & Hwang, Sehee & Moon, Byeongseok & Storni, Charlotte	2014	A randomized double-blind placebo-controlled clinical trial of a product containing pumpkin seed extract and soy germ extract to improve overactive bladder-related voiding dysfunction and quality of life	Journal of Functional Foods	8 (1)	111-117	10.1016/j.jff.2014.03 .010.	Excluded	Not a systematic review
-	Shinto L, Calabrese C, Morris C, et al	2008	A randomized pilot study of naturopathic medicine in multiple sclerosis	Journal of Alternative & Complementary Medicine	14(5)	489-96		Excluded	Not a systematic review
-	Shinto L, Marracci G, Baldauf- Wagner S, et al	2009	Omega-3 fatty acid supplementation decreases matrix metalloproteinase-9 production in relapsing-remitting multiple sclerosis.	Prostaglandins, Leukotrienes and Essential Fatty Acids	80(2-3)	131-6		Excluded	Not a systematic review
-	Shinto L, Quinn J, Montine T, et al	2016	A randomized placebo-controlled pilot trial of omega-3 fatty acids and alpha lipoic acid in Alzheimer's disease	Journal of Alzheimer's Disease	38(1)	111-20		Excluded	Not a systematic review

-	Showell, M. G., R. Mackenzie- Proctor, V. Jordan and R. J. Hart	2017	Antioxidants for female subfertility.	Cochrane Database of Systematic Reviews	bochrane (7). Data   atabase of Coc   vstematic Coll   eviews ion		ISSN: 1465-1858	Excluded	Wrong patient population
-	Shuai Ben, Mulong Du, Gaoxiang Ma, Jianhua Qu, Liyang Zhu, Haiyan Chu, et al.	2019	Vitamin B2 intake reduces the risk for colorectal cancer: a dose-response analysis.	European Journal of Nutrition	58(4)	(4) 1591–1602 N/A		Excluded	Wrong intervention
-	Siegel AB, Narayan R, Rodriguez R, et al	2014	A phase I dose-finding study of silybin phosphatidylcholine (milk thistle) in patients with advanced hepatocellular carcinoma	Integrative Cancer Therapies	13(1)	46-53		Excluded	Not a systematic review
-	Skvarc DR, Dean OM, Byrne LK, Gray L, Lane S, Lewis M, Fernandes BS, Berk M, Marriott A.	2017	The effect of N-acetylcysteine (NAC) on human cognition–A systematic review.	Neuroscience & Biobehavioral Reviews	78	44-56	N/A	Excluded	Wrong intervention
-	Smith DJ, Sarris J, Dowling N, et al	2017	Adjunctive low-dose docosahexaenoic acid (DHA) for major depression: an open-label pilot trial.	Nutritional Neuroscience	21(3)	224-8		Excluded	Not a systematic review
-	Smits, R. M., R. Mackenzie- Proctor, A. Yazdani, M. T. Stankiewicz, V. Jordan and M. G. Showell	2019	Antioxidants for male subfertility.	Cochrane Database of Systematic Reviews	-3	Database Cochrane collaborati on	ISSN: 1465-1858	Excluded	Wrong patient population
-	Sowmya M, Rao R, Sowjanya M, et al	2018	A comparative study on effect of lemon juice with lemon seeds vs. lemon juice alone on high sensitivity C-reactive protein in subjects with obesity undergoing calorie restrictiona pilot study	Journal of Evolution of Medical and Dental Sciences	7(16)			Excluded	Not a systematic review
-	Spence JD, Yi Q, Hankey GJ.	2017	B vitamins in stroke prevention: time to reconsider.	The Lancet Neurology	16 (9)	750-760	N/A	Excluded	Not a systematic review
-	Steel, A, Foley, H et al	2020	Overview of international naturopathic practice and patient characteristics: results from a cross- sectional study in 14 countries	Biomed Central Journal	20(59)		https://doi.org/10.11 86/s12906-020- 2851-7	Excluded	Not a systematic review
-	Steel, A, Foley, H, Bradley, R. et al	2020	Overview of international naturopathic practice and patient characteristics: results from a cross- sectional study in 14 countries	BMC Complementary Medicine and Therapies	20(59)	n/a	https://doi.org/10.11 86/s12906-020- 2851-7	Excluded	Not a systematic review
-	Steel, A, Foley, H, Bradley, R. et al	2020	Overview of international naturopathic practice and patient characteristics: results from a cross- sectional study in 14 countries	BMC Complementary Medicine and Therapies	3MC 20(59) n/a Complementary Medicine and Fherapies		https://doi.org/10.11 86/s12906-020- 2851-7	Excluded	Not a systematic review
-	Steel, A, Foley, H, Bradley, R. et al	2020	Overview of international naturopathic practice and patient characteristics: results from a cross- sectional study in 14 countries	BMC Complementary Medicine and Therapies	20(59)	n/a	https://doi.org/10.11 86/s12906-020- 2851-7	Excluded	Not a systematic review

-	Steel, A. Bradley, R. Wardle, J.	2019	Naturopathic Research: Prevalent, Relevant, But Largely Hidden in Plain Sight	The Journal of Alternative Health and Complementary Medicine	25(2)	123-124	10.1089/acm.2019.2 9065.ast	Excluded	Not a systematic review
-	Steels E, Steele M, Harold M, et al.	2017	Efficacy of a proprietary Trigonella foenum- graecum L. de-husked seed extract in reducing menopausal symptoms in otherwise healthy women: a double-blind, randomized, placebo- controlled study	Phytotherapy Research	31(9)	1316-22		Excluded	Not a systematic review
-	Stephen P. Myers and Vanessa Vigar	2019	The State of the Evidence for WholeSystem, Multi- Modality Naturopathic Medicine: A Systematic Scoping Review.	J Altern Complement Med.	2019 Feb;25(2 )	141-168	doi: 10.1089/acm.2018.0 340	Excluded	Not a priority population- supplement pair
-	Stothers, L.	2002	A randomized trial to evaluate effectiveness and cost effectiveness of naturopathic cranberry products as prophylaxis against urinary tract infection in women	Canadian Journal of Urology	9	1558-1562	ISSN: 1195-9479	Excluded	Not a systematic review
-	Sun Q, Wang B, Li Y, Sun F, Li P, Xia W, et al.	2016	Taurine Supplementation Lowers Blood Pressure and Improves Vascular Function in Prehypertension: Randomized, Double-Blind, Placebo-Controlled Study.	Hypertension	67(3)	541-549	10.1161/HYPERTENS IONAHA.115.06624	Excluded	Not a systematic review
-	Suskind DL, Wahbeh G, Burpee T, et al.	2013	Tolerability of curcumin in pediatric inflammatory bowel disease: a forced dose titration study.	56(3)	277			Excluded	Not a systematic review
-	Szczurko O, Cooley K, Bernhardt B, et al.	2006	Determining the impact of naturopathic treatment on Canadian postal workers with low back pain, a randomised controlled parallel group study	Focus on Alternative and Complementary Therapies	11(Suppl 1)	46		Excluded	Not a systematic review
-	Szczurko O, Cooley K, Busse JW, et al.	2007	Naturopathic care for chronic low back pain: a randomized trial	PLoS One	2 (9)_	E919		Excluded	Not a systematic review
-	Szczurko O, Cooley K, Mills EJ, et al	2009	Naturopathic treatment of rotator cuff tendinitis among Canadian postal workers: a randomized controlled trial	Arthritis Care & Research	61(8)	1037-45		Excluded	Not a systematic review
-	Szczurko O, Cooley K, Mills EJ, Zhou Q, Perri D, Seely D.	2009	Naturopathic treatment of rotator cuff tendinitis among Canadian postal workers: a randomized controlled trial	Arthritis and Rheumatism	61(8)	1037-1045	10.1002/art.24675	Excluded	Not a systematic review
-	Szczurko O, Shear N, Taddio A, et al.	2011	Ginkgo biloba for the treatment of Vitilgo vulgaris: an open label pilot clinical trial.	BMC Complementary and Alternative Medicine	11(1)	21		Excluded	Not a systematic review
-	Tabrizi R, Ostadmohammadi V, Lankarani KB, Peymani P, Akbari M, Kolahdooz F et al.	2018	The effects of inositol supplementation on lipid profiles among patients with metabolic diseases: a systematic review and meta-analysis of randomized controlled trials.	Lipids Health Dis	17(1)	123	10.1186/s12944- 018-0779-4	Excluded	Wrong intervention

-	Talukdar R, Murthy HV, Reddy DN.	2015	Role of methionine containing antioxidant combination in the management of pain in chronic pancreatitis: a systematic review and meta-analysis.	Pancreatology	15(2)	136-144	N/A	Excluded	Not a priority population- supplement pair
-	Taylor JA, Weber W, Standish L, et al	2003	Efficacy and safety of echinacea in treating upper respiratory tract infections in children: a randomized controlled trial	JAMA	290(21)	2824-30		Excluded	Not a systematic review
-	Telles S, Narendran S, Raghuraj P, et al.	1997	Comparison of changes in autonomic and respiratory parameters of girls after yoga and games at a community home	Perceptual and Motor Skills	84(1)	251-7		Excluded	Not a systematic review
-	Telles S, Naveen K, Dash M, et al	2006	Effect of yoga on self-rated visual discomfort in computer users	Head & Face Medicine	2(1)	46		Excluded	Not a systematic review
-	Telles S, Naveen VK, Balkrishna A, et al.	2009	Short term health impact of a yoga and diet change program on obesity	Medical Science Monitor	16(1)	CR35-40		Excluded	Not a systematic review
-	Thakker D, Raval A, Patel I, Walia R.	2015	N-acetylcysteine for polycystic ovary syndrome: a systematic review and meta-analysis of randomized controlled clinical trials. 2015.	Obstetrics and gynecology international	N/A	2015	N/A	Excluded	Wrong intervention
-	Thompson DF, Saluja HS.	2017	Prophylaxis of migraine headaches with riboflavin: a systematic review.	J Clin Pharm Ther	42(4)	394–403	10.1111/jcpt.12548	Excluded	Wrong intervention
-	Tian T, Yang KQ, Cui JG, Zhou LL, Zhou XL.	2017	Folic acid supplementation for stroke prevention in patients with cardiovascular disease	The American journal of the medical sciences.	354(4)	379-387	N/A	Excluded	Not a systematic review
-	Tippens KM, Erlandsen A, Hanes DA, et al.	2019	Impact of a short-term naturopathic whole-foods- based nutrition education intervention on dietary behavior and diabetes risk markers: a pilot study	Journal of Alternative & Complementary Medicine	25(2)	234-40		Excluded	Not a systematic review
-	Tippens KM, Erlandsen A, Hanes DA, et al.	2018	Impact of a short-term naturopathic whole-foods- based nutrition education intervention on dietary behavior and diabetes risk markers: a pilot study	Journal of Alternative & Complementary Medicine	25(2)	234-240		Excluded	Not a systematic review
-	Tippens, K, Erlandsen, A, Hanes, D, Graybill, R, Jackson, C, Briley, J, Zwickey, H	2019	Impact of a Short-Term Naturopathic Whole- Foods-Based Nutrition Education Intervention on Dietary Behavior and Diabetes Risk Markers: A Pilot Study	Journal of Alternative and Complementary Medicine	25(2)	234–240	10.1089/acm.2018.0 025	Excluded	Not a systematic review
-	Tippens, K, Erlandsen, A, Hanes, D, Graybill, R, Jackson, C, Briley, J, Zwickey, H	2019	Impact of a Short-Term Naturopathic Whole- Foods-Based Nutrition Education Intervention on Dietary Behavior and Diabetes Risk Markers: A Pilot Study	Journal of Alternative and Complementary Medicine	25(2)	234–240	10.1089/acm.2018.0 025	Excluded	Not a systematic review
-	Torkelson CJ, Sweet E, Martzen MR, et al	2012	Phase 1 clinical trial of Trametes versicolor in women with breast cancer	ISRN Oncology	2012	1-Jul		Excluded	Not a systematic review
-	Traub ML, Finnell JS, Bhandiwad A, et al	2014	Impact of vitamin D3 dietary supplement matrix on clinical response	The Journal of Clinical	99(8)	2720-8		Excluded	Not a systematic review

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				Endocrinology & Metabolism					
-	Unfer V, Facchinetti F, Orrù B, Giordani B, Nestler J.	2017	Myo-inositol effects in women with PCOS: a meta- analysis of randomized controlled trials.	Endocrine connections	6(8)	647-658	N/A	Excluded	Wrong intervention
-	Usher C, Thompson A, Griebeler M, et al.	2019	Meals, mindfulness, & moving forward: a feasibility study to a multi-modal lifestyle approach in early psychosis	Early Intervention in Psychiatry	13(1)	147-50		Excluded	Not a systematic review
-	Vadiraja H, Rao MR, Nagarathna R, et al.	2009	Effects of yoga program on quality of life and affect in early breast cancer patients undergoing adjuvant radiotherapy: a randomized controlled trial	Complementary Therapies in Medicine	Complementary 17(5) 274-80 herapies in 1edicine			Excluded	Not a systematic review
-	Vadiraja H, Rao RM, Nagarathna R, et al	2017	Effects of yoga in managing fatigue in breast cancer patients: a randomized controlled trial	Indian Journal of Palliative Care	23(3)	247		Excluded	Not a systematic review
-	Vadiraja SH, Rao MR, Nagendra RH, et al.	2009	Effects of yoga on symptom management in breast cancer patients: a randomized controlled trial	International Journal of Yoga	2(2)	73		Excluded	Not a systematic review
-	van de Rest O, Bloemendaal M, de Heus R, Aarts E.	2017	Dose-dependent effects of oral tyrosine administration on plasma tyrosine levels and cognition in aging.	Nutrients	9(12)	E1279	N/A	Excluded	Not a systematic review
-	Venugopal V, Rathi A, Raghuram N	2017	Effect of short-term yoga-based lifestyle intervention on plasma glucose levels in individuals with diabetes and pre-diabetes in the community	Diabetes Metab Syndr	11(Suppl 2)	S597-9		Excluded	Not a systematic review
-	Veselinovic M, Vasiljevic D, Vucic V, Arsic A, Petrovic S, Tomic- Lucic A, Savic M, Zivanovic S, Stojic V, Jakovljevic V.	2017	Clinical benefits of n-3 PUFA and $\pmb{\gamma}$ -linolenic acid in patients with rheumatoid arthritis.	Nutrients	9(4)	325	N/A	Excluded	Not a systematic review
-	Vinutha H, Raghavendra B, Manjunath N.	2015	Effect of integrated approach of yoga therapy on autonomic functions in patients with type 2 diabetes	Indian Journal of Endocrinology and Metabolism	19(5)	653		Excluded	Not a systematic review
-	Vishal AA, Mishra A, Raychaudhuri SP.	2011	A double blind, randomized, placebo controlled clinical study evaluates the early efficacy of aflapin in subjects with osteoarthritis of knee.	Int J Med Sci	8	615–622	N/A	Excluded	Not a systematic review
-	Vitagliano A, Saccone G, Cosmi E, Visentin S, Dessole F, Ambrosini G, et al.	2019	Inositol for the prevention of gestational diabetes: a systematic review and meta-analysis of randomized controlled trials.	Arch Gynecol Obstet	299(1)	55-68	10.1007/s00404- 018-5005-0	Excluded	Wrong intervention
-	Vitetta L, Coulson S, Beck SL, et al.	2013	The clinical efficacy of a bovine lactoferrin/whey protein lg-rich fraction (Lf/lgF) for the common cold: a double blind randomized study	Complementary Therapies in Medicine	7(4)	526-31		Excluded	Not a systematic review
-	Vohra S, Johnston B, Laycock K, et al.	2007	Safety and tolerability of North American ginseng extract in the treatment of paediatric upper	Focus on Alternative and	12(Suppl 1)	52		Excluded	Not a systematic review

			respiratory tract infection: a phase II randomised controlled trial of two dosing schedules.	Complementary Therapies					
-	Waldron M, Patterson SD, Tallent J, Jeffries O.	2018	The effects of oral taurine on resting blood pressure in humans: a meta-analysis.	Curr Hypertens Rep	20(9)	81	10.1007/s11906- 018-0881-z	Excluded	Wrong intervention
-	Wang JY, Wu YH, Liu SJ, Lin YS, Lu PH.	2018	Vitamin B12 for herpetic neuralgia: A meta- analysis of randomised controlled trials.	Complementary therapies in medicine	41	277-282	N/A	Excluded	Wrong intervention
-	Wang WW, Wang XS, Zhang ZR, He JC, Xie CL.	2017	A meta-analysis of folic acid in combination with anti-hypertension drugs in patients with hypertension and hyperhomocysteinemia.	Frontiers in pharmacology	8	585	N/A	Excluded	Wrong intervention
-	Wardle, J	2016	The Australian government review of natural therapies for private health insurance rebates: What does it say and what does it mean?	Advances in Integrative Medicine	3	44107	10.1016/j.aimed.201 6.07.004	Excluded	Wrong outcomes
-	Wardle, J	2016	The Australian government review of natural therapies for private health insurance rebates: What does it say and what does it mean?	Advances in Integrative Medicine	3	3-Oct	10.1016/j.aimed.201 6.07.004	Excluded	Wrong outcomes
-	Wardle, J	2016	The Australian government review of natural therapies for private health insurance rebates: What does it say and what does it mean?	Advances in Integrative Medicine	3	3-Oct	10.1016/j.aimed.201 6.07.004	Excluded	Wrong outcomes
-	Wardle, J, Steel, A, Casteleijn, D, Bowman, D	2019	An evidence-based overview of naturopathic practice in Australia	Australian Journal of Herbal & Naturopathic Medicine	31(1)	41518	10.33235/ajhnm.31. 1.9-13	Excluded	Wrong study design - included SRs searched for eligibility
-	Wardle, J, Steel, A, Casteleijn, D, Bowman, D	2019	An evidence-based overview of naturopathic practice in Australia	Australian Journal of Herbal & Naturopathic Medicine	31(1)	41518	10.33235/ajhnm.31. 1.9-13	Excluded	Wrong study design - included SRs searched for eligibility
-	Wardle, J, Steel, A, Casteleijn, D, Bowman, D	2019	An evidence-based overview of naturopathic practice in Australia	Australian Journal of Herbal & Naturopathic Medicine	31(1)	Sep-13	10.33235/ajhnm.31. 1.9-13	Excluded	Wrong study design - included SRs searched for eligibility
-	Wardle, J, Steel, A, Casteleijn, D, Bowman, D	2019	An evidence-based overview of naturopathic practice in Australia	Australian Journal of Herbal & Naturopathic Medicine	31(1)	Sep-13	10.33235/ajhnm.31. 1.9-13	Excluded	Wrong study design - included SRs searched for eligibility
-	Watson CJ, Grando D, Fairley CK, et al.	2014	The effects of oral garlic on vaginal candida colony counts: a randomised placebo controlled double-blind trial	BJOG: An International Journal of Obstetrics & Gynaecology	121(4)	498-506		Excluded	Not a systematic review
-	Weber W, Taylor JA, Stoep AV, et al	2005	Echinacea purpurea for prevention of upper respiratory tract infections in children	Journal of Alternative &	11(6)	1021-6		Excluded	Not a systematic review

				Complementary Medicine					
-	Weber W, Vander Stoep A, McCarty RL, et al	2008	Hypericum perforatum (St John's wort) for attention-deficit/hyperactivity disorder in children and adolescents: a randomized controlled trial	JAMA	299(22)	2633-41		Excluded	Not a systematic review
-	Westphal, L. M., M. L. Polan, A. S. Trant and S. Mooney	2004	A nutritional supplement for improving fertility in women.	Journal of Reproductive Medicine	49(4)	289-293		Excluded	Not a systematic review
-	Withee ED, Tippens KM, Dehen R, et al	2017	Effects of Methylsulfonylmethane (MSM) on exercise-induced oxidative stress, muscle damage, and pain following a half-marathon: a double-blind, randomized, placebo-controlled trial	Journal of the International Society of Sports Nutrition	14(1)	24		Excluded	Not a systematic review
-	Withee ED, Tippens KM, Dehen R, et al	2015	Effects of MSM on exercise-induced muscle and joint pain: a pilot study	Journal of the International Society of Sports Nutrition	12(Suppl 1)	8		Excluded	Not a systematic review
-	Withee ED, Tippens KM, Dehen R, et al.	2016	Methylsulfonylmethane supplementation as a nonpharmacological option for exercise-induced pain: a pilot study	Integrative Medicine	25(1)	44		Excluded	Wrong outcomes
-	Witte AV, Kerti L, Hermannstädter HM, Fiebach JB, Schreiber SJ, Schuchardt JP, et al.	2014	Long-chain omega-3 fatty acids improve brain function and structure in older adults.	Cereb Cortex	24(11)	3059-3068	10.1093/cercor/bht1 63	Excluded	Not a systematic review
-	World Naturopathic Federation	2018	Research Written by Naturopaths /Naturopathic Doctors	http://worldnaturo pathicfederation.o rg/wp- content/uploads/2 019/04/WNF_Rese arch-Written-by- Naturopaths- Naturopathic- Doctors.pdf		1-50	n/a	Excluded	Not a systematic review
-	World Naturopathic Federation	2018	Research Written by Naturopaths /Naturopathic Doctors	http://worldnaturo pathicfederation.o rg/wp- content/uploads/2 019/04/WNF_Rese arch-Written-by- Naturopaths- Naturopathic- Doctors.pdf		1-50	n/a	Excluded	Not a systematic review

-	World Naturopathic Federation	2019	A comprehensive listing of books, Written by Naturopaths /Naturopathic Doctors	http://worldnaturo pathicfederation.o rg/wp- content/uploads/2 019/04/Book- Project.pdf		1-62	n/a	Excluded	Not a systematic review
-	World Naturopathic Federation	2018	Research Written by Naturopaths /Naturopathic Doctors	http://worldnaturo pathicfederation.o rg/wp- content/uploads/2 019/04/WNF_Rese arch-Written-by- Naturopaths- Naturopathic- Doctors.pdf		1-50	n/a	Excluded	Wrong outcomes
-	World Naturopathic Federation	2019	Research written by Naturopaths/Naturopathic Doctors	http://worldnaturo pathicfederation.o rg/wp- content/uploads/2 019/04/WNF_Rese arch-Written-by- Naturopaths- Naturopathic- Doctors.pdf	n/a	Jan-50	n/a	Excluded	Wrong outcomes
-	World Naturopathic Federation	2017	WNF White Paper: Naturopathic Philosophies, Principals and Theories	http://worldnaturo pathicfederation.o rg/wp- content/uploads/2 019/11/WNF_Whit e_Paper_June- 2017.pdf	n/a	n/a	n/a	Excluded	Wrong outcomes
-	Xin Fang, Hedong Han, Mei Li, Chun Liang, Zhongjie Fan, Aaseth Jan, Jia He, Montgomery Scott, Yang Cao.	2016	Dose-Response Relationship between Dietary Magnesium Intake and Risk of Type 2 Diabetes Mellitus: A Systematic Review and Meta Regression Analysis of Prospective Cohort Studies	Nutrients	8(11)	739	N/A	Excluded	Not a priority population- supplement pair
-	Yadav V, Marracci G, Lovera J, et al	2005	Lipoic acid in multiple sclerosis: a pilot study	Multiple Sclerosis Journal	11(2)	159-65		Excluded	Not a systematic review
-	Yadav V, Marracci GH, Munar MY, et al.	2010	Pharmacokinetic study of lipoic acid in multiple sclerosis: comparing mice and human pharmacokinetic parameters	Mult Scler	16(4)	387-97		Excluded	Not a systematic review
-	Yan JH, Guan BJ, Gao HY, Peng XE.	2018	Omega-3 polyunsaturated fatty acid supplementation and non-alcoholic fatty liver	Medicine	97	37	N/A	Excluded	Wrong patient population

			disease A meta-analysis of randomized controlled trials.						
-	Yang J, Li JH, Deng BH, Wang QZ.	2018	Association of One-Carbon Metabolism-Related Vitamins (Folate, B6, B12), homocysteine and methionine with the risk of lung cancer: systematic review and meta-analysis	Frontiers in oncology	8	493	N/A	Excluded	Wrong intervention
-	Yang K, Zeng L, Bao T, Ge J.	2018	Effectiveness of Omega-3 fatty acid for polycystic ovary syndrome: a systematic review and meta-analysis.	Reproductive Biology and Endocrinology	and 16(1) 27 and 16(1) 27		N/A	Excluded	Wrong patient population
-	Yazaki Y, Faridi Z, Ma Y, et al	2010	A pilot study of chromium picolinate for weight loss	Journal of Alternative & Complementary Medicine	16(3) 291-9			Excluded	Not a systematic review
-	Yu L, Yuan M, Wang L.	2017	The effect of omega-3 unsaturated fatty acids on non-alcoholic fatty liver disease: A systematic review and meta-analysis of RCTs.	Pakistan journal of medical sciences	33(4)	1022-1028	N/A	Excluded	Wrong patient population
-	Yu Y, Zick S, Li X, et al.	2011	Examination of the pharmacokinetics of active ingredients of ginger in humans	AAPS J	13(3)	417		Excluded	Not a systematic review
-	Zhang H, Lv Y, Li Z, Sun L, Guo W.	2019	The efficacy of myo-inositol supplementation to prevent gestational diabetes onset: a meta- analysis of randomized controlled trials.	The Journal Of Maternal-Fetal & Neonatal Medicine: The Official Journal Of The European Association Of Perinatal Medicine	32(13)	2249-2255	N/A	Excluded	Wrong intervention
-	Zhang YY, Liu W, Zhao TY, Tian HM.	2017	Efficacy of omega-3 polyunsaturated fatty acids supplementation in managing overweight and obesity: a meta-analysis of randomized clinical trials.	The journal of nutrition, health & aging	21(2)	187-192	N/A	Excluded	Not a priority population- supplement pair
-	Zhao JV, Schooling CM, Zhao JX.	2018	The effects of folate supplementation on glucose metabolism and risk of type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials.	Ann Epidemiol	28(4)	249-257	10.1016/j.annepide m.2018.02.001	Excluded	Wrong intervention
-	Zheng W, Zhang QE, Cai DB, Yang XH, Qiu Y, Ungvari GS.	2018	N-acetylcysteine for major mental disorders: a systematic review and meta-analysis of randomized controlled trials.	Acta Psychiatr Scand	137(5)	391-400	10.1111/acps.12862	Excluded	Wrong intervention
-	Zhong N, Wang J.	2019	The efficacy of omega-3 fatty acid for gestational diabetes: a meta-analysis of randomized controlled trials.	Gynecological Endocrinology: The Official Journal Of The International Society Of	35(1)	4–9	N/A	Excluded	Not a priority population- supplement pair

				Gynecological					
				Endocrinology.					
-	Zhou Q, Verne ML, Fields JZ, Lefante JJ, Basra S, Salameh H, et al.	2019	Randomised placebo-controlled trial of dietary glutamine supplements for postinfectious irritable bowel syndrome.	Gut	68(6)	996-1002	10.1136/gutjnl-2017- 315136	Excluded	Not a systematic review
-	Zick SM, Blume A, Normolle D, et al		Challenges in herbal research: a randomized clinical trial to assess blinding with ginger	Complementary Therapies in Medicine	13(2)	101-6		Excluded	Not a systematic review
-	Zick SM, Colacino J, Cornellier M, et al.	2017	Fatigue reduction diet in breast cancer survivors: a pilot randomized clinical trial.	Breast Cancer Research and Treatment	16(2)	299-310		Excluded	Not a systematic review
-	Zick SM, Djuric Z, Ruffin MT, et al.	2008	Pharmacokinetics of 6-gingerol, 8-gingerol, 10- gingerol, and 6-shogaol and conjugate metabolites in healthy human subjects	Cancer Epidemiology, Biomarkers & Prevention	17(8)	1930-6		Excluded	Not a systematic review
-	Zick SM, Gillespie B, Aaronson KD	2008	The effect of Crataegus oxycantha special extract WS 1442 on clinical progression in patients with mild to moderate symptoms of heart failure	European Journal of Heart Failure	10(6)	587-93		Excluded	Not a systematic review
-	Zick SM, Ruffin MT, Lee J, et al	2009	Phase II trial of encapsulated ginger as a treatment for chemotherapy-induced nausea and vomiting	Supportive Care in Cancer	17(5)	563-72		Excluded	Not a systematic review
-	Zick SM, Turgeon DK, Ren J, et al.	2015	Pilot clinical study of the effects of ginger root extract on eicosanoids in colonic mucosa of subjects at increased risk for colorectal cancer	Molecular Carcinogenesis	54(9)	908-15		Excluded	Not a systematic review
-	Zick SM, Turgeon DK, Vareed SK, et al.	2011	Phase II study of the effects of ginger root extract on eicosanoids in colon mucosa in people at normal risk for colorectal cancer	Cancer Prevention Research	4(11)	1929-37		Excluded	Not a systematic review
-	Zick SM, Vautaw BM, Gillespie B, et al	2009	Hawthorn extract randomized blinded chronic heart failure (HERB CHF) trial	European Journal of Heart Failure	11(1)	78		Excluded	Not a systematic review
-	Zick SM, Wright BD, Sen A, et al.	2011	Preliminary examination of the efficacy and safety of a standardized chamomile extract for chronic primary insomnia: a randomized placebo- controlled pilot study	BMC Complementary and Alternative Medicine	11(1)	78		Excluded	Not a systematic review

## C3 Citation details of reviews awaiting classification and reports not retrieved

Completed reviews identified as potentially eligible for inclusion that could not be translated are listed below. No other report types were assessed as awaiting classification.

## Table C-17. Citation details of reviews awaiting classification – reviews not published in English.

Priority intervention- population	Title	Authors	Year	Journal	Volume	Issue	Pages
IBS, probiotics	A meta-analysis of probiotics for the treatment of irritable bowel syndrome	Hu, Y.; Tao, L.; Lyu, B.	2015	Zhonghua nei ke za zhi	54	5	445-51
IBS, probiotics	Probiotic agents for the treatment of irritable bowel syndrome in China: a meta-analysis	Yao, Li; Fu, Ling; Zhao, Sheng-Jun	2012	中国循证医学杂志 (Chinese Journal of Evidence-Based Medicine)	12	5	602-607
Depression, Omega 3	Omega 3 fatty acid and schizophrenia treatment: [review]	Zemdegs, Juliane Costa Silva; Pimentel, Gustavo Duarte; Priel, Margareth Rose	2010	Rev. psiquiatr. clín. (São Paulo)	37	5	223-227
Headache and migraine, magnesium	Dietetics and Nutrition Influence in the Migraine	Silva, Lívia Christine Santana e; Freitas, Betânia de Jesus e Silva de Almendra	2016	J. health sci. (Londrina)	NR	NR	NR

## C4 Citation details of ongoing reviews

Citation details of potentially relevant ongoing reviews registered via PROSPERO identified in full-text screening are listed below.

## Table C-18. Citation details of reviews sought for retrieval – ongoing reviews.

Priority intervention- population	Title	Authors	Year	Retrieved from	Details	Reason for exclusion
Anxiety (including post-natal), magnesium	The effectiveness of dietary intervention on anxiety and depression disorders: a systematic review	Amy Gibson, Chante Studin Kirsten Morris Venus So	2019	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42019128321	PROSPERO ID: CRD42019128321	No publication found. Contacted authors; authors do not plan to publish.
Anxiety (including post-natal), magnesium	Intervention of Different Treatments on Type 2 Diabetes Complicated with Anxiety: A Meta- Analysis	YIQIAN QU, ZHAN LI.	2022	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42022330580	PROSPERO ID: CRD42022330580	No publication found. Contacted authors
Irritable bowel syndrome, probiotics	The efficacy of probiotics supplementation on the quality of life of patients with gastrointestinal disease: a systematic review of clinical studies	Amir Saber, Jalal Moludi, Shima Moradi	2022	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42022382414	CRD42022382414	No publication found. Contacted authors
Irritable bowel syndrome, probiotics	Efficacy of complementary and alternative medicine in adults with irritable bowel syndrome: a systematic review of randomized controlled trials.	Andrea Shin	2018	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42018108040	CRD42018108040	No publication found. Contacted authors
Irritable bowel syndrome, probiotics	Functional Abdominal Pain Disorders (FAPDs) in children (4-18 years): a systematic review on the effectiveness and safety of non- pharmacological treatment options.	Clara de Bruijn, Robyn Rexwinkel, Merit Tabbers, Marc Benninga, Morris Gordon	2020	-	CRD42020159847	Now published (DOI: 10.1542/peds.2020-042101) Manually reviewed. Excluded at full text.

Priority intervention- population	Title	Authors	Year	Retrieved from	Details	Reason for exclusion
Irritable bowel syndrome, probiotics	The effect of dairy on the gut microbiome and gastrointestinal health: a systematic review	Cliona Ni Chonnachain, Eileen Gibney Clare Gollogly	2023	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42023392814	CRD42023392814	No publication found. Contacted authors
Irritable bowel syndrome, probiotics	Gut microbiota variations and microbiota- altering treatment on irritable bowel syndrome- a systematic review and network meta-analysis	Hengxiang Su, Ke Ma	2022	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42022314249	CRD42022314249	No publication found. Contacted authors
Irritable bowel syndrome, probiotics	Effectiveness and Safety of Probiotic fermented milk in the treatment of irritable bowel syndrome: A systematic review and meta-analysis	Junjian Tian, Ting Li, Jingwen Sun, Jun Zhao, Da Li, Zhigang Li, Rongxing Shi	2022	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42022334442	CRD42022334442	No publication found. Contacted authors
Irritable bowel syndrome, probiotics	Lactobacillus rhamnosus for treating irritable bowel syndrome in children – a systematic review with meta-analysis	Marek Ruszczynski, Joanna Tarnoruda, Jakub Zolkiewicz, Luiza Sulej, Barbara Bozek, Aleksandra Hoffmann	2021	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42021258186	CRD42021258186	No publication found. Contacted authors
Irritable bowel syndrome, probiotics	Efficacy of probiotics in patients with irritable bowel syndrome: a systematic review and network meta-analysis	Peiwei Xie, Mei Luo, Lishou Xiong	2023	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42023387351	CRD42023387351	Now published (doi.org/10.3390/nu1517385 6) Manually reviewed. Excluded at full text.
Irritable bowel syndrome, probiotics	Drug and non-drug treatment of chronic constipation: a systematic review of randomized controlled trials and a network meta-analysis	Sha Guo, Ran Sun	2021	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42021242937	CRD42021242937	No publication found. Contacted authors
Irritable bowel syndrome, probiotics	Efficacy of Clostridium butyricum in the treatment of irritable bowel syndrome: A systematic review and meta-analysis	Su zhiwei, Feng wen	2022	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42022373766	CRD42022373766	No publication found. Contacted authors
Irritable bowel syndrome, probiotics	The efficacy of probiotics in the treatment of irritable bowel syndrome: a systematic review	Sun Jianrong, Kong Chenfan, Qu Xiangke, Jia Liqun	2019	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42019127391	CRD42019127391	No publication found. Contacted authors
Irritable bowel syndrome, probiotics	Gut microbiota supplementation and replacement for irritable bowel syndrome: a systematic review and meta-analysis of randomized controlled trials	Xiaofeng Xie, Mancai Wang, Yaqing Zhang	2021	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42021289422	CRD42021289422	Now published (DOI: 10.3389/fimmu.2023.1 136343) Manually reviewed. Excluded at title/abstract
Irritable bowel syndrome, probiotics	The effects of complementary and alternative medicine therapy on symptoms and quality of life in patients with irritable bowel syndrome: a systematic review and network meta-analysis	Yan Pengyu, Guo Shijia, Zhang Xinan, Han Juanjuan	2020	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42020147113	CRD42020147113	No publication found. Contacted authors

Priority intervention- population	Title	Authors	Year	Retrieved from	Details	Reason for exclusion
Irritable bowel syndrome, probiotics	The effect of dairy on the gut microbiome and gastrointestinal health: a systematic review	Cliona Ni Chonnachain, Eileen Gibney Clare Gollogly	2023	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42023392814	CRD42023392814	Now published (doi: 10.1017/gmb.2024.2) Manually reviewed. Excluded at title/abstract
Irritable bowel syndrome, probiotics	Probiotics for irritable bowel syndrome (IBS) in children: an individual patient data (IPD) meta-analysis	Joshua Goldenberg, Lyubov Lytvyn Hania Szajewska Ruggiero Francavilla Tucker Winship Jennifer Beardsley Bradley Johnston	2016	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42016038177	CRD42016038177	No publication found. Contacted authors
Irritable bowel syndrome, probiotics	Efficacy and safety of probiotics, prebiotics, synbiotics and fecal microbiota transplantation on irritable bowel syndrome: a systematic review and meta-analysis	Youhe Wu, Yuetong Li, Lanjuan Li	2023	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42023408698	CRD42023408698	No publication found. Contacted authors
Atopic disorders, zinc	Association between Zinc, Copper/Zinc ratio, Selenium and the risk for childhood asthma and wheeze: a systematic review and meta- analysis	Mei Xue, Wenquan Niu Yicheng Zhang Bo Pang Qiong Wang Min Yang Xiangling Deng Shunan Wang Zhixin Zhang	2022	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42022326185	CRD42022326185	Now published (https://doi.org/10.1016/j.ja nd.2020.01.007) Manually reviewed. Excluded at title/abstract
Atopic disorders, zinc	Systematic review and meta-analysis on serum zinc levels and zinc supplementation in psoriasis	Seyed Mohammad Hosein Mousavi Jazayeri, Fatemeh Mirzaiee	2018	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42018089110	CRD42018089110	No publication found. Contacted authors
Fatigue	Effect of co-enzyme Q10 supplementation on clinical symptoms of fibromyalgia patients: a systematic review and meta-analysis of randomized controlled trials	ammar salehi, Samaneh Sadat, Reza Ghiyasvand, Behnood Abbasi	2016	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42016034052	CRD42016034052	No publication found. Contacted authors
Fatigue	The effectiveness of exercise or antioxidants in the management of fatigue in fibromyalgia (FMS)	Deborrah Russell, Inmaculada Concepción Álvarez Gallardo, Joseph McVeigh, Ciara Hughes, Gareth Davison, Borja Sañudo Corrales	2013	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42013004439	CRD42013004439	No publication found. Contacted authors
Fatigue	The effectiveness of coenzyme Q10 supplementation for patients with breast cancer	Kailin Yang, Liuting Zeng Shiying Zhang	2018	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42018089566	CRD42018089566	No publication found. Contacted authors
Fatigue	The effectiveness of coenzyme Q10 supplementation for patients with breast cancer	Kailin Yang, Liuting Zeng, Shiying Zhang	2018	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42018089566	CRD42018089566	No publication found. Contacted authors
Fatigue	Effects of antioxidants micronutrients and essential fatty acids on cystic fibrosis outcomes: a systematic review	Miriam Simon, Gabriele Carra Forte, Roberta Dalle Molle, Paulo Maróstica, Marceli Feldmann, Thais Rodrigues	2018	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42018092042	CRD42018092042	Now published (doi: 10.1007/s12011-023- 03690-4) Manually reviewed. Excluded at title/abstract
Priority intervention- population	Title	Authors	Year	Retrieved from	Details	Reason for exclusion
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Fatigue	Systematic review of Treatments for Chronic Fatigue Syndrome/Myalgic encephalomyelitis on Quality of life	Reynier Lara, YiZhong Zhuang	2022	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42022354101	CRD42022354101	No publication found. Contacted authors
Headache	Magnesium therapy in the treatment of chronic pain: a systematic review	Evan Oliver Matthews, Matthew Bryant, Aman Ahuja, Akhilesh Tiwari	2020	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42020164342	CRD42020164342	No publication found. Contacted authors
Hypertension	Omega-3 fatty acids for vascular access outcomes in patients with chronic kidney disease [Cochrane Protocol]	Mei-Yi Wu, Ka-Wai Tam Fahad Javaid Siddiqui Edwin Chan Tazeen Jafar	2015	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42015020481	CRD42015020481	Now published: https://doi.org/10.1002/14651 858.CD011353.pub2 Manually reviewed. Excluded at title/abstract
Hypertension	The efficacy of n-3 fatty acid supplementation for the prevention of pregnancy-induced hypertension or preeclampsia: a systematic review and meta-analysis of randomized controlled trials	Mouloud Agajani Delavar, Fatemeh Bakouei Sedigheh Esmailzadeh Sepideh Mashayekhamiri Zeynab Taheri	2018	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42018090915	CRD42018090915	Now published: doi: 10.1016/j.tjog.2019.11.002. Manually reviewed. Duplicate excluded.
Hypertension	Which agent most effectively prevents preeclampsia? A systematic review with multi-treatment comparison (network meta- analysis) of large multicenter randomized controlled trials	Jared Roeckner, Luis Sanchez- Ramos Andrew Kaunitz	2016	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42016043584	CRD42016043584	Now published: https://doi.org/10.1016/j.ajog. 2016.11.792 Manually reviewed. Excluded at title/abstract
Hypertension	Omega-3 fatty acids supplementation in patients with peripheral artery disease : a systematic review and meta-analysis	Yingchih cheng, Cheng-We Liu Wei- Cheng Chang MiN- I. Su	2020	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42020168416	CRD42020168416	No publication found. Contacted authors
Hypertension	Blood pressure lowering efficacy of omega-3 polyunsaturated fatty acid for primary hypertension	Chen, Shuo	2017	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42017072569	CRD42017072569	No publication found. Contacted authors
Hypertension	Does omega-3 PUFAs supplementation improve metabolic syndrome and related cardiovascular diseases? A systematic review and meta-analysis of randomized controlled trials	Yongjin Wang, Yandan Wang Gangcheng Wu Xingguo Wang	2022	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42022372178	CRD42022372178	Now published: DOI: 10.1080/10408398.202 3.2212817 Manually reviewed. Duplicate excluded.
Hypertension	N-3 polyunsaturated reduce the risk of cardiovascular adverse events in people with type 2 diabetes:Systematic review and meta- analysis	Yuan Xue, Weichao Bao	2023	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42023423045	CRD42023423045	No publication found. Contacted authors

Priority intervention- population	Title	Authors	Year	Retrieved from	Details	Reason for exclusion
Hypertension	N-3 polyunsaturated reduce the risk of cardiovascular adverse events in people with type 2 diabetes: Systematic review and meta- analysis	Rucheng Cheng, Yanyan Mou Zhaojun Lu Weijun Zheng	2020	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42020211872	CRD42020211872	No publication found. Contacted authors
Hypertension	The effects of Omega-3 fatty acids supplementation on blood pressure in hypertensive adults: a systematic review and dose-response meta-analysis of differences in means	Hossein Shahinfar, Sakineh Shabbidar	2021	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42021266262	CRD42021266262	No publication found. Contacted authors
Hypertension	The impact of eicosapentaenoic and docosahexaenoic acid on measures of arterial pressure: a meta-analysis of randomized-controlled trials protocol	David Brennan, John Babraj Sarah Cottin	2021	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42021261056	CRD42021261056	No publication found. Contacted authors
Hypertension	Effect of Vitamin D and Omega-3 Fatty Acid Co-supplementation on cardiometabolic risk factors	javad Heshmati, Mojgan Morvaridzadeh	2021	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42021242640	CRD42021242640	No publication found. Contacted authors
Hypertension	Comparing the Effects of Docosahexaenoic and Eicosapentaenoic Acids on Cardiovascular Risk Factors: Pairwise and Network Meta-Analyses of Randomized Controlled Trials	Mohammad hassan sohouli, Farzad Shifar	2022	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42022328633	CRD42022328633	No publication found. Contacted authors
Hypertension	Effect of the amount and quality of dietary fat on cardiometabolic risk factors in postmenopausal women: a systematic review and meta-analysis of randomised controlled trials	Joanna Bajerska, Joanna Pieczyńska Aleksandra Skoczek- Rubińska Jakub Noskiewicz Vesna Vufçifá Aleksandra Arsic Snjezana Petrovic Danijela Ristic-Medic	2021	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42021284814	CRD42021284814	No publication found. Contacted authors
Hypertension	Impact of n-3 polyunsaturated fatty acid intake in pregnancy on maternal health and birth outcomes: meta-analyses from randomized controlled trials	Mona AbdelRahman, marina emad ahmed fathy	2022	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42022314485	CRD42022314485	Now published: doi: 10.1007/s00404-022-06533-0 Manually reviewed. Duplicate excluded.
Fibromyalgia	Magnesium therapy in the treatment of chronic pain: a systematic review	Evan Oliver Matthews, Matthew Bryant Aman Ahuja Akhilesh Tiwari	2020	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42020164342	CRD42020164342	No publication found. Contacted authors
Fibromyalgia	Magnesium intake and its relationship with chronic non- cancer pain in adults: a systematic review	Gonzalo Altez, Luisa Saravia Estela Skapino	2020	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42020197189	CRD42020197189	No publication found. Contacted authors
Fibromyalgia	Magnesium for the management of chronic non-cancer pain in adults: a systematic review	Rex Park, Anthony Ho Gisele Pickering Lars Arendt-Nielsen Ian Gilron	2018	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42018103284	CRD42018103284	Now published: https://doi.org/10.1213/ane. 000000000004673 Manually reviewed. Duplicate excluded.

Priority intervention- population	Title	Authors	Year	Retrieved from	Details	Reason for exclusion
Recurrent infection/s	Diagnosis, treatment and prevention of exacerbation of cough in chronic bronchitis and COPD	Mark Maleskar, Priscilla Callahan- Lyon Mark Madison Belinda Ireland	-	Unable to retrieve protocol or study details	-	-
Recurrent infection/s	Zinc supplementation and its role in immunity in childhood	Camila Penso, Elza Mello Sandra Machado	2020	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42020215333	CRD42020215333	No publication found. Contacted authors
Recurrent infection/s	Community based interventions for prevention and control of acute diarrheal disease in children under 5 years of age: an overview of systematic reviews	Jaya Kshatri, Srikanta Kanungo Asit Mansingh Sucharita Panigrahi Sanghamitra Pati	2020	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42020151893	CRD42020151893	No publication found. Contacted authors
Recurrent infection/s	Effect of supplementation with zinc on malaria: A systematic review and meta- analysis	Manas Kotepui, Polrat Wilairatana Kwuntida Uthaisar Kotepui Kinley Wangdi Frederick Ramirez Masangkay Wanida Mala	2023	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42023424345	CRD42023424345	Now published: doi: 10.3390/nu15132855.Manua lly reviewed. Excluded at title/abstract
Recurrent infection/s	Assessing the effects of micronutrients on viral infection in humans: a systematic review and meta-analysis	Muhammad Baig, Mir Moafi Madani Samuel Shim Bo Yang Andrew Zullo Tongzhang Zheng Jie Li Wen-Chih Wu Simin Liu	2021	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42021270615	CRD42021270615	No publication found. Contacted authors
Recurrent infection/s	A systematic review and meta-analysis of observation and intervention studies on the prevention of upper respiratory tract infection: implications for the role of nutrient intake	Tsuyoshi Chiba, Nanae Tanemura Chiharu Nishijima Rie Akamatsu	2020	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42020222530	CRD42020222530	No publication found. Contacted authors
Recurrent infection/s	Zinc supplementation in patients with Cystic fibrosis for respiratory function	Zohaa Shahid, Sandhiya Kumari Nudrat Farheen	2023	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42023388050	CRD42023388050	No publication found. Contacted authors
Diabetes	Effects of coenzyme Q10 supplementation on obesity-related metabolic disorders	Azimeh Izadi	2018	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42018081367	CRD42018081367	No publication found. Contacted authors
Diabetes	Lipoic acid oral supplement in metabolic syndrome: a systematic review and meta- analysis of randomized controlled trials	Fabiana Moura	2017	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42017063940	CRD42017063940	No publication found. Contacted authors
Diabetes	Comparative effects of nutritional supplements on adipokines, oxidative stress and inflammatory markers in adults with metabolic syndrome: a network meta- analysis of randomized controlled trials	Gongquan Wang, Bing Du Jiawei Zhai Jiajia Wang	2023	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42023417473	CRD42023417473	No publication found. Contacted authors
Diabetes	The effectiveness of alpha-lipoic acid supplementation for type 2 diabetes patients	Kailin Yang, Liuting Zeng, Shiying Zhang	2018	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42018088479	CRD42018088479	No publication found. Contacted authors

Priority intervention- population	Title	Authors	Year	Retrieved from	Details	Reason for exclusion
Diabetes	The impact of Coenzyme Q10 on cardiovascular outcomes in diabetic patients: A systematic review and meta- analysis	Phiwayinkosi Dludla, Tawanda M. Nyambuya, Patrick Orlando, Sonia Silvestri, Jacopo Sabbatinelli, Bongani B. Nkambule, Vuyo Mxinwa, Kabelo Mokgalaboni, Johan Louw, Luca Tiano	2020	https://www.crd.york.ac.uk/pr ospero/display_record.php?ID =CRD42020156632	CRD42020156632	Now published; excluded as duplicate.
Diabetes	Effect of coenzyme q10 in patients with metabolic syndrome	Shrouk Ramadan, Mariam Tarek Desouki, Osama Elzankaly, Ahmed Helmi	2023	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42023405471	CRD42023405471	No publication found. Contacted authors
Diabetes	Comparative effects of different types of nutritional supplements on intermediate- disease markers: a network meta-analysis of randomized controlled trials	Suocheng Hui, Kai Wang	2023	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42023397877	CRD42023397877	No publication found. Contacted authors
Diabetes	Alpha Lipoic Acid in the treatment of Diabetic Peripheral Neuropathy– A Systematic Review and Meta-Analysis	Usha Rani Pingali, Padmaja Mekala, Sireesha Kammila, Sravanasandhya Penugonda, Mohammed Abid Ali	2021	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42021284560	CRD42021284560	No publication found. Contacted authors
Diabetes	Effects of coenzyme Q10 supplement on glucose metabolism, lipid profiles, and biomarkers of inflammation: a systematic review and meta-analysis	zhuo liu, Yufan Song, Yanjing Huang, Runan Hu, Fan Li, Fanru Zhou, Yuli Geng, Mingmin Zhang	2022	https://www.crd.york.ac.uk/pro spero/display_record.php?ID=C RD42022313682	CRD42022313682	No publication found. Contacted authors

# C5 Citation details of conference abstracts

Citation details of potentially relevant conference abstracts identified in full-text screening are listed below.

#### Table C-19. Citation details of reviews sought for retrieval – conference abstracts.

Priority intervention- population	Title	Authors	Year	Journal	Volume	Issue	Pages	Details
Irritable bowel syndrome, probiotics	Effectiveness of probiotics in irritable bowel syndrome: A systematic review with meta-analysis	Nikfar, S.; Mozafari, S.; Didari, T.; Abdollahi, M.	2014	Value in Health	17	7	A363	Conference abstract; full- text published and included in full-text review
Irritable bowel syndrome, probiotics	Comparative efficacy of probiotics for treatment of irritable bowel syndrome in children and adults: A systematic review and meta-analysis	Lo Vecchio, A.; Chiatto, F.; Viscovo, S.; Bruzzese, E.; Bruzzese, D.; Giannattasio, A.; Guarino, A.	2014	Digestive and Liver Disease	46		e124- e125	Conference abstract; full- text published and included in full-text review

# Appendix D Characteristics of included reviews.

For each population-supplement pair this appendix provides the citation details of the included studies (if any), as well as the characteristics of included reviews. Tables are organised alphabetically. Preferred reviews are coloured green.

# D1 Anxiety (including post-natal), magnesium

Table D-1. Citation details of included reviews – anxiety (including post-natal), magnesium (n=2).

Review ID	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
Barić 2018	Complementary and Alternative Medicine Treatments for Generalized Anxiety Disorder: Systematic Review and Meta- analysis of Randomized Controlled Trials	Barić H, Đorđević V, Cerovečki I, Trkulja V.	2018	Advances in Therapy	35	3	261-288	10.1007/s12325-018- 0680-6
Tsai 2023	Dietary interventions for perinatal depression and anxiety: a systematic review and meta-analysis of randomized controlled trials	Tsai Z, Shah N, Tahir U, Mortaji N, Owais S, Perreault M, Van Lieshout RJ	2023	Am J Clin Nutr	117	6	1130-1142	10.1016/j.ajcnut.2023. 03.025

Table D-2. Characteristics of included reviews – anxiety (including post-natal), magnesium (n=2).

Review	Review detai	ils			Search deta	ils			Quality ass	essment	Other	
ID	Review design	Aim of the review (as reported by the SR)	Types of studies included	Outcomes relevant to the Overview <sup>^</sup>	# of databases searched	Names of databases searched	Date of last search	Search restrictions	RoB tool used	Certainty of evidence	Conflicts of interest	Funding sources
Barić 2018	Systematic Review and Meta- analysis	To evaluate empirical evidence of clinical efficacy and safety of CAM methods in the treatment of GAD in adults, as assessed in RCTs.	RCTs	1	6	Medline, Web of Science, EBSCO (Academic Search Complete, CINAHL and ERIC), Scopus— Health Sciences, Google Scholar, Cochrane Library	Mar 2017	NR	Cochrane Risk of Bias Tool	GRADE	Nothing to disclose.	No funding or sponsorship was received for this study or publication of this article.
Tsai 2023	Systematic Review and Meta- analysis	To assess the effectiveness of dietary interventions for the treatment of perinatal depression and/or anxiety.	RCTs	1, 4	5	MEDLINE, EMBASE, PsycINFO, CINAHL, Web of Science	Nov 2022	English	Cochrane Risk of Bias Tool	NR	The authors report no conflicts of interest.	The authors reported no funding received for this study.

Abbreviations: CAM=complementary and alternative medicine; CINAHL=Cumulative Index of Nursing and Allied Health Literature; GAD=generalised anxiety disorder; GRADE=Grading of Recommendations Assessment, Development and Evaluation; PMS=premenstrual syndrome; NR=Not reported; RCT=randomised controlled trial

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Anxiety-related emotional functioning/mental health burden;
- 2. Physical function burden from anxiety (gastrointestinal disorders, loss of sexual desire, frequent upper respiratory tract and other infections)
- 3. Improvement in clinical levels of anxiety
- 4. Depression-related emotional functioning/mental health burden
- 5. Stress-related emotional functioning/mental health burden
- 6. Physiological symptoms of anxiety (heart rate, BP, adrenaline, skin conductance, weight gain, weight loss, cortisol levels)
- 7. Health-related quality of life

### D2 Stress (perceived, occupational), magnesium

#### Table D-3. Citation details of included reviews – stress, magnesium (n=0).

Review ID	Title	Authors	Year	r Journal Vo		Issue	Pages	DOI
No reviews we	ere identified for inclusion in the Overview							

#### D3 Irritable bowel syndrome, probiotics

#### Table D-4. Citation details of included reviews – irritable bowel syndrome, probiotics (n=31).

Review ID	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
Abboud 2020	The Health Effects of Vitamin D and Probiotic Co- Supplementation: A Systematic Review of Randomized Controlled Trials	Abboud, M.; Rizk, R.; AlAnouti, F.; Papandreou, D.; Haidar, S.; Mahboub, N.	2020	Nutrients	13	1	111	10.3390/nu13010111
Asha 2020	Efficacy and Safety of Probiotics, Prebiotics and Synbiotics in the Treatment of Irritable Bowel Syndrome: A systematic review and meta-analysis	Asha, M. Z.; Khalil, S. F. H.	2020	Sultan Qaboos University medical journal	20	1	e13-e24	10.18295/squmj.2020. 20.01.003
Connell 2018	Systematic review and meta-analysis: Efficacy of patented probiotic, VSL#3, in irritable bowel syndrome	Connell, M.; Shin, A.; James-Stevenson, T.; Xu, H.; Imperiale, T. F.; Herron, J.	2018	Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society	30	12	e13427	10.1111/nmo.13427
Corbitt 2018	A Systematic Review of Probiotic Interventions for Gastrointestinal Symptoms and Irritable Bowel Syndrome in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME)	Corbitt, M.; Campagnolo, N.; Staines, D.; Marshall-Gradisnik, S.	2018	Probiotics and antimicrobial proteins	10	3	466-477	10.1007/s12602-018- 9397-8

Review ID	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
Ding 2019	Probiotics for paediatric functional abdominal pain disorders: A rapid review	Ding, F. C. L.; Karkhaneh, M.; Zorzela, L.; Jou, H.; Vohra, S.	2019	Paediatrics and Child Health (Canada)	24	6	383- 394	https://dx.doi.org/10. 1093/pch/pxz036
Fatahi 2022	Effects of probiotic supplementation on abdominal pain severity in pediatric patients with irritable bowel syndrome: a systematic review and meta-analysis of randomized clinical trials	Fatahi, S.; Hosseini, A.; Sohouli, M. H.; Sayyari, A.; Khatami, K.; Farsani, Z. F.; Amiri, H.; Dara, N.; de Souza, I. G. O.; Santos, H. O.	2022	World Journal of Pediatrics	18	5	320-332	10.1007/s12519-022- 00516-6
Ford 2014	Efficacy of prebiotics, probiotics, and synbiotics in irritable bowel syndrome and chronic idiopathic constipation: systematic review and meta-analysis	Ford, A. C.; Quigley, E. M.; Lacy, B. E.; Lembo, A. J.; Saito, Y. A.; Schiller, L. R.; Soffer, E. E.; Spiegel, B. M.; Moayyedi, P.	2014	The American journal of gastroenterology	109	10	1547-61	10.1038/ajg.2014.202
Horvath 2011	Meta-analysis: Lactobacillus rhamnosus GG for abdominal pain- related functional gastrointestinal disorders in childhood	Horvath, A.; Dziechciarz, P.; Szajewska, H.	2011	Alimentary pharmacology & therapeutics	33	12	1302-10	10.1111/j.1365- 2036.2011.04665.x
Hoveyda 2009	A systematic review and meta-analysis: probiotics in the treatment of irritable bowel syndrome	Hoveyda, N.; Heneghan, C.; Mahtani, K. R.; Perera, R.; Roberts, N.; Glasziou, P.	2009	BMC gastroenterology	9		15	10.1186/1471-230X-9- 15
Huertas- Ceballos 2009	Dietary interventions for recurrent abdominal pain (RAP) and irritable bowel syndrome (IBS) in childhood	Huertas-Ceballos, A. A.; Logan, S.; Bennett, C.; Macarthur, C.	2009	Cochrane Database of Systematic Reviews	-	1	CD0030 19	https://dx.doi.org/10.1 002/14651858.CD0030 19.pub3
Hungin 2018	Systematic review: probiotics in the management of lower gastrointestinal symptoms - an updated evidence-based international consensus	Hungin, A. P. S.; Mitchell, C. R.; Whorwell, P.; Mulligan, C.; Cole, O.; Agréus, L.; Fracasso, P.; Lionis, C.; Mendive, J.; Philippart de Foy, J. M.; Seifert, B.; Wensaas, K. A.; Winchester, C.; de Wit, N.; European Society for Primary Care, Gastroenterology	2018	Alimentary pharmacology & therapeutics	47	8	1054- 1070	10.1111/apt.14539
Konstantis 2023	Efficacy and safety of probiotics in the treatment of irritable bowel syndrome: A systematic review and meta-analysis of randomised clinical trials using ROME IV criteria	Konstantis, G.; Efstathiou, S.; Pourzitaki, C.; Kitsikidou, E.; Germanidis, G.; Chourdakis, M.	2023	Clinical nutrition (Edinburgh, Scotland)	42	5	800-809	10.1016/j.clnu.2023.03 .019
Korterink 2014	Probiotics for childhood functional gastrointestinal disorders: A systematic review and meta-analysis	Korterink, J. J.; Ockeloen, L.; Benninga, M. A.; Tabbers, M. M.; Hilbink, M.; Deckers-Kocken, J. M.	2014	Acta Paediatrica, International Journal of Paediatrics	103	4	365-372	https://dx.doi.org/10.1 111/apa.12513
Le Morvan 2021	The Effect of Probiotics on Quality of Life, Depression and Anxiety in Patients with Irritable Bowel Syndrome: A Systematic Review and Meta-Analysis	Le Morvan de Sequeira, C.; Kaeber, M.; Cekin, S. E.; Enck, P.; Mack, I.	2021	Journal of clinical medicine	10	16	NR	10.3390/jcm1016349 7
Li 2020	Efficacy and Safety of Probiotics in Irritable Bowel Syndrome: A Systematic Review and Meta-Analysis	Li, B.; Liang, L.; Deng, H.; Guo, J.; Shu, H.; Zhang, L.	2020	Frontiers in pharmacology	11	-	332	10.3389/fphar.2020.0 0332
Liang 2019	Efficacy of different probiotic protocols in irritable bowel syndrome: A network meta-analysis	Liang, D.; Longgui, N.; Guoqiang, X.	2019	Medicine	98	27	e16068	10.1097/MD.00000000 00016068
McFarland 2008	Meta-analysis of probiotics for the treatment of irritable bowel syndrome	McFarland, L. V.; Dublin, S.	2008	World journal of Gastroenterology	14	17	2650-61	10.3748/wjg.14.2650

Review ID	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
McFarland 2021	Strain-specific and outcome-specific efficacy of probiotics for the treatment of irritable bowel syndrome: A systematic review and meta-analysis	McFarland, L. V.; Karakan, T.; Karatas, A.	2021	EClinicalMedicine	41		101154	10.1016/j.eclinm.2021. 101154
Moayyedi 2010	The efficacy of probiotics in the treatment of irritable bowel syndrome: a systematic review	Moayyedi, P.; Ford, A. C.; Talley, N. J.; Cremonini, F.; Foxx-Orenstein, A. E.; Brandt, L. J.; Quigley, E. M.	2010	Gut	59	3	325-32	10.1136/gut.2008.1672 70
Nikfar 2008	Efficacy of probiotics in irritable bowel syndrome: a meta- analysis of randomized, controlled trials	Nikfar, S.; Rahimi, R.; Rahimi, F.; Derakhshani, S.; Abdollahi, M.	2008	Diseases of the colon and rectum	51	12	1775-80	10.1007/s10350-008- 9335-z
Niu 2020	The efficacy and safety of probiotics in patients with irritable bowel syndrome: Evidence based on 35 randomized controlled trials	Niu, H. L.; Xiao, J. Y.	2020	International Journal of Surgery	75	-	116-127	https://dx.doi.org/10.1 016/j.ijsu.2020.01.142
Ortiz-Lucas 2013	Effect of probiotics on symptoms of irritable bowel syndrome: A meta-analysis updated	Ortiz-Lucas, M.; Tobias, A.; Saz, P.; Sebastian, J. J.	2013	Revista Espanola de Enfermedades Digestivas	105	1	19-36	-
Pratt 2020	The Effect of Bifidobacterium on Reducing Symptomatic Abdominal Pain in Patients with Irritable Bowel Syndrome: A Systematic Review	Pratt, C.; Campbell, M. D.	2020	Probiotics and antimicrobial proteins	12	3	834-839	10.1007/s12602-019- 09609-7
Ritchie 2012	A meta-analysis of probiotic efficacy for gastrointestinal diseases	Ritchie, M. L.; Romanuk, T. N.	2012	PloS one	7	4	e34938	https://dx.doi.org/10.1 371/journal.pone.0034 938
Shang 2022	Effectiveness and Safety of Probiotics for Patients with Constipation-Predominant Irritable Bowel Syndrome: A Systematic Review and Meta-Analysis of 10 Randomized Controlled Trials	Shang, X.; E, F. F.; Guo, K. L.; Li, Y. F.; Zhao, H. L.; Wang, Y.; Chen, N.; Nian, T.; Yang, C. Q.; Yang, K. H.; Li, X. X.	2022	Nutrients	14	12	2482	10.3390/nu14122482
Sun 2020	Efficacy and safety of probiotics in irritable bowel syndrome: A systematic review and meta-analysis	Sun, J. R.; Kong, C. F.; Qu, X. K.; Deng, C.; Lou, Y. N.; Jia, L. Q.	2020	Saudi journal of gastroenterology : official journal of the Saudi Gastroenterology Association	26	2	66-77	10.4103/sjg.SJG_384_1 9
Wang 2022	Probiotics therapy for adults with diarrhea-predominant irritable bowel syndrome: a systematic review and meta-analysis of 10 RCTs	Wang, Y.; Chen, N.; Niu, F.; Li, Y.; Guo, K.; Shang, X.; E, F.; Yang, C.; Yang, K.; Li, X.	2022	International journal of colorectal disease	37	11	2263- 2276	10.1007/s00384-022- 04261-0
Wen 2020	The efficacy and safety of probiotics for patients with constipation-predominant irritable bowel syndrome: A systematic review and meta-analysis based on seventeen randomized controlled trials	Wen, Y.; Li, J.; Long, Q.; Yue, C. C.; He, B.; Tang, X. G.	2020	International Journal of Surgery	79		111- 119	https://dx.doi.org/10. 1016/j.ijsu.2020.04.0 63
Xu 2021	Efficacy of probiotic adjuvant therapy for irritable bowel syndrome in children: A systematic review and meta-analysis	Xu, H. L.; Zou, L. L.; Chen, M. B.; Wang, H.; Shen, W. M.; Zheng, Q. H.; Cui, W. Y.	2021	PloS one	16	8	e025516 0	10.1371/journal.pone. 0255160
Yuan 2017	Efficacy of Bifidobacterium infantis 35624 in patients with irritable bowel syndrome: a meta-analysis	Yuan, F.; Ni, H.; Asche, C. V.; Kim, M.; Walayat, S.; Ren, J.	2017	Current Medical Research and Opinion	33	7	1191- 1197	10.1080/03007995.201 7.1292230

Review ID	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
Zhang 2016	Effects of probiotic type, dose and treatment duration on irritable bowel syndrome diagnosed by Rome III criteria: a meta-	Zhang, Y.; Li, L.; Guo, C.; Mu, D.; Feng, B.; Zuo, X.; Li, Y.	2016	BMC gastroenterology	16	1	62	10.1186/s12876-016- 0470-z

Table D-5. Characteristics of included reviews – Irritable bowel syndrome, probiotics (n=31).

Review	Review details	6			Search deta	ils			Quality asse	ssment	Other	
ID	Review design	Aim of the review (as reported by the SR)	Types of studies included	Outcomes relevant to the Overview^	# of databases searched	Names of databases searched	Date of last search	Search restriction s	RoB tool used	Certainty of evidence	Conflicts of interest	Funding sources
Abboud 2020	Systematic review (summarised narratively)	To investigate the literature and summarize the available evidence of RCTs on the various health effects of a combined supplementation of vitamin D and probiotics among children and adults.	RCTs	1	7	PubMed, MEDLINE, CINAHL, EMBASE, Cochrane Library, ClinicalTrials.gov, International Clinical Trials Registry Platform (ICTRP)	Nov 2020	None	Cochrane Risk of Bias Tool	NR	The authors declare that they have no competing interests.	College of Natural and Health Sciences, Zayed University, Dubai, United Arab Emirates. The funding body not involved in the design of the study and collection, analysis, and interpretation of data or in writing the manuscript.
Asha 2020	Systematic review and meta- analysis	A comprehensive evaluation of the efficacy and safety of prebiotics, probiotics and synbiotics in the management of patients with IBS.	RCTs	1, 2, 3	4	MEDLINE, Embase, Cochrane Library, Google Scholar	Jun 2019	English- language, 2000-2019, minimum sample size was 50 patients	Cochrane Risk of Bias Tool	NR	NR	NR
Connell 2018	Systematic review and meta- analysis	To quantify effects of VSL#3 on abdominal pain, stool consistency, overall response, abdominal bloating, and quality of life (QOL) in IBS through meta- analysis.	RCTs	1, 2, 3, 7	4	MEDLINE, EMBASE, Web of Science, Scopus	May 2017	No date limitations or language restrictions . Studies had to be free; excluded if only one out of three keywords	Cochrane Risk of Bias Tool	GRADE	NR	AS is supported, in part, by grants KL2TR001106, and UL1TR001108 (A. Shekhar, PI) from the National Institutes of Health, National Center for Advancing Translational

								were present in the title or abstract.				Sciences, Clinical and Translational Sciences Award.
Corbitt 2018	Systematic review	To conduct a systematic review of these symptoms in CFS/ME, along with any evidence for probiotics as treatment.	Interventi on-based research	1, 3, 7	4	PubMed, Scopus, Medline, EMBASE	Jun 2017	NR	Rosendal Scale	NR	The authors declare that they have no conflicts of interest	NR
Ding 2019	Rapid systematic review	To synthesize the best evidence on the use of probiotics in children with functional abdominal pain disorders (FAPD)	RCTs	2, 5	5	MEDLINE, EMBASE, CINAHL, CENTRAL, Google Scholar	Nov 2017	1990 through November 2017; English	Cochrane Risk of Bias Tool	NR	No reported conflicts of interest.	There are no funders to report for this submission.
Fatahi 2022	Systematic review and meta- analysis	To investigate the overall effects of probiotic supplementation in reducing abdominal pain in paediatric patients with IBS	RCTs	2	5	Scopus, Embase, PubMed, Web of Science, Cochrane library	Apr 2021	None	Cochrane Risk of Bias Tool	NR	None of the authors had any personal or financial conflicts of interest.	None of the authors had any personal or financial conflicts of interest.
Ford 2014	Systematic review and meta- analysis	To examine the efficacy of prebiotics, probiotics, and synbiotics in IBS and CIC.	RCTs	1, 2	3	MEDLINE, EMBASE, CENTRAL	Dec 2013	None	Cochrane Risk of Bias Tool	NR	None	This work was supported by American College of Gastroenterology.
Horvath 2011	Systematic review and meta- analysis	To evaluate systematically the effect of Lactobacillus rhamnosus GG (LGG) for treating abdominal pain-related functional gastrointestinal disorders in children.	RCTs	2,	3	CENTRAL, MEDLINE, EMBASE	Dec 2010	None	Cochrane Risk of Bias Tool	NR	H. Szajewska and A. Horvath served as speakers for Dicopharm, the manufacturer of Lactobacillus GG.	This study was funded in full by The Medical University of Warsaw.
Hoveyda 2009	Systematic review and meta- analysis	To evaluate the efficacy of probiotics in alleviating symptoms in patients with irritable bowel syndrome.	RCTs	1, 2, 3	5	MEDLINE, EMBASE, CINAHL, AMED, Cochrane Library	Aug 2007	A high sensitivity "therapy" (trials) filter was	NR	NR	The authors declare that they have no competing interests.	No funding was sought or obtained for the conduct of this study.

								applied to the EMBASE search.				
Huertas- Ceballos 2009	Systematic review	To examine the effectiveness of dietary interventions in school- age children with RAP.	Random or quasi- random interventi ons	1	9	CENTRAL, MEDLINE, EMBASE, CINAHL, Eric, PsycINFO, Lilacs, SIGLE, JICST	NR	NR	Cochrane Risk of Bias Tool	NR	None known.	External sources: DOH Cochrane Review Incentive Scheme 2006, UK.
Hungin 2018	Systematic review	To give clinicians a practical reference guide on the role of specified probiotics in managing particular lower gastrointestinal symptoms/problems by means of a systematic review-based consensus.	RCTs	1, 2, 3, 6	2	Embase, MEDLINE	Jun 2017	NR	Critical Appraisal Skills Programme (CASP) Checklist for RCTs	GRADE	APSH, LA, PF, CL, JM, BF, K- AW and NdW are committee members of the ESPCG. ASPH has received financial support for the literature review and consensus development activities from Danone, and medical writing assistance from Oxford PharmaGene sis Ltd funded by Danone, for the submitted study. APSH has served as a speaker, a consultant and an advisory board member for	Supported and facilitated by the ESPCG, which received an unrestricted grant from Danone (Paris, France). At the request of the ESPCG, support for the consensus was provided by Dr Catherine Mitchell, Oliver Cole and Dr Chris Winchester (Research Evaluation Unit, Oxford PharmaGenesis Ltd, Oxford, UK). The systematic literature searches and initial title/abstract screening were conducted by Dr Catherine Mitchell (Oxford PharmaGenesis Ltd). Oxford PharmaGenesis Ltd). Oxford PharmaGenesis Ltd). Oxford PharmaGenesis Ltd). Oxford PharmaGenesis Ltd). Oxford PharmaGenesis Ltd received project funding from Danone. The funding body had no input into the

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											PharmaGene sis Holdings Ltd, and is Director of several Oxford PharmaGene sis companies and trustee of a charity. NdW's institution has received a grant from the ESPCG for the submitted study.	
Konstanti s 2023	Systematic review and meta- analysis	The aim of this study was to systematically review available clinical data about the benefit of probiotics in IBS- patients, which were categorized solely using the Rome IV criteria	RCTs	1,2,3	3	MEDLINE, Scopus, Cochrane	Jan 2023	No time or language restrictions	Cochrane Risk of Bias Tool	NR	None declared	None declared
Korterink 2014	Systematic review and meta- analysis	To evaluate the effect of different probiotic strains in the treatment of abdominal pain- and defecation-related FGID.	RCTs	2, 6, 7	4	CENTRAL, MEDLINE, EMBASE, CINAHL	Jun 2013	NR	Cochrane Risk of Bias Tool	NR	NR	NR
Le Morvan 2021	Systematic review and meta- analysis	Providing a synthesis of the evidence regarding the effect of probiotics and paraprobiotics on quality of life, psychiatric symptoms (anxiety and depression) and central functions—the latter defined as neurophysiological parameters measured,	RCTs	3,	3	PubMed, Web of Science, Cochrane Library	Apr 2021	NR	Cochrane Risk of Bias Tool	NR	The authors C.L.M.d.S., S.E.C., M.K. and I.M. declare no conflict of interest. P.E. is a consultant of Alimentary Health, Aptiny, Arena,	I.M. received a grant from the Ministry of Science at Baden- Württemberg and the European Social Fund.

		e.g., functional									Cemet,	
		magnetic resonance									Indigo,	
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Li 2020	Systematic	To examine the efficacy	RCTs	1,2	5	Medline, Embase,	Jan	NR	Cochrane	NR	The authors	This research was
	review and	of global IBS symptoms				CENTRAL,	2019		Risk of Bias		declare that	supported by the
	meta-	improvement, global				ClinicalTrials.gov			Tool		the research	Youth Foundation
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Liang 2019	Network meta analysis	To differentiate the reasonable protocols by assessing the efficacy and safety through the combined way of traditional and network meta-analysis.	RCTs	1,	5	PubMed, Medline, EMBASE, Web Of Science, CENTRAL	April 2019	January 2006 to April 2019	Cochrane Risk of Bias Tool	NR	The authors report no conflicts of interest	NR
McFarlan d 2008	Meta- analysis	To determine the overall efficacy of probiotics for IBS by comparing a common outcome in treated patients with a control group.	RCTs	1, 2	6	PubMed, Medline, Google Scholar, CENTRAL, metaRegister of Controlled Trials, National Institutes of Health	2007	1982-2007	Linde Internal Validity Scale (LIVS)	NR	NR	NR
McFarlan d 2021	Systematic review and meta- analysis	To determine which probiotic strains are safe and effective for the treatment of IBS, accounting for both strain-specificity and based on probiotics with at least one confirmatory trial.	RCTs	1, 2, 3	3	PubMed, Google Scholar, NIH registry of clinical trials	NR	This review is an update from a prior meta- analysis of pro- biotics for IBS, but includes trials and recommen dations published in the subsequen t 13 years	Cochrane Risk of Bias Tool	NR	LVM is on the Scientific Advisory Board of Bio- K+ (Bio-K+, a Kerry company) and on the Biocodex Microbiome Board (Biocodex, France) and has received honoraria from Bio-K+ and Biocodex. TK and AK declared no conflicts of interest.	This study was un- funded. All authors had access to the dataset and decided to submit for publication. This study did not require ethical approval.
Moayyedi 2010	Systematic review	To evaluate the impact of probiotics on IBS and to explore potential reasons for heterogeneity in study findings.	RCTs	1, 2	3	MEDLINE, EMBASE, Cochrane Controlled Trials Register	Dec 2013	Nil	Jadad scale	NR	Declared (the declaration can be viewed on the Gut website at http://www.g	This study was supported by funding from the American College of Gastroenterology

											ut.bmj.com/s upplemental) ·	
Nikfar 2008	Meta- analysis	To evaluate whether probiotics improve symptoms in patients with irritable bowel syndrome.	RCTs	1,	5	PubMed, Embase, Scopus, Web of Science, CENTRAL	Sep 2007	Nil	Jadad score	NR	NR	NR
Niu 2020	Systematic review and meta- analysis	To evaluate the efficacy and safety of probiotics in patients with IBS.	RCTs	1, 2	4	Cochrane Library, PubMed, EMBASE, Web of Science	Apr 2019	NR	Jadad scale	NR	The authors declare no relevant conflict of interest.	There is no funding for this work.
Ortiz- Lucas 2013	Meta- analysis	To assess the efficacy of some probiotic species in alleviating characteristic IBS symptoms	RCTs	2, 3, 6, 7	3	PubMed, Cochrane Library, EMBASE	Jan 2012	English or Spanish	Jadad scale	NR	NR	NR
Pratt 2020	Systematic review	To systematically review human studies in which the efficacy of Bifidobacteria supplementation had been examined as a treatment for abdominal pain in IBS.	RCTs	2	3	MEDLINE, EMBASE, Cochrane Controlled Trials Register	May 2019	None	Cochrane Risk of Bias Tool	NR	The authors declare that they have no competing	This study was funded by the School of Food Science and Nutrition, University of Leeds.
Ritchie 2012	Meta- analysis	To: (i) determine the overall effect of probiotics on diseases of the gastrointestinal tract that have previously been shown to be affected by probiotics, (ii) determine whether certain diseases respond to probiotics more than others (iii) determine whether different species and species combinations differed in their overall effect size, and to (iv) determine whether	RCTs	1	6	PubMed, Medline, Google Scholar, Embase, Biological Abstracts, Science Direct	Jan 2011	None	Jadad scale	NR	The authors have declared that no competing interests exist.	Supported by a National Sciences and Engineering Research Council of Canada (NSERC) Discovery Grant to Tamara Romanuk. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

		efficacy differs based on dosage, length of treatment, and age group.										
Shang 2022	Systematic review and meta- analysis	To investigate the effectiveness and safety of probiotics in IBS-C patients.	RCTs	2, 3, 7	5	PubMed, Embase, the Cochrane Library, Web of Science, China Biology Medicine (CBM)	Mar 2022	NR	Cochrane Risk of Bias Tool	GRADE	The authors declare no conflict of interest.	Supported by the National Natural Science Foundation of China (Project No. 72074103); the Gansu Special Project of Soft Science (20CX9ZA109); the Fundamental Research Funds for the Central Universities: Izujbky-2021-ct06, Izujbky-2021-kb22.
Sun 2020	Systematic review and meta- analysis	To identify the efficacy and safety of probiotics in the treatment of IBS.	RCTs	1, 2, 3	4	MEDLINE, CENTRAL, CINAHL, Embase	Feb 2019	None	Cochrane Risk of Bias Tool	NR	No commercial or associative interest that represents a conflict of interest in connection with the work submitted.	National Natural Science Foundation of China (NSFC) (NO.81573779)
Wang 2022	Systematic review and meta- analysis	To assess the efficacy and safety of probiotics for the treatment of adult IBS-D patients	RCTs	1, 2, 3, 6	8	PubMed, Web of Science, Cochrane Library, Embase, CNKI, CBM, VIP, Wanfang Data	Aug 2021	None	Cochrane Risk of Bias Tool	GRADE	The authors declare no competing interests.	Supported by the National Natural Science Foundation of China: "Reporting Quality Assessment and Key Methods Research for Network Meta- analysis about Acupuncture" (Grant Number: 82004203); and the Fundamental Research Funds for the Central

												Universities: lzujbky-2021-ct06, lzujbky-2021-kb22.
Wen 2020	systematic review and meta- analysis	To evaluate the efficacy and safety of probiotics in patients with IBS-C	RCTs	6, 7	4	Cochrane Library, PubMed, EMBASE, Web of Science	May 2019	NR	Jadad scale	NR	The authors declare no relevant conflict of interest.	No funding.
Xu 2021	Systematic review and meta- analysis	To systematically evaluate the efficacy of probiotics in children with IBS	RCTs	1, 2	5	Web of Science, PubMed, Cochrane Library, Embase, and Clinical Trials	Jan 2021	English	Cochrane Risk of Bias Tool	NR	The authors have declared that no competing interests exist.	This work was funded by the Changzhou Applied Basic Research Project (no. CJ20200005 to WMS), Changzhou City, Jiangsu Province, China.
Yuan 2017	Meta- analysis	To assess the combined effect of B. infantis on reducing the symptom severity of IBS based on the published data.	RCTs	2	3	PubMed, Cochrane Library, EMBASE	Dec 2016	NR	Jadad scale	NR	No significant relationships with or financial interests in any commercial companies related to this study or article. CMRO peer reviewers on this manuscript have no relevant financial or other relationships to disclose.	This study was not funded.
Zhang 2016	Meta- analysis	To assess the efficacy of different probiotic types, doses and treatment durations in IBS patients diagnosed by Rome III criteria via a meta-analysis of RCTs.	RCTs	1, 2, 3	3	Medline, EMBASE, CENTRAL	Oct 2015	NR	Cochrane Risk of Bias Tool	NR	The authors declare that they have no competing interests.	This study was supported by the National Natural Science Foundation of China, grant numbers 81330012 and 81370495.

Abbreviations: CENTRAL=Cochrane Central Register of Controlled Trials; CINAHL=Cumulative Index of Nursing and Allied Health Literature; IBS=irritable bowel syndrome, NR=Not reported; RCT=randomised controlled trial, GRADE=Grading of Recommendations Assessment, Development and Evaluation, QoL=quality of life;

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Global improvement of IBS
- 2. Abdominal pain burden
- 3. Health-related quality of life
- 4. Number of recurrent episodes
- 5. Functioning
- 6. Stool frequency, bowel transit time
- 7. Stool consistency

## D4 Insomnia/sleeping disorders, magnesium

Table D-6. Citation details of included reviews - insomnia/sleeping disorders, magnesium (n=4).

<b>Review ID</b>	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
Chan 2021	Efficacy of dietary supplements on improving sleep quality: a systematic review and meta-analysis	Chan, V.; Lo, K.	2021	Postgraduate medical journal	98		1158	10.1136/postgradmedj- 2020-139319
Mah 2021	Oral magnesium supplementation for insomnia in older adults: a Systematic Review & Meta-Analysis	Mah, J.; Pitre, T.	2021	BMC Complementary Medicine and Therapies	21	1	125	https://dx.doi.org/10.118 6/s12906-021-03297-z
Samara 2020	Network meta-analysis of the efficacy and safety of drugs, psychotherapy and other treatments for elderly people with insomnia	Samara, M. T., Huhn, M., Chiocchia, V., Schneider-Thoma, J., Wiegand, M., Salanti, G., & Leucht, S.	2020	Acta Psychiatr Scand	142	1	6-17	10.1111/acps.13201
Zhan 2023	Comparative efficacy and safety of multiple wake- promoting agents for the treatment of excessive daytime sleepiness in narcolepsy: A network meta-analysis	Shuqin Zhan1, Hui Ye2, Ning Li1, Yimeng Zhang1, Yueyang Cheng1, Yuanqing Wang1,3, Shimin Hu 1, Yue Hou1	2023	Nature and Science of Sleep	15		217-230	10.2147/NSS.S404113

Table D-7. Characteristics of included reviews – Insomnia/sleeping disorders, magnesium (n=4).

Review	<b>Review deta</b>	ils			Search deta	iils			Quality ass	essment	Other	
ID	Review design	Aim of the review (as reported by the SR)	Types of studies included	Outcomes relevant to the Overview <sup>^</sup>	# of databases searched	Names of databases searched	Date of last search	Search restrictions	RoB tool used	Certainty of evidence reported	Conflicts of interest	Funding sources
Chan 2021	Systematic review and meta- analysis	To summarise up- to-date research evidence and to identify the types of	RCTs	2	4	Ovid Emcare, Ovid MEDLINE (R) and Epub Ahead of Print, In-	Jun 2020	NR	Cochrane Risk of Bias Tool	Not conducted	None declared	The authors have not declared a specific grant for this research from any funding agency in the

		dietary supplement that improve subjective sleep quality.				Process & Other Non-Indexed Citations, APA PsycINFO						public, commercial or not-for-profit sectors.
Mah 2021	Systematic review and meta- analysis	To assess the effects and safety of oral magnesium supplementation for older adults with insomnia.	RCTs	1, 2, 4	6	MEDLINE, EMBASE, Allied and Complementary Medicine, clinicaltrials.gov	Oct 2020	NR	Cochrane Risk of Bias Tool	GRADE	None declared	The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.
Samara 2020	Systematic review and network meta- analysis	To conduct a comprehensive systematic review of all currently avail- able treatment options and assess their relative effects via network meta- analysis (NMA).	RCTs	1, 2, 4	7	MEDLINE, Embase, PsycINFO, CENTRAL, Cochrane Database of Systematic Reviews (CDSR), ClinicalTrials.gov, WHO ICTRP	May 2019	NR	Cochrane Risk of Bias Tool	Not conducted	MH has received speaker's honoraria from Janssen. GS was invited to participate in two scientific meetings about the use of real world evidence by Merck (2019) and Biogen (2018). In the last 3 years SL has received honoraria as a consultant or for lectures for LB Pharma, Otsuka, Lundbeck, Boehringer Ingelheim, LTS Lohmann, Janssen, John- son&Johnson , TEVA, MSD, Sandoz, SanofiAventis	This work has been supported by a grant from the German Federal Ministry of Education and Research (Bundesminis- terium fu€r Bildung und Forschung; Grant number: 01GL1731). VC and GS have been supported by a grant from the Swiss National Science Foundation 179185.

											, Angelini, Sunovion, Recordati and Geodon Richter. MTS, VC, JST and MW have no conflicts of interest.	
Zhan 2023	Network meta- analysis	To systematically update the comparative efficacy and detailed safety analysis of approved wake- promoting agents in narcolepsy.	Double- blind RCTs	6	7	PubMed, Embase, CENTRAL, World Health Organization International Trials Registry Platform search portal, United States FDA website, EMA website, ClinicalTrials.gov	May 2022	NR	Cochrane Risk of Bias Tool	Not conducted	Hui Ye is an employee of Ignis Therapeutics. The authors report no other potential conflicts of interest in this work.	The current work was supported by National Natural Science Foundation of China (Grant No. 81571294), National Key R&D program of China (Grant No. 2021YFC2501400), and Research Fund for Chinese Sleep Research Society (Grant No. ZS-KY-2022-01).

Abbreviations: CENTRAL=Cochrane Central Register of Controlled Trials; CINAHL=Cumulative Index of Nursing and Allied Health Literature; NR=Not reported; RCT=randomised controlled trial, GRADE=Grading of Recommendations Assessment, Development and Evaluation

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Improvement in clinical levels of insomnia
- 2. Global improvement in sleep quality or quantity (subjective)
- 3. Global improvement in sleep quality or quantity (objective)
- 4. Improvement in individual sleep parameters (Sleep onset latency, Total sleep duration, Total wake-time, Wake after sleep onset (WASO), Nocturnal and early morning wakening, Sleep efficiency (ratio of time asleep to time in bed), parasomnias)
- 5. Quality of life
- 6. Daytime functioning
- 7. Fatigue

### D5 Depression (including post-natal), omega-3 fatty acids

Table D-8. Citation details of included reviews – depression (including post-natal), omega-3 (n=26).

Review ID	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
Appleton	Omega-3 fatty acids for depression in adults	Appleton, K. M.; Sallis, H. M.; Perry, R.; Ness, A.	2015	Cochrane Database	2015	11	Cd00469	10.1002/14651858.CD
2015		R.; Churchill, R.		Syst Rev			2	004692.pub4

Appleton 2016	ω-3 Fatty acids for major depressive disorder in adults: an abridged Cochrane review	Appleton, K. M.; Sallis, H. M.; Perry, R.; Ness, A. R.; Churchill, R.	2016	BMJ open	6	3	e010172	10.1136/bmjopen- 2015-010172
Appleton 2021	Omega-3 fatty acids for depression in adults	Appleton, K. M.; Voyias, P. D.; Sallis, H. M.; Dawson, S.; Ness, A. R.; Churchill, R.; Perry, R.	202 1	Cochrane Database Syst Rev	11	11	CD0046 92	10.1002/14651858.C D004692.pub5
Bae 2018	Systematic review and meta-analysis of omega-3- fatty acids in elderly patients with depression	Bae, J. H., & Kim, G.	2018	Nutrition Research	50		1-9	doi: 10.1016/j.nutres.2017. 10.013
Bai 2018	Omega-3 polyunsaturated fatty acids and reduction of depressive symptoms in older adults: A systematic review and meta-analysis	Bai, Z. G.; Bo, A.; Wu, S. J.; Gai, Q. Y.; Chi, I.	2018	J Affect Disord	241		241-248	10.1016/j.jad.2018.07. 057
Bai 2020	Efficacy and safety of anti-inflammatory agents for the treatment of major depressive disorder: a systematic review and meta-analysis of randomised controlled trials	Bai, S.; Guo, W.; Feng, Y.; Deng, H.; Li, G.; Nie, H.; Guo, G.; Yu, H.; Ma, Y.; Wang, J.; Chen, S.; Jing, J.; Yang, J.; Tang, Y.; Tang, Z.	2020	Journal of neurology, neurosurgery, and psychiatry	91	1	21-32	10.1136/jnnp-2019- 320912
Chowdhury 2020	Effect of supplementary omega-3 fatty acids on pregnant women with complications and pregnancy outcomes: review from literature	Chowdhury, M. H.; Ghosh, S.; Kabir, M. R.; Mamun, M. A. A.; Islam, M. S.	2020	Journal of Maternal- Fetal and Neonatal Medicine	35	13	2564- 2580	https://dx.doi.org/10.1 080/14767058.2020.17 86522
Farooq 2020	Pharmacological interventions for prevention of depression in high risk conditions: Systematic review and meta-analysis	Farooq, S.; Singh, S. P.; Burke, D.; Naeem, F.; Ayub, M.	2020	Journal of Affective Disorders	269		58-69	10.1016/j.jad.2020.03. 024
Gabriel 2022	Nutrition and bipolar disorder: a systematic review	Gabriel, F. C.; Oliveira, M.; Martella, B. M.; Berk, M.; Brietzke, E.; Jacka, F. N.; Lafer, B.	2022	Nutritional neuroscience	26	7	637-651	10.1080/1028415X.202 2.2077031
Liao 2019	Efficacy of omega-3 PUFAs in depression: A meta- analysis	Liao, Y.; Xie, B.; Zhang, H.; He, Q.; Guo, L.; Subramanieapillai, M.; Fan, B.; Lu, C.; McIntyre, R. S.	2019	Transl Psychiatry	9	1	190	10.1038/s41398-019- 0515-5
Miller 2013	Dietary supplements for preventing postnatal depression	Brendan, J. Miller; Linda, Murray; Michael, M. Beckmann; Terrence, Kent; Bonnie, Macfarlane	2013	Cochrane Database of Systematic Reviews	10	10	CD00910 4	10.1002/14651858.CD 009104.pub2
Mocking 2016	Meta-analysis and meta-regression of omega-3 polyunsaturated fatty acid supplementation for major depressive disorder	Mocking, R. J. T.; Harmsen, I.; Assies, J.; Koeter, M. W. J.; Ruhe, H. G.; Schene, A. H.	2016	Translational Psychiatry	6	3	e756	https://dx.doi.org/10.1 038/tp.2016.29
Mocking 2020	Omega-3 Fatty Acid Supplementation for Perinatal Depression: A Meta-Analysis	Mocking, R. J. T.; Steijn, K.; Roos, C.; Assies, J.; Bergink, V.; Ruhé, H. G.; Schene, A. H.	2020	J Clin Psychiatry	81	5	19r13106	10.4088/JCP.19r13106
Morrell 2016	A systematic review, evidence synthesis and meta-analysis of quantitative and qualitative studies evaluating the clinical effectiveness, the cost-effectiveness, safety and acceptability of interventions to prevent postnatal depression	Morrell, C. J.; Sutcliffe, P.; Booth, A.; Stevens, J.; Scope, A.; Stevenson, M.; Harvey, R.; Bessey, A.; Cantrell, A.; Dennis, C. L.; Ren, S.; Ragonesi, M.; Barkham, M.; Churchill, D.; Henshaw, C.; Newstead, J.; Slade, P.; Spiby, H.; Stewart- Brown, S.	2016	Health Technology Assessment	20	37	1-414	https://dx.doi.org/10.3 310/hta20370
Newberry 2016	Omega-3 Fatty Acids and Maternal and Child Health: An Updated Systematic Review	Newberry, S. J.; Chung, M.; Booth, M.; Maglione, M. A.; Tang, A. M.; O'Hanlon, C. E.; Wang, D. D.; Okunogbe, A.; Huang, C.; Motala, A.; Trimmer,	2016	Evidence report/technology assessment		224	1-826	10.23970/AHRQEPCER TA224

		M.; Dudley, W.; Shanman, R.; Coker, T. R.; Shekelle, P. G.						
Saccone 2016	Omega-3 long-chain polyunsaturated fatty acids and fish oil supplementation during pregnancy: Which evidence?	Saccone, G.; Saccone, I.; Berghella, V.	2016	Journal of Maternal- Fetal and Neonatal Medicine	29	15	2389- 2397	https://dx.doi.org/10.3 109/14767058.2015.10 86742
Sarris 2012	Omega-3 for bipolar disorder: meta-analyses of use in mania and bipolar depression	Sarris, J.; Mischoulon, D.; Schweitzer, I.	2012	The Journal of clinical psychiatry	. 73	1	81-6	10.4088/JCP.10r06710
Suradom 2021	Omega-3 polyunsaturated fatty acid (n-3 PUFA) supplementation for prevention and treatment of perinatal depression: a systematic review and meta-analysis of randomized-controlled trials	Suradom, C.; Suttajit, S.; Oon-Arom, A.; Maneeton, B.; Srisurapanont, M.	202 1	Nord J Psychiatry	75	4	239-246	10.1080/08039488.2 020.1843710
Troeung 2013	A meta-analysis of randomised placebo- controlled treatment trials for depression and anxiety in Parkinson's disease	Troeung, L.; Egan, S. J.; Gasson, N.	2013	PloS one	8	11	e79510	https://dx.doi.org/10.1 371/journal.pone.0079 510
Tsai 2023	Dietary Interventions for Perinatal Depression and Anxiety: A Systematic Review and Meta-Analysis	Tsai, Z., Shah, N., Tahir, U., Mortaji, N., Owais, S., Perreault, M., & Van Lieshout, R. J.	2023	Am J Clin Nutr	117	6	1130- 1142	10.1016/j.ajcnut.2023. 03.025
Tung 2023	Maternal n-3 PUFA Intake During Pregnancy and Perinatal Mental Health Problems: A Systematic Review of Recent Evidence.	Tung, K.T.S., Wong, R.S. & Mak, R.T.W.	2023	Curr Nutr Rep	12		426-438	https://doi.org/10.1007 /s13668-023-00484-x
Viswanathan 2020	Treatment of Depression in Children and Adolescents: A Systematic Review	Viswanathan, M., Kennedy, S. M., McKeeman, J., Christian, R., Coker-Schwimmer, M., Cook Middleton, J., Bann, C., Lux, L., Randolph, C., & Forman-Hoffman, V.	2020	Agency for Healthcare Research and Quality: US	-	-	-	-
Williams 2006	Do essential fatty acids have a role in the treatment of depression?	Williams, A. l; Katz, D.; Ali, A.; Girard, C.; Goodman, J.; Bell, I.	2006	Journal of Affective Disorders	93	1-3	117-123	https://dx.doi.org/10.1 016/j.jad.2006.02.023
Xu 2023	Comparative Efficacy, Acceptability, and Tolerability of Anti-inflammatory Agents on Bipolar disorder: Systematic Review and Network Meta- Analysis	Xu, H., Du, Y., Wang, Q., Chen, L., Huang, J., Liu, Y., Zhou, C., & Du, B	2023	Asian journal of psychiatry	80		103394	https://doi.org/10.1016 /j.ajp.2022.103394
Zhang 2019	Omega-3 fatty acids for the treatment of depressive disorders in children and adolescents: A meta-analysis of randomized placebo-controlled trials	Zhang, L.; Liu, H.; Kuang, L.; Meng, H.; Zhou, X.	201 9	Child and Adolescent Psychiatry and Mental Health	13	1	36	https://dx.doi.org/10. 1186/s13034-019- 0296-x
Zhang 2020	The efficacy and safety of omega-3 fatty acids on depressive symptoms in perinatal women: a meta-analysis of randomized placebo-controlled trials	Zhang, M. M.; Zou, Y.; Li, S. M.; Wang, L.; Sun, Y. H.; Shi, L.; Lu, L.; Bao, Y. P.; Li, S. X.	2020	Translational Psychiatry	10	1	193	10.1038/s41398-020- 00886-3

### Table D-9. Characteristics of included reviews – Depression (including post-natal), omega-3 fatty acids

	Review ID Review details Sea	Gearch details	Quality assessment	Other
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	Review design	Aim of the review (as reported by the SR)	Types of studies included	Outcomes relevant to the Overview <sup>^</sup>	# of databases searched	Names of databases searched	Date of last search	Search restrictions	RoB tool used	Certainty of evidence reported	Conflicts of interest	Funding sources
Appleton 2015	Cochrane review (systematic review and meta- analysis)	To assess the effects of n-3 polyunsaturated fatty acids (also known as omega-3 fatty acids) versus a comparator (e.g. Placebo, antidepressant treatment, standard care, no treatment, wait-list control) for major depressive disorder (MDD) in adults	RCTs	1,6	2	Cochrane Depression, Anxiety and Neurosis Review Group's Specialised Registers, International Trial Registries	May 2015	None	Cochran e Risk of Bias Tool	GRADE	NR	The National Institute for Health Research (NIHR) is the largest single funder of the Cochrane Depression, Anxiety and Neurosis Group.
Appleton 2016	Cochrane review (systematic review and meta- analysis)	To assess the effects of n-3 polyunsaturated fatty acids (n-3PUFAs; also known as $\omega$ -3 fatty acids) compared with comparator for major depressive disorder (MDD) in adults	RCTs	1	3	Cochrane Depression, Anxiety and Neurosis Review Group's Specialised Registers, International Trial Registries, CINAHL	May 2015; Sep 2013	No restrictions on date, language or publication status	Cochran e Risk of Bias Tool	GRADE - low to very low	None	The National Institute for Health Research (NIHR) is the largest single funder of the Cochrane Depression, Anxiety and Neurosis Group
Appleton 2021	Cochrane review (systematic review and meta- analysis)	To assess the effects of n-3 polyunsaturated fatty acids (also known as omega-3 fatty acids) versus a comparator (e.g. Placebo, antidepressant treatment, standard care, no treatment, wait-list control) for major depressive disorder (MDD) in adults.	RCTs	1, 2, 6	4	CENTRAL, Ovid MEDLINE, Embase, PsycINFO	Jan 2021	There were no restrictions by date, language or publication status applied to the overall searches	Cochran e Risk of Bias Tool	GRADE	SD: Is an Information Specialist for Cochrane Common Mental Disorders but was not involved in the editorial approval process for this review. RC: Leads and has	Internal sources • Bournemouth University, UK Researcher time • University of Bristol, UK Researcher time• National Institute for Health Research, NIHR, UK SD and RC contribution to this review update is supported by Cochrane Infrastructure funding to the Common Mental Disorders

											responsibili ty for Cochrane Common Mental Disorders, which has supported parts of the review process and is largely funded by a grant from the National Institute for Health Research (NIHR) in the UK. RC was not involved in the editorial process for this review.	Cochrane Review Group.
Bae 2018	Systematic review and meta- analysis	To provide evidence on the clinical application of omega- 3 fatty acids in the treatment of depressive symptoms in elderly subjects older than 65 years and to compare these results with those of placebo	RCTs	1	7	Ovid MEDLINE, EMBASE, Web of Science, Cochrane Library, KoreaMed, Research Information Service System (Korean database), Korean Studies Information Service system	Sep 2016	NR	Cochran e Risk of Bias Tool	NR	The authors have no conflict of interest	NR
Bai 2018	Systematic review and meta- analysis	The aim of this study is to systematically review the efficacy of omega-3	RCTs	1	9	Medline, Embase, Web of Science, Cochrane	Jun 2018	English and Chinese	Cochran e Risk of Bias Tool	Informal - limited statistica l power	None	This work was supported by the Fundamental Research Funds for

		polyunsaturated fatty acid (n-3 PUFA) supplements in reducing depressive symptoms among older adults aged 60 and above				Library, PsycINFO, Global Health, CINAHL, clinicaltrials.go v, Chinese Biomedical Medicine Database				for moderato r analysis and the results were mixed and are suggestiv e only.		the Central Universities, no. 30918013115
Bai 2020	Systematic review and meta- analysis	To systematically review the efficacy and safety of anti- inflammatory agents for patients with major depressive disorders	RCTs	1	4	PubMed, Embase, Cochrane Library and Web of Science	Dec 2018	NR	Cochran e Risk of Bias Tool	NR	Competing interests None declared	This study was supported by funds from the National Natural Science Foundation of China, grant number: 81873750
Chowdhur y 2020	Systematic review	To assess the current situation of the impact of omega-3 long-chain Poly Unsaturated Fatty Acid (PUFA) supplementation on the outcomes of pregnancy	RCTs + observatio nal studies	1	4	Medline, PubMed, PLOS, Google Scholar	Mar 2017	English; date restriction February 1995 to March 2017	Jadad scale	NR; insufficie nt info to judge	None	NR
Farooq 2020	Systematic review and meta- analysis	We aim to identify and evaluate the efficacy of all pharmacological treatments that have been used for preventing the onset of depressive illness in adult populations.	RCTs	1	4	PubMed, Psych Info, EMBASE, CINHAL	Jan 2020	Date restriction from 1980 to January 2020; language restriction NR	Cochran e Risk of Bias Tool	Insufficie nt informati on to make judgeme nt	None	None
Gabriel 2023	Systematic review	The aim of this review is to summarize the available evidence on nutrition and BD	RCTs and observatio nal	1	2	PubMed, Cochrane Library	Sep 2021	English; date restriction 2001 to 2021	Informal criteria (similar to Cochran e Risk of Bias tool)	Insufficie nt informati on to make judgeme nt	None	MB is supported by a NHMRC Senior Principal Research Fellowship [1156072] and have received other grants and research support, all unrelated to this work. EB receives honoraria as speaker/advisory board member from

(,						
						Daiichi-Sankyo and
						Janssen unrelated to
						the present work. She
						received research
						funding from Faculty
						of Health Sciences
						and Department of
						Psychiatry, Queen's
						University Felice N
						lacka is supported by
						a National Health and
						Modical Passarah
						Council Investigator
						Council Investigator
						Grant (#1194982).
						She has received: (1)
						competitive
						Grant/Research
						support from the
						Brain and Behaviour
						Research Institute,
						the National Health
						and Medical
						Research Council,
						Australian Rotary
						Health, the Geelong
						Medical Research
						Foundation, the lan
						Potter Foundation.
						The University of
						Melbourne: (2)
						industry support for
						research from Meat
						and Livestock
						Australia
						Australia,
						wootworths Limited,
						the A2 Milk Company,
						Be Fit Foods; (3)
						philanthropic support
1 1						from the Fernwood
1 1						Foundation, Wilson
1 1						Foundation, the JTM
1 1						Foundation, the Serp
1						Hills Foundation, the
1						Roberts Family
1						Foundation, the
1						Waterloo Foundation

												and; (4) travel support and speakers honoraria from Sanofi-Synthelabo, Janssen Cilag, Servier, Pfizer, Network Nutrition, Angelini Farmaceutica, Eli Lilly, Metagenics, and The Beauty Chef. Felice Jacka has written two books for commercial publication. BL was supported by FAPESP grants 2017/07089-8; 2018/11963-8; 2020/05087-0 during the preparation of this manuscript.
Liao 2019	Systematic review and meta- analysis	To estimate the efficacy of omega-3 polyunsaturated fatty acids (PUFAs), especially docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), in the improvement of depression	RCTs	1	2	PubMed, Embase	Dec 2017	NR	Cochran e Risk of Bias Tool	NR	None	This study was supported by the National Natural Science Foundation of China (Grant No. 81761128030)
Miller 2013	Systematic review and meta- analysis	To assess the benefits of dietary supplements for preventing postnatal depression either in the antenatal period, postnatal period, or both.	RCTs	1,3	1	Cochrane Pregnancy and Childbirth Group's Trials Register (curated from CENTRAL, MEDLINE, Embase)	Apr 2013	No language restrictions	Cochran e Risk of Bias Tool	NR	None	Brendan Miller received a grant of \$500 from the RANZCOG research foundation which he used to partly fund his attendance at a Cochrane review completion workshop in Melbourne, Australia in May 2012
Mocking 2016	Meta- analysis	To assess "the effects of omega-3 PUFA	RCTs	2	2	Medline, Embase	Dec 2015	NR	Jadad score	NR	None declared	RJTM is supported by a PhD scholarship

		supplementation on depressive symptoms in MDD"										from the Academic Medical Center of the University of Amsterdam. HGR is supported by an NWO/zonmw VENI- Grant #016.126.059. The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.
Mocking 2020	Meta- analysis	Several randomized controlled trials (RCTs) investigated omega-3 polyunsaturated fatty acids (PUFAs) (i.e., fish oil) in perinatal depression, but their efficacy remains unclear. We performed a meta- analysis of RCTs on omega-3 PUFAs for perinatal depression, comparing a priori defined subgroups: pregnant women vs postpartum women and prevention vs treatment of perinatal depression.	RCTs		5	Web of Science, Embase, PsycINFO, CENTRAL	Feb 2019	NR	Cochran e Risk of Bias Tool	GRADE	Drs Mocking, Roos, Assies, Bergink, Ruhé, and Schene and Ms Steijn have no personal affiliations or financial relationshi ps with any commercia l interest to disclose relative to the article. All authors report no conflict of interests with regard to personal dietary preference s	The funding sources by no means influenced the design and conduct of the study; collection, management, analysis, and interpretation of the data; nor preparation, review, or approval of the manuscript; nor decision to submit the manuscript for submission.
Morrell 2016	Systematic review and meta- analysis	To determine the clinical effectiveness of antenatal and postnatal	RCTs	1	14	MEDLINE, MEDLINE In- Process & Other Non-	Jul 2013	English	Cochran e Risk of Bias Tool	NR	NR	National Institute for Health Research (NIHR)

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	interventions for		Indexed					
	preventing PND		Citations.					
			EMBASE					
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			International					
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Newberry 2016	Systematic review	To update a prior systematic review on the effects of omega-3 fatty acids (n-3 FA) on maternal and child health and to assess the evidence for their effects on, and associations with, additional outcomes	RCTs and prospectiv e cohort and nested case control studies sample size >250	1	5	MEDLINE, Embase, CENTRAL, Cochrane Library, Centre for Agriculture and Biosciences (CAB) Abstracts	Aug 2015	Date restriction 2000 to August 2015; English	Cochran e Risk of Bias Tool	Informal rating as low	NR	Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-2012-00006-I)
Saccone 2016	Systematic review and meta- analysis	The aim of this study was to provide evidence-based recommendations for omega-3 supplementation during pregnancy through a systematic review of level-1 data published on this topic	RCTs	1	7	MEDLINE, Scopus, ScienceDirect, clinicaltrials.go v, PROSPERO, EMBASE, CENTRAL	Mar 2015	No restrictions for language or geographic location	Cochran e Risk of Bias Tool	Not formally - level-1 data from this systemati c review indicated no enough evidence to support the routine use of omega-3 supplem entation during pregnanc y	The authors report no conflict of interest. T	This study had no funding source
Sarris 2012	Meta- analysis	Present the significant findings from meta- analyses of omega-3 (as augmentation with standard pharmacotherapy) in the treatment of bipolar depression and bipolar mania	RCTs	2,3	4	PubMed, CINAHL, Web of Science, Cochrane Library	Sep 2010	English	Author's own scale of 1 to 10 (higher = better quality)	NR	Dr Schweitzer has received speaking honoraria from AstraZenec a, Eli Lilly, Lundbeck, Wyeth, Pfizer, Servier and Janssen-	None reported

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Suradom	Systematic	To examine Omega-3	RCTs	1	5	PubMed,	May 2020	NR	Cochran	NR	MS has	This work was
2021	review and	efficacy for the				Scopus, Web of			e Risk of		received	supported by Chiang
	meta-	prevention and				Science,			Bias Tool		grants	Mai University,
	analysis	treatment of perinatal				clinicaltrials.go					and/or	Chiang Mai, Thailand.
		depression and for				v, Cochrane					speaker's	However, Chiang Mai
		mitigating depression				Library					honoraria	University had no role
		at a particular stage of									from	for research
		pregnancy or									Janssens	conception, study
		postpartum									(Thailand),	design, data analysis,
											Lundbeck,	or study report.
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											ticals (Thailand). The remaining authors report no financial or other relation- ship relevant to the subject of this article.	
Troeung 2013	Systematic review and meta- analysis	A meta-analysis of randomised placebo- controlled trials for depression and/or anxiety in PD was conducted to systematically examine the efficacy of current treatments for depression and anxiety in PD.	RCTs	1	6	Medline, PubMed, PsycINFO, Proquest, Cochrane Library, EMBASE	Jul 2013	English only	Cochran e Risk of Bias Tool	Not enough info to judge	None	None
Tsai 2023	Systematic review and meta- analysis	To assess the effectiveness of dietary interventions for the treatment of perinatal depression and/or anxiety	RCTs	1	5	MEDLINE, EMBASE, PsycINFO, CINAHL, Web of Science	Nov 2022	English	Cochran e Risk of Bias Tool	NR; insufficie nt info to judge	None	None
Tung 2023	Systematic review and meta- analysis	To provide an updated review on the association of antenatal n-3 PUFA intake via different sources (seafood, fish, overall diet, and supplementation) with perinatal mental health problems including depression, anxiety, and psychological distress	RCTs, prospectiv e and retrospect ive cohort, case- control, cross- sectional, pilot study	1	4	Web of Science, Embase, PubMed, APA PsycINFO	Jun 2021	English; date restriction 2017 to June 2021	Joanna Briggs Institute' s Critical Appraisal Checklist for Studies Reporting Prevalen ce Data	NR	None declared	NR
Viswanath an 2020	Systematic review	The purpose of the review is to examine the benefits and harms of pharmacological and nonpharmacological treatments for child and adolescent depressive disorders.	RCTs and observatio nal	1, 2	5	MEDLINE, Cochrane Library, CENTRAL, CINAHL, PsycINFO	May 2019	English; Countries with a very high Human Development Index (HDI; at least one country in multiple- country studies had to be on the very high HDI list)	Cochran e Risk of Bias Tool	Informall y as "The evidence is insufficie nt to judge the effective ness of omega-3 when compare d with pill placebo for depressiv e symptom s, response , and remissio n"	None	Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-2015-00011-I)
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Williams 2006	Systematic review	To examine the therapeutic efficacy of essential fatty acids for depression	RCTs, case control studies, reviews, and case reports	1	4	Medline, PsycINFO, AMED, CENTRAL	Sep 2001	English	Cochran e Risk of Bias Tool	NR; insufficie nt info to judge	NR	Project sponsorship from the Centres for Disease Control and Prevention (SIP-14-00 and Grant #U48- CCU115802) is greatly appreciated. Dr. Bell's participation was supported in part by the National Institute of Health grant K24 AT005
Xu 2023	Systematic review and Network meta- analysis	To compare different anti-inflammatory agents to improve the treatment of bipolar disorder (BD) patients	RCTs	1	4	Cochrane Library, Web of Science, PubMed, Embase	Feb 2022	NR	Cochran e Risk of Bias Tool	NR	The authors have no competing interests to report.	There is no financial conflicts of interest to disclosure.
Zhang 2019	Meta- analysis	To investigate the efficacy and safety of omega-3 fatty acids (O3FA) in treating	RCTs	1, 2	7	PubMed, Embase, Cochrane Library, Web of	Jul 2019	No limitations were applied in the search.	Jadad score; Cochran	NR	The authors declare that they have no	Supported by the National Natural Science Foundation of China (Grant No.

		depressive disorders in children and adolescents.				Science, PsycINFO, International trials registers, including WHO's trials portal, US clinicaltrials.go v, EU Clinical Trials Register and Australian New Zealand Clinical Trials Registry			e Risk of Bias tool		competing interests.	81873800 and Grant No. 81701342).
Zhang 2020	Systematic review and meta- analysis	To examine the efficacy and safety of omega-3 fatty acids monotherapy for perinatal depression (PND) compared with placebo	RCTs	1	6	PubMed, Embase, PsycINFO, MEDLINE, Cochrane Library, CINAHL	Nov 2019	None	Cochran e Risk of Bias Tool	Not formally reported	None	Supported in part by the National Natural Science Foundation of China (no. 81871071 and 81171251) and Beijing Municipal Natural Science Foundation (no. 7162101)

Abbreviations: BD=Bipolar disorder; CENTRAL=Cochrane Central Register of Controlled Trials; CINAHL=Cumulative Index of Nursing and Allied Health Literature; MDD=Major depressive disorder, NR=Not reported; RCT=randomised controlled trial, GRADE=Grading of Recommendations Assessment, Development and Evaluation, QoL=quality of life

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Depression-related emotional functioning/mental health burden
- 2. Improvement in clinical levels of depression (including post-natal depression)
- 3. Specific depression dimensions (Anhedonia, Distress, Dysfunctional thoughts, Internalizing problems, Rumination, Self-esteem, Anger, Fatigue, Hopelessness, Irritability, Negative mood, Tension)
- 4. Physiological symptoms of depression (respiration rate and capacity, heart rate, blood pressure, heart rhythm, vital signs, brain beta-nucleoside triphosphate levels, brain phosphodiester levels, brain phosphomonoester levels, serum norepinephrine levels, serum serotonin levels, frontal lobe phosphocreatine levels, body fat, metabolic measures, lactate levels, urinalysis results, lab panel results, weight, height, physical examination, temperature)
- 5. Parent to infant bonding
- 6. Quality of life
- 7. Anxiety-related emotional functioning/mental health burden

### D6 Dysmenorrhea, cruciferous indoles (indole-3-carbinol, di-indolylmethane)

Table D-10. Citation details of included reviews – dysmenorrhea, cruciferous indoles (indole-3-carbinol, di-indolylmethane) (n=0).

Review ID	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
No reviews we	ere identified for inclusion in the Overview							

## D7 Premenstrual syndrome (PMS), cruciferous indoles (indole-3-carbinol, di-indolylmethane)

Table D-11. Citation details of included reviews – premenstrual syndrome (PMS), cruciferous indoles (indole-3-carbinol, di-indolylmethane) (n=0).

Review ID	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
No reviews we	ere identified for inclusion in the Overview							

# D8 Atopic disorders (including eczema, dermatitis, allergic rhinitis, allergies), zinc

Table D-12. Citation details of included reviews – atopic disorders (including eczema, dermatitis, allergic rhinitis, allergies), zinc (n=3).

Review ID	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
Bath-Hextall 2012	Dietary supplements for established atopic eczema	Bath-Hextall, F. J., Jenkinson, C., Humphreys, R., & Williams, H. C	2012	Cochrane Database of Systematic Reviews	2	2	CD005205	10.1002/14651858 .CD005205.pub3
Dhaliwal 2020	Effects of Zinc Supplementation on Inflammatory Skin Diseases: A Systematic Review of the Clinical Evidence	Dhaliwal, S.; Nguyen, M.; Vaughn, A. R.; Notay, M.; Chambers, C. J.; Sivamani, R. K.	2020	American journal of clinical dermatology	21	1	21-39	10.1007/s40257- 019-00484-0
Gray 2019	Zinc and atopic dermatitis: a systematic review and meta-analysis	Gray, N. A.; Dhana, A.; Stein, D. J.; Khumalo, N. P.	2019	Journal of the European Academy of Dermatology and Venereology: JEADV	33	6	1042-1050	10.1111/jdv.15524

#### Table D-13. Characteristics of included reviews – Atopic disorders (including eczema, dermatitis, allergic rhinitis, allergies), zinc (n=3).

Review	Review deta	ails			Search det	tails			Quality assessmer	ıt	Other	
ID	Review design	Aim of the review (as reported by the SR)	Types of studies included	Outcomes relevant to the Overview^	# of databases searched	Names of databases searched	Date of last search	Search restrictions	RoB tool used	Certainty of evidence reported	Conflicts of interest	Funding sources
Bath- Hextall 2012	Cochrane review	To evaluate dietary supplements for treating established atopic eczema/dermatitis.	RCTs	1, 4	9	Cochrane Skin Group Specialised Register, CENTRAL, MEDLINE, EMBASE, PsycINFO, AMED, LILACS, ISI Web of Science, GREAT (Global Resource of EczemA Trials) database	Jul 2010	None	<ul> <li>(a) method of generation of randomisation sequence;</li> <li>(b) method of allocation concealment</li> <li>(c) blinding</li> <li>(d) how many participants were lost to follow up in</li> </ul>	Not reported	NR	NR

									each treatment group, whether reasons for losses were adequately reported, (e) degree of certainty that the participants had atopic eczema; (f) baseline comparability of participants (g) assessment of compliance with treatment.			
Dhaliwal 2020	Systematic Review	To determine the effect of zinc supplementation on inflammatory dermatologic conditions.	Published clinical studies	1, 4	4	CENTRAL, EMBASE, MEDLINE, Ovid	May 2019	English only	Jadad score	Not reported	Raja K. Sivamani serves as a scientific advisor and editor to LearnHealth and as a consultant to Burt's Bees and Derma- la. Cindy J. Chambers serves as a consultant to Burt's Bees. Simran Dhaliwal, Mimi Nguyen, Alexandra R. Vaughn, and Manisha Notay have no conflicts of interest that are directly relevant to the content of this article.	No sources of funding were received for the preparation of this article.
Gray 2019	Systematic review and meta- analysis	To determine (i) the association between zinc levels or zinc deficiency and AD and (ii) the efficacy of oral zinc supplementation in the treatment of AD	Case– control, cross- sectional, cohort, RCT	1,4	3	PubMed, Scopus, Web of Science	Dec 2017	NR	Newcastle–Ottawa Scale (non- randomised studies); Cochrane Risk of Bias tool (RCTs)	Not reported	None declared.	N.A. Gray is funded by the Discovery Foundation.

Abbreviations: AD=atopic dermatitis, CENTRAL=Cochrane Central Register of Controlled Trials; RCT=randomised controlled trial

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Global severity of condition/improvement of symptoms
- 2. Quality of life
- 3. Long-term measure of control of disease
- 4. Individual changes in symptoms (including degree of redness of skin, day-time itch, anterior rhinorrhoea (runny nose): where a study reports 'rhinorrhoea' as the outcome, in the absence of a definition within the paper we assumed that this measured anterior rhinorrhoea. Where the authors reported a combined outcome for anterior and posterior rhinorrhoea and we were not able to obtain individual results, we recorded this as a combined 'anterior and posterior rhinorrhoea' category; posterior rhinorrhoea (post-nasal drip); nasal blockage or congestion or obstruction; nasal itching; sneezing)
- 5. Physical function/ disability (return to work/school)

# D9 Fatigue (general) (including myalgic encephalomyelitis (ME) and Chronic Fatigue Syndrome (CFS)), antioxidants (specifically CoQ10 and alpha-lipoic acid)

Table D-14. Citation details of included reviews – fatigue (general) (including myalgic encephalomyelitis (ME) and Chronic Fatigue Syndrome (CFS)), antioxidants (specifically CoQ10 and alpha-lipoic acid) (n=6).

Review ID	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
Campagnolo 2017	Dietary and nutrition interventions for the therapeutic treatment of chronic fatigue syndrome/myalgic encephalomyelitis: a systematic review	Campagnolo, N.; Johnston, S.; Collatz, A.; Staines, D.; Marshall-Gradisnik, S.	2017	Journal of Human Nutrition and Dietetics	30	3	247-259	https://dx.doi.org/10.1 111/jhn.12435
Kim 2020	Systematic review of randomized controlled trials for chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME)	Kim, D. Y.; Lee, J. S.; Park, S. Y.; Kim, S. J.; Son, C. G.	2020	Journal of translational medicine	18	1	7	10.1186/s12967-019- 02196-9
Marx 2019	The effect of emerging nutraceutical interventions for clinical and biological outcomes in multiple sclerosis: A systematic review	Marx, W.; Hockey, M.; McGuinness, A. J.; Lane, M.; Christodoulou, J.; van der Mei, I.; Berk, M.; Dean, O. M.; Taylor, B.; Broadley, S.; Lechner- Scott, J.; Jacka, F. N.; Lucas, R. M.; Ponsonby, A. L.; Relief Trial team	2019	Multiple sclerosis and related disorders	37		101486	10.1016/j.msard.2019. 101486
Mehrabani 2019	Effect of coenzyme Q10 supplementation on fatigue: A systematic review of interventional studies	Mehrabani, S.; Askari, G.; Miraghajani, M.; Tavakoly, R.; Arab, A.	2019	Complementary therapies in medicine	43		181-187	10.1016/j.ctim.2019.01 .022
Pereira 2018	Dietary supplements and fatigue in patients with breast cancer: a systematic review	Pereira, Ptvt; Reis, A. D.; Diniz, R. R.; Lima, F. A.; Leite, R. D.; da Silva, M. C. P.; Guerra, R. N. M.; de Moraes Vieira É, B.; Garcia, J. B. S.	2018	Breast cancer research and treatment	171	3	515-526	10.1007/s10549-018- 4857-0
Tsai 2022	Effectiveness of Coenzyme Q10 Supplementation for Reducing Fatigue: A Systematic Review and Meta- Analysis of Randomized Controlled Trials	Tsai, I. C.; Hsu, C. W.; Chang, C. H.; Tseng, P. T.; Chang, K. V.	2022	Frontiers in pharmacology	13		883251	10.3389/fphar.2022.88 3251

 Table D-15. Characteristics of included reviews – Fatigue (general) (including myalgic encephalomyelitis and Chronic Fatigue Syndrome), antioxidants (specifically CoQ10 and alpha-lipoic acid)

Review ID	Review det	tails			Search det	tails			Quality assess	sment	Other	
	Review design	Aim of the review (as reported by the SR)	Types of studies included	Outcomes relevant to the Overview^	# of databases searched	Names of databases searched	Date of last search	Search restrictions	RoB tool used	Certainty of evidence reported	Conflicts of interest	Funding sources
Campagnolo 2017	Systematic review	To systematically review original research investigating nutrition interventions in the symptom management of CFS/ME patients measured using patient- centred outcomes including fatigue, quality of life, physical activity and/or psychological wellbeing)	intervention research, defined as studies that evaluated the effective- ness of food and/or nutritional supplement on outcome measures;	1	3	Medline, CINAHL, Scopus	May 2016	English, publication date (year 1994–2016) and humans	Rosendal scale	Not conducted	The authors declare that they have no conflicts of interest.	The Alison Hunter Memorial Foundation, Change for ME, Mason Foundation, the Stafford Medical Research Foundation, the Edward P Evans Foundation, Queens- land Smart State and Advance Queensland provided continued support and funding.
Kim 2020	Systematic review	To systematically review randomized controlled trials (RCTs) for CFS/ME to date.	RCTs	1	2	PubMed, Cochrane library	Apr 2019	None	Jadad scale	Not conducted	The authors declare that they have no competing interests.	This research was supported by the National Research Foundation of Korea (NRF) funded by the Oriental Medicine R&D Project (NRF- 2018R1A6A1A0302522 1).
Marx 2019	Systematic review	To investigate the efficacy and safety of emerging nutraceutical interventions for clinical and biological outcomes in people with MS.	randomized, parallel or cross-over trial	1, 4, 5, 6	5	PubMed, Embase, Cochrane Library, Google Scholar, Natural Medicines Database	Aug 2018	NR	Jadad Scale	Not conducted	NR	No direct funding was used to create this manuscript.
Mehrabani 2019	Systematic review	To investigate the effect of CoQ10 supplementation on fatigue among	interventional studies	1	6	PubMed, Scopus, Cochrane's library, Science direct, Google	Apr 2018	None	Cochrane Risk of Bias Tool	Not conducted	None	NR

		adolescent and adult population				Scholar, ISI web of science databases						
Pereira 2018	Systematic review	To identify dietary supplements that improve fatigue in patients with breast cancer.	Clinical trials	1	5	PubMed, Scopus (Elsevier), MEDLINE, CENTRAL, CINAHL	Aug 2017	None	Cochrane Risk of Bias Tool	GRADE	The authors declare no conflicts of interest.	NR
Tsai 2022	Systematic Review and Meta- Analysis	To investigate the effects of CoQ10 treatment on fatigue symptoms and syndromes.	RCTs	1	5	PubMed, Embase, CENTRAL, Web of Science, ClinicalTrials.g ov	Jan 2022	None	Cochrane Risk of Bias Tool	Not conducted	I-CT is the founder of the company InnovaRad Inc. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.	This study was funded by the National Taiwan University Hospital, Bei-Hu Branch; Ministry of Science and Technology, Taiwan (MOST 106-2314-B- 002-180-MY3 and MOST 109-2314-B- 002-114-MY3); and the Taiwan Society of Ultrasound in Medicine. APC was funded by the Ministry of Science and Technology of Taiwan and Taiwan Society of Ultrasound in Medicine.

Abbreviations: CENTRAL=Cochrane Central Register of Controlled Trials; CINAHL=Cumulative Index of Nursing and Allied Health Literature; NR=Not reported; RCT=randomised controlled trial, GRADE=Grading of Recommendations Assessment, Development and Evaluation, QoL=quality of life

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Global improvement in fatigue severity/burden
- 2. Clinical recovery or improvement (dichotomous)
- 3. Self-perceived change in overall health
- 4. Physical function burden from fatigue
- 5. HRQoL
- 6. Cognitive function burden from fatigue
- 7. Sleep quality/quantity

# D10 Headache and migraine, magnesium

#### Table D-16. Citation details of included reviews – headache and migraine, magnesium (n=6).

Review ID	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
Chiu 2016	Effects of intravenous and oral magnesium on reducing migraine: A meta-analysis of randomized controlled trials	Chiu, H. Y.; Yeh, T. H.; Huang, Y. C.; Chen, P. Y.	2016	Pain Physician	19	1	E97-E112	NR
Okoli 2019	Vitamins and Minerals for Migraine Prophylaxis: A Systematic Review and Meta-analysis	Okoli, G. N.; Rabbani, R.; Kashani, H. H.; Wierzbowski, A. K.; Neilson, C.; Mansouri, B.; Zarychanski, R.; Abou-Setta, A. M.	2019	The Canadian journal of neurological sciences. Le journal canadien des sciences neurologiques	46	2	1-Oct	10.1017/cjn.2018.39 4
Park 2020	Efficacy and safety of magnesium for the management of chronic pain in adults: A systematic review	Park, R.; Ho, A. M. H.; Pickering, G.; Arendt-Nielsen, L.; Mohiuddin, M.; Gilron, I.	2020	Anesthesia and analgesia	131	3	764-775	https://dx.doi.org/10. 1213/ANE.00000000 00004673
Pringsheim 2008	Acute treatment and prevention of menstrually related migraine headache: Evidence-based review	Pringsheim, T.; Davenport, W. J.; Dodick, D.	2008	Neurology	70	17	1555-1563	https://dx.doi.org/10. 1212/01.wnl.000031 0638.54698.36
Pringsheim 2012	Systematic review: medications for migraine prophylaxis ,Äì section II	Pringsheim, Tamara; Davenport, W. Jeptha; Mackie, Gordon; Worthington, Irene; Aubé, Michel; Christie, Suzanne N.; Gladstone, Jonathan; Becker, Werner J.	2012	Canadian Journal of Neurological Sciences	39	Suppl ement 2	S8-S28	http://cjns.metapres s.com/content/b831 1210p2528qt4/?p=4 bc8b3cf0a404edfae1 649923cd403a5π= 0
vonLuckner 2018	Magnesium in Migraine Prophylaxis-Is There an Evidence-Based Rationale? A Systematic Review	von Luckner, A.; Riederer, F.	2018	Headache	58	2	199-209	10.1111/head.13217

#### Table D-17. Characteristics of included reviews – headache and migraine, magnesium (n=6).

<b>Review ID</b>	Review de	tails			Search det	ails			Quality ass	essment	Other		
	Review design	Aim of the review (as reported by the SR)	Types of studies included	Outcomes relevant to the Overview^	# of databases searched	Names of databases searched	Date of last search	Search restrictions	RoB tool used	Certainty of evidence reported	Conflicts of interest	Funding sources	
Chiu 2016	Meta- analysis	To evaluate the effects of intravenous magnesium on acute migraine attacks and oral magnesium supplements on migraine prophylaxis.	RCTs	2, 3	4	EMBASE, PubMed, Wanfang Data Chinese Database, China Knowledge	Feb 2015	NR	Cochrane Risk of Bias Tool	NR	The authors declare no potential conflicts of interest with respect to the authorship and/or publication of this article.	This meta- analysis was supported by a grant from Taipei Medical University, Taiwan (No.	

						Resource Integrated Database						TMU103-AE1- B11).
Okoli 2019	Systematic Review and Meta- analysis	To summarize the findings of randomized controlled trials (RCTs) on the efficacy and safety of vitamins and minerals for migraine prophylaxis.	RCTs	1, 2, 3	5	Medline, Embase, CENTRAL, PsycINFO, CINAHL	Jun 2017	NR	Cochrane Risk of Bias Tool	NR	Dr. Zarychanski is a recipient of the new investigator salary award from the Canadian Institutes of Health Research. Dr. Mansouri has received previous research funding from Allergan Canada Ltd. All other authors declare that they have no competing interests. The primary and corresponding author had full access to data presented in this systematic review and all the authors had final responsibility for the decision to submit a manuscript for publication.	No funding was attained for this project.
Park 2020	Systematic Review	To assess the current evidence of efficacy and safety of magnesium for the treatment of chronic pain	RCTs	2	3	CENTRAL, MEDLINE, EMBASE	NR	excluded studies that were not published in English	Cochrane Risk of Bias Tool	We planned to rate the quality of evidence using the Grading of Recommend ations Assessment, Developmen t and Evaluation approach, by using a "summary of findings" table. However, the summary of findings table was not included	I. Gilron has received support from Biogen, Adynxx, TARIS Biomedical, AstraZeneca, Pfizer, and Johnson and Johnson and has received grants from the Canadian Institutes of Health Research, Physicians' Services Incorporated Foundation, and Queen's University.	This review is grant funded and has undergone a peer-review process through the Queen's University Department of Anesthesiology and Perioperative Medicine Vandewater Endowed Studentship. This proj- ect is also supported, in part, by the Chronic Pain Network of the Canadian

										due to overall lim- ited evidence.		Institutes of Health Research Strategy for Patient- Oriented Research.
Pringsheim 2008	Systematic Review and Meta- analysis	To provide a systematic review and meta-analysis of the existing therapy trials for MRM and evidence-based recommendations for acute and short-term preventive treatment of MRM headache	placebo- controlled, RCTs	1	3	MEDLINE, EMBASE, Cochrane Library	NR	NR	Quality criteria developed by the US Preventive Services Task Force (USPSTF)	NR	Dr. Dodick has provided consulting services for GSK, Merck, Allergan, Endo, Pfizer, Eli Lilly, Addex, Solvay, Neuralieve, and St. Jude, and he has provided research support for Advanced Neurostimulation Systems (ANS) and Medtronic. The other authors report no disclosures.	NR
Pringsheim 2012	Systematic Review	To assess the evidence base for drugs used for prophylaxis of episodic migraine (headache on ≤ 14 days a month) in Canada.	prospective, double- blind, randomized controlled trials (RCTs)	2, 3	3	MEDLINE, EMBASE , Cochrane Collaboration library	Jun 2011	NR	Quality criteria developed by the US Preventive Services Task Force (USPSTF)	GRADE	NR	NR
vonLuckne 2018	r Systematic Review	To systematically evaluate the existing evidence base on magnesium in migraine prophylaxis.	prospective, randomized, double blind, controlled trials	3	2	PubMed, EMBASE	2016	NR	Cochrane Risk of Bias Tool	NR	The authors declare that there is no conflict of interest with regard to this work.	This research received no specific grant from any funding agency in the public, commercial, or not-for- profit sectors. Furthermore, no writing assistance was used.

Abbreviations: CENTRAL=Cochrane Central Register of Controlled Trials; CINAHL=Cumulative Index of Nursing and Allied Health Literature; NR=Not reported; RCT=randomised controlled trial, GRADE=Grading of Recommendations Assessment, Development and Evaluation, QoL=quality of life

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Global improvement in headache/migraine
- 2. Headache pain intensity
- 3. Headache pain frequency
- 4. Headache/migraine-associated symptoms (nausea and vomiting, photophobia and phonophobia, visual aura)
- 5. QoL
- 6. Cognitive function burden
- 7. Medication use

## D11 Arthritis/Osteoarthritis, magnesium

#### Table D-18. Citation details of included reviews – arthritis/osteoarthritis, magnesium (n=0)

Review ID	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
No reviews were identified for inclusion in the Overview								

## D12 Hypertension, omega-3 fatty acids

#### Table D-19. Citation details of included reviews – hypertension, omega-3 fatty acids (n=3)

<b>Review ID</b>	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
Campbell 2013	A systematic review of fish-oil supplements for the prevention and treatment of hypertension	Campbell, F.; Dickinson, H. O.; Critchley, J. A.; Ford, G. A.; Bradburn, M.	2013	Eur J Prev Cardiol	20	1	107-20	10.1177/204748731243705 6
Guo 2019	Effects of EPA and DHA on blood pressure and inflammatory factors: a meta-analysis of randomized controlled trials	Guo, X. F.; Li, K. L.; Li, J. M.; Li, D.	2019	Critical reviews in food science and nutrition	59	20	3380-3393	https://dx.doi.org/10.1080/ 10408398.2018.1492901
Radack 1989	The effects of omega-3 polyunsaturated fatty acids on blood pressure: a methodologic analysis of the evidence	Radack, K.; Deck, C.	1989	Journal of the American College of Nutrition	8	5	376-85	10.1080/07315724.1989.1 0720312

<b>Review ID</b>	D Review details Review Aim of the review (as reported Types of Outco			Search de	tails			Quality asse	ssment	Other		
	Review design	Aim of the review (as reported by the SR)	Types of studies included	Outcomes relevant to the Overview <sup>^</sup>	# of databases searched	Names of databases searched	Date of last search	Search restrictions	RoB tool used	Certainty of evidence reported	Conflicts of interest	Funding sources
Campbell 2013	Systematic review and meta- analysis	To determine the effectiveness of fish-oil supplements on preventing and treating hypertension.	RCTs	1	4	MEDLINE, EMBASE, CENTRAL, Cochrane Collaboration Hypertension Group	Jan 2011	English language reports	NR	NR	None	This research received no specific grant from any funding agency in the public, commercial, or not-for- profit sectors.
Guo 2019	Meta- analysis	To address the question of whether EPA and DHA monotherapy have differential effects on blood pressure (systolic blood pressure (SBP) and diastolic blood pressure (DBP)) and inflammatory factors (CRP, IL-6 and TNF-a)	RCTs	1	2	PubMed, Scopus	Apr 2018	NR	Jadad score	NR	NR	This work is supported by the National Basic Research Program of China (973 Program: 2015CB553604); by National Natural Science Foundation of China (NSFC: 81773433); by the Key scientific Research Projects in Shandong Provence China (2017YYSP007); and by the 2018 Chinese Nutrition Society (CNS) Nutrition Research Foundation-DSM Research Fund (CNS- DSM2018A30). The funders have no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.
Radack 1989	Systematic review and	We attempted to answer the question of whether or not marine $\omega$ -3-PUFAs cause	RCTs	1	2	Medline, Index Medicus	Jan 1988	English, 1970 to January 1988	Seven criteria modified	NR	NR	NR

 Table D-20. Characteristics of included reviews – hypertension, omega-3 fatty acids (n=3).

meta-	clinically and statis tically				from		
analysis	is important reductions in				Chalmers		
	diastolic and systolic BP by				and		
	applying a quantitative method				DerSimonian		
	combining the data from				to assess the		
	randomized controlled trials to				quality of		
	obtain an accurate and reliable				randomized		
	estimate of the effect of $\omega$ -3-				controlled		
	PUFA on BP response.				trials		

Abbreviations: CENTRAL=Cochrane Central Register of Controlled Trials; CINAHL=Cumulative Index of Nursing and Allied Health Literature; LEAD= Lower Extremity Arterial Disease, NR=Not reported; RCT=randomised controlled trial, GRADE=Grading of Recommendations Assessment, Development and Evaluation, QoL=quality of life, EPA=eicosapentaenoic acid, docosahexaenoic acid (DHA).

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Blood pressure (systolic, diastolic)
- 2. Quality of life
- 3. Cardiovascular events (fatal or non-fatal myocardial infaRCTion, excluding heart failure and if possible angina)
- 4. Cerebrovascular events (fatal or non-fatal strokes, excluding transient ischaemic attacks if possible)
- 5. Death from cardiovascular

## D13 Fibromyalgia, magnesium

Table D-21. Citation details of included reviews – fibromyalgia, magnesium (n=3).

Review ID	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
Holdcraft 2003	Complementary and alternative medicine in fibromyalgia and related syndromes	Holdcraft, L. C.; Assefi, N.; Buchwald, D.	2003	Best Practice and Research in Clinical Rheumatology	17	4	667-683	https://dx.doi.org/10.1016/ S1521- 6942%2803%2900037-8
Porter 2010	Alternative medical interventions used in the treatment and management of myalgic encephalomyelitis/chronic fatigue syndrome and fibromyalgia	Porter, N. S.; Jason, L. A.; Boulton, A.; Bothne, N.; Coleman, B.	2010	Journal of Alternative and Complementary Medicine	16	3	235-249	https://dx.doi.org/10.1089/ acm.2008.0376
Thorpe 2018	Combination pharmacotherapy for the treatment of fibromyalgia in adults	Thorpe, J.; Shum, B.; Moore, R. A.; Wiffen, P. J.; Gilron, I.	2018	The Cochrane database of systematic reviews	2		CD010585	10.1002/14651858.CD010 585.pub2

Review	Review details Review Aim of the review (as reported Types of Out				Search details				Quality as:	sessment	Other	
ID	Review design	Aim of the review (as reported by the SR)	Types of studies included	Outcomes relevant to the Overview^	# of databases searched	Names of databases searched	Date of last search	Search restrictions	RoB tool used	Certainty of evidence reported	Conflicts of interest	Funding sources
Holdcraft 2003	Systematic review	Complementary and alternative medicine (CAM) has gained increasing popularity, particularly among individuals with fibromyalgia syndrome (FMS) for which traditional medicine has generally been ineffective. A systematic review of randomized controlled trials (RCTs) and non-RCTs on CAM studies for FMS was conducted to evaluate the empirical evidence for their effectiveness.	RCTs or non-RCTs	1,5	6	Medline, Biosis, Embase, CINAHL, Alternative Medicine Alert, CENTRAL	2002	NR	CONSORT	NR	NR	The sources of the authors' funding had no role in the collection or interpretation of the data.
Porter 2010	Systematic review	To systematically review and evaluate the current literature related to alternative and complementary treatments for ME/CFS and FM	RCT or Controlled Clinical Trials (CCT)	4, unclear	5	MEDLINE, PsycINFO, PubMed, Social Science Citation Index, Cochrane Database of Systematic Reviews	Apr 2007	English	Jadad scale	NR	NR	No competing financial interests exist.
Thorpe 2018	Cochrane review	To assess the efficacy, safety, and tolerability of combination pharmacotherapy compared to monotherapy or placebo, or both, for the treatment of fibromyalgia pain in adults.	RCTs	1,2,5	3	CENTRAL, MEDLINE, Embase	Sep 2017	No language or date restrictions applied to the searches.	Cochrane Risk of Bias Tool	GRADE	JT: none known. BS: none known. RAM has received grant support from Grünenthal relating to individual, patient-level analyses of trial data regarding tapentadol in	Internal sources • Queen's University Department of Anesthesiology & Perioperative Medicine, Canada Research time support External sources • Canadian Institutes of Health Research - Industry-Partnered (Pfizer) Investigator Award to IG, Canada Salary support

Table D-22. Characteristics of included reviews – fibromyalgia, magnesium (n=3).

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						osteoarthritis	
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						(2016) and	
						(2010) and	
						Pharma	
						Pharma	
						(2016) for	
						providing	
						advice on	
						trial and data	
						analysis	
						methods.	
						PW: none	
						known.	
						IG is an	
						anaesthesiol	
						ogist and	
						conducts	
						clinical trials	
						in acute and	
						chronic nain	
						conditions	
						ne nas	
						received	
						lecture/cons	
						ultancy fees	
						from Biogen	
						(2016) and	
						Adynxx	
						(2015). IG,	

		who is the
		lead and
		correspondin
		g author on
		one of the
		included
		studies in
		this review,
		did not
		participate in
		data
		extraction or
		assessments
		pertaining to
		that study.

Abbreviations: CENTRAL=Cochrane Central Register of Controlled Trials; CINAHL=Cumulative Index of Nursing and Allied Health Literature; NR=Not reported; RCT=randomised controlled trial, GRADE=Grading of Recommendations Assessment, Development and Evaluation, CFS=chronic fatigue syndrome, ME= myalgic encephalomyelitis

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Pain
- 2. Function/Disability
- 3. Global assessment of condition
- 4. HRQoL
- 5. Tenderness
- 6. Cognitive function burden from fibromyalgia
- 7. Stiffness

# D14 Recurrent infection/s (including urinary tract infections, cystitis, respiratory tract infection, otitis media in children), zinc

Table D-23. Citation details of included reviews – recurrent infection/s (including urinary tract infections, cystitis, respiratory tract infection, otitis media in children), zinc (n=3).

<b>Review ID</b>	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
Gulani 2014	Zinc supplements for preventing otitis media	Gulani, A.; Sachdev, S. H.	2014	Cochrane Database of Systematic Reviews	6	6	CD006639	10.1002/14651858.C D006639.pub4
Hurley 2020	Antibiotic adjuvant therapy for pulmonary infection in cystic fibrosis	Hurley, M. N.; Smith, S.; Forrester, D. L.; Smyth, A. R.	2020	The Cochrane database of systematic reviews	7	7	CD008037	10.1002/14651858.C D008037.pub4
Manikam 2016	Limited Evidence on the Management of Respiratory Tract Infections in Down's Syndrome: A Systematic Review	Manikam, L.; Reed, K.; Venekamp, R.; Hayward, A.; Littlejohns, P.; Schilder, A.; Lakhanpaul, M.	2016	The Pediatric infectious disease journal	35	10	1075-9	10.1097/INF.000000 0000001243

Table D-24. Characteristics of included reviews – recurrent infection/s (including urinary tract infections, cystitis, respiratory tract infection, otitis media in children), zinc (n=3).

<b>Review ID</b>	Review det	ails	e review (as Types of Outcom		Search de	tails			Quality ass	essment	Other		
	Review design	Aim of the review (as reported by the SR)	Types of studies included	Outcomes relevant to the Overview^	# of databases searched	Names of databases searched	Date of last search	Search restrictions	RoB tool used	Certainty of evidence reported	Conflicts of interest	Funding sources	
Gulani 2014	Cochrane review	To evaluate whether zinc supplements prevent otitis media in adults and children of different ages.	RCTs	1	3	CENTRAL, MEDLINE, EMBASE	Mar 2014	We imposed no language or publication restrictions.	Cochrane Risk of Bias Tool	NR	Harshpal Singh Sachdev: none known. Anjana Gulani: none known.	Internal sources • Sitaram Bhartia Institute of Science and Research, India. External sources • No sources of support supplied	
Hurley 2020	Cochrane review	To determine if antibiotic adjuvants improve clinical and microbiological outcome of pulmonary infection in people with cystic fibrosis.	RCTs) and quasi- RCTs	2,5	2	Cystic Fibrosis Trials Register, Medline	Jan 2020	There are no restrictions regarding language or publication status.	Cochrane Risk of Bias Tool	GRADE	Dr Doug Forrester Dr Doug Forrester declares he has received support from Wellcome Trust as a Wellcome Trust Clinical Research Training Fellow, travel support from Vertex Pharmaceuticals and GSK and consultancy fees from Mologic. Professor Alan Smyth Professor Smyth is lead investigator on one of the trials included in the review (Smyth 2010). He further declares relevant activities of lectures paid for by Teva and Novartis. He is affiliated to a research group which holds a patent: "ALKYL QUINOLONES AS BIOMARKERS OF PSEUDOMONAS AERUGINOSA INFECTION AND USES THEREOF".	Internal sources • Nottingham Respiratory Biomedical Research Unit, UK MH and DF are funded by the Nottingham Respiratory BRU External sources • National Institute for Health Research, UK This systematic review was supported by the National Institute for Health Research, via Cochrane Infrastructure funding to the Cochrane Cystic Fibrosis and Genetic Disorders Group.	

Manikam	Systematic	To systematically review	controlled	1, 5	6	PubMed,	Feb 2015	No limit of	Cochrane	NR	The authors have no	This article presents
2016	Review	the effectiveness of	trials			EMBASE,		search	<b>Risk of Bias</b>		conflicts of interest to	independent research
		preventative and				CINAHL,		strategy to	Tool		disclose.	funded through a PhD
		therapeutic interventions	:			Cochrane		specific study	(			fellowship awarded to
		for respiratory tract				Library, WHO		types,				the first author by the
		infections (RTIs) in				ICTRP,		language or				NIHR. The views
		people with Down's				ClinicalTrials.gov		publication				expressed are those
		syndrome						date				of the authors and not
												necessarily those of
												the NIHR.

Abbreviations: CENTRAL=Cochrane Central Register of Controlled Trials; CINAHL=Cumulative Index of Nursing and Allied Health Literature; NR=Not reported; RCT=randomised controlled trial, GRADE=Grading of Recommendations Assessment, Development and Evaluation; WHO ICTRP=WHO International Clinical Trials Registry Platform (ICTRP)

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Overall control of disease (recurrence)
- 2. Overall severity of symptoms
- 3. Time (days) from initiation of treatment to resolution of symptoms
- 4. HRQoL
- 5. Use of acute and prophylactic antibiotics for conditions where antibiotics are indicated
- 6. Duration of hospital stay

# D15 Diabetes (Type II) (including metabolic syndrome), antioxidants (specifically CoQ10 and alpha-lipoic

### acid)

Table D-25. Citation details of included reviews – diabetes (Type II) (including metabolic syndrome), antioxidants (specifically CoQ10 and alpha-lipoic acid) (n=10).

<b>Review ID</b>	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
Araújo 2022	Efficacy of Antioxidant Supplementation to Non- Surgical Periodontal Therapy on Metabolic Control in Type 2 Diabetes Patients: A Network Meta-Analysis	Araújo, E. G., Oliveira, D. M. S. L., Martins, C. C., & Stefani, C. M.	2022	Antioxidants (Basel, Switzerland)	11	4	621	10.3390/antiox110 40621
Dludla 2020	The impact of coenzyme Q10 on metabolic and cardiovascular disease profiles in diabetic patients: A systematic review and meta-analysis of randomized controlled trials	Dludla, P. V.; Louw, J.; Muller, C. J. F.; Dludla, P. V.; Orlando, P.; Silvestri, S.; Tiano, L.; Nyambuya, T. M.; Mxinwa, V.; Mokgalaboni, K.; Nkambule, B. B.; Nyambuya, T. M.; Louw, J.; Muller, C. J. F.; Muller, C. J. F.	2020	Endocrinol. Diabetes Metab.	3	2	e00118	10.1002/edm2.118
Dludla 2023	Dietary Supplements Potentially Target Plasma Glutathione Levels to Improve Cardiometabolic Health in Patients with Diabetes Mellitus: A Systematic Review of Randomized Clinical Trials	Dludla, P. V.; Ziqubu, K.; Mabhida, S. E.; Mazibuko-Mbeje, S. E.; Hanser, S.; Nkambule, B. B.; Basson, A. K.; Pheiffer, C.; Tiano, L.; Kengne, A. P.	2023	Nutrients	15	4	944	10.3390/nu150409 44
Huang 2018	Effects of coenzyme Q10 on cardiovascular and metabolic biomarkers in overweight and obese	Huang, H.; Chi, H.; Liao, D.; Zou, Y.	2018	Diabetes Metab Syndr Obes.	11		875-886	10.2147/DMSO.S1 84301

<b>Review ID</b>	Title	Authors	Year	Journal	Volume	Issue	Pages	DOI
	patients with type 2 diabetes mellitus: a pooled analysis							
Huo 2022	Efficacy of vitamin and antioxidant supplements for treatment of diabetic peripheral neuropathy: systematic review and meta-analysis of randomized controlled trials	Huo, J.; Xue, Y.; Dong, X.; Lv, J.; Wu, L.; Gao, H.; Yang, X.; Liu, H.; Gao, Q.	2022	Nutritional neuroscience	26	8	778-795	10.1080/1028415X .2022.2090606
Jibril 2022	Efficacy and safety of oral alpha-lipoic acid supplementation for type 2 diabetes management: a systematic review and dose-response meta-analysis of randomized trials	Jibril, A. T.; Jayedi, A.; Shab-Bidar, S.	2022	Endocrine connections	11	10	e220322	10.1530/EC-22- 0322
Kim 2022	Could nutrient supplements provide additional glycemic control in diabetes management? A systematic review and meta-analysis of randomized controlled trials of as an add-on nutritional supplementation therapy	Kim, Y.; Oh, Y. K.; Lee, J.; Kim, E.	2022	Archives of pharmacal research	45	3	185-204	10.1007/s12272- 022-01374-6
Rahimlou 2019	Alpha-lipoic acid (ALA) supplementation effect on glycemic and inflammatory biomarkers: a systematic review and meta-analysis	Rahimlou M, Asadi M, Banaei Jahromi N, Mansoori A.	2019	Clin Nutr ESPEN.	32		16–28	doi: 10.1016/j.clnesp.2 019.03.015
Wang 2022	Effects of Antioxidant Supplementation on Metabolic Disorders in Obese Patients from Randomized Clinical Controls: A Meta-Analysis and Systematic Review	Wang, J.; Liao, B.; Wang, C.; Zhong, O.; Lei, X.; Yang, Y.	2022	Oxid Med Cell Longev	2022		7255413	10.1155/2022/725 5413
Zhang 2018	Effectiveness of Coenzyme Q10 Supplementation for Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis	Zhang, S. Y.; Yang, K. L.; Zeng, L. T.; Wu, X. H.; Huang, H. Y.	2018	International Journal of Endocrinology	2018		6484839	10.1155/2018/648 4839

Table D-26. Characteristics of included reviews – diabetes (Type II) (including metabolic syndrome), antioxidants (specifically CoQ10 and alpha-lipoic acid) (n=10).

Review	Review de	etails			Search de	tails			Quality as	sessment	Other	
ID	Review design	Aim of the review (as reported by the SR)	Types of studies include d	Outcomes relevant to the Overview^	# of databases searched	Names of databases searched	Date of last search	Search restrictions	RoB tool used	Certainty of evidence reported	Conflicts of interest	Funding sources
Araújo 2022	Network Meta- Analysis	To assess whether the adjunctive use of antioxidant supplementation to non-surgical periodontal therapy (NSPT) results in increased metabolic control in patients with T2D and periodontitis.	RCTs	1	7	PubMed, Cochrane, LILACS, Web of Science, Scopus, Embase, LIVIVO	Jan 2022	No restrictions on language or publication period were established	Cochrane Risk of Bias Tool	GRADE	The authors declare no conflict of interest.	This project was funded by the Research Support Foundation of the Federal District (FAP-DF) (process no. 16991.78.45532.26042017 ), and the University of

												Brasilia (Edital DPI 001/2022).
Dludla 2020	Systemati c review and meta- analysis	To understand cardio-protective effects of CoQ10, using data from randomized controlled trials (RCTs) published in the last five years.	RCTs	1, 2	4	MEDLINE, Cochrane Library, Scopus, EMBASE	Sep 2019	no language restrictions	Downs and Black checklist	GRADE	The authors declare no conflict of interest.	This work was supported in part by baseline funding from the Biomedical Research and Innovation Platform of the South African Medical Research Council (SAMRC) and the National Research Foundation (Grant number: 117829).
Dludla 2023	Systemati c review	Tto determine whether supplementation with dietary compounds improves cardiometabolic health in people with diabetes.	RCTs	1, 2	>2	Major databases including PubMed/MEDLINE and Google Scholar	Dec 2022	None	Downs and Black checklist	NR	The authors declare no conflict of interest.	The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.
Huang 2018	Systemati c review and meta- analysis	to perform a pooled analysis to investigate the effects of CoQ10 intervention on cardiovascular disease (CVD) risk factors in overweight/obese patients with type 2 diabetes mellitus (T2DM)	RCTs	1, 2	3	MEDLINE, Embase, CENTRAL	Dec 2017	English and clinical trials	Cochrane Risk of Bias Tool	GRADE	The authors report no conflicts of interest in this work.	NR
Huo 2022	Systemati c review and meta- analysis	To examine whether these supplements are effective in DPN treatment.	RCTs	1	7	PubMed, EMBASE, Web of Science, Chinese Biomedical Database (CBM), Cochrane Library, China National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database	Oct 2021	NR	Cochrane Risk of Bias Tool	GRADE	No potential conflict of interest was reported by the author(s)	This work was supported by Ningxia Natural Science Foundation, China, [grant number: 2021AAC03138]; The National Natural Science Foundation of China [grant number: 82060596].
Jibril 2022	systemati c review and dose- response meta- analysis	To examine the dose-dependent influence of oral alpha-lipoic acid (ALA) supplementation on cardiometabolic risk factors in patients with type 2 diabetes (T2D).	RCTs	1, 2	3	PubMed, Scopus, Web of Science	May 2021	not language restricted	Cochrane Risk of Bias Tool	GRADE	The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of	This work did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector.

											the research reported.	
Kim 2022	Systemati c review and meta- analysis	To compare pharmaconutrients with a placebo in T2DM patients consuming antidiabetics drugs. We aimed to identify add-on pharmaconutrients that exert regulatory effects on glucose levels and insulin resist- ance in patients with T2DM by pooling data from currently available RCTs.	RCTs	1	3	PubMed, EMBASE, CENTRAL	Aug 2021	English	Cochrane Risk of Bias Tool	GRADE	All authors declare that there are no conflicts	This study was supported by Basic Science Research Program through the National Research Foundation of Korea funded by the Ministry of Education (Grant Numbers 2018R1D1A1B07046564 and 2021R1A6A1A03044296) and by NRF grant funded by the Korea government (Ministry of Science and ICT, MICT) (NRF- 2021R1F1A1062044). The funders had no role in study design, data collection, data analysis, or decision to publish and preparation of the manuscript.
Rahimlo u 2019	Systemati c review and meta- analysis	To assess the effect of ALA on some glycemic and inflammatory parameters.	RCTs	1	7	PubMed, Scopus, Cochrane databases, Google Scholar, ProQuest, Web of Science, Embase	Jul 2018	None	Cochrane Risk of Bias Tool	NR	None of the authors declare a conflict of interest.	This work has not received any funding.
Wang 2022	Systemati c review and meta- analysis	To elucidate the heterogeneity in beneficial effects of antioxidant supplementation in obese adults by exploring the differential effects of antioxidant supplementation on basic indicators of obesity, lipid metabolism, systemic antioxidant capacity, inflammatory biomarkers, and liver function.	RCTS	1	5	PubMed, Embase, Cochrane Library, Web of Science, Scopus databases	Aug 2021	English	Cochrane Risk of Bias Tool	NR	The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.	This work was supported by the National Natural Science Foundation of China (No. 82101720), the Scientific Research Elevation Project of Young Faculty from Guangxi Universities (2019KY0567), and the Scientific Research and Techno- logical of Baise in China (20183331).

Zhang 2018	Systemati c review and meta- analysis	To evaluate the effectiveness and safety of coenzyme Q10 for patients with type 2 diabetes mellitus (T2DM).	RCTs	1	10	China National Knowledge Infrastructure (CNKI) Databases, Chinese Biomedical Database (CBM), Cochrane Library, Web of Science, Embase, Wan Fang	Feb 2018	NR	Cochrane Risk of Bias Tool	NR	We declare no competing interests.	This work is supported by the National Natural Science Foundation of China (no. 81373551), the Doctoral Fund of Ministry of Education of China (no. 20134323110001), the key projects of Hunan
						Technology), PubMed, MEDLINE Complete, ClinicalTrials.gov, Chinese Science and Technology Periodical Database (VIP)						S2014S2032)

Abbreviations: CENTRAL=Cochrane Central Register of Controlled Trials; CVD=cardiovascular disease, CINAHL=Cumulative Index of Nursing and Allied Health Literature; T2DM=Type II Diabetes Mellitus, NR=Not reported; RCT=randomised controlled trial, GRADE=Grading of Recommendations Assessment, Development and Evaluation

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Glycemic control
  - HbA1c
  - Fasting glucose
  - Fasting insulin
  - Homeostatic model assessment of insulin resistance
  - 2 hour post-prandial blood sugar
  - Hyperglycemia (frequency)
  - Hypoglycemia (frequency)
- 2. Blood pressure
  - Systolic
  - Diastolic
- 3. Oxidative stress
  - Malonaldehyde
  - Total antioxidant status/capacity
  - Free oxygen radical test
  - Reative oxygen metabolites
  - Biological antioxidant potential
  - Lipo-peroxidation products
  - Catalase
  - Glutathione peroxidase
- 4. Diabetes related symptoms
- 5. Overall diabetes related complications
- 6. HRQoL
- 7. Incidence of type 2 diabetes mellitus

# Appendix E Results of included reviews.

Results are presented separately for preferred reviews (those from which data was used), followed by the remaining included reviews (those which were considered) for each population-supplement pair. Risk of bias for primary studies is only reported for the preferred reviews, but the ROBIS assessment includes whether this was reported.

## E1 Anxiety (including post-natal), magnesium

Revie Outcon w ID e doma	Outcom	Populatio	Population	Type of	Intervention	Comparator	No/type	No of	Outcome	Results			ROBIS
wID	e domain	n group	details	comparison	description	description	s of included studies	participants (total)	measure(s) used	Relative effect (95% CI)	Other reported results	Risk of bias summary (primary studies)	assessment (for the review overall)
Barić 2018	1	With condition	Adults (at least 18 years of age) with GAD diagnosed according to defined criteria	Eligible supplement + naturopathy co- intervention VS placebo	Extract of crataegus oxycantha and Eschscholtzia californica combined with Magnesium	Placebo	1 RCT	81	HAM-A; Patient self- assessment VAS score, CGI	RR = 1.41 (1.04 to 1.93)	Difference in reduction in HAM-A score: –1.7 (–1.8 to – 1.6)	Low risk of bias in included study.	Low risk
Tsai 2023	1	At-risk of condition	During pregnancy or within the first 12 months postpartum	Eligible supplement VS placebo	Magnesium (64.6mg)	Placebo	1 RCT	64	STAI	SMD = - 0.34 (- 0.83 to 0.15)	-	Some concerns of bias in included study.	Low risk
Tsai 2023	4	At-risk of condition	During pregnancy or within the first 12 months postpartum	Eligible supplement VS placebo	Magnesium (64.6mg)	Placebo	1 RCT	64	EPDS	SMD = 0.20 (- 0.29 to 0.69)	-	Some concerns of bias in included study.	Low risk

Table E-1. Results of preferred reviews by outcome domain – anxiety (including post-natal), magnesium

Abbreviations: CGI=Clinician global impression; EPDS= Edinburgh Postnatal Depression Scale; GAD=generalised anxiety disorder; HAM-A=Hamilton Anxiety Rating Scale; RCT=randomised controlled trial; RR=relative risk; STAI=State-Trait Anxiety Inventory; SMD=standardised mean difference

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

1. Anxiety-related emotional functioning/mental health burden;

- 2. Physical function burden from anxiety (gastrointestinal disorders, loss of sexual desire, frequent upper respiratory tract and other infections)
- 3. Improvement in clinical levels of anxiety
- 4. Depression-related emotional functioning/mental health burden
- 5. Stress-related emotional functioning/mental health burden
- 6. Physiological symptoms of anxiety (heart rate, BP, adrenaline, skin conductance, weight gain, weight loss, cortisol levels)
- 7. Health-related quality of life

For Anxiety all included reviews were preferred reviews.

## E2 Stress (perceived, occupational), magnesium

No reviews were identified for inclusion in the Overview.

## E3 Irritable bowel syndrome, probiotics

Table E-2. Results of preferred reviews by outcome domain – irritable bowel syndrome, probiotics.

Revie	Outcom	Populatio	Population	Type of	Intervention	Comparato	No/types of	No of	Outcome	s) Results ROBIS Relative Other Risk of bias t (for the	ROBIS		
w ID	e domain	n group	details	comparison	description	r description	included studies	participant s (total)	measure(s) used	Relative effect (95% Cl)	Other reported results	Risk of bias summary (primary studies)	assessmen t (for the review overall)
Abbou d 2020	1	With condition	Adults or children, healthy or with disease other than those known to influence vitamin D metabolism, and including an intervention group that received a co- supplementatio n of vitamin D and probiotics	Eligible supplement + naturopathy co-intervention VS inactive control (placebo, usual care, no intervention)	Vitamin D3 and probiotic supplement: - Vitamin D3: sublingual liquid spray, 3000 IU daily - Probiotics: Lactobacillus acidophilus, CUL60 (NCIMB 30157), CUL21 (NCIMB 30156), Bifidobacteriu m bifidum CUL20 (NCIMB 30153) and Bifidobacteriu m animalis	C1: Double placebo C2: Placebo and Vitamin D3 (400 IU daily) Similar in form, containing identical buffers	1	NR	Questionnair e assessing abdominal pain (pain severity and number of days with pain), bloating, bowel habits (minimum and maximum bowel movement per day and satisfaction with bowel habit) and quality of life	NR	No significant between- group differences for any symptom tested, and total symptom severity	Low risk of bias in included study.	Low risk

					subsp. Lactis CUL34 (NCIMB 30172) 2.5 × 1010 CFU per capsule								
Ding 2019	2	With condition	Children 0 to 18 years old	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	6	329	NR	NR	Five of six RCTs (n=279) demonstrated a beneficial effect of probiotic, however, the specific pain parameter affected was heterogeneou s among the studies. Three out of four trials using LGG demonstrated an improvement in pain severity or frequency in the probiotic group. One trial using a bifidobacteria combination product and one using VSL #3, each showed some benefits for pain resolution and pain severity.	Low risk of bias assessed across most domains for most studies.	High risk
Ding 2019	5	With condition	Children 0 to 18 years old with IBS (ROME Criteria)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	4	NR	Functional Disability Inventory, Functional scale by LS3,	NR	Four studies evaluated the functional impact of probiotic use,	Low risk of bias assessed across most domains for most studies.	High risk

									Family life disruptions by caregiver's report, School absenteeism (n)		with three studies finding a positive result for probiotic usage.		
Le Morva n 2021	3	With condition	Adults of both sexes and of all ages with IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	11	1501	IBS-QOL questionnair e	SMD = 0.36 (0.07 to 0.64); p = 0.01	Heterogeneity was high with I2 = 86%. In subgroup analysis of single-strain versus multi- strain studies in, no significant subgroup effects were found (p = 0.37). However, heterogeneity decreased slightly when analysing only single-strain probiotic studies (I2 = 72%) but remained similarly high for multi- strain probiotic studies (I2 = 91%).	Eight of 11 studies had low risk of bias across all assessed domains.	Unclear risk
Li 2020	1	With condition	≥ 18 years with IBS diagnosis	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	35 comparison s from 29 trials	3726	IBS-SSS, Subject's Global Assessment, Global symptoms score (GSS), GSRS, GSRS-	SMD = – 0.18 (–0.30 to -0.06)	Heterogeneity was significant (l <sup>2</sup> = 65%, P < 0.001).	Most (23/29) studies did not describe the details of the sequence generation process or allocation	Low risk

Li 2020	2	With condition	≥ 18 years with IBS diagnosis	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	44 comparison s from 38 trials	4579	IBS, Likert scale, IBS SSI, VAS, Birmingham IBS Symptom Questionnair e Likert scale, VAS, Numerical scale, GSRS, IBS-SSS	RR = 1.52 (1.32 to 1.76)	l <sup>2</sup> = 71%, p<0.001	concealment. The risk of outcome assessment was mostly unclear. Attrition bias, reporting bias, and other biases were low.	Low risk
Li 2020	2	With condition	≥ 18 years with IBS diagnosis	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	44 comparison s from 38 trials	4579	Likert scale, VAS, Numerical scale, GSRS, IBS-SSS	RR = 1.52 (1.32 to 1.76)	l <sup>2</sup> = 71%, p<0.001	-	Low risk
Wen 2020	6	With condition	Adult populations aged ≥16 y with functional chronic constipation defined by clinical symptoms, a physician's opinion, or the Rome I, II, or III criteria.	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	11 comparison s from 10 trials	1139	BMs per week	MD = 1.29 bowel movement s (BMs) per week (0.69 to 1.89 BMs per week) P < 0.0001)	As significant heterogeneity was observed (p < 0.00001 and I <sup>2</sup> = 90), the pooled analysis was perform with random- effect model. There was no significant funnel plot asymmetry (Egger test = 1.44; 95% CI: 22.02–9.10; P = 0.183), suggesting no evidence of publication bias.	Studies assessed as good methodologic al quality. All RCTs showed a low risk of bias regarding random sequence generation (selection bias) and performance bias. Unclear risk of bias was mainly observed in detection and other bias. No high risk of bias was	Low risk
Wen 2020	6	With condition	Adult populations aged ≥16 y with functional chronic constipation	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	2	141	Rectosigmoi d transit time	4.0 hours (-7.6 to -0.4 hours) P = 0.03)		observed.	Low risk

			defined by clinical symptoms, a physician's opinion, or the Rome I, II, or III criteria.									
Wen 2020	6	With condition	Adult populations aged ≥16 y with functional chronic constipation defined by clinical symptoms, a physician's opinion, or the Rome I, II, or III criteria.	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	2	141	Right colonic transit time	MD = -4.9 hours (-10.5 to 0.8 hours) p = 0.09		Low risk
Wen 2020	6	With condition	Adult populations aged ≥16 y with functional chronic constipation defined by clinical symptoms, a physician's opinion, or the Rome I, II, or III criteria.	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	2	141	Left colonic transit time	MD = -4.9 hours (-10.2 to 0.3 hours), p = 0.07		Low risk
Wen 2020	6	With condition	Adult populations aged ≥16 y with functional chronic constipation defined by clinical symptoms, a physician's opinion, or the	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	3 comparison s from 2 trials	140	Gut transit time	12.36 hours (-20.74 to -3.98 hours), p = 0.004	As no significant heterogeneity between studies was observed (Ph = 0.27 and I <sup>2</sup> = 23), the pooled analysis was perform with	Low risk

			Rome I, II, or III criteria.								fixed-effect model	
Wen 2020	7	With condition	Adult populations aged ≥16 y with functional chronic constipation defined by clinical symptoms, a physician's opinion, or the Rome I, II, or III criteria.	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	10 comparison s from 9 trials	NR	Stool frequency, Bristol Stool Form Scale or modified versions of it	SMD = 0.55 (0.27 to 0.82) P = 0.0001	As significant heterogeneity between studies was observed (Ph < 0.00001 and l <sup>2</sup> = 80), the pooled analysis was performed with random- effect model (Fig. 5). There was no funnel plot asymmetry (Egger test = 0.57; 95% Cl: 24.87–8.09; P = 0.583), suggesting no evidence of publication bias.	Low risk

Abbreviations: BM=bowel movement; IBS=irritable bowel syndrome; IBS-SSS=IBS Symptom Severity Scale; GSS= Global symptoms score; GSRS=Gastrointestinal Symptom Rating Scale; LGG= Lactobacillus rhamnosus GG; MD=mean difference; NR=Not reported; RR=relative risk; SMD=Standard mean difference; VAS=visual analogue scale

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Global improvement of IBS
- 2. Abdominal pain burden
- 3. Health-related quality of life
- 4. Number of recurrent episodes
- 5. Functioning
- 6. Stool frequency, bowel transit time
- 7. Stool consistency

#### Table E-3. Results of included (non-preferred) reviews by outcome domain - irritable bowel syndrome, probiotics

Review ID	Outcome	Populatio	Population	Type of	Intervention	Comparat	No/type	No of	Results	ROBIS
	domain	n group	details	comparison	description	or	s of	particip		assessment

						descriptio n	included studies	ants (total)	Outcome measure(s) used	Relative effect (95% CI)	Other reported results	Risk of bias summary (primary studies)	(for the review overall)
Asha 2020	1	With condition	Adult IBS patients (aged ≥18 years)	Eligible supplement VS placebo/inactiv e control	Probiotics (single strain or multiple strain)	Placebo	17	2431	NR	SMD = -0.32 (-0.48 to -0.15)	Significant heterogeneit y (I <sup>2</sup> = 72%; p < 0.001).	NA	High risk
Asha 2020	2	With condition	Adult IBS patients (aged ≥18 years)	Eligible supplement VS placebo/inactiv e control	Probiotics (single strain or multiple strain)	Placebo	26	3678	NR	SMD = -0.18 (-0.43 to 0.07)	Significant heterogeneit y (I <sup>2</sup> = 92%; p < 0.001)	NA	High risk
Asha 2020	3	With condition	Adult IBS patients (aged ≥18 years)	Eligible supplement VS placebo/inactiv e control	Probiotics (single strain or multiple strain)	Placebo	NR	NR	NR	NR	Nil	NA	High risk
Connell 2018	1	With condition	Patients with IBS	Eligible supplement VS placebo/inactiv e control	VSL no. 3.	Placebo	3	177		RR = 1.39 (0.98 to 1.96)	No significant heterogeneit y ( $l^2 = 0\%$ , p = 0.63).	NA	Low risk
Connell 2018	2	With condition	Patients with IBS	Eligible supplement VS placebo/inactiv e control	VSL no. 3.	Placebo	5	243	VAS, Gastrointestina I Symptom Rating Scale (GSRS)	SMD = 0.03 (-0.22 to 0.29)	No significant heterogeneit y ( $l^2 = 0\%$ , P- value for Cochrane's Q = 0.7).	NA	Low risk
Connell 2018	3	With condition	Patients with IBS	Eligible supplement VS placebo/inactiv e control	VSL no. 3.	Placebo	3	170		SMD = -0.08 (-0.39 to 0.22)	No significant heterogeneit y ( $I^2 = 0\%$ , P = 0.65).	NA	Low risk
Connell 2018	7	With condition	Patients with IBS	Eligible supplement VS placebo/inactiv e control	VSL no. 3.	Placebo	3	177		Overall MD = 0 (-0.09 to 0.08)	There was no observed heterogeneit y across studies ( $I^2 =$ 0%, p = 0.71)	NA	Low risk
Corbitt 2018	1	With condition	Adults aged 18 years and above	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo, parallel group, no control	21		Patient diaries, GSRS, 7-point Likert, IBS-SSI, IBS Sum Score, Birmingham	NR	The results were variable, with 8 (of 24) studies	NA	High risk

									IBS Symptom Questionnaire, Integrative Medicine Patient Satisfaction Scale (IMPSS), VAS, single question		finding that a probiotic significantly improved IBS symptoms compared to the control		
Corbitt 2018	3	With condition	Adults aged 18 years and above	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo, parallel group, no control	15		IBS-QOL, SF- 12, SF-36, Quality of Life Questionnaire for Functional Digestive Disorders (FDDQL), RAND 36-Q, HR-QOL, patient diaries	NR	Four studies reported a significant improvemen t in QoL, one study reported a significant improvemen t in both groups.	NA	High risk
Corbitt 2018	7	With condition	Adults aged 18 years and above	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo, parallel group, no control	5		Patient reporting of number of bowel movements per day	NR	Two studies reported an improvemen t in stool frequency. It was also noted that the improvemen t in stool frequency was attributed to two different IBS sub- groups.	NA	High risk
Ding 2019	2	With condition	Children 0 to 18 years old	Eligible supplement VS placebo/inactiv e control	Probiotics	РІасево	6	329	NR	NR	Five of six RCTs (n=279) demonstrate d a beneficial effect of probiotic, however, the	Most (5/6) studies had low risk of bias for randomisati on, allocation concealme nt, blinding,	High risk

							1	1					
											specific pain parameter affected was heterogeneo us among the studies. Three out of four trials using LGG demonstrate d an improvemen t in pain severity or frequency in the probiotic group. One trial using a bifidobacteri a combination product and one using VSL #3, each showed some benefits for pain resolution and pain severity.	data collection, and selective reporting. Five studies were sponsored by a pharmaceu tical company.	
Fatahi 2022	2	With condition	Children and adolescents (under or equal to 18 years of age) with IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	7	441	Faces pain scale, Subject's global assessment of relief, Likert	WMD = -2.36 (-4.12 to -0.60)	The length of supplement ation longer than four weeks was more effective (WMD = -2.43; -2.76 to $-2.09$ ). None of the subgroup analyses for the age of the	NA	Low risk

											participants and the duration of the intervention could find a possible source of heterogeneit y. Significant heterogeneit y (Cochran Q test, p < 0.001, l <sup>2</sup> = 99.9%)		
Ford 2014	1	With condition	Adult patients (over the age of 16 years) with IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	23	1642	NR	RR = 0.79 (0.70 to 0.89)		NA	Low risk
Ford 2014	2	With condition	Adult patients (over the age of 16 years) with IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	25	2026	NR	SMD = -0.25 (-0.36 to -0.14)	No significant heterogeneit y ( $I^2 = 27\%$ , P = 0.11	NA	Low risk
Horvath 2011	2	With condition	Children up to 18 years of age	Eligible supplement VS placebo/inactiv e control	Lactobacillus GG	Placebo	2	117	NR	RR = 1.70 (1.27 to 2.27)	P = 0.22; I <sup>2</sup> = 33%	NA	Unclear risk
Hoveyda 2009	1	With condition	Patients with IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	7	895	Dichotomous data	OR = 1.63 (1.23 to 2.17)	P = .22, I <sup>2</sup> = 27.5%	NA	Unclear risk
Hoveyda 2009	1	With condition	Patients with IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	6	657	Continuous data	SMD = 0.23 (0.07 to 0.38)	P = 0.8, I <sup>2</sup> = 0%	NA	Unclear risk
Hoveyda 2009	2	With condition	Patients with IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	7	398	Dichotomous data	OR = 2.88 (1.84 to 4.50)	P = .25, I <sup>2</sup> = 24.1%	NA	Unclear risk
Hoveyda 2009	3	With condition	Patients with IBS	Eligible supplement VS	Probiotics	Placebo	4	362	IBS specific QoL		No significant	NA	Unclear risk

				placebo/inactiv e control					questionnaire and the Hospital Anxiety and Depression Scale (HAD).	change in the QoL or HAD scores was reported with any of the probiotic dosages in comparison to placebo.		
Hoveyda 2009	3	With condition	Patients with IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	4	274	Functional Digestive Disorders Quality of Life questionnaire	Global score did not differ significantly between the probiotic group and the control group	NA	Unclear risk
Hoveyda 2009	3	With condition	Patients with IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	4	103	RAND 36 item health survey	Mean QoL was somewhat higher in the probiotic group, but the difference between the groups was non- significant compared with the baseline. There was no change in the mean score at three months or six months in either group.	NA	Unclear risk
Hoveyda 2009	3	With condition	Patients with IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	4	80	IBS-specific questionnaire	For most domains, QoL scores were	NA	Unclear risk

											numerically lower than those for placebo for the patients randomized to the pro- biotics, but reached statistical significance versus placebo, during the treatment phase only, for health worry for bifidobacteri um (at the 0.05 level) and dysphoria for lactobacillus at the 0.10 level.		
Huertas- Ceballos 2009		condition	School-age children (5-18 years old) with recurrent abdominal pain (defined as at least three episodes of pain interfering with normal activities within a three- month period)	Eligible supplement VS placebo/inactiv e control	Lactobacillus	Placebo	2	154	GSRS, other	1.17 (0.62 to 2.21	P=0.99; I* =0%	NA	High risk
Hungin 2018	1	With condition	Adult patients (>= 18 years) with IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	23	3112			15 evaluated overall IBS symptoms as a primary endpoint, of which 8	NA	High risk

						1				1		
										reported a significant beneficial effect of 8 different probiotic products (dosed at 3.4 9 107 to 2.5 9 1010 CFU per day) compared with placebo, 5 reported no significant differences between 2 specific probiotic treatments and placebo, and 2 reported mixed results.		
Hungin 2018	2	With condition	Adult patients (>= 18 years) with IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	30	3771		7 studies showed a significant beneficial effect of specific probiotic treatments compared with placebo.	NA	High risk
Hungin 2018	3	With condition	Adult patients (>= 18 years) with IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	6	NR		Two studies of 2 different probiotics reported a significantly greater improvemen t in HRQoL with	NA	High risk
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					probiotic	
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					probiotics in	
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					(physical,	
					social and	ļ
					mental;	ļ
					primary	
					endpoint);	ļ

										however, use of the 36-item Short-Form Health Survey (SF- 36; secondary endpoint) revealed significant improvemen ts in		
Hungin 2018	7	With condition	Adult patients (>= 18 years) with IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	25	3069		Two studies of 2 different probiotics (administere d at doses of between 1.3 9 108 and 9 9 109 CFU per day) evaluated bowel habit as a primary endpoint, with 1 study (included in the original consensus) reporting no significant difference in weekly defecation frequency between the probiotic and placebo groups, although a significant positive effect of the specific probiotic	NA	High risk

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											only. Fourteen of these (evaluating 12 different probiotics) found no difference between treatment groups in measures of HRQoL, whereas 5 studies (all in patients with IBS) reported significant benefits of 5 different probiotic treatments for some aspects of HRQOL.		
Konstantis 2023	1	With condition	IBS patients categorized solely according to the Rome IV criteria, adult	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	4	NR - in table	IBS-Symptom Severity Score	WMD = 43.2 (87.5 to 1.02)	l <sup>2</sup> = 82.9%	NA	Low risk
Konstantis 2023	2	With condition	IBS patients categorized solely according to the Rome IV criteria, adult	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	6	NR - in table	VAS optical scale to assess pain, APS-NRS score, Likert scale	SMD = 0.94 (1.53 to 0.35)	l <sup>2</sup> = 92.2%	NA	Low risk
Konstantis 2023	3	With condition	IBS patients categorized solely according to the Rome IV criteria, adult	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	5	NR - in table	VAS, qol-score	SMD = - 0.64, (- 1.27 to 0.00)	l <sup>2</sup> = 93,9%	NA	Low risk

Korterink 2014	2	With condition	Children and adolescents with functional gastrointestina l disorders - IBS subgroup analysis	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	4	NR	NR	RR = 1.62 (1.27 to 2.06)	l <sup>2</sup> = 20%, p = 0.29	NA	High risk
Korterink 2014	6, 7	With condition	Children and adolescents with functional gastrointestina l disorders - IBS subgroup analysis	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	2	NR	The questionnaires used gathered information about defecation frequency and consistency.	NR	One study did not find a significant improvemen t in stool pattern comparing LGG with placebo (50 participants, p = 0.61). The other study also failed to show a significant effect of VSL#3 on improving stool pattern in children with IBS (59 participants, p = 0.06).	NA	High risk
Liang 2019	1	With condition	Adult patients (age ≥18 years) with IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	13	1573	Dichotomous data are "responders" which reflect the global efficacy of probiotics, defined as reporting "adequate relief (AR)" or "satisfactory relief (SR)" of IBS symptoms	RR = 1.27 (1.13 to 1.44); P < .001	<sup>2</sup> = 34%	NA	Low risk

									for >50% of the time				
Mcfarland 2008	1	With condition	NR	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	14 compari sons from 12 trials	NR	NR	RR = 0.77 (0.62 to 0.94)	I <sup>2</sup> = 68.3%, P = 0.000	NA	Low risk
Mcfarland 2008	2	With condition	NR	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	11 compari sons from 8 trials	NR	NR	RR = 0.78 (0.69 to 0.88)	The pooled RR for abdominal pain was similar when weighted by study quality (RR pooled = 0.61; 95% CI, 0.45- 0.81) and after exclusion of the two trials conducted in children (RR pooled = 0.77; 95% CI, 0.68- 0.88).	NA	Low risk
Mcfarland 2021	1	With condition	Adult or pediatric patients diagnosed with IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	15 compari sons from 12 trials	NR	Change in IBS symptom scores	SMD = – 2.39 (– 3.32 to – 1.46)	Heterogeneit y in the 21 RCTs with this outcome was high ( $I^2 =$ 97.9%).	NA	Unclear risk
Mcfarland 2021	2	With condition	Adult or pediatric patients diagnosed with IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	32 compari sons from 29 trials	NR	Change in IBS abdominal pain scores	SMD = - 1.47 (1.95 to -0.99)	Overall, the heterogeneit y in the 29 RCTs with this outcome was high (I <sup>2</sup> = 95.9%),	NA	Unclear risk
Mcfarland 2021	2	With condition	Adult or pediatric patients	Eligible supplement VS	Probiotics	Placebo	32 compari sons	NR	Frequency reporting less	SMD = 1.94	Overall, the heterogeneit y in the 13	NA	Unclear risk

	1	1				1	1	1		1			
			diagnosed with IBS	placebo/inactiv e control			from 11 trials		abdominal pain by study end	(1.39 to 2.71)	RCTs with this outcome was high (l <sup>2</sup> =87%),		
Moayyedi 2010	1	With condition	Adult patients with IBS (over the age of 16 years)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	10	533	Dichotomous outcome	SMD = 0.71 (0.57 to 0.88)	l <sup>2</sup> = 68.2%	NA	Unclear risk
Moayyedi 2010	1	With condition	Adult patients with IBS (over the age of 16 years)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	15	533	Continuous outcome	SMD = - 0.34 (- 0.6 to - .07)	l <sup>2</sup> = 79.1%	NA	Unclear risk
Moayyedi 2010	2	With condition	Adult patients with IBS (over the age of 16 years)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	10	834	Continuous outcome	SMD = - 0.51 (- 0.91 to - 0.09), p = 0.016	l <sup>2</sup> =85%	NA	Unclear risk
Nikfar 2008	1	With condition	Only Rome criteria were accepted for diagnosis of IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	8	1011	"Clinical improvement", measures NR	RR = 1.22 (1.07, 1.40), p = 0.0042	The Cochrane Q test for heterogeneit y (P = 0.4482) indicated that the studies are homogenou s and could be combined thus the fixed effects for individual and summary of RR for meta- analysis of studies have been applied.	NA	Low risk
Niu 2020	1	With condition	> 16 years, patients diagnosed with IBS based on a physician's	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	23	2575		RR = 0.79 (0.70 to 0.89), P	Significant heterogeneit y was observed (Ph	NA	Low risk

			opinion or symptom- based diagnostic criteria							< 0.0001)	< 0.00001 and I <sup>2</sup> = 72).		
Niu 2020	1 and 2 (combine d reporting)	With condition	> 16 years, patients diagnosed with IBS based on a physician's opinion or symptom- based diagnostic criteria	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	25	2001	Global symptom score (GSS) or abdominal pain score (APS)	SMD = - 0.25 (- 0.36 to - 0.14)	Probiotics significantly reduced the GSS or APS.	NA	Low risk
Ortiz-Lucas 2013	3	With condition	Adult patients >= 18 years, with IBS - Rome criteria I, II, or III for the diagnosis of IBS	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	12	NR	NR	NR	Probiotics significantly improved QoL in 5 studies.	NA	High risk
Pratt 2020	2	With condition	Adult patients with IBS, Rome- diagnosed	Eligible supplement VS placebo/inactiv e control	Bifidobacteri a via malted milk beverage	РІасеро	8	1045	Likert scales		50% (n = 4) of studies found a statistically significant improvemen t in abdominal pain following Bifidobacteri a supplement ation compared to placebo, 38% (n = 3) of studies found non- significant improvemen ts, and 12% (n = 1)	NA	High risk

											showed a statistically significant dose- response effect of improvemen t.		
Ritchie 2012	1	With condition	Humans with gastrointestina l disease (AAD, CDD, HPP, IBS, ID, NE, Pouch, TD) - IBS results could be determined separately	Eligible supplement VS inactive control (usual care, no intervention)	Probiotics	No interventio n	16 compari sons across 14 trials	NR	NR	RR = 0.77 (0.65 to 0.92)		NA	Unclear risk
Shang 2022	2	With condition	IBS-C patients diagnosed with specific criteria (Rome I, II, III, IV)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	4	488	NR	SMD = -0.28 (-0.60, 0.05) p > 0.05	When one study was excluded, the combined results and heterogeneit y changed significantly. The meta- analysis results demonstrate that probiotics significantly reduced abdominal pain scores in IBS-C patients compared to placebos (SMD = -0.20, 95% CI [-0.38, -0.01], p <	NA	Low risk

											0.05, I <sup>2</sup> = 0%).		
Shang 2022	3	With condition	IBS-C patients diagnosed with specific criteria (Rome I, II, III, IV)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	3	487	NR	SMD = -3.92 (-8.09 to 0.25), p > 0.05		NA	Low risk
Shang 2022	7	With condition	IBS-C patients diagnosed with specific criteria (Rome I, II, III, IV)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	3	71	NR	MD = 0.72 (0.18 to 1.26), p < 0.05	In the subgroup analysis, an eight-week duration - 9 of 21 showed a good effect on stool consistency (MD = 0.71, 95% CI [0.11, 1.32], p < 0.05), but twelve weeks showed no effect (MD = 0.75, 95% CI [-0.53, 2.03], $p >$ 0.05	NA	Low risk
Sun 2020	1	With condition	Adult patients (age >16 years); IBS based on either a clinician's opinion or meeting specific diagnostic criteria (Rome I, II, III, IV)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	22	3144	NR	RR = 1.50 (1.23 to 1.83)	Statistically significant heterogeneit y detected between studies (l <sup>2</sup> = 68%, P < 0.01). There was statistically significant asymmetry detected in the funnel plot (Egger test, P =	NA	High risk

											0.04), to suggest publication bias or other small study effects.		
Sun 2020	3	With condition	Adult patients (age >16 years); IBS based on either a clinician's opinion or meeting specific diagnostic criteria (Rome I, II, III, IV)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	5	856	NR	SMD = - 0.07 (- 0.74 to 0.6)		NA	High risk
Sun 2020	1 and 2 (combine d reproting)	With condition	Adult patients (age >16 years); IBS based on either a clinician's opinion or meeting specific diagnostic criteria (Rome I, II, III, IV)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	20 compari sons from 18 trials	2766	NR	SMD = - 0.31 (- 0.45 to - 0.17)	Significant heterogeneit y (I <sup>2</sup> = 66%, P < 0.01). There was no significant asymmetry detected in the funnel plot (Egger test, P = 0.84), to suggest no publication bias or other small study effects.	NA	High risk
Wang 2022	1	With condition	Subjects were at least 18 years old and met the diagnostic criteria for IBS- D	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	8	846	NR	SMD = -0.55 (-0.83 to -0.27), P < 0.05		NA	Low risk
Wang 2022	2	With condition	Subjects were at least 18	Eligible supplement VS	Probiotics	Placebo	8	829	NR	SMD = -0.43		NA	Low risk

			years old and met the diagnostic criteria for IBS- D	placebo/inactiv e control						(-0.57 to -0.29), P < 0.05			
Wang 2022	3	With condition	Subjects were at least 18 years old and met the diagnostic criteria for IBS- D	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	7	806	NR	SMD = 0.31 (-0.26 to 0.89), P > 0.05		NA	Low risk
Wang 2022	6	With condition	Subjects were at least 18 years old and met the diagnostic criteria for IBS- D	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	2	97	NR	SMD = 0.06, (-0.47 to 0.59), p > 0.05		NA	Low risk
Xu 2021	1	With condition	4-18 years with IBS diagnosis (Rome II~IV)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	2	159	SGARC score	MD = – 3.84, (– 6.49 to – 1.20), P = 0.004	l <sup>2</sup> = 95%	NA	Unclear risk
Xu 2021	2	With condition	4-18 years with IBS diagnosis (Rome II~IV)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	7	508	Abdominal pain score	SMD = - 1.15, (- 2.05 to - 0.24), P = 0.01	l <sup>2</sup> = 95%	NA	Unclear risk
Xu 2021	2	With condition	4-18 years with IBS diagnosis (Rome II~IV)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	7	508	Standard abdominal pain	MD = - 0.15 (- 0.27 to - 0.04), P = 0.01	l <sup>2</sup> = 94%	NA	Unclear risk
Xu 2021	2	With condition	4-18 years with IBS diagnosis (Rome II~IV)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	3	167	Abdominal pain relief	RR = 1.48 (0.96 to 2.28), P = 0.08	l <sup>2</sup> = 40%	NA	Unclear risk
Xu 2021	2	With condition	4-18 years with IBS diagnosis (Rome II~IV)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	3	163	Abdominal pain treatment success	RR = 3.44, (1.73 to 6.87),	l <sup>2</sup> = 0%	NA	Unclear risk

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										p=0.000 5			
Xu 2021	2	With condition	4-18 years with IBS diagnosis (Rome II~IV)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	3	147	Frequency of abdominal pain	MD = - 0.82 (- 1.57 to - 0.07), p=0.03	l <sup>2</sup> = 2%	NA	Unclear risk
Yuan 2017	2	With condition	Rome criteria I, II, or III for the diagnosis of IBS; (3) age greater than 15 years old	Eligible supplement VS placebo/inactiv e control	Probiotics containing B. Infantis	Placebo	5	666	NR	M = 0.23 (-0.03 to 0.49)		NA	Unclear risk
Zhang 2016	1	With condition	IBS diagnosis (Rome III criteria)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	18 compari sons from 16 trials	1275	Overall symptom response defined as a >50% reduction in IBS pain and discomfort or adequate relief of IBS symptoms for >50% of the time in 7 of 15 studies. Other definitions included an improvement of ≥ 50 points in the global IBS- SSS, global relief of IBS symptoms, or good and excellent overall efficacy.	RR = 1.82 (1.27 to 2.60)	l <sup>2</sup> =82.2%, p<0.001	NA	Unclear risk
Zhang 2016	2	With condition	IBS diagnosis (Rome III criteria)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	13	889	100-mm VAS, 7-point Likert scale, 5-point Likert scale, other, NR.	SMD = -0.25 (-0.62 to 0.13)	No significant funnel plot asymmetry observed (Egger test,	NA	Unclear risk

											p=0.90), suggesting no evidence of publication bias or other small-study effects.		
Zhang 2016	3	With condition	IBS diagnosis (Rome III criteria)	Eligible supplement VS placebo/inactiv e control	Probiotics	Placebo	9	529	SF-12, 5-point Likert scale	SMD = 0.29 (0.08 to 0.50)	l <sup>2</sup> = 36.2%	NA	Unclear risk

Abbreviations: APS=abdominal pain score; BM=bowel movement; CI=confidence interval; CFU=colony forming units; FDQoL=Functional Digestive Disorders Quality of Life ; GI=gastrointestinal; GIQLI=Gastrointestinal Quality of Life Index; HAD= Hospital Anxiety and Depression Scale; HRQoL=health-related quality of life; IBS=irritable bowel syndrome; IBS-C=IBS-constipation subtype; IBS-SSS=IBS Symptom Severity Scale; GSS=Global symptoms score; GSRS=Gastrointestinal Symptom Rating Scale; LGG= Lactobacillus rhamnosus GG; MD=mean difference; NA=Not applicable; NR=Not reported; QoL=quality of life; RCT=randomised controlled trial; RR=relative risk; SF-36=36-item Short-Form Health Survey; SMD=Standard mean difference; VAS=visual analogue scale; WMD=weighted mean difference;

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 8. Global improvement of IBS
- 9. Abdominal pain burden
- 10. Health-related quality of life
- 11. Number of recurrent episodes
- 12. Functioning
- 13. Stool frequency, bowel transit time
- 14. Stool consistency

### E4 Insomnia/sleeping disorders, magnesium

Table E-4. Results of preferred reviews by outcome domain - insomnia/sleeping disorders, magnesium

Revie	Outcom	Populatio	Populatio	Type of	Intervention	Comparat	No/type	No of	Outcome	Results					ROBIS
wID	e domain	n group	n details	comparison	description	or descriptio	s of include	participa nts	measure(s) used	Results effects	- absolute	Relative effect	Other reported	Risk of bias	assess ment
						n	d studies	(total)		Risk with contro l	Risk with interventio n	(95% CI)	results	summar y (primary studies)	(for the review overall)

Mah 2021	4 - total sleep time	With condition	Older adults ≥55 years old with insomnia	Eligible supplement VS placebo/inactiv e control	Oral magnesium supplementation	Placebo	2	55	Time from sleep onset to offset (min)	NR	NR	The mean post- interventio n TST in the interventio n group was 16.06 min higher (95% Cl: – 5.99 to 38.12; p = 0.15)	Serious or concerning methodolo gical limitations were detected in all studies, especially poor internal validity in the	Unclear risk
Mah 2021	4 - Sleep onset latency (SOL)	With condition	Older adults ≥55 years old with insomnia		Oral magnesium supplementation	Placebo	2	55	Time from wakefulness to initiation of sleep (min)	NR	NR	The mean post- interventio n SOL in the interventio n group was – 17.36 min lower (95% CI: – 27.27 to – 7.44, p = 0.0006)	randomiza tion process and bias arising from deviations from intended outcomes	Unclear risk
Mah 2021	4 - Sleep efficiency (SE)	With condition	Older adults ≥55 years old with insomnia		Oral magnesium supplementation	Placebo	1	43	Sum of REM & non REM sleep / total time in bed (h)	MD = -0.00 ± 0.05	MD = −0.06 ± 0.01h	NR	Only one study included. Some concerns	Unclear risk
Mah 2021	4 - Early morning awakening (EMA)	With condition	Older adults ≥55 years old with insomnia		Oral magnesium supplementation	Placebo	1	43	Premature termination of sleep (h)	MD = 1.03 ± 0.02	MD = 1.01 ± 0.05	NR	for risk of bias in the randomiza tion process	Unclear risk

Mah 2021	1	With condition	Older adults ≥55 years old with insomnia		Oral magnesium supplementation	Placebo	1	43	ISI, score from 0 to 28; ≥ 15 = clinical insomnia, Lower scores indicate better sleep quality.	MD = - 0.5 ± 1.71	MD = -2.38 ± 2.24	NR		and bias arising from deviations from intended outcomes (same as above) mainly due to poor reporting.	Unclear risk
Mah 2021	2	With condition	Older adults ≥55 years old with insomnia		Oral magnesium supplementation	Placebo	1	96	PSQI, Score from 0 (1) to 21; ≥ 5 = poor sleeper (8 weeks)	MD = -4.1	MD = -3.4	NR		Only one study included. High risk of bias from selective reporting.	Unclear risk
Samara 2020	5	With condition	Insomnia in elderly patients (>65 years)	Eligible supplement + naturopathy co-intervention	Melatonin 5mg + magnesium 225mg + zinc 11.5mg/day	Placebo	1	43	NR	NR	NR	0.61 (0.00 to 1.22)	NR	NR	Unclear risk
Samara 2020	4	With condition	Insomnia in elderly patients (>65 years)	VS placebo	Melatonin 5mg + magnesium 225mg + zinc 11.5mg/day	Placebo	1	43	NR	NR	NR	MD = 62.27 (28.80 to 95.74	NR	NR - Stud- ies that demonstra ted a high	Unclear risk
Samara 2020	2	With condition	Insomnia in elderly patients (>65 years)		Melatonin 5mg + magnesium 225mg + zinc 11.5mg/day	Placebo	1	43	NR	NR	NR	SMD = -1.9 (-2.63, - 1.17)	NR	risk of bias for sequence generation or allocation concealme nt were excluded	Unclear risk
Zhan 2023	6	With condition	Aged ≥18 years, diagnosed with narcolepsy	Eligible supplement + naturopathy co-intervention VS placebo	LXB - Calcium, Magnesium, Potassium, and Sodium	Placebo	1	136	ESS	NR	NR	MD=-3.00; 95% CI=-5.88 to -0.12	NR	Low risk of bias for primary study across all assessed domains.	Unclear risk

Abbreviations: EMA=early morning awakening; ESS=Epworth Sleepiness Scale; ISI=Insomnia Severity Index; M=mean; MD=mean difference; NA=not applicable; NR=Not reported; PSQI=Pittsburgh Sleep Quality Index; RR=relative risk; SMD=Standard mean difference; SOL=sleep onset latency; ^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Improvement in clinical levels of insomnia
- 2. Global improvement in sleep quality or quantity (subjective)
- 3. Global improvement in sleep quality or quantity (objective)
- 4. Improvement in individual sleep parameters (Sleep onset latency, Total sleep duration, Total wake-time, Wake after sleep onset (WASO), Nocturnal and early morning wakening, Sleep efficiency (ratio of time asleep to time in bed), parasomnias)
- 5. Quality of life
- 6. Daytime functioning
- 7. Fatigue

#### Table E-5. Results of included (non-preferred) reviews by outcome domain – insomnia/sleeping disorders, magnesium

I	Revie	Outcom	Populatio	Populatio	Type of	Intervention	Comparato	No/type	No of	Outcome	Results					ROBIS
	w ID	e domain	n group	n details	comparison	description	r descriptio n	s of include d studies	participa nts (total)	measure(s) used	Results effects Risk with contro l	- absolute Risk with interventio n	Relative effect (95% CI)	Other reported results	Risk of bias summar y (primary studies)	assess ment (for the review overall)

Chan 2021	2	At-risk of condition	Adults with poor sleep quality	Eligible supplement VS inactive control	320 mg/day magnesium citrate	Sodium citrate	1	100	PSQI	NR	NR	NR	Significant reduction in PSQI values in both groups and there was no significant difference between two groups	NA	High risk
Chan 2021	2	With condition	Participants with NLC, nocturnal leg cramps	Eligible supplement VS placebo/inactiv e control	Magnesium oxide and magnesium oxide monohydrate 865 mg	Placebo	1	94	PSQI	NR	NR	NR	There was no statisticall y significant difference between two groups.	NA	High risk
Chan 2021	2	With condition	Participants with primary insomnia	Eligible supplement + naturopathy co-intervention VS inactive control	5mg of melatonin, 225mg of magnesium, 11.25mg of zinc	100 g pear pulp	1	43	PSQI	NR	NR	NR	There was a significantl y improved overall PSQI score in the interventio n group but not in the placebo group.	NA	High risk

Abbreviations: NA=not applicable; NR=Not reported; PSQI=Pittsburgh Sleep Quality Index

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

8. Improvement in clinical levels of insomnia

9. Global improvement in sleep quality or quantity (subjective)

10. Global improvement in sleep quality or quantity (objective)

- 11. Improvement in individual sleep parameters (Sleep onset latency, Total sleep duration, Total wake-time, Wake after sleep onset (WASO), Nocturnal and early morning wakening, Sleep efficiency (ratio of time asleep to time in bed), parasomnias)
- 12. Quality of life
- 13. Daytime functioning

14. Fatigue

# E5 Depression (including post-natal), omega-3 fatty acids

### Table E-6. Results of preferred reviews by outcome domain – depression (including post-natal), omega-3 fatty acids

Review	Outco	Population	Population	Type of	Interventio	Compar	No/t	No of	Outco	Results					ROBIS
	domai n	group	uetaits	n	description	descript ion	of inclu	pants (total)	measu re(s)	Results - effects	absolute	Relative effect (95% CI)	Other reported	Risk of bias	ment (for the
							ded studi es		used	Risk with control	Risk with interventio n		results	summary (primary studies)	review overall)
Appleton 2021	1	With condition	Adults with a diagnosis of "depression" or "depressive disorder", given by a trained professional meeting a recognised diagnostic schedule	Eligible supplement Vs placebo/ inactive control	n3 PUFAs	Placebo/ inactive control	33	1848	Depressi ve sympto mology (continu ous)	NR	NR	SMD = -0.40 (- 0.64 to 0.16)		High risk of bias in all studies, and different effects when comparing analyses including only those studies with judgements of low risk of selection bias (allocation concealment ), performance bias (blinding of participants and personnel), or attrition bias (incomplete outcome data), and analyses including all studies.	Low risk
Appleton 2021	2						8	609	Depressi ve	329 per 1000	356 per 1000	OR = 1.13 (0.74 to 1.72)	-	Judgements of high risk of	Low risk

									sympto mology (dichoto mous - remissio n)					bias in all studies included in this analysis.	
Appleton 2021	2						17	794	Depressi ve sympto mology (dichoto mous - response )	445 per 1000	490 per 1000	OR = 1.20 (0.80 to 1.79)	-		Low risk
Appleton 2021	6						12	476	-	-	Mean QoL in the intervention groups was 0.38 standard deviations lower (0.82 lower to 0.06 higher). This rep- resents a small to modest difference between groups, equivalent to a CGI score of 0.38 (95% CI 0.06 to 0.82)	SMD = -0.38 (- 0.82 to 0.06)	-		Low risk
Suradom 2021	1	At-risk of condition	At-risk of perinatal depression	Eligible supplement Vs placebo/inac tive control	Range of combinations of DHA alone, or DHA + EPA, 6-16 weeks	Placebo/i nactive control	10 compa risons in 9 trials	779	BDI, EPDS, PDSS, CES-D, BDI-II, HAMD, MINI	-	-	SMD = -0.03 (- 0.20 to 0.13)	I <sup>2</sup> = 24%, ns	One trial possessed high-risk bias due to its high attrition rate and imbalanced	Low risk
Suradom 2021	1	With condition	Perinatal depression	Eligible supplement Vs	Combination DHA + EPA (609-1638mg	Placebo/i nactive control	4	141	EPDS HAMD CGI	-	-	SMD = -0.14 (- 0.55 to 0.27)	l <sup>2</sup> = 31%, ns	reasons for dropouts, the others had	

				placebo/inac tive control	DHA, 414- 2200mg EPA), 6-12 weeks				MADRS, BDI, BDI- II, MINI					low- risk of bias across the domains	
Zhang 2019	1	With condition	Children or adolescents with depression	Eligible supplement Vs placebo/inac tive control	Omega-3, 1- 3.4g daily, 10- 16 weeks	Placebo/i nactive control	4	153	End- point score of depressi ve scale	-	-	SMD = -0.12 (-0.53 to 0.30), P=0.58;	l <sup>2</sup> =30%, P=0.23	Low quality assessed for all studies. In one primary study the	Low risk
Zhang 2019	2	With condition	Children or adolescents with depression	Eligible supplement Vs placebo/inac tive control	Omega-3, 1- 3.4g daily, 10- 16 weeks	Placebo/i nactive control	4	153	Respons e rate was defined as ≥ 50% change from baseline on depressi on score or a score of ≤ 28 at the endpoint of a trial on the CDRS-R	-	-	OR = 1.57 (0.26 to 9.39), P=0.62	l <sup>2</sup> =71%, P=0.03	capsule used in the O3FA group was different from the one used in the placebo group in tone of internal colour. This could result in failure in blinding of intervention.	Low risk
Zhang 2019	1	With condition	Children or adolescents with depression	Eligible supplement Vs placebo/inac tive control	Omega-3, 1- 3.4g daily, 10- 16 weeks	Placebo/i nactive control	4	153	End- point score of depressi ve scale	-	-	SMD = -0.12 (-0.53 to 0.30), P=0.58	I <sup>2</sup> =30%, P=0.23		Low risk
Zhang 2019	2	With condition	Children or adolescents with depression	Eligible supplement Vs placebo/inac tive control	Omega-3, 1- 3.4g daily, 10- 16 weeks	Placebo/i nactive control	4	153	Respons e rate was defined as ≥ 50% change from baseline on depressi on score or a	-	-	OR = 1.57 (0.26 to 9.39), P=0.62	l <sup>2</sup> =71%, P=0.03		Low risk

				score of			
				≤ 28 at			
				the			
				endpoint			
				of a trial			
				on the			
				CDRS-R			

Abbreviations: BDI=Beck Depression Index; CES-D=Center for Epidemiological Studies Depression Scale; CGI=Clinical Global Impressions Scale; DHA=Docosahexaenoic acid; EPA=eicosapentaenoic acid; EPDS=Edinburgh Postnatal Depression Scale; CDRS-R= Children's Depression Rating Scale—Revised; HAMD, HDRS=Hamilton Depression Rating Scale; DSM=Diagnostic and Statistical Manual of Mental Disorders; MADRS= Montgomery–Åsberg Depression Rating Scale; MINI=Mini-International Neuropsychiatric Interview; PDSS=Postpartum Depression Screening Scale; OR=Odds ratio; QoL=Quality of life; SMD=standardised mean difference

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Depression-related emotional functioning/mental health burden
- 2. Improvement in clinical levels of depression (including post-natal depression)
- 3. Specific depression dimensions (Anhedonia, Distress, Dysfunctional thoughts, Internalizing problems, Rumination, Self-esteem, Anger, Fatigue, Hopelessness, Irritability, Negative mood, Tension)
- 4. Physiological symptoms of depression (respiration rate and capacity, heart rate, blood pressure, heart rhythm, vital signs, brain beta-nucleoside triphosphate levels, brain phosphodiester levels, brain phosphomonoester levels, serum norepinephrine levels, serum serotonin levels, frontal lobe phosphocreatine levels, body fat, metabolic measures, lactate levels, urinalysis results, lab panel results, weight, height, physical examination, temperature)
- 5. Parent to infant bonding
- 6. Quality of life
- 7. Anxiety-related emotional functioning/mental health burden

Review ID		Population group	Population details	Type of compariso	Intervention description	Compar ator	No/ types of	No of participant	Outcome measure(s)	Results			ROBIS assessment
	Outcome domain	8 F		n		descripti on	included studies	s (total)	used	Relative effect (95% CI)	Other reported results	Risk of bias summary (primary studies)	(for the review overall)
Bae 2023	1	With condition	Adults >65 years of age with depression	Eligible supplement VS placebo/ inactive control	Omega-3 fatty acids	Placebo	4	NR	NR	Hedge's g = -0.94 (-1.37 to -0.50)	No heterogeneity in the effect size was detected (I 2 = 32.7%, P = .216). Low RoB across most studies/outcome domains.	NA	Low risk
Bai 2018	1	With condition	Adults >60 years with mild to moderate depression at baseline (DSM criteria for MDD or	Eligible supplement VS placebo/ inactive control	180-1970 EPAg/day 120- 1720 DHAg/d; duration 2-6 months	Placebo	3	126	Change from baseline using any validated instrument e.g.	SMD = -0.555 (- 1.185 to 0.075)	No significant effect on depressive symptoms	NA	Unclear risk

#### Table E-7. Results of included (non-preferred) reviews by outcome domain - depression (including post-natal), omega-3 fatty acids

			dysthymia; or expressed depressive symptoms and scored above cut-off scores on validated depression scales)						HDRS, BDI, GDS, MADRAS				
Bai 2020	1	With condition	Adults with MDD based the DSM-IV, DSM-IV-TR or DSM-5	Eligible supplement VS placebo/ inactive control	Omega-3 fatty acids	Placebo	12	746	NR	SMD = -0.35 (- 0.60 to -0.09)	Heterogeneity among studies was found to be moderate (X2=33.67, p<0.00001, l <sup>2</sup> = 61%	NA	High risk
Chowdhu ry 2020	1	With condition	18–35 years of age with postpartum depressive symptomatology	Eligible supplement VS placebo/ inactive control	300mg DHA/day; 24 through 40 weeks' gestation	Placebo	1	42	PDSS	Total scores were significantly lowe (p = 0.016; Mean = 46.03, SD = 2.17, intervention vs. Mean = 52.11 SD = 2.4, placebo)	-	NA	High risk
Chowdhu ry 2020	1	With condition	18–45 years of age who were either pregnant (12-32 weeks' gestation) or postpartum (within 6 months of childbirth) and met criteria for MDD	Eligible supplement Vs placebo/inac tive control	Omega-3 FA 1.9g/d; 8 weeks	placebo	1	59	Depressive symptomatolog y as measured by EPDS and HDRS	There were no significant effects of omega-3 FA for either EPDS (b=0.2, z=1.15, p=0.25) or HDRS scores (b=0.06, z=0.34, p=0.73)	-	NA	High risk
Farooq 2020	1	At-risk of condition	Adult with hepatitis C + previous history of depression, but who were not suffering from depression at the beginning of the trial. The onset of depressive illness was defined using standard diagnostic criteria, such as International Classification of Disease (ICD-10), or the Diagnostic and Statistical Manual	NR	2 groups EPA or DHA but dose NR; duration 24 weeks	unknown	1	152	MINI	NR	-	NA	Low risk

			(DSM), based on standardised clinical interview or using score above cut off point on standardised and valid rating scales.										
Farooq 2020	1	At-risk of condition	Postnatal women at increased risk of depression	NR	EPA & DHA (fish oil supplement); dose NR; duration 12 weeks	unknown	1	60	EPDS	NR	-	NA	Low risk
Gabriel 2023	1	With condition	>18 years with BPD	Eligible supplement Vs placebo/inac tive control	Omega-3 - variable doses and duration; unsure of nature of control groups	NR	5	NR	Various depression scales including BDI, EPDS, IDS	NR; very small study samples; heterogenous studies	Small effect-size for Omega-3 supplementation in BD in secondary biological outcomes, but which was not translated into meaningful symptomatic improvement	NA	High risk
Liao 2019	1	With condition	adults with a diagnosis of clinical depression (DSM-III-R/DSM-IV) or depressive symptoms according to validated psychometric instruments (with or without comorbid medical conditions)	Eligible supplement Vs placebo/inac tive control	omega-3 PUFAs	combinati on of with and without antidepres sant co- therapy	32	2160	HRSD, MADRS, BDI, GDI	SMD = 0.28 (- 0.47, -0.09)	I <sup>2</sup> = 75%, significant evidence of heterogeneity between trials	NA	Low risk
Miller 2013	1	At-risk of condition	Not have been depressed at the beginning of the trial >18, 12-22 weeks	Eligible supplement Vs placebo/inac	2 arms - a) EPA-rich fish oil supplement	Placebo	1	126	BDI for EPA	MD = 0.70, 95% CI -1.78 to 3.18 (no significant effect)		NA	Unclear risk
Miller 2013	1	At-risk of condition	gestation, at risk for depression, based on (i) a history of MDD, (ii) a history of	tive control	(1060 mg EPA plus 274 mg DHA) b) DHA- rich fish oil		1	126	BDI for DHA	MD = -0.20, 95% CI -2.61 to 2.21 (no significant effect)		NA	Unclear risk

Miller 2013	3	At-risk of condition	postpartum depression, or (iii) an EPDS score between		supplement (900 mg DHA plus 180 mg		1	126	EPA-Incidence of MDD	1.58 (0.28 to 8.94)	No significant effect on incidence of MDD	NA	Unclear risk
Miller 2013	3	At-risk of condition	9 and 19		EPA) for 6 weeks postpartum		1	126	DHA-Incidence of MDD	1.08 (0.16 to 7.28)	No significant effect on incidence of MDD	NA	Unclear risk
Mocking 2016	1	With condition	Adult patients with MDD according to the Diagnostic and Statistical Manual of Mental Disorders (DSM) as assessed by a standardized clinical interview	Eligible supplement Vs placebo/inac tive control	DHA 2g/day for 42 weeks	placebo	1	35	Mean change in MADRAS; SMD in MADRAS between groups	SMD = 0.42; SE = 0.34 Hedge's g = 0.41; SE = 0.33	-	NA	Low risk
Mocking 2016	1	With condition	Adult patients with MDD according to the Diagnostic and Statistical Manual of Mental Disorders (DSM) as assessed by a standardized clinical interview	Eligible supplement Vs placebo/inac tive control	EPA 1050mg/d + DHA 150mg/d for 56 weeks	placebo	1	29	SMD in HDRS- 21 score	SMD = -0.66; SE = 0.38	-	NA	Low risk
Mocking 2016	1	With condition	Adult patients with MDD according to the Diagnostic and Statistical Manual of Mental Disorders (DSM) as assessed by a standardized clinical interview	Eligible supplement Vs placebo/inac tive control	EPA 1000mg/d for 56 weeks	placebo	1	35	SMD in HDRS- 17 score	SMD = 0.54; SE = 0.35	-	NA	Low risk
Mocking 2016	1	With condition	Adult patients with MDD according to the Diagnostic and Statistical Manual of Mental Disorders (DSM) as assessed by a standardized clinical interview	Eligible supplement Vs placebo/inac tive control	EPA 180mg/d + DHA 900mg/d for 56 weeks	placebo	1	20	SMD in HDRAS- 17	SMD = 0.05; SE = 0.18	-	NA	Low risk
Mocking 2016	1	With condition	Adult patients with MDD according to the Diagnostic and Statistical Manual of Mental Disorders (DSM) as assessed by	Eligible supplement Vs placebo/inac tive control	EPA 1060mg/d + DHA 274mg/d for 56 weeks	placebo	1	20	SMD in HDRS- 17 score	SMD = 0.18; SE = 0.18	-	NA	Low risk

			a standardized clinical interview										
Mocking 2020	1	With condition	Perinatal depression	Eligible supplement Vs placebo/inac tive control	-	Placebo/in active control	7	NR	BDI, combined	SDM = 0.545 (-1.182 to 0.093)	l <sup>2</sup> = 91.40; Q = 69.78; P < .001	NA	Low risk
Mocking 2020	1	At-risk of condition	At-risk of perinatal depression (not depressed at baseline)	Eligible supplement Vs placebo/inac tive control	-	Placebo/in active control	3	NR	EPDS, EPDS >12, combined	SDM = -0.073 (-0.255 to 0.108)	no significant heterogeneity in this subgroup (l <sup>2</sup> = 0.000; Q = 0.384; P = .825)	NA	Low risk
Mocking 2020	1	With condition	Perinatal depression	Eligible supplement Vs placebo/inac tive control	-	Placebo/in active control	7	NR	BDI, combined	SDM = 0.545 (-1.182 to 0.093)	l <sup>2</sup> = 91.40; Q = 69.78; P < .001	NA	Low risk
Mocking 2020	1	At-risk of condition	At-risk of perinatal depression (not depressed at baseline)	Eligible supplement Vs placebo/inac tive control	-	Placebo/in active control	3	NR	EPDS, EPDS >12, combined	SDM = -0.073 (-0.255 to 0.108)	no significant heterogeneity in this subgroup (l <sup>2</sup> = 0.000; Q = 0.384; P = .825)	NA	Low risk
Morrell 2016	1	With condition	Postnatal women at increased risk of depression	Eligible supplement Vs usual care	DHA	Usual care	1	2399	Universal preventive interventions EPDS threshold score at 6 weeks postnatally	OR = 0.87 (0.41 to 1.83)		NA	Low risk
Newberry 2016	1	With condition	pregnant women who planned to breast feed for at least 4 months	Eligible supplement Vs placebo/inac tive control	DHA 0.200 g/d beginning within first week of delivery for four months	placebo	1	138	SMD of EPDS score at any of the timepoints (3 weeks, 2 months, 4 months, 18 months)	Exact effect measure NR; no significant SMD in depressive symptoms scores between groups at any of the time points (3 weeks, 2 months, 4 months, 18 months postpartum)	-	NA	Low risk
Saccone 2016	1	At-risk of condition	Pregnant women	Eligible supplement Vs	DHA 800 mg + EPA 100 mg	Usual care	1	2399	NR	RR = 0.85 (0.70 to 1.02)	The only RCT available (including 2399	NA	Unclear risk

				placebo/inac tive control							singleton gestations) failed to demonstrate a clear and statistically significant benefit of omega-3 supplementation during pregnancy in preventing depressive post- partum symptoms		
Sarris 2012	1	With condition	All ages with DSM diagnosis of BPD or score above cut-off for a validated depression rating instrument	Eligible supplement + non- naturopathy co- intervention VS placebo/inac tive control	Omega-3 - various doses - 6.6g/d ALA for 16 weeks, EPA only 1g/d- 6g/d for 12-16 weeks, EPA/DPA combination - either EPA 4.4g + DHA 2.4g or EPA 6.2g + DHA 3.4g for 4 and 16 weeks respectively	placebo + psychotro pic pharmaco herapy	6	320	SMD between treatment and placebo between baseline and endpoint using a validated scale i.e., HDRS, CDRS or IDS-CR	SMD = 0.338 (0.035 to 0.641), p=0.029	For MA of depression studies: I <sup>2</sup> =30%, p=0.213 Large heterogeneity to the type of omega-3 preparation; moderate to low risk of bias for individual studies	NA	Low risk
Troeung 2013	1	With condition	idiopathic PD; DSM or ICD diagnosis of depression	Eligible supplement Vs placebo/inac tive control	Omega-3 dose NR	placebo	1	29	MADRS	d= .92 (0.15 to 1.69)	-	NA	Low risk
Tsai 2023	1	With condition	Women with perinatal depression	Eligible supplement Vs placebo/inac tive control	Omega-3 - variable doses and duration	combinati on of placebo, different dose of omega-3, adjunct non- naturopath	13	1153	Various depression scales including BDI, EPDS, PDSS, CES-D	SMD = -0.11 (0.26 to 0.0)	I <sup>2</sup> =23% p>0.05	NA	Low risk

						y interventio n							
Tung 2023	1	With condition	Pregnant women with EPDS >=11 or depressive symptoms intervention initiated 22 -24 weeks gestation	Eligible supplement Vs placebo/inac tive control	EPA 1.08/DHA 0.72 g/day for 16 weeks	placebo	1	60	SMD in EPDS between groups; SMD change in EPDS at the following assessment times: 5th to13th, 22nd to 24th, and 30th to 32nd gestational weeks, and 4 to 6 weeks postpartum	Exact effect measures NR; no significant difference in EPDS between groups nor changes over time for EPDS scores during pregnancy and postpartum	insufficient information	NA	High risk
Tung 2023	1	With condition	Pregnant women with EPDS ≥ 12; probable depressive disorders	Eligible supplement Vs placebo/inac tive control	Fish oil (DHA 120 mg, EPA 180mg, ALA 400mg) for 24 weeks from end of 20th gestational week until 1 month postpartum	placebo	1	150	Mean EPDS score; SMD change in EPDS at the following assessment times: 5th to13th, 22nd to 24th, and 30th to 32nd gestational weeks, and 4 to 6 weeks postpartum	Exact effect measures NR; significant decrease in EPDS in intervention group at 35-37 weeks gestation; no significant difference in EPDS at other measurement periods	insufficient information	NA	High risk
Viswanat han 2020	1	With condition	Children and adolescents (6 to 14 years) with a confirmed diagnosis of a depressive disorder (DD)—major depressive disorder (MDD), persistent depressive disorder (previously termed dysthymia) or DD not otherwise specified	Eligible supplement Vs placebo/inac tive control	Omega-3, dose NR, 12- 16 weeks	placebo	1	20	Depressive symptoms, clinician report	SMD (CDRS) cannot be calculated but authors report that mean difference is - 20.72, p=0.03 at the end of treatment	-	NA	High risk
Viswanat han 2020	1	With condition	Children and adolescents (6 to 14 years) with a	Eligible supplement Vs	Omega-3, dose NR, 12- 16 weeks	placebo	1	34	Depressive symptoms, clinician report	SMD = 0.0 (-0.67 to 0.67)	-	NA	High risk

			confirmed diagnosis of a depressive disorder (DD)—major depressive disorder (MDD), persistent depressive disorder (previously termed dysthymia) or DD not otherwise specified	placebo/inac tive control									
Viswanat han 2020	2	With condition	Children and adolescents (6 to 14 years) with a confirmed diagnosis of a depressive disorder (DD)—major depressive disorder (MDD), persistent depressive disorder (previously termed dysthymia) or DD not otherwise specified	Eligible supplement Vs placebo/inac tive control	Omega-3, dose NR, 12- 16 weeks	placebo	1	20	Response - CDRS score <29	RR (CDRS score of <29) = 15.0 (0.97 to 1.86)	-	NA	High risk
Viswanat han 2020	2	With condition	Children and adolescents (6 to 14 years) with a confirmed diagnosis of a depressive disorder (DD)—major depressive disorder (MDD), persistent depressive disorder (previously termed dysthymia) or DD not otherwise specified	Eligible supplement Vs placebo/inac tive control	Omega-3, dose NR, 12- 16 weeks	placebo	1	20	Remission (loss of diagnosis)	RR (more than 50% reduction in CDRS score) = 9.00 (0.55 to 147.96)	-	NA	High risk
Viswanat han 2020	2	With condition	Children and adolescents (6 to 14 years) with a confirmed diagnosis of a depressive disorder (DD)—major depressive disorder (MDD), persistent depressive disorder (previously termed dysthymia) or DD not otherwise specified	Eligible supplement Vs placebo/inac tive control	Omega-3, dose NR, 12- 16 weeks	placebo	1	34	Remission (loss of diagnosis)	RR (CDRS score ≤ 28) = 0.79 (0.39 to 1.57)	-	NA	High risk

Williams 2006	1	With condition	Adults with bipolar disorder	Eligible supplement + non- naturopathy co- intervention VS placebo/inac tive control	Omega-3 dose NR; duration 30 days	placebo	1	14	No formal measure - "duration of time to exit double-blind treatment due to exacerbation of symptoms of bipolar disorder"	Significantly longer period of remission than the placebo group (favourable)	-	NA	High risk
Xu 2023	1	With condition	patients (over 18 years of age, with no upper limit) were diagnosed with bipolar I disorder (BD- I), bipolar II disorder (BD-II), or BD not otherwise specified according to the Diagnostic and Statistical Manual of Mental Disorders criteria (DSM-III, DSMIV, DSM-IV-TR, DSM-V) or International Classification of Diseases, 10th Revision (ICD-10) in any phase of illness;	-	-	-	5	NR	NR	Omega 3 was not statistically superior to placebo. OR = -0.43 (-0.88 to 0.02) in NMA	-	NA	Unclear risk
Zhang 2020	1	With condition	Pregnant or postnatal women with DSM diagnosis of MDD or score above cut-off for a validated depression rating instrument	Eligible supplement Vs placebo/inac tive control	Omega-3 - various doses (1-6g/d) and durations (4 to 14 weeks)	Placebo	8	638	SMD between treatment and placebo between baseline and endpoint using a validated scale i.e., HDRS, CDRS or IDS	SMD = 0.65 (0.10 to 1.20), P = 0.02	High heterogeneity T2=0.56 Chl <sup>2</sup> =74.24, df=7, p<0.001, l <sup>2</sup> =91%	NA	Low risk

Abbreviations: BDI=Beck Depression Index; CES-D=Center for Epidemiological Studies Depression Scale; CGI=Clinical Global Impressions Scale; DHA=Docosahexaenoic acid; EPA=eicosapentaenoic acid; EPDS=Edinburgh Postnatal Depression Scale; CDRS-R=Children's Depression Rating Scale—Revised; DSM=Diagnostic and Statistical Manual of Mental Disorders; GDI=Geriatric Depression Inventory; HAMD, HDRS=Hamilton Depression Rating Scale; IDS=Inventory for Depressive Symptomatology; IDS-CR=Inventory for Depressive Symptomatology – Clinician Reported; MADRS, MADRAS=Montgomery–Åsberg Depression Rating Scale; MDD=major depressive disorder; MINI=Mini-International Neuropsychiatric Interview; NA=Not applicable; NMA=network meta-analysis; NR=Not reported; PDSS=Postpartum Depression Screening Scale; OR=Odds ratio; QoL=Quality of life; RCT=randomised controlled trial; RR=relative risk; SD=standard deviation; SMD=standardised mean difference

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Depression-related emotional functioning/mental health burden
- 2. Improvement in clinical levels of depression (including post-natal depression)
- 3. Specific depression dimensions (Anhedonia, Distress, Dysfunctional thoughts, Internalizing problems, Rumination, Self-esteem, Anger, Fatigue, Hopelessness, Irritability, Negative mood, Tension)
- 4. Physiological symptoms of depression (respiration rate and capacity, heart rate, blood pressure, heart rhythm, vital signs, brain beta-nucleoside triphosphate levels, brain phosphodiester levels, brain phosphomonoester levels, serum norepinephrine levels, serum serotonin levels, frontal lobe phosphocreatine levels, body fat, metabolic measures, lactate levels, urinalysis results, lab panel results, weight, height, physical examination, temperature)
- 5. Parent to infant bonding
- 6. Quality of life
- 7. Anxiety-related emotional functioning/mental health burden

### E6 Dysmenorrhea, cruciferous indoles (indole-3-carbinol, di-indolylmethane)

No reviews were identified for inclusion in the Overview.

### E7 Premenstrual syndrome (PMS), cruciferous indoles (indole-3-carbinol, di-indolylmethane)

No reviews were identified for inclusion in the Overview.

## E8 Atopic disorders (including eczema, dermatitis, allergic rhinitis, allergies), zinc

Table E-8. Results of preferred reviews by outcome domain - atopic disorders (including eczema, dermatitis, allergic rhinitis, allergies), zinc.

Review ID	Outcome domain	Population group	Population details	Type of comparison	Intervention description	Comparator description	No/types of included studies	No of participants (total)	Outcome s measure(s) used	Results			ROBIS
										Relative effect (95% CI)	Other reported results	Risk of bias summary (primary studies)	assessment (for the review overall)
Bath- Hextall 2012	1	With condition	Atopic eczema as diagnosed by a doctor (paediatric)	Eligible supplement VS placebo/inactive control	Z Span capsules (sustained release capsules each containing 61.8 mg zinc sulphate, equivalent to 22.5 mg zinc)	Placebo	1	50	Surface area of body affected by eczema – 4 weeks	MD = 4.20 (-6.19 to 14.59)	NR	Unclear risk for selection bias, performance and detection bias, baseline comparability, conflict of interest and compliance. Smith, Kline, & French Laboratories supplied active and placebo capsules. The lead author was <b>also</b> supported by grants from Glaxo Group Research and Glaxo Laboratories	Unclear risk
	1	With condition					1	50	Surface area of body affected by eczema – 8 weeks	MD = 2.90 (-6.08 to 11.88)	NR		Unclear risk
	1	With condition					1	50	Combined disease severity score – 4 weeks	MD = 4.00 (-43.07 to 51.07)	NR		Unclear risk
	1	With condition					1	50	Combined disease severity score – 8 weeks	MD = 9.40 (-25.87 to 44.67)	NR		Unclear risk
	4	With condition					1	50	Mean itch score – 4 weeks	Effect sizes NR (NS)	NR		Unclear risk
	4	With condition					1	50	Mean itch score – 8 weeks	MD = 1.20 (0.02 to 2.38)	NR		Unclear risk
	4	With condition					1	50	Erythema – 4 weeks	MD = 0.00 (-0.53, 0.53)	NR		Unclear risk
	4	With condition					1	50	Erythema – 8 weeks	MD = 0.50 (-0.04, 1.04)	NR		Unclear risk

Abbreviations: AD=atopic dermatitis; CI=Confidence Interval; MD=mean difference; NS=not significant; NR=Not reported

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Global severity of condition/improvement of symptoms
- 2. Quality of life
- 3. Long-term measure of control of disease
- 4. Individual changes in symptoms (including degree of redness of skin, day-time itch, anterior rhinorrhoea (runny nose): where a study reports 'rhinorrhoea' as the outcome, in the absence of a definition within the paper we assumed that this measured anterior rhinorrhoea. Where the authors reported a combined outcome for anterior and posterior rhinorrhoea and we were not able to obtain individual results, we recorded this as a combined 'anterior and posterior rhinorrhoea' category; posterior rhinorrhoea (post-nasal drip); nasal blockage or congestion or obstruction; nasal itching; sneezing)
- 5. Physical function/ disability (return to work/school)
| Review           | Outcome | Population        | Population                      | Type of  | Intervention       | Comparator  | No/types                  | No of                   | Outcome   | Results                        |  |   | ROBIS  |
|------------------|---------|-------------------|---------------------------------|--|--------------------|-------------|---------------------------|-------------------------|---|--------------------------------|--|---|--|
| ID               | domain  | group             | details                         | comparison   | description        | description | of<br>included<br>studies | participants<br>(total) | measure(s)<br>used                                  | Relative<br>effect<br>(95% CI) | Other reported results   | Risk of bias<br>summary<br>(primary<br>studies) | assessment<br>(for the<br>review<br>overall) |
| Dhaliwal<br>2020 | .1      | With<br>condition | 1 to 16<br>years old<br>with AD | Eligible<br>supplement VS<br>placebo/inactive            | Z Span<br>capsules | Placebo     | 1                         | 50                      | Severity  |                                | Between the two groups there were no significant differences in severity scores (p = 0.60).                    | NA  | Unclear risk                                 |
|                  | 4       | With<br>condition |                                 | control  |                    |             | 1                         | 50                      | Mean itch<br>score                                  |                                | The results showed that at 8 weeks, the mean itch score was significantly higher in the zinc group (p = 0.01). | NA  | Unclear risk                                 |
|                  | 4       | With condition    |                                 |  |                    |             | 1                         | 50                      | Daytime<br>itch                                     |                                | No significant changes in other mean symptom scores  | NA  | Unclear risk                                 |
| Gray<br>2019     | 1       | With<br>condition | 1 to 16<br>years old<br>with AD | Eligible<br>supplement VS<br>placebo/inactive<br>control | Z Span<br>capsules | Placebo     | 1                         | 50                      | Surface<br>area of<br>body<br>affected by<br>eczema |                                | No significant difference between groups.  | NA  | Unclear risk                                 |
|                  | 1       | With<br>condition |                                 |  |                    |             | 1                         | 50                      | Combined<br>disease<br>severity<br>score            |                                | No significant difference between groups.  | NA  | Unclear risk                                 |
|                  | 4       | With<br>condition |                                 |  |                    |             | 1                         | 50                      | Mean itch<br>score                                  |                                | Itch scores at 8 weeks were<br>significantly higher in children receiving<br>zinc supplementation (P = 0.01).  | NA  | Unclear risk                                 |
|                  | 4       | With condition    |                                 |  |                    |             | 1                         | 50                      | Erythema  |                                | No significant difference between groups.  | NA  | Unclear risk                                 |

Table E-9. Results of included (non-preferred) reviews by outcome domain – atopic disorders (including eczema, dermatitis, allergic rhinitis, allergies), zinc.

Abbreviations: AD=atopic dermatitis; CI=Confidence Interval; MD=mean difference; NS=not significant; NA=Not applicable

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Global severity of condition/improvement of symptoms
- 2. Quality of life
- 3. Long-term measure of control of disease
- 4. Individual changes in symptoms (including degree of redness of skin, day-time itch, anterior rhinorrhoea (runny nose): where a study reports 'rhinorrhoea' as the outcome, in the absence of a definition within the paper we assumed that this measured anterior rhinorrhoea. Where the authors reported a combined outcome for anterior and posterior rhinorrhoea and we were not able to obtain individual results, we recorded this as a combined 'anterior and posterior rhinorrhoea' category; posterior rhinorrhoea (post-nasal drip); nasal blockage or congestion or obstruction; nasal itching; sneezing)

5. Physical function/ disability (return to work/school)

# E9 Fatigue (general) (including myalgic encephalomyelitis (ME) and Chronic Fatigue Syndrome (CFS)), antioxidants (specifically coq10 and alpha-lipoic acid)

Table E-10. Results of preferred reviews by outcome domain – fatigue (general) (including myalgic encephalomyelitis (ME) and Chronic Fatigue Syndrome (CFS)), antioxidants (specifically coq10 and alpha-lipoic acid)

Revie	Outcom	Populatio	Populatio	Type of	Interventio	Comparato	No/type	No of	Outcome	Results			ROBIS
wID	e domain	n group	n details	compariso n	n description	r description	s of included studies	particip ants (total)	measure(s) used	Relativ e effect (95% CI)	Other reported results	Risk of bias summary (primary studies)	assessmen t (for the review overall)
Marx 2019	5	At-risk of condition	Secondary progressiv e multiple sclerosis	Eligible supplement VS placebo	ALA (1200 mg per day)	placebo	1	54	SF-36	NR	No significant effect on quality of life	Jadad score=5	Unclear risk
Marx 2019	1	At-risk of condition	Relapse remitting multiple sclerosis	Eligible supplement VS placebo	ALA (1200 mg per day)	placebo	1	39	FSS	NR	No significant between- group difference in fatigue	Jadad score=4	Unclear risk
Marx 2019	1	At-risk of condition	Relapse remitting multiple sclerosis	Eligible supplement VS placebo	CoQ10 500mg/day	placebo	1	48	FSS	NR	Participants reported reduced fatigue (using the Fatigue Severity Scale) (p < 0.001) after 12 weeks	Jadad score=3	Unclear risk
Tsai 2022	1	At-risk of condition	Fatigue- associated diseases	Eligible supplement VS placebo	CoQ10 60- 500mg/day	placebo	10	899	Minnesota Living with Heart Failure Questionnaire fatigue score (0- 5), FSS (9-63), FIQ fatigue score (0- 10), POMS-F (0- 4), FIS (0-160), Fatigue Scale (0- 32), MAF (1-50), FACIT-F (0-44)	Hedges' g = -0.433 (-0.732, -0.133)		5 studies assessed as low risk of bias; 5 studies assessed as some risk of bias	Low risk

Abbreviations: CFS=Chronic Fatigue Syndrome; CoQ10=Coenzyme Q10; FSS=Fatigue Severity Scale; FACIT-F= Functional Assessment of Chronic Illness Therapy-Fatigue; FIS= Fatigue Impact Scale; FIQ= Fibromyalgia Impact Questionnaire; ME=myalgic encephalomyelitis; NR=not reported; POMS-F=Profile of Mood States-Fatigue, LASA-F= Linear Analog Scale Assessment – Fatigue, MAF= Multidimensional Assessment of Fatigue; SF-36= RAND 36-Item Short Form Health Survey

- 1. Global improvement in fatigue severity/burden
- 2. Clinical recovery or improvement (dichotomous)
- 3. Self-perceived change in overall health
- 4. Physical function burden from fatigue

- 5. HRQoL
- 6. Cognitive function burden from fatigue7. Sleep quality/quantity

Table E-11. Results of included (non-preferred) reviews by outcome domain – fatigue (general) (including myalgic encephalomyelitis (ME) and Chronic Fatigue Syndrome (CFS)), antioxidants (specifically coq10 and alpha-lipoic acid)

Review ID	Outcom	Populatio	Population details	Type of	Intervention	Compar	No/types	No of	Outcome	Results			ROBIS
	e domain	n group		compariso n	description	ator descripti on	of included studies	partici pants (total)	measure(s) used	Relative effect (95% CI)	Other reported results	Risk of bias summary (primary studies)	assessmen t (for the review overall)
Campagnol o 2017	1	With condition	CFS/ME diagnosis according to Fukuda (2), Canadian (2003) (14) or International Consensus Criteria (ICC) (2011) (1); (iii) adults aged 18 years and over;	Eligible supplemen t VS placebo	NADH (200 mg day) + CoQ10 (20 mg day)	placebo	1	73	Fatigue Index Symptom Questionnaire	NR	Significant reduction of fatigue after 8 weeks of treatment compared to placebo (p < 0.05)	NA	Unclear risk
Campagnol o 2017	1	With condition	CFS/ME diagnosis according to Fukuda (2), Canadian (2003) (14) or International Consensus Criteria (ICC) (2011) (1); (iii) adults aged 18 years and over;	Eligible supplemen t VS placebo	Ubiquinol-10 (150 mg day post meal)	placebo	1	31	Chalder Fatigue Scale	NR	No significant difference.	NA	Unclear risk
Kim 2020	1	With condition	Patients with CFS/ME	Eligible supplemen t VS placebo	NADH (200 mg day) + CoQ10 (20 mg day)	placebo	1	73	Fatigue Index Symptom Questionnaire	NR	Significant reduction of fatigue after 8 weeks of treatment compared to placebo (p < 0.05)	NA	Unclear risk
Mehrabani 2019	1	At-risk of condition	Fibromyalgia	Eligible supplemen t VS placebo	CoQ10 (100- 400mg/day)	placebo	4 RCT and 1 quasi- experiment al study	35 (quasi) , 154 in RCTs	FIQ, Chalder Fatigue Scale, VAS	NR	Fatigue reduced significantly in all trials (ps < 0.05)	NA	Unclear risk
Mehrabani 2019	1	At-risk of condition	Statin-associated myopathy	Eligible supplemen t VS placebo	CoQ10 200mg/day	placebo	1 RCT	60	VAS	NR	Fatigue reduced significantly, p < 0.01	NA	Unclear risk
Mehrabani 2019	1	At-risk of condition	Poliomyelitis	Eligible supplemen t VS placebo	CoQ10 100mg/day	placebo	1 RCT	101	FSS, MAF	NR	Both measures failed to show any statistically significant (p > 0.05) reduction in fatigue	NA	Unclear risk
Mehrabani 2019	1	At-risk of condition	Multiple sclerosis	Eligible supplemen t VS placebo	CoQ10 500mg/day	placebo	1 RCT	45	FSS	NR	Fatigue symptoms had a significant reduction, p < 0.001	NA	Unclear risk
Mehrabani 2019	1	At-risk of condition	End-stage heart failure	Eligible supplemen t VS placebo	CoQ10 60mg/day	placebo	1 RCT	32	FSS	NR	Significant reduction (p < 0.001) in fatigue symptoms in the intervention group compared with control	NA	Unclear risk

Mehrabani 2019	1	With condition	CFS	Eligible supplemen t VS placebo	CoQ10 150mg/day	placebo	1 RCT	32	FSS	NR	Failed to reveal any significant improvements (p > 0.05) in fatigue after supplementation with CoQ10	NA	Unclear risk
Mehrabani 2019	1	At-risk of condition	Breast cancer	Eligible supplemen t VS placebo	CoQ10 300mg/day	placebo	1 RCT	236	POMS-F, FACIT-F, LASA- F	NR	Did not show any significant efficacy (p > 0.05) for CoQ10 supplementation in fatigue reduction in newly diagnosed patients with breast cancer	NA	Unclear risk
Pereira 2018	1	At-risk of condition	Patients aged 18 years and older diagnosed with breast cancer	Eligible supplemen t + naturopath y co- interventio n VS naturopath y co- interventio n	300 mg CoQ10 combined with 300 IU vitamin E (divided into 3 doses with meals)	Placebo combine d with 300 IU vitamin E (divided into 3 doses with meals)	1	236	POMS-F, FACT- F, LASA-F	NR	CoQ10 was not associated with improvement of fatigue after 24 weeks or at any time during the study	NA	Low risk

Abbreviations: CFS=Chronic Fatigue Syndrome, CoQ10=Coenzyme Q10, FSS=Fatigue Severity Scale, FACIT-F= Functional Assessment of Chronic Illness Therapy-Fatigue, FIS= Fatigue Impact Scale, FIQ= Fibromyalgia Impact Questionnaire, POMS-F=Profile of Mood States-Fatigue, LASA-F= Linear Analog Scale Assessment – Fatigue, MAF= Multidimensional Assessment of Fatigue, ME=myalgic encephalomyelitis, NR=Not reported; NA=not applicable; SF-36= RAND 36-Item Short Form Health Survey

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Global improvement in fatigue severity/burden
- 2. Clinical recovery or improvement (dichotomous)
- 3. Self-perceived change in overall health
- 4. Physical function burden from fatigue
- 5. HRQoL
- 6. Cognitive function burden from fatigue
- 7. Sleep quality/quantity

### E10 Headache and migraine, magnesium

Table E-12. Results of preferred reviews by outcome domain - headache and migraine, magnesium.

Review ID	Outcome	Population	Population details	Type of	Intervention	Comparator	No/types	No of	Outcome	Results			ROBIS
	domain	group		comparison	description	description	of included studies	particip ants (total)	measure(s) used	Relative effect (95% CI)	Other reported results	Risk of bias summary (primary studies)	assessment (for the review overall)
Okoli 2019	1	With condition	average-risk individuals (no history of head trauma or	Eligible supplement VS placebo/inactive control	Magnesium (600mg per day)	Placebo	1	81	Migraine duration (hours)	MD = -0.21 (-0.70 to 0.28)		Moderate to high risk of bias for 5/6 domains in primary study.	High risk
Okoli 2019	1	With condition	neurological disease), irrespective of health status, with	Eligible supplement VS placebo/inactive control	Magnesium (250-600mg per day)	Placebo	3	226	Days with migraine	MD = -3.00 (-5.02 to -0.98)		All trials judged as unclear risk of bias overall. unclear risk of bias for sequence	High risk
Okoli 2019	2	With condition	migraines	Eligible supplement VS placebo/inactive control	Magnesium (250-600mg per day)	Placebo	3	226	Migraine severity (intensity)	RoM = −0.17 (−0.36 to 0.02);	l <sup>2</sup> = 48%	generation, bias for allocation concealment, incomplete outcome	High risk
Okoli 2019	3	With condition		Eligible supplement VS placebo/inactive control	Magnesium (250-600mg per day)	Placebo	4	266	Migraine frequency	MD -2.57 (-4.21 to -0.94)	$I^2 = 88\%$	participants and personnel, and outcome assessment.	High risk

Abbreviations: MD=mean difference; RoM=ratio of means;

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Global improvement in headache/migraine
- 2. Headache pain intensity
- 3. Headache pain frequency
- 4. Headache/migraine-associated symptoms (nausea and vomiting, photophobia and phonophobia, visual aura)
- 5. Qol
- 6. Cognitive function burden
- 7. Medication use

#### Table E-13. Results of included (non-preferred) reviews by outcome domain – headache and migraine, magnesium.

Review ID		Populatio	Population	Type of	Intervention	Comparator	No/types	No of	Outcome	Results			ROBIS
	Outcome domain	n group	details	comparison	description	description	of included studies	participants (total)	measure(s) used	Relative effect (95% CI)	Other reported results	Risk of bias summary (primary studies)	assessment (for the review overall)
Chiu 2016	2	With condition	participants≥ 17 years diagnosed	Eligible supplement VS	magnesium (500-600mg per day)	placebo/usu al care	3	189	VAS	PE = 0.10 (0.01 to 1.07), ns		NA	Low risk

			with migraine, exclude MRM	placebo/inactive control									
Chiu 2016	3	With condition		Eligible supplement VS placebo/inactive control	magnesium (500-600mg per day)	placebo/usu al care	3	189	VAS	PE = 0.02 (0.00 to 2.33), ns		NA	Low risk
Park 2020	2	With condition	participants with migraine	Eligible supplement VS placebo/inactive control	oral magnesium administered for 3 months	placebo	3	190	Migraine severity/inte nsity, VAS		All 3 studies investigated oral magnesium administered for 3 months compared to placebo. One study found some benefit, where magnesium demonstrated a lower median post/pretreatment ratio for migraine severity compared to placebo. Two studies found no significant difference between magnesium and placebo in reducing pain intensity.	NA	Unclear risk
Pringsheim 2008	1	With condition	women (18 or older) with MRM or PMM	Eligible supplement VS placebo/inactive control	Magnesium 120 mg TID for last 2 weeks of menstrual cycle vs placebo, 2 cycles assessed	placebo	1	110	Pain Total Index	p<0.03	Short-term prevention of MRM.	NA	High risk
Pringsheim 2012	2	With condition	adults meeting criteria for the diagnosis of migraine headache, or trial publications had to provide sufficient detail of the headache characteristic s to support the diagnosis of migraine	Eligible supplement VS placebo/inactive control	magensium 243mg twice daily	placebo	1	69	NR		10 mmol elemental magnesium twice daily (243 mg elemental magnesium twice daily, contained in magnesium-L-aspartate- hydrochloride trihydrate) to placebo for 12 weeks following a four-week baseline period. The percentage of patients achieving their primary outcome, a reduction of 50% in the duration of migraine (in hours) or in the intensity of migraine at the end of the third month of treatment compared to	NA	High risk

										baseline, was not significantly different between groups. The main side effect experienced by patients in the treatment group was soft stools or diarrhea.		
Pringsheim 2012	3	With condition	adults meeting criteria for the diagnosis of migraine headache, or trial publications had to provide sufficient detail of the headache characteristic s to support the diagnosis of migraine	Eligible supplement VS placebo/inactive control	magnesium (600mg per day)	placebo	2	121	NR	After a one-month baseline period, Peikert et al randomized patients to 24 mmol elemental magnesium (600 mg elemental magnesium as trimagnesium dicitrate) or placebo daily for 12 weeks. Patients treated with magnesium had a significantly higher reduction in attack frequency in the final month of treatment compared to baseline than the placebo group. ("fair" quality). In a "poor" study, Köseoglu compared magnesium citrate (600 mg elemental magnesium daily) to a placebo control. All patients had migraine without aura. The study was rated as poor because, although 30 patients received magnesium, the placebo control group consisted of only ten patients (randomization 4:1). Migraine attack frequencies during a one- month baseline period were compared to the last month of a three-month treatment period. Attack frequency was reduced more in the group receiving magnesium as compared to the control	NA	High risk

										group when post/pre- treatment ratios of attack frequency were compared (P = 0.005)		
vonLuckne r 2018	3	With condition	patients 18-65 with migraine	Eligible supplement VS placebo/inactive control	magnesium	placebo	5	240	attacks/mont h	Three out of five randomized, double-blind, and placebo controlled studies showed a statistically significant decrease in number of migraine attacks, the primary efficacy measure when compared with placebo	NA	Low risk

Abbreviations: MD=mean difference; MRM=Menstrually related migraine; PMM=pure menstrual migraine; NA=Not applicable; PE=point estimate; RoM=ratio of means; VAS=visual analogue scale

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Global improvement in headache/migraine
- 2. Headache pain intensity
- 3. Headache pain frequency
- 4. Headache/migraine-associated symptoms (nausea and vomiting, photophobia and phonophobia, visual aura)
- 5. Qol
- 6. Cognitive function burden
- 7. Medication use

### E11 Arthritis/osteoarthritis, magnesium

No reviews were identified for inclusion in the Overview.

### E12 Hypertension, omega-3 fatty acids

Table E-14. Results of preferred reviews by outcome domain – hypertension, omega-3 fatty acids.

<b>Review ID</b>	Outcome	Population	Population	Type of	Intervention	Comparator	No/types	No of	Outcome	Results			ROBIS
	domain	group	details	comparison	description	description	of included studies	participants (total)	measure(s) used	Relative effect (95% CI)	Other reported results	Risk of bias summary (primary studies)	assessment (for the review overall)
Campbell 2013	1. Diastolic BP	With condition	hypertensive patients (considered to have hypertension if BP was raised: a minimum of 140mmHg for SBP or 90 mmHg for DBP)	Eligible supplement VS placebo/inactive control	Fish oil	Placebo	8	475		MD = -1.47 mmHg, 95% Cl -0.41 to - 2.53	l <sup>2</sup> = 10.6%	7/8 studies assessed at moderate risk of bias	Low risk
Campbell 2013	1. Systolic BP	With condition	hypertensive patients (considered to have hypertension if BP was raised: a minimum of 140mmHg for SBP or 90 mmHg for DBP)	Eligible supplement VS placebo/inactive control	Fish oil	Placebo	8	475		MD = -2.56 mmHg, 95% Cl -0.58 to - 4.53	l <sup>2</sup> = 0%		Low risk

Abbreviations: CI=confidence interval; DBP=diastolic blood pressure; MD=mean difference; SBP=systolic blood pressure;

- 1. Blood pressure (systolic, diastolic)
- 2. Quality of life
- 3. Cardiovascular events (fatal or non-fatal myocardial infaRCTion, excluding heart failure and if possible angina)
- 4. Cerebrovascular events (fatal or non-fatal strokes, excluding transient ischaemic attacks if possible)
- 5. Death from cardiovascular

Table E-15. Results of included (non-preferred) reviews by outcome domain – hypertension, omega-3 fatty acids.

Revie	Outcom	Populati	Population	Type of	Intervention	Comparato	No/type	No of	Outcome	Results			ROBIS
w ID	e domain	on group	details	comparison	description	r description	s of included studies	partici pants (total)	measure(s) used	Relative effect (95% CI)	Other reported results	Risk of bias summary (primary studies)	assessmen t (for the review overall)
Guo 2019	1. SBP	At-risk of conditio n	subjects whose baseline SBP was >130mmHg	Eligible supplement VS placebo/inactiv e control	EPA	Placebo	4	NR	mean differences between baseline and endpoint	Pooled effect=- 5.30 mmHg; 95%Cl: -10.50, -0.09 mmH	l <sup>2</sup> = 0%	NA	Low risk
Guo 2019	1. SBP	At-risk of conditio n	subjects whose baseline SBP was >125mmHg	Eligible supplement VS placebo/inactiv e control	DHA	Placebo	4	NR	mean differences between baseline and endpoint	Pooled effect=- 2.06 mmHg; 95%Cl: -7.41, 3.29 mmH	l <sup>2</sup> = 0%	NA	Low risk
Radac k 1989	1. DBP	With conditio n	Male/females with mild- moderate hypertension	Eligible supplement VS placebo/inactiv e control	Encapsulate d fish oil; 16.5 g/day	NR	1	16		ES = -0.08 (- 0.58-0.42)		NA	Unclear risk
Radac k 1989	1. SBP	With conditio n	Male/females with mild- moderate hypertension	Eligible supplement VS placebo/inactiv e control	Encapsulate d fish oil; 16.5 g/day	NR	1	16		ES= -0.44 (- 0.94-0.06)	Effect size is the mean change in the treatment group (i.e., $\omega$ -3 fatty acid) minus the mean change in the control group, divided by the pooled standard deviation. Therefore, an effect size is a measure of the degree of improvement in standard deviation units. Negative effect sizes indicate that to-3 fatty acids were more effective than control. Positive effect sizes indicate that control was more effective	NA	Unclear risk

Abbreviations: CI=confidence interval; DBP=diastolic blood pressure; MD=mean difference; NA=Not applicable; NR=Not reported; SBP=systolic blood pressure;

- 1. Blood pressure (systolic, diastolic)
- 2. Quality of life
- 3. Cardiovascular events (fatal or non-fatal myocardial infaRCTion, excluding heart failure and if possible angina)
- 4. Cerebrovascular events (fatal or non-fatal strokes, excluding transient ischaemic attacks if possible)
- 5. Death from cardiovascular

## E13 Fibromyalgia, magnesium

### Table E-16. Results of preferred reviews by outcome domain – fibromyalgia, magnesium.

Review		Population	Population	Type of comparison	Intervention	Comparator	No/types	No of	Outcome	Results			ROBIS
ID	Outcome domain	group	details		description	description	of included studies	participants (total)	measure(s) used	Relative effect (95% CI)	Other reported results	Risk of bias summary (primary studies)	assessment (for the review overall)
Thorpe 2018	1	With condition	Adult participants (18 years and older) with a diagnosis of fibromyalgia.	Eligible supplement + naturopathy co- intervention VS placebo/inactive control/inactive control	3 tablets (200 mg malic acid (Super Malic) + 50 mg magnesium hydroxide per tablet) twice a day for 4 weeks	Placebo	1	24	Pain VAS	No statistically significant differences were seen between any outcomes measured during placebo treatment and combination treatment (VAS pain scores, tender point index, tender point average, Health Assessment Questionnaire scores, Center for Epidemiologic Studies Depression scale scores, and anxiety assessed by the Hassle scale scores).		Unclear risk of bias for selection bias, detection bias, reporting bias and trial duration (3-6 weeks). High risk of bias for size of study.	Low risk
Thorpe 2018	2	With condition	Adult participants (18 years and older) with a diagnosis of fibromyalgia.	Eligible supplement + naturopathy co- intervention VS placebo/inactive control/inactive control	3 tablets (200 mg malic acid (Super Malic) + 50 mg magnesium hydroxide per tablet) twice a day for 4 weeks	Placebo	1	24	Health Assessment Question- naire score				Low risk

Review		Population	Population	Type of comparison	Intervention	Comparator	No/types	No of	Outcome	Results			ROBIS
ID	Outcome domain	group	details		description	description	of included studies	participants (total)	measure(s) used	Relative effect (95% CI)	Other reported results	Risk of bias summary (primary studies)	assessment (for the review overall)
Thorpe 2018	5	With condition	Adult participants (18 years and older) with a diagnosis of fibromyalgia.	Eligible supplement + naturopathy co- intervention VS placebo/inactive control/inactive control	3 tablets (200 mg malic acid (Super Malic) + 50 mg magnesium hydroxide per tablet) twice a day for 4 weeks	Placebo	1	24	tender point index (sum of tenderness severity at 18 tender points				Low risk
Thorpe 2018	5	With condition	Adult participants (18 years and older) with a diagnosis of fibromyalgia.	Eligible supplement + naturopathy co- intervention VS placebo/inactive control/inactive control	3 tablets (200 mg malic acid (Super Malic) + 50 mg magnesium hydroxide per tablet) twice a day for 4 weeks	Placebo	1	24	tender point average (mean tenderness at 18 tender points measured by dolorimeter)				Low risk

Abbreviations: VAS=visual analogue scale

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Pain
- 2. Function/Disability
- 3. Global assessment of condition
- 4. Hrqol
- 5. Tenderness
- 6. Cognitive function burden from fibromyalgia
- 7. Stiffness

Table E-17. Results of included (non-preferred) reviews by outcome domain – fibromyalgia, magnesium.

<b>Review ID</b>	Outcome	Populatio	Population	Type of comparison	Intervention	Comparator	No/types	No of	Outcome	Results			ROBIS
	domain	n group	details		description	description	of included studies	s (total) used Pain VAS	Relative effect (95% CI)	Other reported results	Risk of bias summary (primary studies)	assessment (for the review overall)	
Holdcraft 2003	1	With condition	fibromyalgia syndrome (FMS)	Eligible supplement + naturopathy co- intervention VS placebo/inactive	Supermalic (200 mg malic acid and 50 mg magnesium), 1 month	Placebo	2		Pain VAS	NR	No treatment effects were observed as measured by tender point index,	NA	High risk

<b>Review ID</b>	Outcome	Populatio	Population	Type of comparison	Intervention	Comparator	No/types	No of	Outcome	Results			ROBIS
	domain	n group	details		description	description	of included studies	participant s (total)	measure(s) used	Relative effect (95% CI)	Other reported results	Risk of bias summary (primary studies)	assessment (for the review overall)
				control/inactive control							dolorimetery reading of the tender point average, or pain as rated on a VAS.		
Holdcraft 2003	1	With condition	fibromyalgia syndrome (FMS)	Eligible supplement + naturopathy co- intervention VS placebo/inactive control/inactive control	magnesium (300– 600 mg) and malate (1200–2400 mg) over 8 weeks	Placebo	2		Pain VAS	NR		NA	High risk
Holdcraft 2003	5	With condition	fibromyalgia syndrome (FMS)	Eligible supplement + naturopathy co- intervention VS placebo/inactive control/inactive control	Supermalic (200 mg malic acid and 50 mg magnesium), 1 month	Placebo	2		tender point index,	NR	No treatment effects were observed as measured by tender point index, dolorimetery reading of the tender point average, or pain as rated on a VAS.	NA	High risk
Holdcraft 2003	5	With condition	fibromyalgia syndrome (FMS)	Eligible supplement + naturopathy co- intervention VS placebo/inactive control/inactive control	Supermalic (200 mg malic acid and 50 mg magnesium), 1 month	Placebo	2		tender point average from dolorimeter	NR	No treatment effects were observed as measured by tender point index, dolorimetery reading of the tender point average, or pain as rated on a VAS.	NA	High risk
Holdcraft 2003	5	With condition	fibromyalgia syndrome (FMS)	Eligible supplement + naturopathy co- intervention VS placebo/inactive control/inactive control	magnesium (300– 600 mg) and malate (1200–2400 mg) over 8 weeks	Placebo	2		tender point index,	NR	Significant differences in tender point index scores between the intervention and control condition subjects were observed, , as well	NA	High risk

<b>Review ID</b>	Outcome	Populatio	Population	Type of comparison	Intervention	Comparator	No/types	No of	Outcome	Results			ROBIS
	domain	n group	details		description	description	of included studies	participant s (total)	measure(s) used	Relative effect (95% CI)	Other reported results	Risk of bias summary (primary studies)	assessment (for the review overall)
											as a significant worsening of these scores when six subjects were crossed-over to placebo group		
Holdcraft 2003	5	With condition	fibromyalgia syndrome (FMS)	Eligible supplement + naturopathy co- intervention VS placebo/inactive control/inactive control	magnesium (300– 600 mg) and malate (1200–2400 mg) over 8 weeks	Placebo	2		tender point average from dolorimeter	NR		NA	High risk
Porter 2010	4	At-risk of condition	CFS/ME	Eligible supplement VS placebo/inactive control	Magnesium	Placebo	1	34	NR	NR	positive outcome	NA	High risk
Porter 2010	Unclear - "physical"	With condition	FM	Eligible supplement VS placebo/inactive control	Magnesium	Placebo	2	39	NR	NR	positive outcome	NA	High risk
Porter 2010	Unclear - "physical"	At-risk of condition	CFS/ME	Eligible supplement VS placebo/inactive control	Magnesium	Placebo	1	34	NR	NR	positive outcome	NA	High risk

Abbreviations: CFS=Chronic fatigue syndrome; FMS= fibromyalgia syndrome; ME=myalgic encephalomyelitis; NA=Not applicable; NR=Not reported; VAS=visual analogue scale

- 1. Pain
- 2. Function/Disability
- 3. Global assessment of condition
- 4. Hrqol
- 5. Tenderness
- 6. Cognitive function burden from fibromyalgia
- 7. Stiffness

# E14 Recurrent infection/s (including urinary tract infections, cystitis, respiratory tract infection, otitis media in children), zinc

Table E-18. Results of preferred reviews by outcome domain – recurrent infection/s (including urinary tract infections, cystitis, respiratory tract infection, otitis media in children), zinc.

Review	Outcom	Populatio	Populatio	Type of	Intervention description	Comparat	No/type	No of	Outcome	Results			ROBIS
ID	e domain	n group	n details	comparison		or descriptio n	s of included studies	participan ts (total)	measure(s) used	Relative effect (95% CI)	Other reported results	Risk of bias summary (primary studies)	assessment (for the review overall)
Gulani 2014	1	At-risk of condition	Children aged 6 to 31 months	Eligible supplement VS placebo/inactiv e control	Zinc gluconate syrup taker daily for 4 months (contained 10 mg elemental zinc for infants and 20 mg for older children); 12.5 mg zinc sulphate, in tablet form, daily (except Sundays) for 6 months	placebo	2	3191	Number of participants with at least one episode of definite acute otitis media (AOM) during follow-up	RR = 1.05 [0.82, 1.36]	I <sup>2</sup> =17.69%	Low risk of bias in all domains for included primary studies	Low risk
Gulani 2014	1	At-risk of condition	Children aged 6 to 30 months	Eligible supplement VS placebo/inactiv e control	Zinc gluconate syrup taker daily for 4 months (contained 10 mg elemental zinc for infants and 20 mg for older children)	placebo	1	2482	Number of episodes of definite AOM per participant per year of follow-up	RR = 1.08 [0.50, 2.36]			Low risk
Hurley 2020	2	With condition	Children with cystic fibrosis	Eligible supplement VS placebo/inactiv e control	Zinc supplementation (30 mg orally once daily)	placebo	2	62	Respiratory function mean FEV1 % predicted Follow- up: 24 months		One trial showed no difference between groups, MD - 5.46 (95% CI - 19.44 to 8.52). A further paper reported that the median (IQR) FEV1 % predicted value was 8.97% (- 18.23% to	rRsk of bias within 1 of the included trials; there were concerns across 5 out of the 6 domains for assessing risk of bias.	Low risk

											0.33%) lower than baseline in the zinc group and 9.55% (-9.59% to 12.88%) higher in the placebo group (P = 0.08) (Sharma 2016).		
Hurley 2020	5	With condition	Children with cystic fibrosis	Eligible supplement VS placebo/inactiv e control	Zinc supplementation (30 mg orally once daily)	placebo	1	37	Pulmonary exacerbations number of participants re- quiring IV antibiotics Follow-up: 12 months	RR = 1.85 (0.65 to 5.26)		No assessed risk of bias	Low risk
Hurley 2020	5	With condition	Children with cystic fibrosis	Eligible supplement VS placebo/inactiv e control	Zinc supplementation (30 mg orally once daily)	placebo	2	62	Need for antibiotics number of days on IV or oral antibiotics Follow-up: 24 months		Fewer oral antibiotics alone were needed by participants in the zinc group, MD = -17.74 (95% CI -26.98 to -8.50); but there was no significant difference between groups in the need for IV antibiotics alone, $MD =$ 0.52 (95% CI - 3.07 to 4.11). Another trial found no significant difference in the number of days on IV or oral antibiotics (P = 0.76).	Risk of bias within 1 of the included trials; there were concerns across 5 out of the 6 domains for assessing risk of bias.	Low risk

Manika m 2016	1	At-risk of condition	Children with Down's syndrome	Eligible supplement VS placebo/inactiv e control	Zinc sulfate 25mg/d for 1– 9 yr and 50 mg/d for older children for 6 months	placebo	1	64	Number of children with URTI	no significant differences in terms of URTI episodes	Moderate risk of bias overall, study with critical risk of bias	Unclear risk
Manika m 2016	5	At-risk of condition	Children with Down's syndrome	Eligible supplement VS placebo/inactiv e control	Zinc sulfate 25mg/d for 1– 9 yr and 50 mg/d for older children for 6 months	placebo	1	64	Antibiotic use	no significant differences in terms of antibiotic use	excluded.	Unclear risk

Abbreviations: AOM=acute otitis media; CI=confidence interval; FEV1=Forced expiratory volume; IQR=interquartile range; IV=intravenous; MD=mean difference; RR=relative risk; URTI=upper respiratory tract infection;

^Outcome domains identified as part of the Outcome Prioritisation Exercise:

- 1. Overall control of disease (recurrence)
- 2. Overall severity of symptoms
- 3. Time (days) from initiation of treatment to resolution of symptoms
- 4. Hrqol
- 5. Use of acute and prophylactic antibiotics for conditions where antibiotics are indicated
- 6. Duration of hospital stay

For recurrent infections all included reviews were preferred reviews.

# E15 Diabetes (Type II) (including metabolic syndrome), antioxidants (specifically coq10 and alpha-lipoic acid)

Table E-19. Results of preferred reviews by outcome domain – diabetes (Type li) (including metabolic syndrome), antioxidants (specifically coq10 and alphalipoic acid).

Review ID	Outcome	Population	Population	Type of	Intervention	Comparator	No/types	No of	Outcome	Results			ROBIS
	domain	group	details	comparison	description	description	of included studies	participant s (total)	measure(s) used	Relative effect (95% Cl)	Other reported results	Risk of bias summary (primary studies)	assessment (for the review overall)
Dludla 2020	1 - FBI	With condition	Adults (>18 years) with diabetes or metabolic syndrome	Eligible supplement VS placebo/inactive control	CoQ10	Placebo	5	308		SMD = 0.19 [-0.30, 0,68]	l <sup>2</sup> = 78%	All included studies had low internal and reporting bias. However,	Low risk
Dludla 2020	1 - FPG/FBG	With condition	Adults (>18 years) with diabetes or	Eligible supplement VS	CoQ10	Placebo	9	457		SMD = 0.14 [-0.11, 0,39]	l <sup>2</sup> = 38%	included studies scored poor on	Low risk

						T			· · · · · · · · · · · · · · · · · · ·				1
			metabolic syndrome	placebo/inactive control								external validity.	
Dludla 2020	1 - Hb1AC	With condition	Adults (>18 years) with diabetes or metabolic syndrome	Eligible supplement VS placebo/inactive control	CoQ10	Placebo	8	419	Hb1AC	SMD in the - intervention group was 0.35 lower (0.03 lower to 0.67 lower)	NR	•	Low risk
Dludla 2020	2 - SBP	With condition	Adults (>18 years) with diabetes or metabolic syndrome	Eligible supplement VS placebo/inactive control	CoQ10	Placebo	4	187		SMD = -0.07 [-0.35, 0,22]	l <sup>2</sup> = 0%		Low risk
Jibril 2022	1 - FPG/FBG	With condition	Type 2 diabetes patients (men and women), 18 years and above,	Eligible supplement VS placebo/inactive control	Oral supplementation of ALA ≥4 weeks	Placebo	9	620		MD: -6.08 mg/dl; 95% Cl: -9.74 to -2.42, P = 0.001	<sup>2</sup> =94.2%, P < 0.001). Exclusio n of each study at a time did not change the pooled effect size. Subgrou p analysis showed the risk of bias partly explaine d the heteroge neity, where a greater decrease was observed in the	All included studies were at low risk of bias in terms of incomplete outcome data, selective reporting, and other	Low risk

										studies with a low risk of bias.		
Jibril 2022	1 - Hb1AC	With condition	Type 2 diabetes patients (men and women), 18 years and above,	Eligible supplement VS placebo/inactive control	Oral supplementation of ALA ≥4 weeks	Placebo	11	782	MD: -0.17%; 95% CI: -0.30 to -0.05, P = 0.008	<sup>2</sup> = 91.5%, P < 0.001		Low risk
Jibril 2022	2 - SBP	With condition	Type 2 diabetes patients (men and women), 18 years and above,	Eligible supplement VS placebo/inactive control	Oral supplementation of ALA ≥4 weeks	Placebo	5	388	MD: -1.71 mmhg; 95% Cl: -5.48 to 2.07			Low risk
Kim 2022	1 - FPG/FBG	With condition	Patients with T2DM;	Eligible supplement VS placebo/inactive control	Coq10	Placebo/non- exposure	9	NR	MD = -8.84 (- 16.94, -0.75)	l <sup>2</sup> = 6%	High and unclear risk of bias in included	Low risk
Kim 2022	1 - Hb1AC	With condition	Patients with T2DM;	Eligible supplement VS placebo/inactive control	Coq10	Placebo/non- exposure	11	NR	MD=-0.23 (- 0.40, -0.05)	l <sup>2</sup> = 3%	studies.	Low risk
Kim 2022	1 - HOMA- IR	With condition	Patients with T2DM;	Eligible supplement VS placebo/inactive control	Coq10	Placebo/non- exposure	4	228	MD = -0.83 (- 2.12, 0.47)	High heteroge neity observed		Low risk
Wang 2022	1 - FPG/FBG	At-risk of condition	Patients had obesity (BMI ≥30 kg/m2) who did not habitually use antioxidant supplements	Eligible supplement VS placebo/inactive control	Antioxidant	Placebo	6	315	MD=-4.92 [- 6.87, -2.98]	l <sup>2</sup> = 45%	Unclear risk of bias in allocation bias, attrition bias, attrition bias and reporting bias	Unclear risk
Wang 2022	1- HOMA-ir	At-risk of condition	Patients had obesity (BMI ≥30 kg/m2) who did not habitu- ally use antioxidant supplements	Eligible supplement VS placebo/inactive control	Antioxidant	Placebo	8	395	MD = -0.45 [-0.61, - 0.30]	l <sup>2</sup> = 48%	for all primary studies.	Unclear risk

Abbreviations: BMI=body mass index; CoQ10=Coenzyme Q10, CI=Confidence interval; DBP=diastolic blood pressure; FBG=fasting blood glucose; FPG=fasting plasma glucose; MD=Mean difference, NR=Not reported, T2DM=Type II Diabetes Mellitus; Homeostatic Model Assessment for Insulin Resistance=HOMA-ir; Hb1AC=Hemoglobin A1C; SBP=systolic blood pressure

- 1. Glycemic control
  - Hba1c
  - Fasting glucose
  - Fasting insulin
  - Homeostatic model assessment of insulin resistance
  - 2 hour post-prandial blood sugar
  - Hyperglycemia (frequency)
  - Hypoglycemia (frequency)
- 2. Blood pressure
  - Systolic
  - Diastolic
- 3. Oxidative stress
  - Malonaldehyde
  - Total antioxidant status/capacity
  - Free oxygen radical test
  - Reative oxygen metabolites
  - Biological antioxidant potential
  - Lipo-peroxidation products
  - Catalase
  - Glutathione peroxidase
- 4. Diabetes related symptoms
- 5. Overall diabetes related complications
- 6. Hrqol
- 7. Incidence of type 2 diabetes mellitus

Table E-20. Results of included (non-preferred) reviews by outcome domain -	- diabetes (Type li) (including metabolic syndrome), antioxidants (specifically
coq10 and alpha-lipoic acid).	

Review ID	Outcome	Population	Population	Type of	Intervention	Comparator	No/types	No of	Outcome	Results			ROBIS
	domain	group	details	comparison	description	description	of included studies	participant s (total)	measure(s) used	Relative effect (95% CI)	Other reported results	Risk of bias summary (primary studies)	assessment (for the review overall)
Araújo 2022	1 - Hb1AC	With condition	Adult patients with diagnosed T2DM (controlled or not) under treatment (including diet, exercises,	Eligible supplement + non-naturopathy co-intervention VS non-naturopathy co-intervention	Alpha Lipoic Acid 600 mg thrice a day for 12 weeks + NSPT	NSPT	1	40	Hba1c level change from baseline to 8 or 12 weeks	P < 0.001		NA	Low risk

			pharmacological therapy or any combination of those) and untreated periodontitis (according to the case definition of the new Periodontal Diseases Classification, patients with interdental clinical attachment level (CAL) detectable at 22 non-adiacent									
			teeth, or buccal or oral CAL ≥ 3 mm with pocketing > 3 mm detectable at ≥2 teeth									
Huang 2018	1 - FBI	With condition	Adults aged ≥18 years) with a body mass index (BMI) of ≥25 kg/m2 and diagnosed with T2DM	Eligible supplement VS placebo/inactive control	Coq10	Placebo	5	NR	WMD = – 1.87 µiu/ml; 95% CI=– 4.51 to 0.77; P=0.17	l <sup>2</sup> = 71%	NA	Low risk
Huang 2018	1 - FPG/FBG	With condition	Adults aged ≥18 years) with a body mass index (BMI) of ≥25 kg/m2 and diagnosed with T2DM	Eligible supplement VS placebo/inactive control	Coq10	Placebo	12	NR	WMD = – 0.59 mmol/L; 95% CI=– 1.05 to – 0.12; P=0.01	<sup>2</sup> = 37%	NA	Low risk
Huang 2018	1 - hba1c	With condition	Adults aged ≥18 years) with a body mass index (BMI) of ≥25 kg/m2 and diagnosed with T2DM	Eligible supplement VS placebo/inactive control	Coq10	Placebo	13	NR	WMD = – 0.28%; 95% CI=–0.53 to – 0.03; P=0.03	l <sup>2</sup> = 33%	NA	Low risk
Huang 2018	1 - HOMA- IR	With condition	Adults aged ≥18 years) with a body mass index (BMI) of ≥25 kg/m2 and	Eligible supplement VS placebo/inactive control	Coq10	Placebo	5	NR	WMD = - 1.03; 95% CI=-2.06 to - 0.00; P=0.05	l <sup>2</sup> = 71%	NA	Low risk

			diagnosed with T2DM									
Huang 2018	2 - SBP	With condition	Adults aged ≥18 years) with a body mass index (BMI) of ≥25 kg/m2 and diagnosed with T2DM	Eligible supplement VS placebo/inactive control	Coq10	Placebo	6	NR	WMD = 1.84 mmhg; 95% CI=-5.60 to 1.92; P=0.34	l <sup>2</sup> = 80%	NA	Low risk
Huo 2022	1 - Hb1AC	With condition	Diabetic patients who have been diagnosed with DPN	Eligible supplement VS placebo/inactive control	Coq10 (400mg/day 4 months)	Placebo	1	49	MD = -0.20, 95% CI (-1.04, 0.64)		NA	Low risk
Huo 2022	1 - Hb1AC	With condition	Diabetic patients who have been diagnosed with DPN	Eligible supplement VS placebo/inactive control	ALA (1200mg/day for 24 months)	Placebo	1	38	MD = -1.10, 95% CI (- 2.36, 0.16)		NA	Low risk
Rahimlou 2019	1 - FPG/FBG	With condition	Patients with T2DM;	Eligible supplement VS placebo/inactive control	ALA	Placebo/non- exposure	NR	NR	WMD = 9.89, 95% Cl: 16.96 to 2.82, P 1⁄4 0.006		NA	Low risk
Zhang 2018	1 - FBI	With condition	Patients with T2DM	Eligible     supplement VS     placebo/inactive     control     Eligible     supplement +     naturopathy co-     intervention VS     naturopathy co-     intervention     Eligible     supplement +     non-naturopathy     co-intervention VS     non-naturopathy     co-intervention	CoQ10	Control	4	228	WMD = -0.48; 95% Cl -2.54, 1.57; P = 0 65	l <sup>2</sup> = 77%	NA	High risk
Zhang 2018	1 - FPG/FBG	With condition	Patients with T2DM	<ul> <li>Eligible</li> <li>supplement VS</li> <li>placebo/inactive</li> <li>control</li> <li>Eligible</li> <li>supplement +</li> <li>naturopathy co-</li> </ul>	CoQ10	Control	10	619	WMD = -11.21; 95% CI -18.99, -3.43; P = 0 005	l <sup>2</sup> = 85%	NA	High risk

				intervention VS naturopathy co- intervention • Eligible supplement + non-naturopathy co-intervention VS non-naturopathy co-intervention								
Zhang 2018	1 - Hb1AC	With condition	Patients with T2DM	Eligible     supplement VS     placebo/inactive     control     Eligible     supplement +     naturopathy co-     intervention VS     naturopathy co-     intervention     Eligible     supplement +     non-naturopathy     co-intervention VS     non-naturopathy     co-intervention	CoQ10	Control	13	765	WMD = -0.29; 95% CI -0.54, -0.03; P = 0 03	l <sup>2</sup> = 88%	NA	High risk
Zhang 2018	1 - HOMA- IR	With condition	Patients with T2DM	Eligible     supplement VS     placebo/inactive     control     Eligible     supplement +     naturopathy co-     intervention VS     naturopathy co-     intervention     Eligible     supplement +     non-naturopathy     co-intervention VS	CoQ10	Control	4	228	MD = -0.89; 95% Cl -2.25, 0.48; P = 0 20	l <sup>2</sup> = 92%	NA	High risk

Abbreviations: ALA=alpha-linolenic acid, BMI=body mass index; CoQ10=Coenzyme Q10, CI=Confidence interval; DBP=diastolic blood pressure; FBG=fasting blood glucose; FPG=fasting plasma glucose; MD=Mean difference, NR=Not reported; T2DM=Type II Diabetes Mellitus; HOMA-ir= Homeostatic Model Assessment for Insulin Resistance; Hb1AC=Hemoglobin A1C; NA=Not applicable; SBP=systolic blood pressure; WMD=weighted mean difference

- 1. Glycemic control
  - Hba1c
  - Fasting glucose
  - Fasting insulin
  - Homeostatic model assessment of insulin resistance
  - 2 hour post-prandial blood sugar
  - Hyperglycemia (frequency)
  - Hypoglycemia (frequency)
- 2. Blood pressure
  - Systolic
  - Diastolic
- 3. Oxidative stress
  - Malonaldehyde
  - Total antioxidant status/capacity
  - Free oxygen radical test
  - Reative oxygen metabolites
  - Biological antioxidant potential
  - Lipo-peroxidation products
  - Catalase
  - Glutathione peroxidase
- 4. Diabetes related symptoms
- 5. Overall diabetes related complications
- 6. Hrqol
- 7. Incidence of type 2 diabetes mellitus

## Appendix F ROBIS assessments

This appendix provides the three questions described in ROBIS used to arrive at a final risk of bias judgement, for each included review. We did not provide narrative domain or overall summary judgements for systematic reviews due to the volume of included reviews.

Table F-1. ROBIS assessment for includ	ed reviews -	- anxiety, magnesium
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Review ID	Baric 2018	Tsai 2023
ROBIS DOMAINS		
Answer code: Y=YES, PY=PROBABLY YES, PN=PROBABLY NO, N=NO, NI=NO INFORMATION		
Domain 1: Study eligibility criteria		
Did the review adhere to pre-defined objectives and eligibility criteria?	PY	Y
Were the eligibility criteria appropriate for the review question?	Y	Y
Were eligibility criteria unambiguous?	Y	Y
Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?	PY	PY
Were any restrictions in eligibility criteria based on sources of information appropriate (publication status or format, language, availability of data)?	PY	PY
Concerns regarding specification of study eligibility criteria LOW, HIGH, UNCLEAR	Low	Low
Domain 2: Identification and selection of studies		
Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?	Y	Y
Were methods additional to database searching used to identify relevant reports?	Y	Y
Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible?	PY	Y
Were restrictions based on date, publication format, or language appropriate?	PN	PN
Were efforts made to minimise error in selection of studies?	NI	Y
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR	Unclear	Unclear
Domain 3: Data collection and study appraisal		
Were efforts made to minimise error in data collection?	Y	NI
Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?	Y	Y
Were all relevant study results collected for use in the synthesis?	Y	Y
Was risk of bias (or methodological quality) formally assessed using appropriate criteria?	Y	Y
Were efforts made to minimise error in risk of bias assessment?	Y	NI
Concerns regarding methods used to collect data and appraise studies: LOW, HIGH, UNCLEAR	Low	Low
Domain 4: Synthesis and findings		

Did the synthesis include all studies that it should?	PY	PY
Were all pre-defined analyses reported or departures explained?	PY	Y
Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies?	Y	Y
Was between-study variation (heterogeneity) minimal or addressed in the synthesis?	Y	Y
Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?	Y	Y
Were biases in primary studies minimal or addressed in the synthesis?	Y	Y
Concerns regarding the synthesis and finding: LOW, HIGH, UNCLEAR	Low	Low
Risk of bias in the review		
Did the interpretation of findings address all of the concerns identified in Domains 1-4?	Y	Y
Was the relevance of identified studies to the review's research question appropriately considered?	Y	Y
Did the reviewers avoid emphasizing results on the basis of their statistical significance?	Y	Y
Overall risk of bias	Low risk	Low risk

### Table F-2. ROBIS assessment for included reviews – irritable bowel syndrome, probiotics

Review ID	Abboud 2020	Asha 2020	Connell 2018	Corbitt 2018	Ding 2019	Fatahi 2022	Ford 2014	Horvath 2011	Hovevda 2009	Huertas-Ceballos 2009	Hungin 2018	Konstantis 2023	Korterink 2014	Le Morvan 2021	Li 2020	Liang 2019	McFarland 2008	McFarland 2021	Moayyedi 2010	Nikfar 2008	Niu 2020	Ortiz-Lucas 2013	Pratt 2020	Ritchie 2012	Shang 2022	Sun 2020	Wang 2022	Wen 2020	Xu 2021	Yuan 2017	Zhang 2016
ROBIS DOMAINS																															
Answer code: Y=YES, PY=PROBABLY YES, PN=PROBABLY NO, N=NO, NI=NO INFORMATION																															
Domain 1: Study eligibility criteria																															
Did the review adhere to pre-defined objectives and eligibility criteria?	N I	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	Y	P Y	Y	P Y	Y	P Y	P Y	P Y	Y	Y	P Y	P Y	P Y	P Y	P Y	P Y	Y	P Y	P Y	Y	P Y	P Y
Were the eligibility criteria appropriate for the review question?	Y	Υ	Y	Υ	Υ	Y	Y	Y	Y	Y	Y	Υ	Υ	Υ	Y	Y	Y	Y	Υ	Υ	Y	Υ	Υ	Υ	Υ	Y	Υ	Υ	Υ	Y	Υ
Were eligibility criteria unambiguous?	P Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Υ	Y	Y	Y

Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?	Y	P N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were any restrictions in eligibility criteria based on sources of information appropriate (publication status or format, language, availability of data)?	Y	P Y	Y	P N	P Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Concerns regarding specification of study eligibility criteria LOW, HIGH, UNCLEAR	Low	High	Low	High	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Domain 2: Identification and selection of studies																															
Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were methods additional to database searching used to identify relevant reports?	Y	Y	Y	P N	P N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Υ	Y	Y
Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible?	P Y	P Y	Y	P Y	Y	P Y	Y	Y	P Y	Y	P Y	Y	P Y	Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	Y	Y	Y	P N	P Y	P Y	P Y
Were restrictions based on date, publication format, or language appropriate?	Y	P N	P N	Ν	P N	Y	Y	Y	P N	Y	P N	Y	Y	Y	Y	P N	Y	Y	Y	Y	N I	P N	Y	Y	P N	Y	Y	N I	P N	P N	N I
Were efforts made to minimise error in selection of studies?	Y	Y	Y	N I	N I	N I	Y	Y	N I	Y	N I	Y	Y	Y	N I	N I	Y	Y	Y	Y	Y	N I	Y	N I	Y	Y	Y	Y	Y	Y	N I
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR	Low	Unclear	Unclear	High	High	Low	Low	Low	Unclear	Low	Unclear	Low	Low	Low	Unclear	Unclear	Low	Low	Low	Low	Unclear	Unclear	Low	Unclear	Unclear	Low	Low	Unclear	Unclear	Unclear	Unclear
Domain 3: Data collection and study appraisal																														T	
Were efforts made to minimise error in data collection?	Y	N I	Y	N I	P Y	Y	Y	Y	Y	Y	N I	Y	Y	N I	Y	Y	N I	Y	Y	Y	Y	N I	N I	N I	Y	Y	Y	Y	Y	N I	Y
Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were all relevant study results collected for use in the synthesis?	Y	Y	Υ	Y	Υ	Υ	Υ	Υ	Y	Υ	Y	Υ	Y	Υ	Y	Y	Y	Υ	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Υ
Was risk of bias (or methodological quality) formally assessed using appropriate criteria?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were efforts made to minimise error in risk of bias assessment?	Y	N I	Y	N I	N I	Y	Y	Y	Y	Y	N I	N I	N I	N I	Y	Y	Y	Y	Y	N I	Y	N I	Y	N I	Y	Y	N I	Y	N I	N I	Y

Concerns regarding methods used to collect data and appraise studies: LOW, HIGH, UNCLEAR	Low	Unclear	Low	Unclear	Unclear	Low	Low	Low	Low	Low	Unclear	Low	Low	Unclear	Low	Low	Low	Low	Low	Low	Low	Unclear	Low	Unclear	Low	Low	Low	Low	Low	Unclear	Low
Domain 4: Synthesis and findings																															
Did the synthesis include all studies that it should?	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y
Were all pre-defined analyses reported or departures explained?	N I	P Y	P Y	P Y	P Y	P Y	P Y	P Y	P Y	Y	P Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	P Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was between-study variation (heterogeneity) minimal or addressed in the synthesis?	P Y	Y	Y	P N	P N	Y	Y	Y	Y	P N	P N	Y	P N	Y	Y	Y	Y	Y	Y	Y	Y	P N	N I	Y	Y	Ν	Y	Y	Y	Y	Y
Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?	P Y	Ν	Y	P N	P N	Y	Y	N	Y	P N	Ν	Y	Ν	N I	Y	Y	Y	P N	P N	Y	Y	N	N I	Y	N I	P N	N I	Y	N I	Y	Y
Were biases in primary studies minimal or addressed in the synthesis?	Y	Y	Y	P Y	P Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Concerns regarding the synthesis and finding: LOW, HIGH, UNCLEAR	Low	Unclear	Low	Unclear	Unclear	Low	Low	Unclear	Low	High	High	Low	High	Unclear	Low	Low	Low	Unclear	Unclear	Low	Low	High	High	Low	Low	High	Low	Low	Unclear	Unclear	Unclear
Risk of bias in the review																															
Did the interpretation of findings address all of the concerns identified in Domains 1-4?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Υ	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the relevance of identified studies to the review's research question appropriately considered?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Υ	Y	Υ	Y	Y	Y	Y	Y	Υ	Y	Y	Y	Y	Y	Y	Y
Did the reviewers avoid emphasizing results on the basis of their statistical significance?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Overall risk of bias	Low risk	High risk	Low risk	High risk	High risk	Low risk	Low risk	Unclear	Unclear	High risk	High risk	Low risk	High risk	Unclear	Low risk	Low risk	Low risk	Unclear	Unclear	Low risk	Low risk	High risk	High risk	Unclear	Low risk	High risk	Low risk	Low risk	Unclear	Unclear	Unclear

### Table F-3. Results of included reviews by outcome domain – insomnia/sleeping disorders, magnesium

Review ID	Chan 2021	Mah 2021	Samara 2021	Zhan 2023
ROBIS DOMAINS				
Answer code: Y=YES, PY=PROBABLY YES, PN=PROBABLY NO, N=NO, NI=NO INFORMATION				
Domain 1: Study eligibility criteria				
Did the review adhere to pre-defined objectives and eligibility criteria?	Y	Y	PY	Y
Were the eligibility criteria appropriate for the review question?	Y	Y	Y	Y
Were eligibility criteria unambiguous?	PY	Y	Y	Y
Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?	Y	Y	Y	Y
Were any restrictions in eligibility criteria based on sources of information appropriate (publication status or format, language, availability of data)?	Y	Y	Y	Y
Concerns regarding specification of study eligibility criteria LOW, HIGH, UNCLEAR	Low	Low	Low	Low
Domain 2: Identification and selection of studies				
Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?	Y	Y	Y	Y
Were methods additional to database searching used to identify relevant reports?	Y	Y	Y	Y
Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible?	Y	Y	Y	Y
Were restrictions based on date, publication format, or language appropriate?	PN	PN	Y	PN
Were efforts made to minimise error in selection of studies?	Y	Y	Y	Y
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR	Unclear	Unclear	Low	Unclear
Domain 3: Data collection and study appraisal				
Were efforts made to minimise error in data collection?	Y	Y	Y	Y
Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?	Y	Y	Y	Y
Were all relevant study results collected for use in the synthesis?	Y	Y	Y	Y
Was risk of bias (or methodological quality) formally assessed using appropriate criteria?	Y	Y	Y	Y
Were efforts made to minimise error in risk of bias assessment?	NI	PY	NI	Y
Concerns regarding methods used to collect data and appraise studies: LOW, HIGH, UNCLEAR	Low	Low	Low	Low
Domain 4: Synthesis and findings				
Did the synthesis include all studies that it should?	PY	PY	PY	PY
Were all pre-defined analyses reported or departures explained?	Y	Y	Y	Y

Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies?	Y	Y	Y	Y
Was between-study variation (heterogeneity) minimal or addressed in the synthesis?	Y	Y	Y	Y
Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?	Y	NI	NI	PN
Were biases in primary studies minimal or addressed in the synthesis?	Ν	Y	Y	Y
Concerns regarding the synthesis and finding: LOW, HIGH, UNCLEAR	High	Unclear	Unclear	High
Risk of bias in the review				
Did the interpretation of findings address all of the concerns identified in Domains 1-4?	Y	Y	Y	Y
Was the relevance of identified studies to the review's research question appropriately considered?	Y	Y	Y	Y
Did the reviewers avoid emphasizing results on the basis of their statistical significance?	Y	Y	Y	Y
Overall risk of bias	High risk	Unclear risk	Unclear risk	Unclear risk

### Table F-4. Results of included reviews by outcome domain – depression, omega-3 fatty acids

Review ID	Appleton 2015	Appleton 2016	Appleton 2021	Bae 2018	Bai 2018	Bai 2020	Chowdhury 2020	Farooq 2020	Gabriel 2023	Liao 2019	Miller 2013	Mocking 2016	Mocking 2020	Morrell 2016	Newberry 2016	Saccone 2016	Sarris 2012	Suradom 2021	Troeung 2013	Tsai 2023	Tung 2023	Viswanathan 2020	Williams 2006	Xu 2023	Zhang 2019	Zhang 2020
ROBIS DOMAINS																										
Answer code: Y=YES, PY=PROBABLY YES, PN=PROBABLY NO, N=NO, NI=NO INFORMATION																										
Domain 1: Study eligibility criteria																										
Did the review adhere to pre-defined objectives and eligibility criteria?	Y	Y	PY	PY	PY	Y	PY	Y	Y	PY	Y	Y	Y	Y	Y	Y	Y	Y	PY	Y	PY	Y	Y	PY	PY	Y
Were the eligibility criteria appropriate for the review question?	Y	Y	Y	Y	Y	Y	Υ	Y	Y	Υ	Y	Y	Y	Υ	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were eligibility criteria unambiguous?	Υ	Υ	Υ	Υ	Υ	Y	Υ	Υ	Υ	Y	Υ	Υ	Y	Υ	Υ	Υ	Υ	Υ	Υ	Υ	Y	Υ	Y	Υ	Y	Υ
Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	PY	Y	Y	PY	Y	Y	Y

Were any restrictions in eligibility criteria based on sources of information appropriate (publication status or format, language, availability of data)?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	PY	Y	Y	Y	Y	Y	Y
Concerns regarding specification of study eligibility criteria LOW, HIGH, UNCLEAR	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Domain 2: Identification and selection of studies																										
Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were methods additional to database searching used to identify relevant reports?	Y	Y	Y	Y	Y	Υ	Y	Y	Y	Y	Υ	Y	Υ	Υ	Υ	Υ	Υ	Y	Y	PY	Υ	Υ	PN	Y	PY	Y
Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible?	Y	Y	Y	Y	Y	Y	PN	ΡY	ΡY	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NI	PN	Y	Y	Y
Were restrictions based on date, publication format, or language appropriate?	Y	Y	Y	NI	PN	Y	N	PN	N	NI	Ν	Y	Y	PN	N	Y	Y	PY	PN	PN	Ν	Ν	Y	PN	Y	Y
Were efforts made to minimise error in selection of studies?	Y	Y	Y	Y	Y	Υ	N	PY	N	Y	Υ	Y	Y	Υ	Υ	Υ	Υ	Y	NI	Υ	Υ	Υ	Y	Y	Y	Y
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR	Low	Low	Low	Unclear	Unclear	Low	High	Unclear	High	Unclear	High	Low	Low	Unclear	Unclear	Low	Low	Low	Unclear	Unclear	High	High	High	Unclear	Low	Low
Domain 3: Data collection and study appraisal																										
Were efforts made to minimise error in data collection?	Y	Y	Y	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NI	Y	Y	NI	Y	Y	Y
Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were all relevant study results collected for use in the synthesis?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was risk of bias (or methodological quality) formally assessed using appropriate criteria?	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were efforts made to minimise error in risk of bias assessment?	Y	Y	Y	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y	Y	Υ	Y	NI	NI	Y	Y	Y	Y	Y	Y

Concerns regarding methods used to collect data and appraise studies: LOW, HIGH, UNCLEAR	Low	Low	Low	Low	Low	Low	Unclear	Low	High	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Unclear	Low	Low	Low	Low	Low	Low
Domain 4: Synthesis and findings																										
Did the synthesis include all studies that it should?	PY	PY	PY	PY	PY	PY	PY	PY	PY	PY	PY	PY	PY	PY	PY	PY	PY	PY	PY	PY	PY	PY	ΡY	PY	PY	PY
Were all pre-defined analyses reported or departures explained?	Y	Y	Y	Y	PY	Y	NI	NI	NI	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was between-study variation (heterogeneity) minimal or addressed in the synthesis?	Υ	Υ	Y	Y	Y	Υ	NI	Y	NI	PY	N	Y	Υ	Y	Y	PY	Y	Y	Υ	Υ	PY	PY	PY	NI	PY	Υ
Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?	N	N	N	Y	N	Y	NI	Y	NI	Y	N	Y	Y	N	Y	NI	Y	Y	Y	Y	NI	NI	NI	NI	NI	Y
Were biases in primary studies minimal or addressed in the synthesis?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Concerns regarding the synthesis and finding: LOW, HIGH, UNCLEAR	High	High	High	Low	Unclear	Low	Unclear	Low	Unclear	Low	High	Low	Low	High	Low	Unclear	Low	Low	Low	Low	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Risk of bias in the review																										
Did the interpretation of findings address all of the concerns identified in Domains 1-4?	Y	Y	Y	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the relevance of identified studies to the review's research question appropriately considered?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Did the reviewers avoid emphasizing results on the basis of their statistical significance?	Y	Υ	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Υ	Y	Υ	Y	Y	Y	Y
Overall risk of bias	Low risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	High risk	Low risk	High risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	Low risk	Low risk	High risk	High risk	High risk	Unclear risk	Low risk	Low risk

Review ID	Bath- Hextall 2012	Dhaliwal 2023	Gray 2019
ROBIS DOMAINS			
Answer code: Y=YES, PY=PROBABLY YES, PN=PROBABLY NO, N=NO, NI=NO INFORMATION			
Domain 1: Study eligibility criteria			
Did the review adhere to pre-defined objectives and eligibility criteria?	Y	PY	Y
Were the eligibility criteria appropriate for the review question?	Y	Y	Y
Were eligibility criteria unambiguous?	Y	PN	Y
Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?	Y	PY	Y
Were any restrictions in eligibility criteria based on sources of information appropriate (publication status or format, language, availability of data)?	Y	PY	Y
Concerns regarding specification of study eligibility criteria LOW, HIGH, UNCLEAR	Low	Unclear	Low
Domain 2: Identification and selection of studies			
Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?	Y	Y	Y
Were methods additional to database searching used to identify relevant reports?	Y	Y	Y
Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible?	Y	PY	Y
Were restrictions based on date, publication format, or language appropriate?	Y	PN	Y
Were efforts made to minimise error in selection of studies?	Y	Y	Y
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR	Low	Unclear	Low
Domain 3: Data collection and study appraisal			
Were efforts made to minimise error in data collection?	Y	NI	Y
Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?	Y	Y	Y
Were all relevant study results collected for use in the synthesis?	Y	Y	Y
Was risk of bias (or methodological quality) formally assessed using appropriate criteria?	Y	Y	Y

### Table F-5. Results of included reviews by outcome domain – atopic disorders (including eczema, dermatitis, allergic rhinitis, allergies), zinc

Were efforts made to minimise error in risk of bias assessment?	Y	NI	Y
Concerns regarding methods used to collect data and appraise studies: LOW, HIGH, UNCLEAR	Low	Unclear	Low
Domain 4: Synthesis and findings			
Did the synthesis include all studies that it should?	PY	PY	PY
Were all pre-defined analyses reported or departures explained?	Y	Y	Y
Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies?	Y	Y	Y
Was between-study variation (heterogeneity) minimal or addressed in the synthesis?	PY	PY	PY
Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?	NI	NI	NI
Were biases in primary studies minimal or addressed in the synthesis?	Y	Y	Y
Concerns regarding the synthesis and finding: LOW, HIGH, UNCLEAR	Unclear	Unclear	Unclear
Risk of bias in the review			
Did the interpretation of findings address all of the concerns identified in Domains 1-4?	Y	Y	Y
Was the relevance of identified studies to the review's research question appropriately considered?	Y	Y	Y
Did the reviewers avoid emphasizing results on the basis of their statistical significance?	Y	Y	Y
Overall risk of bias	Unclear risk	Unclear risk	Unclear risk

Table F-6. ROBIS assessments – fatigue (general) (including myalgic encephalomyelitis (ME) and Chronic Fatigue Syndrome (CFS)), antioxidants (specifically coq10 and alpha-lipoic acid)

Review ID	Campagnolo 2017	Kim 2020	Marx 2019	Mehrabani 2019	Pereira 2018	Tsai 2022
ROBIS DOMAINS						
Answer code: Y=YES, PY=PROBABLY YES, PN=PROBABLY NO, N=NO, NI=NO INFORMATION						
Domain 1: Study eligibility criteria						
Did the review adhere to pre-defined objectives and eligibility criteria?	PY	PY	Y	Y	Y	Y
Were the eligibility criteria appropriate for the review question?	Y	Y	Y	Y	Y	Y
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Were eligibility criteria unambiguous?	Y	PY	PY	PY	Y	Y
Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?	Y	Y	Y	Y	Y	Y
Were any restrictions in eligibility criteria based on sources of information appropriate (publication status or format, language, availability of data)?	PY	Y	Y	Y	Y	Y
Concerns regarding specification of study eligibility criteria LOW, HIGH, UNCLEAR	Low	Low	Low	Low	Low	Low
Domain 2: Identification and selection of studies						
Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?	Y	PY	Y	Y	Y	Y
Were methods additional to database searching used to identify relevant reports?	Y	Ν	Y	Y	Y	Y
Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible?	PY	PY	PY	PY	PY	Y
Were restrictions based on date, publication format, or language appropriate?	PN	Y	NI	PN	Y	Y
Were efforts made to minimise error in selection of studies?	Y	NI	Y	NI	Y	Y
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR	Unclear	Unclear	Low	Unclear	Low	Low
Domain 3: Data collection and study appraisal						
Were efforts made to minimise error in data collection?	NI	NI	NI	Y	NI	Y
Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?	Y	Y	Y	Y	Y	Y
Were all relevant study results collected for use in the synthesis?	Y	Y	Y	Y	Y	Y
Was risk of bias (or methodological quality) formally assessed using appropriate criteria?	Y	Y	Y	Y	Y	Y
Were efforts made to minimise error in risk of bias assessment?	NI	NI	NI	Y	Y	NI
Concerns regarding methods used to collect data and appraise studies: LOW, HIGH, UNCLEAR	Unclear	Unclear	Unclear	Low	Low	Low

Did the synthesis include all studies that it should?	PY	PY	PY	PY	PY	PY
Were all pre-defined analyses reported or departures explained?	Y	Y	Y	Y	Y	Y
Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies?	Y	Y	Y	Υ	Y	Y
Was between-study variation (heterogeneity) minimal or addressed in the synthesis?	PY	PY	PY	PY	PY	Y
Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?	NI	NI	NI	NI	NI	PY
Were biases in primary studies minimal or addressed in the synthesis?	Y	Y	Y	Y	Y	Υ
Concerns regarding the synthesis and finding: LOW, HIGH, UNCLEAR	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Concerns regarding the synthesis and finding: LOW, HIGH, UNCLEAR Risk of bias in the review	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Concerns regarding the synthesis and finding: LOW, HIGH, UNCLEAR Risk of bias in the review Did the interpretation of findings address all of the concerns identified in Domains 1-4?	Unclear Y	Unclear Y	Unclear Y	Unclear Y	Unclear Y	Low
Concerns regarding the synthesis and finding: LOW, HIGH, UNCLEAR Risk of bias in the review Did the interpretation of findings address all of the concerns identified in Domains 1-4? Was the relevance of identified studies to the review's research question appropriately considered?	Unclear Y Y	Unclear Y Y	Unclear Y Y	Unclear Y Y	Unclear Y Y	Low Y Y
Concerns regarding the synthesis and finding: LOW, HIGH, UNCLEAR Risk of bias in the review Did the interpretation of findings address all of the concerns identified in Domains 1-4? Was the relevance of identified studies to the review's research question appropriately considered? Did the reviewers avoid emphasizing results on the basis of their statistical significance?	Unclear Y Y Y Y	Unclear Y Y Y	Unclear Y Y Y	Unclear Y Y Y Y	Unclear Y Y Y	Low Y Y Y

#### Table F-7. Results of included reviews by outcome domain – headache and migraine, magnesium

Review ID	Chiu 2016	Okoli 2019	Park 2020	Pringsheim 2008	Pringsheim 2012	vonLuckner 2018
ROBIS DOMAINS						
Answer code: Y=YES, PY=PROBABLY YES, PN=PROBABLY NO, N=NO, NI=NO INFORMATION						
Domain 1: Study eligibility criteria						
Did the review adhere to pre-defined objectives and eligibility criteria?	PY	Y	Y	PY	PY	PY
Were the eligibility criteria appropriate for the review question?	Y	Y	Y	Y	Y	Y
Were eligibility criteria unambiguous?	PY	Y	Y	Y	Y	Y

Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?	Y	Y	Y	Y	Y	Y
Were any restrictions in eligibility criteria based on sources of information appropriate (publication status or format, language, availability of data)?	Y	Y	Y	Y	Y	Y
Concerns regarding specification of study eligibility criteria LOW, HIGH, UNCLEAR	Low	Low	Low	Low	Low	Low
Domain 2: Identification and selection of studies						
Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?	Y	Y	Y	Y	Y	Y
Were methods additional to database searching used to identify relevant reports?	Y	Y	Y	Y	Y	Y
Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible?	PY	Y	Y	Y	Y	Y
Were restrictions based on date, publication format, or language appropriate?	PN	Y	PN	NI	NI	NI
Were efforts made to minimise error in selection of studies?	Y	Y	Y	Y	Y	Y
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR	Unclear	Low	Unclear	Unclear	Unclear	Unclear
Domain 3: Data collection and study appraisal						
Domain 3: Data collection and study appraisal Were efforts made to minimise error in data collection?	Y	Y	Y	Y	Y	Y
Domain 3: Data collection and study appraisal Were efforts made to minimise error in data collection? Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?	Y Y	Y Y	Y Y	Y Y	Y Y	Y Y
Domain 3: Data collection and study appraisal Were efforts made to minimise error in data collection? Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? Were all relevant study results collected for use in the synthesis?	Y Y Y Y	Y Y Y Y	Y Y Y	Y Y Y Y	Y Y Y Y	Y Y Y
Domain 3: Data collection and study appraisal Were efforts made to minimise error in data collection? Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? Were all relevant study results collected for use in the synthesis? Was risk of bias (or methodological quality) formally assessed using appropriate criteria?	Y Y Y Y	Y Y Y Y Y	Y Y Y Y	Y Y Y Y Y	Y Y Y Y	Y Y Y Y
Domain 3: Data collection and study appraisal         Were efforts made to minimise error in data collection?         Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?         Were all relevant study results collected for use in the synthesis?         Was risk of bias (or methodological quality) formally assessed using appropriate criteria?         Were efforts made to minimise error in risk of bias assessment?	Y Y Y Y Y	Y Y Y Y Y Y	Y Y Y Y Y Y	Y Y Y Y NI	Y Y Y Y NI	Y Y Y Y NI
Domain 3: Data collection and study appraisal         Were efforts made to minimise error in data collection?         Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?         Were all relevant study results collected for use in the synthesis?         Was risk of bias (or methodological quality) formally assessed using appropriate criteria?         Were efforts made to minimise error in risk of bias assessment?         Concerns regarding methods used to collect data and appraise studies: LOW, HIGH, UNCLEAR	Y Y Y Y Y Low	Y Y Y Y Y Low	Y Y Y Y Y Low	Y Y Y Y NI Low	Y Y Y Y NI Low	Y Y Y Y NI Low
Domain 3: Data collection and study appraisal         Were efforts made to minimise error in data collection?         Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?         Were all relevant study results collected for use in the synthesis?         Was risk of bias (or methodological quality) formally assessed using appropriate criteria?         Were efforts made to minimise error in risk of bias assessment?         Concerns regarding methods used to collect data and appraise studies: LOW, HIGH, UNCLEAR         Domain 4: Synthesis and findings	Y Y Y Y Y Low	Y Y Y Y Y Low	Y Y Y Y Y Low	Y Y Y Y NI Low	Y Y Y Y NI Low	Y Y Y Y NI Low
Domain 3: Data collection and study appraisal         Were efforts made to minimise error in data collection?         Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?         Were all relevant study results collected for use in the synthesis?         Was risk of bias (or methodological quality) formally assessed using appropriate criteria?         Were efforts made to minimise error in risk of bias assessment?         Concerns regarding methods used to collect data and appraise studies: LOW, HIGH, UNCLEAR         Domain 4: Synthesis and findings         Did the synthesis include all studies that it should?	Y Y Y Y Y Low PY	Y Y Y Y Y Low PY	Y Y Y Y Low PY	Y Y Y Y NI Low PY	Y Y Y Y NI Low PY	Y Y Y Y NI Low PY

Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies?	Y	Y	Y	Y	Y	Y
Was between-study variation (heterogeneity) minimal or addressed in the synthesis?	Y	Ν	PY	Ν	Ν	PY
Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?	Y	N	PY	Ν	N	NI
Were biases in primary studies minimal or addressed in the synthesis?	Y	Y	Y	Y	Y	Y
Concerns regarding the synthesis and finding: LOW, HIGH, UNCLEAR	Low	High	Unclear	High	High	Unclear
Risk of bias in the review						
Did the interpretation of findings address all of the concerns identified in Domains 1-4?	Y	Y	Y	Y	Y	Y
Was the relevance of identified studies to the review's research question appropriately considered?	Y	Y	Y	Y	Y	Y
Did the reviewers avoid emphasizing results on the basis of their statistical significance?	Y	Y	Y	Y	Y	Y
Overall risk of bias	Low risk	High risk	Unclear risk	High risk	High risk	Low risk

#### Table F-8. Results of included reviews by outcome domain – hypertension, omega-3 fatty acids

Review ID	Campbell 2013	Guo 2019	Radack 1989
ROBIS DOMAINS			
Answer code: Y=YES, PY=PROBABLY YES, PN=PROBABLY NO, N=NO, NI=NO INFORMATION			
Domain 1: Study eligibility criteria			
Did the review adhere to pre-defined objectives and eligibility criteria?	PY	PY	PY
Were the eligibility criteria appropriate for the review question?	Y	Y	Y
Were eligibility criteria unambiguous?	Y	Y	Y
Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?	Y	Y	Y

Were any restrictions in eligibility criteria based on sources of information appropriate (publication status or format, language, availability of data)?	Y	Y	Y
Concerns regarding specification of study eligibility criteria LOW, HIGH, UNCLEAR	Low	Low	Low
Domain 2: Identification and selection of studies			
Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?	Y	Y	Y
Were methods additional to database searching used to identify relevant reports?	Y	Y	Y
Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible?	Y	PY	PY
Were restrictions based on date, publication format, or language appropriate?	PN	Y	PN
Were efforts made to minimise error in selection of studies?	PY	NI	NI
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR	Unclear	Unclear	Unclear
Domain 3: Data collection and study appraisal			
Were efforts made to minimise error in data collection?	Y	NI	NI
Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?	Y	Y	Y
Were all relevant study results collected for use in the synthesis?	Y	Y	Y
Was risk of bias (or methodological quality) formally assessed using appropriate criteria?	Y	Y	Y
Were efforts made to minimise error in risk of bias assessment?	NI	NI	NI
Were efforts made to minimise error in risk of bias assessment? Concerns regarding methods used to collect data and appraise studies: LOW, HIGH, UNCLEAR	NI Low	NI	NI Unclear
Were efforts made to minimise error in risk of bias assessment?         Concerns regarding methods used to collect data and appraise studies: LOW, HIGH, UNCLEAR         Domain 4: Synthesis and findings	NI Low	NI	NI Unclear

Were all pre-defined analyses reported or departures explained?	Y	Y	Y
Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies?	Y	Y	Y
Was between-study variation (heterogeneity) minimal or addressed in the synthesis?	Y	Y	Y
Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?	Y	Y	РҮ
Were biases in primary studies minimal or addressed in the synthesis?	Y	Y	Y
Concerns regarding the synthesis and finding: LOW, HIGH, UNCLEAR	Low	Low	Low
Risk of bias in the review			
Did the interpretation of findings address all of the concerns identified in Domains 1-4?	Y	Y	Y
Was the relevance of identified studies to the review's research question appropriately considered?	Y	Y	Y
Did the reviewers avoid emphasizing results on the basis of their statistical significance?	Y	Y	Y
Overall risk of bias	Low risk	Low risk	Unclear risk

#### Table F-9. Results of included reviews by outcome domain – fibromyalgia, magnesium

Review ID	Holdcraft 2003	Porter 2010	Thorpe 2018
ROBIS DOMAINS			
Answer code: Y=YES, PY=PROBABLY YES, PN=PROBABLY NO, N=NO, NI=NO INFORMATION			
Domain 1: Study eligibility criteria			
Did the review adhere to pre-defined objectives and eligibility criteria?	РҮ	РҮ	Y
Were the eligibility criteria appropriate for the review question?	Y	Y	Y

Were eligibility criteria unambiguous?	PY	PY	Y
Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?	Y	Y	Y
Were any restrictions in eligibility criteria based on sources of information appropriate (publication status or format, language, availability of data)?	Y	Υ	Υ
Concerns regarding specification of study eligibility criteria LOW, HIGH, UNCLEAR	Low	Low	Low
Domain 2: Identification and selection of studies			
Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?	Y	Y	Y
Were methods additional to database searching used to identify relevant reports?	Y	Y	Y
Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible?	РҮ	PY	Y
Were restrictions based on date, publication format, or language appropriate?	NI	PN	Y
Were efforts made to minimise error in selection of studies?	N	Υ	Y
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR	Unclear	Unclear	Low
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR Domain 3: Data collection and study appraisal	Unclear	Unclear	Low
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR Domain 3: Data collection and study appraisal Were efforts made to minimise error in data collection?	Unclear NI	Unclear PY	Low Y
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR Domain 3: Data collection and study appraisal Were efforts made to minimise error in data collection? Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?	Unclear NI N	Unclear PY N	Low Y Y
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR Domain 3: Data collection and study appraisal Were efforts made to minimise error in data collection? Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? Were all relevant study results collected for use in the synthesis?	Unclear NI N Y	Unclear PY N N	Low Y Y Y
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR Domain 3: Data collection and study appraisal Were efforts made to minimise error in data collection? Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? Were all relevant study results collected for use in the synthesis? Was risk of bias (or methodological quality) formally assessed using appropriate criteria?	Unclear NI N Y Y	Unclear PY N N Y	Low Y Y Y Y Y
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR Domain 3: Data collection and study appraisal Were efforts made to minimise error in data collection? Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? Were all relevant study results collected for use in the synthesis? Was risk of bias (or methodological quality) formally assessed using appropriate criteria? Were efforts made to minimise error in risk of bias assessment?	Unclear NI N Y Y NI	Unclear PY N N Y PY	Low Y Y Y Y Y Y
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR Domain 3: Data collection and study appraisal Were efforts made to minimise error in data collection? Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? Were all relevant study results collected for use in the synthesis? Was risk of bias (or methodological quality) formally assessed using appropriate criteria? Were efforts made to minimise error in risk of bias assessment? Concerns regarding methods used to collect data and appraise studies: LOW, HIGH, UNCLEAR	Unclear       Unclear       NI       N       Y       Y       NI       High	Unclear PY N N Y PY High	Low Y Y Y Y Y Y Low
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR Domain 3: Data collection and study appraisal Were efforts made to minimise error in data collection? Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? Were all relevant study results collected for use in the synthesis? Was risk of bias (or methodological quality) formally assessed using appropriate criteria? Were efforts made to minimise error in risk of bias assessment? Concerns regarding methods used to collect data and appraise studies: LOW, HIGH, UNCLEAR Domain 4: Synthesis and findings	Unclear NI NI Y Y NI High	Unclear PY N N Y PY High	Low Y Y Y Y Y Low Low

Were all pre-defined analyses reported or departures explained?	РҮ	PY	Y
Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies?	Υ	Υ	Υ
Was between-study variation (heterogeneity) minimal or addressed in the synthesis?	PY	PY	PY
Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?	NI	NI	NI
Were biases in primary studies minimal or addressed in the synthesis?	Υ	Y	Y
Concerns regarding the synthesis and finding: LOW, HIGH, UNCLEAR	Unclear	Unclear	Unclear
Risk of bias in the review			
Did the interpretation of findings address all of the concerns identified in Domains 1-4?	Υ	Y	Y
Was the relevance of identified studies to the review's research question appropriately considered?	Υ	Y	Y
Did the reviewers avoid emphasizing results on the basis of their statistical significance?	Υ	Y	Y
Overall risk of bias	High risk	High risk	Low risk

Table F-10. Results of included reviews by outcome domain – recurrent infection/s (including urinary tract infections, cystitis, respiratory tract infection, otitis media in children), zinc

Review ID	Gulani 2014	Hurley 2020	Manikam 2016
ROBIS DOMAINS			
Answer code: Y=YES, PY=PROBABLY YES, PN=PROBABLY NO, N=NO, NI=NO INFORMATION			
Domain 1: Study eligibility criteria			
Did the review adhere to pre-defined objectives and eligibility criteria?	Y	Y	Y
Were the eligibility criteria appropriate for the review question?	Y	Y	Y
Were eligibility criteria unambiguous?	Y	Y	Y

Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?	Y	Y	Y
Were any restrictions in eligibility criteria based on sources of information appropriate (publication status or format, language, availability of data)?	Y	Y	Y
Concerns regarding specification of study eligibility criteria LOW, HIGH, UNCLEAR	Low	Low	Low
Domain 2: Identification and selection of studies			
Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?	Y	Y	Y
Were methods additional to database searching used to identify relevant reports?	Y	Y	Y
Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible?	Y	Y	Y
Were restrictions based on date, publication format, or language appropriate?	Y	Y	Y
Were efforts made to minimise error in selection of studies?	Y	Y	Y
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR	Low	Low	Low
Domain 3: Data collection and study appraisal			
Were efforts made to minimise error in data collection?	Y	Y	PY
Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?	Y	Y	Y
Were all relevant study results collected for use in the synthesis?	Y	Y	Y
Was risk of bias (or methodological quality) formally assessed using appropriate criteria?	Y	Y	Y
Were efforts made to minimise error in risk of bias assessment?	Y	Y	Y
Concerns regarding methods used to collect data and appraise studies: LOW, HIGH, UNCLEAR	Low	Low	Low
Domain 4: Synthesis and findings			
Did the synthesis include all studies that it should?	PY	PY	PY
Were all pre-defined analyses reported or departures explained?	Y	Y	Y

Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies?	Y	Y	Y	
Was between-study variation (heterogeneity) minimal or addressed in the synthesis?	PY	PY	NI	
Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?	NI	NI	NI	
Were biases in primary studies minimal or addressed in the synthesis?	Y	Y	Y	
Concerns regarding the synthesis and finding: LOW, HIGH, UNCLEAR	Unclear	Unclear	Unclear	
Risk of bias in the review				
Did the interpretation of findings address all of the concerns identified in Domains 1-4?	Y	Y	Y	
Was the relevance of identified studies to the review's research question appropriately considered?	Y	Y	Y	
Did the reviewers avoid emphasizing results on the basis of their statistical significance?	Y	Y	Y	
Overall risk of bias	Low risk	Low risk	Unclear risk	

Table F-11. Results of included reviews by outcome domain – diabetes (Type II) (including metabolic syndrome), antioxidants (specifically coq10 and alphalipoic acid)

Review ID	Araújo 2022	Dludla 2020	Dludla 2023	Huang 2018	Huo 2022	Jibril 2022	Kim 2022	Rhimlou 2019	Wang 2022	Zhang 2018
ROBIS DOMAINS										
Answer code: Y=YES, PY=PROBABLY YES, PN=PROBABLY NO, N=NO, NI=NO INFORMATION										
Domain 1: Study eligibility criteria										
Did the review adhere to pre-defined objectives and eligibility criteria?	Y	Y	Y	PY	PY	Y	Y	Y	PY	Y
Were the eligibility criteria appropriate for the review question?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were eligibility criteria unambiguous?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were any restrictions in eligibility criteria based on sources of information appropriate (publication status or format, language, availability of data)?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Concerns regarding specification of study eligibility criteria LOW, HIGH, UNCLEAR	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Domain 2: Identification and selection of studies										
Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were methods additional to database searching used to identify relevant reports?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible?	Y	PY	PY	PY	PY	Y	Y	Y	PY	Y
Were restrictions based on date, publication format, or language appropriate?	Y	Y	NI	PN	NI	PN	Y	Y	PN	Y
Were efforts made to minimise error in selection of studies?	Y	Y	NI	NI	Y	Y	Y	Y	Y	Y
Concerns regarding methods used to identify and/or select studies: LOW, HIGH, UNCLEAR	Low	Low	Unclear	Unclear	Low	Unclear	Low	Low	Unclear	Low
Domain 3: Data collection and study appraisal										
Were efforts made to minimise error in data collection?	Y	Y	NI	NI	Y	Y	Y	NI	NI	Y
Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were all relevant study results collected for use in the synthesis?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was risk of bias (or methodological quality) formally assessed using appropriate criteria?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Were efforts made to minimise error in risk of bias assessment?	Y	Y	NI	Y	Y	Y	Y	NI	NI	Y
Concerns regarding methods used to collect data and appraise studies: LOW, HIGH, UNCLEAR	Low	Low	Unclear	Low	Low	Low	Low	Unclear	Unclear	Low
Domain 4: Synthesis and findings										
Did the synthesis include all studies that it should?	PY	PY	PY	PY	PY	PY	PY	PY	PY	PY
Were all pre-defined analyses reported or departures explained?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was between-study variation (heterogeneity) minimal or addressed in the synthesis?	PY	Y	NI	Y	PY	PY	Y	PY	PY	PN

Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?	PY	Y	NI	Y	Y	Y	Y	Y	ΡY	PN
Were biases in primary studies minimal or addressed in the synthesis?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Concerns regarding the synthesis and finding: LOW, HIGH, UNCLEAR	Low	Low	Unclear	Low	Low	Low	Low	Low	Low	High
Risk of bias in the review										
Did the interpretation of findings address all of the concerns identified in Domains 1-4?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Was the relevance of identified studies to the review's research question appropriately considered?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Did the reviewers avoid emphasizing results on the basis of their statistical significance?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Overall risk of bias	Low risk	Low risk	Unclear risk	Low risk	Unclear risk	High risk				

## Appendix G Differences between protocol and overview

#### G1 Methods not implemented

#### G1.1 Types of reviews

#### 1. Criteria for considering reviews for this overview - Review is up to date

This criterion was listed in the protocol as "Additional primary studies which may impact conclusions of the systematic review are not available. This will be confirmed by searching MEDLINE from the date of final search in the systematic review". Per "inclusion of supplemental primary studies" deviation, given the volume of primary studies across all included PICOs, this was determined as not feasible. The impact of potentially more recent primary studies than the included systematic review are noted in limitations of the overview.

#### 2. Criteria for considering reviews for this overview - Best practice methods are used

This criterion was listed in the protocol as "Appropriate methodologies and risk of bias tools must be used". When conducting screening and assessment of studies, this criterion was considered vague and potentially excluding reviews which could be used with the concerns addressed in the overview. The concerns about methodological rigour of the included reviews were addressed with ROBIS and in GRADE assessments.

#### G1.2 Types of participants, interventions comparators and outcomes

#### 3. Primary study overlap.

We had listed in the protocol that the degree of overlap would be addressed using corrected covered area. In completing the overview, we determined this was no longer necessary considering results were reported from one systematic review only for each PICO. Therefore, for any particular comparison and outcome, there was not overlap in primary studies.

#### G1.3 Review selection

#### 4. Inclusion of supplemental primary studies.

The protocol allowed for inclusion of supplementary studies where a population-supplement pair was not adequately covered by a preferred systematic review. Four pairings were not covered by any relevant review: magnesium for stress (perceived, occupational), cruciferous indoles for dysmenorrhea, cruciferous indoles for premenstrual syndrome (PMS), and magnesium for arthritis/osteoarthritis. However, the protocol for inclusion of supplemental primary studies was not followed due to the volume of primary studies needed for conclusions amounting to completing a full systematic review for each population-supplement pair. This is based on guidance in the Cochrane Handbook.

#### 5. Incompletely reported results in SRs - Contacting systematic review authors

Where there were incompletely reported results in systematic reviews (either meta-analysis or primary studies), review authors were not contacted as intended in the protocol. Where results were not reported adequately (e.g. no effect estimates or confidence intervals, no information about inconsistency (such as a forest plot displaying effect estimates for individual studies) or no heterogeneity statistics), this was considered in GRADE assessments.

#### 6. Addressing discrepant data from systematic reviews

As only one systematic review for each PICO was presented (i.e. the most comprehensive and/or highest quality), addressing discrepant data across included systematic reviews was not necessary.

#### 7. Requests for data – conference abstracts

It was intended that authors of eligible systematic reviews only available as conference abstracts were to be contacted through an open-ended request for data or further information. However, no non-published potentially relevant conference abstracts were found.

#### G1.4 Data collection

#### 8. PRISMA versus PRIOR flow diagram

We had intended to present information on the review selection process as a PRIOR flow diagram (3), however found a PRSIMA diagram for each population-supplement pair more informative and necessary given fifteen separate searches were completed.

#### 9. Extraction of all reported outcomes for included reviews

Only prioritised outcomes were extracted and reported in "Results of included reviews" tables due to the volume of information being too high (many reviews with many outcomes), and it was determined that this information would not contribute greatly to findings/conclusions relevant to the overview's objective.

#### 10. Extraction of risk of bias assessments for non-preferred reviews

We had intended to extract risk of bias results for primary studies for all reviews, however given the volume of work and that this would not contribute to evidence evaluation, risk of bias assessments were not extracted for non-preferred reviews. This did not impact ROBIS assessments, as these were completed by reading and considering the entire article as published, rather than referring only to extracted information.

#### G1.5 Data analysis and synthesis

#### 11. Limitations of each review described in 'Characteristics of included reviews' tables

It was intended in the protocol that limitations of each systematic review (including a rationale for judgements with supporting information) would be described in the 'Characteristics of included reviews' table. This was not done due to the volume of included reviews, and ROBIS signalling questions are provided instead.

#### 12. Reporting of results - timepoints

The protocol specified that outcomes reported at different timepoints would be grouped and considered as short term, intermediate term, long term, or not specified. This was not completed due to issues in the reporting in many of the systematic reviews so that timepoints could not be accurately determined.

#### 13. Stratification of results by comparator

It was intended in the protocol that "where possible and appropriate, the analysis will stratify the evidence into comparator groups (placebo, usual care, active)". This was not done due to paucity of evidence.

#### G1.6 Risk of bias assessment

#### 14. Subgroup analyses

As part of the protocol, it was specified that subgroup analyses were not planned, however if there was inconsistency between effect estimates, subgroup analysis may be used to explore possible sources of heterogeneity. Given that no re-analysis was undertaken per the overview's methods, this was not completed. However, subgroup analyses conducted by preferred reviews was considered as part of the GRADE process.

# 15. Assessment of risk of bias of primary studies by the overview (if not completed as part of the review)

It was intended that where risk of bias was not reported on primary studies, an independent assessment of the risk of bias would be conducted. However, this was not necessary given the minimum quality criteria specified risk of bias assessment as required for inclusion of a review.

#### 16. ROBIS assessment judgements

We also stated in the protocol that a ROBIS assessment for each outcome for each priority population-supplement pair would be presented in the main report, however this was determined as not necessary as primary study risk of bias informed Summary of Findings and GRADE assessments.

### **G2** Clarifications from protocol

#### 1. Definition of "at-risk".

The definition of "at-risk" required clarification from the protocol as there are many interpretations of "at-risk populations". Results for populations "at-risk" were therefore only included if it was: (1) a specific population identified by the review authors to be at-risk, and therefore formed part of the research question in terms of prevention (e.g. pregnant people are at-risk of postnatal anxiety); and/or (2) preclinical conditions (e.g. people with pre-diabetes are at risk of diabetes). Conditions which were comorbid alone were excluded (e.g. hypertension and diabetes; fibromyalgia and CFS/ME).

#### 2. Definition of "recurrent" infection.

Many infections are at risk of recurrence (depending on their definition). To keep scope manageable, articles were only included if they were focused on prevention and treatment of relapse, reinfection, or recurrence of an infection (and not on initial infection that may reoccur). This had to be clearly specified in the review of interest.

#### 3. Inclusion of active comparators

There were some confusing statements in the protocol about inclusion or exclusion of active comparators. Active comparators were not included, as the overview was trying to determine the effect of chosen supplements with or without co-interventions, and not to compare against other interventions. Including active comparators would have made the analysis unmanageable in size. Eligible types of comparisons are listed in Appendix A3.4.

# Appendix H How comments from methodological review were addressed

Methodological review (or peer review) was conducted to appraise the methodological quality and assess the appropriateness of reporting for this overview (including appendices).

For reporting, the methodological review assessed the overview against the PRIOR Checklist (3) and where applicable, the MECIR (Methodological Expectations of Cochrane Intervention Reviews) manual (6).

The ROBIS (Risk of Bias in Systematic Reviews) tool was also used to assess the methodological quality of the overview, to ensure it was designed and conducted in accordance with:

- NHMRC's Developing your Guideline module in NHMRC's Guidelines for Guidelines Handbook
- Cochrane Handbook for Systematic Reviews of Interventions (updated 2022) Chapter on Overviews
- GRADE guidance and GRADE working group criteria for determining whether the GRADE approach was used (GRADE handbook).

The assessment included specification and application for considering systematic reviews for the overview, search methods, data extraction and analysis, assessment of risk of bias, assessment of the certainty of evidence using GRADE, and the interpretation and summary of findings.

The overview (including appendices) has been updated to reflect the amendments suggested by methodological review and NHMRC's Natural Therapies Working Committee, where appropriate. In summary, updates included additional information and/ or clarification of the Plain Language Summary, Executive Summary, Results sections and Appendices, including:

- Clarification of methods used, particularly regarding selecting preferred reviews
- Thresholds used for judging certainty of evidence
- Clarifying presentation of the results in the discussion.

A detailed record of responses to all comments indicating changes that were made was provided to NHMRC together with the amended Report and Appendices documents.

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