National Health and Medical Research Council

Whole system, multi-modal or single modal interventions delivered in the context of naturopathic practice, for preventing and treating health conditions

Evidence Evaluation

18 September 2023

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Report information

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Fodero L, Stathis S, Soh N. Whole system, multi-modal or single modal interventions delivered in the context of naturopathic practice, for preventing and treating health conditions. 2023

Dates

This evidence evaluation report and accompanying technical report received approval from the National Health and Medical Research Council (NHMRC) Natural Therapies Working Committee (NTWC) on 18 September 2023. The protocol for the evidence evaluation received approval from the NTWC on 8 June 2021 (PROSPERO: CRD42021266381).

Funding:

This review is funded by the Australian Government Department of Health and Aged Care via the NHMRC, under Official Order 2019-20P047.

Acknowledgements:

Thank you to members of the Department of Health and Aged Care'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. Practitioner Research and Collaboration Initiative (PRACI) data was provided by Dr Amie Steel, University of Technology (UTS), Sydney.

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

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

https://www.nhmrc.gov.au/about-us/leadership-and-governance/committees/natural-therapies-working-committee

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List of Abbreviations

ABS	Australian Bureau of Statistics
AIHW	Australian Institute of Health and Welfare
ARONAH	Australian Register of Naturopaths and Herbalists
AMED	Allied and Complementary Medicine Database
BAI	Beck Anxiety Inventory
BDI	Beck Depression Inventory
BMI	Body Mass Index
CABG	Coronary artery bypass graft
CENTRAL	Cochrane Central Register of Controlled Trials
COMET	Core Outcome Measures in Effectiveness Trials
CIM	complementary and integrative medicine
CINAHL	Cumulative Index of Nursing and Allied Health Literature
CM	Complementary medicine
CHD	Coronary heart disease
CNS	Central nervous system
CT	Computerised tomography
CVD	Cardiovascular disease

DMT	Disease modifying treatments
DSM	Diagnostic and Statistical Manual of Mental
EDSS	Expanded Disability Status Scale
FAI	free androgen index
FBG	Fasting blood glucose
FLIC	Functional Living Index Cancer
FSH	Follicle-stimulating hormone
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HRT	Hormone replacement therapy
ITT	intention to treat
LBP	Low back pain
LDL	Low density lipoprotein
LH	luteinizing hormone
MCID	Minimally clinically important difference
MD	Mean difference
MET	metabolic equivalent task
MFIS	Modified Fatigue Impact Scale
MI	Myocardial infarct
MRI	Magnetic resonance imaging
MS	Multiple sclerosis
MSFC	Multiple Sclerosis Functional Composite
MYMOP	Measure Yourself Medical Outcomes Profile
NHMRC	National Health and Medical Research Council
NHS	National Health Survey
NRSI	Non-randomised studies of interventions
NTREAP	Natural Therapies Review Expert Advisory Panel
NTWC	Natural Therapies Working Committee
OGTT	Oral glucose tolerance test
OR	Odds ratios
OIS	optimal information size
ONHMRC	Office of the National Health and Medical Research Council
PCOS	polycystic ovary syndrome
PASAT-3	Paced Auditory Serial Addition Test 3
PCOSQ	Polycystic Ovary Syndrome Questionnaire
PBRN	Practice-based research network
PCI	Percutaneous coronary intervention
PET	Positron emission tomography
PRACI	Practitioner Research and Collaboration Initiative
QOL	Quality of life
QUICKI	Quantitative Insulin Sensitivity Check Index
RCT	Randomised controlled trials
ROB	Risk of bias
RoB2	Revised Cochrane risk of bias tool for randomised control trials
ROBINS-I	Risk of bias of non-randomised studies of interventions
SHBG	sex hormone-binding globulin
SPADI	Shoulder Pain and Disability Index
STAI	State Trait Anxiety Inventory
T2DM	type 2 diabetes mellitus
TSH	Thyroid-stimulating hormone
UTS	University of Technology
VAS	Visual Analogue Scale

Plain Language Summary

What was the aim of the review?

The aim of this review was to identify eligible studies and assess whether they demonstrate that whole-system naturopathy (referred to as 'naturopathy') is effective in preventing and/or treating injuries, diseases, medical conditions or pre-clinical conditions. Naturopathy is a system of healthcare that uses several natural therapy modalities or 'tools of the trade' used by naturopaths to treat patients, including herbal medicine and nutritional medicine. This review was intended to inform decisions by the Australian Government Department of Health and Aged Care about whether certain natural therapies, including naturopathy, have enough evidence of effectiveness to be considered re-eligible for private health insurance rebates. This review was not intended to inform decisions about whether an individual should use naturopathy or a practitioner practise naturopathy.

Key messages

For the populations (or conditions) assessed, naturopathy appears to provide people with some benefit for some of the conditions and outcomes assessed in this review, when compared with people who do not use naturopathy. The evidence assessed in this review provides low certainty and more studies on naturopathy are needed to confirm the findings.

What was studied in this review?

This review identified studies using a planned literature search, with no limit on publication date. Included studies needed to compare the results of people who received naturopathy to a group of people who did not and assess naturopathic practice that included at least one core modality or 'tool of the trade' used by naturopaths (e.g. western herbal medicine, nutritional medicine etc.), consistent with how naturopathy is practised in Australia. Studies were excluded if their treatments were not delivered by a naturopath or in a naturopathic context or if they were "single-arm", meaning all participants received the same treatment and a comparator group (a group that did not receive the treatment) was absent. Assessment of cost effectiveness, safety and studies of healthy populations were not included in this review. Studies published in a language other than English were listed, but not included in the assessment.

Studies were assessed for certainty using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) framework. GRADE is a method to assess how confident (or certain) systematic review authors can be that the results reported in studies (estimates of effect) are accurate. Statements about the evidence are written in two parts, the first tells the reader what the certainty is, the second tells the reader the size of an effect. The certainty is described as either:

- high certainty – meaning the authors have a lot of confidence that the true effect is similar to the estimated effect.
- moderate certainty – meaning that the true effect is probably close to the estimated effect
- low certainty – meaning the true effect might be markedly different from the estimated effect
- very low certainty - meaning the true effect is probably markedly different from the estimated effect

What studies did we identify in this review?

Using a planned approach, 5,887 studies from six databases were collected and examined, as well as 437 studies submitted by the public via the Department of Health and Aged Care's public call for evidence.

Out of these, 16 studies covering 14 populations were assessed in the evidence evaluation and are included in the results. A further nine studies were in languages other than English and 36 studies had been registered as ongoing but not published at the time of the search. Of the registered ongoing studies 9 were listed as complete (but without available data), 20 studies were not recruiting participants and 5 were recruiting participants; one study was cancelled.

What were the main results of the review?

The evidence provides low certainty that naturopathy is more effective than not using naturopathy for some outcomes in people with polycystic ovarian syndrome. The evidence also provides low certainty that naturopathy has little (to no) benefit for some of the conditions assessed in this review. For most of the conditions and outcomes assessed in this review the effect of naturopathy is very uncertain or unknown.

The evidence provides low certainty that naturopathy is effective in:

- improving quality of life and menstrual regularity in people with polycystic ovary syndrome (PCOS) (one study, 122 participants). Participants received a lifestyle intervention, consultations with a qualified naturopath and herbal supplements.

The evidence provides low certainty that naturopathy has little (to no) effect on:

- cognitive impairment in people with multiple sclerosis (one study, 30 participants). Participants received naturopathic treatment plus usual care, which included visits with a naturopath, daily supplementation with multivitamins and minerals, fish oils and alpha-lipoic acid, intramuscular vitamin B12 and dietary intervention.
- cardiovascular risk factors (i.e. risk of heart attack, LDL cholesterol levels), prevalence of metabolic syndrome and impact on severity of type II diabetes (i.e. blood sugar levels) in people at risk of cardiovascular disease (one study, 246 participants). Participants received naturopathic care plus enhanced usual care, which included visits with a naturopath, individualised naturopathic treatments, diet and lifestyle recommendations and natural dietary supplements.

The evidence provides very low certainty of the effect of naturopathy on many of the prioritised outcomes for colon cancer, prostate cancer, type II diabetes, PCOS, overweight and obesity, anxiety, multiple sclerosis, cardiovascular disease, allergic rhinitis, low back pain, rotator cuff tendinitis and menopause.

Of the populations (conditions) identified in this review, the effect of naturopathy for 44 outcomes considered critical or important by the Natural Therapies Working Committee (NTWC) remain unknown, as no studies were found that assessed these outcomes.

Implications for health policy and research

This review assesses the evidence for certain conditions and groups of people to inform the Australian Government about health policy decisions for private health insurance rebates. This review does not cover all the reasons that people use naturopathy, or the reasons practitioners prescribe naturopathic treatments and is not intended to inform decisions about whether an individual should use naturopathy or a practitioner practise naturopathy.

The results of this review indicate that naturopathy may improve some conditions and outcomes and not others. However, these conclusions are based on a small number of studies with limited numbers of participants, with results across studies often imprecise and patient-relevant outcomes often not reported. Given naturopathy is a system of healthcare made up of individual treatments modalities, the evidence base is likely to focus on single treatments (such as herbal medicine and nutritional medicine). This review included studies which assessed single treatments when given in the context of naturopathic practice; however, did not assess these treatments when given in isolation. It is likely that the available evidence for whole-system naturopathic treatment is limited due to it being a system of health care and not an individual treatment.

Future research could be improved by undertaking more studies of whole-system naturopathy versus control (i.e. usual care) which include more participants and measure outcomes that are considered critical or important for decision-making.

In considering the evidence on the overall effectiveness of naturopathy, this review will be accompanied by two companion evidence reviews which will assess the main treatments or 'tools of the trade' used by naturopaths. The two companion reviews include (1) an overview of systematic reviews that will assess the clinical effectiveness of selected nutritional supplements for certain conditions/ populations (PROSPERO CRD42023410906) and (2) an overview of systematic reviews that will assess the clinical effectiveness of western herbal medicines for certain conditions and populations (PROSPERO CRD42021243337).

How up to date is the review?

Searches were conducted from the earliest date included in the databases until 6 July 2021. Studies published after this date are not included in this review.

Executive Summary

Background

Naturopathy has been defined by the World Naturopathic Federation as a system of healthcare with a deep history of traditional philosophies, utilising several natural therapy modalities, such as herbal medicine and nutritional medicine, to treat patients.[1] It is used by populations to either prevent health conditions or to treat, manage or delay the progression of existing health conditions.

In 2015, an overview of systematic reviews of naturopathy, as a health service, conducted for the Australian Government found no reliable evidence demonstrating its effectiveness in treating any clinical condition. The current review includes a broader range of study types, including randomised controlled trials and non-randomised studies of interventions. The review assesses the effectiveness of naturopathy as a whole-system treatment, including single and multi-modality treatments given in the context of naturopathic practice and delivered in a range of settings relevant to the practice of naturopathy in Australia.

Objectives

The objective of this review was to evaluate the effectiveness of naturopathy (whole system, multi-modal or single modal treatments delivered in the context of naturopathic practice) in individuals with a described injury, disease, medical condition, or preclinical condition, including primary prevention in at-risk individuals, on outcomes that align with the reasons why people commonly utilise naturopathy in Australia.This information will be used by the Australian Government to inform its decision about whether to reinclude naturopathy as eligible for private health insurance rebates after naturopathy was excluded in 2019. This review was not designed to include all the reasons that people use naturopathy, or the reasons practitioners practise naturopathy and was not intended to inform decisions about whether an individual should use naturopathy or a practitioner practise naturopathy.

Search methods

Literature searches were conducted in Medline, Embase, CENTRAL, CINAHL, and AMED to identify relevant studies published up to 6 July 2021. The public were also invited by the Department to submit references for published evidence. There were no limitations on language or date of publication in the search.

Selection criteria

Randomised controlled trials and non-randomised studies that examined whole system multi-modal or single modal interventions, delivered in the context of naturopathic practice and compared to control or another intervention, were eligible for inclusion. Quasi-randomised studies, as well as cluster-randomised or crossover trials, were also eligible. To be eligible, the naturopathic treatment needed to include at least one of the modalities central to naturopathy in Australia i.e. herbal medicine, complementary medicine prescription (e.g. nutritional supplements), dietary or lifestyle advice and be delivered in the context of naturopathic practice. Single modalities not central to naturopathic practice in Australia were excluded, except when incorporated within a multi-modal naturopathy treatment applicable to naturopathy in Australia. There were no limits on the setting in which the naturopathic intervention was delivered, the intensity, or the frequency. Studies were excluded if their interventions were not delivered by a naturopath or in the naturopathic context or if they were single-arm without a contemporaneous comparator group.

The search included studies of people of any age with any injury, disease, medical condition, or preclinical condition. Studies examining naturopathy for individual at-risk participants, but not studies assessing at-risk populations in general, were also eligible for inclusion.

The search was not restricted by comparators, noting that the evidence was stratified into two comparisons, (i) control (inclusive of no intervention, waitlist, or usual care if considered inactive) and (ii) other (inclusive of active comparators). Outcomes were not part of the eligibility criteria and were not included in the search terms but were prioritised as described below. Studies were not excluded based on country of origin, however studies published in a language other than English were not translated but were listed in an inventory for completeness.

Data collection and analysis and collection

After initial searching and screening and to determine what data to extract from studies, a blinded outcome prioritisation process was conducted by NTWC, with input from the Department of Health and Aged Care's Natural Therapies Review Expert Advisory Panel (NTREAP). Harms and cost effectiveness measures were out of scope.

At least two researchers collected data using data extraction forms, with the second researcher checking the forms for completeness and accuracy. Risk of Bias of the eligible studies was conducted using the most appropriate risk of bias assessment tool recommended by the Cochrane Collaboration (according to study type).

In the data analysis for each identified population, the overall certainty of evidence for a maximum of seven critical or important outcome domains were reported in GRADE summary of findings tables, with corresponding evidence statements assigned to each outcome. Data for reported outcomes at 'end of treatment' were assessed against a threshold such as minimal clinically important differences (MCID) or minimal important difference (MID) (where available). In instances where MCID were unavailable, effect estimates were assessed using a threshold of (1) small mean difference (MD <10% of the scale) (2) moderate (MD between 10% to 20% of the scale), or (3) large (MD more than 20% of the scale). If there were insufficient data to calculate effect sizes, a relative risk increase of 25% or more was used as a default threshold of appreciable harm or benefit.

Main results

A total of 16 studies covering 14 different populations (conditions) were identified as eligible for inclusion in this review. At the time of the search there were 9 studies awaiting classification (published in a language other than English) and 36 studies ongoing (registered but not published, more than half of these were listed as not recruiting).

All included studies examined naturopathy delivered in a manner that was considered applicable to the Australian context and included a large range of naturopathic treatment modalities and regimens. The treatment provider was usually reported as a naturopathic doctor or licensed naturopath (12 studies), with three studies not specifying the provider and one study reporting that the treatment was delivered by a doctor or diabetologist (doctor specialising in diabetes).

There were 14 studies covering 12 populations (conditions) that compared naturopathy with an inactive control (no intervention, wait list, or usual care) and two studies covering two populations which compared naturopathy to an active control.

Studies were assessed using the GRADE framework. GRADE combines information to assess how certain systematic review authors can be that the overall estimates of the effect (reported across a study/s for each critical or important outcome) are correct. High certainty means the authors have a lot of confidence that the true effect is similar to the estimated effect. Moderate

certainty means that the true effect is probably close to the estimated effect. Low certainty means the true effect might be markedly different from the estimated effect. Very low certainty means the true effect is probably markedly different from the estimated effect.

This review identified 14 populations (conditions) for which there was evidence about the effect of naturopathy on an outcome ranked critical or important by NTWC (with input from NTREAP). The evidence provides:

- **low certainty that naturopathy may result in:**
  - a moderate improvement in quality of life of people with polycystic ovary syndrome (PCOS) (one study, 122 participants)
  - a slight improvement in menstrual regularity in people with PCOS (one study, 122 participants)
- **low certainty that naturopathy results in little to no difference in:**
  - cognitive impairment in people with multiple sclerosis (one study, 30 participants)
  - cardiovascular risk factors (i.e. cardiovascular risk scores, LDL cholesterol levels), prevalence of metabolic syndrome and impact on severity of type II diabetes (i.e. HbA1c levels) in people at risk of cardiovascular disease (one study, 246 participants).

The evidence provides very low certainty of the effect of naturopathy on 51 prioritised outcomes for colon cancer, prostate cancer, type II diabetes, PCOS, overweight and obesity, anxiety, multiple sclerosis, cardiovascular disease, allergic rhinitis, low back pain, rotator cuff tendinitis and menopausal symptoms.

Of the populations (conditions) identified in this review, the effect of naturopathy on 44 outcomes considered critical or important by the NTWC remain unknown, as no studies were found that assessed these outcomes. An assessment of the harms/ adverse effects or cost effectiveness of naturopathy was out of scope for this review.

Limitations

This review is limited to studies which assess naturopathy as a whole-system treatment and did not assess individual treatment modalities or 'tools of the trade' (e.g. herbal medicines, nutritional supplements etc.) unless a study demonstrated that the individual (or combination) treatment modality was given in the context of naturopathic practice. The NTWC considered that the available evidence for naturopathy as a whole-system treatment is likely limited and has sought two companion reviews to accompany the totality of the evidence for naturopathy for Government decision making. The two companion reviews will assess the clinical effectiveness of certain nutritional supplements and western herbal medicines that are commonly utilised in naturopathic practice.

The outcomes assessed in this review were limited to those deemed critical or important by NTWC (with input from NTREAP) for each identified population or condition. All but one condition had no available evidence for some of the critical or important outcomes.

The populations and conditions were limited to one or two small studies, with participants ranging from 51 to 246 participants. The exception was one observational study with 922 participants, this study focussed on a post-operative naturopathic support of patients with cardiovascular disease.

Given the limited number of studies and the difficulties of assessing a whole-system treatment, it is challenging to conclude the effectiveness of naturopathy as a whole-system treatment for the populations and conditions identified in this review.

Conclusions

The evidence provides very low to low certainty that naturopathy as a whole-system treatment, is more effective than not using naturopathy for some of the conditions and outcomes assessed in this review. However, the evidence also provides low certainty that naturopathy as a whole-system treatment has little (to no) benefit on some of the conditions and outcomes assessed in this review. There are many conditions and outcomes assessed in this review where the effect of naturopathy is unknown.

The results of this review are generally consistent with other systematic reviews published up to July 2021, which conclude that there is an absence of high certainty evidence that using naturopathy as a whole-system treatment is more effective than not using naturopathy. More research is needed to reach a definitive conclusion on the effectiveness of naturopathy as a whole-system treatment for preventing and treating health conditions.

1. Background

NHMRC was engaged by the Department of Health and Aged care to update the evidence underpinning the 2015 Review of the Australian Government Rebate on Natural Therapies for Private Health Insurance. Following a decision to exclude 16 natural therapies from private health insurance rebates on 1 April 2019.

Naturopathy is one of the 16 natural therapies currently under review as part of the update. In 2015, an overview of systematic reviews assessing naturopathy as a health service found no reliable evidence demonstrating its efficacy in treating any clinical condition (refer to section 1.3).

This update will assess the clinical effectiveness of whole system, multi-modal, or single modal interventions delivered in the context of naturopathic practice and is designed to include a broader range of study types, including primary studies (i.e. randomised controlled trials and non-randomised studies of interventions). Further details regarding similarities and differences between this Review and the 2015 Review are described in Section 1.3.

In considering the evidence on the overall effectiveness of naturopathy, this review will be accompanied by two companion evidence reviews which will assess the main treatment modalities or 'tools of the trade' used by naturopaths. The two companion reviews include (1) an overview of systematic reviews that will assess the clinical effectiveness of selected nutritional supplements for certain conditions/ populations (PROSPERO CRD42023410906) and (2) an overview of systematic reviews that will assess the clinical effectiveness of western herbal medicines for certain conditions and populations (PROSPERO CRD42021243337).

1.1. Description of intervention

For the purposes of this Review, the interventions of interest are whole system, multi-modal or single modal interventions delivered in the context of naturopathic practice:

- **'Whole system'** in the context of naturopathy 'refers to the practice of naturopathy as a complex health care system that addresses simultaneously the multiple dimensions (physical, mental, spiritual, family, community, and environment) of an individual patient as pragmatically practised by naturopathic clinicians'.[3]
- **'Multi-modality'** refers to 'a minimum of two modalities as part of a single clinical approach to the treatment of an individual'.[3]
- **'Single modality'** refers to the individual modalities used by a naturopath.

Naturopathy can be defined as a system of healthcare with a deep history of traditional philosophies and principles, utilising several natural therapy modalities to treat patients.[1] A naturopath typically sees patients via consultation in private clinical practice. An initial consultation is usually between 60 – 120 minutes duration[5] with follow-up consultations about 30 - 60 minutes.[6] In a typical consultation a naturopath takes a detailed case history and performs physical examinations such as pulse and tongue diagnosis, iridology, and blood pressure.[5] A naturopath may also send a patient for laboratory testing (e.g. stool testing or pathology) to assist in determining a naturopathic diagnosis. Once a naturopathic diagnosis is confirmed, naturopaths usually develop a treatment plan using one or more modalities such as diet and lifestyle advice[5] or recommend other treatments like yoga and exercise.[6,7] Naturopaths also provide maintenance for long term health[8], with some clients requiring follow-up appointments to refine treatment plans or maintenance appointments for a few months for chronic or ongoing conditions.[9]

The core naturopathic philosophies, principles, and treatment modalities that form naturopathic practice and diagnosis are explained in more detail below.[10]

In Australia, 'Naturopathy' is not a regulated or registered profession. However, while not regulated, for naturopaths to obtain professional indemnity insurance, they need to be affiliated with a professional association. In recent years, naturopaths have developed an independent register for qualified naturopaths through the Australian Register of Naturopaths and Herbalists (ARONAH), which requires practitioners to meet competency standards and have a minimum qualification.[11] Typical naturopathic training involves a diploma or degree level qualification and some naturopathic organisations have minimum requirements in naturopathy such as an advanced diploma, a bachelor's degree, or another qualification in naturopathy or Western herbal medicine providing the practitioner can show evidence that they have been in regular practice in the last two to ten years.[12]

1.1.1. Description of the condition

This review is not limited by population and includes any population undertaking naturopathic treatment/s for prevention of health condition/s (in at-risk populations); or to treat, manage or delay the progression of existing health conditions.

Naturopaths treat a wide variety of conditions. The Practitioner Research and Collaboration Initiative (PRACI) which is the largest national practice-based research network (PBRN) for complementary healthcare (including naturopathy) in Australia,[13] has collected data on the most commonly self-reported conditions treated by naturopathic practitioners in Australia.

Conditions which more than 50% of naturopaths surveyed as "often seen" include:[13]

- Fatigue (95% of respondents)
- Digestive Disorders (84%)
- Mental illness (77%)
- Irritable bowel syndrome (67%)
- Menstrual disorders (61%)
- Insomnia/sleeping disorders (61%).

Conditions that were reported as "sometimes seen", by more than 50% of naturopaths surveyed, include:[13]

- Hay fever (64% or respondents)
- Eczema/Psoriasis (57%)
- Headache/migraine (57%)
- Recurrent infections (54%)
- Arthritis (51%).

1.1.2. Core philosophies

Two core naturopathic philosophies are holism and vitalism. Holism refers to the 'whole' being greater than the sum of its 'parts'. In naturopathic practice, to treat 'holistically' means treating both a health condition/ disease and an individual as a 'whole,' not in isolation and considers both internal (disease process) and external (environmental, social, cultural) factors that may contribute to the health of an individual.

Vitalism refers to the theory that every living organism has an innate 'vital force' or natural wisdom. To treat a condition using a 'vitalistic' approach is to encourage the body's natural ability to heal itself, rather than suppressing or masking symptoms (e.g. encouraging a fever, rather than suppressing it).[10,14]

1.1.3. Principles

Traditional principles form the basis of naturopathic practice.[14,15] These principles include: first, do no harm (primum non nocere), (supporting the) healing power of nature (vis medicatrixnaturae), treat the cause (not just the symptoms) (tollecausam), treat the whole person (rather than individual disease) (tolletotum), doctor as teacher (to educate the patient) (docere), disease prevention and health promotion, and wellness or wellbeing. [10,15]

1.1.4. Theories

The theories are concepts that have been incorporated into the principles of naturopathic practice (e.g. treat the whole person) or which are used to guide naturopathic practice (e.g. value of a fever).[10] According to the World Naturopathic Federation, key theories that underlie naturopathic practice include:[10]

(1) Vital Force and Theory of Vitality – synonymous with the naturopathic philosophy of vitalism.

(2) Integration of the Individual – aligns with the naturopathic principle of treating the whole person.

(3) Naturopathic Cures – refers to the therapeutic concept of detoxification (e.g. fasting), revitalisation (e.g. in the form of mental therapy such as yoga), stabilisation (of an individual's health (e.g. through lymphatic drainage), and regeneration (e.g. in the form of mental therapy such as counselling).

(4) Value of a Fever – based on the understanding that fever helps the body fight an infection and helps the body to heal itself.

(5) Therapeutic Order – refers to the recommendation that naturopathic treatment is best applied in a certain order to resolve a patient's symptoms and address them with the least potential for damage.

(6) Naturopathic Triad of Health – represented in the principle of 'treating the whole person' by addressing mind, body, and spirit.

(7) Unity of Disease – all disorders can be traced back to three primary manifestations, namely: lowered vitality, abnormal composition of blood and lymph, and accumulation of waste materials, morbid matter, and poisons.

(8) Hering's Law of Cure – stipulates the direction in which symptoms are cured: from the inside out, from the head down, from most important to least important organs, in reverse order of how they first appeared.

(9) Theory of Toxaemia – the main cause of disease is the accumulation of toxins (harmful materials or chemicals) from, for example, too much stress or eating too much of the wrong foods.

(10) Emunctory Theory – elimination of toxins from the body is vital to achieving optimal health.

(11) Humoral Theory – spans all aspects of the naturopathic therapeutic encounter, including assessment, diagnosis, and treatment.

These philosophies, principles, and theories focus on the treatment and prevention of conditions, and promotion of health through naturopathic treatment modalities.

1.1.5. Modalities

In Australia, the most commonly prescribed modalities in naturopathic clinical practice include nutritional medicine (e.g. nutraceuticals and supplements), dietary and lifestyle counselling, and

herbal medicine prescription.[15,16] Some naturopaths also use homeopathy and manual therapies (e.g. massage) as part of their practice. Naturopaths also report prescribing other interventions; such as meditation, yoga, and exercise to support their patients.[10,13]

In a recent survey,[13] Australian naturopathic practitioners reported that the most common modalities they use in their interventions are:

(1) lifestyle modifications (98% of practitioners)
(2) dietary modifications (90%)
(3) herbal medicine (90%)
(4) meditation (88%)
(5) exercise prescription (83%)
(6) yoga (75%)
(7) nutritional supplementation (65%)
(8) homeopathy (36%).

1.2. How the intervention might work

Naturopathic treatment often uses multi-modal interventions such as herbal medicine, nutritional supplementation, diet, and lifestyle modifications in combination with other supporting modalities, for example, homeopathy and manual therapies.[16] Some research suggests that the aforementioned whole system, multi-modal or single modal interventions delivered in the context of naturopathic practice can improve health outcomes and improve quality of life (QOL) in patients with chronic conditions or who are at-risk of chronic conditions such as cardiovascular disease (CVD), chronic pain, type 2 diabetes mellitus (T2DM) and/or anxiety.[3,4] Some interventions delivered or prescribed by naturopaths aim to improve patient's diet or lifestyle (e.g. exercise prescription, reducing intake of sugary or processed foods), with the health benefits of physical activity and a healthy diet are well-documented in the scientific literature.[17]

According to the Australian Burden of Disease Study in 2015, 7.3% of the total burden of disease was due to poor diet while physical inactivity contributed to 2.5% of the total burden.[18] Using CVD as an example, dietary risks contribute 40.2% of the total burden of disease, while alcohol use contributed 3.6%, tobacco use 11.5%, and physical inactivity 8.0%.[18] However, the risk factors contributing to the burden of disease are not additive and have been described as having a 'joint effect', given the complex interactions between them.[18] Australian naturopaths may apply dietary advice and help develop a healthier diet based on the evidence-based Australian Dietary Guidelines[17] to improve a patient's risk of CVD or other chronic conditions,[17,19] among counselling for other lifestyle modalities. Given the synergistic effect of smoking, poor diet, and physical inactivity on chronic conditions,[17,19] adhering to lifestyle advice for these modalities may therefore have a synergistic effect on improving health.

The way naturopathy is practised may also enhance the effects of the naturopathic modalities administered or prescribed by the practitioner. Benefits of naturopathic practice may arise from the practitioner-patient relationship.[16] For example, compared to family physicians, naturopaths practise with relatively longer consultation times with their clients.[20] This may enhance communication which in turn enhances adherence to therapeutic advice, including advice on lifestyle factors, although additional consultation time alone does not directly result in improved care.[21] However, longer consultation times may allow a naturopath to assess more of a patient's issues than a family physician can in a shorter consultation, which could influence patient-practitioner interactions.[20]

Although Zolnierek (2009) did not investigate naturopathic practitioners, their meta-analysis reported good physician communication is associated with greater patient adherence to treatment. The rationale is that open communication and shared beliefs elicit clinical and psychosocial

information from clients. Good communication also enables client involvement in decision-making and the discussion of benefits, risks, and barriers to treatment adherence, and develops rapport, trust, and encouragement with clients.[16,22] To further illustrate the relationship between communication and treatment adherence, clients of complementary medicine (CM) practitioners (which also encompass naturopathic practitioners) in Australia reported elements that helped change their health behaviour included the practitioner teaching them what to do, monitoring their progress, providing encouragement and directing them to information and resources they could use independently[23] All of these are components of good clinician communication. The most frequently reported health behaviour changes made by clients of CM practitioners in Australia were the lifestyle changes of improved diet and increased exercise.[23] As stated in Section 1.1.5, dietary advice was also the most common treatment provided by naturopathic practitioners, followed by Western herbal medicine, lifestyle advice, and exercise advice.[24] Thus, where there is adherence to behavioural change advice (dietary, lifestyle, and exercise advice), there may be resulting health benefits.

1.3. Why it is important to do this review

Australia has one of the highest rates of CM practitioner use among developed countries and naturopathy is one of the most popular forms of CM.[14,25] The number of naturopathic consultations exceeds 4.9 million annually.[14] However, naturopathic practice has been accused of lacking an evidence base.[14,26] Naturopathy is not regulated in Australia (i.e. it is self-regulated) which means any individual can currently practice naturopathy with or without appropriate training.[15,27] Further research into the effects of naturopathic practice and regulations, as practised in Australia, is required.[15] Hence, this Review will identify and evaluate the evidence for the clinical effectiveness of whole system, multi-modal or single modal interventions delivered in the context of naturopathic practice. The Review will inform the Australian Government's decisions about private health insurance rebates for natural therapies.

Previously, the Australasian Cochrane Centre, Monash University was commissioned by the NHMRC to conduct an overview of systematic reviews to synthesise the effectiveness of naturopathy as a health service.[2] The overview, which was finalised in 2015, was part of the 'Review of the Australian Government Rebate on Private Health Insurance for Natural Therapies'. It considered systematic reviews published between 2008 and May 2013. It identified one unpublished systematic review of whole system naturopathic medicine in chronic conditions, which was later published (Oberg, 2015). Of the 13 studies included in the unpublished systematic review, six were randomised controlled trials (RCTs), which were further assessed. These studies evaluated the effectiveness of naturopathic practice in CVD, multiple sclerosis (MS), anxiety, and musculoskeletal pain. The primary outcomes included measures of pain, QOL, anxiety, and CVD risk. The quality of the evidence was assessed by Cochrane as very low, and the overview authors noted among the limitations that studies were restricted to those conducted in North America. The overview authors concluded that while there was some evidence to suggest naturopathy as a health service improved patient health for several chronic health conditions, they urged caution given the differences in naturopathic practice, training, and accreditation between North America and Australia.[2]

The 2015 overview did not include individual modal therapies used in naturopathic practice.[2] The Department of Health's Natural Therapies Review Advisory Committee[28] noted that the authors may have missed systematic reviews that were published as grey literature, as searching was restricted to bibliographic databases. While the 2015 overview did not apply language restrictions in its search, its inclusion criteria limited studies to the English language only. The unpublished systematic review it identified had itself restricted languages to English, Spanish and French, in view of its North American focus.

This Review aims to evaluate and synthesise the evidence for the effectiveness of whole system, multi-modal or single modal interventions delivered in the context of naturopathic practice. In contrast with the 2015 overview, this Review evaluates primary evidence from RCTs and non-randomised studies of interventions (NRSIs) and includes the most common (single) modalities of a therapy administered in the context of naturopathic practice. There is no restriction on date of studies.

2. Objectives

The main objective of this Review is to assess the effectiveness of whole system, multi-modal or single modal interventions delivered in the context of naturopathic practice for preventing, managing, treating, and/ or delaying the progression of health conditions in people with a clinical condition, pre-clinical condition or at-risk of illness or injury.

3. Summary of methods

Methods reported in this systematic review align, where possible, with the those described in the *Cochrane Handbook of Systematic Reviews of Interventions.* Screening, selection and data extraction of citations was conducted using Rayyan (https://www.rayyan.ai/). We intended to use RevMan 5.3 for the main analyses, however meta-analyses could not be performed for studies identified for any of the prioritised outcomes (see Appendix B.3.4). GRADE methodology was used to produce the summary of findings tables and overall certainty of the evidence for each identified population and prioritised outcome, using GRADEPro GDT software (www.gradepro.org).

Population and conditions identified in eligible studies were ordered by the International Classification of Disease (ICD-11) categories. Up to seven critical and important outcomes were prioritised per identified population to inform data synthesis for the systematic review. Outcomes were prioritised by NTWC (with input from NTREAP) using a blinded process; in which NTWC was not aware of the number of studies identified per population, nor characteristics of included studies, such as study design, number of participants or quality (See Appendix A.4.5). In deciding up to seven critical or important outcomes, NTWC applied principles outlined by the GRADE framework (see Appendix A.4.5).

Using appropriate risk of bias tools (see Appendix B.1.1) for RCTs and NRSIs, risk of bias was assessed across all identified populations and conditions and where possible for the primary outcome of the study. Where usable data was identified, data was extracted into data tables and results summarised.

Summary of findings tables were developed for studies which compared naturopathy to an eligible comparator of interest (see Appendix A.4.4) for outcomes considered critical or important by NTWC. Findings from RCTs and NRSI are presented separately in each summary of findings table. The certainty of the evidence, along with reasons for downgrading, are presented for each outcome per table. The tables were generated using GRADEPro software.

The research protocol and methods for this Review was registered with PROSPERO (CRD42021266381) on 8 June 2021.

Further details about methods and criteria for considering studies for this review are outlined in Appendix A to Appendix D of the technical report. The following appendices outline:

- Appendix A.4.1 – Types of studies
- Appendix A.4.2 – Types of participants
- Appendix A.4.3 –Types of interventions
- Appendix A.4.4 – Types of comparators
- Appendix A.4.5 – Types of outcome measures
- Appendix B – Data appraisal, extraction, analysis, and reporting for included studies
- Appendix C – Excluded studies
- Appendix D – Details of Included studies including risk of bias.

4. Results

4.1. Literature search results

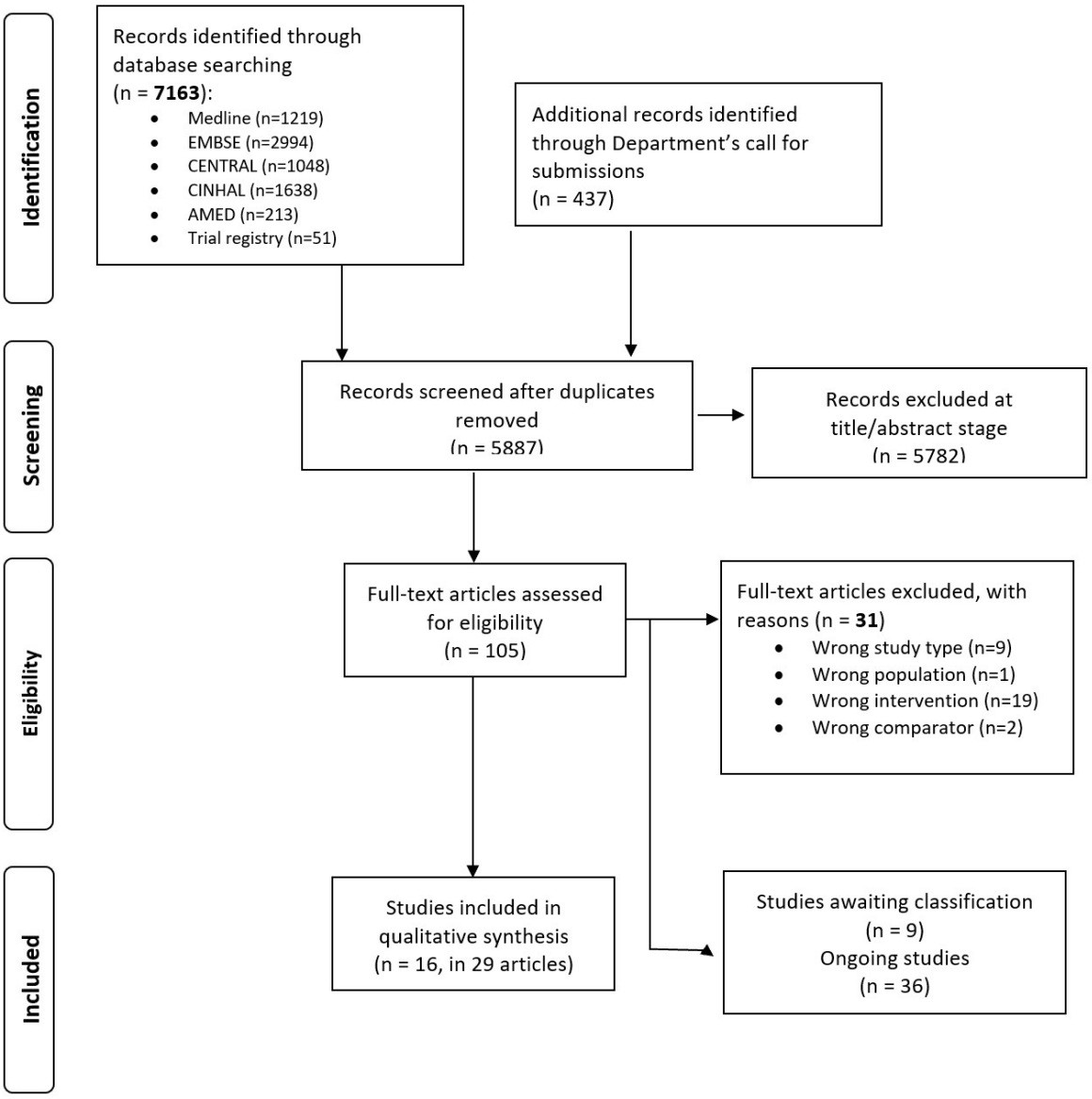
The search retrieved 7,600 citations, including 437 provided by the Department of Health and Aged Care's public call for evidence. After removing duplicates, 5,887 unique citations were screened by title and abstract including 378 entries from the public call for evidence. A total of 105 full-text citations were retrieved for screening by full text. Screening at full text identified 30 publications that were excluded for not matching inclusion criteria for study type, population, intervention, comparator or outcomes (see Appendix C *Excluded Studies*). Studies awaiting classification included 9 in languages other than English (see Appendix C.3) and 36 ongoing studies (see Appendix C.4). If an NRSI is assessed as being at critical risk of bias in any one domain, its details were to be recorded in the characteristics of included studies tables and the reason for critical risk of bias rating documented, but it would not be further assessed and would not contribute to data synthesis. As there were a limited number of studies, no meta-analyses for data synthesis were conducted.

Twenty-nine publications for 16 studies were included in this review (see Appendix D) with 14 populations and conditions identified. Erratum (or retraction) were reviewed to confirm that the included studies were still eligible for inclusion in this review (see Appendix A.1.2.).

The search and screening results are presented in a PRISMA flow diagram at Figure 1.

A summary of studies identified in this review is provided at Table 1 *Summary of publications investigated in this review*. Appendix D to Appendix E provides detailed descriptions of studies, including the PICO criteria, risk of bias assessments of included studies and study results data.

Figure 1: PRISMA flowchart



Abbreviations: AMED, Allied and Complementary Medicine Database; CENTRAL, Cochrane Central Register of Controlled Trials; CINAHL, Cumulative Index to Nursing and Allied Health Literature

Table 1: Summary of publications investigated in this review

Condition groups [a]	Population	RCT	NRSI
Neoplasms	Breast cancer		✓
	Colon cancer	✓	
	Prostate cancer		✓
Endocrine, nutritional, or metabolic diseases	T2DM	✓	✓
	PCOS	✓	✓
	Overweight and obesity		✓
Mental, behavioural or neurodevelopmental disorders	Anxiety	✓	
Diseases of the nervous system	MS	✓	
Diseases of the circulatory system	CVD		✓
Diseases of the respiratory system	Allergic rhinitis	✓	
Musculoskeletal system conditions	Back pain	✓	
	Rotator cuff tendonitis	✓	
Genitourinary system conditions	Menopausal symptoms		✓
Other: Prevention of disease, injury, or illness in at-risk populations	CVD risk	✓ [b]	

Abbreviations: CVD = Cardiovascular disease; MS = Multiple sclerosis; PCOS = Polycystic ovarian syndrome; T2DM = Type 2 diabetes mellitus

a conditions are based on WHO ICD-11 for Mortality and Morbidity Statistics https://icd.who.int/browse11/l-m/en

b Two duplicate data sets with different first author studies were identified for this population

4.2. Breast cancer

4.2.1. Description of the condition

Breast cancer is abnormal growth of the cells lining the breast lobules or ducts. Symptoms include lumps, change in shape, discharge, dimpling or discomfort. Breast cancer diagnosis may include physical examination, mammogram, ultrasound and/or biopsy. Prognosis is determined by individual circumstances such as type of breast cancer (i.e. genetic or strong family history or unaffected[29]), test results, tumour growth rate, age, fitness and medical history.[30] In Australia, in 2021 there were an estimated 20,030 new cases with 3,138 deaths, with an incidence rate of 67.8 and mortality rate of 9.8 and per 100,000 persons (females and males).[31] Breast cancer is the most common cancer affecting Australian women.[32]

4.2.2. Description of studies

Andersen 2018, a NRSI matched longitudinal study in USA investigated 568 women, aged 42 to 65 years who were breast cancer survivors. Breast cancer survivors who did not and did choose to supplement their breast cancer treatment with naturopathy within two years of diagnosis participated. Participants were followed for 12 months, although data are only reported at baseline and 6 months; the majority were at stage I and stage II breast cancer.[33]

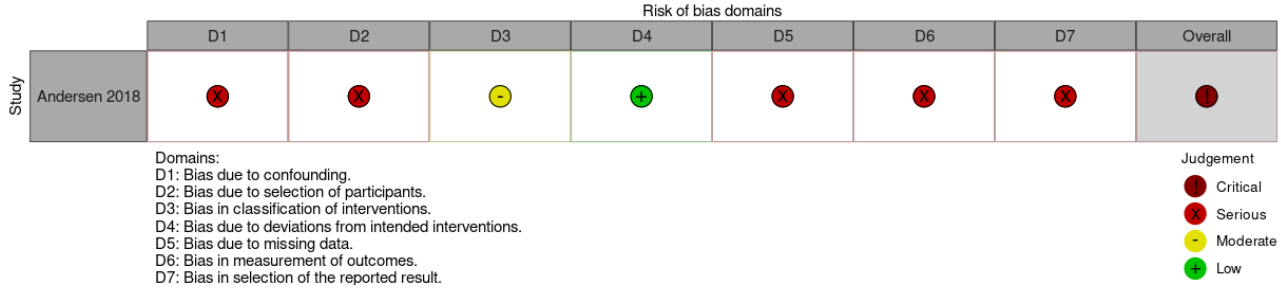
Andersen 2018 compared the effectiveness of naturopathic oncology (complementary and alternative medicine care) in participants recruited from naturopathic doctors' clinics against usual care (further details in Appendix D.1.).

4.2.3. Risk of bias

Risk of bias assessment for Andersen 2018 was assessed using ROBINS-I[34] for non-randomised studies of interventions, and overall was rated as 'critical' (see figure 2). As per the protocol methodology, given the study (NRSI) is assessed as being at critical risk of bias it was not assessed further and did not contribute to data synthesis.

Details of the risk of bias assessment are provided at Appendix D.2.2. Details of the study characteristics are provided at Appendix D1.1 and outcome data details are available at Appendix E1.2.

Figure 2: Andersen 2018 Risk of bias - SF-36



Abbreviations: SF-36=short form 36

Source: Risk of bias visual graphic performed in *McGuinness, LA, Higgins, JPT. Risk of bias VISualization (robvis): An R package and Shiny web app for visualizing risk of bias assessments. Res Syn Meth. 2020; 1- 7.* https://doi.org/10.1002/jrsm.1411

Note: All SF-36 domains have the same ROB score

The following outcomes were selected (in order of importance):

- quality of life
- fatigue
- pain
- physical function
- psychosocial function
- sleep
- cognitive function

4.3. Colon cancer

4.3.1. Description of the condition

Colon cancer is usually preceded by growths called polyps and develops in the lining of the bowel. Symptoms include change in bowel habits, change in appearance or bowel movement consistency, pain, blood in stool or urine, weight loss and fatigue. Colon cancer diagnosis may include blood tests, immunochemical faecal occult blood test, colonoscopy, flexible sigmoidoscopy, magnetic resonance imaging (MRI), computerised tomography (CT) and positron emission tomography (PET) scans. Prognosis is determined by individual circumstances such as type, stage of cancer, age and general health at the time of diagnosis.[37] In Australia, in 2021 there were an estimated 10,881 new cases of colon cancer with 1,220 deaths, with an incidence rate of 34.6 and mortality rate of 3.6 and per 100,000 persons.[31]

4.3.2. Description of studies

Raghunath 2020 conducted an RCT in India of 116 adult patients with a median age of 48 years who underwent surgery and adjuvant chemotherapy in the management of stage II and III adenocarcinoma of the colon. Confirmed medical diagnosis of adenocarcinoma of the colon was based on the American Joint Committee on Cancer and a National Cancer Institute and Prognostic criterion, belonging to both genders, between the age group of 18 and 65 years, 21 days from surgery without radiation with adequate renal and liver functions and Eastern Cooperative Oncology Group (ECOG) performance status − 0, 1, and 2. ECOG performance status 3 and 4, and stage IV colon cancer patients were excluded from the study. Recruitment was from the out-patient and in-patient departments of Basavatarakam Indo-American Cancer Hospital, Hyderabad. Haematological, biochemical and psychological evaluations were performed at set intervals during a total period of eighteen months starting from the first cycle of adjuvant chemotherapy.[38]

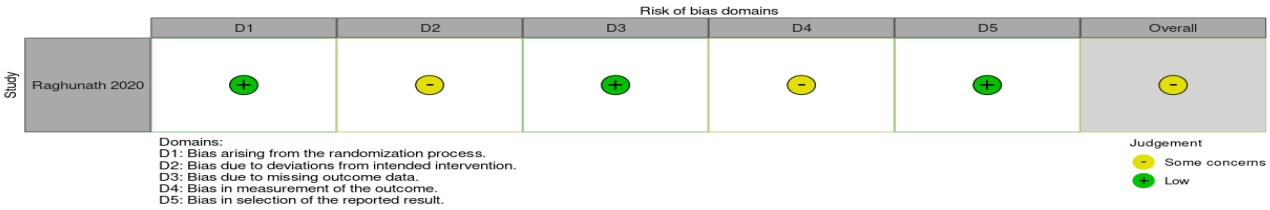
Raghunath 2020 compared the effectiveness of naturopathy (consisting of yoga, and dietary interventions) against usual care (psychosocial counselling). With both the intervention and control groups receiving adjuvant chemotherapy (further details in Appendix D.1.).

4.3.3. Risk of bias

Risk of bias for Raghunath 2020 was assessed using the RoB 2[39] tool for randomised controlled trials, and overall was rated as ‘some concerns’ (see Figures 3, 4 and 5) as participants were not blinded and the outcomes were measured by self-report methods. There were some concerns about deviations from intended interventions and in the measurement of outcomes, with the biases potentially favouring naturopathy.

Details of the risk of bias assessment are provided at Appendix D.2.2. Details of the study characteristics are provided at Appendix D1.2 and outcome data details are available at Appendix E1.1.

Figure 3: Raghunath 2020 Risk of bias – FLIC



Abbreviations: FLIC=Functional Living Index Cance

Source: Risk of bias visual graphic performed in *McGuinness, LA, Higgins, JPT. Risk of bias VISualization (robvis): An R package and Shiny web app for visualizing risk of bias assessments. Res Syn Meth. 2020; 1- 7.* https://doi.org/10.1002/jrsm.1411

4.3.4. Summary of findings

Table 2: Colon cancer summary of findings

Naturopathy compared to control (usual care or control) for colon cancer						
Patient or population: Colon cancer **Setting:** Cancer treatment centre **Intervention:** Naturopathy **Comparison:** Control (no intervention, usual care)						
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with control	Risk with Naturopathy				
Quality of life assessed with FLIC Scale 22-154 (higher is better) follow-up: 18 months	The mean quality of life was **82.54**	MD **7 points higher**; no CI	-	116 (1 RCT)	⊕◯◯◯ VERY LOW[a,b,c]	The evidence is very uncertain about the effect of Naturopathy on quality of life in people with colon cancer **
Adverse effects	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on adverse effects in people undergoing cancer treatment is unknown
Pain	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on pain in people undergoing cancer treatment is unknown
Fatigue	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on pain in people undergoing cancer treatment is unknown
Tumour progression	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on pain in people undergoing cancer treatment is unknown
Overall survival	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on pain in people undergoing cancer treatment is unknown

Naturopathy compared to control (usual care or control) for colon cancer

Patient or population: Colon cancer
Setting: Cancer treatment centre
Intervention: Naturopathy
Comparison: Control (no intervention, usual care)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with control	Risk with Naturopathy				

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
** The MCID in colon cancer is unknown. Using the FLIC scale a change score of ~ 5% is small #
***The MCID in people with colon cancer is unknown. An MCID of 10 for STAI is likely important.[40] A change score of ~ 40% is large #
****The MCID in people with colon cancer is unknown. A change of ~22% is large #

Effect estimates were considered on three levels: small (MD <10% of the scale), moderate (MD between 10% to 20% of the scale) or large (MD more than 20% of the scale).

BDI: Beck's Depression Inventory; **CI:** confidence interval; **FLIC:** Functional Living Index Cancer; **MCID:** Minimal clinically important difference; **MD:** Mean difference; **RCT:** Randomised controlled trial; **STAI:** State Trait Anxiety Inventory

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations
a. Downgraded one level for risk of bias: for risk of bias there were some concerns about deviations from intended interventions and in measurement of the outcome
b. Downgraded two level for imprecision: standard deviation (SD) and 95% confidence intervals were also not reported. The results could be compatible with appreciable benefit and little to no difference or possibly appreciable harm. Effect sizes calculated from scale were large in a small population
c. Inconsistency could not be assessed as only one study measured this outcome. No downgrading. Publication bias not suspected. No downgrading.

Forest plots could not be generated as the study did not report standard deviations or confidence intervals for their mean scores.

4.4. Prostate cancer

4.4.1. Description of the condition

Prostate cancer develops when prostate gland cells grow abnormally and form a tumour. Localised prostate cancer refers to cancer cells that have not spread beyond the prostrate, local advanced is where the cancer has spread to outside to nearby prostate parts and metastatic prostate cancer is where it has spread to distant body parts. Early prostate cancer is asymptomatic. Advanced prostate cancer symptoms include frequent, painful, or weak urination, pain in the back or weakness in legs. Prostate cancer diagnosis includes a prostate specific antigen blood test, rectal examination, biopsy or MRI, CT, or bone scans. Prognosis similar to breast and colon cancer is determined by type, test results, tumour growth, age, fitness, and medical history. Prostate cancer grows slowly and has a five year survival rate of 95%.[41] In Australia, in 2021 there were an estimated 18,110 new cases of prostate cancer with 3,323 deaths, an incidence rate of 55.9 and mortality rate of 9.5 and per 100,000 persons in Australia.[31]

4.4.2. Description of studies

Braun 2013 an NRSI retrospective study in USA investigated 134 men, aged 46 to 81 years who had undergone radiation therapy for localised adenocarcinoma of the prostate. All participants

received radiation therapy, while just over half (~57%) received hormone ablation therapy as well. All supplement-treated patients continued supplements for at least 24 months following the end of radiation therapy. Patients were stratified according to their pre-treatment Prostate-Specific Antigen (PSA) level as being of low (range 4–10 ng), intermediate (range 10–20 ng), or high risk (> 20 ng). The majority were low (~76%). Overall the majority were tumour staged 1 and 2; intervention group 83% and control group 78%.[42]

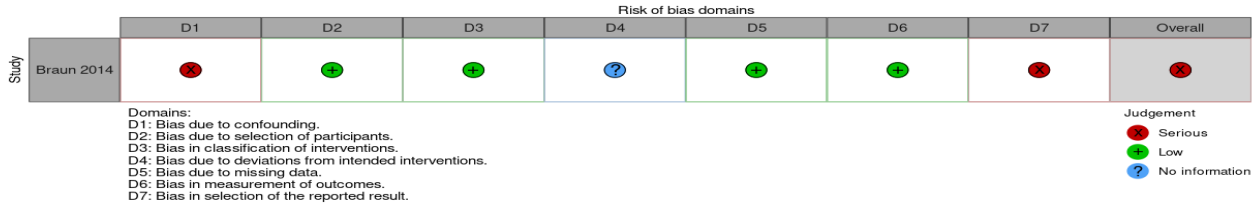
Braun 2013 compared the effectiveness of those who received naturopathic/nutritional antioxidant supplements (i.e. green tea extract, melatonin, vitamin C and vitamin E) against those who elected not to receive antioxidant treatment (further details in Appendix D.1.).

4.4.3. Risk of bias

Risk of bias for Braun 2013 was assessed using ROBINS-I[34] and overall was rated 'serious' (see Figure 6) due to confounding variables not being adjusted in PSA measures, there was a suggestion of selective reporting among multiple analyses, as all of the outcomes had both mean and median values and their statistical comparisons reported, but only median values were reported for time to reach PSA nadir.

Details of the risk of bias assessment are provided at Appendix D.2.2. Details of the study characteristics are provided at Appendix D1.3 and outcome data details are available at Appendix E1.2.

Figure 4: Braun 2013 Risk of bias – tumour progression



Abbreviations: ROBINS-I= Risk Of Bias In Non-randomised Studies of Interventions

Source: Risk of bias visual graphic performed in *McGuinness, LA, Higgins, JPT. Risk of bias VISualization (robvis): An R package and Shiny web app for visualizing risk of bias assessments. Res Syn Meth. 2020; 1- 7. https://doi.org/10.1002/jrsm.1411*

4.4.4. Summary of findings

Table 3: Prostate cancer summary of findings

Naturopathy compared to control (usual care or control) for prostate cancer						
Patient or population: Prostate cancer **Setting:** Cancer treatment centre **Intervention:** Naturopathy **Comparison:** Control (no intervention, usual care)						
Outcomes	Anticipated absolute effects* (95% CI)		Risk ratio** (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with control	Risk with Naturopathy				
Quality of Life	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on Quality of Life in people undergoing cancer treatment is unknown

Naturopathy compared to control (usual care or control) for prostate cancer

Patient or population: Prostate cancer
Setting: Cancer treatment centre
Intervention: Naturopathy
Comparison: Control (no intervention, usual care)

Outcomes	Anticipated absolute effects* (95% CI)		Risk ratio** (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with control	Risk with Naturopathy				
Adverse effects	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on adverse effects in people undergoing cancer treatment is unknown
Pain	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on pain in people undergoing cancer treatment is unknown
Fatigue	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on pain in people undergoing cancer treatment is unknown
Tumour progression (hormonal ablation) assessed with: % with biochemical failure (PSA >2ng/ml above PSA nadir) (lower is better) follow-up: range ≥24 months	5.3%	ARD **0.2% lower**, (CI not calculated for ARD)	RR 0.97 (0.14, 6.57)	77 (1 observational study)	⨁◯◯◯ VERY LOW a,b,c,d,	The evidence is very uncertain about the effect of naturopathy on tumour progression assessed by biochemical failure in men with prostate cancer**
Tumour progression (no hormonal ablation) assessed with: % with biochemical failure (PSA >2ng/ml above PSA nadir) (lower is better) follow-up: range ≥24 months	0%	ARD **3.3% higher**, CI not reported for ARD	RR 2.71 (0.12, 3.84)	57 (1 observational study)	⨁◯◯◯ VERY LOW a,b,c,d,	The evidence is very uncertain about the effect of naturopathy on tumour progression assessed with biochemical failure in men with prostate cancer ***
Overall survival	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on pain in people undergoing cancer treatment is unknown

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). The difference between the two groups is 3.1%
** The MCID in people with prostate cancer is unknown. A threshold of PSA >2ng/ml above PSA nadir is reported in Braun 2013.
*** The MCID in people with prostate cancer is unknown. A threshold of PSA >2ng/ml above PSA nadir is reported in Braun 2013.
# Effect estimates were considered on three levels: small (MD <10% of the scale), moderate (MD between 10% to 20% of the scale) or large (MD more than 20% of the scale).

ARD: Absolute risk difference; **CI:** confidence interval; **MCID:** Minimal clinically important difference; **MD:** Mean difference; **PSA**: Prostate-specific antigen; **RR:** Relative risk

Naturopathy compared to control (usual care or control) for prostate cancer						
Patient or population: Prostate cancer **Setting:** Cancer treatment centre **Intervention:** Naturopathy **Comparison:** Control (no intervention, usual care)						
Outcomes	Anticipated absolute effects* (95% CI)		Risk ratio** (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with control	Risk with Naturopathy				
GRADE Working Group grades of evidence **High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect. **Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. **Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect. **Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.						

Explanations

a. Downgraded two levels for risk of bias: for very serious risk of bias arising from unadjusted confounding and selective reporting of results from multiple analyses

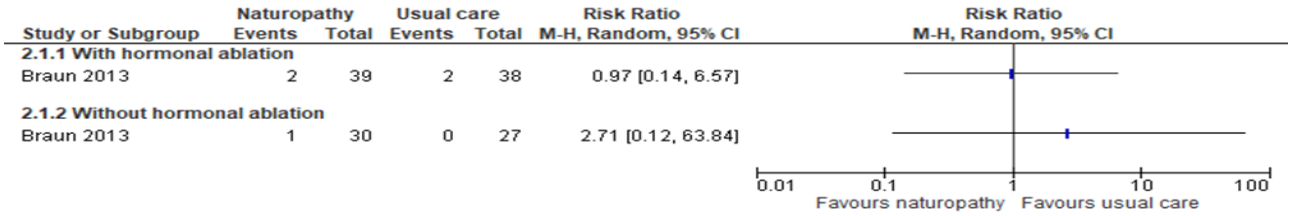
b. Downgraded one level for indirectness: PSA levels are not a direct measure of prostate cancer progression, they are a surrogate outcome

c. Downgraded two levels for imprecision: A confidence interval could not be calculated from the data reported in the study and therefore imprecision cannot be assessed. The results are compatible with appreciable benefit and little to no difference and appreciable harm. The sample size (77 and 57) and the event rate are low (4 and 1 event/s only, respectively). Naturopathy is trending towards being more harmful, higher chance of biomechanical failure in none ablated participants (ARD).

d. Inconsistency could not be assessed as only one study measured this outcome. No downgrading. Publication bias not suspected. No downgrading..

Figure 7 shows the forest plot comparing tumour progression in prostate cancer with biochemical failure (with and without hormonal ablation). Confidence intervals are wide and cross the line of no effect.

Figure 5: Prostate cancer forest plots



Abbreviations: M-H=Mantel-Haenszel

Note: Risk ratio and 95% confidence interval were calculated post-hoc for this Review by RevMan 5.3

% with biochemical failure (PSA >2ng/ml above PSA nadir)

4.5. Type 2 diabetes mellitus

4.5.1. Description of the condition

Type II diabetes (T2DM) is a metabolic condition where the body becomes resistant to insulin and loses capacity to produce enough insulin in the pancreas. T2DM may be asymptomatic, or include the following symptoms: excessive thirst, passing more urine, lethargy, hunger and delayed wound healing.[43] T2DM diagnosis includes the following blood tests: fasting blood glucose (FBG), glucose and haemoglobin joined together as 'glycated' haemoglobin (HbA1c)[44] or oral glucose tolerance test (OGTT).[45] Heart attacks, stroke, blindness, kidney failure and amputations are most threatening to long term prognosis of people with T2DM. T2DM complications can be reduced

through lifestyle modification (e.g. exercise and weight loss) and medication.[43] In 2020-2021 4.5% of people had T2DM diabetes in Australia.[46]

4.5.2. Description of studies

One NRSI (Bairy 2020)[47] and one RCT (Stier-Jarmer 2021)[48] were identified that assessed naturopathy for T2DM. Bairy 2020 is a prospective cohort study in India investigating 211 adults, aged 41 to 59 with a confirmed history of T2DM for the past 1 year or more, a HbA1c >7%, dependant on oral or parenteral hypoglycaemic agents and with Zubrod's performance status 0–2. The interventions were administered for three months, and participants followed for 12 months. Patients were stratified by those who agreed to undergo intensive residential naturopathy and yoga-based lifestyle intervention recruited as cases. Those who agreed to participate in the study but were not undergoing residential naturopathy and yoga intervention, were recruited as controls.

Stier-Jarmer 2021 conducted an RCT in Germany investigating 98 overweight and obese adults, mean age 62 years with T2DM. The naturopathy intervention was administered for three weeks and follow up reported at six months. Participants were 'randomly' allocated to naturopathy administered at a health resort in Munich, Germany or assigned to a control group, a diabetes friendly holiday.

Note: Stier-Jarmer 2021 is an abstract only and presented due to paucity of evidence for naturopathy and being a near completed study. [1] The German Clinical trials Registry report for this study is DRKS00010714 which provides trial description details.

Bairy 2020 compared the effectiveness of those who received an intensive residential naturopathy and yoga-based lifestyle intervention against those who did no. The 3-month residential naturopathy intervention program comprised of diet, yoga, hydriatic treatments, massage, and didactic and interactive lectures on lifestyle modification and T2DM self-management (further details in Appendix D.1.).

Stier-Jarmer 2021 compared the effectiveness of those who received 'Oberstaufen Schrothkur (a low-calorie diet and daily adjustments of low to high fluid intake, physical activity and cold damp body packs) carried out in the 'Oberstaufen' health resort against those who received a diabetes-friendly holiday, which was described as a holiday specifically tailored to diabetics, although no specific details were provided (further details in Appendix D.1.).

4.5.3. Risk of bias

Risk of bias of Bairy 2020[34] was assessed using ROBINS-I[34] and overall was rated as 'serious' due to potential confounders that may not have been controlled for. There was also a risk of selective reporting for body weight, as BMI was recorded according to the methodology but results were not presented (see Figure 8 and 9).

The risk of bias of Stier-Jarmer 2021[48] was assessed using RoB 2[39] and rated as 'high' due to outcome data only being available from the publication abstract and due to lack of information on whether the data were analysed by intention-to-treat or per-protocol methods. We were unable to obtain the full text for this RCT (See Figure).

Details of the risk of bias assessments are provided at Appendix D.3. Details of the study characteristics are provided at Appendix D1.4 and outcome data details are available at Appendix E.2.

[1] Authors *Stier-Jarmer M and Frisch D* were contacted 17 August 2021

Figure 6: Bairy 2020 Risk of bias - change in HbA1c

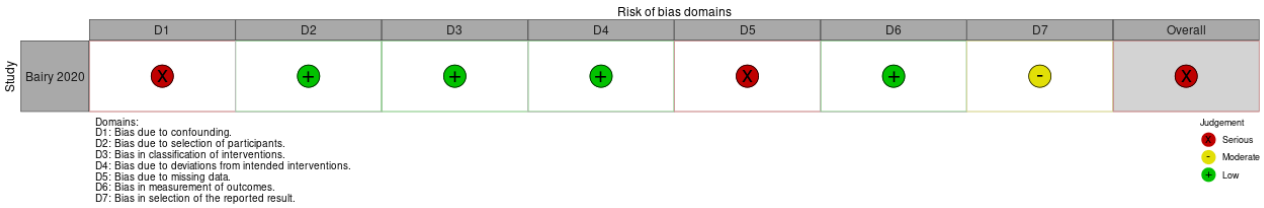


Figure 7: Bairy 2020 Risk of bias - change in body weight

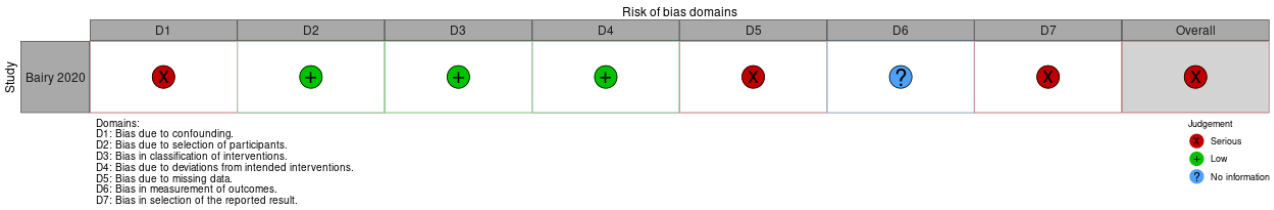
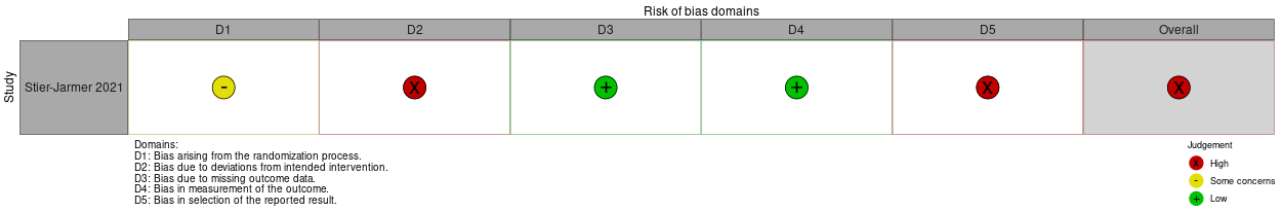


Figure 8: Stier-Jarmer 2021 Risk of bias - changes in HbA1c and body weight



Abbreviations: HbA1c=haemoglobin A1c

Source: Risk of bias visual graphic performed in *McGuinness, LA, Higgins, JPT. Risk of bias VISualization (robvis): An R package and Shiny web app for visualizing risk of bias assessments. Res Syn Meth. 2020; 1- 7.* https://doi.org/10.1002/jrsm.1411

4.5.4. Summary of findings

Table 4: T2DM summary of findings

Naturopathy compared to control (usual care or control) for type 2 diabetes mellitus						
Patient or population: Type 2 diabetes mellitus **Setting:** Health resort (RCT); residential naturopathy centre (NRSI) **Intervention:** Naturopathy **Comparison:** Control (active control, waitlist[1])						
Outcomes	**Anticipated absolute effects* (95% CI)**		Risk ratio (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with control	**Risk with Naturopathy**				
Glycaemic control assessed with: HbA1c (%) change from baseline (lower is better) follow-up: 12 months	The mean HbA1c was **0.5% points** (0.90 lower to 0.10 lower)	MD **0.60% points lower** (1.21 lower to 0.01 higher) ^	-	211 (1 observational study)	⨁◯◯◯ VERY LOW[a,b]	The evidence is very uncertain about the effect of Naturopathy on HbA1c in people with type 2 diabetes**

Naturopathy compared to control (usual care or control) for type 2 diabetes mellitus

Patient or population: Type 2 diabetes mellitus
Setting: Health resort (RCT); residential naturopathy centre (NRSI)
Intervention: Naturopathy
Comparison: Control (active control, waitlist[1])

Outcomes	Anticipated absolute effects* (95% CI)		Risk ratio (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with control	**Risk with Naturopathy**				
Glycaemic control assessed with: HbA1c (%)[2] change from baseline (lower is better) follow-up: 6 months	The mean HbA1c was **0.55% points** (0.93 lower to 0.40 lower)	MD **0.12% points lower** (0.46 lower to 0.22 higher) ^	-	106 (1 RCT)	⊕◯◯◯ VERY LOW[d,e]	The evidence is very uncertain about the effect of Naturopathy on HbA1c changes in people with type 2 diabetes **
Quality of life – not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on quality of life in people with type 2 diabetes is unknown
Cardiovascular measures – not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on cardiovascular measures in people with type 2 diabetes is unknown
Bodyweight assessed with: kg, change from baseline (lower is better) follow-up: 6 months	Mean changes in body weight from baseline to 6 months were not reported by the NRSI, only that there was a significant decrease in the naturopathy group. There was a significant difference between the groups for the mean change, but the magnitude and direction were not indicated. Data for changes from baseline to 12 months were not presented.		-	211 (1 observational study)	⊕◯◯◯ VERY LOW[a,c]	The evidence is very uncertain about the effect of naturopathy in bodyweight in people with type 2 diabetes***
Bodyweight assessed with: kg, change from baseline (lower is better) follow-up: 6 months	**The mean was 4.0 kg** (5.3 lower to 2.6 lower)	MD **0.76 kg lower** (2.38 lower to 1.02 higher) ^	-	106 (1 RCT)	⊕◯◯◯ VERY LOW[d,e]	The evidence is very uncertain about the effect of Naturopathy on bodyweight in people with type 2 diabetes***
Activities of daily living – not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on activities of daily living in people with type 2 diabetes is unknown
Adverse events– not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on adverse events in people with type 2 diabetes is unknown

Naturopathy compared to control (usual care or control) for type 2 diabetes mellitus

Patient or population: Type 2 diabetes mellitus
Setting: Health resort (RCT); residential naturopathy centre (NRSI)
Intervention: Naturopathy
Comparison: Control (active control, waitlist[1])

Outcomes	Anticipated absolute effects* (95% CI)		Risk ratio (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with control	Risk with Naturopathy				

* **The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
^ MD and 95% CI calculated post-hoc by RevMan 5.3

** The HbA1c MCID in people with type 2 diabetes is 0.3%. [49,50]
*** The weight decrease MCID in people with type 2 diabetes is 3kg.[51]

Effect estimates were considered on three levels: small (MD <10% of the scale), moderate (MD between 10% to 20% of the scale) or large (MD more than 20% of the scale).

1.Bairy 2020, NRSI, waitlist, recruited controls who did not take part in residential naturopathy/yoga intervention. Stier-James 2021 active control, recruited controls who participated in a 'diabetes holiday'
2.Stier-Jarmer 2021, RCT define HbA1c of 0.3% points as clinically relevant

CI: confidence interval; **HbA1c:** haemoglobin A1c; **kg:** kilogram; **MCID:** Minimal clinically important difference; **MD:** mean difference; **mITT:** modified intention to treat; **NRSI:** Non-randomised Studies of Interventions; **OIS**: optimal information size; **RCT:** Randomised controlled trial; **SAP:** statistical analysis plan; **T2DM:** Type 2 diabetes mellitus

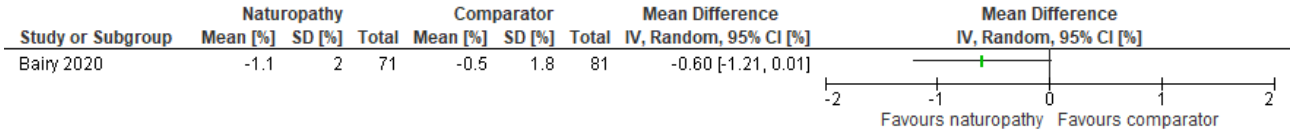
GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded two levels for risk of bias: due to confounding (unadjusted estimates; multivariate analyses were mentioned, although authors did not state which variables were adjusted); and missing outcome data (there was no reporting of weight at 12 months. Significant differences from baseline were presented, but not non-significant differences, and no means or standard deviations for any time point).
b. Downgraded one level for imprecision: due to few participants (n=211), few events and thus wide confidence intervals. Forest plot (see Figure 9 below) just cross the null, line of no effect, and appreciable harm, favouring both intervention and the comparator. Bairy 2020 HbA1c was clinically meaningful, see above**) and significant
c. Downgraded two levels for imprecision: narrative synthesis was conducted; estimates are not precise due to lack of effect sizes and confidence intervals
d. Downgraded two levels for risk of bias: due to from deviations from intended interventions (all participants were unblinded and treated in the same facility, with access to same facilities as control, therefore could deviate from intended intervention; mITT used but did not include participants that dropped out post randomisation) and selection of reported results (SAP not presented; trial registered retrospectively; 3-month data not reported; selected reporting of body weight outcomes)
e. Downgraded one level for imprecision: due to few participants (n=106), few events and thus wide confidence intervals (particularly for body weight at 6 months). Both forest plots (see Figure 12 and 13 below) cross the null, line of no effect and appreciable benefit and harm, favoring both intervention and comparator and are not clinically meaningful, see above**/***). The RCT is consistent with the NRSI (Bairy 2020) showing reduction in HbA1c at 6 months is greater in the naturopathy group than in the comparator group, although this was not statistically significant in the RCT (Stier-Jarmer 2021).

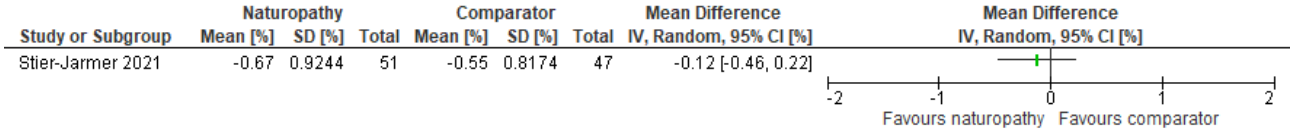
Figure 11 presents Bairy 2020, change in HbA1c from baseline to 12 months. Figure 12 presents Stier-Jarmer 2021, glycaemic control as assessed by HbA1c, from baseline to 6 months. Figure 13 presents Stier-Jarmer 2021, change in body weight from baseline to 6 months. All confidence intervals are wide and cross the line of no effect.

Figure 9: T2DSM forest plot – change in HbA1c from baseline to 12 months



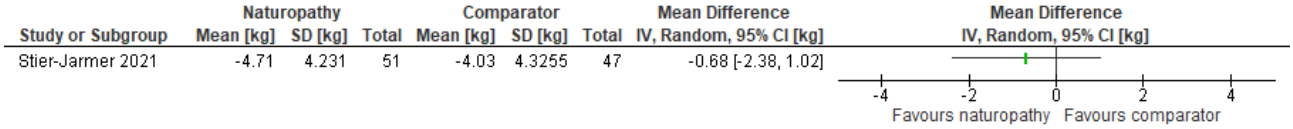
HbA1c (%) change from baseline (lower is better). Reference range 3.5% to 6.0% (Royal College of Pathologists Australasia https://www.rcpa.edu.au/Manuals/RCPA-Manual/Pathology-Tests)

Figure 10: T2DM forest plot – change in HbA1c from baseline to 6 months



HbA1c (%) change from baseline (lower is better). Reference range 3.5% to 6.0% (Royal College of Pathologists Australasia https://www.rcpa.edu.au/Manuals/RCPA-Manual/Pathology-Tests)

Figure 11: T2DM forest plot – change in body weight from baseline to 6 months



Body weight change from baseline (lower is better). No reference range.

Abbreviations: IV= Inverse variance; SD=Standard deviation; T2DM=Type 2 diabetes mellitus

Note: SDs of mean changes from baseline, mean differences between groups and 95% confidence intervals were calculated post-hoc for this review by RevMan.5.3

4.6. Polycystic ovarian syndrome

4.6.1. Description of the condition

Polycystic ovary syndrome (PCOS) is a hormonal condition. Symptoms include hirsutism (excess hair) acne, weight gain, abnormal menstrual cycle, infertility, insulin resistance, cardiovascular risk, and depression.[52] PCOS diagnosis is dependent on two of the three features: oligo/anovulation, hyperandrogenism and/or multiple cysts on ovaries by ultrasound, as per the Rotterdam criteria. Prognosis can be improved for woman with PCOS by treating symptoms with lifestyle modification (e.g. exercise and weight loss) and medication.[53] In Australia, PCOS is more prevalent in First Nations women with around 21% of First Nations women affected.[54] Overall, PCOS is estimated to affect 8–13% of reproductive age women.[54]

4.6.2. Description of studies

One RCT (Arentz 2017) [55] and one NRSI (Ratnakumari 2018)[56] were identified that assessed naturopathy for PCOS. Arentz 2017 conducted a parallel RCT in Australia that investigated 122 women, aged between 18 and 44 years with a confirmed medical diagnosis of PCOS according to the Rotterdam criteria (ESHRE, 2004) in overweight women (BMI≥24.5kg/m^2). The interventions

were administered for 3 months and stratified by BMI. Ratnakumari 2018, conducted an NRSI single-blinded prospective, pre-post clinical trial conducted in India, which investigated 50 PCOS patients aged between 18 and 35 years who satisfied the Rotterdam PCOS criteria.

Arentz 2017 compared the effectiveness of a lifestyle intervention plus herbal medicine (Cinnamomum verum, Glycyrrhiza glabra, Hypericum perforatum, Paeonia lactiflora and Tribulus terrestris) against lifestyle alone (further details in Appendix D.1).

Ratnakumari 2018 investigated the efficacy of yoga (asanas (yoga postures), pranayama, relaxation techniques, and kriyas and naturopathy (hydrotherapy, mud therapy, manipulative therapy, fasting, and natural diet therapy) for the management of PCOS observing the morphological changes, to a waitlist control group (further details in Appendix D.1).

4.6.3. Risk of bias

Risk of bias for Arentz 2017 was assessed using RoB 2[39] and overall was rated 'high' due to participants being aware of which group they were assigned (through self-reporting of quality of life measures), large effect size from a small sample size and selective reporting of results (i.e. mean days between menstrual periods) as oligomenorrhoea in the control group (106 days) is longer than the follow-up period (3 months ~90 days). For the subgroup analysis 'some concerns' were reported due to unblinded selective hormonal testing based on self-reported outcomes (wanting to conceive) and missing outcome data (see Figures 14 to 17).

Risk of bias for Ratnakumari 2018 was assessed using ROBINS-I[34] and rated as 'critical' due to confounding variables not adjusted for, wide inter quartile ranges were reported that provided information on distribution of effects, not the confidence in the estimate (see Figure 18). As per the protocol methodology, given the study (NRSI) is assessed as being at critical risk of bias it was not assessed further and did not contribute to data synthesis.

Details of the risk of bias assessments are provided at Appendix D.3. Details of the study characteristics are provided at Appendix D1.5 and outcome data details are available at Appendix E.2.

Figure 12: Arentz 2017 Risk of bias - Oligomenorrhoea

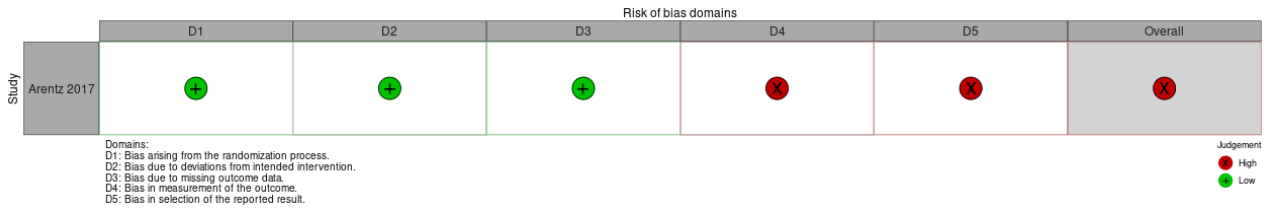


Figure 13: Arentz 2017 Risk of bias QOL - PCOSQ

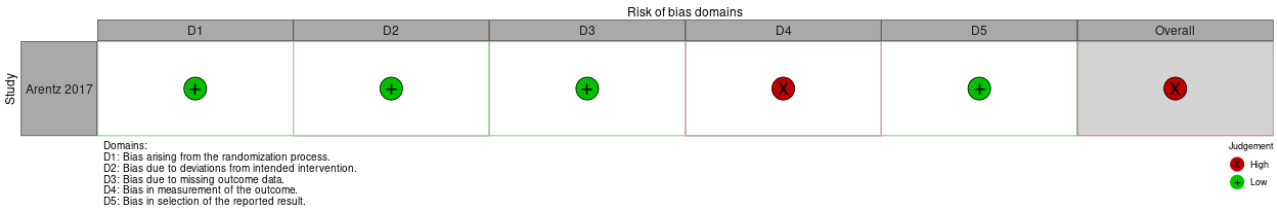


Figure 14: Arentz 2017 Risk of bias subgroup – QUICKI

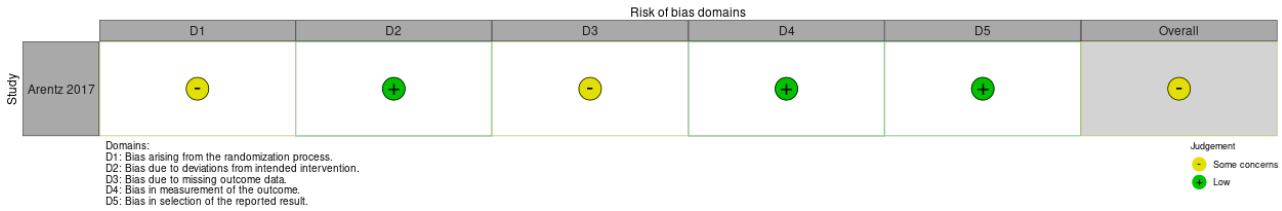
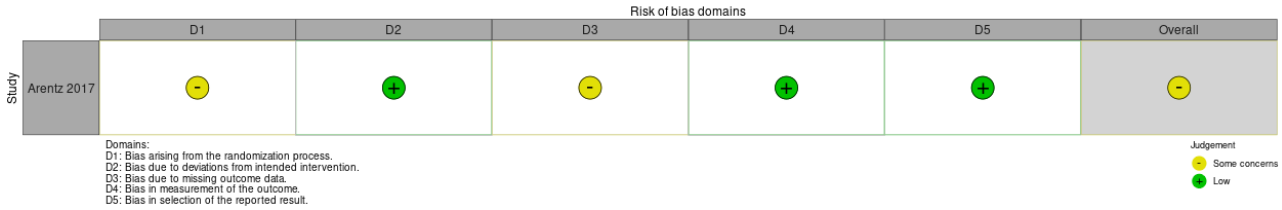


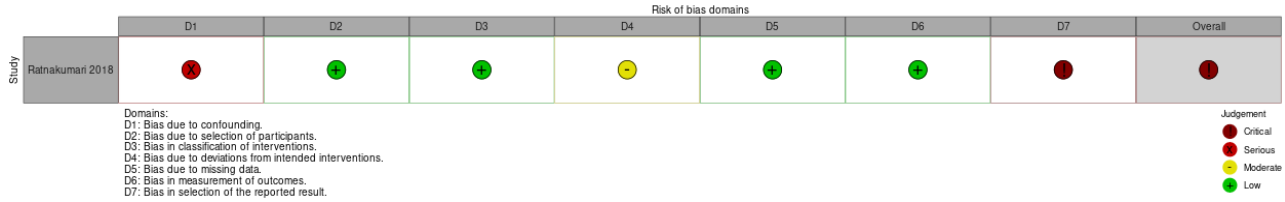
Figure 15: Arentz 2017 Risk of bias subgroup – Testosterone



Abbreviations: PCOSQ=Polycystic Ovary Syndrome Questionnaire; QUICKI=Quantitative Insulin Sensitivity Check Index;

Source: Risk of bias visual graphic performed in *McGuinness, LA, Higgins, JPT. Risk of bias VISualization (robvis): An R package and Shiny web app for visualizing risk of bias assessments. Res Syn Meth. 2020; 1- 7.* https://doi.org/10.1002/jrsm.1411

Figure 16: Ratnakumari 2018 Risk of bias – Oligomenorrhoea



Abbreviations: ROBINS-I= Risk Of Bias In Non-randomised Studies of Interventions

Source: Risk of bias visual graphic performed in *McGuinness, LA, Higgins, JPT. Risk of bias VISualization (robvis): An R package and Shiny web app for visualizing risk of bias assessments. Res Syn Meth. 2020; 1- 7.* https://doi.org/10.1002/jrsm.1411

4.6.4. Summary of findings

Table 5: PCOS summary of findings

Naturopathy compared to control (usual care or control) for PCOS						
Patient or population: PCOS **Setting:** Community **Intervention:** Naturopathy **Comparison:** Control (no intervention, usual care)						
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with control	Risk with naturopathy				
Menstrual regularity assessed with: No of days between menstrual periods (lower is better)[1] follow-up: 3 months	The mean number of days between menstrual periods was **106.6** days	Adjusted MD **42.9 days less** (64.8 lower to 21.1 lower)	-	122^ (1 RCT)	⊕⊕◯◯ LOW a,b	Naturopathy may result in a slight improvement in menstrual regularity**

Naturopathy compared to control (usual care or control) for PCOS

Patient or population: PCOS
Setting: Community
Intervention: Naturopathy
Comparison: Control (no intervention, usual care)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with control	Risk with naturopathy				
Quality of life assessed with: PCOSQ Scale: 25-182 (lower is better) Follow-up: 3 months[2]	The mean quality of life score was **109.3** points	Adjusted MD **31.1 points lower** (41.4 lower to 20.7 lower)	-	122^ (1 RCT)	⊕⊕◯◯ LOW c,d,e	Naturopathy may result in a moderate improvement in quality of life***
Metabolic indices/outcomes assessed with: QUICKI (higher is better) follow-up: 3 months	The mean QUICKI score was **0.32** points	Adjusted MD **0.002 points higher** (0.06 lower to 0.12 higher)[3]	-	51^ (1 RCT)	⊕◯◯◯ VERY LOW e,f,g	The evidence is very uncertain about the effect of naturopathy on insulin resistance ****
Pregnancy related measures and outcomes as measured by: Serum beta human chorionic gonadotropin (BHCG) concentration – Not reported	-	-	-	(0 studies)	-	No studies found that reported usable data. The effect of naturopathy on BHCG is unknown
Reproductive outcomes – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on reproductive outcomes is unknown
Reproductive hormonal profile assessed with: testosterone level (lower is better) Follow-up: 3 months	The mean testosterone level was **1.59** nmol/L	Adjusted MD **0.04 nmol/L lower** (0.33 lower to 0.25 higher)	-	71^ (1 RCT)	⊕◯◯◯ VERY LOW e,f,h	The evidence is very uncertain about the effect of naturopathy on testosterone levels*****
Abdominal endometrial proliferation (atypical hyperplasia and endometrial cancer) – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on abdominal proliferation is unknown

Naturopathy compared to control (usual care or control) for PCOS

Patient or population: PCOS
Setting: Community
Intervention: Naturopathy
Comparison: Control (no intervention, usual care)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with control	Risk with naturopathy				

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
** The MCID in people with PCOS is unknown. The norm is 28 days (21-40 days).[57] Oligomenorrhoea is greater than 35 days apart.[58]
*** Using the PCOSQ scale 25-182 (range of 157 points). A change score of ~19-20% is moderate #
**** QUICKI index ranges from 0.45 in healthy individuals to 0.30 in people with diabetes.[59]
*****Testosterone range is 0.3-1.8nmo/L[60]

^Outcomes were assessed by the one study, but were analysed by subgroup for QUICKI and testosterone outcomes.
Effect estimates were considered on three levels: small (MD <10% of the scale), moderate (MD between 10% and 20% of the scale) or large (MD than 20% of the scale).

1.Arentz 2017 define a normal cycle as 20-34 days (p.1334)

2.The PCOSQ was scored with lower scores indicative of better quality of life. This is the reverse of conventional scoring. Results are reported after adjustment for variation in baseline values

3. Log transformations were carried out on the data before analyses

4. All results are reported after adjustment for baseline values

BHCG: beta human chorionic gonadotropin; **CI**: Confidence interval; **MCID:** Minimal clinically important difference; **MD**: Mean difference; **PCOS**: Polycystic ovary syndrome; **PCOSQ:** Polycystic ovary Syndrome Questionnaire; **QUICKI**: Quantitative Insulin Sensitivity Check Index; **RCT:** Randomised controlled trial

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded one level for risk of bias: A large effect has been observed in a small study due to selective reporting bias as the mean days between menstrual periods in the control group (106 days) is longer than the follow-up period (3 months ~90 days)
b. Downgraded one level for imprecision: Lower CI ~21 days includes possible benefit; although 18% and 26%, intervention and control, respectively reported 'regular cycle' at baseline (25–34 days). Both the point estimate (~43 days) and the upper CI ~65 days are above the oligomenorrhoea threshold of 35 days apart
c. Downgraded one level for risk of bias: High risk of bias arising from self-reported measurement method
d. Downgraded one level for imprecision: It is presumed adjusted results were reported because it was not possible to present a CI for unadjusted. The 95% CIs are wide but upper and lower bounds both indicate a reduction that is potentially important, small and large, respectively. Using the PCOSQ scale 25-182 (range of 157 points), the point estimate change score of 19-20% is moderate#
e. Inconsistency could not be assessed as only one study measured this outcome. No downgrading
f. Downgraded two level for risk of bias: Due to inadequate randomisation on selection of subgroup for analysis; either 51 out of 122 were investigated i.e. less than half; or 71 out of 122 over half of participants
g. Downgraded one level for imprecision: The 95% CIs are wide; the lower CI represents insulin resistance, and the upper CI is just under the 0.45 healthy threshold
h. Downgraded one level for imprecision: Sample size is small subgroup of 71 participants; the point estimate (1.55nmo/L), lower (1.3nmo/L) and upper (1.88nmo/L) CIs are all grouped on and towards the upper limit of the range indicating worse disease.

Forest plots could not be generated as adjusted mean differences and their 95% confidence intervals were reported, but not the standard deviations, standard errors, or 95% confidence intervals of the mean values for the treatment groups.

4.7. Overweight and obesity

4.7.1. Description of the condition

Overweight and obesity is characterised by excess body weight that is a risk factor for chronic disease such as CVD, T2DM, high blood pressure, asthma, back pain, some cancers and a higher death rate. Overweight and obesity occurs because of an imbalance between energy intake, from the diet and energy expenditure, through physical activity. Overweight and obesity is classified by Body Mass Index (BMI). Waist circumference is an alternative to BMI to assess the risk of developing obesity related chronic disease. In 2017–2018, an estimated 67% of Australians aged 18 and over, were overweight (36%) or obese (31%) and 24% of children aged 5–14 and over, were overweight (17%) or obese (7%).[61]

4.7.2. Description of studies

One NRSI study was identified (Beer 2014) that assessed 275 overweight or obese adults, aged 44 to 65 years with naturopathy. Diagnosis was confirmed as overweight (BMI ≥ 25 kg/m^2) or obese (BMI ≥ 30 kg/m^2) as part of an inpatient naturopathic treatment to receive either fasting therapy or a weight reduction diet between 1999 and 2002. Follow up data was collected by telephone interview at an average of 6.8 years after the inpatient therapy.[62]

Beer 2014 compared the effectiveness of fasting (fluids for three days and exercise with the gradual return of solid foods after three days) with a weight reduction diet (low-fat wholefood caloric restricted weight reduction diet with exercise) delivered as inpatient naturopathic care (further details in Appendix D.1.).

4.7.3. Risk of bias

Risk of bias for Beer 2014 was assessed using ROBINS-I[34] and overall was rated 'serious' across all outcome domains. Due to non-measurement and no adjustment of potential confounding variables, participants were selected based on characteristics after the start of treatment, most outcome measurements were self-reported at the time of the telephone interview and without standardised questionnaires (i.e. subject to recall bias). Possible issues with selective reporting of weight and weight loss results where BMI was documented at baseline but not reported at other timepoints (Details of the risk of bias assessments are provided at Appendix D.3. Details of the study characteristics are provided at Appendix D1.6 and outcome data details are available at Appendix E.2. Figure 19 to 23).

Details of the risk of bias assessments are provided at Appendix D.3. Details of the study characteristics are provided at Appendix D1.6 and outcome data details are available at Appendix E.2.

Figure 17: Beer 2014 Risk of bias – change in inpatient weight

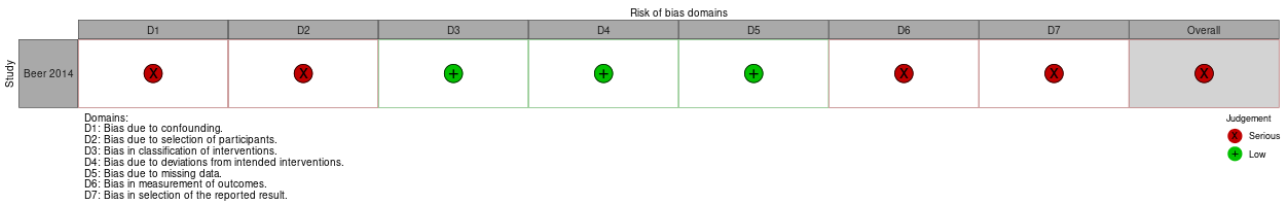


Figure 18: Beer 2014 Risk of bias– rebound weight

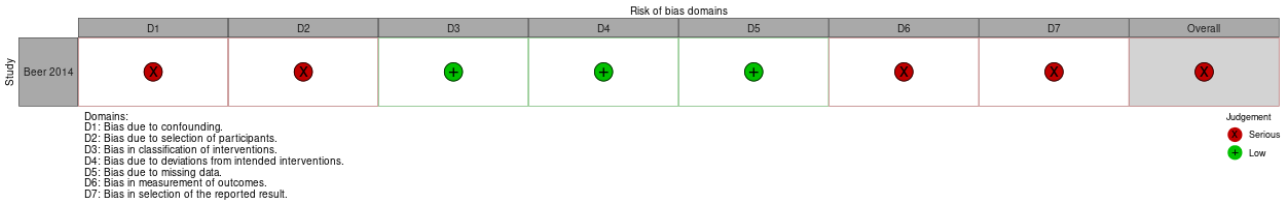


Figure 19: Beer 2014 Risk of bias – weight change at interview

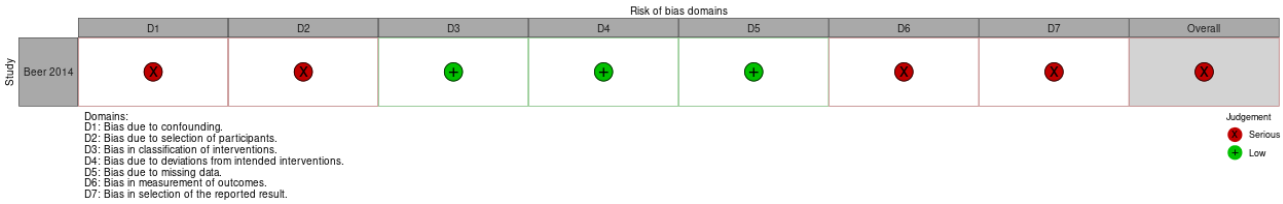


Figure 20: Beer 2014 Risk of bias – QOL non standardised questionnaire

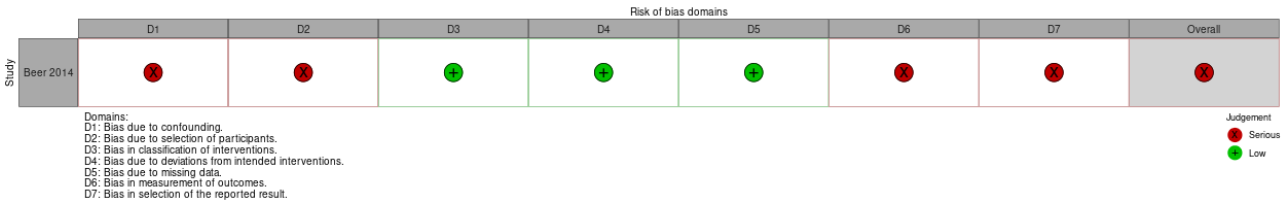
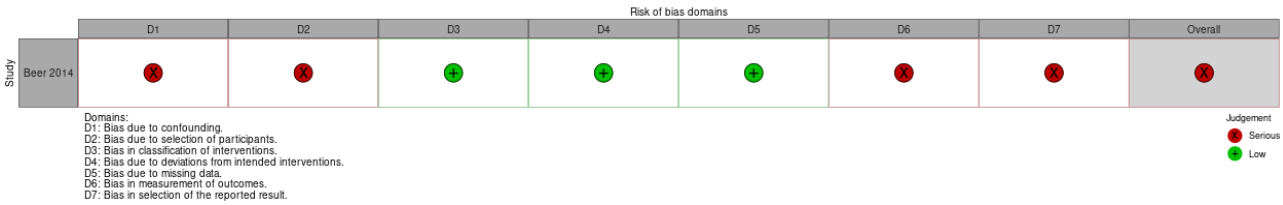


Figure 21: Beer 2014 Risk of bias – physical activity non standardised questionnaire



Source: Risk of bias visual graphic performed in *McGuinness, LA, Higgins, JPT. Risk of bias VISualization (robvis): An R package and Shiny web app for visualizing risk of bias assessments. Res Syn Meth. 2020; 1- 7. https://doi.org/10.1002/jrsm.1411*

4.7.4. Summary of findings

Table 6: Overweight and obesity summary of findings

Naturopathy compared to control (usual care or control) for overweight and obesity						
Patient or population: Overweight and obesity **Setting:** Post inpatient naturopathic treatment **Intervention:** Fasting diet **Comparison:** Control (weight reduction diet)						
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with control	Risk with naturopathy				
Change in rebound weight from admission to interview assessed with: kg (lower is better) follow up: 6.8 ± 1.1 years post intervention	Mean change was **2.6 kg lower** (95% CI not reported)	Not estimable	-	169 (1 observational study)	⊕◯◯◯ VERY LOW [a,b,e]	The evidence is very uncertain about the effect of Naturopathy on rebound weight
Quality of life assessed with: three closed questions in a questionnaire (higher is better) follow up: 6.8 ± 1.1 years post intervention	A higher proportion of fasting patients had improvement for some time in their quality of life, from the time of inpatient admission to the time of the interview, compared to patients who were treated with dietary therapy. A greater proportion of patients who had received weight-reducing diets had either no improvement or a sustained improvement in their quality of life. The differences were statistically significant overall, but it is unclear which group had an overall better outcome.		-	169 (1 observational study)	⊕◯◯◯ VERY LOW [c,d,e]	The evidence is very uncertain about the effect of fasting therapy on quality of life
Anthropometric measurements/changes other than weight – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on anthropomorphic changes other than weight is unknown
Metabolic indices – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on metabolic indices is unknown
Change in physical activity assessed with: seven closed questions with sub questions in a questionnaire (higher is better) follow up: 6.8 ± 1.1 years post intervention	Both fasting and weight-reducing dietary groups experienced a non-significant increase in their physical activity. A greater proportion of the weight-reducing diet group had a persistent increase in their leisure time activity compared to the fasting group. However, a greater proportion of the fasting group had no increase in their leisure time activity or an increase for some of the time compared to the weight-reducing diet group. The difference between the treatment groups was significant, but it is not clear overall which group had an overall better outcome.		-	169 (1 observational study)	⊕◯◯◯ VERY LOW [c,d,e]	The evidence is very uncertain about the effect of fasting therapy on quality of life

Naturopathy compared to control (usual care or control) for overweight and obesity						
Patient or population: Overweight and obesity **Setting:** Post inpatient naturopathic treatment **Intervention:** Fasting diet **Comparison:** Control (weight reduction diet)						
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with control	Risk with naturopathy				
Cardiovascular risk – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on cardiovascular risk in people who are overweight or obese is unknown
Morbidity – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on morbidity in people who are overweight or obese is unknown

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
MD and 95% CI calculated post-hoc for this Review by RevMan 5.3
** The MCID in overweight and obese people is unknown. Guidelines and experts describe 5% to 10% reductions in body weight as `clinically important'[63]

Effect estimates were considered on three levels: small (MD <10% of the scale), moderate (MD between 10% and 20% of the scale) or large (MD than 20% of the scale).

CI: confidence interval; **kg:** kilogram; **MD:** mean difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded two levels for risk of bias: for very serious risk of bias arising from confounding, selection of participants into the study, measurement of outcomes, and selection of reported results
b. Downgraded two levels for imprecision: evidence limited by imprecise data i.e. small sample size (n=169)
c. Downgraded two levels for risk of bias: serious risk of bias arising from confounding, selection of participants into the study, measurement of outcomes, and selection of reported results. Measures were self-reported by closed questions in a questionnaire
d. Downgraded one level for imprecision: Data not presented, the CI includes the possibility of both important benefit and harm
e. Inconsistency could not be assessed as only one study measured this outcome. No downgrading. Publication bias not suspected. No downgrading.

Forest plots could not be generated for change in body weight from admission to follow-up interview, QOL or changes in physical activity.

4.8. Anxiety

4.8.1. Description of the condition

Generalised anxiety is characterised by feeling anxious most of the time, not just to specific situations. Symptoms include excessive worrying, restlessness, panic attacks, tachycardia, hot and cold flushes and social avoidance.[64] Anxiety diagnosis is defined by Diagnostic and Statistical Manual of Mental Disorders (DSM) and self-assessment questionnaires (i.e. Beck Anxiety Inventory (BAI)). Prognosis can be improved by medication (i.e. antidepressants) and cognitive behaviour therapy.[65] In 2017-18, 3.2 million Australians (13%) had an anxiety related condition, an

increase from 11% in 2014-15. The increase was due to a higher number of people reporting anxiety-related conditions in the population age 15-24 years.[66]

4.8.2. Description of studies

One RCT was identified (Bernhardt 2009)[2] which assessed naturopathy for anxiety. The study was conducted in Canada and investigated 81 employees of 'Canada Post' aged 43 to 63, with moderate to severe anxiety (diagnosed with BAI) for longer than six weeks. Participants were excluded if they had mild or no anxiety at the time of assessment (BAI score,10). The interventions were administered for 12 weeks.[67]

Bernhardt 2009 compared the effectiveness of naturopathic care (dietary counselling, deep breathing relaxation techniques, a standard multi-vitamin, and the herb Withania somnifera) against psychotherapy (psychotherapy, matched deep breathing relaxation techniques and placebo) (further details in Appendix D.1.).[67]

4.8.3. Risk of bias

Risk of bias for Bernhardt 2009 ROB was assessed with RoB 2[39] and overall was rated 'high' across all outcome domains, due to all measurement tools being self-reported, potentially favouring the naturopathy treatment group (Details of the risk of bias assessments are provided at Appendix D.4. Details of the study characteristics are provided at Appendix D1.7 and outcome data details are available at Appendix E.3. Figure 25 to Figure 27).

Details of the risk of bias assessments are provided at Appendix D.4. Details of the study characteristics are provided at Appendix D1.7 and outcome data details are available at Appendix E.3.

Figure 22: Bernhardt 2009 Risk of bias – BAI

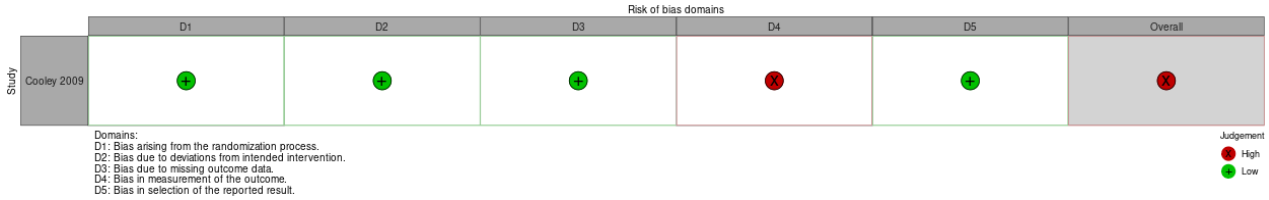
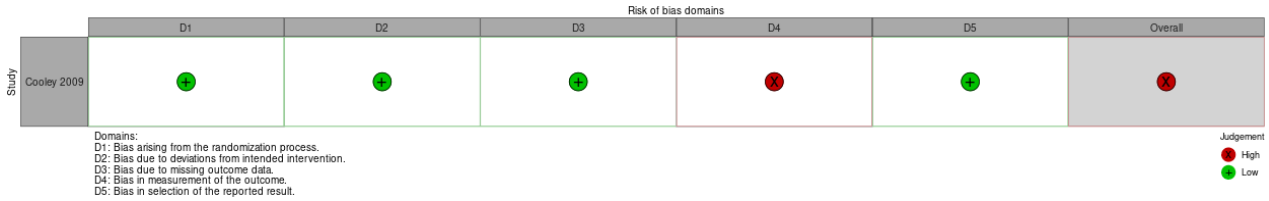
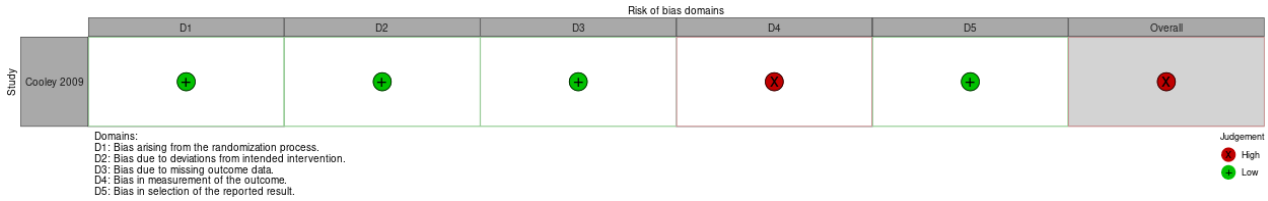


Figure 23: Bernhardt 2009 Risk of bias– SF36



[2] Duplicate citation identified: Cooley K, Szczurko O, Perri D, et al. Naturopathic care for anxiety: a randomized controlled trial ISRCTN78958974. PLoS One. 2009;4(8):e6628.

Figure 24: Bernhardt 2009 Risk of bias– VAS



Abbreviations: BAI= Beck Anxiety Inventory; RoB2=Risk of Bias 2; SF-36=Short form 36; VAS= Visual analogue scale

Source: Risk of bias visual graphic performed in *McGuinness, LA, Higgins, JPT. Risk of bias VISualization (robvis): An R package and Shiny web app for visualizing risk of bias assessments. Res Syn Meth. 2020; 1- 7.* https://doi.org/10.1002/jrsm.1411

4.8.4. Summary of findings

Table 7: Anxiety summary of findings

Naturopathy compared to control (psychotherapy) for anxiety						
Patient or population: Anxiety **Setting:** Community, postal workers **Intervention:** Naturopathy **Comparison:** Control (psychotherapy)						
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI) **	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statement
	Risk with Control	Risk with Naturopathy				
Anxiety assessed with: BAI (lower is better) Scale from: 0 to 63 follow-up: 12 weeks	The mean anxiety score was **7.15 points lower** (9.84 lower to 4.47 lower)	MD **6.16 points lower** (10.24 lower to 2.08 lower)	-	81 (1 RCT)	⊕◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of Naturopathy on anxiety in people with anxiety***
Depressive symptoms – Not Reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on depressive symptoms in people with anxiety is unknown
Quality of life physical assessed with: SF-36 (higher is better) Scale from: follow-up: 12 weeks	The mean quality of life physical summary score was **0.50** (1.91 lower to 2.91 higher)	MD **3.26 points higher** (0.15 lower to 6.66 higher)	-	81 (1 RCT)	⊕◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of Naturopathy on quality of life in people with anxiety****
Quality of life mental assessed with: SF-36 (higher is better) Scale from: follow-up: 12 weeks	The mean quality of life mental summary score was **2.23** (1.54 lower to 5.99 higher)	MD **10.34 points higher** (5.21 higher to 15.46 higher)	-	81 (1 RCT)	⊕◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of Naturopathy on the mental function of people with anxiety****
Symptom burden/severity assessed with: VAS (lower is better) Scale from: 7 points follow-up: 12 weeks	The mean symptom burden/severity score was **0.10** (0.27 lower to 0.49 higher)	MD **0.81 points higher** (0.24 higher to 1.37 higher)	-	81 (1 RCT)	⊕◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of Naturopathy on perceived stress in people with anxiety*****

Naturopathy compared to control (psychotherapy) for anxiety						
Patient or population: Anxiety **Setting:** Community, postal workers **Intervention:** Naturopathy **Comparison:** Control (psychotherapy)						
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI) **	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statement
	Risk with Control	Risk with Naturopathy				
Treatment sustainability/ Relapse – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on treatment sustainability in people with anxiety is unknown
Improvement in social functioning – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on improvement in social functioning in people with anxiety is unknown
Additional benzodiazepines	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on additional benzodiazepines in people with anxiety is unknown

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
**Relative effect 95% CI
Effect sizes calculated post-hoc for this Review
*** An MCID of at least 5 points is likely important.[68]
**** An MCID of at least 5 points difference on PCS and MSC scores is likely important.[68]
*****An MCID of at least 5 points is likely important.[40]

CI: confidence interval; **BAI:** Beck Anxiety Inventory; **MCID**: Minimal important clinical difference; **MD:** mean difference; **MSC:** mental component summary; **PCS:** physical component summary; **RCT:** Randomised controlled trial; **RoB2**: Risk of Bias 2; **SF-36:** Short form 36; **VAS:** Visual analogue scale

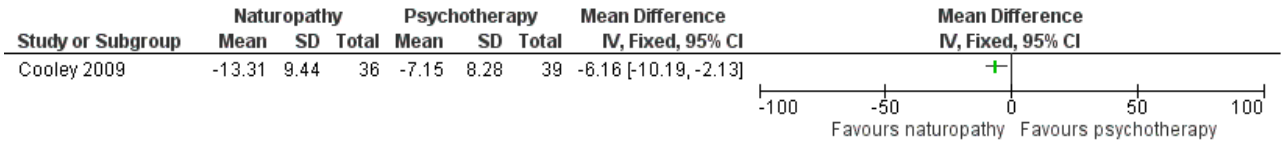
GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded one level for risk of bias: arising from the measurement of the outcome. For all three outcome domains, the measurement methods were appropriate but were self-reported. Thus, the assessors were the participants, who were aware of which treatment they were receiving. There may be strong beliefs about naturopathic care, which could influence the assessment of outcomes in favour of naturopathy.
b. Downgraded two levels for imprecision: due to few participants (n=81) (OIS underpowered), few events therefore imprecise and lowering the certainty of evidence. Forest plots (see Figure 28 SF-36 physical, below) cross the null, line of no effect and are not clinically meaningful, see above/***). Wide CI for QOL SF-36 mental component and symptom severity/burden, indicating lack of precision and reducing confidence in effect.
c. Inconsistency could not be assessed as only one study measured this outcome. No downgrading. Publication bias not suspected no downgrading.

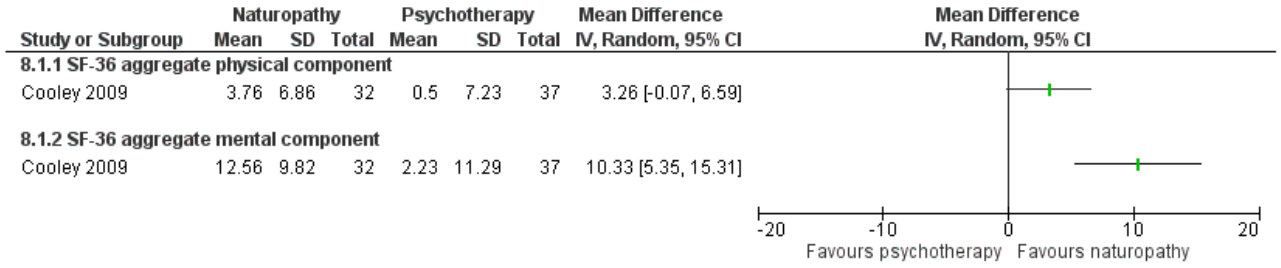
Figure 28 presents the forest plot for changes in anxiety levels from baseline, as measured by the BAI. Figure 29 shows the forest plot for changes in QOL as measured by the SF-36 aggregate physical and mental components. Figure 30 shows the forest plot for the changes in symptom severity and burden from baseline, as measured by the VAS

Figure 25: Anxiety forest plot



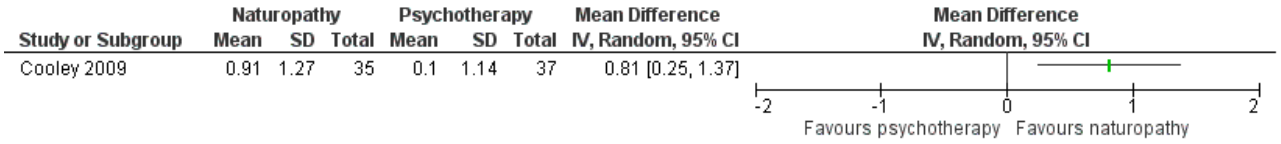
BAI (lower is better). Scale from 0 to 63.

Figure 26: QOL SF-36 forest plots



SF-36 score 0-100 (higher is better)

Figure 27: Symptom severity/burden forest plot



VAS, 7-point scale (lower is better)

Abbreviations: BAI= Beck Anxiety Inventory; IV= Inverse variance; RoB2=Risk of Bias 2; SD= Standard deviation; SF-36=Short form 36; VAS= Visual analogue scale

Note: Standard deviations calculated post-hoc for this Review; 95% confidence intervals for Mean Difference calculated by RevMan 5.3

4.9. Multiple sclerosis

4.9.1. Description of the condition

Multiple Sclerosis (MS) is an autoimmune disease affecting the central nervous system (CNS) characterised by inflammation, demyelination and axonal/neuronal destruction, which leads to severe disability. Scars occur within the CNS and depending on where they develop, manifest into various symptoms.[69] Symptoms include numbness, electric shock sensation, tremor, loss of vison, slurred speech and fatigue. There are three main types of MS: relapsing remitting MS (RRMS), secondary progressive MS (SPMS) and primary progressive MS (PPMS). The classification of MS depends on its activity and progression. Diagnosis may include blood tests, lumbar puncture, MRI and evoked potential tests.[70,71] Prognosis for people with MS can be improved by disease modifying treatments (DMT) combined with other medication to alleviate symptoms. In Australia more than 25,600 people live with MS.[72]

4.9.2. Description of studies

One RCT (Shinto 2008) was identified which assessed naturopathy alongside usual care for MS. The study was a 3-arm RCT in the USA and investigated 41 people, aged 34 to 53 years. Diagnosis was confirmed as relapsing–remitting MS with an Expanded Disability Status Score

(EDSS) ≤6.0 indicating the ability to ambulate 100 meters (mild–moderate neurologic impairment). Naturopathy treatment was administered for 6 months.[73]

Shinto 2008 compared the effectiveness and safety of a naturopathy intervention (dietary therapy, and dietary supplements and education with support from a nurse specialising in MS care) combined with usual care against usual care only (further details in Appendix D.1.).

4.9.3. Risk of bias

Risk of bias for Shinto 2008 was assessed with RoB 2[39] and overall rated as 'high' due to self-report methods for assessing the fatigue and QoL outcome domains (Figure 32), (Details of the risk of bias assessments are provided at Appendix D.5. Details of the study characteristics are provided at Appendix D1.8 and outcome data details are available at Appendix E.4. Figure 31). The function/ disability outcome domain was rated as 'some concerns' due to a lack of reporting of how randomisation was conducted (Figure 33).

Details of the risk of bias assessments are provided at Appendix D.5. Details of the study characteristics are provided at Appendix D1.8 and outcome data details are available at Appendix E.4.

Figure 28: Shinto 2008 risk of bias – overall

Figure 29: Shinto 2008 Risk of bias - QOL

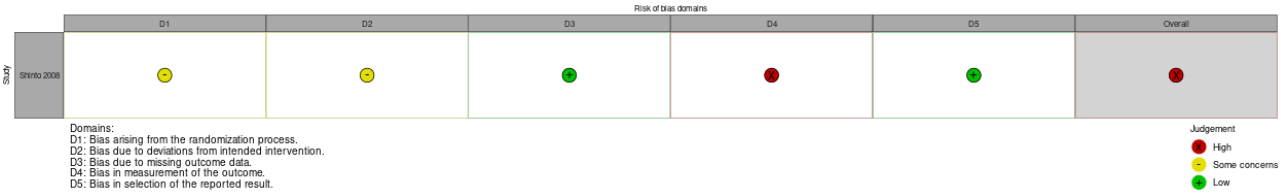


Figure 30: Shinto 2008 risk of bias – function

Abbreviations: QOL=Quality of life

Source: Risk of bias visual graphic performed in *McGuinness, LA, Higgins, JPT. Risk of bias VISualization (robvis): An R package and Shiny web app for visualizing risk of bias assessments. Res Syn Meth. 2020; 1- 7. https://doi.org/10.1002/jrsm.1411*

4.9.4. Summary of findings

Table 8: MS summary of findings

Naturopathy compared to Control (no intervention, waitlist, usual care) for multiple sclerosis						
Patient or population: Multiple sclerosis **Setting:** Community **Intervention:** Naturopathy **Comparison:** Control (no intervention, usual care)						
Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with Control	**Risk with Naturopathy[1]**				
Fatigue assessed with: MFIS (lower is better) Scale from: 0 to 84 follow-up: 6 months	Mean change in fatigue from baseline was **0.2 points lower**	**MD 1.13 points higher** (1.48 lower to 3.74 higher)	-	30 (1 RCT)	⊕◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of naturopathy on fatigue in people with multiple sclerosis**
Quality of life – physical assessed with: SF-36 (higher is better) Scale from: 0 to 100 follow-up: 6 months	Mean change of physical QOL from baseline was **0.3 points lower**	**MD 1.80 points higher** (2.61 lower to 6.21 higher)	-	30 (1 RCT)	⊕◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of naturopathy on physical wellbeing in people with multiple sclerosis***
Quality of life - mental assessed with: SF-36 (higher is better) Scale from:1 to 100 follow-up: 6 months	Mean change of mental QOL from baseline was **1.2 points lower**	**MD 1.30 points higher** (4.32 lower to 6.92 higher)	-	30 (1 RCT)	⊕◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of naturopathy on mental wellbeing in people with multiple sclerosis***
Quality of life assessed with: SF-36 general health (higher is better) Scale from: 0 to 100 follow-up: 6 months	Mean change from baseline was **3.1 points lower**	**MD 11.00 points higher** (0.39 higher to 21.61 higher)	-	30 (1 RCT)	⊕◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of Naturopathy on general health in people with multiple sclerosis ***
Function/disability assessed with: EDSS, (lower is better) Scale from: 0 to 10 follow-up: 6 months	Mean change in functionality from baseline was **0.33 points lower**	**MD 0.53 points higher** (0.17 higher to 0.89 higher)	-	30 (1 RCT)	⊕◯◯◯ VERY LOW b,c,d	The evidence is very uncertain about the effect of naturopathy in function/disability in people with multiple sclerosis****
Function/disability assessed with: MSFC (higher is better) Scale from: z score change follow-up: 6 months	Mean change from baseline was **0.09 points higher**	**MD 0.00 points** (0.27 lower to 0.27 higher)	-	30 (1 RCT)	⊕◯◯◯ VERY LOW b,c,d	The evidence is very uncertain about the effect of naturopathy on function/disability in people with multiple sclerosis*****
Cognitive impairment assessed with: PASAT-3 (higher is better) Scale from: 0 to 60 follow-up: 6 months	Mean change in cognitive impairment from baseline was **0.15 points higher**	**MD 0.03 points higher** (0.24 lower to 0.30 higher)	-	30 (1 RCT)	⊕⊕◯◯ LOW b,c,d	Naturopathy may result in little to no difference on function/disability in people with multiple sclerosis******
Relapse – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on relapse in people with MS is unknown

Naturopathy compared to Control (no intervention, waitlist, usual care) for multiple sclerosis						
Patient or population: Multiple sclerosis **Setting:** Community **Intervention:** Naturopathy **Comparison:** Control (no intervention, usual care)						
Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with Control	**Risk with Naturopathy**[1]				
Spasms – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on spasms in people with MS is unknown

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
**The MCID for MFIS is 4 points (for improvement).[74]
***An MCID of at least 5 points difference on PCS and MSC scores is likely important.[76]
****The MCID for EDSS is 1.0 point change when the EDSS score was less than 5.5, and a 0.5 point change when the EDSS score was between 5.5 and 8.5.[75]
*****The MCID for MSFC is unknown. The score is 0.
******The MCID for PASAT-3 is unknown. The change score of 0.03 is small#

#Effect estimates were considered on three levels: small (MD <10% of the scale), moderate (MD between 10% to 20% of the scale) or large (MD more than 20% of the scale).

1. MD and 95% CI calculated post-hoc for this Review by RevMan 5.3 (see Shinto 2008, Table 4 (p. 494) reports mean change from baseline between groups with standard deviations)

CI: confidence interval; **EDSS**: Expanded Disability Status Score; **MD:** mean difference; **MFIS:** Modified Fatigue Impact Scale; **MSFC:** Multiple Sclerosis Functional Composite; **MSQLI:** Multiple Sclerosis Quality of Life Inventory; **PASAT-3:** Paced Auditory Serial Addition Test 3; **SF-36:** Short Form 36

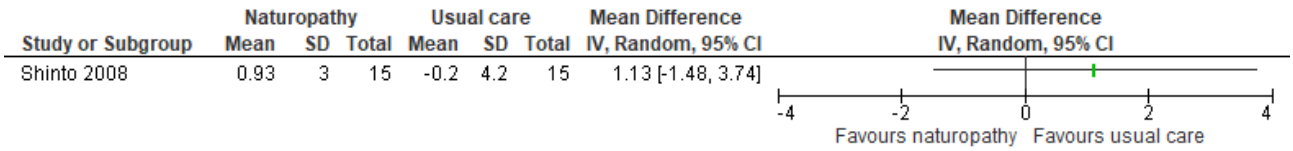
GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded two levels for risk of bias: for very serious risk of bias arising from the measurement of the outcome (self-reported). There were some concerns arising from the randomisation process (no information) and missing outcome data (only SF-36 and MFIS were included from ten MSQLI battery tests).
b. Downgraded two levels for imprecision: small sample size (n=45) and wide CIs overall. MCIDs were not exceeded for MFIS, EDSS and SF-36 (aggregated). Only the upper CIs for SF-36 for PCS and MSC (aggregated) exceeded the MCID, MFIS and EDSS did not.
c. Inconsistency could not be assessed as only one study measured this outcome. No downgrading. Publication bias not suspected. No downgrading.
d. Downgraded one level for risk of bias: There were some concerns arising from missing outcome data (only SF-36 and MFIS were included from ten MSQLI battery tests).

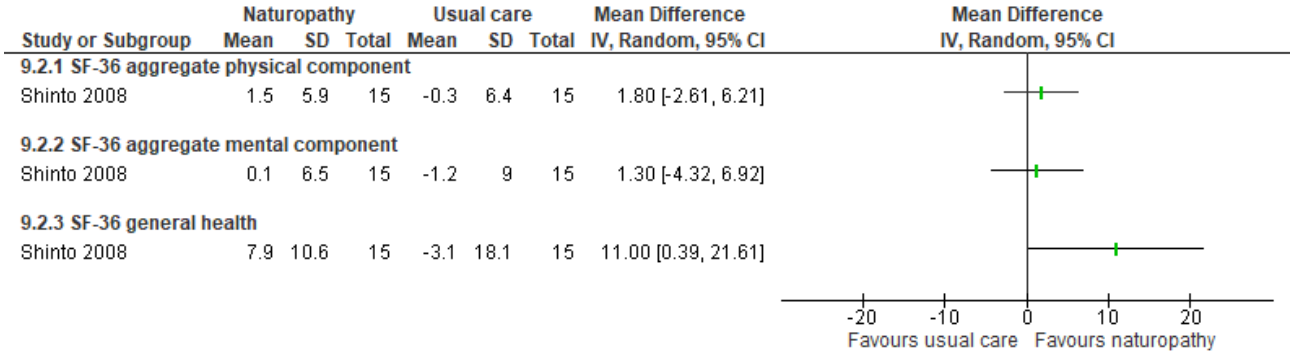
Figure 34 presents the forest plot for changes in fatigue between naturopathy and usual care only groups, as measured by the Modified Fatigue Impact Scale. Figure 35 presents the forest plot for changes in QOL from baseline as measured by the SF-36, for the naturopathy and usual care only groups. Figure 36 presents the forest plot for changes in function and disability from baseline as measured by the EDSS, for naturopathy and usual care only groups. Figure 36 presents the forest plot for changes in function and disability from baseline as measured by the Multiple Sclerosis Functional Composite (MSFC), for the naturopathy and usual care only groups. Figure 37 and Figure 38 presents the forest plot for changes in cognitive impairment from baseline as measured by the Paced Auditory Serial Addition Test 3 (PASAT-3), for the naturopathy and usual care only groups.

Figure 31: MS fatigue forest plot



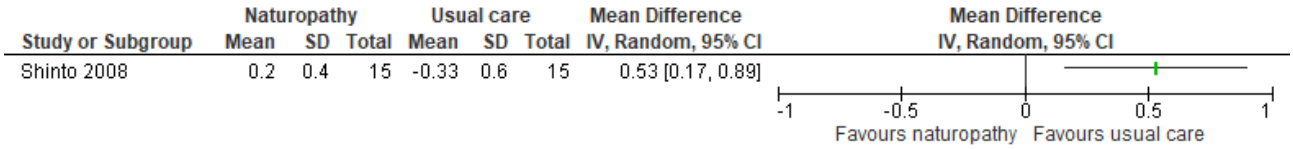
MFIS, scale from 0 to 84 (lower is better)

Figure 32: MS QOL forest plots

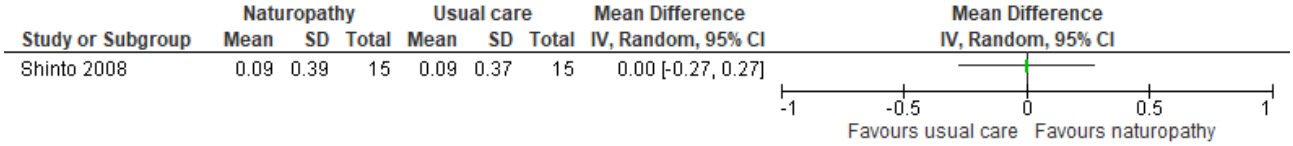


SF-36, scale from 0 to 100 (higher is better)

Figure 33: MS EDSS forest plot

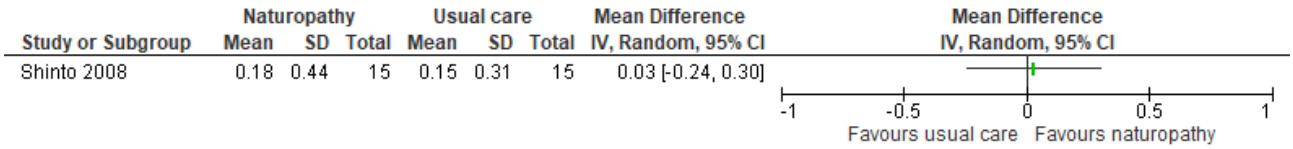


EDSS, scale from 0 to 10 (lower is better)Figure 34: MS MSFC forest plot



MSFC, z-score change (higher is better)

Figure 35: MS cognitive impairment forest plot



PASAT-3, scale from 0 to 60 (higher is better)

Abbreviations: EDSS= Expanded Disability Status Score; IV= Inverse variance; MS=Multiple sclerosis; MSFC= Multiple Sclerosis Functional Composite; SD=Standard deviation; QOL=quality of life

Note: For all outcomes the number of events were calculated post-hoc for this Review. Risk ratio and 95% CI calculated post-hoc for this Review by RevMan 5.3.

4.10. Cardiovascular disease

4.10.1. Description of the condition

Cardiovascular disease (CVD) or coronary heart disease (CHD) affects the blood vessels that supply blood to the heart. CHD can lead to myocardial infarct (MI) or angina (chest pain) and risk factors may include smoking, poor diet, insufficient physical activity, hypertension and obesity. Symptoms of MI include chest or arm pain, nausea and shortness of breath. Cardiovascular diagnosis includes cholesterol blood tests, blood pressure check, electrocardiogram or angiogram. Prognosis of CHD is related to the number of affected blood vessels and the degree of dysfunction of the left ventricle, invasive treatment can include percutaneous coronary intervention and coronary artery bypass grafting to restore blood flow to the heart. In 2017-18, an estimated 580,000 Australians aged 18 and over (2.8% of the adult population) had CHD.[77] In 2022, CHD is the leading single cause of death in Australia.[78]

4.10.2. Description of studies

One NRSI (Braun 2014) was identified that assessed naturopathy (as an adjunct to usual care) against usual care alone for CVD patients. The study was conducted in Australia and involved patients who received elective cardiothoracic surgery (mean age 65-68 years), stratified by either coronary artery bypass surgery[80] or valve surgery.[79,81]

Braun 2014[79] compared the effectiveness and safety of naturopathy (i.e. an integrative cardiac wellness program combined with metabolic therapy (i.e. coenzyme Q10, R-S-alpha lipoic acid, magnesium orotate, D-alpha-tocopherol, omega 3 triglycerides) and ward-based individualised health promotion (dietary advice, stress management, activity etc.) as an adjunct to standard pharmaceutical and surgical care to those who received usual care alone (further details in Appendix D.1).

4.10.3. Risk of bias

Risk of bias for Braun 2014 was assessed using ROBINS-I[34] and overall was rated as 'serious' due to a lack of information and no information regarding the start of follow-up for the historical comparator group, further the study did not assess compliance with the intervention (Details of the risk of bias assessments are provided at Appendix D.6. Details of the study characteristics are provided at Appendix D1.9 and outcome data details are available at Appendix E.5. Figure 39 to Figure 41).

Details of the risk of bias assessments are provided at Appendix D.6. Details of the study characteristics are provided at Appendix D1.9 and outcome data details are available at Appendix E.5.

Figure 36: Braun 2014 Risk of bias - Non-fatal cardiovascular events

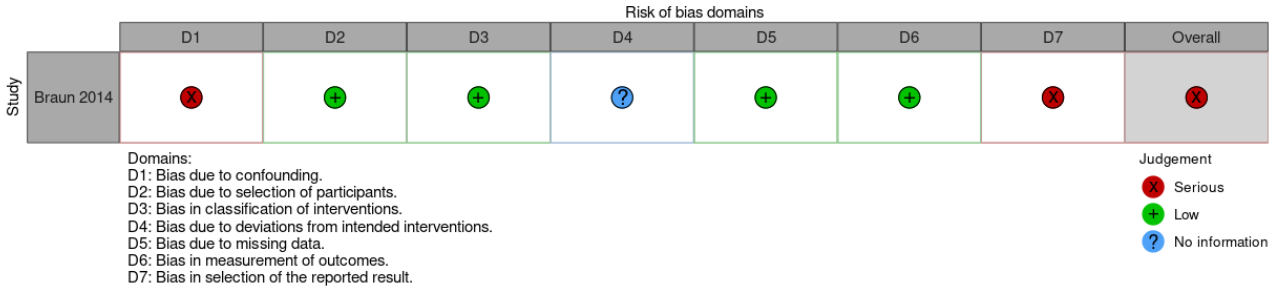


Figure 37: Braun 2014 Risk of bias - Hospital length of stay

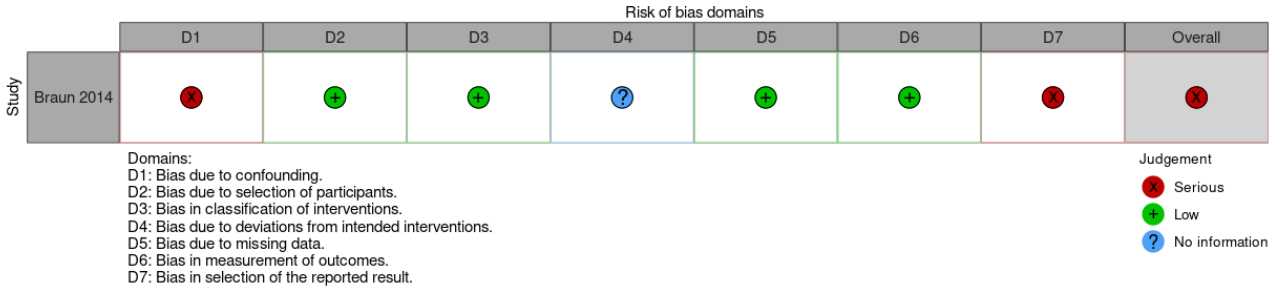
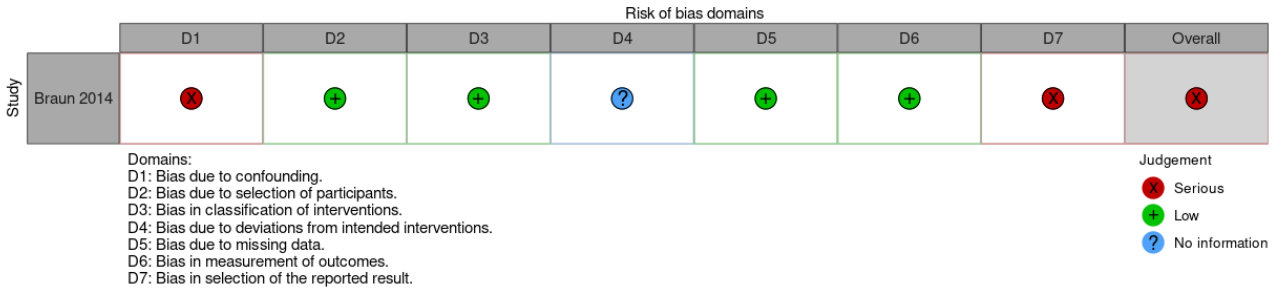


Figure 38: Braun 2014 Risk of bias - Arrhythmia requiring treatment



Abbreviations: ROBINS-I= Risk Of Bias In Non-randomised Studies of Interventions

Source: Risk of bias visual graphic performed in *McGuinness, LA, Higgins, JPT. Risk of bias VISualization (robvis): An R package and Shiny web app for visualizing risk of bias assessments. Res Syn Meth. 2020; 1- 7.* https://doi.org/10.1002/jrsm.1411

4.10.4. Summary of findings

Table 9: CVD summary of findings

Naturopathy compared to control (usual care or control) for cardiovascular disease (CABG and valve surgery)						
Patient or population: Cardiovascular disease (CABG and valve surgery) **Setting:** Inpatient **Intervention:** Naturopathy **Comparison:** Control (usual care or control)						
Outcomes	Anticipated absolute effects*		Relative risk (95% CI) ^	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with Usual Care	Risk with Naturopathy				
Non-fatal cardiovascular events (CABG) assessed with: Incidence of returning to theatre (lower is better) Follow up: 4 weeks	31 per 1,000	17 per 1,000 (5 to 60)	RR 0.55 (0.16 to 1.94)	530^^^ (1 observational study)	⨁◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of naturopathy on return to theatre in CABG patients**
Non-fatal cardiovascular event (valve surgery) assessed with: Incidence of returning to theatre (lower is better) Follow up: 4 weeks	39 per 1,000	37 per 1,000 (14 to 102)	RR 0.96 (0.35 to 2.63)	392^^^ (1 observational study)	⨁◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of naturopathy on return to theatre in valve surgery patients**

Naturopathy compared to control (usual care or control) for cardiovascular disease (CABG and valve surgery)

Patient or population: Cardiovascular disease (CABG and valve surgery)
Setting: Inpatient
Intervention: Naturopathy
Comparison: Control (usual care or control)

Outcomes	Anticipated absolute effects*		Relative risk (95% CI) ^	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with Usual Care	Risk with Naturopathy				
Cardiovascular mortality – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on cardiovascular mortality is unknown
Cerebrovascular complications – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on cerebrovascular complications is unknown
30-day rehospitalisation – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on 30-day rehospitalisation is unknown
Hospital length of stay (CABG) assessed with: Days (lower is better) Follow up: 4 weeks	Median **6 days** (IQR 5 to 8)	Median **6.5 days** (IQR 6 to 8)	-	530^^^ (1 observational study)	⨁◯◯◯ VERY LOW [a,b,c]	The evidence is very uncertain about the effect of naturopathy on length of hospital stay CABG patients***
Hospital length of stay (valve surgery) assessed with: Days (lower is better) Follow up: 4 weeks	Median **8 days** (IQR 6 to 13)	Median **8 days** (IQR 7 to 12)	-	392^^^ (1 observational study)	⨁◯◯◯ VERY LOW [a,b,c]	The evidence is very uncertain about the effect of naturopathy on length of hospital stay valve surgery patients***
Prevalence of atrial fibrillation (CABG) assessed with: number of cases (lower is better) ^^ Follow up: 4 weeks	356 per 1,000	260 per 1,000 (196 to 349)	RR 0.73 (0.55 to 0.98)	530^^^ (1 observational study)	⨁◯◯◯ VERY LOW [a,b,c]	The evidence is very uncertain about the effect of naturopathy on atrial fibrillation prevalence CABG patients****
Prevalence of atrial fibrillation (valve surgery) assessed with: number of cases (lower is better) ^^ Follow up: 4 weeks	359 per 1,000	341 per 1,000 (26 to 45)	RR 0.95 (0.72 to 1.25)	392^^^ (observational studies)	⨁◯◯◯ VERY LOW [a,b,c]	The evidence is very uncertain about the effect of naturopathy on atrial fibrillation prevalence valve surgery patients****

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
** The MCID or threshold for returning to theatre in CABG or value surgery patients is unknown.
*** Among those hospitalised for one night or more with CVD as a principal diagnosis, the average length of stay was 6.0 days in 2018–19.[82] Valve patients stayed longer than CABG patients by 2 days. Those that received the naturopathy intervention stayed half a day longer than usual care patients.
**** The MCID or threshold for atrial fibrillation prevalence in CABG or value surgery patients is unknown.

^Risk ratios were calculated post-hoc by RevMan 5.3 for this Review.
^^Only percentages were reported by the study, not the number of participants
^^^Outcomes were analysed by subgroups CABG (n=530) and valve surgery recipients (n=392) from the one study.

CABG: Coronary artery bypass graft; **CI:** confidence interval; **CVD:** Cardiovascular disease; **IQR:** Interquartile range; **RR:** Relative risk;

Naturopathy compared to control (usual care or control) for cardiovascular disease (CABG and valve surgery)						
Patient or population: Cardiovascular disease (CABG and valve surgery) **Setting:** Inpatient **Intervention:** Naturopathy **Comparison:** Control (usual care or control)						
Outcomes	Anticipated absolute effects*		Relative risk (95% CI) ^	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with Usual Care	Risk with Naturopathy				
GRADE Working Group grades of evidence **High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect. **Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. **Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect. **Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.						

Explanations

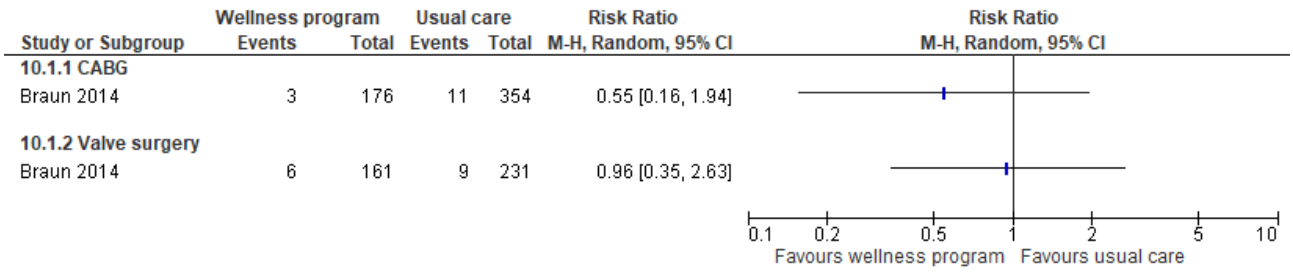
a. Downgraded two levels for risk of bias: the risk of bias was assessed as 'no information' for selection of participants into the study and deviations from intended intervention. There was no information regarding the start of follow-up for the historical comparator group and the study did not assess compliance with the intervention. Moderate risk of bias arising from confounding and selection of reported results.

b. Downgraded one level for imprecision: wide confidence intervals that cross over the null, line of no effect and appreciable harm in all outcomes expect CABG atrial fibrillation prevalence. (Note: that relative risk and 95% confidence intervals were calculated post-hoc for this Review).

c. Inconsistency could not be assessed as only one study measured this outcome. No downgrading. Publication bias not suspected. No downgrading.

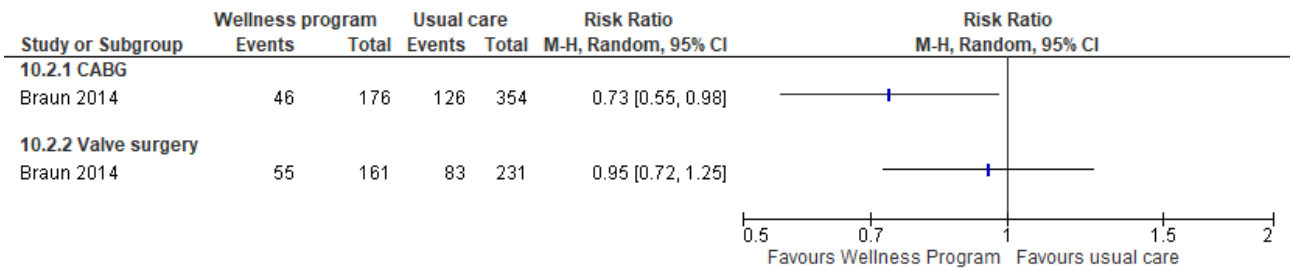
Figure 42 shows the forest plot for both CABG and valve surgery patients and the risk ratio for non-fatal cardiovascular events comparing the Wellness Program to usual care. Figure 43 shows the forest plot for both CABG and valve surgery patients and the risk ratio for arrhythmias requiring treatment, comparing the Wellness Program to usual care.

Figure 39: Non-fatal cardiovascular event forest plot



Incidence of returning to theatre, no reference range (lower is better)

Figure 40: Arrhythmia prevalence of atrial fibrillation - forest plot



Atrial fibrillation, number of cases, no reference range (lower is better)

Abbreviations: CABG= Coronary artery bypass graft; M-H= Mantel-Haenszel

Note: For valve surgery, the number of events were calculated post-hoc for this Review. Risk ratio and 95% CI calculated post-hoc for this Review by RevMan 5.3.

Note: Forest plots could not be generated from the median hospital length of stay.

4.11. Allergic rhinitis

4.11.1. Description of the condition

Allergic rhinitis also known as hay fever is an immune response to allergens. Symptoms include watery eyes and blocked nose. Most people manage hay fever at home with pharmacy medications. Although a skin prick test can be used in some circumstances by clinicians to confirm diagnosis. Prognostically most people live normal lives with symptom management.[83] In 2020-21 an estimated 20.3% or one in five Australians experienced allergic rhinitis.[84]

4.11.2. Description of studies

One RCT (Mittman 1990)[85] was identified that investigated naturopathy for allergic rhinitis. The study was a parallel double blind RCT in the USA that investigated 98 adults, aged 20 to 74 years with at least two allergic rhinitis symptoms that were rated 'moderately severe': rhinorrhoea, sinus congestion, or excessive lacrimation (watery eyes). The intervention was administered for one week.

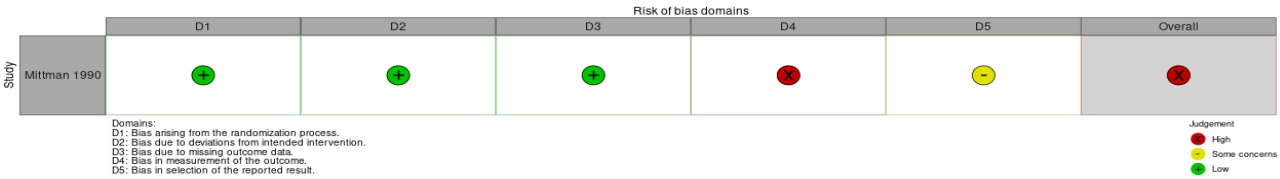
Mittman 1990 compared the effectiveness of urtica dioica (stinging nettles administered as a freeze-dried herb in tablet form at 600mg dose) to placebo. The intervention was administered for one week (further details in Appendix D.1.).

4.11.3. Risk of bias

Risk of bias for Mittman 1990 was assessed using RoB 2[39] and overall rated as 'high' due to the outcome measurement method being highly subjective and non-standardised. Ordinal data was presented, and the CI could not be generated (Details of the risk of bias assessments are provided at Appendix D.7. Details of the study characteristics are provided at Appendix D1.10 and outcome data details are available at Appendix E.6. Figure 44).

Details of the risk of bias assessments are provided at Appendix D.7. Details of the study characteristics are provided at Appendix D1.10 and outcome data details are available at Appendix E.6.

Figure 41: Mittman 1990 Risk of bias - symptom response



Source: Risk of bias visual graphic performed in *McGuinness, LA, Higgins, JPT. Risk of bias VISualization (robvis): An R package and Shiny web app for visualizing risk of bias assessments. Res Syn Meth. 2020; 1- 7. https://doi.org/10.1002/jrsm.1411*

4.11.4. Summary of findings

Table 10: Allergic rhinitis summary of findings

Naturopathy compared to control (usual care or control) for allergic rhinitis

Patient or population: Allergic rhinitis
Setting: Community
Intervention: Naturopathy
Comparison: Control (usual care or control)

Outcomes	Proportion		Risk ratio(95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statement
	Risk with placebo	Risk with Urtica dioico (stinging nettle)				
Dramatically improved >50% time assessed with: % follow-up: 1 week	3%	**16%**	1.23 [0.39, 3.85]	69 (1 RCT)	⨁◯◯◯ VERY LOW [a,b,d]	The evidence is very uncertain about the effect of *U. dioica* on the proportion of participants reporting dramatically improved symptoms more than 50% of the time**
Moderate improved >50% time follow-up: 1 week	32%	**48%**	0.90 [0.49, 1.67]	69 (1 RCT)	⨁◯◯◯ VERY LOW [a,b,d]	The evidence is very uncertain about the effect of *U. dioica* on the proportion of participants reporting moderate improvements more than 50% of the time**
No change >50% of the time follow-up: 1 week	71%	**61%**	0.86 [0.61, 1.22]	69 (1 RCT)	⨁◯◯◯ VERY LOW [a,b,d]	The evidence is very uncertain about the effect of *U. dioica* on the proportion of participants reporting no change more than 50% of the time**
Worse symptoms >50% of the time follow-up: 1 week	3%	**0%**	0.41 [0.02, 9.64]	69 (1 RCT)	⨁◯◯◯ VERY LOW [a,c,d]	The evidence is very uncertain about the effect of *U. dioica* on the proportion of patients who experience worse symptoms more than 50% of the time**
Quality of Life – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on Quality of Life is unknown
Airflow measures – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on Airflow measures is unknown
Avoidance of Surgery – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on Avoidance of Surgery is unknown
Efficacy Outcomes – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on Efficacy Outcomes is unknown
Adverse effects – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on adverse effects is unknown

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
**MCID for ordinal data are not appropriate

Effect estimates were considered on three levels: small (MD <10% of the scale), moderate (MD between 10% and 20% of the scale) or large (MD than 20% of the scale)

CI: confidence interval; **RCT**: Randomised controlled trial; ***U dioica*:** Urtica dioico

Naturopathy compared to control (usual care or control) for allergic rhinitis

Patient or population: Allergic rhinitis
Setting: Community
Intervention: Naturopathy
Comparison: Control (usual care or control)

Outcomes	Proportion		Risk ratio(95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statement
	Risk with placebo	**Risk with Urtica dioico (stinging nettle)**				

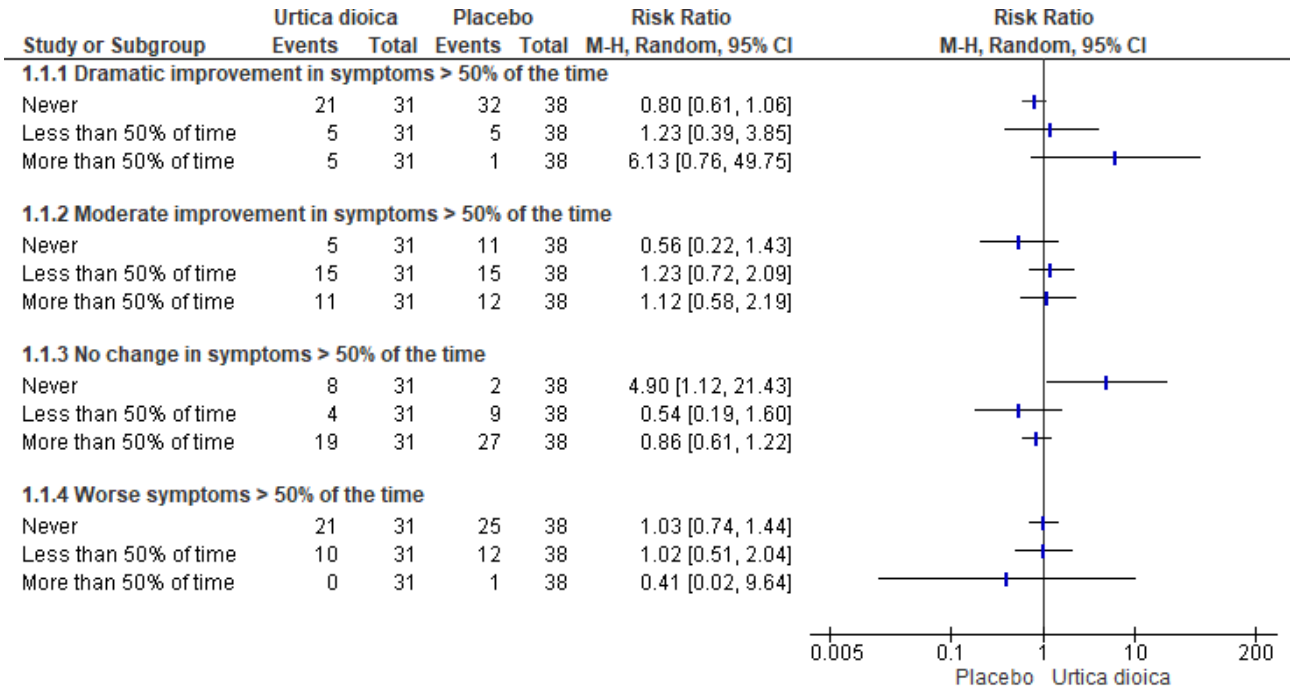
GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded two levels for risk of bias: serious risk of bias arising from the measurement of the outcome; ordinal data from a unvalidated symptom questionnaire over 1 week
b. Downgraded one level for imprecision: small sample size (n= 69). All confidence intervals crossed the line of no effect except for never no change 50% of the time favoring the intervention (i.e no response from U dioico)
c. Downgraded one for imprecision: The CI is exceptionally wide due to exceptionally low event rate. Result is not statistically significant
d. Inconsistency could not be assessed as only one study measured this outcome. No downgrading. Publication bias not suspected. No downgrading.

The forest plot (Figure 45) shows the risk ratios and 95% confidence intervals calculated by RevMan 5.3, for the likelihood that participants receiving *U. dioica* would rate the effectiveness of their treatment compared to the placebo group for each category.

Figure 42: Effectiveness ratings for allergic rhinitis forest plot



No reference ranges.

Note: Risk ratios and 95% confidence intervals were calculated post-hoc for this Review by RevMan 5.3

4.12. Low back pain

4.12.1. Description of the condition

Nonspecific low back pain (LBP) is chronic and characterised by recurrent and transient episodes of LBP.[90] LBP is a symptom rather than a condition.[91] Diagnosis of nonspecific LBP without radiating, nerve or acute pain is by physical examination.[92] With 85-90% of LBP presentations to primary care not having a pathoanatomical cause for their pain.[93] Evidence suggests diagnostic imaging is not appropriate for most LBP diagnoses.[90] Staying physically active increases the chance of a good prognosis for nonspecific LBP.[92] In Australia around 25% suffer from back pain daily and 50% have suffered back pain in the past month.[94] Based on self-reported data from the ABS 2017–18 National Health Survey (NHS) about 4.0 million Australians (16% of the total population) have back problems.[95]

4.12.2. Description of studies

One RCT (Szczurko 2007) was identified that assessed naturopathy for low back pain. The RCT was conducted in Canada and investigated 75 people employed as postal workers, aged 38 to 56 years with a non-specific low back pain in the preceding six weeks. Diagnosis was by physical examination and completion of the Oswestry Low Back Pain Disability Questionnaire and the Roland and Morris low back pain Disability Questionnaire. The interventions were administered for 12 weeks.[96]

Szczurko 2007 compared the effectiveness of naturopathy treatment (acupuncture treatment for LBP and diaphragmatic deep breathing exercises, dietary and physical activity advice) to standardised physiotherapy advice. Both the treatment and control groups were administered by naturopathic physicians (further details in Appendix D.1.).

4.12.3. Risk of bias

Risk of bias for Szczurko 2007 was assessed using RoB 2[39] and rated as 'high' due to study design being open label, attrition rates being substantially greater in the comparator group than the intervention group, and due to self-reported measurement methods that may favour the intervention (Figure 46).[39]

Details of the risk of bias assessments are provided at Appendix D.9. Details of the study characteristics are provided at Appendix D1.12 and outcome data details are available at Appendix E.8.

Figure 43: Szczurko 2007 Risk of bias – pain and function/disability

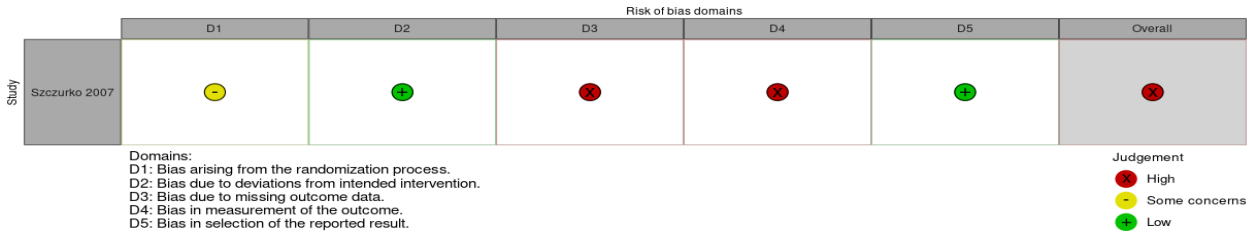
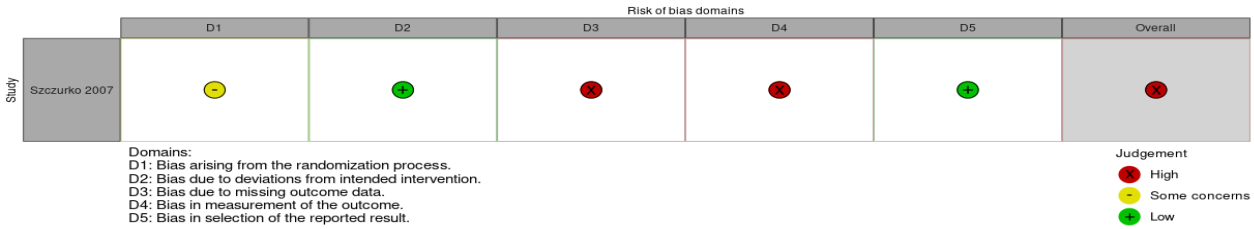


Figure 44: Szczurko 2007 Risk of bias – QOL



Source: Risk of bias visual graphic performed in *McGuinness, LA, Higgins, JPT. Risk of bias VISualization (robvis): An R package and Shiny web app for visualizing risk of bias assessments. Res Syn Meth. 2020; 1- 7. https://doi.org/10.1002/jrsm.1411*

4.12.4. Summary of findings

Table 11: LBP summary of findings

Naturopathy compared to Control (no intervention, usual care) for low back pain						
Patient or population: Low back pain Setting: Community, postal workers Intervention: Naturopathy Comparison: Control (no intervention, usual care)						
Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with Control	**Risk with Naturopathy**				
Pain assessed with: VAS change from baseline (lower is best) Scale: 10 points follow-up: 12 weeks	The median change in pain was **0 points**	MD **1.17 points lower** (1.63 lower to 0.70 lower) ^	-	75 (1 RCT)	⊕◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of naturopathy on pain in people with low back pain**
Quality of life - mental assessed with: SF-36 (higher is best) Scale from: 0 to 100 follow-up: 12 weeks	The mean quality of life – mental summary score was **2.74 point decrease**	MD **7.00 points higher** (2.25 higher to 11.75 higher) ^^	-	75 (1 RCT)	⊕◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of naturopathy on mental wellbeing in people with low back pain***
Function/disability assessed with: Oswestry disability questionnaire (lower is best) Scale from: 0 to 100 follow-up: 12 weeks	The median change in function/disability was **0 points**	MD **5.33 points lower** (7.48 lower to 3.19 lower) ^	-	75 (1 RCT)	⊕◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of naturopathy on function/disability in people with low back pain****
Improvement – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on improvement in people with LBP is unknown
Psychological Function – Not reported	-	-	-	(0 studies)		No studies found. The effect of naturopathy on psychological function in people with LBP is unknown

Naturopathy compared to Control (no intervention, usual care) for low back pain

Patient or population: Low back pain
Setting: Community, postal workers
Intervention: Naturopathy
Comparison: Control (no intervention, usual care)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with Control	Risk with Naturopathy				

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
^MD and 95% CI for pain and function/disability estimated post-hoc from median changes from baseline and IQR reported by study authors, using equation #15 (Wan 2014) and RevMan 5.3
^^MD and 95% CI for S-36 scales were reported by the study authors. Median differences for pain VAS and Oswestry questionnaires were calculated post-hoc from the median changes from baseline to 12 weeks

**The MCID in people with back pain is 2.3 points.[99]
***An MCID of 5 points for MSC is likely important.[98]
****The MCID in people with back pain is 12.8 points.[97]

Effect estimates were considered on three levels: small (MD <10% of the scale), moderate (MD between 10% to 20% of the scale) or large (MD more than 20% of the scale).

CI: confidence interval; **IQR:** Interquartile range; **MCID:** Minimal clinically important difference; **MD:** mean difference; **MSC:** Mental component summary; **PCS:** physical component summary; **RCT:** Randomised Controlled trial: **VAS:** Visual Analogue Scale

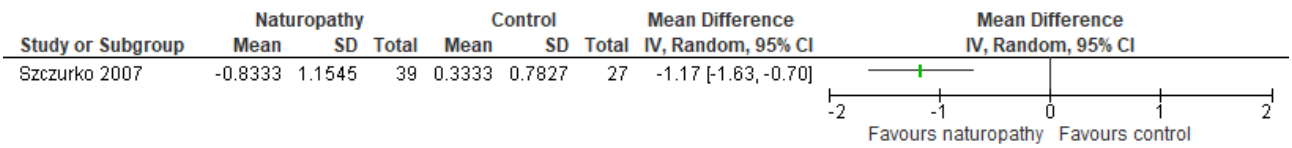
GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded two levels for very serious risk of bias: due to missing outcome data, measurement of the outcome and selection of the reported result. All three outcome domains assessed were at high risk of bias due to the open-label design of the study, the attrition rates being substantially greater in the comparator group than the intervention group, and the self-reported measurement methods. The bias is likely to favour naturopathic treatment.
b. Downgraded two levels for imprecision: Small sample size (n=75), low event rate and wide CIs
c: Inconsistency could not be assessed as only one study measured this outcome. No downgrading. Publication bias not suspected. No downgrading.

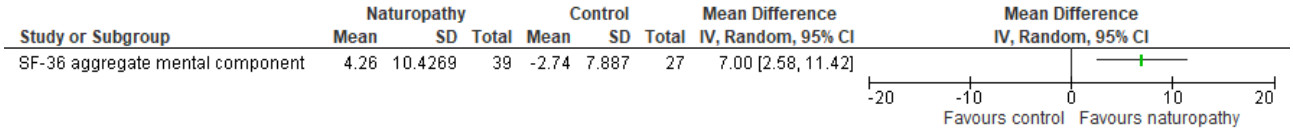
Figure 48 shows the forest plot for the change in the QOL in participants with LBP. Forest plots could not be generated for pain or disability/functioning.

Figure 45: LBP – change in pain from baseline to 12 weeks



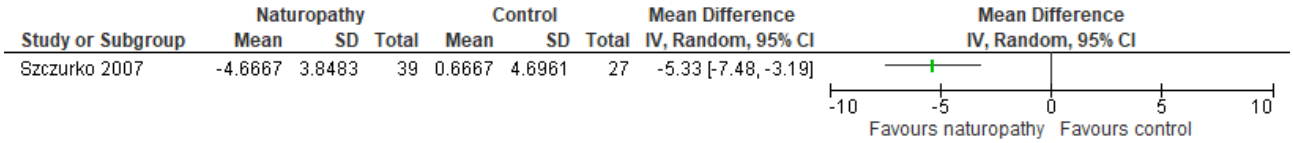
VAS, 10 point scale. Change from baseline (lower is best)

Figure 46: LBP - QOL



SF-36, scale from 0 to 100 (higher is best)

Figure 47: LBP – change in function/disability (Oswestry questionnaire) from baseline to 12 weeks



Oswestry disability questionnaire, scale from 0 to 100 (lower is best) Abbreviations: IV= Inverse variance; SD= Standard deviation; SF-36=Short form 36

Note: SD values and upper limit of 95% confidence intervals for mean changes from baseline for each group, mean difference and 95% confidence intervals for between groups were calculated post-hoc by RevMan 5.3. Mean and SD values for naturopathy and control groups calculated post-hoc from median and IQR values reported by the study (Wan 2014).

4.13. Rotator cuff tendinitis

4.13.1. Description of the condition

Rotator cuff disease is an umbrella term and includes partial and/or complete rotator cuff tears, calcific tendinitis and subacromial bursitis. Symptomatic rotator cuff disease includes shoulder pain, in the upper outer arm aggravated by overhead activities and often worse at night.[100] Diagnosis is by clinical examination and/or diagnostic imaging, although evidence to support diagnostic imaging is uncertain.[101] Prognostically most patients recover from rotator cuff tendinitis with non-operative management.[102] There is a paucity of Australian prevalence data for rotator cuff disease. In Australia, a 2016 estimate of 65-70% of all shoulder pain was due to rotator cuff disease. Based on these figures approximately 13.3 per 1,000 patients per year present to GPs with a rotator cuff syndrome.[103]

4.13.2. Description of studies

One RCT (Szczurko 2009)[104] was identified that assessed naturopathy for rotator cuff tendinitis. The RCT was conducted in Canada and investigated 85 adults employed as postal workers who were diagnosed with rotator cuff tendinitis. Participants were aged between 42 and 59 years. Diagnosis was by biometric tests, specific shoulder range of motion and orthopaedic tests. Additionally rotator cuff tendinitis was confirmed by a blinded co-ordinator. The interventions were administered for 12 weeks.

Szczurko 2009 compared the effectiveness of naturopathic care (including acupuncture, dietary changes, and the supplement Phlogenzym containing hydrolytic enzymes, bromelain, trypsin, and bioflavonoid rutin) delivered by two naturopathic doctors against physical exercise. Participants in the comparator group (physical exercise group) received a placebo supplement but were not provided with dietary counselling, and the treatment provider was not reported (further details in Appendix D.1.).

4.13.3. Risk of bias

Risk of bias for Szczurko 2009 was assessed using RoB 2[39] and overall rated as 'high' due to a higher proportion of participants dropping out of the comparator group, versus the naturopathy group with no reason given for drop-out rates. For the pain, QOL (Details of the risk of bias assessments are provided at Appendix D.9. Details of the study characteristics are provided at Appendix D1.13 and outcome data details are available at Appendix E.8. Figure 51, Figure 53) treatment success self-report measures were used, which may favour the intervention (Details of the risk of bias assessments are provided at Appendix D.9. Details of the study characteristics are provided at Appendix D1.13 and outcome data details are available at Appendix E.8. Figure 51 to Figure 53).

Details of the risk of bias assessments are provided at Appendix D.9. Details of the study characteristics are provided at Appendix D1.13 and outcome data details are available at Appendix E.8.

Figure 48: Szczurko 2009 Risk of bias – pain and QOL

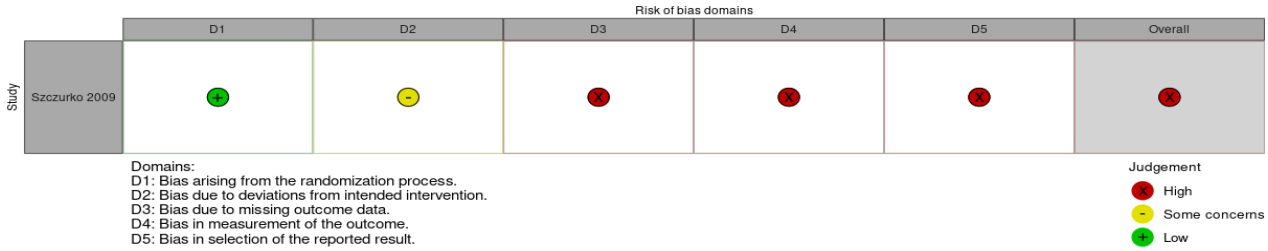


Figure 49: Szczurko 2009 Risk of bias – range of motion

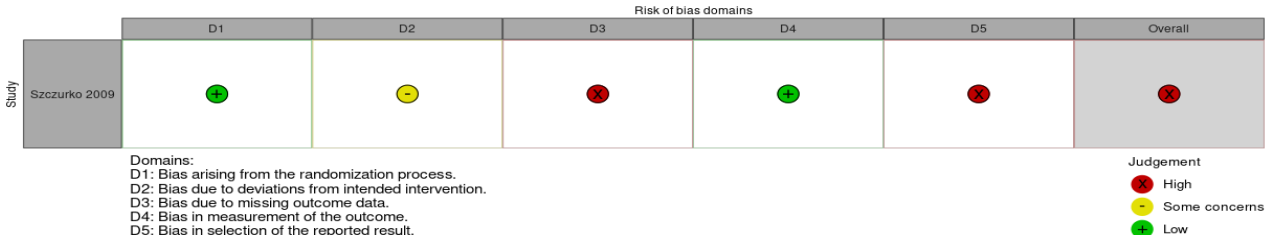
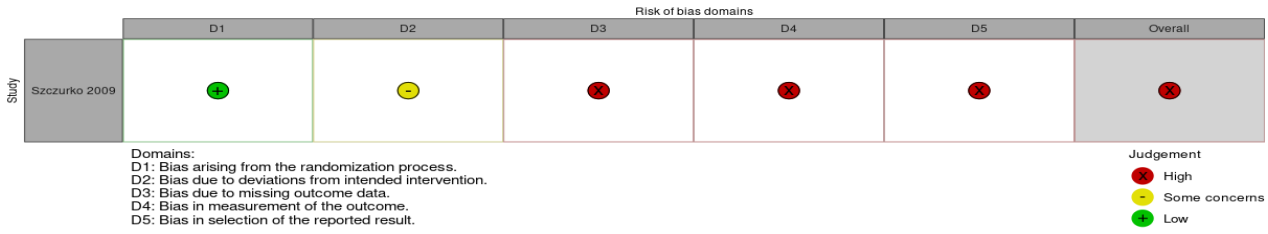


Figure 50: Szczurko 2009 Risk of bias – treatment success



Source: Risk of bias visual graphic performed in *McGuinness, LA, Higgins, JPT. Risk of bias VISualization (robvis): An R package and Shiny web app for visualizing risk of bias assessments. Res Syn Meth. 2020; 1- 7. https://doi.org/10.1002/jrsm.1411*

4.13.4. Summary of findings

Table 12: Rotator cuff tendinitis summary of findings

Naturopathy compared to Control (no intervention, usual care) for rotator cuff tendinitis

Patient or population: Rotator cuff tendinitis
Setting: Community, postal workers
Intervention: Naturopathy
Comparison: Control (no intervention, usual care)

Outcomes	Mean change from baseline* (95% CI)		Relative effects (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statement
	Risk with control	**Risk with Naturopathy**				
Pain assessed with: VAS (lower is best) Scale from: 0 to 7 follow-up: 12 weeks	The mean change in pain was **0.67 points lower**	MD **1.67 points lower** (2.47 lower to 0.88 lower)	-	85 (1 RCT)	⊕◯◯◯ VERY LOW a,b,c,d	The evidence is very uncertain about the effect of naturopathy on pain in people with rotator cuff**
Quality of life - mental assessed with: SF-36 (higher is best) Scale from: 0 to 100 follow-up: 12 weeks	The mean quality of life – mental summary score was **0.13 points higher**	MD **5.73 higher** (1.37 higher to 10.09 higher)	-	85 (1 RCT)	⊕◯◯◯ VERY LOW a,b,c,d	The evidence is very uncertain about the effect of naturopathy on mental wellbeing in people with rotator cuff***
Functionality assessed with: SPADI (lower is best) Scale from: 0 to 130^ follow-up: 12 weeks	The mean change in range of motion was **12.68 points lower**	MD **29.66 points lower** (42.35 lower to 16.98 lower)	-	85 (1 RCT)	⊕◯◯◯ VERY LOW a,b,c,d	The evidence is very uncertain about the effect of naturopathy on functionality in people with rotator cuff****
Abduction assessed with: Goniometer readings (higher is better) Scale from: 0 to 180 degrees follow-up: 12 weeks	The mean change in abduction from baseline was 0.89 degree increase	MD **46.57 degrees higher** (31.21 higher to 61.94 higher)	-	85 (1 RCT)	⊕◯◯◯ VERY LOW a,b,c,d	The evidence is very uncertain about the effect of naturopathy on abduction in people with rotator cuff*****
Treatment success assessed with: MYMOP Symptom 1^^ (lower is best) Scale: 7-points follow-up: 12 weeks	The mean change in treatment success was **1.29 points lower**	MD **0.91 points lower** (1.68 lower to 0.13 lower)	-	85 (1 RCT)	⊕◯◯◯ VERY LOW a,b,c,d	The evidence is very uncertain about the effect of naturopathy on treatment success in people with rotator cuff******
Treatment success assessed with: MYMOP Symptom 2^^ (lower is best) Scale: 7-points follow-up: 12 weeks	The mean change in treatment success was **0.66 points lower**	MD **1.86 points lower** (2.73 lower to 1.00 higher)	-	85 (1 RCT)	⊕◯◯◯ VERY LOW a,b,c,d	The evidence is very uncertain about the effect of naturopathy on treatment success in people with rotator cuff******
Strength - Not Reported	-	-	-	(0 studies)		No studies found. The effect of naturopathy on strength in people with rotator cuff is unknown

Naturopathy compared to Control (no intervention, usual care) for rotator cuff tendinitis

Patient or population: Rotator cuff tendinitis
Setting: Community, postal workers
Intervention: Naturopathy
Comparison: Control (no intervention, usual care)

Outcomes	Mean change from baseline* (95% CI)		Relative effects (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statement
	Risk with control	Risk with Naturopathy				
Disability - Not Reported	-	-	-	(0 studies)		No studies found. The effect of naturopathy on disability in people with rotator cuff is unknown

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
^ MD and 95% CI were reported by Szczurko 2009
^^ For the MYMOP measure, patients choose 2 personally relevant symptoms of greatest importance to their health and rate these symptoms on a 7-point VAS. The study did not report which symptoms the patients selected for each of the two MYMOP "subscales". Thus, it was decided to retain both scales in the SoF. The paper does not specify, so the scale is assumed to be the original MYMOP not MYMOP 2.

**An MCID of 1.37 is likely important.[105]
***The MCID for SF-36 in rotator cuff is unknown. An MCID of 5 is likely important.[98]
****The MCID for SPADI in rotator cuff, unspecified and shoulder tears is 8, 10, 13.2[105] and 14.1, 20.6 in shoulder arthroplasty, instability and fracture.[105]
***** The MCID for flexion, extension, abduction, adduction is unknown. Range of motion normal values for flexion are 180, extension 50, abduction 180 and adduction 50.[106]
******The MCID of MYMOP 1 is unknown. A change score of 13% is moderate.# The MCID of MYMOP 2 is unknown. A change score of 26% is large.#

Effect estimates were considered on three levels: small (MD <10% of the scale), moderate (MD between 10% to 20% of the scale) or large (MD more than 20% of the scale).

CI: confidence interval; **MD:** mean difference **MCID:** Minimal clinically important differences; **MYMOP:** Measure Yourself Medical Outcome Profile; **RCT:** Randomized controlled trial; **SF-36:** 36-Item Short Form Health Survey; **SPADI:** Shoulder Pain and Disability Index; **VAS:** Visual Analogue Scale

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded one level for serious risk of bias: due to missing outcome data, measurement of the outcome and selection of the reported results
b. Downgraded one level for indirectness: it is not known what symptoms were self-selected by participants to assess treatment success.
c. Downgraded two levels for imprecision: small sample size (n=85) and few events leading to larger CIs. Confidence intervals cross the line of no effect for Adduction and MYMOP 2
d. Inconsistency could not be assessed as only one study measured this outcome. No downgrading. Publication bias not suspected. No downgrading.

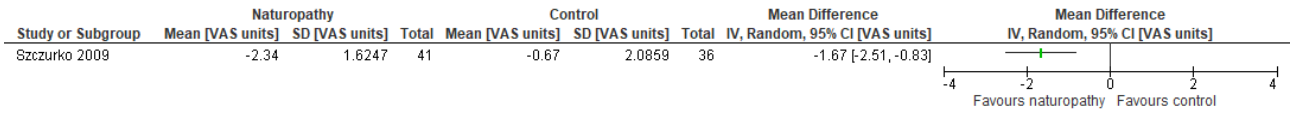
The forest plot for pain Figure 54 shows the MD between the groups for mean changes from baseline, indicating greater pain reduction in the naturopathy group.

The forest plot for QOL Figure 55 shows how both the physical and mental components for QOL improved from baseline to a greater degree in the naturopathy group compared to the standardised physical exercises group.

The forest plot Figure 56 shows the naturopathy group had a greater improvement in shoulder range of motion compared to the standardised physical exercises group, as measured by SPADI.

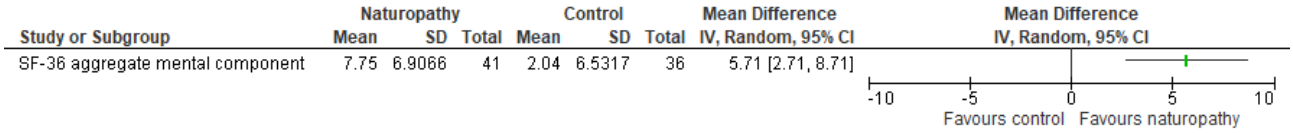
The forest plot Figure 57 shows the difference in mean change from baseline in maximal range of motion as measured by goniometer readings. Naturopathy resulted in a greater improvement in flexion, extension, and abduction than standardised physical exercises, while there was no difference between the groups for adduction. The forest plot Figure 58 shows the naturopathy group had greater treatment success compared to the standardised therapy group, from baseline to 12 weeks of treatment), as measured by the Measure Yourself Medical Outcomes Profile (MYMOP) for two symptoms.

Figure 51: Rotator cuff tendinitis – mean change in pain from baseline to 12 weeks



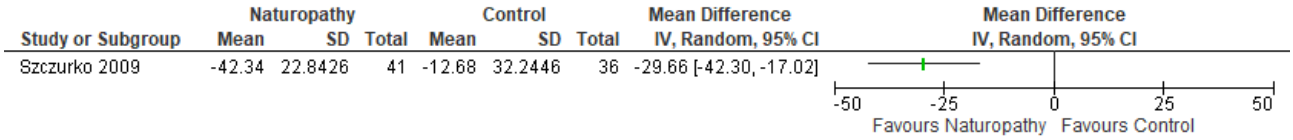
VAS, scale from 0 to 7 (lower is best)

Figure 52: Rotator cuff tendinitis – mean changes in QOL (SF-36) from baseline to 12 weeks forest plot



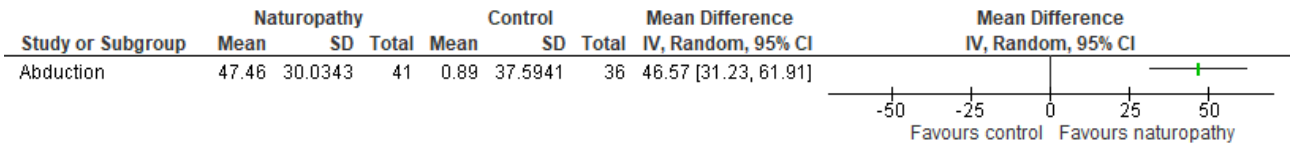
SF-36, scale from 0 to 100 (higher is best)

Figure 53: Rotator cuff tendinitis - mean changes in functionality (SPADI) from baseline to 12 weeks forest plot



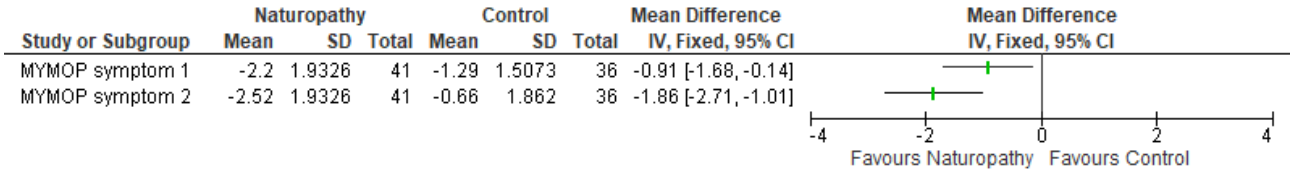
SPADI, scale from 0 to 130 (lower is best)

Figure 54: Rotator cuff tendinitis – mean changes in range of motion from baseline to 12 weeks forest plot



Goniometer readings for abduction, scale from 0 to 180 degrees (higher is better)

Figure 55: Rotator cuff tendinitis – mean changes in treatment success (MYMOP) from baseline to 12 weeks forest plot



MYMOP , 7-point scale (lower is best)

Abbreviations: MYMOP, Measure Yourself Medical Outcome; SD, Standard deviation

Note: SD values and upper limit of 95% confidence intervals for mean changes from baseline for each group, mean difference and 95% confidence intervals for between groups were calculated post-hoc by RevMan 5.3.

4.14. Menopausal symptoms

4.14.1. Description of the condition

Menopause is a decline in female reproductive hormones where menstruation ceases. Symptoms of menopause include hot flushes, night sweats and vaginal dryness. Diagnosis is made by signs and symptoms. Although blood tests, follicle-stimulating hormone (FSH) and estrogen (oestradiol), or thyroid-stimulating hormone (TSH) may be recommended. [107] Prognostically on average symptoms last for up to eight years.[108] Prevalence of menopause symptoms in Australian women ranged from 30% peri menopause to 80% post menopause for hot flushes, 47% to 67% for insomnia and 4% to 57% for anxiety.[109]

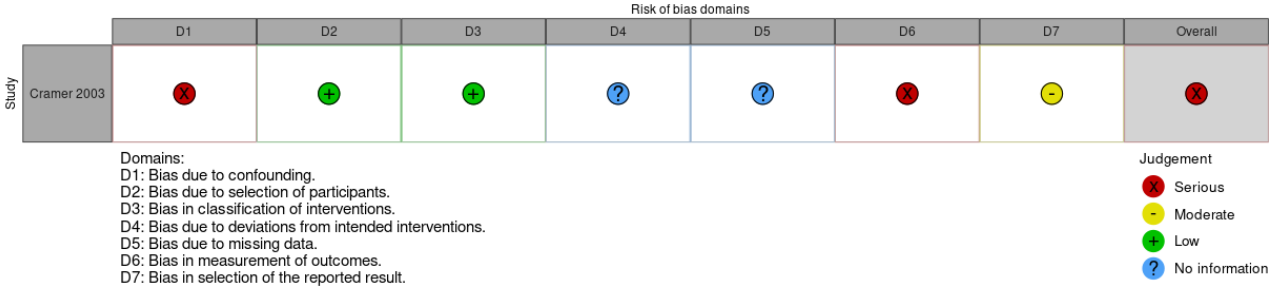
4.14.2. Description of studies

One NRSI (Cramer 2003) [110] was identified that assessed naturopathy for menopausal symptoms. The study was a retrospective study in the USA that investigated 239 women aged between 50 to 52 years with menopausal symptoms who were also taking hormonal replacement therapy. The intervention compared a comprehensive aggregate system of naturopathic care to conventional therapy (further details in Appendix D.1).

4.14.3. Risk of bias

Risk of bias of Cramer 2003 was assessed using ROBINS-I[34] and overall rated as 'serious' due to no adjustment of confounding variables in the analyses, the outcome assessors not being blinded, and the lack of information on how the outcomes were measured when recorded by clinicians (Details of the risk of bias assessments are provided at Appendix D.10. Details of the study characteristics are provided at Appendix D1.14 and outcome data details are available at Appendix E.9. Figure 59).[34]

Figure 56: Cramer 2003 Risk of bias – all menopause symptoms [a]



Source: Risk of bias visual graphic performed in *McGuinness, LA, Higgins, JPT. Risk of bias VISualization (robvis): An R package and Shiny web app for visualizing risk of bias assessments. Res Syn Meth. 2020; 1- 7. https://doi.org/10.1002/jrsm.1411*

a Menopause symptoms are: vasomotor symptoms, decreased energy, menstrual changes, insomnia, and anxiety

4.14.4. Summary of findings

Table 13: Menopausal symptoms summary of findings

Naturopathy compared to Control (no intervention, usual care) for menopausal symptoms

Patient or population: Menopausal symptoms
Setting: Community
Intervention: Naturopathy
Comparison: Control (no intervention, usual care)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect^ (95% CI)[1]	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements[2]
	Risk with Control	Risk with Naturopathy†				
Menopausal symptoms - Improvements in vasomotor assessed with: Proportion with symptoms who improved (higher is better) Follow-up: not stated	303 per 1,000	454 per 1,000 (95% CI not estimable)	Adjusted OR 1.40 (0.68, 2.88)	239 (1 observational study)	⊕◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of naturopathy on vasomotor symptoms in menopausal women **
Menopausal symptoms - decreased energy assessed with: Proportion with symptoms who improved (higher is better) Follow-up: not stated	154 per 1,000	364 per 1,000 (95% CI not estimable)	Adjusted OR 6.55 (0.96, 44.74)	239 (1 observational study)	⊕◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of naturopathy on decreased energy in menopausal women**
Menopausal symptoms - menstrual changes assessed with: Proportion with symptoms who improved (higher is better) Follow-up: not stated	337 per 1,000	257 per 1,000 (95% CI not estimable)	Adjusted OR 0.98 (0.43, 2.24)	239 (1 observational study)	⊕◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of naturopathy on menstrual changes in menopausal women**
Menopausal symptoms - insomnia assessed with: Proportion with symptoms who improved (higher is better) Follow-up: not stated	170 per 1,000	378 per 1,000 (95% CI not estimable)	Adjusted OR 6.77 (1.71, 26.63)	239 (1 observational study)	⊕◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of naturopathy on insomnia in menopausal women**
Menopausal symptoms - anxiety assessed with: Proportion with symptoms who improved (higher is better) Follow-up: not stated	329 per 1,000	455 per 1,000 (95% CI not estimable)	Adjusted OR 1.27 (0.63, 2.56)	239 (1 observational study)	⊕◯◯◯ VERY LOW a,b,c	The evidence is very uncertain about the effect of naturopathy on anxiety in menopausal women**
Satisfaction (acceptability of therapy) – Not reported	-	-	-	(0 studies)	-	No studies found. The satisfaction of naturopathy in menopause is unknown

Naturopathy compared to Control (no intervention, usual care) for menopausal symptoms

Patient or population: Menopausal symptoms
Setting: Community
Intervention: Naturopathy
Comparison: Control (no intervention, usual care)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect^ (95% CI)[1]	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements [2]
	Risk with Control	Risk with Naturopathy†				

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
** The MCID for menopause symptoms is unknown.

Effect estimates were considered on three levels: small (MD <10% of the scale), moderate (MD between 10% to 20% of the scale) or large (MD more than 20% of the scale).

†Absolute difference for outcomes: Vasomotor absolute difference = 15% improvement; Decreased energy absolute difference = 21% improvement; Menstrual changes absolute difference = 8% reduction; Insomnia absolute difference = 21% improvement; Anxiety absolute difference = 13% improvement

1. Adjusted OR and 95% CI were reported by Cramer 2003 and were adjusted for age, weight, smoking status, monthly income, regular exercise program, antihypertensive therapy
2. Adjusted OR >1.25
Note: Odds ratios were adjusted for age, weight, smoking status, monthly income, regular exercise program, antihypertensive therapy
^ Odds ratios calculated post-hoc by RevMan 5.3 (unadjusted). The odds ratios calculated by RevMan 5.3 differ from the crude odds ratios reported by the study authors.

Adj OR: adjusted odds ratios; **CI:** confidence interval; **MD:** Mean difference; **OR:** Odds ratio

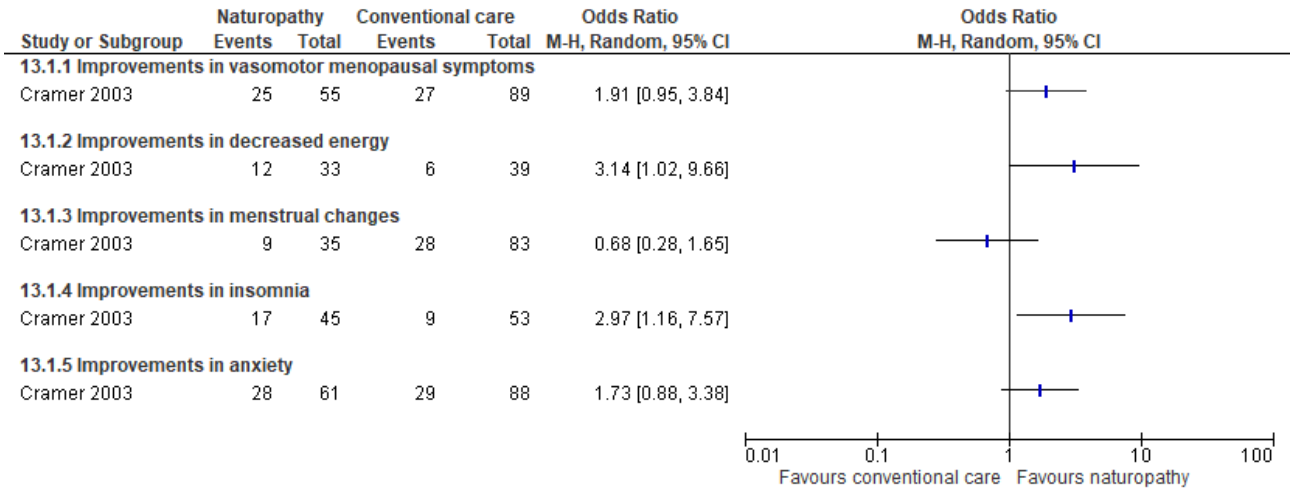
GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded by two levels for very serious risk of bias: due to confounding (estimates not adjusted for important variables) and measurement of outcomes (clinicians delivering intervention and assessors were aware of intervention received)
b. Downgraded by two levels for very serious imprecision: Forest plot (see Figure 58 below) all cross the null, line of no effect, except for insomnia. Due to few participants (n=211 or n=239), few events and thus wide confidence intervals.
c. Inconsistency could not be assessed as only one study measured this outcome. No downgrading. No publication bias suspected. No downgrading.

Figure 60 shows the forest plot for the unadjusted odds ratios for the prioritised outcome measures for vasomotor menopausal symptoms, decreased energy, menstrual changes, sleep, and anxiety.

Figure 57: Menopausal symptoms forest plot



No reference range or scale, higher score is better

Note: Odds ratios calculated post-hoc by RevMan 5.3 (unadjusted). The odds ratios calculated by RevMan 5.3 differ from the crude odds ratios reported by the study authors.

4.15. Cardiovascular disease risk

4.15.1. Description of the condition

Cardiovascular disease risk factors increase the likelihood of a person developing cardiovascular disease. CVD is a group of diseases that affect the heart and blood vessels including coronary heart disease, stroke, cardiomyopathy and atrial fibrillation.[111] Risk factors can be behavioural such as low fruit and vegetable consumption, lack of physical activity and increased alcohol and tobacco consumption. Biomedical risk factors can include overweight, obesity, dyslipidaemia, hypertension and hyperglycaemia. Additionally having two or three behavioural or biomedical risk factors at the same time can increase CVD risk.[112] In Australia, CVD was the underlying cause of 25% (42,300) of deaths in 2019.[113]

4.15.2. Description of studies

One RCT (Seely 2013)[114] was identified that assessed naturopathy for cardiovascular risk. The study was conducted in Canada and assessed 246 adults at multiple postal work sites from 2008 to 2010 over 12 months. Participants were screened as having the highest CVD risk and were aged 25-65 years. Participants were randomised to two treatments: naturopathic treatment combined with enhanced usual care against enhanced usual care only.

Seely 2013 compared naturopathy (including diet and lifestyle recommendations natural health products (i.e. omega-3 fatty acids, soluble fibre, coenzyme Q10, and plant sterols) and physical activity) combined with enhanced usual care (routine visits to physicians) to enhanced usual care alone (further details in Appendix D.1.).

Note: Seely 2013[114] is the primary publication reporting on population grouping 10: Prevention of disease, injury or illness in at-risk populations. Note: Herman 2014[115] is a cost-effectiveness analysis reporting on the same population as Seeley 2013 but contained no unique or complete outcome data that is within the scope of the review. The clinical trials registry report for both Seely 2013 and Herman 2014 is https://clinicaltrials.gov/ct2/show/NCT00718796.

4.15.3. Risk of bias

Risk of bias for Seely 2013 was assessed using RoB 2[39] and overall rated as 'high' due to no *a priori* plan, additional time point (26 weeks) included and additional secondary outcomes were reported. There was some selective reporting for some of the outcomes (Figure 62 to Figure 64).

Details of the risk of bias assessments are provided at Appendix D.11. Details of the study characteristics are provided at Appendix D1.15 and outcome data details are available at Appendix E.10.

Figure 58: Seely 2013 Risk of bias– 1 year CVD risk

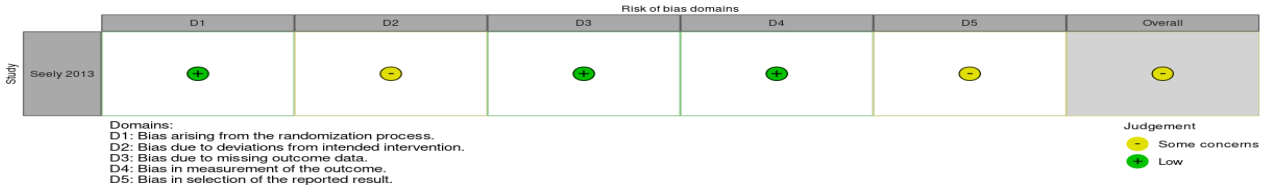


Figure 59: Seely 2013 Risk of bias– 10 year CVD risk

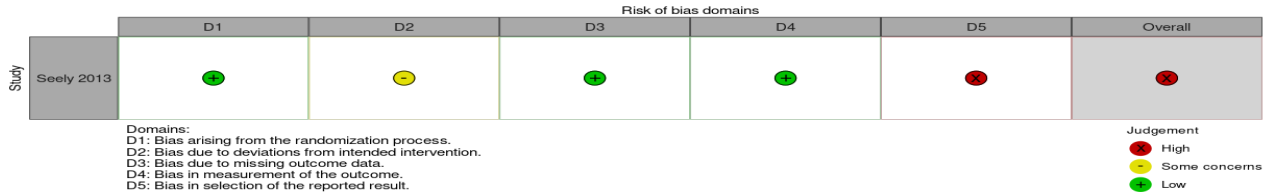


Figure 60: Seely 2013 Risk of bias– cholesterol

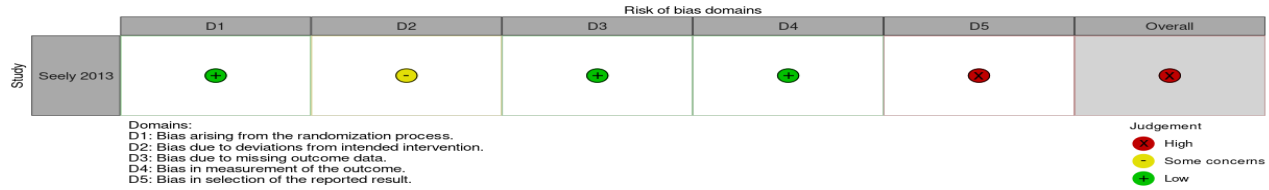


Figure 61: Seely 2013 Risk of bias– metabolic syndrome

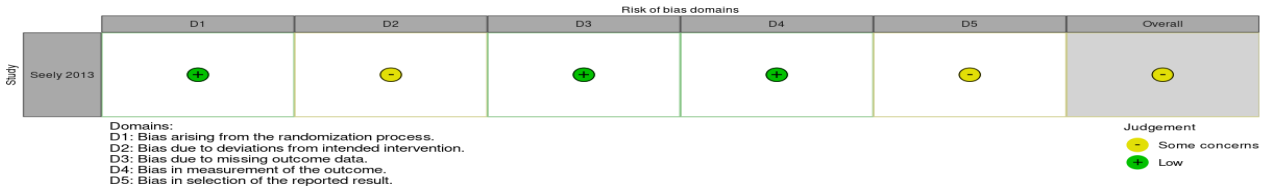
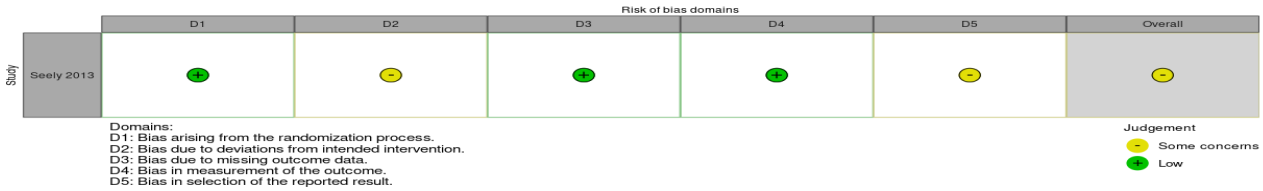


Figure 62: Seely 2013 Risk of bias – HbA1c



Abbreviations: CVD=Cardiovascular disease; HbA1c=haemoglobin A1c; RoB2= Risk of Bias 2

Source: Risk of bias visual graphic performed in *McGuinness, LA, Higgins, JPT. Risk of bias VISualization (robvis): An R package and Shiny web app for visualizing risk of bias assessments. Res Syn Meth. 2020; 1- 7.* https://doi.org/10.1002/jrsm.1411

4.15.4. Summary of findings

Table 14: CVD risk summary of findings

Naturopathy compared to control (usual care or control) for CVD risk summary						
Patient or population: CVD risk **Setting:** Community, postal workers **Intervention:** Naturopathy **Comparison:** Control (no intervention, usual care)						
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect* (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with Usual care	Risk with Naturopathy				
Cardiovascular risk score at 10 years assessed with: Framingham 10 year cardiovascular risk score (lower is better) follow-up: 12 months	The mean cardiovascular risk score was **10.81%** (9.88 to 11.74)	Adjusted MD **3.07% lower** (4.35 lower to 1.78 lower)	-	246 (1 RCT)	⊕⊕◯◯ LOW a,b,c	Naturopathy may result in little to no difference in CVD risk score**
LDL cholesterol assessed with: mmol/L (lower is better) follow-up: 12 months	The mean LDL cholesterol was **3.50 mmol/L** (3.32 to 3.68)	Adjusted MD **0.01mmol/L lower** (0.28 lower to 0.25 higher)		246 (1 RCT)	⊕⊕◯◯ LOW b,c,d	Naturopathy may result in little to no difference in CVD risk***
Prevalence of metabolic syndrome at 12 months (lower is better) Follow up: 12 months	The mean prevalence of metabolic syndrome was **48.48%** (SE 0.05%)	Adjusted MD **16.90% lower** prevalence (29.55 lower to 4.25 lower)	-	246 (1 RCT)	⊕⊕◯◯ LOW a,b,c	Naturopathy may result in little to no difference in CVD risk****
T2DM severity assessed with: HbA1c (%) (lower is better) follow-up: 12 months	The mean HbA1c was **5.78%** (5.68 to 5.89)	Adjusted MD **0.14% lower** (0.29 lower to 0)	-	246 (1 RCT)	⊕⊕◯◯ LOW a,b,c,	Naturopathy may result in little to no difference in CVD risk****
Cerebrovascular complications – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on cerebrovascular complications in people with CVD is unknown
Non-fatal ASCVD – Not reported	-	-	-	(0 studies)	-	No studies found. The effect of naturopathy on ASCVD in people with CVD is unknown

Naturopathy compared to control (usual care or control) for CVD risk summary

Patient or population: CVD risk
Setting: Community, postal workers
Intervention: Naturopathy
Comparison: Control (no intervention, usual care)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect* (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Evidence statements
	Risk with Usual care	Risk with Naturopathy				

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
** The MCID for CVD risk is unknown. CHD risk at 10 years in percent can be calculated with the Framingham Risk Score. Individuals with low risk have 10% or less CHD risk at 10 years, with intermediate risk 10-20%, and with high risk 20% or more.[116]
***The MCID for LDL in CVD risk is unknown. LDL-Cholesterol ≤3.0 mmol/L.[118] LDL cholesterol (mmol/L) MCID=0.10 in low and very low carbohydrate diets for T2DM remission.[117]
**** The MCID for metabolic syndrome in CVD risk is unknown. The prevalence of the metabolic syndrome using the ATPIII, WHO, IDF, and EGIR definitions was 22.1% (95%CI: 18.8, 25.4), 21.7% (19.0, 24.3), 30.7% (27.1, 34.3), and 13.4% (11.8, 14.9), respectively.[119]
***** The HbA1c MCID in people with type 2 diabetes is 0.3%.[49,50]

Effect estimates were considered on three levels: small (MD <10% of the scale), moderate (MD between 10% and 20% of the scale) or large (MD than 20% of the scale)

ATPIII: US National Cholesterol Education Program (ATPIII) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults **CI:** confidence interval; **CHD:** Coronary heart disease; **CVD:** Cardiovascular disease; **EGIR:** European Group for the Study of Insulin Resistance; **HbA1c:** Haemoglobin A1c; **IDF:** International Diabetes Federation; **LDL:** Low density lipoprotein; **SD:** Standard deviation; **MD:** mean difference; **WHO:** World Health Organization

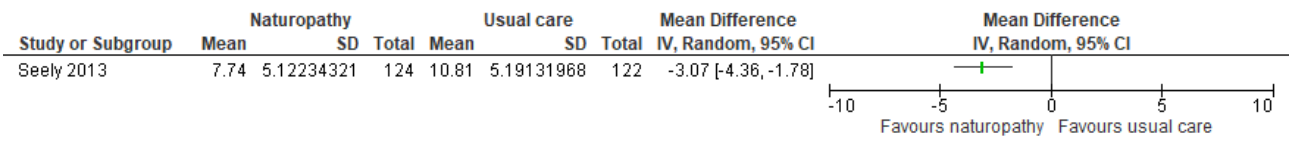
GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Downgraded one level for risk of bias: some concerns with blinding of participants and outcome assessors
b. Downgraded one level for imprecision: low event rate and small trial (n=246)
c. Inconsistency could not be assessed as only one study measured this outcome. No downgrading
d. Downgraded one level for risk of bias: outcome was not pre specified

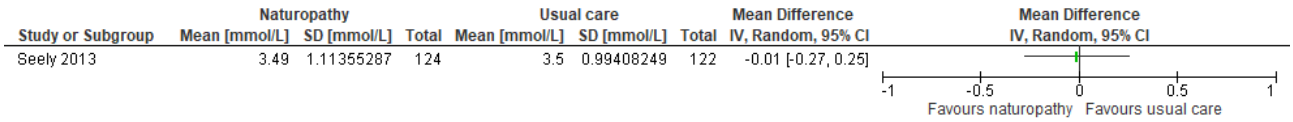
Figure 66 presents the MD in 10-year cardiovascular risk at 12 months (Framingham risk score) calculated by RevMan 5.3, showing the risk difference is in favour of naturopathy (Seely 2013). Figure 67 shows the forest plot for blood cholesterol profiles as measured by LDL levels. The MD between treatment groups was small. Figure 68 presents the forest plot for HbA1c levels at 12 months, as a measure of T2DM severity. The MD between the treatment groups was small. A forest plot for the prevalence of metabolic syndrome could not be generated.

Figure 63: 10-year cardiovascular risk 12 months forest plot



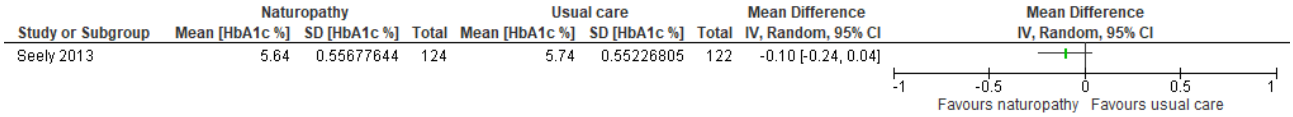
Framingham 10 year cardiovascular risk score, % (lower is better)

Figure 64: LDL levels 12 months forest plot



LDL mmol/L (lower is better). Therapeutic target < 2.5 mmol/L (Royal College of Pathologists Australasia https://www.rcpa.edu.au/Manuals/RCPA-Manual/Pathology-Tests)

Figure 65: HbA1c 12 months forest plot



HbA1c (%) (lower is better). Reference range 3.5% to 6.0% (Royal College of Pathologists Australasia https://www.rcpa.edu.au/Manuals/RCPA-Manual/Pathology-Tests)

Abbreviations: HbA1c=Haemoglobin A1c; LDL=Low density lipoprotein; SD=Standard deviation

Note: Standard deviations were calculated post-hoc for this Review.

5. Discussion

5.1. Summary of main results

We conducted a systematic review of RCTs and NRSIs to evaluate the effectiveness of naturopathy in Australia. People of any age with any injury, disease, medical condition, or preclinical condition, including individuals at-risk, were eligible for inclusion. In total 14 populations were identified for inclusion in the review.

A total of 16 studies (29 reports of 9 RCTs and 7 NRSIs) were eligible for inclusion in the results. Critical or important outcomes prioritised by NTWC for the 16 studies were included in the analysis and presented in the summary of findings tables.

Meta-analyses could not be undertaken for any of the populations and outcomes in this review. For most outcomes there were fewer than two studies or studies were unable to be synthesised due to differences in study design (e.g. RCT and NRSI).

Studies were assessed using the GRADE framework. GRADE combines information to assess overall how certain systematic review authors can be that the estimates of the effect (reported across a study/s for each critical or important outcome) are correct.

Certainty of evidence is interpreted as follows:

Certainty	Definition
High certainty	The authors have a lot of confidence that the true effect is similar to the estimated effect.
Moderate certainty	The true effect is probably close to the estimated effect.
Low certainty	The true effect might be markedly different from the estimated effect.
Very low certainty	The true effect is probably markedly different from the estimated effect.

This review identified 14 populations or conditions for which evidence provided low to very low certainty about the effect of naturopathic practice on an outcome considered critical or important by NTWC. The evidence provides:

- **low certainty that naturopathy may result in:**
  - a moderate improvement in quality of life and a slight improvement in menstrual regularity of people with polycystic ovary syndrome (PCOS) (one study, 122 participants). Participants received a lifestyle intervention, consultations with a qualified naturopath and herbal supplements.
- **low certainty that naturopathy results in little to no difference in:**
  - cognitive impairment in people with multiple sclerosis (one study, 30 participants). Participants received naturopathic treatment plus usual care, which included visits with a naturopath, daily supplementation with multivitamins and minerals, fish oils and alpha-lipoic acid, intramuscular vitamin B12 and dietary intervention.
  - cardiovascular risk factors (i.e. cardiovascular risk scores, LDL cholesterol levels), prevalence of metabolic syndrome and impact on severity of type II diabetes (i.e. HbA1c levels) in people at risk of cardiovascular disease (one study, 246 participants). Participants received naturopathic care plus enhanced usual care, which included visits with a naturopath, individualised naturopathic treatments, diet and lifestyle recommendations and natural dietary supplements.

The evidence provides very low certainty of the effect of naturopathy on 51 prioritised outcomes for colon cancer, prostate cancer, type II diabetes, PCOS, overweight and obesity, anxiety, multiple sclerosis, cardiovascular disease, allergic rhinitis, low back pain, rotator cuff tendinitis and symptoms of menopause.

Of the population (conditions) identified in this review, the effect of naturopathy on 44 outcomes considered critical or important by the NTWC remain unknown, as no studies were found that assessed these outcomes.

An assessment of benefits and harms of naturopathy was not conducted for this review, as it was out of scope of this review to assess adverse effects of naturopathy or naturopathic treatments.

Overall, the evidence suggests that naturopathy may provide people with polycystic ovarian syndrome with a moderate or slight improvement, for a small number of relevant outcomes when compared with control (no intervention, wait list or inactive control). For most outcomes, effect estimates were based on one or two small studies (typically 51 to 246 participants, except one observational study with 922 total participants) with concerns of bias that may favour the intervention. For several outcomes, a clinically important difference was not observed (possibly relating to study design, size or duration).

5.2. Overall completeness and applicability of evidence

This review sought to identify the available evidence on the effectiveness of naturopathy as a whole-system practice, including both multi-modal and single modal treatments for conditions identified in the literature and relevant to the practice of naturopathy in Australia. Included studies were either RCTs or NRSIs.

The literature search was not restricted by country; however consideration was given to how applicable the evidence was to the Australian context. Of the eligible studies, two were conducted in Australia[55,79] and the remaining conducted in countries where naturopathic practice is considered generally applicable to the Australian context, including United States,[33,42,85,110] India,[38,47,56] Germany,[62,48] and Canada.[120,73,96,114,67]

Studies published in a language other than English were not translated and were not included in the report but were listed in an inventory for completeness (See Appendix F). Databases in languages other than English were not searched. There were nine publications identified in a language other than English. Given these studies were not translated or assessed, we cannot comment on whether the results of these studies would impact the overall conclusions of the review.

The review includes studies published up to July 2021. There were 36 studies considered ongoing (registered but not published) at the time of the search. Of these 9 were listed as complete (but without available data), 20 studies were not recruiting participants, 5 were recruiting participants and one study was cancelled. It is unknown whether these studies would meet the eligibility criteria for this review and therefore impact the overall results.

5.3. Certainty of the evidence

Most studies in this review were assessed as having concerns with bias for one or more of the following factors: self-reporting of outcome assessments, lack of blinding of outcome assessors, selective reporting of results (e.g. missing reported results, or results being reported outside the study timeline) and presentation of unadjusted estimates or selected results, which appear to be those with a statistically significant effect. Other factors affecting certainty include the use of non-

validated, non-standardised outcome measurement tools and imprecision with small sample sizes and low event rates overall.

As most population groups were represented by only one study, inconsistency of the evidence could not be evaluated. For most population groups, the certainty of the evidence was rated as 'low' to 'very low' mainly due to issues with risk of bias and imprecision.

5.4. Potential biases in the review process

To ensure transparency in the review process the final NTWC endorsed research protocol was published on PROSPERO.

To capture all relevant studies, we searched for published peer-reviewed studies and screened citations, including grey literature, provided by stakeholders via the Department's public call for evidence. No restrictions were applied to language, date of publication, population, or study design (i.e. included RCTs, quasi RCTs and NRSIs) at search. We did independently search for unpublished trials, which are a potential source of reporting bias.

Studies published in a language other than English were not translated or included in this review but were listed in an inventory (Appendix F) for completeness. We cannot comment on whether inclusion of these studies would impact (or not impact) the overall conclusions of the review.

To ensure consistent methodology throughout the review, we utilised the methodological approach described in the *Cochrane Handbook of Systematic Reviews of Interventions* and other best practice methodology.

Using standardised procedures, data were extracted from published sources by at least two researchers to ensure data was collected accurately, with a secondary reviewer independently assessing an initial 20% of citations to achieve 80% inter-rater agreement. Where sufficient data were published, standard deviations and 95% confidence intervals for reported means and mean differences were reported. Missing mean values for outcomes were not imputed, although mean differences and risk ratios were calculated post-hoc where studies reported sufficient data to do so. Where studies reported insufficient information to impute measures of variation (standard deviations, standard errors, or 95% confidence intervals), the certainty of the evidence may have been overestimated as demonstrated by imprecision. One author (Stier-Jarmer 2021) was contacted to obtain a full publication of their study but did not respond.

Outcomes included in the analysis were agreed by NTWC (with input from NTREAP) who underwent an outcome prioritisation process to identify up to seven critical and important outcomes per population. NTWC and NTREAP were blinded to the number of studies and study details (see Appendix A.6.2.).

Reporting bias could not be assessed using funnel plots, as fewer than 10 publications were identified per outcome across populations. However, the potential for reporting bias cannot be excluded.

5.5. Agreements and disagreements with other studies or reviews

We identified one overview of systematic reviews that was conducted by Monash University[2] in 2014 for the 2015 review of natural therapies. This overview included the then unpublished manuscript of a systematic review by Oberg 2015 (now published).[4] An additional systematic review was identified by Myers 2019.[3] Neither the Oberg 2015 nor Myers 2019 systematic reviews included GRADE certainty ratings for included studies.

This Review includes five RCTs that were included in the previous overview of systematic reviews conducted by Monash University[2] in 2014 (Bernhardt 2009, Seely 2013, Shinto 2008, Szczurko 2007 and Szczurko 2009). The 2014 overview included six RCTs overall, all from North America, and concluded that there was some evidence to suggest that whole system naturopathic practice is effective in improving patient health for a range of chronic health conditions. The Monash overview rated the certainty of the evidence in Oberg (2015) as 'very low'. The findings in this review are consistent with the overview results.

The systematic review by Oberg 2015[4] included 15 studies in their systematic review of whole system naturopathic medicine but restricted their search to treatments delivered by North American naturopathic doctors. The included studies were RCTs, observational studies, and cost-effectiveness analyses. Seven studies included by Oberg 2015 were also included in this Review (Bernhardt 2009, Cramer 2003, Herman 2014, Seely 2013, Shinto 2008, Szczurko 2007 and Szczurko 2009). The review concluded that in North America, naturopathic medicine is associated with improved health outcomes and improved QOL in patients with or at-risk for chronic conditions. Effect sizes were generally small for clinical outcomes and mostly moderate for QOL measures, but certainty of the evidence was not reported.

In comparison, the systematic review by Myers 2019[3] included 33 studies, including RCTs, NRSIs, case series, and poster presentations. Seven of the studies included by Myers were also included in this review (Arentz 2017, Bernhardt 2009, Braun 2014, Seely 2013, Shinto 2008, Szczurko 2007, and Szczurko 2009). Similar to this review, studies included by Myers 2019 were from a wider range of countries, such as India, Australia, Canada, USA, UK, Germany and Japan. The range of populations, naturopathic modalities, and study designs were broader in the Myers 2019 systematic review than the scope of the current review. Myers 2019 stated that the studies mainly reported positive health outcomes and QOL, for the chronic conditions of CVD, T2DM, chronic pain, anxiety and depression, hepatitis C, menopausal symptoms, bipolar disorder, asthma, PCOS and cancer survival times, which is broadly consistent with this review. Myers 2019 reported no difference between treatment groups for MS (Shinto 2008) and acknowledged that there was a lack of data to make a clinical assessment of naturopathic treatment in HIV. Although risk of bias was assessed for the RCTs and with similar results to this review, the certainty of the evidence was not reported.

The studies both Myers 2019 and Oberg 2015 included, and which were also included by the current review, were Bernhardt 2009, Seely 2013, Shinto 2008, Szczurko 2007 and Szczurko 2009. Braun 2014 and Arentz 2017 were included by Myers 2019 but not Oberg 2015; in comparison, Herman 2014 (from the same trial as Seely 2013) and Cramer 2003 were included by Oberg 2015 but not by Myers 2019. Studies that were included by Myers 2019[3] and Oberg 2015[4] but were excluded by the current review had been excluded because they did not meet the inclusion criteria. The excluded studies were the wrong study type (e.g., case reports, single arm studies without a contemporaneous control group) or were not in scope (e.g., were cost-effectiveness studies).

The findings of this Review broadly align with other systematic reviews of naturopathy as a whole-system treatment.

5.6. Limitations of the Review

Overall, the review is intended to inform the Australian Government about health policy decisions for private health insurance rebates. This review is not designed to assess all the reasons that people use naturopathy or the reasons practitioners prescribe naturopathic treatments and is not intended to inform individual choices about using naturopathy.

At the review level, this review was limited to studies which assessed naturopathy as a whole-system treatment and was not designed to assess individual treatment modalities or 'tools of the trade' (e.g. herbal medicines, nutritional supplements etc.), unless a study demonstrated that the individual (or combination) treatment modality was given in the context of naturopathic practice. The NTWC considered that the available evidence for naturopathy as a whole-system treatment was likely to be limited and has sought two companion reviews to accompany the totality of the evidence for naturopathy for Government decision making. The two companion reviews will assess the clinical effectiveness of certain nutritional supplements and western herbal medicines that are commonly utilised in naturopathic practice.

At the study level, the outcomes assessed in this review were limited to those deemed critical or important by NTWC (with input from NTREAP) for each identified population or condition. All but one condition had no available evidence for some of the critical or important outcomes.

Most of the populations and conditions were limited to one or two small studies, with participants ranging from 51 to 246 participants. The exception was one observational study with 922 participants, this study focussed on a post-operative naturopathic support of patients with cardiovascular disease. Nine studies were published in languages other than English and were not included in the synthesis (but listed for completeness), which may or may not impact overall conclusions of the Review.

It is acknowledged that the nature of naturopathic treatment makes blinding of participants impractical in trials, and that patient-relevant outcomes such as pain and QOL are often assessed by self-report, inevitably increasing risk of bias. While this Review focused on naturopathic treatment as a whole system being delivered by naturopaths or in the naturopathic context, there was great heterogeneity in the composition of the treatments across the studies, in the naturopathic modalities that were incorporated into care. Further, there was also heterogeneity in the comparator treatments, in what was deemed 'usual care'.

Given the limited number of studies and the difficulties of assessing a whole-system treatment, it is challenging to conclude the effectiveness of naturopathy as a whole-system treatment for the populations and conditions identified in this review and more studies of whole-system naturopathy are needed to confirm findings.

6. Conclusions

6.1. Implications for health policy

This report was commissioned by the Australian Government as part of the Natural Therapies Review, with findings intended to inform decisions relating to whether private health insurance cover should be reinstated to naturopathy. As such, specific recommendations are not provided.

There is an absence of high certainty evidence examining the effectiveness of naturopathy as a whole-system treatment compared with no intervention and usual care for the 14 populations and conditions identified in the literature. The evidence provides:

- **low certainty that naturopathy provides:**
  - a moderate improvement in quality of life and a slight improvement in menstrual regularity of people with polycystic ovary syndrome (PCOS) (one study, 122 participants)
- **low certainty that naturopathy has little (to no) benefit in:**
  - cognitive impairment in people with multiple sclerosis (one study, 30 participants).
  - improving cardiovascular risk factors (i.e. decreasing risk of heart attack, number of cardiovascular events, lowering LDL cholesterol levels), prevalence of metabolic syndrome and impact on severity of type II diabetes (i.e. blood sugar levels) in people at risk of cardiovascular disease (one study, 246 participants).

The effect of naturopathy for most of the prioritised outcomes for colon cancer, prostate cancer, type II diabetes, overweight and obesity, anxiety, multiple sclerosis, cardiovascular disease, allergic rhinitis, low back pain, rotator cuff tendinitis and menopause remains uncertain.

Naturopathic practice in Australia generally aligns with that practiced internationally (e.g. USA, UK and Europe), so the evidence is likely to be applicable for most studies identified in this review. Adverse events and safety were not within scope for this Review.

In considering the evidence on the overall effectiveness of naturopathy, this review will be accompanied by two companion evidence reviews which will assess the main treatment modalities or 'tools of the trade' used by naturopaths. The two companion reviews include (1) an overview of systematic reviews that will assess the clinical effectiveness of selected nutritional supplements for certain conditions/ populations (PROSPERO CRD42023410906) and (2) an overview of systematic reviews that will assess the clinical effectiveness of western herbal medicines for certain conditions and populations (PROSPERO CRD42021243337).

6.2. Implications for research

There is a need for more robust trials evaluating the effectiveness of naturopathy as a whole-system treatment in the Australian context. However, it is likely that the available evidence for whole-system naturopathic treatment is limited due to it being a system of health care and not an individual treatment modality.

The available evidence could be enhanced by larger studies (more participants enrolled), improved registering and reporting of the methods use, analysis of results from all randomised participants (or better transparency of missing data), as well as measuring and reporting outcomes that are considered critical or important for decision-making.

7. Author contributions and declaration of interests

Dr Lisa Fodero: systematic review protocol design; critical quality assurance and review; oversight of systematic review.

Shari Stathis: systematic review protocol design; development of search methodology and search strategy; critical quality assurance; database searches; screening of publications; report writing, ROB assessments; certainty of evidence assessments; oversight of evidence evaluation and technical reports.

Dr Nerissa Soh: systematic review protocol design; screening of publications; data extractions; data synthesis; ROB assessments; certainty of evidence assessments; report writing.

Katrin Schultz: systematic review protocol design.

The authors declare that they have no conflicts of interest.

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