YOGA FOR PREVENTING AND TREATING HEALTH CONDITIONS

TECHNICAL REPORT
APPENDICES D TO H

prepared by
HTANALYSTS

for
National Health and Medical Research Council

NHMRC | Natural Therapies Working Committee
Canberra ACT 2601

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Report information

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Dates

This technical report and accompanying evidence evaluation report received approval from the National Health and Medical Research Council (NHMRC) Natural Therapies Working Committee (NTWC) on 04 Dec 2023.

The protocol for the evidence evaluation received approval from the NHMRC NTWC on 25 May 2020 (PROSPERO: CRD42020200084).

History

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

To support NHMRC in their evidence review, Health Technology Analysts (HTAnalysts) has been engaged to conduct a systematic review of the evidence of clinical effectiveness of Yoga. Eligible studies received from the Department's public call for evidence, the Natural Therapies Review Expert Advisory Panel (NTREAP) and the Natural Therapies Working Committee (NTWC) will also be included in the evidence evaluation.

This technical report has been developed by HTAnalysts in conjunction with NHMRC, NTWC, and NTREAP. It provides the appendices (Appendix A to Appendix H) and supplementary data related to an evidence valuation of the effect of yoga for preventing and treating health conditions. The main body of evidence is presented in the evidence evaluation report. All associated materials have been developed in a robust and transparent manner in accordance with relevant best practice standards (2-5).

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List of abbreviations

OA	Osteoarthritis
BRISA	Regional Base of Health Technology Assessment Reports of the Americas
CINAHL	Cumulative Index to Nursing and Allied Health Literature
COMET	Core Outcome Measures in Effectiveness Trials
GRADE	Grading of Recommendations Assessment, Development and Evaluation
ITT	Intent-to-treat
NHMRC	National Health and Medical Research Council
NRSI	Nonrandomised study of an intervention
NTREAP	Natural Therapies Review Expert Advisory Panel
NTWC	Natural Therapies Working Committee
OR	Odds ratios
PAHO	Pan American Health Organization
PICO	Population, Intervention, Comparator, Outcome
PP	Per protocol
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT	Randomised controlled trial
RoB	Risk of bias
RR	Risk ratios
SR	Systematic review
SD	Standard deviation
TIDIER	Template for Intervention Description and Replication

Appendix D Details of included studies

This appendix documents the studies that met the prespecified inclusion criteria for a systematic review on the effect of yoga for preventing and treating any health condition and were prioritised at the population prioritisation phase. It provides an overview of the PICO criteria of these studies, a summary of the risk of bias assessment, and results of the data synthesis for the main comparison.

Additional details concerning the risk of bias judgements for each study are provided in Appendix E and characteristics of the included studies are provided in Appendix F1. Outcome data for outcomes considered to be critical or important for this review are provided in Appendix F2.

D1 Mental, behavioural or neurodevelopmental disorders

D1.1 Anxiety

D1.1.1 List of studies

An overview of the PICO criteria of included studies is provided in Table D-1. Study details, including all outcome domains and measures reported by the included studies are provided in Appendix F1. Outcome data for critical or important outcomes are provided in Appendix F2.

Table D-1 Overview of PICO criteria of included studies: Anxiety

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
Yoga versus control (no intervention, waitlist, inactive usual care)*						
Armat 2020 (6)	RCT	Symptoms of anxiety and/or depression (female, older than 50 years)	Laughter yoga	Control (usual activities)	None reported	Depression symptoms Anxiety symptoms
de Manincor 2016 (7, 8)	RCT	Symptoms of anxiety and/or depression	Yoga	Control (waitlist)	None reported	Mental health Depression Anxiety Stress Psychological distress Emotional function Physical function Psychological wellbeing Quality of life Resilience Exercise
Han 2015 (9)	Quasi RCT	Anxiety disorder (female, aged 40 to 55 years)	Yoga OR Yoga plus auricular plaster therapy ^	Auricular plaster therapy	None reported	Anxiety symptoms Anxiety cure rate Physical function Mental function Anxiety recurrence
Parthasarathy 2014 (10)	RCT	Anxiety disorder (female, aged 25 to 35 years)	Yoga (asanas, pranayamas & relaxation) OR Integrated yoga †	Control (no intervention)	None reported	Anxiety symptoms Frustration

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
Yoga versus 'other' intervention**						
Bazzano 2018 (11)	RCT	Symptoms of anxiety (children)	Yoga Ed	Control (usual care including counselling) ††	Teacher training	Life satisfaction Quality of life
Gupta 2013 (12)	Quasi RCT	Anxiety disorder	Yoga	Naturopathy	None reported	Anxiety symptoms
Shaikh 2013 (13)	RCT	Symptoms of anxiety	Yoga	Relaxation training	None reported	Anxiety symptoms

Abbreviations: RCT, randomised controlled trial

* Studies that compared yoga with an inactive control were eligible for inclusion in the evidence synthesis and are included in the Summary of findings tables if they reported outcomes considered critical or important to this review.

** Studies that compared yoga with an active intervention are included in the supplementary outcome tables (Appendix F2) if they reported data for outcomes considered critical or important to this review.

^ Study included 3 groups (yoga, auricular plaster therapy, and a combination group). Auricular plaster therapy is considered a co-intervention for the main comparison (combination versus auricular plaster therapy alone).

† Sitilikarana vyayama, suryanamaskar, asanas, pranayama and yoga nidra

†† Control (usual care including counselling) is considered an active comparator for the purpose of this comparison.

D1.1.2 Risk of bias per item

The risk of bias for each item in the included studies for anxiety is described below and shown graphically in Figure D-1 (details are provided in Appendix E).

Bias arising from the randomisation process

One study (Shaikh 2013) was assessed to be at low risk of bias. The other studies were assessed to have some concerns due to bias arising from the randomisation process. Concerns were primarily related to lack of information regarding the allocation concealment process or the method of generating the random sequence.

Bias due to deviations from intended interventions

All studies had a lack of blinding due to the nature of the intervention. Three studies (Bazzano 2018, de Manincor 2016, Shaikh 2013) were assessed to be at low risk of bias as intention to treat analysis was specified and followed. Three studies (Gupta 2013, Han 2015, Parthasarathy 2014) were assessed to have some concerns due to the lack of information presented regarding the method of analysis. One study (Armat 2020) was assessed at high risk of bias due to participants switching intervention groups after randomisation and using an as-treated analysis approach.

Bias due to missing outcome data

All studies were assessed to have some concerns for this domain. Most studies did not report the number of participants who had missing outcome data or the reasons for any missingness, leading to some concerns. Of the studies that did report the rate of drop out (Armat 2020, de Manincor 2016), insufficient information was provided to assess whether this would meaningfully impact the result.

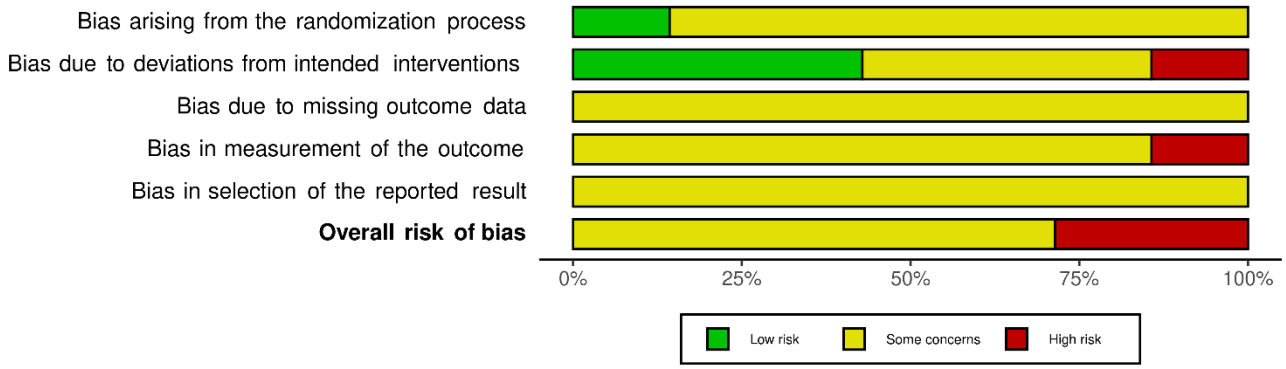
Bias in measurement of the outcome

All studies were assessed to have at least some concerns for this domain, owing to the non-blinded nature of the studies and the self-reported nature of the outcome measures. One study (Bazzano 2018) was assessed to be at high risk of bias for this domain due to reported excitement to participate in yoga which would likely bias the reporting of results.

Bias in selection of the reported result

All studies were assessed to have some concerns for this domain. There were no pre-specified analysis plans available for the included studies, making it impossible to assess whether the reported result had been selected on the basis of multiple analyses. There was no indication of inappropriate multiple analysis.

Figure D-1 Risk of bias summary: review authors' judgements about each risk of bias item expressed as percentages across all RCTs – Anxiety



D1.1.3 Effect of intervention

Outcomes considered by the NTWC to be critical or important for decision-making in people with anxiety are listed in Table D-2.

Table D-2 Outcomes considered by the NTWC to be critical or important for decision-making: Anxiety

Outcome domain	Measured with	Consensus rating	Data available for main comparison?	Armat 2020	De Manincor 2016	Han 2015	Parthasarathy 2014
Anxiety symptoms	HAM-A, BAI (or other validated measure)	Critical	Yes	✓	✓	✓	✓
Health-related quality of life	WHO QoL-BREF (or other validated measure)	Critical	Yes	--	--	--	--
Perceived stress	Perceived Stress Scale (or other validated measure)	Critical	Yes	--	✓	--	--
Emotional function	PROMIS-29 Mental Health (or other validated measure)	Critical	Yes	--	✓	✓	--
Physical function	PROMIS-29 Physical Health (or other validated measure)	Critical	Yes	--	✓	✓	--
Sleep quality	Pittsburgh Sleep Quality Index (or other validated measure)	Critical	No	--	--	--	--
Life satisfaction	BMSLSS	Critical	Yes	--	--	--	--

Abbreviations: BAI, Beck Anxiety Inventory; BMSLSS, Brief Multidimensional Student Life Satisfaction Scale; HAM-A, Hamilton Anxiety Rating Scale; PROMIS, Patient Reported Outcomes Measurement Information System; WHO QoL-BREF, World Health Organization Quality of Life Brief Version

✓ A study result is available for inclusion in the synthesis

X No study result is available for inclusion, (probably) because the P value, magnitude or direction of the results generated were considered unfavourable by the study investigators

-- No study result is available for inclusion, (probably) because the outcome was not assessed, or for a reason unrelated to the P value, magnitude or direction of the results

? No study result is available for inclusion, and it is unclear if the outcome was assessed in the study

Main comparison (vs control)

Three RCTs (Armat 2020, de Manincor 2016, Parthasarathy 2014) and one quasi RCT (Han 2015) comparing yoga with no intervention, usual care or waitlist control in people with anxiety or symptoms of anxiety were eligible for this comparison and contributed data to 4 of the 7 outcomes considered critical or important for this review.

There were 3 studies awaiting classification (total 152 participants) and one ongoing study (total 60 participants) that compared yoga with inactive control that could have contributed data to anxiety, life-satisfaction and quality of life outcomes (see Appendix C6). There were also 3 ongoing studies (total 529 participants) that had either completed recruitment or were still recruiting participants (see Appendix C5).

Anxiety symptoms

Three studies (193 participants) reported anxiety symptoms measured with the Hamilton Anxiety Rating Scale (HAM-A), Beck Anxiety Inventory (BAI), or the Depression, Anxiety and Stress Scale (DASS-21) at the end of treatment (range: 6 to 12 weeks).

The HAM-A is widely used in both clinical and research settings to measure the severity of anxiety symptoms. The scale consists of 14 items each scored on a scale from 0 (not present) to 4 (severe) to yield a total score from 0-56 where a higher score indicates more severe anxiety. The results from one study (30 participants) (Han 2015) showed a moderate difference in anxiety symptoms in the yoga group compared to the control group (SMD –0.72; 95% CI –1.46, 0.02; $p = 0.06$).

The BAI is a 21 item self-reported inventory measuring the severity of anxiety symptoms in adults. Each item is scored on a scale from 0 (not at all) to 3 (severely) to yield a total score from 0 to 63 where a higher score indicates more severe anxiety. The results from one study (62 participants) (Armat 2020) showed an improvement in anxiety symptoms in the yoga group compared to the control group (SMD –2.41; 95% CI –3.07, –1.75; $p < 0.00001$). The study informing this result was judged to be at high risk of bias.

The DASS-21 is a quantitative measure of distress along the 3 emotional states of depression, anxiety and stress. Each subscale consists of 7 questions, scored on a scale from 0 to 3 (14, 15). The anxiety scale assesses autonomic arousal, skeletal muscle effects, situational anxiety, and subjective experience of anxious affect. Total scores from the DASS-21 are multiplied by 2 to align with the original DASS-42 scoring (total score range 0 to 42). The DASS-21 is intended to be a dimensional rather than a categorical assessment of psychological disorders, but recommended cut-offs for the anxiety domain are: 0-7 is considered normal, 8-9 is indicative of mild anxiety, 10-14 is representative of moderate anxiety, 15-19 of severe anxiety and 20+ of extremely severe anxiety (16). The results from one study (101 participants) (de Manincor 2016) showed no difference in anxiety symptoms in the yoga group compared to the control group (SMD –0.34; 95% CI –0.73, 0.05; $p = 0.09$).

Outcome data from one additional study (number of participants unknown) which measured anxiety using the Taylor's Manifest Anxiety Scale is not included in this meta-analysis. This study reported a significant effect in favour of yoga but did not report sample size or standard deviation and therefore was unable to be included in the meta-analysis.

Pooled results suggest a large difference in anxiety symptoms between the yoga group compared to the control group, however heterogeneity was substantial (SMD –1.14; 95% CI –2.41, 0.13; $p = 0.08$; $I^2 = 93\%$) *(GRADE: Very low)*. Based on Cohen's guidance, the size of the effect was considered large (i.e. SMD greater than 0.8).

In a sensitivity analysis examining the impact of one RCT at high risk of bias, the size of the effect estimate decreased (small to moderate) (SMD –0.42; 95% CI –0.77, –0.07; $p = 0.02$; $I^2 = 0\%$).

Perceived stress

No studies were found that measured perceived stress, but one study (101 participants) reported stress measured with the DASS-21 (stress) at the end of treatment (8 weeks) (de Manincor 2016).

The DASS-21 is a quantitative measure of distress along the 3 emotional states of depression, anxiety and stress. Each subscale consists of 7 questions, scored on a scale from 0 to 3 (14, 15). The stress scale is sensitive to levels of chronic nonspecific arousal and assesses difficulty relaxing, nervous arousal, and being easily upset/agitated, irritable/over-reactive and impatient. Total scores from the DASS-21 are multiplied by 2 to align with the original DASS-42 scoring (total score range 0 to 42). The DASS-21 is intended to be a dimensional rather than a categorical assessment of psychological disorders, but recommended cut-offs for the stress subscale are: 0-14 is considered normal, 15-18 is indicative of mild stress, 19-25 is representative of moderate stress, 26-33 of severe stress and 34+ of extremely severe stress (16).

The results showed a reduction in distress in the yoga group compared to the control group (MD –4.12; 95% CI; –7.54, –0.70; p = 0.02) *(GRADE: Low)*. In the absence of an MCID, this was considered a small change (i.e. MD <10% of the scale).

No sensitivity analysis was performed examining the impact of studies at high risk of bias as only one study contributed data to this outcome.

Emotional function

Two studies (131 participants) reported emotional function measured with either the SF-12 or the Generic Quality of Life Inventory-74 (GQOL-74) at end of treatment (range: 6 to 12 weeks).

The SF-12 measures the impact of one's health on everyday life across 8 domains. The mental component summary score includes the domains of vitality, social functioning, role emotional, and mental health and is summarised on a scale from 0 (worse) to 100 (best). A higher score indicates improved emotional function. The results from one study (101 participants) (de Manincor 2016) suggested an improvement in emotional function in the yoga group compared to the control group (SMD –0.59; 95% CI –0.99, –0.19; p = 0.004).

The GQOL-74 is used to evaluate the life quality of participants across psychological, social, and physical indicators. The GQOL-74 psychological test consists of 5 questions and is scored on a 100-point scoring system. A higher score indicates improved psychological functioning. The results from one study (30 participants) (Han 2015) showed an improvement in psychological functioning in the yoga group compared to the control group (SMD –0.88; 95% CI –1.63, –0.12; p = 0.02).

Pooled results suggest an improvement in emotional functioning in the yoga group compared to the control group (SMD –0.66; 95% CI –1.01, –0.30; p = 0.0003; I^2 = 0%) *(GRADE: Moderate)*. Based on Cohen's guidance, this was considered a moderate change (i.e. SMD between 0.5 and 0.8).

No sensitivity analysis examining the impact of RCTs at high risk of bias was conducted, as neither study contributing data was judged at high risk of bias.

Physical function

Two studies (131 participants) reported physical function measured with either the SF-12 or the GQOL-74 at end of treatment (range: 6 to 12 weeks).

The SF-12 physical component summary score includes the domains general health, physical functioning, role-physical and bodily pain and is summarised on a scale from 0 (worse) to 100 (best). A higher score indicates improved physical function. The results from one study (101 participants) (de Manincor 2016) showed no difference in physical functioning between the yoga and control groups (SMD 0.22; 95% CI –0.17, 0.66; p = 0.26).

The GQOL-74 physical test consists of 5 questions and is scored on a 100-point scoring system. A higher score indicates improved physical functioning. The results from one study (30 participants) (Han 2015) showed an improvement in physical functioning in the yoga group compared to the control group (SMD –1.98; 95% CI –2.88, –1.09; p < 0.0001).

Pooled results suggest there is no difference between the yoga and control groups on physical functioning (SMD –0.84; 95% CI –3.00, 1.32; p = 0.45; I^2 = 95%) *(GRADE: Very low)*.

Comparison 2 (vs other intervention)

Three RCTs comparing yoga with 'other' interventions in people with anxiety or symptoms of anxiety were eligible for this comparison and contributed data for 3 outcomes. Data from these studies are presented in Appendix F2 Supplementary outcome .

D1.2 Depression

D1.2.1 List of studies

An overview of the PICO criteria of included studies is provided in Table D-3. Study details, including all outcome domains and measures reported by the included studies are provided in Appendix F1. Outcome data for critical or important outcomes are provided in Appendix F2.

Table D-3 Overview of PICO criteria of included studies: Depression (clinical)

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
Yoga versus control (no intervention, waitlist, inactive usual care)*						
Bressington 2019 (17)	RCT	Depression, clinical	Laughter yoga	Control (no intervention)	Standard medical care	Depression symptoms Anxiety symptoms Stress symptoms Physical wellbeing Mental wellbeing
Buttner 2015 (18)	RCT	Depression, postpartum	Vinyasa yoga	Control (waitlist)	None reported	Depression General wellbeing Anxiety HRQoL
Chu 2017 (19)	RCT	Depression, mild to moderate (female)	Yoga	Control (no intervention)	Standard medical care (antidepressants)	Depression Stress Heart rate variability
Falsafi 2016 (20)	RCT	Depression and/or anxiety	Hatha yoga	Control (no intervention) OR Mindfulness meditation ^	None reported	Depression severity Anxiety symptoms Stress symptoms Mindfulness Self-compassion
Kumar 2019b (21)	RCT	Major depressive disorder	Yoga	Control (no intervention)	Standard medical care (antidepressants and counselling)	Depression severity Anxiety severity
Sarubin 2014 (22)	Quasi-RCT	Major depressive disorder	Yoga	Control (no intervention)	Standard medical care (quetiapine fumarate 300 mg/day or escitalopram 10 mg/day	Depression severity HPA sensitivity
Shahidi 2011 (23)	Quasi-RCT	Symptoms of depression (female, aged 60 to 80 years)	Laughter yoga	Control (no intervention) OR Physical activity ^	None reported	Depression Mood Sleep quality Pain Perceived stress Spirituality Mindfulness
Sharma 2005 (24, 25)	Quasi-RCT	Major depressive disorder	Sahaj Yoga Meditation	Control (no intervention)	None reported	Depression severity Anxiety severity
Sharma 2015a (26, 27)	RCT	Major depressive disorder	Sudarshan Kriya Yoga †	Control (no intervention)	Standard medical care (antidepressants)	Depression severity Anxiety severity
Tolahunase 2018b (28)	RCT	Major depressive disorder	Yoga	Control (no intervention)	Standard medical care	Depression symptoms Neuroplasticity

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
Whiddon 2011 (29)	Quasi-RCT	Symptoms of depression	Hatha yoga	Control (waitlist)	None reported	Depression symptoms
Woolery 2004 (30)	Quasi-RCT	Symptoms of depression	Yoga	Control (usual care)	None reported	Depression Anxiety Mood Stress biomarker
Yoga versus 'other' intervention**						
Janakiramaiah 2000 (31)	Quasi-RCT	Melancholic depression	Sudarshan Kriya Yoga	ECT OR Pharmacotherapy (imipramine)	None reported	Depression severity
Kinser 2013 (32)	RCT	Major depressive disorder	Hatha yoga	Attention control (wellness education programme)	None reported	Depression severity Anxiety symptoms Stress symptoms Rumination Interpersonal sensitivity and hostility
Prathikanti 2017 (33, 34)	RCT	Major depressive disorder	Hatha yoga	Attention control (Yoga-themed education programme)	None reported	Depression severity Self-efficacy Self-esteem
Ravindran 2020 (35)	RCT	Unipolar and bipolar depression	Yoga (pranayama and asanas)	Attention control (wellness education programme)	Standard medical care (antidepressants, mood stabilisers)	Depression severity Stress symptoms HRQoL
Tolahunase 2018a (36)	RCT	Major depressive disorder	Yoga-based lifestyle intervention #	Pharmacotherapy (SSRI)	None reported	Depression severity
Uebelacker 2017 (37-39)	RCT	Major depressive disorder	Hatha yoga	Attention control (wellness education programme)	Standard medical care (antidepressants)	Depression severity Depression symptoms Social functioning Role-function Physical pain Physical functioning General health perception
Wahbeh 2019 (40)	Quasi-RCT	Depression (aged 55 to 90 years)	Meditation program (based on yoga Nidra techniques)	2-day retreat	None reported	Depression Mood Sleep quality Pain Stress
Weinstock 2016 (41)	RCT	Bipolar depression	Hatha yoga	Bibliotherapy (Self-help book)	Standard medical care (antidepressants)	Depression symptoms Mania symptoms HRQoL

Abbreviations: ECT, electroconvulsive therapy; HPA, hypothalamic pituitary adrenal; HRQoL, health-related quality of life; RCT, randomised controlled trial

* Studies that compared yoga with an inactive control were eligible for inclusion in the evidence synthesis and are included in the Summary of findings tables if they reported outcomes considered critical or important to this review.

** Studies that compared yoga with an active intervention are included in the supplementary outcome tables (Appendix F2) if they reported data for outcomes considered critical or important to this review.

^ Study included 3 groups. The inactive control is considered in the evidence synthesis.

† a breathing-based meditative technique plus yoga postures, sitting meditation and stress education

Includes interactive lectures on yoga, lifestyle, lifestyle diseases including major depressive disorder, and the importance of their prevention and management

D1.2.2 Risk of bias per item

The risk of bias for each item in the included studies for depression is described below and shown graphically in Figure D-2 (details are provided in Appendix E).

Bias arising from the randomisation process

Six studies (Buttner 2015, Prathikanti 2017, Ravindran 2020, Tolahunase 2018a, Tolahunase 2018b, Uebelacker 2017b) were at low risk of bias in this domain. There were 13 studies with some concerns of bias relating to a lack of information on the allocation concealment process (Bressington 2019, Chu 2017, Falsafi 2016, Janakiramaiah 2000, Kinser 2013, Kumar 2019b, Sarubin 2014, Shahidi 2011, Sharma 2005, Sharma 2015, Wahbeh 2019, Weinstock 2016, Woolery 2004). One study (Whiddon 2011) was assessed to be at high risk of bias as the authors did not provide information about the randomisation sequence, allocation concealment or baseline characteristics.

Bias due to deviations from intended interventions

There were 17 studies assessed to have low risk of bias (Bressington 2019, Buttner 2015, Chu 2017, Falsafi 2016, Janakiramaiah 2000, Prathikanti 2017, Shahidi 2011, Sharma 2005, Sharma 2015, Tolahunase 2018a, Tolahunase 2018b, Uebelacker 2017b, Wahbeh 2019, Weinstock 2016, Whiddon 2011, Woolery 2004). One study (Ravindran 2020) was judged to have some concerns of bias for this domain, arising from dropout rate considered related to trial context. Three studies were assessed to be at high risk of bias. Two of these (Kumar 2019b, Sarubin 2014) utilised an inappropriate method of analysis (per protocol). Kinser 2013 was considered high risk of bias due to a high dropout rate that was not balanced between study groups.

Bias due to missing outcome data

Six studies were assessed to have low risk of bias as data was available for all, or nearly all, participants (Buttner 2015, Janakiramaiah 2000, Sharma 2005, Uebelacker 2017b, Wahbeh 2019, Whiddon 2011). Eleven studies were judged to have some concerns for bias in this domain due to missing data, however missing data was not considered to be related to outcome (Bressington 2019, Chu 207, Falsafi 2016, Kinser 2013, Prathikanti 2017, Sarubin 2014, Shahidi 2011, Sharma 2015, Tolahunase 2018b, Weinstock 2016, Woolery 2004). Three studies were assessed to be at high risk of bias, as missingness of data was considered likely due to relation to outcome (Kumar 2019b, Ravindran 2020, Tolahunase 2018a).

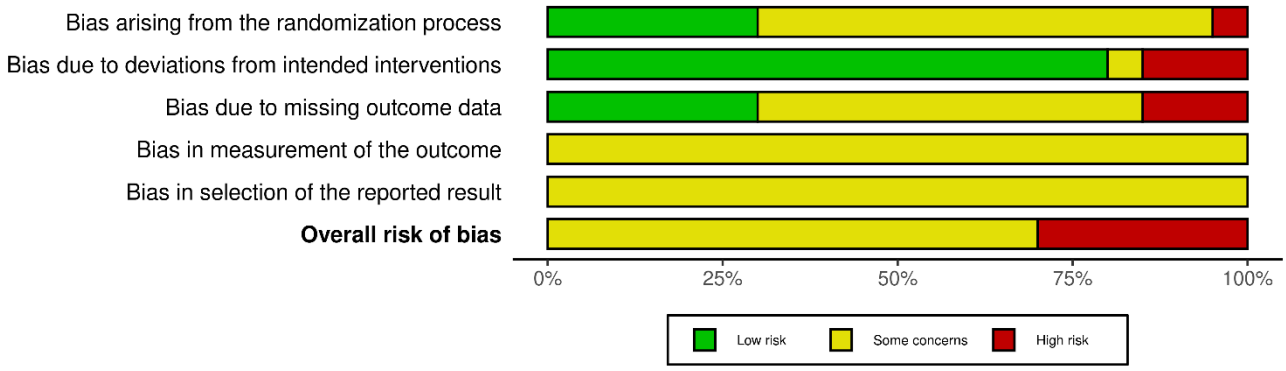
Bias in measurement of the outcome

All studies were assessed to have some concerns regarding the measurement of outcomes. The method of measuring outcomes was appropriate; however participants were not blinded to their allocation due to the nature of the intervention. As outcome measures were self-reported, lack of blinding raised some concerns that reporting of outcomes may be biased. There was no evidence to indicate that participants were likely to differentially report outcomes between the intervention and control groups.

Bias in selection of the reported result

All studies were considered to have some concerns of bias, as no information regarding the researcher's pre-specified analysis plan is available. There was no indication of inappropriate multiple analysis in each study.

Figure D-2 Risk of bias summary: review authors' judgements about each risk of bias item expressed as percentages across all RCTs – Depression



D1.2.3 Effect of intervention

Outcomes considered by the NTWC to be critical or important for decision-making in people with depression (or symptoms of depression) are listed in Table D-4.

Table D-4 Outcomes considered by the NTWC to be critical or important for decision-making: Depression

Outcome domain	Measured with	Consensus rating	Data available for main comparison?	Bressington 2019	Buttner 2015	Chu 2017	Falsafi 2016	Kumar 2019b	Sarubin 2014	Shahidi 2011	Sharma 2005	Sharma 2015	Tolahunase 2018b	Whiddon 2011	Woolery 2004
HRQoL	WHO QoL-BREF (or other)	Critical	Yes	--	✓	--	--	--	--	--	--	--	--	--	--
Life-satisfaction	Diener life satisfaction scale (or other)	Critical	Yes	--	--	--	--	--	--	✓	--	--	--	--	--
Depression symptoms	HAM-D (or other)	Critical	Yes	✓	✓	✓	✓	✓	✓	✓	✓	✓	--	✓	✓
Psychological distress	Brief Symptom Inventory (or other)	Critical	No	✓	--	--	--	--	--	--	--	--	--	--	--
Emotional function	Profile of Mood States (or other)	Critical	No	✓	--	--	--	--	--	--	--	--	--	--	X
Perceived stress	Perceived Stress Scale (or other)	Critical	Yes	--	--	✓	✓	--	--	--	--	--	--	--	--
Self-efficacy/ esteem / compassion	General Self-efficacy Scale (or other)	Critical	Yes	--	--	--	✓	--	--	--	--	--	--	--	--

Abbreviations: HAM-D Hamilton Depression Rating Scale; WHO QoL-BREF, World Health Organization Quality of Life Scale - Abbreviated
✓ A study result is available for inclusion in the synthesis
X No study result is available for inclusion, (probably) because the P value, magnitude or direction of the results generated were considered unfavourable by the study investigators
-- No study result is available for inclusion, (probably) because the outcome was not assessed, or for a reason unrelated to the P value, magnitude or direction of the results
? No study result is available for inclusion, and it is unclear if the outcome was assessed in the study

Main comparison (vs control)

Seven RCTs (Bressington 2019, Buttner 2015, Chu 2017, Falsafi 2016, Kumar 2019b, Sharma 2015a, Tolahunase 2018b) and 5 quasi-RCTs (Sarubin 2014, Shahidi 2011, Sharma 2005, Whiddon 2011, Woolery 2004) comparing yoga with no intervention, waitlist or usual care in people with depression or symptoms of depression were eligible for this comparison and contributed data to 6 of the 7 outcomes considered critical or important for this review.

There were 3 studies awaiting classification (155 participants) and 5 ongoing studies (503 participants) that were completed with results not available or of unknown status that compared yoga with inactive control that could have contributed data to this comparison.

Quality of life

One study (56 participants) reported quality of life measured with the SF-36 at the end of treatment (8 weeks). The other eligible RCTs did not report QoL, probably because the outcome was not assessed in the studies.

The SF-36 is a self-reported multidimensional measure assessing the impact of one's health on everyday life. Eight domains are summarised on a scale from 0 (worse) to 100 (best), which can be summarised into 2 component scores. The physical component summary (PCS) score includes the domains of general health, physical functioning, role physical and body pain. The mental component summary (MCS) score includes the domains of vitality, social functioning, role emotional, and mental health. The PCS and MCS are derived by aggregating individual scores. The MCID for the SF-36 is estimated to be around 2 to 4 points for the general population (i.e. ~0.5 of the SD) (42).

Results from one study (56 participants) (Buttner 2015) showed an effect in SF-36 total score favouring yoga when compared to the control group (MD 12.01; 95% CI 4.67, 19.35; p = 0.001) (*GRADE: Low*). The mean difference between the yoga and control group was between 10% and 20% of the scale, representing a moderate effect.

No sensitivity analysis was conducted to assess the impact of RCTs at high risk of bias as there was only one study.

Life satisfaction

One study (40 participants) reported life satisfaction measured with the Diener satisfaction with life scale (SWLS) at the end of treatment (mean: 10 session) (Shahidi 2011). The other eligible RCTs did not report life satisfaction, probably because the outcome was not assessed in the studies.

The SWLS is designed to assess life pleasure in general. Participants indicate how much they agree or disagree with each of the 5 items using a 7-point scale that ranges from 1 strongly disagree to 7 strongly agree. Scores range from 5 to 35 with a higher score indicating a greater life satisfaction. An MCID for the Diener life satisfaction scale in people with depression has not been established.

Results suggest an effect favouring yoga when compared to the control group (MD –5.90; 95% CI –9.22, –2.58; p = 0.0005). Considering the observed change is between 10% and 20% of the scale this was considered a moderate effect. (*GRADE: Low*)

No sensitivity analysis was conducted to assess the impact of RCTs at high risk of bias as there was only one study.

Depression

Twelve studies (513 participants) reported depression measured with the Hamilton depression rating scale (HAM-D), the Beck depression inventory (BDI-II), the depression, anxiety and stress scale (DASS-21), the Montgomery-Asberg depression rating scale (MADRS) or the geriatric depression scale (GDS) at the end of treatment (range: 25 days to 12 weeks).

The HAM-D measures the severity of current depressive symptoms and consists of 17 or 21-items scored on a 3 or 5 point scale. Individual scores are summed with a higher score indicating a greater level of depressive symptoms. Pooled results from 3 studies (111 participants) (Buttner 2015, Sharma 2005, Sharma 2015a) suggest a large effect favouring yoga when compared to the control group (SMD –0.80; 95% CI –1.36, –0.24; p = 0.005) (i.e. SMD ≥ 0.8). Results from one additional study (53 participants) that measured depression using the HAM-D but did not report post-baseline scores is not included in this estimate.

The BDI-II assesses the behavioural and cognitive symptoms of depression and consists of 21 questions, each on a 4-point scale. Scores range from 0 to 63 with a higher score indicating a greater level of depressive symptoms. Pooled results from 4 studies (152 participants) (Chu 2017, Falsafi 2016, Tolahunase 2018b, Whiddon 2011, Woolery 2004) suggest a large effect favouring yoga when compared to the control group (SMD –1.08; 95% CI –1.53, –0.63; p < 0.00001) (i.e. SMD ≥ 0.8). Results from one additional study (26 participants) that measured depression using the BDI-II but did not report individual treatment group scores is not included in this estimate but reported a point-estimate which favours yoga.

The DASS-21 is a quantitative measure of distress along 3 emotional states of depression, anxiety and stress. Each subscale consists of 7 questions, scored on a scale from 0 to 3 (14, 15). The depression scale assesses dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest / involvement, anhedonia and inertia. Total scores from the DASS-21 are multiplied by 2 to align with the original DASS-42 scoring (total score range 0 to 42). The DASS-21 is intended to be a dimensional rather than a categorical assessment of psychological disorders, but recommended cut-offs for the depression subscale are: 0-9 is considered normal, 10-13 is indicative of mild depression, 14-20 is representative of moderate depression, 21-27 of severe depression and 28+ of extremely severe depression (16). Results from one study (50 participants) (Bressington 2019) show no important difference between yoga when compared to the control group (SMD –0.10; 95% CI –0.66, 0.46; p = 0.72) (i.e. SMD ≤ 0.2).

The MADRS is a 10-item scale that measures severity of depressive symptoms. Based on clinical interview, each item can be scored from 0 to 6, with the cumulative score ranging between 0 and 60. A higher score indicates a greater level of depressive symptoms. Results from one study (80 participants) (Kumar 2019b) showed no difference between groups when comparing yoga to the control (SMD –0.36; 95% CI –0.80, 0.08; p = 0.11) (i.e. SMD ≤ 0.2).

The GDS consists of 30 yes or no questions that divides individuals into those without depression (0-9), those who are moderately depressed (10-19) and those who are severely depressed (20-30). Results from one study (40 participants) (Shahidi 2011) showed a moderate effect favouring yoga when compared to the control group (SMD –0.78; 95% CI –1.43, –0.14; p = 0.02). (i.e. SMD between 0.5 and 0.8).

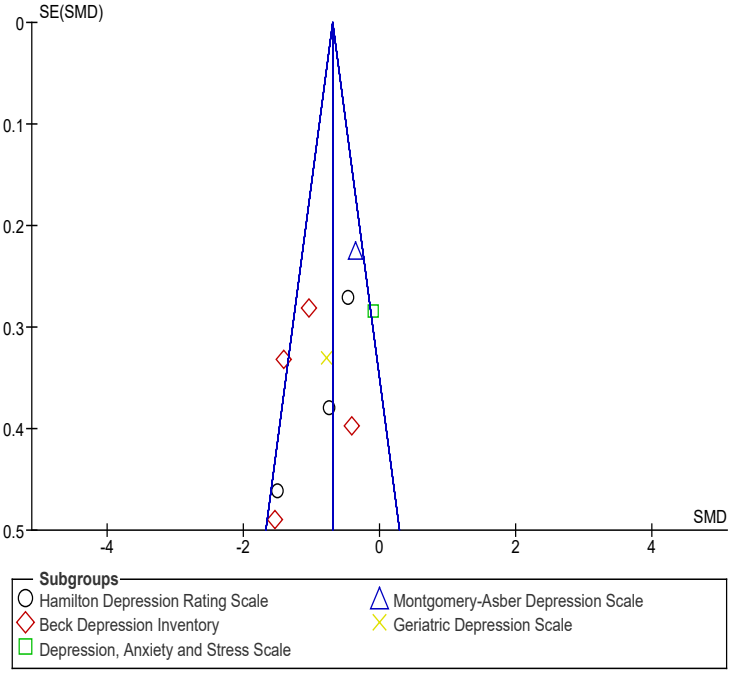
Pooled results from all 10 studies (434 participants) suggest a moderate reduction in depression in the yoga group when compared to the control group (SMD –0.76; 95% CI; –1.07, –0.46; p < 0.00001, I^2 = 55%) (i.e. SMD between 0.5 and 0.8) (*GRADE: Moderate*). The magnitude of statistical heterogeneity was high (I^2 > 50%) and may be due to the differences in the study populations (geriatric, postpartum, clinical depression) or the type of interventions measured.

Visual inspection of the funnel plot (see Figure D-3) suggests that poor methodological quality may have led to exaggerated effects in smaller studies, with slight asymmetry indicating that smaller studies without statistically significant effects remain unpublished (43) [1]. Of the two studies with results not included in the meta-analysis, Sarubin 2014 reported no difference between the yoga and control groups whereas Whiddon 2011 reported an effect favouring the yoga group when compared to the control.

In a sensitivity analysis that examined the impact of RCTs judged to be at high risk of bias (Sarubin 2014, Tolahunase 2018b, Whiddon 2011) the size of the effect estimate did not substantially change (SMD –0.73: 95% CI –1.06, –0.40; p < 0.0001; I^2 = 56%).

[1] It is noted that funnel plots of the SMD plotted against the SE are susceptible to distortion, leading to overestimation of the existence and extent of publication bias.

Figure D-3 Funnel plot of comparison: Yoga vs control (no intervention, waitlist, usual activities): Depression, outcome: Depression (end of treatment)



Psychological distress

The DASS-21 is a quantitative measure of distress along 3 emotional states of depression, anxiety and stress. Each subscale consists of 7 questions, scored on a scale from 0 to 3 (14, 15). The stress scale is sensitive to levels of chronic nonspecific arousal and assesses difficulty relaxing, nervous arousal, and being easily upset/agitated, irritable/over-reactive and impatient. Total scores from the DASS-21 are multiplied by 2 to align with the original DASS-42 scoring (total score range 0 to 42). The DASS-21 is intended to be a dimensional rather than a categorical assessment of psychological disorders, but recommended cut-offs for the stress subscale are: 0-14 is considered normal, 15-18 is indicative of mild stress, 19-25 is representative of moderate stress, 26-33 of severe stress and 34+ of extremely severe stress (16).

Results from one study (50 participants) show no difference between the yoga group when compared to the control group (MD 1.08; 95% CI –3.17, 5.33; p = 0.62). (*GRADE: Low*)

Emotional function

Two studies (78 participants) measured emotional function with the Profile of Mood States (POMS) or the SF-12 MCS at the end of treatment (5 weeks), but no data were provided (Woolery 2004).[2]

The SF-12 is a shorter version of the SF-36 quality of life questionnaire, which measures health related quality of life across eight domains. The MCS score includes the domains of vitality, social functioning, role emotional, and mental health. Total scores range from 0 to 100, with a higher score indicating improved emotional function.

Results from one study (50 participants) showed no difference between the yoga and control groups in SF-12 MCS score at 4 weeks (MD –0.32; 95% CI –4.94, 4.30; p = 0.89) (*GRDAE: Low*).

[2] Woolery 2004 was a pilot study. The authors report a significant change in total mood scores comparing pre-class and post-class scores, but no end-of-treatment data are provided.

No sensitivity analysis was conducted to assess the impact of RCTs at high risk of bias as there was only one study.

Perceived stress

Two studies (72 participants) reported stress measured with the perceived stress scale (PSS-14) or the student-life stress inventory (SSI) at the end of treatment (range: 8 to 12 weeks).

The 14-item PSS assesses the perception of stressful experiences, with participants asked to rate how overwhelmed they are by their current life circumstances over the preceding 30 days on a 5-point scale. Total scores range from 0 to 56 with higher scores indicating greater perceived stress. Results from one study (26 participants) (Chu 2017) show no difference between yoga when compared to the control group (SMD –0.21; 95% CI –0.98, 0.56; p = 0.59).

The SSI is a 51-item questionnaire that measures a students' exposure to stressors (frustrations, conflicts, pressure, changes, self-imposed) and their response to stressors (physiological, emotional, behavioural, cognitive). Total scores from the 9 domains are summed, with a higher score indicating higher exposure and worse response to stressors. Results from one study (26 participants) (Falsafi 2016) show an effect favouring yoga when compared to the control group (SMD –0.75; 95% CI –1.35, –0.15; p = 0.01).

Taken together, the pooled results suggest a moderate effect favouring the yoga group when compared to the control group (SMD –0.54; 95% CI; –1.06, –0.02; p = 0.04, I^2 = 16%) (i.e. SMD between 0.5 and 0.8) (*GRADE: Low*).

No sensitivity analysis was conducted as none of the RCTs included were assessed to be at high risk of bias.

Self-compassion

One study (26 participants) reported self-compassion measured with a 12-item self-compassion scale at the end of treatment (mean: 8 weeks) (Falsafi 2016).

The 12-item self-compassion scale is an abbreviated version of the 26-item questionnaire that assesses 6 different aspects of self-compassion (self-kindness, self-judgement, common humanity, isolation, mindfulness, and over-identification). Overall scores are calculated after reversing coding responses to the negatively worded items comprising self-judgement, isolation, and over-identification subscales. The means for each of the 6 subscales are then used to calculate a total mean (the average of the 6 subscale means). Higher scores indicate better self-compassion, with general cut-offs being as follows: low (between 1.0 and 2.49), moderate (between 2.5 and 3.5) and high (between 3.51 and 5.0) (44).

The results show a large effect favouring yoga when compared to the control group (SMD –0.83; 95% CI –1.44, –0.23; p = 0.007) (i.e. SMD ≥ 0.8). (*GRADE: Low*). Participants in the control group continue to have low self-compassion.

No sensitivity analysis was conducted as there was only one study.

Comparison 2 (vs other intervention)

Ten RCTs comparing yoga with 'other' interventions in people with depression or symptoms of depression were eligible for this comparison. Data from these studies are presented in Appendix F2 Supplementary outcome .

D1.3 Post-traumatic stress disorder

D1.3.1 List of studies

An overview of the PICO criteria of included studies is provided in Table D-5. Study details, including all outcome domains and measures reported by the included studies are provided in Appendix F1. Outcome data for critical or important outcomes are provided in Appendix F2.

Table D-5 Overview of PICO criteria of included studies: Post-traumatic stress disorder

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
Yoga versus control (no intervention, waitlist, inactive usual care)						
Jindani 2015 (45)	RCT	Post-traumatic stress disorder	Kundalini yoga	Control (waitlist)	None reported	Emotional function Sleep quality Anxiety Depression
Martin 2015 (46)	RCT	Post-traumatic stress disorder	Kripalu yoga	Control (no intervention)	None reported	Emotional function Physical function
Quinones 2015 (47)	RCT	Post-traumatic stress disorder	Satyananda yoga	Control (usual care)	None reported	Emotional function
Reddy 2013 (48-52)	RCT	Post-traumatic stress disorder (female)	Hatha yoga	Control (usual activities)	Educational advice ^	Emotional function Anxiety Depression
Reinhardt 2018 (53)	RCT	Post-traumatic stress disorder (veterans)	Kripalu yoga	Control (no intervention)	None reported	Emotional function
Seppala 2014 (54)	RCT	Post-traumatic stress disorder (veterans, male)	Sudarshan Kriya yoga	Control (waitlist)	None reported	Emotional function Physical function
Telles 2010 (55)	RCT	Post-traumatic stress disorder (male)	Yoga	Control (waitlist)	None reported	Physical function
Yoga versus 'other' intervention						
Culver 2015 (56)	Quasi RCT	Post-traumatic stress disorder (children)	Hatha yoga	Physical activity (dance)	None reported	Trauma related symptoms Emotional function
Davis 2020 (57)	RCT	Post-traumatic stress disorder (veterans)	Holistic yoga program	Wellness lifestyle programme	None reported	Emotional function Sleep quality Depression Anxiety Physical functioning
Huberty 2018 (58, 59)	RCT	Post-traumatic stress disorder (mothers experiencing stillbirth)	yoga	Physical activity (stretching/ toning)	None reported	Emotional function Anxiety Depression Quality of life Sleep quality
Van Der Kolk 2014 (60, 61)	Quasi RCT	Post-traumatic stress disorder (female, treatment resistant)	Trauma informed yoga	Wellness education program	None reported	Emotional function Physical function Depression

*Studies that compared yoga with an inactive control were eligible for inclusion in the evidence synthesis and are included in the Summary of findings tables if they reported outcomes considered critical or important to this review.

**Studies that compared yoga with an active intervention are included in the supplementary outcome tables (Appendix F2) if they reported data for outcomes considered critical or important to this review.

^ Information sheet about yoga for PTSD, local resources for psychotherapy and domestic violence and a list of VA services provided to veterans

D1.3.2 Risk of bias summary

The risk of bias for each item in the included studies for people with PTSD is described below and shown graphically in Figure D-4 (details are provided in Appendix E).

Bias arising from the randomisation process

Three studies (Culver 2015, Huberty 2018, Telles 2010) provided sufficient information on the randomisation process and were considered at low risk of bias for this domain. Eight studies had concerns of bias due to lack of information regarding concealment of group allocation (Davis, 2020, Jindani 2015, Martin 2015, Quinones 2015, Reddy 2013, Reinhardt 2018, Seppala 2014). One study (Van der Kolk 2014) had concerns of bias raised due to a lack of information regarding the randomisation process and concealment of group allocation.

Bias due to deviations from intended interventions

All studies had a lack of blinding due to the nature of the intervention. Three studies were judged to be at low risk of bias for this domain (Culver 2015, Martin 2015, Telles 2010).

Six studies had some concerns as there were deviations from the treatment allocation possibly related to the trial context, but their impact on the outcome was expected to be slight (Davis 2020, Huberty 2018, Quinones 2015, Reddy 2013, Seppalla 2014, Van der Kolk 2014)Two studies (Jindani 2015, Reinhardt 2018) were considered to be at high risk of bias because of deviations from the intended intervention probably relating to the trial context, indicated by a high and unbalanced dropout rate.

Bias due to missing outcome data

Three studies were judged to be low risk of bias for this domain as all data was available for the measured outcomes (Martin 2015, Telles 2010) or any missing data was balanced across groups and considered unlikely to influence the effect estimate (Quinones 2015). In 6 studies the number of participants with missing outcome data was balanced between groups, but there were concerns of missing outcome data being related to the trial context (Davis 2020, Huberty 2018, Reddy 2013, Reinhardt 2018, Seppala 2014, Van Der Kolk 2014).

Two studies were assessed to have high risk of bias due to unbalanced missingness of data and a lack of sensitivity analysis conducted to determine impact of missing data (Culver 2015, Jindani 2015). Culver 2015 did not report reasons for drop out whereas Jindani 2015 reported 10 participants withdrew prior to classes due to scheduling and 10 withdrew following the first class for the same reasons, 6 participants cited medical/ health reasons and 4 cited personal reasons for drop out.

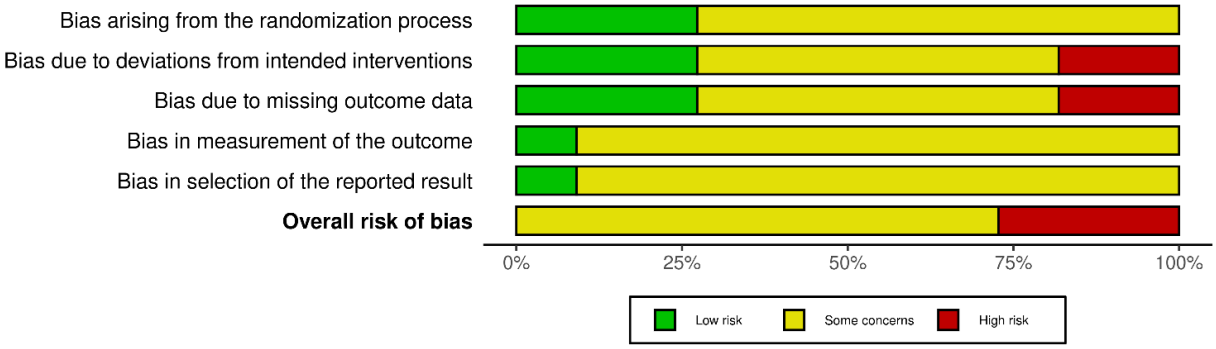
Bias in measurement of the outcome

All studies were assessed to have at least some concerns of bias for this domain, due to the non-blinded nature of the studies and the self-reported nature of the outcome measures. Telles 2010 was determined to be at low risk of bias for one outcome (heart rate variability) as outcome assessors were blinded to the intervention received.

Bias in selection of the reported result

Huberty 2018 provided a pre-specified analysis plan. The remaining studies were assessed to have some concerns for this domain as a pre-specified analysis plans was not available, making it impossible to assess whether the reported result had been selected on the basis of multiple analyses. There was no indication of inappropriate multiple analysis or selection of results.

Figure D-4 Risk of bias summary: review authors' judgements about each risk of bias item expressed as percentages across all RCTs – PTSD



D1.3.3 Effect of intervention

Outcomes considered by the NTWC to be critical or important for decision-making in people with PTSD are listed in Table D-6.

Table D-6 Outcomes considered by the NTWC to be critical or important for decision-making: Post-traumatic stress disorder

Outcome domain	Measured with	Consensus rating	Data available for main comparison?	Jindani 2015	Martin 2015	Quinones 2015	Reddy 2013	Reinhardt 2018	Seppala 2014	Telles 2010
Anxiety	HAM-A (or other validated measure)	Critical	Yes	✓	--	--	✓	--	✓	✓
Perceived stress	PSS (or other validated measure)	Critical	Yes	✓	--	--	--	--	--	--
Emotional function	Inventory of altered self-capacities (or other)	Critical	Yes	✓	--	--	--	--	--	--
Physical function/ mobility	No eligible measures reported	Critical	No	--	--	--	--	--	--	--
Health-related quality of life	SF-36 or other validated measure	Critical	Yes	✓	--	--	--	--	--	--
Depression	BDI or other validated measure	Critical	Yes	✓	--	--	✓	--	--	--
Sleep quality	PSQI	Critical	Yes	✓	--	--	--	--	--	✓

Abbreviations: BDI, Beck Depression Inventory; HAM-A, Hamilton Anxiety Scale; PSQI, Pittsburgh Sleep Quality Index; PSS, Perceived stress scale; SF-36, 36-item short form

✓ A study result is available for inclusion in the synthesis

X No study result is available for inclusion, (probably) because the *p*-value, magnitude or direction of the results generated were considered unfavourable by the study investigators

--No study result is available for inclusion, (probably) because the outcome was not assessed, or for a reason unrelated to the *p*-value, magnitude or direction of the results

? No study result is available for inclusion, and it is unclear if the outcome was assessed in the study

Main comparison (vs control)

Seven studies comparing yoga with control (no intervention, waitlist, usual activities) in people with PTSD were eligible for this comparison. Four studies contributed data relevant to at least one of the 7 outcomes considered critical or important for this review (Jindani 2015, Reddy 2013, Seppala 2014, Telles 2010). Three studies (Martin 2015, Quinones 2015, Reinhardt 2018) did not measure outcomes considered critical or important for this review.

There were no additional studies awaiting classification and 5 ongoing studies (4 were complete, but results were not available and one with unknown status) that compared yoga with control (no intervention, waitlist, usual activities) in people with PTSD (276 participants) that could have contributed data to 6 of the 7 outcomes (perceived stress, depression, anxiety, emotional function, sleep quality and quality of life) considered critical or important for this review (see Appendix C6).

Anxiety

Four studies (118 participants) reported anxiety measured with the Depression, Anxiety and Stress Scale (DASS-21), Mood and Anxiety Symptoms Questionnaire (MASQ), State-Trait Anxiety Inventory (STAI) or Visual Analogue Scale (VAS) at the end of treatment (range: 7 days to 8 weeks).

The DASS-21 is a quantitative measure of distress along the 3 emotional states of depression, anxiety and stress. Each subscale consists of 7 questions, scored on a scale from 0 to 3 (14, 15). The anxiety scale assesses autonomic arousal, skeletal muscle effects, situational anxiety, and subjective experience of anxious affect. Total scores from the DASS-21 are multiplied by 2 to align with the original DASS-42 scoring (total score range 0 to 42). The DASS-21 is intended to be a dimensional rather than a categorical assessment of psychological disorders, but recommended cut-offs for the anxiety domain are: 0-7 is considered normal, 8-9 is indicative of mild anxiety, 10-14 is representative of moderate anxiety, 15-19 of severe anxiety and 20+ of extremely severe anxiety (16). Results from one study (50 participants) (Jindani 2015) showed little to no difference between yoga when compared to the control group (SMD –0.43; 95% CI –1.00, 0.14; p = 0.14).

The MASQ assesses general and specific components of anxiety and depression via 4 subscales: general distress, anxiety, anxious arousal, general distress-depressive, and anhedonic depression. Results from one study (20 participants) (Seppala 2014) suggested an effect favouring the yoga group when compared to the control group, but it did not reach statistical significance (SMD –0.82; 95% CI –1.74, 0.10; p = 0.08).

The STAI is a 40-item test divided into two domains pertaining to state (obvious) and trait (hidden) anxiety. State anxiety evaluates an individual's feeling in the moment and trait anxiety measures an individual's usual and general feelings. All items are rated on a 4-point scale from 'almost never' to 'almost always'; with total scores for each domains ranging from 20 to 80 (higher is worse). Determining meaningful difference can be difficult for the trait anxiety subscale as it is intended to identify susceptibility and is less responsive to change compared to state anxiety. For the state anxiety subscale, a cut point of 39-40 is suggested to detect clinically significant symptoms (62). Results from one study (26 participants) (Reddy 2013) showed no difference in state-anxiety between the yoga group when compared to the control group (SMD 0.08; 95% CI –0.69, 0.85; p = 0.84).

The VAS is subjective tool that can be used to measure a variety of outcomes. Measured on a continuous scale (cm), with one end (score 10 cm) of the scale indicating the highest intensity of a feeling/symptom and the other end (score 0 cm) indicating the lowest intensity of feeling / symptom. One study (22 participants) measured anxiety (Telles 2010), with little to no difference in anxiety observed between the yoga group when compared to the control group (SMD –0.13; 95% CI –0.97, 0.71; p = 0.76).

Taken together, the pooled results suggest a small effect favouring the yoga group when compared to the control group, but it did not reach statistical significance (SMD –0.32; 95% CI –0.68, 0.05; p = 0.47; I^2 = 0%) (*GRADE: Very low*). (i.e. SMD between 0.2 and 0.5)

In a sensitivity analysis that examined the impact of one RCT judged to be at high risk of bias (Jindani 2015) the size (but not overall direction) of the effect estimate was slightly decreased (SMD –0.24; 95% CI –0.76, 0.27; p = 0.32; I^2 = 12%).

Perceived stress

One study (50 participants) reported perceived stress as measured by the Perceived Stress Scale (PSS-10) (Jindani 2015) at end of treatment (8 weeks).

The PSS-10 is an abbreviated version of the 14-item Perceived Stress Scale where participants indicate how often they have found their lives unpredictable, uncontrollable, and overloaded. Participants rate the frequency with which they experienced 10 stress symptoms over the preceding 30 days on a 5-point scale. Total scores range from 0 to 40 with higher scores indicating greater perceived stress. An MCID for the PSS-10 in people with PTSD has not been established, but is estimated to be between 2.19 and 2.66 points among undergraduate students with elevated stress (63) and around 11 points in people with work-related stress complaints (64).

The results suggest a large effect favouring the yoga group when compared to the control group (MD –9.20; 95% CI –13.83, –4.57; $p < 0.0001$) (*GRADE: Very low*) (i.e. MD >20% of the scale). Based on an MCID of 11 points, this difference may not be considered clinically important.

The study was at high risk of bias, but no sensitivity analysis could be performed as only one study contributed data.

Emotional function

One study (50 participants) reported emotional function measured with the Resilience Scale at the end of treatment (8 weeks) (Jindani 2015).

The 25-item Resilience Scale measures the degree of individual perceived ability to bounce back or recover from stress or negative emotions. The scale includes positively and negatively worded items with a total score ranging from 25 to 175. A higher score is indicative of higher resilience. The MCID for the Resilience Scale in people with PTSD is not established. Results suggest a small effect favouring yoga when compared to the control group (MD –13.60; 95% CI –26.86, –0.34; $p = 0.04$) (*GRADE: Very low*). (i.e. MD <10% of the scale)

The study was at high risk of bias, but no sensitivity analysis could be performed as only one study contributed data.

Depression

Two studies (76 participants) reported depression measured with the Depression, Anxiety and Stress Scale (DASS-21) (Jindani 2015) or the Centre for Epidemiological Studies – Depression Scale (CES-D) (Reddy 2013) at the end of treatment (mean: 8 weeks).

The DASS-21 is a quantitative measure of distress along 3 dimensions: depression, anxiety and stress. Each subscale consists of 7 questions, scored on a scale from 0 to 3 (14, 15). The depression scale assesses dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest / involvement, anhedonia and inertia. Total scores from the DASS-21 are multiplied by 2 to align with the original DASS-42 scoring (total score range 0 to 42). The DASS-21 is intended to be a dimensional rather than a categorical assessment of psychological disorders, but recommended cut-offs for the depression subscale are: 0-9 is considered normal, 10-13 is indicative of mild depression, 14-20 is representative of moderate depression, 21-27 of severe depression and 28+ of extremely severe depression (16). Results suggest no difference between the yoga group and the control group (SMD –0.25; 95% CI –0.82, 0.31; $p = 0.38$).

The CES-D measures depression symptomatology and consists of 4 subscales: negative affect, positive affect, interpersonal symptoms, and somatic and vegetative activity. Higher scores indicate greater depressive symptoms. Results suggest no difference in depression between yoga when compared to the control group (SMD 0.06; 95% CI –0.71, 0.83; $p = 0.08$).

Pooled results (76 participants) suggested no difference in depression between the yoga group compared to the control group (SMD –0.14; 95% CI –0.60, 0.31; $p = 0.52$; $I^2 = 0\%$) (*GRADE: Very low*).

In a sensitivity analysis that examined the impact of one RCT judged to be at high risk of bias (Jindani 2015) the point estimate shifted to favour control (SMD 0.06; 95% CI –0.71, 0.83; p = 0.88) but did not materially change the result.

Sleep quality

Two studies (72 participants) reported sleep quality as measured by the Insomnia Severity Index (ISI) or with a visual analogue scale (VAS) at the end of treatment (range: 7 days to 8 weeks).

The ISI is a 7-item questionnaire assessing the nature, severity and impact of insomnia, with the focus being on subjective feelings about insomnia symptoms. The ISI uses a 5-point Likert scale to rate each item with the total score ranging from 0 to 28. A higher score corresponds to more severe symptoms of insomnia. Results from one study (50 participants) (Jindani 2015) suggest a large effect favouring yoga when compared to the control group (SMD –0.90; 95% CI –1.49, –0.31; p = 0.003). (i.e. SMD ≥ 0.8) (*GRADE: Very low*).

The study was at high risk of bias, but no sensitivity analysis could be performed as only one study contributed data.

One study (22 participants) (Telles 2010) measured sleep disturbance using a 10 cm VAS but further details about the measure were not provided. It is assumed scores ranged from 0 (no sleep disturbance) to 10 (severe sleep disturbance). Results suggested little to no difference between yoga when compared to the control group (SMD –0.26; 95% CI –1.10, 0.58; p = 0.55).

Results from these studies were not pooled as correlation between the ISI and the VAS is not established.

Comparison 2 (vs other intervention)

Four RCTs (Culver 2015, Davis 2020, Huberty 2018, Van Der Kolk 2014) comparing yoga with 'other' interventions in people with PTSD were eligible for this comparison. Data from these studies are presented in Appendix F2 Supplementary outcome .

D2 Sleep-wake disorders

D2.1 Insomnia

D2.1.1 List of studies

An overview of the PICO criteria of included studies is provided in Table D-7. Study details, including all outcome domains and measures reported by the included studies are provided in Appendix F1. Outcome data for critical or important outcomes are provided in Appendix F2.

Table D-7 Overview of PICO criteria of included studies: Insomnia

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
Yoga versus control (no intervention, waitlist, inactive usual care)*						
Afonso 2012 (65)	Quasi RCT	Insomnia (females aged 50 to 65 years, menopausal)	Yoga	Control (no intervention) OR Physical activity (Stretching)^	None specified	Sleep severity Daytime functioning Stress
Sobana 2013 (66)	RCT	Insomnia (males)	Yoga	Control (no intervention)	None specified	Stress Self-confidence
Yoga versus 'other' intervention**						
Tapas 2013 (67)	Quasi RCT	Insomnia	Yoga	Ayurvedic healing (Sirodhara [tila taila])	None specified	Daytime functioning Cardiovascular Sleep quality Wake time after sleep onset Mood/stress

Abbreviations: RCT, randomised controlled trial

*Studies that compared yoga with an inactive control were eligible for inclusion in the evidence synthesis and are included in the Summary of findings tables if they reported outcomes considered critical or important to this review.

**Studies that compared yoga with an active intervention are included in the supplementary outcome tables (Appendix F2) if they reported data for outcomes considered critical or important to this review.

^ Study included 3 groups. The inactive control is considered in the evidence synthesis.

† Slowly pouring a steady stream of medicated oil or other warm liquid over your forehead.

D2.1.2 Risk of bias summary

The risk of bias for each item in the included studies for insomnia is described below and shown graphically in Figure D-5 (details are provided in Appendix E).

Bias arising from the randomisation process

Two studies (Afonso 2012, Tapas 2013) were judged to be at high risk of bias as the studies did not specify the randomisation sequence and did not report on allocation concealment. One study (Sobana 2013) was judged as being at low risk of bias for this domain, with no concern raised about the randomisation process.

Bias due to deviations from intended interventions

One study (Afonso 2012) was judged to be high risk of bias as most participants did not complete the intervention and deviations were not balanced between treatment arms, suggesting deviations were influenced by the trial context (e.g., lost interest in participating). Two studies (Tapas 2013, Sobana 2013) had no concerns raised and were judged as low risk of bias for this domain.

Bias due to missing outcome data

One study (Tapas 2013) was judged to be at high risk of bias for this domain as there was no information regarding the extent of missing data. Two studies (Afonso 2012, Sobano 2013) were judged as low risk of bias for this domain as data were available for all (or almost all) participants.

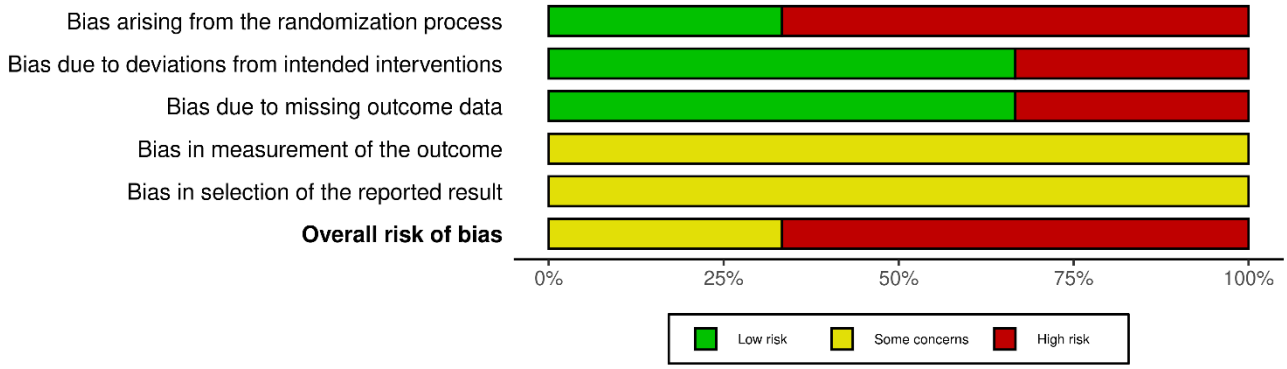
Bias in measurement of the outcome

All 3 studies (Afonso 2012, Tapas 2013, Sobana 2013) had some concern of bias raised as all primary outcomes were participant-reported and participants were aware of the intervention they were receiving; which could have influenced their response.

Bias in selection of the reported result

All 3 studies (Afonso 2012, Tapas 2013, Sobana 2013) were judged to have some concerns of bias for this domain. There were no pre-specified analysis plans available for the included studies, making it impossible to assess whether the reported result had been selected on the basis of multiple analyses. There was no indication of inappropriate multiple analysis.

Figure D-5 Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included RCTs: Insomnia



D2.1.3 Effect of intervention

Outcomes considered by the NTWC to be critical or important for decision-making in people with insomnia are listed in Table D-8.

Table D-8 Outcomes considered by the NTWC to be critical or important for decision-making: Insomnia

Outcome domain	Measured with	Consensus rating	Data available for main comparison?	Afonso 2012	Sobana 2013
Sleep quality/ satisfaction	PSQI, Insomnia Severity Index	Critical	Yes	✓	--
Daytime functioning	Epworth sleepiness scale, Stanford Sleepiness Scale	Critical	No	--*	--
Stress	Inventory of Stress Symptoms for Adults	Important	Yes	✓	--†
Fatigue	Any validated measure	Important	No	--	--
HRQoL (global)	Any validated measure	Important	No	--	--

Abbreviations: HRQoL, Health-related quality of life; PSQI, Pittsburgh Sleep Quality Index

✓ A study result is available for inclusion in the synthesis

X No study result is available for inclusion, (probably) because the *p*-value, magnitude or direction of the results generated were considered unfavourable by the study investigators

-- No study result is available for inclusion, (probably) because the outcome was not assessed, or for a reason unrelated to the *p*-value, magnitude or direction of the results

? No study result is available for inclusion, and it is unclear if the outcome was assessed in the study

* Epworth Sleepiness Scale only reported as n and observed power (OP) of the applied questionnaires. It was unclear which control group the reported p-values were associated with.

† Although stress was assessed, the measures used were not prioritised by the NTWC and therefore not included in the synthesis.

Main comparison (vs control)

Two studies (Afonso 2012, Sobana 2013) comparing yoga with control (no intervention) in people with insomnia were eligible for this comparison. One study (Afonso 2012) contributed data to 2 of the 5 outcomes considered critical or important for this review. The other study (Sobana 2013) could have contributed data but did not report outcomes or measures eligible for inclusion in this review.

There were 2 ongoing studies (total 108 participants) that compared yoga with no intervention in people with insomnia that were complete and could have contributed data to outcomes considered by the NTWC to be critical or important for decision-making, but there were no data available to make any judgements.

Results for all outcomes were at high risk of bias but no sensitivity analysis examining the impact of RCTs at high risk of bias could be conducted, as only one RCT contributed data.

Sleep quality (severity)

One study (30 participants) reported sleep quality measured with the Insomnia Severity Index (ISI) at the end of treatment (16 weeks) (Afonso 2012).

The ISI is a 7-item questionnaire assessing the nature, severity and impact of insomnia, with the focus being on subjective feelings about insomnia symptoms. Each question is summed to give a total score that ranges from 0 to 28. Scores are categorised as follows: 0-7, no clinical insomnia; 8-14, subclinical insomnia; 15-21, clinical insomnia (moderate); 22-28, clinical insomnia (severe). A cut-off score of 10 has been found to maximise sensitivity and specificity in a community sample (68). In a clinical sample of people seeking treatment for insomnia, an improvement of 8.4 points corresponded to a moderate improvement in insomnia (68).

Results show a small decrease in ISI score in the yoga group compared to the control group at end of treatment (MD –4.00; 95% CI –7.33, –0.67; p = 0.02) (*GRADE: Very low*). This difference does not reach the proposed MCID of 8.4 points, and mean post treatment scores in both treatment arms represented subclinical insomnia (score between 8 to 14 points).

Daytime functioning

One study (30 participants) measured daytime functioning with the Epworth Sleepiness Scale but did not report the end of treatment (16 weeks) data for this outcome (Afonso 2012).

Stress (symptoms)

One study (30 participants) reported stress as measured by Lipp's Stress Symptom Inventory for Adults (LSSI) (Afonso 2012).

The LSSI is a 53-item screening tool that assesses physical and psychological symptoms of stress in the last 24 hours (alert phase), the last week (resistance phase), or the last month (exhaustion phase). Results from each phase are reported separately, with the interpretation of results based on quartiles that denote stress can manifest from minimal to severe (69). Severe psychological distress is indicated by the following scores: alert phase – greater than 6; resistance phase – greater than 3; and exhaustion phase – greater than 8 (70).

Results suggest there is little to no difference in stress scores comparing the yoga and control groups in both the alert (MD –1.50; 95% CI –3.44, 0.44; p = 0.13) and exhaustion phases (MD –2.20, 95% CI –4.69, 0.29, p = 0.08). An effect favouring yoga was observed for the resistance phase (MD –3.10; 95% CI –5.04, –1.16; p = 0.002) (*GRADE: Very low*). The clinical significance of the observed effect is uncertain. At the end of treatment, participants in the yoga and control groups do not have severe distress in the alert or exhaustion phases but remain with severe distress (scores above 3) in the resistance phase.

Comparison 2 (vs other intervention)

Two RCTs (Afonso 2012, Tapas 2013) comparing yoga with 'other' interventions in people with insomnia were eligible for this comparison. Data from these studies are presented in Appendix F2 Supplementary outcome

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D3 Diseases of the nervous system

D3.1 Headache disorders

D3.1.1 List of studies

An overview of the PICO criteria of included studies is provided in Table D-9. Study details, including all outcome domains and measures reported by the included studies are provided in Appendix F1. Outcome data for critical or important outcomes are provided in Appendix F2.

Table D-9 Overview of PICO criteria of included studies: Headache disorders

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
Yoga versus control (no intervention, waitlist, inactive usual care)*						
John 2007 (71)	RCT	Migraine (without aura)	Yoga	Education	Standard medical care	Headache frequency Headache severity Anxiety Depression Pain Medication use
Kumar 2019a (72, 73)	RCT	Migraine (episodic)	Yoga	Control (no intervention)	Standard medical care	Headache intensity Headache frequency Headache-specific disability Medication use
Latha 1992 (74)	Quasi-RCT	Migraine and tension headache	Yoga	Control (no intervention)	Standard medical care	Headache duration Headache intensity Headache frequency Stress Medication use
Naji-Esfahani 2014 (75, 76)	RCT	Migraine (females)	Yoga (hatha)	Control (no intervention)	Standard medical care	Headache frequency Headache severity Headache duration Headache-specific disability Blood nitric oxide
Talakad 2013 (77, 78)	RCT	Migraine (with or without aura)	Yoga	Control (no intervention)	Standard medical care	Headache-specific disability Headache intensity Headache frequency Autonomic function
Yoga versus 'other' intervention**						
Sethi 1981 (79)	Quasi-RCT	Headache (tension-type)	Yoga (shavashana)	Electromyographic biofeedback	Not reported	Headache severity Headache frequency Social adjustment

Abbreviations: RCT, randomised controlled trial

*Studies that compared yoga with an inactive control were eligible for inclusion in the evidence synthesis and are included in the Summary of findings tables if they reported outcomes considered critical or important to this review.

**Studies that compared yoga with an active intervention are included in the supplementary outcome tables (Appendix F2) if they reported data for outcomes considered critical or important to this review.

D3.1.2 Risk of bias summary

The risk of bias for each item in the included studies for headache is described below and shown graphically in Figure D-6 (details are provided in Appendix E).

Bias arising from the randomisation process

Two studies (Kumar 2019a, Talakad 2013) were judged to be at low risk of bias for this domain as they provided sufficient information regarding the randomisation sequence and allocation concealment. Two studies (John 2007, Naji-Esfahani 2013) had some concerns as they did not report on allocation concealment. Two studies (Latha 1992, Sethi 1981) were judged to be at high risk of bias for this domain as they did not provide sufficient information regarding the randomisation sequence, allocation concealment or baseline characteristics of included participants.

Bias due to deviations from intended interventions

Three studies (John 2007, Latha 1992, Sethi 1981) were judged at low risk of bias for this domain as there were no reported deviations from the trial protocol that were expected to be due to the trial context and an appropriate method of analysis was used. One study (Kumar 2019a) was judged to have some concerns, as a substantial proportion of participants did not complete the trial, however this was balanced between groups.

Two studies (Naji-Esfahani 2014 and Talakad 2013) were judged at high risk of bias for this domain. Naji-Esfahani 2014 used an unclear method of analysis, with participant numbers from the consort diagram not aligning to the number of participants with reported results, raising concerns about inappropriate exclusion of participants from the results. Talakad 2013 had a large, unequal proportion of participants not completing the intervention, and it appears that a per protocol analysis was used, with some participants in the yoga group being excluded from the analysis.

Bias due to missing outcome data

One study (Latha 1992) was judged at low risk of bias for this domain as it was interpreted that all participants had outcome data available. Three studies (John 2007, Kumar 2019a, Sethi 1982) were judged to have some concerns as there was a substantial proportion of participants with missing outcome data, but reasons for drop out were provided and in most cases did not appear to be related to the intervention or outcome. Two studies (Naji-Esfahani 2014, Talakad 2013) were judged at high risk of bias for this domain as a significant and uneven proportion of participants with missing outcome data that was considered plausibly related to the outcome.

Bias in measurement of the outcome

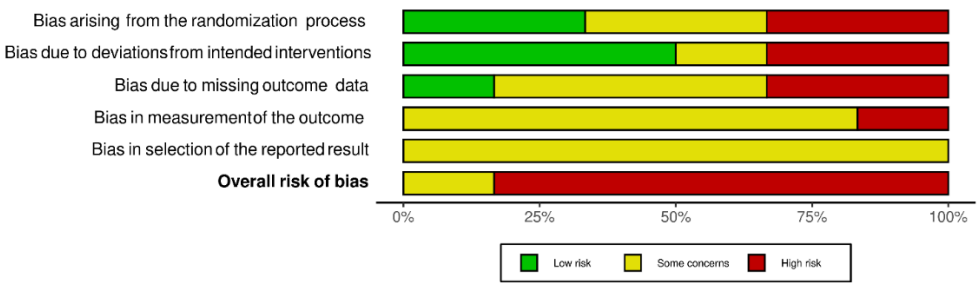
Five studies (Kumar 2019a, Latha 1992, Naji-Esfahani 2013, Sethi 1982, Talakad 2013) were judged to have some concerns in this domain, as most outcomes were self-reported by non-blinded participants. There was no reason to suggest that participants would be biased in their reporting of the outcome.

One study (John 2007) was judged to be at high risk of bias for this domain. Participants were required to pay a fee to enrol in the yoga program, which is considered likely to bias reporting of the outcome as participants would have increased motivation for the intervention to be effective.

Bias in selection of the reported result

All studies (John 2007, Kumar 2019a, Latha 1992, Naji-Esfahani 2013, Sethi 1981, Talakad 2013) were judged to have some concerns of bias due to a lack of information regarding a pre-specified analysis plan.

Figure D-6 Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included RCTs: Headache disorders



D3.1.3 Effect of intervention

Outcomes considered by the NTWC to be critical or important for decision-making in people with headache or migraine are listed in Table D-10.

Table D-10 Outcomes considered by the NTWC to be critical or important for decision-making: Headache disorders

Outcome domain	Measured with	consensus rating	Data available for main comparison?	John 2007	Kumar 2019a	Latha 1992	Naji-Esfahani 2014	Talakad 2013
Pain	MPQ or VAS	Critical	Yes	✓	--	--	--	--
Headache severity	VAS	Critical	Yes	✓	✓	✓^	✓	✓
Headache frequency	Headache diary	Critical	Yes	✓	✓	✓^	✓	✓
Headache-specific disability	HIT6 or MIDAS	Critical	Yes	?	✓	--	✓	✓
Emotional function	HADS	Critical	Yes	✓	--	--	--	--
Medication use	Medication use	Critical	Yes	✓	✓	X	--	--

Abbreviations: HADS, Hospital Anxiety and Depression Scale; HIT-6, Headache Impact Test-6; MIDAS, Migraine Disability Assessment Questionnaire; MPQ, McGill Pain Questionnaire; VAS, Visual Analogue Scale

^ Study reports this outcome but does not report standard deviation or confidence intervals and is therefore unable to be included in the meta-analysis. Results are considered in the narrative synthesis.

✓ A study result is available for inclusion in the synthesis

X No study result is available for inclusion, (probably) because the P value, magnitude or direction of the results generated were considered unfavourable by the study investigators

-- No study result is available for inclusion, (probably) because the outcome was not assessed, or for a reason unrelated to the P value, magnitude or direction of the results

? No study result is available for inclusion, and it is unclear if the outcome was assessed in the study

Main comparison (vs control)

Four RCTs (John 2007, Kumar 2019a, Naji-Esfahani 2014, Talakad 2013) and one quasi-RCT (Latha 1992) comparing yoga with control (no intervention, waitlist or usual care) in people with headache or migraine were eligible for this comparison. The studies contributed data to 6 of the 6 outcomes considered critical or important for this review.

There were 9 studies awaiting classification (>350 participants) and 2 ongoing studies (98 participants) that could have contributed data to 6 of the 6 outcomes. Missing results are (probably) because the *p* value, magnitude or direction of effect was considered unfavourable by the study investigators.

Pain

One study (65 participants) reported pain measured using the Short-Form McGill Pain Questionnaire (SF-MPQ) at end of treatment (12 weeks).

The SF-MPQ is a self-reported measure of pain, which assesses both the quality and the intensity of subjective pain. It consists of 15 words (11 sensory, 4 affective), of which respondents choose those that best describe their experience of pain. Three pain scores are derived from the sum of the intensity rank values for sensory, affective, and total pain score which ranges from 0-45 (80). The measure also includes a present pain intensity index and visual analogue scale for pain. A higher score is indicative of more severe pain. An MCID of at least 5 points has been proposed in a sample of people with musculoskeletal and rheumatic pain (80). No MCID in people with headache was identified.

The results suggest an improvement in pain in the yoga group compared to the control group (MD –2.28; 95% CI –2.54, –2.02; $p < 0.00001$) but, based on an MCID of 5 points, the effect may not be clinically meaningful (or MD <10% of the scale). *(GRADE: Very low)*

Headache severity

Four studies (317 participants) reported headache severity measured using a 10 cm VAS at end of treatment (range: 6 to 12 weeks) (John 2007, Kumar 2019a, Naji-Esfahani 2014, Talakad 2013).

A VAS is a unidimensional measure of pain where participants are asked to rate their pain on a scale from 0 (best) to 10 (worst). The reported MCID for pain measured by the VAS is influenced by baseline pain (81) and no MCID in participants with headache disorders was identified.

The results showed a large reduction in headache severity in the yoga group compared to the control group, however statistical heterogeneity was substantial (MD –2.85, 95% CI –4.81, –0.90; p = 0.004; I^2 = 97%) *(GRADE: Very low)*. (i.e. MD >20% of the scale).

In a sensitivity analysis examining the impact of 3 RCTs at high risk of bias (John 2007, Naji-Esfahani 2014, Talakad 2013) the size of the effect estimate decreased to moderate (>10% of the scale) but remained in favour of the yoga group (MD –1.10; 95% CI –1.76, –0.4; p = 0.001; I^2= NA [one study]).

Outcome data was missing from one study (Latha 1992; 20 participants) that reported an improvement in headache severity in the yoga group compared to the control group, but the authors did not report standard deviation or confidence intervals and could not be included in the meta-analysis.

Headache frequency

Four studies (317 participants) reported headache frequency measured by self-report at end of treatment (range: 6 to 12 weeks). Frequency was reported as headache days per month (John 2007, Kumar 2019a, Talakad 2013) or unspecified (Naji-Esfahani 2014). A 30% to 50% reduction in the frequency of days with headache or migraine is considered clinically meaningful (82, 83).

The results suggest a large reduction in headache frequency in the yoga group compared to the control group, however statistical heterogeneity was substantial (MD –3.52; 95% CI –5.14, –1.90; p < 0.0001; I^2 = 88%) *(GRADE: Low)*.

In a sensitivity analysis examining the impact of 3 RCTs at high risk of bias (John 2007, Naji-Esfahani 2014, Talakad 2013), the size of the effect estimate decreased but remained in favour of the yoga group (MD –2.10; 95% CI –3.14, –1.06; p < 0.0001; I^2= NA [one study]).

Outcome data was missing from one additional study (Latha 1992; 20 participants) which reported an improvement in headache frequency in the yoga group compared to the control group but did not report standard deviation or confidence intervals and could not be included in the meta-analysis.

Headache-specific disability

Three studies (252 participants) reported headache-specific disability measured using the Headache Impact Test-6 (HIT-6) at the end of treatment (range: 6 to 12 weeks) (Kumar 2019a, Naji-Esfahani 2014, Talakad 2013).

The HIT-6 measures the impact of headache on the ability to function at work, school, home and in social situations and covers 6 quality of life domains: pain, social functioning, role functioning, vitality, cognitive functioning, and psychological distress. Each item is answered on a 5-point Likert scale, with the total score ranging between 36 and 78. A higher score indicates a greater impact, with scores 49 or less representing little or no impact; between 50 and 55 representing some impact; between 56 and 59 representing substantial impact; and scores 60 or indicate severe impact. In headache populations a 2.3-point decrease reflects a clinically meaningful improvement (84, 85).

The results showed a large effect favouring the yoga group when compared with the control group, however heterogeneity was substantial (MD –15.22; 95% CI –32.16, 1.71; p = 0.08; I^2 = 98%) *(GRADE: Very low)*. Based on a proposed MCID of 2.3 points, this would be considered clinically important.

In a sensitivity analysis examining the impact of 2 RCTs at high risk of bias (Naji-Esfahani 2014, Talakad 2013), the size of the effect estimate decreased but remained in favour of the yoga group (MD –7.1; 95% CI –10.20, –4.00; p < 0.00001; I^2 = NA [one study]).

One study (Kumar 2019a) also reported headache-specific disability measured using the Migraine Disability Assessment Questionnaire (MIDAS). The result of this analysis using the MIDAS outcome did not differ substantially from the HIT-6, and thus the HIT-6 was chosen for consistency with the other studies included in this comparison.

Emotional function

One study (65 participants) reported emotional function measured using the Hospital Anxiety and Depression Scale (HADS) at the end of treatment (12 weeks) (John 2007).

The HADS is a self-report instrument used to assess the severity of anxiety and depression symptoms. Each domain contains 7 items, which participants rate on a scale from 0 (not at all) to 3 (definitely, most of the time). Total scores for each domain range from 0 to 21, with higher scores indicative of worse emotional function. The MCID in HADS score is proposed to be a change of 1.5 points in people with chronic obstructive pulmonary disease (86) and 1.7 points in people with cardiovascular disease (87). No MCID in people with headache was identified.

The results suggest a large improvement in emotional function in the yoga group compared to the control group for both anxiety (MD –8.70; 95% CI –9.47, –7.93; $p < 0.00001$) (*GRADE: Low*) and depression (MD –8.87; 95% CI –9.67, –8.07; $p < 0.00001$) *(GRADE: Low).* Based on a proposed MCID of 1.5 points, this would be considered clinically important.

Medication use

Two studies (225 participants) reported medication use as measured by a medication score at end of treatment (12 weeks) (John 2007, Kumar 2019a). Outcome data was missing from one additional study (Latha 1992; 20 participants) that noted analgesic use decreased during and after the training period in the yoga group compared with increased use in the control group, but no data were reported.

The medication score is the number of acute rescue pills used by participants during headache attacks (in addition to prescribed prophylactic drugs). According to the American Headache Society (83) acute treatments should be limited to an average of 2 headache days per week, with patients who exceed this limit offered preventive treatment. Patients who continue to overuse acute medication while receiving preventive therapy may require escalation.

The pooled results showed a reduction in medication use in the yoga group compared to the control group (MD –2.36; 95% CI –3.03, –1.69; $p < 0.00001$; $I^2 = 33\%$). *(GRADE: Low).*

In a sensitivity analysis examining the impact of one RCT at high risk of bias (John 2007), the size of the effect estimate decreased but the overall direction did not change (MD –1.80; 95% CI –2.93, –0.67; $p = 0.002$; I^2 = NA [one study]).

Comparison 2 (vs other intervention)

One RCT (Sethi 1981) comparing yoga with 'other' interventions in people with headache disorders was eligible for this comparison. Data from this study are presented in Appendix F2 Supplementary outcome.

D4 Diseases of the circulatory system

D4.1 Hypertensive heart disease

D4.1.1 List of studies

An overview of the PICO criteria of included studies is provided in Table D-11Table D-1. Study details, including all outcome domains and measures reported by the included studies are provided in Appendix F1. Outcome data for critical or important outcomes are provided in Appendix F2.

Table D-11 Overview of PICO criteria of included studies: Hypertension

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
Yoga versus control (no intervention, waitlist, inactive usual care)*						
Ankolekar 2019 (88)	Quasi RCT	Hypertension (pre)	Yoga	Control (no intervention)	None reported	CVD-risk
Cohen 2013 (89-92)	RCT	Hypertension (pre & Stage 1)	Yoga # OR Yoga plus wellness education program	Wellness education program †	None reported	CVD-risk
Cramer 2018 (93, 94)	RCT	Hypertension	Yoga (with postures) OR Yoga (without postures) ##	Control (waitlist)	Standard medical care (antihypertensives)	CVD-risk Perceived stress Quality of life
McCaffrey 2005 (95)	RCT	Hypertension (nonmedicated)	Yoga (pranayama and asanas)	Control (no intervention)	Educational advice	CVD-risk
Misra 2019 (96)	RCT	Hypertension (uncontrolled)	Yogic breathing (group class with home practise) OR Yogic breathing (group class with DVD-guided practise)	Control (no intervention)	Standard medical care (+/- antihypertensives)	CVD-risk
Mourya 2009 (97)	RCT	Hypertension	Yogic breathing (fast) OR Yogic breathing (slow)	Control (no intervention)	Standard medical care (+/- antihypertensives)	CVD-risk
Murugesan 2000 (98)	RCT	Hypertension (nonmedicated)	Yoga	Control (no intervention)^ OR Medical care (antihypertensives)	None reported	CVD-risk
Punita 2016 (99)	RCT	Hypertension	Yoga	Control (no intervention)	Standard medical care (antihypertensives)	CVD-risk
Pushpanathan 2015 (99)	RCT	Hypertension	Yoga	Control (no intervention)	Standard medical care (antihypertensives)	CVD-risk

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
Saptharishi 2009 (100, 101)	RCT	Hypertension (pre & Stage 1)	Yoga	Control (no intervention) ^ OR Physical activity (walking) OR Diet (salt intake reduction)	None reported	CVD-risk
Shetty 2017 (102)	RCT	Hypertension (pre & Stage 1)	Yogic breathing (sheetali and sheetkari pranayama)	Control (waitlist)	Standard medical care (antihypertensives)	CVD-risk
Sujatha 2014 (103)	Quasi RCT	Hypertension	Yoga	Control (no intervention)	Standard medical care (antihypertensives)	CVD-risk Anxiety Perceived stress
Thanalakshmi 2020 (104)	RCT	Hypertension	Yogic breathing (sheetali pranayama)	Control (no intervention)	None reported	CVD-risk
Thiyagarajan 2015 (105)	RCT	Hypertension (pre)	Yoga	Control (no intervention)	Lifestyle modification	CVD-risk
Tolbanos Roche 2014 (106)	RCT	Hypertension	Integrative Yoga Program	Control (no intervention)	Standard medical care (antihypertensives)	CVD-risk Perceived stress
Tolbanos Roche 2017 (107)	RCT	Hypertension	Integrative Yoga Program	Control (no intervention) ^ OR HT meditation OR Pranayama	Standard medical care (antihypertensives)	CVD-risk Perceived stress
Wolff 2016 (108)	RCT	Hypertension	MediYoga	Control (usual care)	Standard medical care (antihypertensives)	CVD-risk Quality of life Perceived stress
Yoga versus 'other' intervention**						
Cohen 2011a (109)	RCT	Hypertension (pre & Stage 1)	Iyengar yoga	Enhanced usual care (behavioural modification classes)	None reported	CVD-risk Perceived stress Quality of life
Ghati 2020 (110)	RCT	Hypertension	Bee-Humming Breathing (BHB) exercise	Attention control (breathing exercises)	Standard medical care (antihypertensives)	CVD-risk
Hagins 2014 (111)	RCT	Hypertension (pre & Stage 1)	Yoga	Physical activity (nonaerobic)	None reported	CVD-risk

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
Patil 2014 (112)	RCT	Hypertension (nonmedicated)	Yoga	Physical activity (walking/ stretching)	None reported	CVD-risk
Sieverdes 2014 (113)	Quasi RCT	Hypertension (normo & pre, 12-13 yrs.)	Hatha yoga	Attention control (music or art class)	None reported	CVD-risk
Sriloy 2015 (114)	RCT	Hypertension	Yogic breathing	Acupuncture	None reported	CVD-risk
Yadav 2012 (115)	RCT	Hypertension	Yogic breathing (anuloma-viloma pranayama)	Attention control (breathing awareness) OR Attention control (reading)	Standard medical care (antihypertensives)	CVD-risk

Abbreviations: CVD, Cardiovascular disease; RCT, Randomised Controlled Trial; HT, Himalayan tradition

* Studies that compared yoga with an inactive control were eligible for inclusion in the evidence synthesis and are included in the Summary of findings tables if they reported outcomes considered critical or important to this review.

** Studies that compared yoga with an active intervention are included in the supplementary outcome tables (Appendix F2) if they reported data for outcomes considered critical or important to this review.

† Small group blood pressure education classes and a walking program.

Study included 3 intervention groups (yoga alone vs education and walking program vs yoga + education and walking program). The Yoga delivered as an adjunct to the education and walking program was considered in the evidence synthesis.

Study include 3 intervention groups. The Yoga group (with postures) was considered in the evidence synthesis.

^ Study include 3 or 4 intervention groups. The Yoga vs Control (no intervention) was considered in the evidence synthesis.

D4.1.2 Risk of bias summary

The risk of bias for each time in the included studies for chronic pain is described below and shown graphically in Figure D-7 (details are provided in Appendix E).

Bias arising from the randomisation process

12 studies (Cohen 2013, Cramer 2018, Ghati 2020, Hagins 2014, Misra 2019, Punita 2016, Pushpanathan 2015, Saptharishi 2009, Sriloy 2015, Thanalakshmi 2020, Thiyagarajan 2015, Wolff 2016) provided sufficient information on the randomisation process and were considered at low risk of bias for this domain.

10 studies were assessed to have some concerns of bias. Eight of these studies (Cohen 2011, McCaffrey 2005, Mourya 2009, Murugesan 2000, Patil 2014, Shetty 2017, Sieverdes 2014, Sujatha 2014) had some concerns due to missing information about methods of concealing treatment allocation. The other 2 studies (Ankolekar 2019, Yadav 2012) did not provide information regarding allocation concealment or baseline differences between intervention groups.

Two studies (Tolbanos Roche 2014, Tolbanos Roche 2017) were assessed as high risk of bias for this domain as authors did not report concealment of intervention allocation and did not provide information regarding baseline differences between intervention groups.

Bias due to deviations from intended interventions

All studies had a lack of blinding due to the nature of the intervention. 15 studies were assessed as low risk of bias as intention to treat analysis was specified and followed.

Four studies were assessed to be at some risk of bias. Two of these studies (Punita 2016, Tolbanos Roche 2014) had high but balanced drop out, related to the trial context. Murugesan 2000 did not provide information regarding study retention and Shetty 2017 used per protocol analysis which is considered an inappropriate means of estimating effect of assignment to intervention.

Four studies (Cohen 2011, Cohen 2013, Misra 2019, Tolbanos Roche 2017) were assessed as high risk of bias due to high dropout, related to trial context. One study (Thiyagarajan 2015) was assessed to be at high risk of bias due to use of per protocol analysis and high dropout related to trial context.

Bias due to missing outcome data

15 studies (Cramer 2018, Ghati 2020, McCaffrey 2005, Mourya 2009, Patil 2014, Punita 2016, Pushpanathan 2015, Shetty 2017, Sieverdes 2014, Sriloy 2015, Sujatha 2014, Thanalakshmi 2020, Thiyagarajan 2015, Wolff 2016, Yadav 2012) were determined to have low risk of bias for this domain. Three studies (Hagins 2014, Misra 2019, Tolbanos Roche 2014) reported a balanced number of participants with missing outcome data and were considered to have some concerns for bias. No reasons for drop out were provided by any of the studies. Six studies (Ankolekar 2019, Cohen 2011, Cohen 2013, Murugesan 2000, Saptharishi 2009, Tolbanos Roche 2017) were assessed to have high risk of bias due to unbalanced missingness of data and a lack of sensitivity analysis conducted to determine impact of missing data. Cohen 2011 stated that 6 participants dropped out as per the protocol criteria, 3 participants had adverse events and one participant dropped out for personal reasons. Cohen 2013 stated that 24 participants dropped out as a result of not adhering to protocol criteria and 23 dropped out for personal reasons. Ankolekar 2019, Murugesan 2000, Saptharishi 2009 and Tolbanos Roche 2017 did not provided reasons for drop out.

Bias in measurement of the outcome

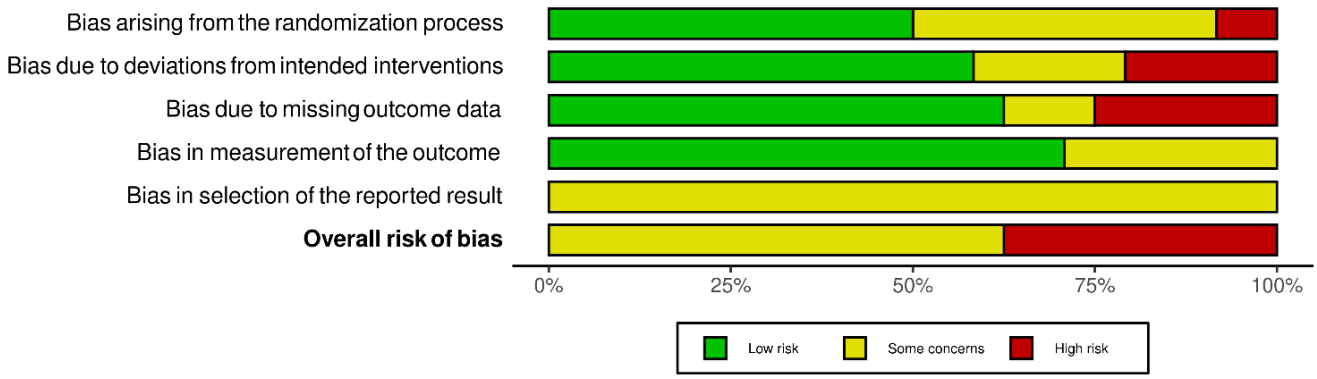
Seven studies (Ankolekar 2019, Cohen 2011, Cohen 2013, Sujatha 2014, Tolbanos Roche 2014, Tolbanos Roche 2017, Wolff 2016) were assessed to have at least some concerns for this domain, due to the non-blinded nature of the studies and the self-reported nature of the outcome measures. The remaining studies were determined to be at low risk of bias due to the objective outcome measure used in this population.

Bias in selection of the reported result

Cohen 2013 provided a pre-specified analysis plan however there were inconsistencies between pre-specified plan and final report, hence the study was considered at some concerns for this domain.

The remaining studies were assessed to have some concerns for this domain. There were no pre-specified analysis plans available for the included studies, making it impossible to assess whether the reported result had been selected on the basis of multiple analyses. There was no indication of inappropriate multiple analysis.

Figure D-7 Risk of bias summary: review authors' judgements about each risk of bias item expressed as percentages across all RCTs – Hypertension



D4.1.3 Effect of intervention

Outcomes considered by the NTWC to be critical or important for decision-making in people with Hypertension are listed in Table D-12.

Table D-12 Outcomes considered by the NTWC to be critical or important for decision-making: Hypertension

Outcome domain	Measured with	Consensus rating	Data available for main comparison?	Ankolekar 2019	Cohen 2011a	Cramer 2018	McCaffrey 2005	Misra 2019	Mourya 2009	Murugesan 2000	Punita 2016	Pushpanathan 2015	Saptharishi 2009	Shetty 2017	Sujatha 2014	Thanalakshmi 2020	Thiyagarajan 2015	Tolbanos Roche 2014	Tolbanos Roche 2017	Wolff 2016
CVD risk	Blood pressure (SBP, DBP)	Critical	Yes	✓	✓	✓	✓	✓	✓^	✓	✓	✓^	✓	✓	✓	✓	✓	✓	✓	✓
Fitness / exercise capacity	No eligible measures	Critical	No	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
Physical function / mobility	Six-minute walk test	Critical	No	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
Perceived Stress	Perceived stress scale (or other)	Critical	Yes	--	✓^	✓	--	--	--	--	--	--	--	--	✓^	--	--	✓	✓	✓
Quality of life	SF-12/ SF-36/ WHOQOL-BREF	Critical	Yes	--	✓^	✓	--	--	--	--	--	--	--	--	--	--	--	--	--	✓
Anxiety	STAI or other validated measure	Important	Yes	--	--	✓	--	--	--	--	--	--	--	--	✓	--	--	--	✓	✓
Medication use	Medication intake	Important	No	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

Abbreviations: DBP, diastolic blood pressure; CVD, cardiovascular disease; SBP, systolic blood pressure; SF-12, 12-item short form survey; SF-36, 36-item short form survey; STAI, State-Trait Anxiety Inventory WHOQOL-BREF, World Health Organisation Quality of Life Questionnaire.

✓ A study result is available for inclusion in the synthesis

X No study result is available for inclusion, (probably) because the P value, magnitude or direction of the results generated were considered unfavourable by the study investigators

-- No study result is available for inclusion, (probably) because the outcome was not assessed, or for a reason unrelated to the P value, magnitude or direction of the results.

^ Study data were not in an extractable form (column/line graph)

Main comparison (vs. control)

Seventeen RCTs comparing yoga with control (no intervention, waitlist or usual care) in people with pre- and/or primary hypertension were eligible for this comparison (Ankolekar 2019, Cohen 2013, Cramer 2018, McCaffrey 2005, Misra 2019, Mourya 2009, Murugesan 2000, Punita 2016, Pushpanathan 2015, Saptharishi 2009, Shetty 2017, Sujatha 2014, Thanalakshmi 2020, Thiyagarajan 2015, Tolbanos Roche 2014, Tolbanos Roche 2017, Wolff 2016) and contributed data relevant to at least one of the 7 outcome domains considered critical or important for this review.

There were 5 studies awaiting classification (total 270 participants) and 5 ongoing studies[3] (total 533 participants) that compared yoga with control (no intervention, waitlist or usual care) in people with pre- and/or primary hypertension that could have contributed data for 4 outcomes considered critical or important for this review (cardiovascular disease-risk, quality of life, perceived stress, and anxiety) (see Appendix C6).

Cardiovascular disease risk

Seventeen studies (total 1279 participants) reported cardiovascular disease risk measured by systolic and diastolic blood pressure (mm Hg) at the end of treatment (range: 30 days to 24 weeks). Two of the studies (Misra 2019, Pushpanathan 2015) reported SBP but not DBP. Blood pressure was measured by a clinician using a sphygmomanometer or a blood pressure monitoring device.

There were 2 other studies (Mourya 2009, Pushpanathan 2015) that did not provide any extractable data for either outcome so were unable to be included in the quantitative synthesis. Both studies reported a significant reduction in SBP and DBP for participants who practised yoga when compared with control.

Systolic blood pressure (SBP) measures the force produced by the heart when it pumps out bloods to the rest of the body. In the general adult population, an SBP below 120 mmHg is considered normal, whereas an SBP between 120 to 129 mmHg indicates high/elevated or prehypertension (i.e. increased cardiovascular disease risk. Diastolic blood pressure (DBP) measures the pressure in your arteries when the heart is at rest. In the general adult population, a DBP around 80 mmHg is considered normal, whereas a score between 85 to 89 mmHg indicates high/elevated DBP. The closer the score to 120/80 mmHg, the more stable the cardiorespiratory health, with a 2 mmHg size difference in SBP associated with 4% lower risk of coronary death and 6% lower risk of stroke death in middle age (116).

Pooled results suggest a large effect favouring yoga when compared with the control group for SBP (MD –7.95; 95% CI –12.31, –3.59; $p < 0.00001$; $I^2 = 93\%$) (*GRADE: Low*) and a large effect favouring yoga for DBP (MD –5.61; 95% CI –8.69, –2.54; $p < 0.00001$; $I^2 = 93\%$) (*GRADE: Low*).

Visual inspection of the funnel plots suggests poor methodological quality may have led to inflated effects in smaller studies (for SBP – see Figure D-8) and that smaller studies without statistically significant effects remain unpublished (and DBP – see Figure D-9). This is in line with 8 studies (Ankolekar 2019, Cohen 2013, Misra 2019, Murugesan 2000, Saptharishi 2009, Thiyagarajan 2015, Tolbanos Roche 2014, Tolbanos Roche 2017) being judged to be at high risk of bias and 5 ongoing studies identified in the literature search that are completed but results not published.

In a sensitivity analysis that examined the impact of the RCTs judged to be at a high risk of bias the size of the effect estimate increased for SBP (MD –0.79; 95% CI –18.64, –2.93; $p < 0.00001$; $I^2 = 95\%$) but did not materially change for DBP (MD –4.90; 95% CI –9.46, –0.35; $p < 0.00001$, $I^2 = 95\%$).

[3] Complete, results not published or of unknown status

Figure D-8 Funnel plot of comparison: Yoga vs control (no intervention, waitlist, usual activities): Hypertension, outcome - systolic blood pressure

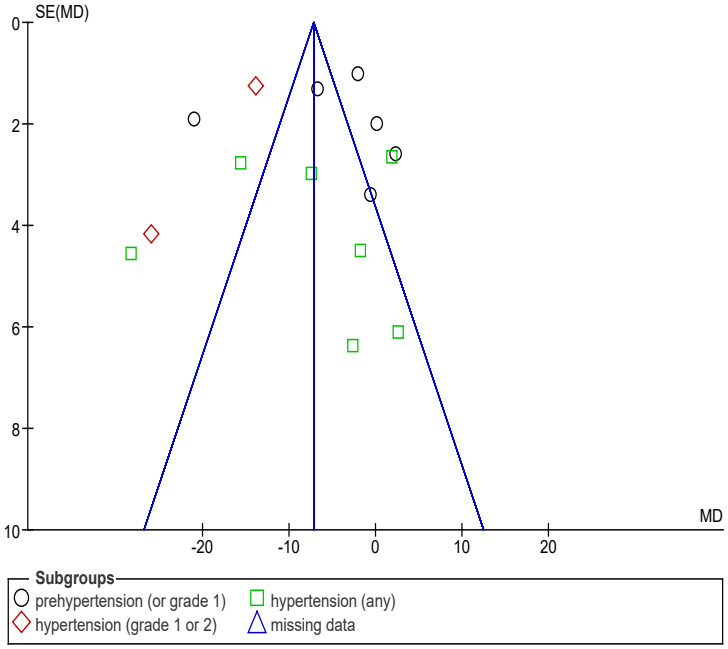
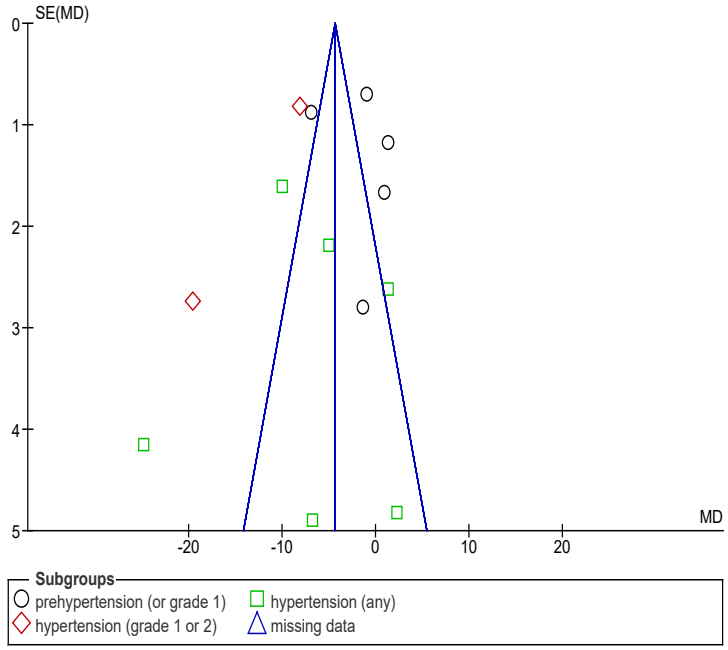


Figure D-9 Funnel plot of comparison: Yoga vs control (no intervention, waitlist, usual activities): Hypertension, outcome - diastolic blood pressure



Perceived stress

Four studies (total 486 participants) reported perceived stress measured with the Perceived Stress Scale (PSS-10) at the end of treatment (range: 8 to 12 weeks) (Cramer 2018, Sujatha 2014, Tolbanos Roche 2017, Wolff 2016). One study (Sujatha 2014) did not report any extractable data and was unable to be included in the quantitative synthesis for this outcome. The authors reported a significant reduction in perceived stress for participants completing the yoga intervention.

The PSS-10 is an abbreviated version of the 14-item Perceived Stress Scale, which measures how overwhelmed a person is by their current life circumstances. Participants rate the frequency with which they experienced 10 stress symptoms over the preceding 30 days on a 5-point scale. Total scores range from 0 to 40 with higher scores indicating greater perceived stress. An MCID for the PSS-10 in people with hypertension has not been established, but is estimated to be between 2.19 and 2.66 points among undergraduate students with elevated stress (63) and around 11 points in people with work-related stress complaints (64).

Pooled results suggest little to no difference between the groups when comparing yoga with the control (MD –1.75; 95% CI –4.89, 1.38; $p = 0.18$; $I^2 = 41\%$) *(GRADE: Low)*.

In a sensitivity analysis that examined the impact of one RCT judged to be at a high risk of bias (Tolbanos Roche 2017) the size of the effect estimate decreased (MD –0.56; 95% CI –2.33, 1.22; $p = 0.54$ $I^2 = 0\%$).

Quality of life

Two studies (221 participants) reported quality of life measured with the SF-36, the WHOQOL-BREF at the end of treatment (12 weeks) (Cramer 2018, Wolff 2016). One other study (Cohen 2013) measured quality of life with the SF-36, but results were not published.

The SF-36 assesses the impact of one's health on everyday life. Eight domains are summarised on a scale from 0 (worse) to 100 (best), which can be summarised into 2 component scores. The physical component summary (PCS) score includes the domains of general health, physical functioning, role physical and body pain. The mental component summary (MCS) score includes the domains of vitality, social functioning, role emotional, and mental health. The PCS and MCS are derived by aggregating individual scores. The MCID for the SF-36 is estimated to be around 2 to 4 points for the general population (i.e. ~0.5 of the SD) (42).

The WHOQOL-BREF contains 26 items that assess quality of life in the context of an individual's culture, value systems, personal goals, standards and concerns. Items are scored on a scale from 1 (disagree) to 5 (completely agree or extremely) and are summarised in 4 domains, being: physical health, psychological health, social relationships, and environment. There are also 2 additional items that measure an individual's overall perception of quality of life (WHOQOL-BREF 1) and health satisfaction (WHOQOL-BREF 2). The study (Wolff 2016) only reported the WHOQOL-BREF 1 and WHOQOL-BREF 2 scores. The WHOQOL-BREF 1 score was used in this analysis, as this measures quality of life rather than health satisfaction.

The results suggested there is little to no difference in quality of life comparing the yoga and control groups for any specified measure *(GRADE: Very low)*:

- SF-36 PCS (SMD 0.06; 95% CI –0.49, 0.61; $p = 0.83$)
- SF-36 MCS (SMD –0.39; 95% CI –0.95, 0.17; $p = 0.17$)
- WHOQOL-BREF 1 (SMD –0.00; 95% CI –0.30, 0.30; $p = 1.00$)

Results from one additional study (Ankolekar 2019, 102 participants) suggests a small effect that favours the yoga group compared with control (SMD –0.49; 95% CI –0.89, –0.10; $p = 0.01$). The measure used to assess quality of life was not specified in this study, and as such the results were not able to be included in the meta-analysis.

No sensitivity analysis was conducted that examined the impact of RCTs judged to be at high risk of bias, as all studies contributing data were not judged to be at high risk of bias.

Anxiety

Four studies (485 participants) reported anxiety measured with the Hospital Anxiety and Depression scale (HADS), the Beck Anxiety Inventory (BAI), or the State Trait Anxiety Inventory (STAI) at the end of treatment (range: 2 months to 12 weeks) (Cramer 2018, Tolbanos Roche 2017, Sujatha 2014, Wolff 2016).

The HADS is a self-report instrument used to assess the severity of anxiety and depression symptoms. Each domain contains 7 items, which participants rate how they currently feel on a scale from 0 (not at all) to 3 (definitely, most of the time). The HADS-A assessed generalized anxiety including tension, worry, fear, panic, difficulties in relaxing, and restlessness. Total scores for each domain range from 0 to 21, with higher scores indicative of worse emotional function. The MCID in HADS score is proposed to be a change of 1.7 points in people with cardiovascular disease (87). The results from 2 studies (221 participants) showed no improvement in anxiety symptoms in the yoga group compared to the control group (MD[4] 0.21, 95% CI –0.55, 0.96, p = 0.59, I^2=0%).

The BAI is a 21 item self-reported inventory that focuses on the somatic symptoms of anxiety such as nervousness, dizziness, inability to relax felt by a participant in the past week. Each item is scored on a scale from 0 (not at all) to 3 (severely) to yield a total score from 0 to 63. A higher score indicates more severe anxiety. The results from one study (24 participants) suggested little to no improvement in anxiety symptoms in the yoga group compared to the control group (MD –3.27; 95% CI –12.21, 5.67; p = 0.47). (i.e. MD < 10% of the scale)

The STAI consists of 20 questions evaluating obvious (state) anxiety and 20 questions evaluating hidden (trait) anxiety. All items are rated on a 4-point scale from 'almost never' to 'almost always'. State anxiety evaluates an individual's feeling in the moment and trait anxiety measures an individual's usual and general feelings. Total scores for each measure range between 20 to 80, with higher scores relating to higher levels of anxiety. Determining meaningful difference can be difficult for the trait anxiety subscale as it is intended to identify susceptibility and is less responsive to change compared to state anxiety. For the state anxiety subscale, a cut point of 39-40 is suggested to detect clinically significant symptoms (62). No MCID for the STAI in people with hypertension was found. The results from one study suggest an effect favouring yoga when compared to control group for both state (MD –8.65; 95% CI –10.59, –6.71; p < 0.00001) and trait anxiety (MD –8.28; 95% CI –10.30, –6.26; p < 0.00001). Participants in both groups continue to have clinically significant state anxiety (total scores > 40).

Pooled results[5] suggest little to no effect favouring yoga when compared with the control group (SMD –0.33; 95% CI –1.07, 0.41; p < 0.00001; I^2 = 92%) (*GRADE: Very low*). (i.e. SMD between 0.2 and 0.5).

In a sensitivity analysis that examined the impact of one RCT judged to be at a high risk of bias (Tolbanos Roche 2017) the size of the effect estimate decreased but did not materially change (SMD –0.34; 95% CI –1.23, 0.55; p = 0.45; I^2 = 95%).

Comparison 2 (vs other intervention)

There were 12 studies comparing Yoga with 'other' interventions in people at risk of hypertensive heart disease that were eligible for this comparison. Data from these studies are presented in Appendix F2 Supplementary outcome .

[4] MD reported here for interpretation of the MCID. Forest plots (Figure 33 of the evaluation report) report the SMD as it is combined with other measures.

[5] State-anxiety results included in the meta-analysis as this correlates better with HADS and BAI than the trait anxiety domain.

D5 Diseases of the respiratory system

D5.1 Asthma

D5.1.1 List of studies

An overview of the PICO criteria of included studies is provided in Table D-13. Study details, including all outcome domains and measures reported by the included studies are provided in Appendix F1. Outcome data for critical or important outcomes are provided in Appendix F2.

Table D-13 Overview of PICO criteria of included studies: Asthma

Study ID	Study design	POPULATION	INTERVENTION	COMPARATOR	Co-interventions	OUTCOME DOMAINS
Yoga versus control (no intervention, waitlist, inactive usual care)*						
Agnihotri 2013 (117, 118)	RCT	Asthma (mild to moderate)	Yoga	Control (no intervention)	Standard medical care	Quality of life Pulmonary function Biochemical parameters
Agnihotri 2017 (119)	RCT	Asthma (mild to moderate)	Yoga	Control (no intervention)	Standard medical care	Quality of life Emotional function Response to environmental stimuli Activity limitation Asthma symptoms
Bidwell 2012 (120)	Quasi RCT	Asthma (mild to moderate)	Yoga (Hatha)	Control (no intervention)	Standard medical care	Quality of life Pulmonary function Physical activity Cardiac autonomic function Haemodynamic response
Malarvizhi 2019 (4)	RCT	Asthma (mild to moderate)	Yoga	Control (no intervention)	Standard medical care	Quality of life
Mekonnen 2010 (121)	RCT	Asthma (mild to moderate)	Yoga	Control (no intervention)	Standard medical care	Pulmonary function Medication use Asthma experience
Prem 2013 (122)	RCT	Asthma (mild to moderate)	Yogic breathing	Control (no intervention) ^ OR Buteyko breathing	Standard medical care	Quality of life Asthma symptoms Pulmonary function
Pushpa 2018 (123)	Quasi RCT	Asthma (mild to moderate)	Yogic breathing	Control (no intervention)	Standard medical care	Pulmonary function
Satpathy 2012 (124)	Quasi RCT	Asthma (mild to moderate)	Yogic breathing	Control (no intervention)	Standard medical care	Pulmonary function
Sodhi 2009 (125)	Quasi RCT	Asthma (mild to moderate)	Yogic breathing	Control (no intervention)	Standard medical care	Pulmonary function
Turan 2020 (126)	RCT	Asthma (mild to moderate)	Yoga	Control (no intervention)	None reported	Quality of life Asthma symptoms Pulmonary function
Yoga versus 'other' intervention**						
Jiandani Mariya 2013 (127)	RCT	Asthma (mild to moderate)	Yoga	Physiotherapy	Standard medical care Education program	Quality of life Pulmonary function

Study ID	Study design	POPULATION	INTERVENTION	COMPARATOR	Co-interventions	OUTCOME DOMAINS
Manocha 2002 (128)	RCT	Asthma (moderate to severe)	Yoga (Shaja)	Relaxation methods	Standard medical care	Quality of life Pulmonary function Emotional function Metacholine challenge test
Raghavendra 2016 (129)	RCT	Asthma (mild to moderate)	Yogic breathing	Attention control (deep breathing)	None reported	Pulmonary function
Sabina 2005 (130)	RCT	Asthma (mild to moderate)	Yoga (Iyengar)	Stretching exercises	Standard medical care	Pulmonary function Quality of life Medication use Asthma symptoms
Saravanan 2019 (131)	RCT	Asthma (mild to moderate)	Yoga mudra	Attention control (deep breathing)	None reported	Pulmonary function
Saxena 2009 (132)	Quasi RCT	Asthma (mild to moderate)	Yogic breathing	Meditation	None reported	Pulmonary function Asthma symptoms
Yuce 2009 (133)	RCT	Asthma (mild to moderate)	Yogic breathing	Progressive relaxation	Standard medical care	Pulmonary function Quality of life Asthma symptoms

Abbreviations: RCT, randomised controlled trial

*Studies that compared yoga with an inactive control were eligible for inclusion in the evidence synthesis and are included in the Summary of findings tables if they reported outcomes considered critical or important to this review.

**Studies that compared yoga with an active intervention are included in the supplementary outcome tables (Appendix F2) if they reported data for outcomes considered critical or important to this review.

^ Study included 3 groups. The inactive control is considered in the evidence synthesis.

D5.1.2 Risk of bias summary

The risk of bias for each item in the included studies for asthma is described below and shown graphically in Figure D-10 (details are provided in Appendix E).

Bias arising from the randomisation process

Four studies (Malarvizhi 2019, Manocha 2002, Prem 2013, Yuce 2020) provided sufficient information regarding allocation concealment, the randomisation sequence and baseline characteristics. These studies were considered at low risk of bias. Thirteen studies had concerns regarding bias arising from the randomisation process (Agnihotri 2013, Agnihotri 2017, Bidwell 2012, Jiandani Mariya 2013, Mekonnen 2010, Pushpa 2018, Raghavendra 2016, Sabina 2005, Saravanan 2019, Satpathy 2012, Sodhi 2009).

Bias due to deviations from the intended interventions

Fifteen studies (Agnihotri 2013, Agnihotri 2017, Bidwell 2012, Jiandani Mariya 2013, Malarvizhi 2019, Manocha 2002, Mekonnen 2010, Prem 2013, Pushpa 2018, Raghavendra 2016, Sabina 2005, Saravanan 2019, Satpathy 2012, Saxena 2009, Sodhi 2009, Turan 2020, Yuce 2020) were judged to be at low risk of bias for this domain as they had no deviations from the intervention that were considered to have arisen from the trial context. Two studies (Prem 2013, Sabina 2005) were judged to be at high risk of bias for this domain due to high discontinuation rate (27%) of participants and exclusion of participants (15%) for noncompliance which is considered higher than what would occur in usual practice.

Bias due to missing outcome data

Twelve studies (Agnihotri 2013, Bidwell 2012, Jiandani Mariya 2013, Malarvizhi 2019, Mekonnen 2010, Pushpa 2018, Raghavendra 2016, Saravanan 2019, Satpathy 2012, Saxena 2009, Sodhi 2009, Turan 2020) were judged at low risk of bias for this domain as outcome data was available for most or all participants. Five studies (Agnihotri 2017, Manocha 2002, Prem 2013, Sabina 2005, Yuce 2020) had some concerns due to a large proportion of missing data, with no reason provided for drop out or how missing data was handled.

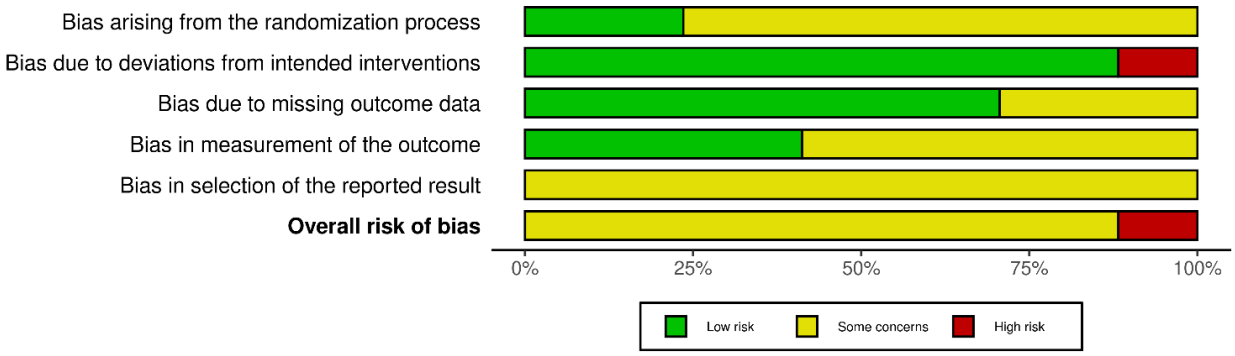
Bias in measurement of the outcome

Seven studies (Pushpa 2018, Raghavendra 2016, Sabina 2005, Saravanan 2019, Satpathy 2012, Saxena 2009, Sodhi 2009) were assessed to have a low risk of bias with participants unaware of treatment allocation or objectively measured outcomes. The remaining 10 studies (Agnihotri 2013, Agnihotri 2017, Bidwell 2012, Jiandani Mariya 2013, Malarvizhi 2019, Manocha, 2002, Mekonnen 2010, Prem 2013, Sabina 2005, Satpathy 2012, Saxena 2009, Sodhi 2009, Turan 2020, Yuce 2020) had some concerns regarding the measurement of outcomes, with participants aware of treatment allocation and primary outcomes being subjectively measured, which could be influenced by knowledge of the intervention.

Bias in selection of the reported results

All studies were assessed at some concern at risk of bias for this domain as no pre-specified analysis plan was available to confirm the reported results was analysed in a pre-determined manner.

Figure D-10 Risk of bias summary: review authors' judgements about each risk of bias item expressed as percentages across all RCTs – Asthma



D5.1.3 Effect of intervention

Outcomes considered by the NTWC to be critical or important for decision-making in people with asthma are listed in Table D-14.

Table D-14 Outcomes considered by the NTWC to be critical or important for decision-making: Asthma

Outcome domain	Measured with	Consensus rating	Data available for main comparison?	Agnihotri 2013	Agnihotri 2017	Bidwell 2012	Malarvizhi 2019	Mekonnen 2010	Prem 2013	Pushpa 2018	Satpathy 2012	Sodhi 2009	Turan 2020
Asthma symptoms	Asthma control questionnaire	Critical	Yes	--	--	--	--	--	✓	--	--	--	✓
Pulmonary function	FEV_1/FVC	Important	Yes	✓	?	X	?	X	✓	✓	✓	✓	✓
Health-related quality of life	AQLQ/ SGRQ	Important	Yes	✓	✓	✓	✓	--	✓	?	?	✓	✓
Emotional function	POMS	Important	No	--	--	--	--	--	--	--	--	--	--
Medication use	As reported	Important	Yes	--	--	--	--	✓	--	--	--	--	--
Days off work/ school	Count data	Important	No	--	--	--	--	--	--	--	--	--	--
Asthma specific hospitalisation	Incident rate	Important	No	--	--	--	--	--	--	--	--	--	--

Abbreviations: AQLQ, asthma quality of life questionnaire; FEV_1, forced expiratory volume; Forced vital capacity; POMS, Profile of mood states; SGRQ, St. George Respiratory Questionnaire

✓ A study result is available for inclusion in the synthesis

X No study result is available for inclusion, (probably) because the P value, magnitude or direction of the results generated were considered unfavourable by the study investigators

-- No study result is available for inclusion, (probably) because the outcome was not assessed, or for a reason unrelated to the P value, magnitude or direction of the results

? No study result is available for inclusion, and it is unclear if the outcome was assessed in the study

Main comparison (vs control)

Ten RCTs (Agnihotri 2013, Agnihotri 2017, Bidwell 2012, Malarvizhi 2019, Mekonnen 2010, Prem 2013, Pushpa 2018, Satpathy 2012, Sodhi 2009, Turan 2020) comparing yoga with control (no intervention, waitlist or usual care) in people with asthma were eligible for this comparison and contributed data relevant to 4 of the 7 outcomes considered critical or important for this review.

There were 8 studies awaiting classification (total 353 participants) and one ongoing study (total 60 participants) that could have contributed data to these outcomes (see Appendix C6). The available information is insufficient to make a judgement about the nonreporting of results.

Asthma symptoms

Two studies (total 188 participants) reported asthma symptoms measured with the Asthma Control Questionnaire (ACQ) or the Asthma Control Test (ACT) before and after treatment (range: 6 to 12 weeks) (Prem 2013, Turan 2020).

The ACT is a self-reported questionnaire consisting of 5 items that assess how well an individual manages their asthma. Participants rate their experience on the following subdomains, frequency of shortness of breath, general asthma symptoms, use of rescue medications, effect of asthma on daily functioning and overall self-assessment of asthma control. The total scores range from 5 (poor control of asthma) to 25 (complete control of asthma). A score greater than 19 indicates well-controlled asthma. The MCID is determined as 3 points between 2 groups or for changes over time (134). The results from one study (Turan 2020) (112 participants) suggests a large effect favouring the yoga group when compared to the control group (SMD –4.53; 95% CI –5.24, –3.82; $p < 0.00001$).

The ACQ measures the adequacy of how well asthma is managed due to treatment in the past week. There are 7 subdomains assessing asthma symptoms (5 items), use of rescue bronchodilator (1 item) and FEV_1% (1 item). Items are scored from (0 (no impairment) to 6 (maximum impairment) for symptoms and rescue use; and 7 categories for FEV_1%). A lower score indicates no impairment whereas a higher score indicates severely uncontrolled asthma. The MCID is determined as a 0.5 change in score (135). The results from one study (Prem 2013) (76 participants) suggests no difference between the yoga and the control group (SMD 0.02; 95% CI –0.43, 0.47; $p = 0.91$).

Pooled results suggest an effect favouring the yoga group, but there is substantial statistical heterogeneity that may be related to differences in the intervention delivered (yogic breathing, yoga with postures) (SMD –2.24; 95% CI –6.71, 2.22; $p = < 0.00001$; I^2=99%). (*GRADE: Very low*).

In a sensitivity analysis that examined the impact of one RCT judged to be at a high risk of bias (Prem 2013) the size of the effect estimate increased substantially (SMD –4.53; 95% CI –5.24, –3.82; $p < 0.00001$; $I^2 = 0$%). The direction of bias may be against the intervention.

Pulmonary function

Six studies (680 participants) reported pulmonary function measured by FEV_1/FVC ratio at the end-of treatment (range: 6 weeks to 6 months) (Agnihotri 2013, Bidwell 2012, Prem 2013, Pushpa 2018, Satpathy 2012; Sodhi 2009, Turan 2020).

The FEV1/FVC ratio measures the ratio of forced expiratory volume (FEV) in 1 second to forced vital capacity (FVC). Normal values typically range between 75% to 85%, depending on sex and age, with a 5 point percentage lower than normal suggestive of airflow obstruction (136) (lower is worse). An MCID for the change in FEV_1/FVC has not been established, but the normalisation of the ratio, secondary to an improvement in FEV_1, could be considered clinically important (137).

The pooled results from 5 studies suggests little to no difference between the yoga and control groups (MD 2.71; CI –3.76, 9.19; $p = 0.41$; $I^2 = 97\%$) (*GRADE: Low*)., with substantial statistical heterogeneity. One study (Bidwell 2012) did not provide any data but reported that no difference between groups was observed.

In a sensitivity analysis that examined the impact of one RCT judged to be at a high risk of bias (Prem 2013) the size of the effect estimate increased (MD 4.48; CI –2.93, 11.88; $p = 0.24$; $I^2 = 97\%$).

Quality of life

Six studies (total 826 participants) reported quality of life measured with the Asthma Quality of Life Questionnaire (15-item or 32-item) or the St. George's Respiratory Questionnaire (SGRQ) at the end of treatment (range: 6 weeks to 6 months) (Agnihotri 2013, Agnihotri 2017, Malarvizhi 2019, Prem 2013, Sodhi 2009, Turan 2020).

The 15- and 32-item Asthma Quality of Life Questionnaire (AQLQ) measures the functional impairments for people with asthma which they experience in their daily lives[6]. There are 4 subdomains encompassing symptoms (12 items), activity limitation (11 items), emotional function (5 items) and environmental stimuli (4 items). Patients respond to each question on a 7-point scale from 1 (maximum impairment) to 7 (no impairment) (i.e. higher is better). Scores are calculated as averages of all items on that domain (range 1 to 7). The MCID for AQLQ in people with asthma is determined to be 0.5 (range: 0.42 to 0.58) for overall quality of life and for each of the individual domains (138). Pooled results from 5 studies (total 806 participants) suggests a large effect favouring the yoga group when compared with the control group (SMD –3.26; CI –5.24, –1.27; $p = 0.001$; $I^2 = 99\%$).

The SGRQ records quality of life in participants with asthma in the preceding month (part 1) and in the current state (part 2). There are 3 subscales: symptoms (frequency and severity), activity (cause or limited by breathlessness), and impacts (social functioning and psychologic disturbances), with a total score expressed as a percentage (0-100) of overall impairment. A higher score indicates worse quality of life. The MCID for the SGRQ indicates a mean change score of 4 units is associated with slightly efficacious treatment, 8 units for moderately efficacious change and 12 units for very efficacious treatment. Result from one study (Bidwell 2012) show an improvement in the yoga group compared to the control group (SMD –3.89; 95% CI –5.50, –2.27; $p < 0.00001$).

Taken together, the pooled results suggest a large effect favouring the yoga group when compared to control, but there is substantial statistical heterogeneity (SMD –3.35; 95% CI –5.18, –1.53; $p = 0.0003$; $I^2 = 99\%$). (*GRADE: Low*).

In a sensitivity analysis that examined the impact of one RCT (Prem 2013) judged to be at high risk of bias, the size of the effect estimate did not materially change (SMD –3.97; 95% CI –6.25, –1.69; $p = 0.0006$; $I^2 = 99\%$).

Medication use

One study (total 24 participants) reported the use of medication measured by the change (reduction or increase) in salbutamol use (utilised as a tablet or inhaler) at the end of treatment (4 weeks) (Mekonnen 2010). No other details on the measure were provided.

Results suggested that participants in the yoga group reduced salbutamol inhaler use (RR 0.40; 95% CI 0.17, 0.93; $p = 0.03$) and salbutamol tablet use (RR 0.45; 95% CI 0.23, 0.91; $p = 0.03$) when compared with control. (*GRADE: Very low*).

[6] The Mini AQLQ is a modified, 15-item version of the AQLQ but includes the same subdomains.

No sensitivity analysis was conducted that examined the impact of RCTs judged to be at high risk of bias, as only one study was included in this comparison.

Comparison 2 (vs other intervention)

There were 8 studies comparing Yoga with 'other' interventions in people with asthma that were eligible for this comparison. Data from these studies are presented in Appendix F2 Supplementary outcome .

D6 Symptoms, signs or clinical findings, not elsewhere classified

D6.1 Chronic pain conditions

D6.1.1 List of studies

An overview of the PICO criteria of included studies is provided in Table D-15. Study details, including all outcome domains and measures reported by the included studies are provided in Appendix F1. Outcome data for critical or important outcomes are provided in Appendix F2.

Table D-15 Overview of PICO criteria of included studies: Chronic pain conditions

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
Yoga versus control (no intervention, waitlist, inactive usual care)*						
Bedekar 2012 (139)	Quasi RCT	Osteoarthritis (Rehabilitation after unilateral total knee replacement)	Yoga	Control (no intervention)	Conventional physiotherapy	Pain Stiffness Physical function
Bhandari 2009 (140, 141)	Quasi RCT	Inflammatory arthropathies (Rheumatoid arthritis)	Yoga	Control (no intervention)	Standard medical care	Pain Stiffness Blood pressure Inflammatory biomarkers
Carson 2010 (142, 143)	RCT	Chronic pain (Fibromyalgia)	Yoga of Awareness program	Control (waitlist)	Standard medical care	Pain Physical function Mental health Fibromyalgia symptoms
Cheung 2014 (144)	RCT	Osteoarthritis (knee)	Hatha yoga	Control (waitlist)	None specified	Pain Stiffness Physical function Sleep quality Quality of life
Deepeshwar 2018 (145)	Quasi RCT	Osteoarthritis (knee)	Integrated Approach of Yoga Therapy	Control (usual care)	None specified	Functional mobility Flexibility Strength Falls self-efficacy
Evans 2011a (146-148)	RCT	Inflammatory arthropathies (Rheumatoid or Juvenile idiopathic arthritis)	Iyengar yoga	Control (waitlist)	Standard medical care	Quality of life Pain Disease activity Inflammatory biomarkers Sleep quality Mental health Arthritis functioning
Ganesan 2020 (149)	RCT	Inflammatory arthropathies (Rheumatoid arthritis)	Yoga	Control (waitlist)	Standard medical care	Disease activity Inflammatory biomarkers Blood pressure Arthritis functioning
Gautam 2019 (150)	RCT	Inflammatory arthropathies (Rheumatoid arthritis)	Yoga	Control (usual care)	Standard medical care (DMARDS)	Inflammatory biomarkers Disease activity Arthritis functioning

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
						Depression
Khan 2018 (151)	Quasi RCT	Chronic pain (Myofascial pain syndrome)	Raj-yoga meditation and pranayama	Control (no intervention) ^ OR Raj-yoga alone	Standard medical care	Pain Inflammation Mental health
Moonaz 2015 (152)	RCT	Arthropathies, mixed (Rheumatoid or osteoarthritis, knee)	Hatha Yoga	Control (waitlist)	Standard medical care	Physical function Flexibility Strength Mental health Arthritis symptoms Quality of life
Schmid 2018 (153-157)	RCT	Chronic pain (attending pain clinic)	Yoga	Control (usual care)	Standard medical care (monthly visits with medical provider)	Pain, Balance Quality of life Strength Physical function
Ward 2014 (158-160)	RCT	Inflammatory arthropathies (Rheumatoid arthritis)	Yoga	Control (no intervention)	Standard medical care	Pain Sleep quality Arthritis functioning Disease activity Quality of life Mental health Fatigue
Yoga versus 'other' intervention**						
Cheung 2016 (161, 162)	RCT	Osteoarthritis (knee)	Hatha yoga	Educational advice # OR Physical exercise (aerobic / strengthening)	None specified	Pain Stiffness Physical function Mental health Quality of life
Ebnezar 2011 (163-166)	RCT	Osteoarthritis (knee)	Integrated Approach of Yoga Therapy	Physical exercise (aerobic / strengthening)	Physiotherapy with transcutaneous electrical stimulation	Physical function Mental health Pain Flexibility
Flehr 2019 (167)	RCT	Chronic pain (female with history of trauma)	Bikram yoga	Physical exercise (HIIT)	None specified	Pain Quality of life Mental health Cardiovascular health Physical function
Kuntz 2016 (168, 169)	RCT	Osteoarthritis (knee)	Yoga	Physical exercise (aerobic / strengthening) OR Guided relaxation	None specified	Pain Physical function Strength Depression Quality of life
McCaffrey 2019 (170)	RCT	Osteoarthritis (hip, knee, or other lower extremity)	Chair yoga	Chair exercises for older adults	None specified	Pain Functional mobility Physical function
Park 2011 (171)	Quasi RCT	Osteoarthritis (with chronic pain)	Chair yoga	Reiki	None specified	Pain Stiffness Physical function Depression

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
Park 2016 (172-174)	RCT	Osteoarthritis (hip, knee, or other lower extremity)	Chair yoga	Wellness education program	None specified	Pain Physical function Functional mobility Mental health Fatigue

Abbreviations: HIIT, high intensity interval training; RCT, randomised controlled trial

* Studies that compared yoga with an inactive control were eligible for inclusion in the evidence synthesis and are included in the Summary of findings tables if they reported outcomes considered critical or important to this review.

** Studies that compared yoga with an active intervention are included in the supplementary outcome tables (Appendix F2) if they reported data for outcomes considered critical or important to this review.

inclusive of weekly phone calls

D6.1.2 Risk of bias summary

The risk of bias for each time in the included studies for chronic pain conditions is described below and shown graphically in Figure D-11 (details are provided in Appendix E).

Bias arising from the randomisation process

15 studies (Carson 2010, Cheung 2014, Cheung 2016, Ebnezar 2011, Flehr 2019, Ganesan 2020, Gautam 2019, Kuntz 206, Moonaz 2015, Park 2016, Schmid 2018, Ward 2014) provided sufficient information on the randomisation sequence, allocation concealment and baseline characteristics, and were assessed to be at low risk of bias for this domain. Five studies (Bhandari 2009, Deepeshwar 2018, Evans 2011a, McCaffrey 2019, Park 2011) provided some information, but generally lacked reporting of allocation concealment, and were assessed to have some concerns for this domain.

Two studies (Bedekar 2012, Khan 2018) provided insufficient information relating to the randomisation process, and insufficient baseline characteristics to assess potential differences between the intervention groups. These studies were assessed to be at high risk of bias for this domain.

Bias due to deviations from the intended intervention

15 studies (Bedekar 2012, Bhandari 2009, Carson 2010, Cheung 2014, Cheung 2016, Deepeshwar 2018, Ebnezar 2011, Evans 2011a, Flehr 2019, Ganesan 2020, Gautam 2019, McCaffrey 2019, Moonaz 2015, Park 2011, Ward 2014) were assessed to be at low risk of bias for this domain. There were minimal reported deviations from the intended intervention, mostly pertaining to drop out which was not considered related to the trial context. An appropriate method of analysis (intention to treat or modified intention to treat) was used.

Four studies were assessed to have some concerns (Kuntz 2016) or at high risk of bias (Khan 2018, Park 2016, Schmid 2018) for this domain. Concerns related to high or uneven rates of drop out between groups, and inappropriate methods of analysis that excluded participants.

Bias due to missing outcome data

Nine studies (Bedekar 2012, Bhandari 2009, Cheung 2014, Deepeshwar 2018, Ebnezar 2011, Flehr 2019, Kuntz 2016, McCaffrey 2019, Ward 2014) had outcome data available for a sufficiently high proportion of participants to be considered low risk of bias for this domain.

Five studies (Carson 2010, Cheung 2016, Evans 2011a, Gautam 2019, Khan 2018) had a moderate level of missing data and did not provide sufficient analysis to assess the impact of this missingness. It was not considered likely that missingness related to the true value of the outcome. These studies were assessed to have some concerns for this domain.

Five studies (Ganesan 2020, Moonaz 2015, Park 2011, Park 2016, Schmid 2018) were assessed to be at high risk of bias as they had moderate or high levels of missing data and did not provide sufficient analysis to assess the impact of this missingness. It was considered likely that drop outs could be related to the true value of the outcome, as they were either unbalanced between groups or reasons suggested a relationship to the intervention or outcome.

Bias in measurement of the outcome

Three studies (Deepeshwar 2018, Flehr 2019, Gautam 2019) were assessed to be at low risk of bias for this domain. Outcomes were measured using validated instruments. Primary outcome measures were objective and a blinded assessor was specified. In one study (Flehr 2019) the outcome was self-reported, but participants were not aware of which arm of the trial was the 'intervention', and were considered sufficiently blinded when reporting the outcome.

14 studies (Bedekar 2012, Bhandari 2009, Carson 2010, Cheung 2014, Cheung 2016, Ebnezar 2011, Ganesan 2020, Khan 2018, Kuntz 2016, McCaffrey 2019, Moonaz 2015, Park 2011, Schmid 2018, Ward 2014) were assessed to have some concerns in this domain. Outcomes were measured using validated instruments, but self-reported primary outcomes were reported by non-blinded participants. There was no indication of bias in reporting of the outcome.

Two studies (Evans 2011a, Park 2016) were assessed at high risk of bias for this domain. Outcomes were measured using validated instruments, but self-reported primary outcomes were reported by non-blinded participants. There was evidence that participants would be biased in their reporting of the outcome, due to strong belief in the effectiveness of the intervention.

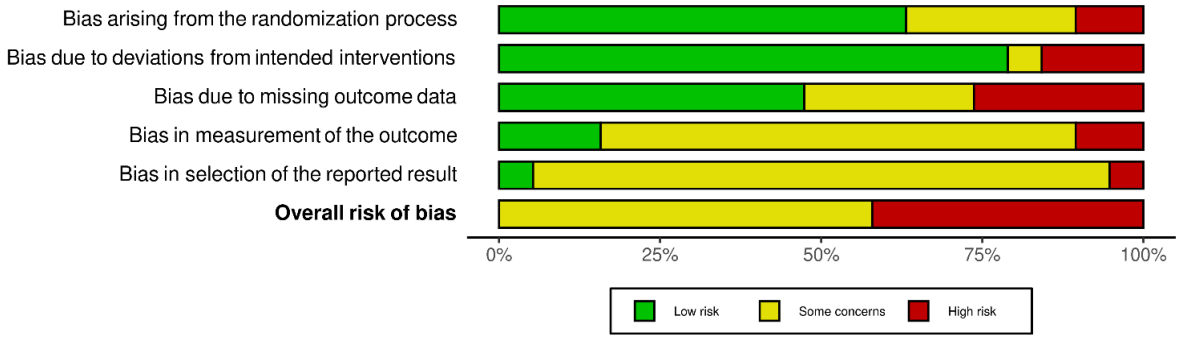
Bias in selection of the reported result

One study (Ward 2014) was assessed at low risk of bias for this domain. A pre-specified statistical analysis plan is available and data were analysed in accordance with this plan.

17 studies (Bedekar 2012, Bhandari 2009, Carson 2010, Cheung 2014, Cheung 2016, Deepeshwar 2018, Ebnezar 2011, Flehr 2019, Ganesan 2020, Gautam 2019, Khan 2018, Kuntz 2016, McCaffrey 2019, Moonaz 2015, Park 2011, Park 2016, Schmid 2018) were assessed to have some concerns for this domain. No pre-specified analysis plan was provided, but there was no evidence of bias in the selection of the reported result.

One study (Evans 2011) was assessed to be at high risk of bias for this domain. The reported result did not align with the pre-specified analysis plan, and the reported results appeared to be selected from multiple subscales of outcome measures.

Figure D-11 Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included RCTs – Chronic pain conditions



D6.1.3 Effect of intervention

Outcomes considered by the NTWC to be critical or important for decision-making in people with chronic pain conditions are listed in Table D-16.

Table D-16 Outcomes considered by the NTWC to be critical or important for decision-making: chronic pain conditions

Outcome domain	Measured with	Condition/s	consensus rating	Data available for main comparison?	Bedekar 2012	Bhandari 2009	Carson 2010	Cheung 2014	Deepshwar 2018	Evans 2011	Ganesan 2020	Gautam 2019	Khan 2018	Moonaz 2015	Schmid 2018	Ward 2014
Health-related quality of life	FIQ, SF-36, EQ-5D-3L	OA, RA, JIA, nonspecific pain, fibromyalgia	Critical	Yes	--	--	✓	✓	--	✓	--	--	--	✓	✓	✓
Pain	Any multidimensional measure of pain	OA, RA, JIA, nonspecific pain	Critical	Yes	✓	✓	✓†	✓	--	X	--	--	?	✓^	✓	✓
Perceived stress	Depression, Anxiety and Stress Scale (42-item)	OA, RA, JIA, nonspecific pain	Critical	No	--	--	NA	--	--	--	--	--	X	✓	--	--
Emotional function	SF-36 or SF-12 mental component	nonspecific pain	Critical	Yes	--	--	NA	✓	--	--	--	--	--	✓	--	--
Physical function / mobility	FIQ – function	OA, RA, JIA, nonspecific pain, fibromyalgia	Critical	Yes	✓	--	✓	✓	--	--	--	--	--	✓	--	--
	6MWT	RA, nonspecific pain	Critical	Yes	--	--	--	--	--	--	--	--	--	✓	✓	--
Symptom severity	Disease specific measures (Life stressor checklist, FIQ)	trauma-related pain, fibromyalgia	Critical	No	NA	NA	✓	NA	NA	NA	NA	NA	--	NA	--	NA
Self-efficacy	Chronic pain self-efficacy scale	OA, RA, JIA, nonspecific pain	Critical	Yes	--	--	NA	--	--	--	--	--	--	--	✓	--
Fatigue	FIQ – fatigue	Fibromyalgia	Critical	Yes	NA	NA	✓†	NA	NA	NA	NA	NA	NA	NA	NA	NA
Medication use	As reported	OA, RA, JIA,	Critical	No	--	--	--	--	--	X	--	--	--	--	--	--
Coping	Coping strategies questionnaire	OA, RA, JIA,	Important	Yes	--	--	NA	--	--	✓	--	--	--	--	--	--

Abbreviations: 6MWT, 6-minute walk test; FIQ, Fibromyalgia impact questionnaire; JIA, juvenile idiopathic arthritis; NA, not applicable; OA, osteoarthritis; RA, rheumatoid arthritis; SF-36, 36-item short form; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

✓ A study result is available for inclusion in the synthesis

X No study result is available for inclusion, (probably) because the P value, magnitude or direction of the results generated were considered unfavourable by the study investigators

-- No study result is available for inclusion, (probably) because the outcome was not assessed, or for a reason unrelated to the P value, magnitude or direction of the results

? No study result is available for inclusion, and it is unclear if the outcome was assessed in the study
^ Outcome included in under HRQoL
† Outcome included under fibromyalgia symptoms severity
Shaded studies are in people with chronic pain (fibromyalgia, myofascial pain, not specified). Others are people with OA, RA or JIA.

Main comparison (vs control)

There were 12 RCTs comparing yoga with no intervention, waitlist or usual care in people with chronic pain conditions that were eligible for this comparison and contributed data to 9 outcomes considered critical or important for this review (Bedekar 2012, Bhandari 2009, Carson 2010, Cheung 2014, Deepeshwar 2018, Evans 2011a, Ganesan 2020, Gautam 2019, Khan 2018, Moonaz 2015, Schmid 2018, Ward 2014).

There were 10 studies awaiting classification (total 450+ participants) and 5 ongoing studies (total 450+ participants) that were complete (or unknown status) that compared yoga with inactive control that could have contributed data to this comparison (see Appendix C6). The available information is insufficient to make a judgement about the nonreporting of results.

Quality of life

Four studies (192 participants) reported quality of life measured using the Fibromyalgia Impact Questionnaire (FIQ), the SF-36, or the EQ-5D-3L at the end of treatment (range: 6 to 8 weeks) (Carson 2010, Evans 2011a, Schmid 2018, Ward 2014).

The Fibromyalgia impact questionnaire (FIQ) is a self-administered questionnaire that measures the impact of symptom burden and functional limitations on quality of life. Composed of 10 items, the first item contains 11 questions related to physical functioning, items 2 and 3 require patient to mark the number of days they felt well and the number of days they were unable to work (including housework) because of fibromyalgia symptoms. Items 4 through 10 are horizontal linear scales marked in 10 increments on which the patient rates pain, tenderness, fatigue, morning tiredness, stiffness, anxiety and depression. Each item is normalised to a maximum possible score of 10, thus the total maximum score is 100 (higher is worse). A 14-point change in the FIQ total score is considered clinically relevant (175).

Results from one study of fibromyalgia (53 participants) (Carson 2010) suggested an effect that favoured the yoga group when compared to the control group (SMD –0.71, 95% CI –1.27, –0.15; p = 0.01) (*GRADE: Low*), but the change score (MD 13.20; 95% CI –23.03, –3.37) did not reach the MCID.

For non-fibromyalgia studies, the EQ-5D-3L measures the individual's health state on 5 scales: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The responses were weighted with the time trade-off method, which gives quality adjusted life year values anchored between 0 and 1; where 1 is a year lived in full health and 0 (zero) represents death (176) Results from one study (26 participants) (Ward 2014) suggested there was no difference between the yoga and the control groups (SMD –0.14, 95% CI –0.91, 0.63; p = 0.72).

The SF-36 is a self-reported, multidimensional measure assessing the impact of one's health on everyday life. Eight domains are summarised on a scale from 0 (worse) to 100 (best), which can be summarised into 2 component scores. The physical component summary (PCS) score includes the domains of general health, physical functioning, role physical and body pain. The mental component summary (MCS) score includes the domains of vitality, social functioning, role emotional and mental health. The PCS and MCS are derived by aggregating individual scores. The MCID for the SF-36 is estimated to be around 2 to 4 points for the general population (i.e. ~0.5 of the SD) (42).

Pooled results from 2 studies (149 participants) that reported a total SF-36 score (Evans 2011a, Schmid 2018) suggested no effect of yoga on HRQoL when compared to the control (SMD 0.06, 95% CI –0.31, 0.43; p = 0.76; I^2 = 0%). Both studies contributing data to this measure were at high risk of bias.

Pooled results from 3 studies (139 participants) suggest no difference in quality of life between the yoga group and control group (SMD –0.02; 95% CI –0.35, 0.31; p = 0.91) (*GRADE: Low*). One study in people with fibromyalgia (53 participants) was not included in this meta-analysis as the populations and outcome measures used were considered sufficiently heterogenous (subgroup differences with the fibromyalgia population, I^2 = 60.5%).

Pain

Four studies (total 196 participants) reported pain measured with a Visual Analogue Scale (VAS), the Brief Pain Inventory (BPI), or Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index – pain and stiffness[7] subscale at the end of treatment (range: 40 days to 9 weeks) (Bedekar 2012, Cheung 2014, Ward 2014, Schmid 2018). One additional study (Carson 2010) measuring pain severity using the FIQ-pain scale is included in the evidence synthesis for fibromyalgia symptoms.

The VAS is subjective tool that can be used to measure a variety of outcomes. It is measured on a continuous scale (mm) from 0 (no pain) to 100 (worst imaginable pain), with higher scores indicating a higher intensity of a feeling/symptom. The median absolute MCID on a VAS scale in people with chronic pain is reported to be 20 mm (IQR 15–30) (81). Results from one study (total 26 participants) showed no effect of yoga on pain compared to the control group (SMD 0.00, 95% CI –0.77, 0.77; p = 1.00).

The BPI assesses pain severity and its interference on various aspects of life (including general activity, mood, sleep, mobility, activities of daily living, role-social, enjoyment). Each item is rated on a scale from o to 10, with the total scores calculated as an average of each item (score range 0 to 10). Higher scores mean worse pain. The 11-item measure can be reported as 2 subscales: pain severity (4-items) and pain interference (7-items). The MCID for the BPI in people with fibromyalgia is around 2.2 points (177). Results from one study (total 83 participants) suggested no difference in BPI scores (total) for the yoga group when compared to the control group (SMD –0.03, 95% CI –0.46, 0.40; p = 0.89).

The WOMAC is a self-administered questionnaire used to evaluate the impact of hip and knee osteoarthritis (OA) on daily living. It consists of 24 items divided into 3 subscales: pain, stiffness, and physical function. The WOMAC pain score includes five items (total score range from 0 to 20) with higher scores equating to greater pain with activities of daily living. The MCID for the WOMAC pain subscale varies, with estimate being between 7 to 12 points among people with knee OA (178, 179). The WOMAC Stiffness score includes 2 items (total score range from 0 to 8) with higher scores equating to greater stiffness in activities of daily living. For the WOMAC stiffness subscale, the MCID is 19 points in people with knee OA (180, 181).

Pooled results from 2 studies (total 87 participants) (Bedekar 2012, Cheung 2014) show an effect favouring yoga when compared to the control group (SMD –1.51, 95% CI –2.78, -0.23; p = 0.0.02; I^2 = 85%).

Taken together, the pooled results (total 196 participants) show no significant difference between the yoga and control groups, however there is substantial statistical heterogeneity (SMD –0.75, 95% CI –1.72, 0.22; p = 0.13; I^2 = 89%) *(GRADE: Very low)*.

In sensitivity analysis examining the impact of the 2 RCTs at high risk of bias (Bedekar 2012, Schmid 2018), the size of the effect estimate was smaller, but the direction did not materially change (SMD –0.45, 95% CI –1.29, 0.39; p = 0.30; I^2 = 63%).

Results from three additional studies (130 participants) were not included in the meta-analysis due to non-reporting of post-treatment scores (Bhandari 2009), non-reporting of the outcome measure (Khan 2018), or non-reporting of results despite being a pre-specified outcome according to the study protocol (Evans 2011).

Perceived stress

One study (total 75 participants) reported perceived stress measured with the Perceived Stress Scale (PSS-10) at the end of treatment (8 weeks) (Moonaz 2015). The PSS is a 14-item scale that measures how overwhelmed a person is by their current life circumstances. Participants rate the frequency with which they experienced 10 stress symptoms over the preceding 30 days on a 5-point scale. Total scores range from 0 to 40 with higher scores indicating greater perceived stress. An MCID for the PSS in people with chronic pain has not been established, but is estimated to be between 2.19 and 2.66 points among undergraduate students with elevated stress (63) and around 11 points in people with work-related stress complaints (64).

[7] Included here because one study (Bedekar 2012) reported a combined score for pain and stiffness.

The results suggest there is little to no difference in perceived stress comparing yoga with control group (MD –1.90, 95% CI –0.07, 5.27; p = 0.34) (*GRADE: Very low*). The study was at high risk of bias.

One study (Khan 2018) (20 participants) reported psychological distress[8] measured using the Depression Anxiety and Stress scale (DASS) at the end of treatment (3 months). The DASS is a quantitative measure of distress along 3 emotional states of depression, anxiety and stress, with the stress subscale sensitive to levels of chronic nonspecific arousal and assesses difficulty relaxing, nervous arousal, and being easily upset/agitated, irritable/over-reactive and impatient. The study did not provided any usable data.

Emotional function

Two studies (111 participants) reported emotional wellbeing measured with the SF-12 or SF-36 MCS score at the end of treatment (8 weeks) (Chueng 2014, Moonaz 2015).

The SF-36 and SF-12 are self-reported quality of life questionnaires assessing quality of life across eight domains. The MCS score includes the domains of vitality, social functioning, role emotional and mental health. Total scores range from 0 (worst) to 100 (best), with a higher score indicating improved emotional function.

Pooled results from two studies show no difference in emotional function between the yoga and control group, however the statistical heterogeneity was high (SMD 0.01; 95% –0.76, 0.78; p = 0.98; I^2 = 73%) (*GRADE: Low*).

In a sensitivity analysis, removing one study at high risk of bias (Moonaz 2015), resulted in a reduced estimate of effect (SMD –0.41; 95% CI –1.08, 0.24; p = 0.21).

Physical function

Four studies (216 participants) reported physical function measured using the FIQ – function domain, SF36 PCS or the WOMAC OA index – function domain at the end of treatment (range: 8 weeks to 3 months) (Bedekar 2012, Carson 2010, Cheung 2014, Moonaz 2015).

For fibromyalgia, the FIQ is a self-administered questionnaire composed of 10 items, the first of which contains 11 questions related to physical functioning. Each item is rated on a 4 point Likert type scale from 0 (always) to 3 (never), with the total score ranging from 0 to 33 (higher is worse). The MCID for the FIQ-function domain is not established but is estimated to be 14% change for the overall score (175). Results from one study (Carson 2010) showed little to no difference between the yoga and control groups (SMD –0.37, 95% CI –0.92, 0.71; p = 0.18).

The WOMAC is self-administered questionnaire used to evaluate the impact of hip and knee osteoarthritis on daily living. It consists of 24 items divided into 3 subscales: pain, stiffness, and physical function. The physical function subscale consists of 17 items including everyday activities such as stair use, standing up from a sitting or lying position, bending, walking, etc. Scores range between 0 and 68 with higher scores indicating worse functional limitation. The MCID for the WOMAC function subscale is estimated to be between 10.1 and 14.5 points in people with knee OA (180, 181).

Results from 2 studies (87 participants) suggest an effect favouring yoga compared to the control group (SMD –0.88; 95% CI –1.76, 0.00; p = 0.05, I^2 = 74%), but statistical heterogeneity was high and the confidence interval was wide.

The SF-36 and SF-12 are self-reported quality of life questionnaires assessing quality of life across eight domains. The physical component summary (PCS) score includes the domains of general health, physical functioning, role physical and body pain. Total scores range from 0 (worst) to 100 (best), with a higher score indicating improved emotional function. Results for SF-36 PCS were inverted for consistency with other physical function outcome measures.

[8] The DASS- stress subscale is not a measure of perceived stress, rather is focused on nervous tension, difficulty relaxing and irritability.

Results from one study (75 participants) suggest an effect favouring yoga compared to the control group (SMD –0.80; 95% CI –1.28, –0.33; p = 0.0009).

For non-fibromyalgia studies, the pooled results suggest a moderate effect favouring the yoga group when compared to the control groups (SMD –0.86, 95% CI –1.32, –0.39; p = 0.0003, I^2 = 0%) (*GRADE: Very low*).

In a sensitivity analysis examining the impact of two RCTs at high risk of bias (Bedekar 2012, Moonaz 2015), the size of the effect estimate decreased and was not statistically significant (SMD –0.42, 95% CI –1.08, 0.24; p = 0.21).

Mobility

Two studies (93 participants) reported mobility measured using the 6-minute walk test (6MWT) at the end of treatment (range: 7 days to 8 weeks) (Moonaz 2015, Schmid 2018). Noting, Schmid 2018 was a secondary analysis in a subgroup of participants with chronic pain and type 2 diabetes.

The 6MWT evaluates the functional endurance and mobility of an individual by assessing the distance they can walk over 6 minutes (further is better). The expected walking distance in healthy adults aged ~20 to 75 years is around 581 metres (range 383 to 800 m) for females and around 608 metres (range 410 to 875 m) for males (182). Among a range of conditions, a change of 14.0 to 30.5 metres is reported to be clinically important across multiple patient groups (183).

Results suggest no difference between the yoga and control groups (MD –18.76, 95% CI –178.28, 140.76; p = 0.82, I^2 = 62%) (*GRADE: Low*). Both studies were assessed to be at high risk of bias, so no sensitivity analysis was conducted.

Symptom severity (fibromyalgia)

One study (53 participants) reported fibromyalgia symptoms (pain, stiffness, tenderness and morning tiredness, fatigue) measured using the FIQ at the end of treatment (8 weeks) (Carson 2010).

The FIQ is a self-administered questionnaire that measures the impact of symptom burden and functional limitations on quality of life. Items 4 through 10 are horizontal linear scales marked in 10 increments on which the patient rates pain, tenderness, fatigue, morning tiredness, stiffness, anxiety and depression. Each item has a maximum possible score of 10. MCIDs for the FIQ symptom items are not established, but is estimated to be 14% change for the overall score, and 13% for stiffness (175).

The results from one study suggest a small but not important effect favouring the yoga group when compared to control for pain (MD –1.02; 95% CI –2.18, 0.14; p = 0.09), stiffness (MD -1.10; 95% CI -2.10, -0.10; p = 0.03), tenderness (MD –0.96; 95% CI –2.42, 0.50; p = 0.20), or morning tiredness (MD –0.39; 95% CI –2.01, 0.1.23; p = 0.64)*(GRADE: Low).* An effect favouring the yoga group is suggested for fatigue (MD –2.01; 95% CI –3.16, -0.86; p = 0.0006) *(GRADE: Low).*

Self-efficacy

One study (83 participants) reported self-efficacy measured using the chronic pain self-efficacy scale (CPSS) at the end of treatment (8 weeks) (Schmid 2018).

The CPSS is a 22-item scale that measures perceived self-efficacy to cope with the consequences of chronic pain over 3 domains: pain management, physical functioning and coping with symptoms. Participants indicate their confidence to address each item on a scale from 0 (no confidence) to 100 (highest confidence).

The results from one study suggest little to no effect of yoga when compared to the control group (MD –6.08, 95% CI –14.85, 2.69; p = 0.19) *(GRADE: Very low).* This study was at high risk of bias, but no sensitivity analysis could be conducted as there was only one study contributing data.

Pain acceptance/coping

Two studies (83 participants) assessed pain acceptance using the chronic pain acceptance questionnaire (CPAQ) at the end of treatment (8 weeks) (Carson 2010, Evans 2011a).

The CPAQ is a 20-item questionnaire for self-assessment of activity engagement (participation in daily activities regardless of pain) and pain willingness (willingness to tolerate pain). Items are rated on a 7-point scale from 0 (never true) to 6 (always true). Total scores range from 0 to 120, with higher scores indicating greater pain acceptance. No MCID for the CPAQ was found, but studies suggest there are 3 discrete groups of patients based on levels of pain acceptance: aligned with a mean CPAQ score of 23.6 (low acceptance). 47.5 (medium), 74.9 (high); as well as a group with a high level of activity engagement and low willingness to have pain (mean CPAQ score of 56) (184).

Results from one non-fibromyalgia study suggested there was no difference between the yoga group when compared to the control group (MD –5.00; 95% CI –16.38, 6.38; p = 0.39) *(GRADE: Very Low).*

Results from one study in people with fibromyalgia showed an effect favouring the yoga group (MD –9.79; 95% CI –18.08, –1.50; p = 0.03). (*GRADE: Low*)

Comparison 2 (vs other intervention)

Eight studies comparing yoga with 'other' interventions in people with chronic pain conditions were eligible for this comparison (Cheung 2016, Ebnezar 2011, Flehr 2019, Khan 2018, Kuntz 2016, McCaffrey 2019, Park 2011, Park 2016).

Data from these studies are presented in Appendix F2 Supplementary outcome .

D6.2 Low back pain

D6.2.1 List of studies

An overview of the PICO criteria of included studies is provided in Table D-17. Study details, including all outcome domains and measures reported by the included studies are provided in Appendix F1. Outcome data for critical or important outcomes are provided in Appendix F2.

Table D-17 Overview of PICO criteria of included studies: Low back pain

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
Yoga versus control (no intervention, waitlist, inactive usual care)*						
Aboagye 2015 (185, 186)	RCT	Low back pain (nonspecific)	Kundalini Yoga	Educational advice # OR Exercise therapy (strength training) ^	None reported	QoL
Cox 2010a (187)	RCT	Low back pain (chronic, nonspecific)	Yoga for Healthy Lower Backs	Control (usual care)	Educational advice and standard medical care	Disability Pain General health QoL Pain self-efficacy
Cox 2010b (188-190)	RCT	Low back pain (chronic, nonspecific)	Yoga for Healthy Lower Backs	Control (usual care)	Educational advice and standard medical care	Disability General health Pain Pain self-efficacy
Galantino 2004 (191)	RCT	Low back pain (chronic, nonspecific)	Hatha yoga	Control (waitlist)	None reported	Functional disability Depression Lower back flexibility Balance
Groessl 2016 (192-194)	RCT	Low back pain (chronic, nonspecific)	Hatha yoga	Control (waitlist)	None reported	Disability Pain intensity Pain interference Fatigue QoL Self-efficacy Anxiety Depression Sleep quality
Highland 2018 (195)	RCT	Low back pain (chronic, nonspecific)	Therapeutic Yoga ^	Control (usual care)	Standard medical care †	Past 24 hr Pain Disability Physical functioning Symptom burden
Jacobs 2004 (196, 197)	RCT	Low back pain (mechanical)	Iyengar yoga	Control (waitlist)	None reported	Pain QoL Functional disability Depression Anxiety Healthcare utilisation
Monro 2015 (198-200)	RCT	Low back pain, sciatica, disc extrusion or bulges (mechanical)	Yoga	Control (usual care)	Standard medical care †	Disability Pain Functional strength Palpation of the spine Structural Changes Pain

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
						State anxiety Spinal flexibility Heart rate variability Respiratory rate
Pushpika Attanayake 2010 (201)	RCT	Low back pain (acute and/or chronic, nonspecific)	Yogic treatment plan	Control (no intervention)	Diet and lifestyle modification plan	Pain
Saper 2009 (202)	RCT	Low back pain (chronic, nonspecific)	Yoga	Control (waitlist)	Educational advice and standard medical care	Pain Disability Pain medication use Global improvement QoL
Saper 2014 (203-214)	RCT	Low back pain (chronic, nonspecific)	Yoga	Educational advice ## OR Standard exercise therapy ^	None reported	Disability Pain Pain medication use Global improvement Patient satisfaction QoL Sleep quality Anxiety Depression Sleep quality Treatment response Perceived Stress Perceived treatment effect
Sherman 2005 (215)	RCT	Low back pain (chronic, nonspecific)	Viniyoga	Educational advice # OR Standard exercise therapy ^	None reported	Disability Pain QoL Pain medication use Degree of restricted activity
Sherman 2010 (216-219)	RCT	Low back pain (chronic, nonspecific)	Viniyoga	Educational advice # OR Standard exercise therapy^	None reported	Disability Symptom bothersomeness Fear avoidance Self-efficacy Awareness Psychological distress Perceived stress Positive states of mind Sleep Quality Endocrine function
Teut 2016 (220)	RCT	Low back pain (chronic, nonspecific)	Yoga	Control (waitlist) OR Qigong ^	Standard medical care ††	Pain Back function Pain medication Frequency of falls Risk of falls QoL Depression Body self-efficacy Handgrip strength

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
Williams 2005 (221)	RCT	Low back pain (chronic, nonspecific)	Iyengar Yoga	Control (no intervention)	Educational advice and standard medical care	Functional disability Pain Fear of movement Pain attitudes Coping strategies Pain self-efficacy ROM Pain medication use
Williams 2009 (222)	RCT	Low back pain (chronic, nonspecific)	Yoga	Control (waitlist)	Standard medical care	Functional disability Present pain intensity Depression Pain medication use
Yoga versus 'other' intervention**						
Demirel 2019 (223)	RCT	Low back pain (chronic, nonspecific)	Yoga	Stabilisation exercises	None reported	Pain severity Physical performance Perceived effect Functional disability
Kim 2014b (224)	RCT	Low back pain (chronic, nonspecific)	WiiFit Yoga program	Stabilisation exercises plus physical therapy	None reported	Pain Pain sensitivity Functional disability Disability Fear of low back pain
Nambi 2014 (225)	RCT	Low back pain (chronic, nonspecific)	Iyengar yoga	Standard exercise program	Educational advice	Pain QoL
Neyaz 2019 (226)	RCT	Low back pain (chronic, nonspecific)	Hatha Yoga	Standard exercise program	None reported	Pain Disability Pain medication use Perceived recovery
Patil 2018 (227)	RCT	Low back pain (chronic, nonspecific)	Integrated Approach of Yoga Therapy	Standard exercise program	None reported	QoL
Tekur 2008 (228, 229)	RCT	Low back pain (chronic, nonspecific)	Yoga	Standard exercise program	Counselling and education sessions	Functional disability QoL Perceived Stress Mobility State anxiety Depression Pain Flexibility

Abbreviations: RCT, randomised controlled trial; ROM, range of motion, QoL, quality of life

* Studies that compared Yoga with an inactive control were eligible for inclusion in the evidence synthesis and are included in the Summary of findings tables if they reported outcomes considered critical or important to this review.

** Studies that compared Yoga with an active intervention are included in the supplementary outcome tables (Appendix F2) if they reported data for outcomes considered critical or important to this review.

^ Study included 3 groups. The inactive control (educational advice) is considered in the evidence synthesis.

The Back Pain Helpbook includes information on chronic LBP self-management, stretching, strengthening and role of emotions and fear avoidance.

The Back Pain Helpbook. Every 3 weeks, participants also received a 5-10 minute check-in call and a 1-2 page newsletter summarising main points from assigned chapters.

^^ Restorative Exercise and Strength Training for Operational Resilience and Excellence

† Inclusive of pain medication, physical therapy, chiropractic care, injections, acupuncture, massage, supplements, or other therapies.

†† Not including physiotherapy or pain medication that targets the central nervous system.

D6.2.2 Risk of bias summary

The risk of bias for each time in the included studies for chronic pain is described below and shown graphically in Figure D-6 (details are provided in Appendix E).

Bias arising from the randomisation process

There were 13 studies (Cox 2010a, Cox 2010b, Groessl 2016, Highland 2018, Jacobs 2004, Monro 2015, Neyaz 2019, Saper 2009, Sherman 2005, Sherman 2010, Tekur 2008, Teut 2016, Williams 2009) that provided sufficient information on the randomisation process and were at low risk of bias for this domain.

Three studies (Kim 2014, Nambi 2014, Patil 2018) had some concerns due to missing information about methods of concealing treatment allocation. Two studies (Aboagye 2015, Saper 2014) had some concerns due to differences between groups with regards to baseline characteristics, suggesting issues with the randomisation process. Pushpika Attanayake 2010 had some concerns regarding methods used for concealing treatment allocation and baseline differences between groups. Demirel 2019 had some concerns regarding method of randomisation.

Two studies (Galantino 2004, Williams 2005) were considered to be at high risk of bias for this domain as no details were provided regarding allocation concealment method and baseline differences between groups were unbalanced, suggesting issues with the randomisation process.

Bias due to deviations from intended intervention

11 studies were judged to be at low risk of bias for this domain (Cox 2010a, Demirel 2019, Highland 2018, Patil 2018, Pushpika Attanayake 2010, Saper 2009, Saper 2014, Sherman 2005, Sherman 2010, Tekur 2008, Teut 2016).

Six studies had some concerns raised for this domain as there were deviations from the treatment allocation possibly related to the trial context, but their impact on the outcome was expected to be slight (Aboagye 2015, Kim 2014, Monro 2015, Nambi 2014, Neyaz 2019, Williams 2005). Four studies were considered to be high risk of bias for this domain because of deviations from intended outcomes, due to trial context, indicated by unbalanced dropout rate (Cox 2010, Galantino 2004, Groessl 2016, Williams 2009). Tekur 2008 was considered to be high risk of bias due to the use of per protocol analysis.

Bias due to missing outcome data

15 studies were assessed to be at low risk of bias for this domain as outcome data was available for all (or nearly all) participants (Cox 2010a, Demirel 2019, Groessl 2016, Highland 2018, Jacobs 2004, Kim 2014, Nambi 2014, Patil 2018, Pushpika Attanayake 2010, Saper 2009, Saper 2014, Sherman 2005, Sherman 2010, Tekur 2008, Teut 2016).

Three studies (Monro 2015, Neyaz 2019, Williams 2005) had some concerns raised as outcome data was not available for all (or nearly all) participants however, missingness of data was considered not likely to substantially impact the results as drop out was balanced between groups. In Monro 2015, 10 participants declined followup and two drop outs from the control group required spinal surgery. Neyaz 2019 provided no reasons for drop out. Reasons for drop out from the control group in Williams 2005 include lost to follow up (3 participants), ineligible due to participation in another complementary alternative medicine (2 participants) and one no show to baseline testing. Reasons for drop out in yoga group in Williams 2005 included 3 no shows, 3 participants that quit, 2 that became medically ineligible, one participant that experienced an adverse event (that was deemed unrelated to the performance of yoga postures) and one participant that was unwilling to perform active postures.

Four studies (Aboagye 2015, Cox 2010, Galantino 2004, Williams 2009) were considered at high risk of bias as they had missing data that was not balanced between treatment groups. Reasons for missing outcome data provided by Cox 2010a include participants moving to different area, travelling, dealing with childcare problems or illness. Reasons for missing outcome data provided by Williams 2009 included scheduling conflicts, lost job, family illness, and exacerbation of LBP by yoga. No reasons for missing outcome data were provided by Aboagye 2015 and Galantino 2004. Additionally, the analysis conducted was unlikely to have adjusted for any impact the missingness of the outcome could have on the results.

Bias in the measurement of the outcome

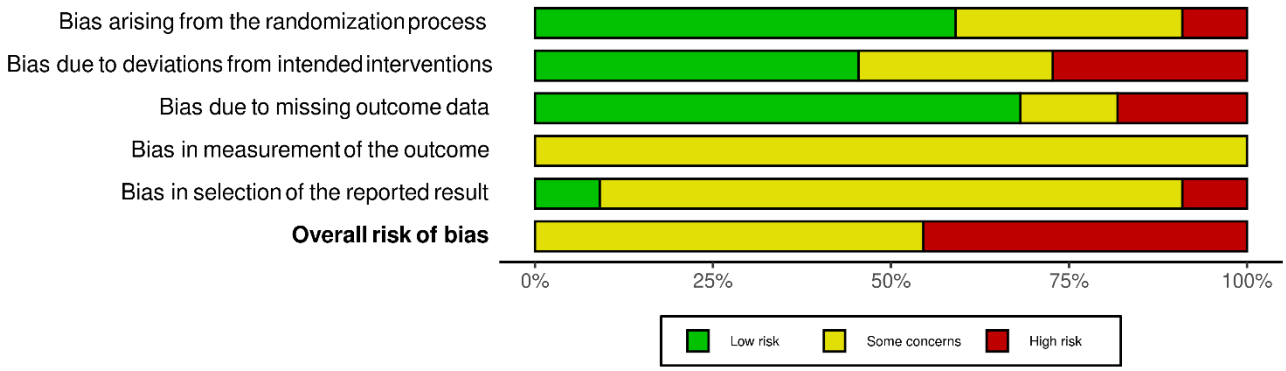
All studies had some concerns for this domain because participant-reported outcomes could be influenced by knowledge of the intervention received. There were no reasons to suspect the patient-reported outcomes were substantially influenced by their treatment experience.

Bias in selection of reported result

Two studies were assessed to be at low risk of bias as authors provided and reported results in accordance with a pre-specified analysis plan (Groessl 2016, Sherman 2010). In the absence of an available analysis plan, 16 studies reported all eligible pre-specified results and were judged to be of some concern of bias in this domain (Aboagye 2015, Cox 2010a, Cox 2010b, Demirel 2019, Galantino 2004, Highland 2018, Kim 2014, Monro 2015, Nambi 2014, Patil 2018, Saper 2009, Saper 2014, Sherman 2010, Teut 2016, Williams 2005, Williams 2009).

Two studies were determined to have some concerns for risk of bias as authors did not report analysis intentions in sufficient detail to enable an assessment (Jacobs 2004), or data was not analysed in accordance with pre-specified analysis plan (Sherman 2005). Two studies were judged to be at high risk of bias because of incomplete reporting suggesting selective reporting of outcome results (Neyaz 2019, Pushpika Attanayake 2010).

Figure D-6 Risk of bias summary: review authors' judgements about each risk of bias item expressed as percentages across all RCTs – Low back pain



D6.2.3 Effect of intervention

Outcomes considered by the NTWC to be critical or important for decision-making in people with low back pain are listed in Table D-18.

Table D-18 Outcomes considered by the NTWC to be critical or important for decision-making: Low back pain

Outcome domain	Measured with	Consensus rating	Data available for main comparison?	Aboagye 2015	Cox 2010a	Cox 2010b	Galantino 2004	Groessl 2016	Highland 2018	Jacobs 2004	Monro 2015	Pushpika Attanavake 2010	Saper 2009	Saper 2014	Sherman 2005	Sherman 2010	Teut 2016	Williams 2005	Williams 2009
Pain	McGill Pain Questionnaire (or other)	Critical	Yes	--	✓	✓	--	✓	✓	--	✓	X	✓	✓	?	?	✓	✓	✓
Health-related quality of life	EQ5D-3L (or other)	Critical	Yes	✓	✓	✓	--	✓	?	--	--	--	X	--	X	--	--	--	--
Coping strategies	Coping strategies questionnaire-revised	Critical	No	--	--	--	--	--	--	--	--	--	--	--	--	--	--	?	--
Medication use	Narcotic, Non-narcotic	Important	Yes	--	--	--	--	--	--	--	--	--	✓	✓	✓	--	✓	✓	X
Work status	Return to work (or other)	Important	No	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--
Physical function	PROMIS-29 physical functioning subscale (or other)	Important	Yes	--	✓	✓	--	--	✓	--	--	--	X	✓	X	✓	✓	--	--
Emotional function	Multidimensional measure of mood-state	Important	Yes	--	✓	✓	--	--	?	--	--	--	X	✓	X	✓	✓	--	--

Abbreviations: PROMIS-29 physical functioning subscale, Patient Reported Outcome Measurement Information System-29 physical functioning subscale;EQ5D-3L, EuroQol- 5 Dimension 3 level.

✓ A study result is available for inclusion in the synthesis

-- No study result is available for inclusion, (probably) because the outcome was not assessed, or for a reason unrelated to the P value, magnitude or direction of the results

? No study result is available for inclusion, and it is unclear if the outcome was assessed in the study

X No study result is available for inclusion, (probably) because the P value, magnitude or direction of the results generated were considered unfavourable by the study investigators

Main comparison (vs control)

Sixteen RCTs comparing yoga with control (no intervention, usual care, educational advice) in people with low back pain were eligible for this comparison. Thirteen RCTs contributed data relevant to at least one of the 7 outcomes considered critical or important for this review (Aboagye 2015, Cox 2010a, Cox 2010b, Groessl 2016, Highland 2018, Monro 2015, Saper 2009, Saper 2014, Sherman 2005, Sherman 2010, Teut 2016, Williams 2005, Williams 2009).

Three studies were not included in the evidence synthesis because data were not in an extractable form (Pushpika Attanayake 2010) or the studies assessed feasibility (or pilot) and did not report outcomes considered critical or important to this review (Galantino 2004, Jacobs 2004).

There were 4 studies awaiting classification (360+ participants) and 3 ongoing studies[9] (300+ participants) that compared yoga with control (no intervention or educational advice) in people with low back pain that could have contributed data to 4 outcomes (pain, disability, quality of life and emotional function) (see Appendix C6).

Pain

10 studies (total 1101 participants) assessed pain measured with the Aberdeen Back Pain Scale (APBS), the Brief Pain Inventory (BPI) or by using a Numerical Pain Rating Scale (NPRS) or Visual Analog Scale (VAS) at the end of treatment (range: 6 to 24 weeks) (Cox 2010a, Cox 2010b, Groessl 2016, Highland 2018, Monro 2015, Saper 2009, Saper 2014, Teut 2016, Williams 2005, Williams 2009). The results of one study (12 participants) (Pushpika Attanayake 2010) were not included in the evidence synthesis for this outcome as the authors only reported data dichotomised according to participants with statistically significant change scores.

The Aberdeen Back Pain Scale is a multidimensional measure of the effect of pain on function. It includes 19 items of how back pain affects activities like self-care, sitting, standing, sport, housework, resting, bending and sleep. Points for each item range from 0 to 5, with the total score range from 0 (no pain) to 100 (worst possible pain). The results from 3 studies (Cox 2010a, Cox 2010b, Monro 2015) suggested little to no effect favouring the yoga group when compared to control (SMD –0.18; 95% CI; –0.38, 0.02; p = 0.08, I^2 = 0%). (i.e. SMD ≤ 0.2).

The BPI assesses pain severity and its interference on various aspects of life (including general activity, mood, sleep, mobility, activities of daily living, role-social, enjoyment). Each item is rated on a scale from 0 to 10, with the total scores calculated as an average of each item (score range 0 to 10). Higher scores mean worse pain. The 11-item measure can be reported as 2 subscales: pain severity (4-items) and pain interference (7-items). An MCID for the BPI in people with low back pain is not established, but is around 2.2 points in people with fibromyalgia (177). The results from one study (Groessl 2016) suggested an effect in favour of the yoga group for pain severity[10] when compared to control (SMD –0.46; 95% CI; –0.79, –0.14; p = 0.005), but it is likely not clinically important (i.e. MD < 2.2 points).

The VAS is a subjective assessment of pain, reported by participants and measured on a continuous scale (mm) from 0 (no pain) to 100 (worst imaginable pain). Higher values indicate worse pain. Among patients with subacute or chronic low back pain, the MCID for pain on a VAS should at least be 20 mm and for acute low back pain it is suggested that the MCID should be at the level of approximately 35 mm (230). Results from 3 studies (Teut 2016, Williams 2005, Williams 2009) suggests an effect favouring yoga when compared to control (SMD –0.51; 95% CI –0.82, –0.20; p = 0.001, I^2 = 36%); but the clinical importance of the change is not reached. (i.e. MD < 20 mm).

[9] complete, results not published or of unknown status.

[10] The BPI-pain severity measure has better correlation with the NPRS and VAS therefore was used in the evidence synthesis. The result for BPI-pain interference were similar (SMD –0.33; 95% CI –0.65, –0.01; p = 0.04).

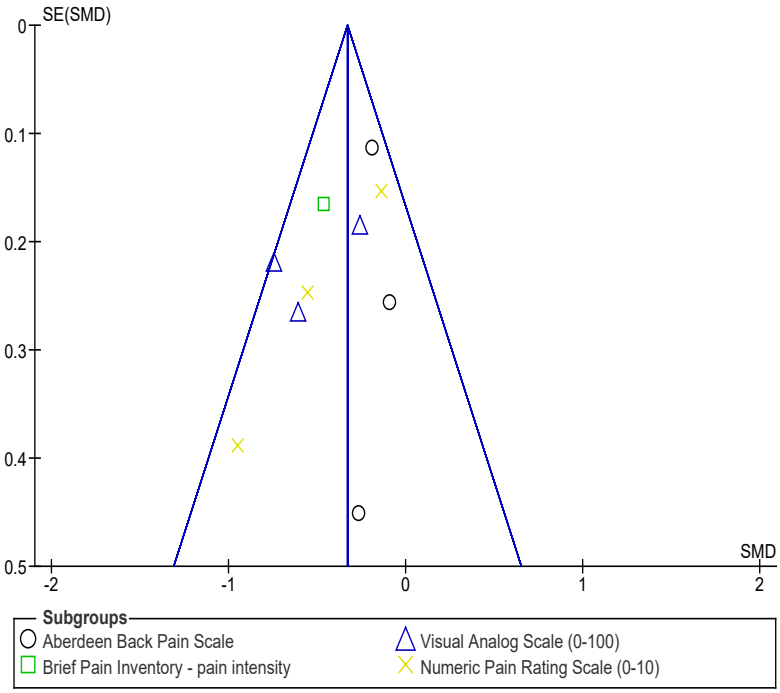
The NPRS is a segmented numeric version of the VAS that is administered verbally or graphically for self-completion. The 11-point numeric scale ranges from 0 (representing no pain) to 10 (representing pain as bad as you can imagine). The participant selects the whole number (between 0 and 10) that best represents the intensity of their pain. A reduction of 2 points (or 30%) on the NPRS is estimated to be clinically important in people with diabetic neuropathy, postherpetic neuralgia, chronic low back pain, fibromyalgia and osteoarthritis (231). The results from 3 studies (Highland 2018, Saper 2009, Saper 2014) suggest an effect favouring the yoga group compared to control (SMD –0.45; 95% CI –0.89, –0.01; $p = 0.04$; $I^2 = 59\%$), but the clinical importance of the change is not reached. (i.e. MD < 2 points).

Taken together, the pooled results suggest a slight reduction in pain in the yoga group compared to the control group (SMD –0.36; 95% CI –0.51, –0.21; $p < 0.00001$, $I^2 = 29\%$) *(GRADE: Low)*, but the clinical importance of this change is unclear. The observed effect estimate is smaller when only measures that consider sensory, emotional, and functional aspects of the pain experience are considered (i.e. ABPS and BPI) (SMD –0.26, 95% CI –0.43, –0.09; $p = 0.003$, $I^2 = 0\%$).

Visual inspection of the funnel plot (see Figure D-12) suggests slight asymmetry indicating that studies without statistically significant effects remain unpublished (43)[11] and that poor methodological quality may have led to exaggerated effects in smaller studies. This is in line with 4 studies being considered at high risk of bias (Cox 2010b, Groessl 2016, Williams 2005, Williams 2009) and several ongoing studies that are completed but results not published.

In a sensitivity analysis that examined the impact of 4 RCTs judged to be at high risk of bias (Cox 2010a, Groessl 2016, Williams 2005, Williams 2009) the size (but not overall direction) of the effect estimate was reduced (SMD –0.25; 95% CI –0.41, –009; $p = 0.003$; $I^2 = 15\%$).

Figure D-12 Funnel plot of comparison: Low back pain, outcome: Pain (end of treatment)



[11] It is noted that funnel plots of the SMD plotted against the SE are susceptible to distortion, leading to overestimation of the existence and extent of publication bias.

Quality of life

Four studies (590 participants) reported quality of life measured with the EQ-5D at the end of treatment (range: 6 to 12 weeks) (Aboagye 2015, Cox 2010a, Cox 201b, Groessl 2016). There were 2 studies (96 participants) that assessed QoL measured with the SF-36 at the end of treatment (12 weeks). Both studies (Saper 2009, Sherman 2005) indicated that there was no significant difference between treatment groups over time, but no data were provided.

Three other studies (446 participants) also assessed QoL measured with the SF-36 at the end of treatment (12 weeks), reporting summary scores for the physical and mental components (Saper 2014, Sherman 2010, Teut 2016). These studies are considered under the evidence synthesis for physical function and emotional function.

The EQ-5D measures the individual's health state on 5 scales: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The responses are weighted with the time trade-off method, which gives quality adjusted life year values anchored between 0 and 1, where 0 represents death and 1 is a year lived in full health. The minimal change score for the EQ-5D in participants with chronic lower back pain is estimated to be 0.03 (232).

Pooled results show an effect favouring yoga when compared to the control groups (MD –0.06; 95% CI –0.10, –0.02; $p < 0.0010$; $I^2 = 11\%$) *(GRADE: Moderate)*. (i.e. MD > 0.03).

In a sensitivity analysis that assessed the impact of 3 RCTs at high risk of bias (Aboagye 2015, Cox 2010a, Groessl 2016), the size of the effect estimate did not materially change (MD –0.06; 95% CI –0.10, –0.01; $p = 0.01$; I^2 = NA).

Pain medication use

Five studies (total 465 participants) assessed pain medication use at the end of treatment (range: 12 to 16 weeks), or end of followup (26 weeks). Four studies reported the proportion of patients using pain mediation in the previous week (Saper 2009, Saper 2014, Sherman 2005, Teut 2016) and one study reported the proportion of patients with no change or increase in pain medication use (Williams 2005). One other study (90 participants) (Williams 2009) indicated that there was a non-significant reduction in pain medication use in the yoga group, but no data were provided.

Pooled results suggest an effect that favours the yoga group when compared to the control group (RR 0.52; 95% CI; 0.32, 0.87; $p = 0.01$; $I^2 = 70\%$) *(GRADE: Low)*.

In a sensitivity analysis that assessed the impact of 1 RCT at high risk of bias (Williams 2005), the size of the effect estimate did not materially change (RR 0.60; 95% CI 0.38, 0.96; $p = 0.03$; $I^2 = 66\%$).

Physical function

Five studies (710 participants) reported physical function measured with the PROMIS-29[12] Physical Functioning Subscale or the SF-12/SF-36 Physical Component Score (PCS) at the end of treatment (range: 6 to 12 weeks) (Highland 2018, Cox 2010a, Cox 2010b, Saper 2014, Teut 2016). Two other studies (Saper 2009, Sherman 2005) reported SF-36 total scores and were considered in the evidence synthesis for health-related quality of life.

The PROMIS-29 is a National Institutes of Health self-report measure designed to assess functioning and wellbeing across 8 health domains (physical function, fatigue, pain intensity, pain interference, depressive symptoms, anxiety, ability to participate in social roles and activities, and sleep disturbance) (233). Each domain contains 4 items that are rated on a 5-point descriptive scale, except pain intensity, which measured using a single 0–10 numeric rating item. Raw scores are converted to a T-score, which is standardised to a population mean of 50 and SD of 10 (range 0 to 100). Higher scores indicate better health outcomes. The MCID for the PROMIS-29 scales are estimated to be 5-points (i.e. 0.5 of the SD) (234).

[12] The Patient-Reported Outcomes Measurement Information System.

Results from one study (Highland 2018) suggested an effect that favoured the yoga group when compared to the control group (MD –4.72; 95% CI –7.84, 1.60; p = 0.003), but the difference was not clinically important (MD < 5).

The SF-36 is a self-reported multidimensional measure assessing the impact of one's health on everyday life. Eight domains are summarised on a scale from 0 (worse) to 100 (best), which can be condensed into 2 component scores. The PSC score includes the domains of general health, physical functioning, role physical and body pain. The PCS is derived by aggregating individual scores, which have been standardised to a population mean of 50 and standard deviation of 10. The MCID for the SF-36 is estimated to be around 2 to 4 points for the general population (i.e. ~0.5 of the SD) (42).

Results from 4 studies (Cox 2010a, Cox 2010b, Saper 2014, Teut 2016) showed little to no difference in SF-36 PCS scores between the yoga group compared to the control group (MD –0.87; 95% CI –2.31, 0.57; p = 0.24; I^2 = 0%) (i.e. MD < 2).

Taken together, the pooled results suggest little to no effect of yoga on physical function when compared to the control group (MD –1.57; 95% CI –3.34, 0.19; p = 0.08, I^2 = 38%) *(GRADE: LOW)*.

In a sensitivity analysis that examined the impact of one RCT judged to be at high risk of bias (Cox 2010a) the effect estimate did not materially change (MD –1.72; 95% CI –3.44, 0.01; p = 0.05, I^2 = 40%).

Emotional function

Four studies (642 participants) reported emotional function measured with the SF-12 or SF-36 mental component score (MCS) at the end of treatment (mean: 12 weeks) (Cox 2010a, Cox 2010b, Saper 2014, Teut 2016). Two other studies (Saper 2009, Sherman 2005) reported SF-36 total scores and were considered in the evidence synthesis for health-related quality of life.

The SF-36 is a self-reported multidimensional measure assessing the impact of one's health on everyday life Eight domains are summarised on a scale from 0 (worse) to 100 (best), which can be condensed into 2 component scores. The MCS score includes the domains of vitality, social functioning, role emotional and mental health. The MCS is derived by aggregating individual scores, which have been standardised to a population mean of 50 and standard deviation of 10. The MCID for the SF-36 is estimated to be around 2 to 4 points for the general population (i.e. ~0.5 of the SD) (42).

The pooled results show little to no effect of yoga on emotional function when compared to control (MD –1.59; 95% CI –3.35, 0.16; p = 0.08; I^2 = 0%). (i.e. MD < 2).

In a sensitivity analysis that examined the impact of one RCT judged to be at high risk of bias (Cox, 2010a) the effect estimate did not materially change (MD –1.57; 95% CI –3.34, 0.20; p = 0.08; I^2 = 0%).

Comparison 2 (vs other intervention)

There were 11 studies comparing yoga with 'other' interventions in people with low back pain that were eligible for this comparison and contributed data relevant to 5 of the 7 outcomes (Aboagye 2015, Demirel 2019, Kim 2014b, Nambi 2014, Neyaz 2019, Patil 2018, Saper 2014, Sherman 2005, Sherman 2010, Tekur 2008, Teut 2016). Data from these studies are presented in Appendix F2 Supplementary outcome .

D6.3 Neck and/or shoulder pain

D6.3.1 List of studies

An overview of the PICO criteria of included studies is provided in Table D-19. Study details, including all outcome domains and measures reported by the included studies are provided in Appendix F1. Outcome data for critical or important outcomes are provided in Appendix F2.

Table D-19 Overview of PICO criteria of included studies: Neck and shoulder pain

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
Yoga vs control (no intervention, waitlist, inactive usual care)*						
Jain 2020 (235)	Quasi RCT	Shoulder pain (adhesive capsulitis)	SGA Yoga	Control (no intervention)	Physical therapy & NSAIDs	Pain Disability
Rajalaxmi 2018 (236)	RCT	Neck pain (chronic, mechanical)	Yoga	Control (no intervention) ^ OR Pilates OR Tai Chi	Isometric neck exercises	Pain Kinesiophobia
Yoga vs 'other' intervention**						
Cramer 2013 (237)	RCT	Neck pain (chronic, nonspecific)	Yoga	Self-directed exercise	None reported	Pain HRQoL Function/disability
Michalsen 2012 (238)	RCT	Neck pain (chronic)	Iyengar Yoga	Self-directed exercise	None reported	Pain HRQoL Function/disability
Ulug 2018 (239)	RCT	Neck pain (chronic, nonspecific)	Yoga	Pilates OR Isometric exercise	Physical therapy (TENS, hot pack, ultrasound)	Pain HRQoL Function/disability
Yogitha 2010 (240)	RCT	Neck pain (chronic)	Yoga Mind Sound Resonance Technique	Attention control (non-guided supine rest)	Physical therapy	Pain Function/disability

Abbreviations: HRQoL, health-related quality of life; NSAIDS, nonsteroidal anti-inflammatory drugs; RCT, randomised controlled trial; SPA, Standing Group of Asanas

* Studies that compared Yoga with an inactive control were eligible for inclusion in the evidence synthesis and are included in the Summary of findings tables if they reported outcomes considered critical or important to this review.

** Studies that compared Yoga with an active intervention are included in the supplementary outcome tables (Appendix F2) if they reported data for outcomes considered critical or important to this review.

^ Study included 3 groups. The control (no intervention) is considered in the evidence synthesis

D6.3.2 Risk of bias summary

Bias arising from the randomisation process

Four studies were at low risk of bias for this domain (Cramer 2013, Jain 2020, Michalsen 2012, Ulug 2018). Two studies (Rajalaxmi 2018, and Yogitha 2010) were assessed to have some concerns for bias in this domain. Concerns of bias arose due to neither study reporting whether or how the allocation process was concealed.

Bias due to deviations from intended interventions

All studies lacked blinding due to the nature of the intervention. Five studies (Cramer 2013, Jain 2020, Rajalaxmi 2018, Ulug 2018, Yogitha 2010) were judged to be at low risk of bias for this domain, as any discontinuations from intended interventions in were judged to be unrelated to the trial context. Limited information relating to deviations was provided for 2 studies (Rajalaxmi 2018, Yogitha 2010). One study (Michalsen 2018) was judged to have some concerns due to deviations from the intervention which could plausibly have been due to the trial context and were unbalanced between arms.

Bias due to missing outcome data

Four studies were at low risk of bias for this domain (Cramer 2013, Jain 2020, Michalsen 2012, Rajalaxmi 2018). One study (Ulug 2018) was judged to have some concerns due to the moderate rate of missing data (10% for each yoga and control), with no reasons for drop out provided, however missingness was balanced between arms. One study (Yogitha 2010) was judged at high risk of bias due to the proportion of missing data which was unbalanced between arms. Reasons for drop out were provided and were related to the outcome of pain in some cases.

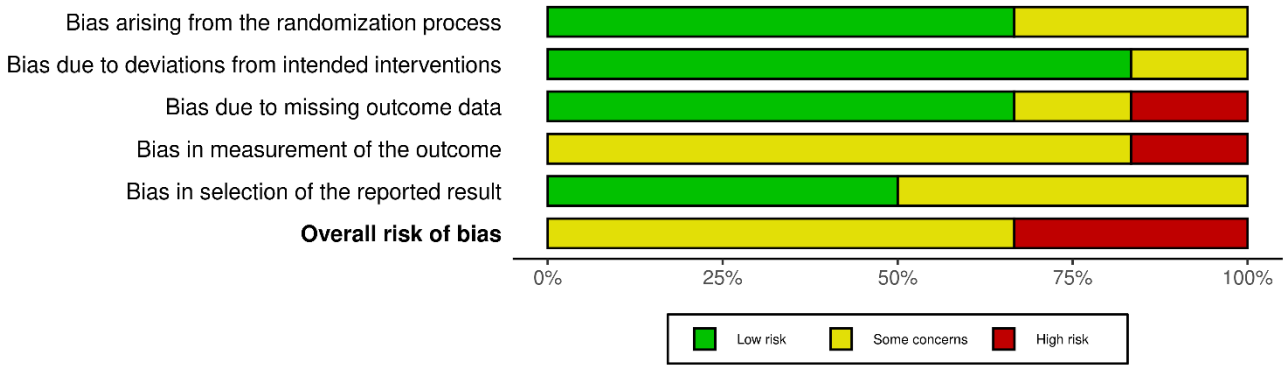
Bias in measurement of the outcome

Five studies were assessed to have some concerns of bias in this domain (Cramer 2013, Jain 2020, Rajalaxmi 2018, Ulug 2018 and Yogitha 2010). Due to the nature of the intervention, participant reported outcomes could be influenced by knowledge of the intervention received. In all cases there was no reason to believe the patient reported outcomes were substantially influenced by knowledge of the intervention. One study (Michalsen 2012) was assessed at high risk of bias for this domain as there was a high rate of discontinuations in the control arm, which suggests that participants in this study were particularly invested in the yoga intervention, and therefore likely to be biased in their reporting of outcomes.

Bias in selection of the reported result

Three studies were assessed to have low concerns for risk of bias in this domain (Cramer 2013, Michalsen 2012, Rajalaxmi 2018). Three studies (Jain 2020, Ulug 2018, Yogitha 2010) were assessed to have some concern for risk of bias in this domain. There were no pre-specified analysis plans available for these two studies.

Figure D-13 Risk of bias summary: review authors' judgements about each risk of bias item expressed as percentages across all RCTs – Neck and shoulder pain



D6.3.3 Effect of intervention

Outcomes considered by the NTWC to be critical or important for decision-making in people with neck and/or shoulder pain are listed in Table D-20.

Main comparison (vs control)

Two RCTs comparing yoga with no intervention (delivered as an adjunct to isometric neck exercises or physical therapy) were eligible for this comparison and contributed data to 3 of the 7 outcomes considered critical or important for this review (Jain 2020, Rajalaxmi 2018).

There were 2 studies awaiting classification (total 106 participants) and one ongoing study (10 participants) that was complete (results not published) that compared yoga with control (no intervention) in people with shoulder pain that could have contributed data to this comparison (see Appendix C6). The available information is insufficient to make a judgement about the nonreporting of results.

Table D-20 Outcomes considered by the NTWC to be critical or important for decision-making: Neck Pain

Outcome domain	Measured with	Consensus rating	Data available for main comparison?	Jain 2020	Rajalaxmi 2018
Pain	MPQ, NPQ, VAS (or other)	Critical	Yes	✓	✓
Health-related quality of life	SF-36, Nottingham Health Profile	Critical	No	--	--
Physical function/ disability	Neck Disability Index (or shoulder)	Critical	Yes	✓	?
Emotional function	SF-36-MCS Beck Depression Inventory	Important	No	--	--
Return to work	Work ability index	Important	No	--	--
Kinesiophobia	Tampa scale for kinesiophobia	Important	Yes	--	✓
Global perceived effect	Patient-rated improvement (or other)	Important	No	--	--

Abbreviations: MCS, mental component score; MPQ, McGill Pain Questionnaire; NPQ, Northwick Park neck pain questionnaire; SF-36, 36-item short form; VAS, visual analogue scale

✓ A study result is available for inclusion in the synthesis

-- No study result is available for inclusion, (probably) because the outcome was not assessed, or for a reason unrelated to the P value, magnitude or direction of the results

? No study result is available for inclusion, and it is unclear if the outcome was assessed in the study

^ Study data was not in an extractable form

Pain

Two studies (total 92 participants) reported pain measured with the Northwick Park Neck Pain Questionnaire (NPQ) or the Shoulder Pain and Disability Index (SPADI) at the end of treatment (range: 3 to 4 weeks) (Jain 2020, Rajalaxmi 2018).

The NPQ is a multi-dimensional measure of pain disability that covers 9 parameters related to pain intensity, duration of symptoms, numbness at night, pain affecting sleep, effect on social life, carrying, reading/watching television, working/housework, and driving (241). Each parameter is assigned a score that corresponds to the degree of difficulty, from 0 (no difficulty) to 4 (severe difficulty). The overall score is calculated by taking the sum of the scores for each parameter and converting this to a percentage, where a higher score relates to more severe disability/pain. The NPQ has been validated in people with neck pain, and the proposed MCID is a reduction of at least 25% from baseline (241).

The results from one study (20 participants) showed an improvement in neck pain in the yoga group compared to the control group (MD –31.40; 95% CI –35.71, –27.09 ; $p < 0.000001$) *(GRADE: Low)*. The mean difference between the yoga and control group exceeds 25% of the baseline scores for each group, suggesting that this is a clinically meaningful difference.

The SPADI is a self-administered questionnaire that consists of 2 dimensions, one for pain and the other for functional activities. The pain dimension consists of 5 questions regarding the severity of an individual's pain. Each item is rated on 10 cm visual analogue scale using verbal anchors from 0 (no pain at all) to 10 (worst pain imaginable). The pain score is then aggregated to 100 (higher is worse). An MCID for the pain score was not found but is estimated to be between 8 and 13.2 when the combined with the disability score (242). The results from one study (72 participants) showed no difference between the yoga and control groups (MD 0.33; 95% CI –1.18, 1.84; $p = 0.67$) *(GRADE: Low)*.

The results of these studies were not pooled, as they were considered sufficiently different (subgroup difference $I^2 = 99.5\%$).

Disability

One study (72 participants) reported disability measured with the Shoulder Pain and Disability Index (SPADI) at the end of treatment (4 weeks) (Jain 2020).

The SPADI is a self-administered questionnaire that consists of 2 dimensions, one for pain and the other for functional activities. Functional activities are assessed with 8 questions designed to measure the degree of difficulty an individual has with various activities of daily living that require upper-extremity use. Each item is rated on 10 cm visual analogue scale using verbal anchors from 0 (no difficulty) to 10 (so difficult it required help). The disability score is then aggregated to 100 (higher is worse). An MCID for the disability score was not found but is estimated to be between 8 and 13.2 when the combined with the pain score (242).

The results from one study (72 participants) showed no difference between the yoga and control groups (MD 0.77; 95% CI –1.81, 3.35; $p = 0.56$) *(GRADE: Low*).

Kinesiophobia

One study (20 participants) reported kinesiophobia with the Tampa Scale for Kinesiophobia (TSK) at the end of treatment (3 weeks) (Rajalaxmi 2018).

The TSK is a self-completed 17-item questionnaire used to assess the subjective rating of kinesiophobia (a debilitating fear of physical movement due to pain). Total scores range from 17 to 68, where a higher score indicates an increasing degree of kinesiophobia. Scores above 37 indicate kinesiophobia is present in people with chronic low back pain (243), which can reasonably be applied to people with neck pain.

The results suggest a moderate effect that favours the yoga group compared to the control group (MD –8.50; 95% CI –11.25, –5.75; $p < 0.000001$) (*GRADE: Low*). (i.e. MD is between 10% to 20% of the scale). However, post-treatment scores indicate that both the yoga and control groups still experience kinesiophobia (mean score in both groups is greater than 37).

Comparison 2 (vs other intervention)

There were 5 studies comparing Yoga with ‘other’ interventions in people with neck pain that were eligible for this comparison. All 5 RCTs (Cramer 2013, Michalsen 2012, Rajalaxmi 2018, Ulug 2018, Yogitha 2010) contributed data relevant to 3 of the 7 outcomes. Data from these studies are present in Appendix F2 Supplementary outcome .

There were 2 ongoing studies and one study awaiting classification that compared yoga with 'other' interventions.

D7 Factors influencing health status

D7.1 Stress

D7.1.1 List of studies

An overview of the PICO criteria of included studies is provided in Table D-21. Study details, including all outcome domains and measures reported by the included studies are provided in Appendix F1. Outcome data for critical or important outcomes are provided in Appendix F2.

Table D-21 Overview of PICO criteria of included studies: Stress

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
Yoga versus control (no intervention, waitlist, inactive usual care)*						
Daukantaitė 2018 (244)	RCT	Elevated perceived stress	Yoga (Yin)	Control (waitlist) OR Yoga plus psychoeducation and mindfulness ^	None reported	Perceived stress Anxiety Depression Sleep quality Coping strategies Diet Emotional function Life satisfaction Mindfulness Avoidance Compassion Stress biomarkers Glucose tolerance Gut microbiota Heart rate variability
Godse 2015 (245)	RCT	Elevated perceived stress (students)	Yoga (Suryanamaskar)	Control (waitlist)	None reported	Stress disposition Stress symptoms
Harkess 2016 (246-248)	RCT	Elevated perceived stress (professional females)	Yoga (Ashtanga)	Control (waitlist)	None reported	Psychological distress Perceived stress Mindfulness Life satisfaction Emotional wellbeing Physical activity Obesity disease risk Stress biomarkers Physical function Anger Loneliness Heart rate Blood pressure Flexibility Patient experience
Hartfiel 2012 (249)	RCT	Elevated perceived stress (government workers)	Yoga (Dru)	Control (waitlist)	None reported	Perceived stress Functional disability Emotional wellbeing Positive and negative affect
Hewett 2017 (250, 251)	RCT	Elevated perceived stress (sedentary)	Yoga (Bikram)	Control (waitlist)	None reported	Heart rate variability Perceived stress Self-efficacy

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
						Augmentation index
Köhn 2013 (252, 253)	RCT	Stress-related symptoms (adults seeking treatment)	Yoga (medical)	Control (no intervention)	Standard medical treatment	Perceived stress Burnout Anxiety Depression Psychological distress Pain Sleep problems HRQoL Heart rate Blood pressure Peripheral oxygen saturation
Maddux 2018 (254)	RCT	Elevated perceived stress (university staff)	Power yoga	Control (waitlist)	None reported	Perceived stress Psychological distress Anxiety Depression Sleep problems Life satisfaction Harmony in life Mindfulness Avoidance behaviour
Michalsen 2012a (255)	RCT	Elevated perceived stress (females)	Yoga (Iyengar) †	Control (waitlist)	None reported	Perceived stress Depression Anxiety Psychological distress Emotional wellbeing Mood HRQoL Somatic complaints General wellbeing Pain
Yoga versus 'other' intervention**						
Granath 2006 (256)	Quasi RCT	Elevated perceived stress (finance workers)	Yoga (Kundalini)	Cognitive Behaviour Therapy	None reported	Perceived stress Stress experience Exhaustion Anger HRQoL Stress biomarkers Blood pressure Heart rate
Grensman 2018 (257)	RCT	Burnout (workers on leave)	Yoga	Mindfulness based cognitive psychotherapy OR Cognitive behavioural therapy	None reported	HRQoL
Kumar 2016 (258)	RCT	Elevated perceived stress (students)	Yoga	Mental imagery	None reported	Mood Stress response Pulse rate Blood pressure Respiratory rate

STUDY ID	Study design	POPULATION	INTERVENTION	COMPARATOR	CO-INTERVENTION	OUTCOME DOMAINS
Smith 2007 (259)	RCT	Elevated perceived stress	Yoga (Hatha)	Relaxation (muscle)	None reported	Anxiety Psychological distress General health perceptions Blood pressure

Abbreviations: HRQoL; Health-related quality of life; RCT, randomised controlled trial

*Studies that compared yoga with an inactive control were eligible for inclusion in the evidence synthesis and are included in the Summary of findings tables if they reported outcomes considered critical or important to this review.

**Studies that compared yoga with an active intervention are included in the supplementary outcome tables (Appendix F2) if they reported data for outcomes considered critical or important to this review.

^ Study included 3 groups. The inactive control is considered in the evidence synthesis.

† Study includes two yoga groups at different doses (once and twice per week). The results for both yoga groups are combined in the evidence synthesis.

D7.1.2 Risk of bias summary

The risk of bias for each item in the included studies for stress is described below and shown graphically in Figure D-14 (details are provided in Appendix E).

Bias arising from the randomisation process

Five studies (Daukantaitė 2018, Hewett 2017, Köhn 2013, Michalsen 2012a Smith 2007) provided sufficient information regarding allocation concealment, the randomisation sequence and baseline characteristics, and were considered at low risk of bias. The remaining studies had some concerns relating to lack of information on allocation concealment (Hartfiel 2012, Harkess 2016, Maddux 2018, Godse 2015), insufficient baseline characteristics presented (Grensman 2018) or no information on the generation of the randomisation sequence (Granath 2006, Kumar 2016).

Bias due to deviations from intended interventions (effect of assignment to intervention [ITT])

Eight studies (Granath 2006, Harkess 2016, Hartfiel 2012, Hewett 2017, Köhn 2013, Kumar 2016, Michalsen 2012a, Smith 2007) were judged to be at low risk of bias for this domain as they had no deviations from the intervention that were considered to have arisen from the trial context and used an appropriate analysis method to estimate the effect of assignment to the intervention (ITT or modified ITT). One study had some concerns (Grensman 2018) due to deviations from the intended intervention, however the rate was considered relatively small and not likely to have affected the outcome. Three studies (Daukantaitė 2018, Godse 2015, Maddux 2018) were assessed to be at high risk of bias due to high rates of deviations from the intended intervention which were considered to have arisen due to the trial context and which occurred unevenly between the intervention groups, and an inappropriate method of analysis (per protocol) being sued to estimate the effect of assignment to intervention (Daukantaitė 2018 and Godse 2015).

Bias due to missing outcome data

Three studies (Köhn 2013, Kumar 2016, Michalsen 2012a) were judges at low risk of bias for this domain as outcome data was available for most or all participants randomised. Five studies (Granath 2016, Grensman 2018, Harkess 2016, Hewett 2017, Smith 2007) had some concerns due to a large proportion of missing data, however reasons for drop out were presented and did not appear related to the study outcomes. Four studies (Daukantaitė 2018, Godse 2015, Hartfiel 2012, Maddux 2018) were judged at high risk of bias due to a large proportion of missing outcome data with no analysis presented to adjust for missingness and no reasons for missing outcomes provided.

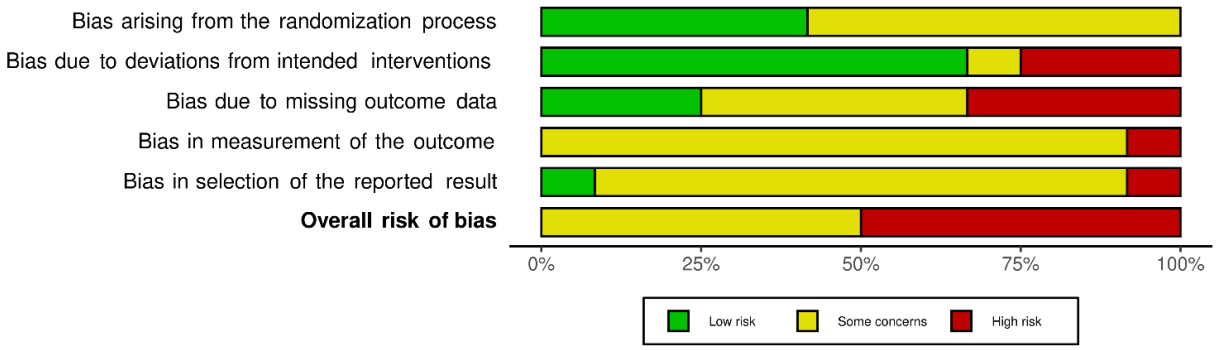
Bias in measurement of the outcome

All studies were assessed to have at least some concerns regarding the measurement of outcomes. None of the included studies blinded participants and the primary outcomes were subjective, results of which could be influenced by knowledge of the intervention. Smith 2007 was assessed at high risk of bias as study participants were reported to have expectations of the yoga program including for relaxation and lifestyle changes which are considered *likely* to bias reporting of the outcome.

Bias in selection of the reported result

One study (Daukantaitė 2018) was assessed at low risk of bias for this domain as the analysis presented aligned with the pre-specified analysis plan. Some outcomes mentioned in the protocol were not reported. The impact of this known missing outcome data will be considered as part of the overall certainty of the evidence for each outcome domain. The remaining studies were either considered to have some concerns or at high risk of bias (Michalsen 2012a) as no pre-specified analysis plan was available to confirm the reported result was analysed in a pre-determined manner. One study (Michalsen 2012a) was assessed at high risk of bias as only significant outcomes were reported, with non-significant results reported in-text but unable to be extracted for quantitative synthesis.

Figure D-14 Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included RCTs – Stress



D7.1.3 Effect of intervention

Outcomes considered by the NTWC to be critical or important for decision-making in people with elevated perceived stress are listed in Table D-22.

Table D-22 Outcomes considered by the NTWC to be critical or important for decision-making: Stress

Outcome domain	Measured with	consensus rating	Data available for main comparison?	Daukantaitė 2018	Godse 2015	Harkess 2016	Hartfiel 2012	Hewett 2017	Köhn 2013	Maddux 2018	Michalsen 2012a
Health-related Quality of life	Quality of Life Inventory (or other)	Critical	Yes	--	--	--	--	--	✓	--	--
Stress	Perceived Stress Scale (or other)	Critical	Yes	✓	--	✓	✓	✓	✓	✓	✓
Emotional wellbeing	PANAS (or other)	Critical	Yes	--	--	✓	✓	✓	--	--	✓
Life satisfaction	Harmony in Life Scale (or other)	Important	Yes	X	--	✓	--	--	--	✓	--
Fatigue (including burnout)	Shirom-Melamed Burnout Questionnaire (or other)	Important	Yes	--	--	--	--	--	✓	--	--
Cognitive function	SWED-QUAL cognitive domain (or other)	Important	No	--	--	--	--	--	--	--	--
Sleep quality	Insomnia Severity Index (or other)	Important	Yes	✓	--	--	--	--	✓	✓	--

Abbreviations: SWED-QUAL, Swedish Quality of Life Inventory
✓ A study result is available for inclusion in the synthesis

X No study result is available for inclusion, (probably) because the P value, magnitude or direction of the results generated were considered unfavourable by the study investigators
-- No study result is available for inclusion, (probably) because the outcome was not assessed, or for a reason unrelated to the P value, magnitude or direction of the results
? No study result is available for inclusion, and it is unclear if the outcome was assessed in the study

Main comparison (vs control)

Eight RCTs (Daukantaitė 2018, Godse 2015, Harkess 2016, Hartfiel 2012, Hewett 2017, Köhn 2013, Maddux 2018, Michalsen 2012a) comparing yoga with control (no intervention, waitlist or usual care) in people with elevated perceived stress were eligible for this comparison. The RCTs contributed data to 6 outcomes considered critical or important for this review.

There was one study awaiting classification that compared yoga with no intervention in military personnel at risk of stress, anxiety or depression (total participants unknown) that could have contributed data to two outcomes (see Appendix C6)). There were no ongoing studies that compared yoga to usual care that could have contributed data to this comparison.

Quality of life

Three RCTs (172 participants) reported health-related quality of life measured with either the SF-36 or the EuroQoL Visual Analogue Scale (EuroQoL VAS) at the end of treatment (range: 12 to 16 weeks) (Köhn 2013).

The SF-36 is a self-reported multidimensional measure that assesses the impact of one's health on everyday life across. Eight domains are summarised on a scale from 0 (worse) to 100 (best), which can be summarised into 2 component scores. The physical component summary (PCS) score includes the domains of general health, physical functioning, role physical and body pain. The mental component summary (MCS) score includes the domains of vitality, social functioning, role emotional, and mental health. The results from one study (63 participants) suggest a significant improvement in each of the SF-36 domains in the yoga group compared to the control group. The MCID for the SF-36 is estimated to be around 2 to 4 points for the general population (i.e. ~0.5 of the SD) (42).

Individual domain scores were reported in one study (63 participants) (Hewett 2017) that suggested an effect favouring the yoga group when compared with control for all 4 domains in the MCS, and one domain within the PCS as follows (*GRADE: Low*):

- mental health (MD –13.50; 95% CI –22.14, –4.86; p = 0.002)
- social functioning (MD –12.00; 95% CI –23.64, –0.36; p = 0.04)
- role-emotional (MD –31.60; 95% CI –50.94, –12.26; p = 0.001)
- vitality (MD –11.00; 95% CI –19.89, –2.11; p = 0.02)
- general health perception (MD –11.20; 95% CI –21.40, –1.00; p = 0.03)
- physical functioning (MD –5.90 95% CI –15.36, 3.56; p = 0.22)
- bodily pain (MD –4.00; 95% CI –13.35, 5.35; p = 0.40)
- role-physical (MD –12.70; 95% CI –29.65, 4.25; p = 0.14)

One study (72 participants) (Michalsen 2012) did not report individual group post-treatment or change from baseline scores and could not be included in the analysis. Between group differences in the change scores were reported for the for the PCS (MD –0.1, 95% CI –0.4, 0.2; p = 0.653) and the MCS (MD 0.6; 95% CI 0.1, 1.1; p = 0.012).

The EuroQoL VAS records the participant's self-rated health on a visual analogue scale where the ends are labelled "the best health you can imagine" (a score of 100) and "the worst health you can imagine" (a score of 0). The MCID for EuroQoL VAS in people with elevated perceived stress has not been established. Results from one study (37 participants) (Köhn 2013) suggested an improvement in QoL scores in the yoga group compared to the control group (MD 20.60; 95% CI 7.42, 33.78; p = 0.002) (*GRADE: Low*). In the absence of an established MCID, this is considered a moderate change (i.e. 20% of the scale).

No sensitivity analysis was conducted that examined the impact of RCTs judged to be at high risk of bias, as only two studies was included in the comparison, and they were not judged to be at high risk of bias.

Perceived stress

Six studies (401 participants) reported perceived stress measured using the Perceived Stress Scale (PSS) at the end of treatment (range: 5 to 16 weeks). Five studies used the 10-item PSS (Daukantaitė 2018, Harkess 2016, Hartfiel 2012, Hewett 2017, Maddux 2018) and one study used the 14-item PSS (Köhn 2013). Outcome data for one additional study (Michalsen 2012a; 72 participants) was not included in the meta-analysis as it did not report post-treatment or change from baseline scores. This study noted a significant (p = 0.003) between-group difference in favour of yoga.

The PSS is a widely used psychological instrument for measuring people's perception of stress and measures the degree to which situations in one's life are stressful. Some questions are positively stated, then reverse coded. Scores for the 10-item PSS range from 0 to 40, and scores for the 14-item PSS range from 0 to 56, with higher scores indicating greater perceived stress. An MCID for the PSS-10 is estimated to be between 2.19 and 2.66 points among undergraduate students with elevated stress (63) and around 11 points in people with work-related stress complaints (64).

Pooled results suggest a moderate improvement in perceived stress scores in the yoga group compared to the control group (SMD –0.60; 95% CI –0.96, –0.23; p = 0.001; I^2 = 68%) (*GRADE: Low*) (i.e. SMD between 0.5 and 0.8). However, the clinical importance of the difference is not clear (MD is more than 2.5 but less than 11 points).

In a sensitivity analysis that examined the impact of 3 RCTs (Daukantaitė 2018, Hartfiel 2012, Maddux 2018) that were judged to be at high risk of bias, the size of the effect estimate increased (SMD –0.87; 95% CI –1.60, –0.14; p = 0.02; I^2 = 82%); however, heterogeneity was substantial.

Emotional wellbeing

Two studies (159 participants) reported emotional function measured using the Positive and Negative Affect Schedule (PANAS) or the PANAS-X – an expanded version of the original PANAS – at the end of treatment (range: 8 to 16 weeks) (Harkess 2016, Hartfiel 2012).

The PANAS is a self-report questionnaire that consists of two 10-item scales that measure positive and negative affect (260). Participants rate their mood on a scale from one (not at all) to 5 (very much), responding to different words or phrases that describe feelings and emotions. For the positive affect scale, higher scores represent better propensity to experience positive emotions and interact with others positively; for the negative affect scale, higher scores represent higher propensity for experiencing the world in a more negative way. Scores for each of the positive and negative affect scales range from 10-50. There are no established norms (or cut-offs) for the PANAS and no MCID was found.

The results from one study (total 100 participants) suggests an small effect favouring yoga when compared to control for positive emotions (SMD 0.39; 95% CI 0.79, –0.01; p = 0.05) (*GRADE: Low*) (i.e. SMD between 0.2 and 0.5) and little to no effect on negative emotions (SMD –0.17; 95% CI –0.57, 0.22; p = 0.39) (*GRADE: Low*) (i.e. SMD less than 0.2).

In addition to the general positive and negative affects states in the original PANAS, the PANAS-X also includes additional items for basic negative and positive emotions, and other affective states such as shyness or surprise which are neither positive nor negative (261). Similar to the PANAS, participants rate their experience of each item on a scale from one (not at all) to 5 (very much). The overall score for PANAS-X ranges from 60-300 with higher score indicating improved emotional function. There are no established norms (or cut-offs) for the PANAS-X and no MCID was found.

The results from one study (total 59 participants) showed a large effect for emotional wellbeing in the yoga group compared to the control group (SMD 0.90; 95% CI 0.36, 1.44; p = 0.001) (*GRADE: Low*) (i.e. SMD greater than 0.8). This study was judged to be at high risk of bias.

Life satisfaction (subjective wellbeing)

Two studies (178 participants) reported life satisfaction (subjective wellbeing) measured using the Harmony in Life Scale (HILS) or the Personal Wellbeing Index – Adult (PWI-A) at end of treatment (range: 5 weeks to 8 weeks) (Maddux 2018, Harkess 2016).

The HILS is a 7-item measure of subjective wellbeing, emphasising psychological balance and flexibility in life (262). Participants rate each statement on a scale from one (strongly disagree) to 7 (strongly agree). Total scores range from 5 to 35, with higher scores indicating improved subjective wellbeing. An MCID for the HILS has not been established. The results from one study (78 participants) suggest an effect with wide confidence intervals in favour of the yoga group compared to the control group (SMD 0.39; 95% CI –0.06, 0.84; p = 0.09).

This study also reported life satisfaction measured by a Numeric Rating scale from 0 to 7 for 3 questions: (1) "How satisfied are you with your current life?"; (2) "To what extent are you pleased with your current life?"; (3) "How do you value your life?", with a higher score indicating greater life satisfaction. Results using this measure did not substantially differ from the HILS (results not shown here), and so the validated outcome measure was used for this analysis.

The PWI-A is a 7-item scale that measures life satisfaction in the following domains: standard of living, health, life achievement, personal relationships, personal safety, community connectedness, and future security. Each item is scored on a scale from 0 to 10, with higher scores indicating improved life satisfaction. Scores for each domain can be summed to yield a total score between 0 and 70. The PWI-A has been shown to have good correlation with the Satisfaction with Life Scale and has demonstrated good test-re-test reliability (263). The results from one study (100 participants) suggested no difference between the yoga and control groups (SMD 0.06; 95% CI –0.33, 0.45; p = 0.76).

Taken together, the pooled results (total 178 participants) suggested no difference between yoga and control for the outcome of life satisfaction (SMD 0.21; 95% –0.11, 0.52; p = 0.20; I^2 = 13%) (*GRADE: Low*).

The result does not include data from one study (64 participants) (Daukantaite 2018) that did not report data for this outcome, despite being pre-specified in the clinical trial record. Missing data is likely to be related to the direction or magnitude of effect being considered unfavourable by the study authors.

In a sensitivity analysis that examined the effect of one RCT at high risk of bias (Maddux 2018), the size of the effect estimate decreased (SMD 0.06; 95% CI –0.33, 0.45; p = 0.76).

Fatigue (including burnout)

One study (37 participants) reported fatigue measured by the Shirom-Melamad Burnout Questionnaire (SMBQ) at end of treatment (12 weeks) (Köhn 2013).

The SMBQ is a burnout measure that includes 22 questions graded on a scale from 1 (almost never) to 7 (almost always). A modified version of the SMBQ, removing 4 items related to tension, has been validated in a clinical sample of people seeking medical care for stress-related problems (264). Scores are calculated as the average of each question, with the total score ranging from 1 to 7 (265). A higher score indicates a higher level of burnout and cut-off values of 4.00 and 3.75 have previously been used, where a score above this indicates clinically significant burnout (265).

The results showed an effect in favour of the yoga group for improvement in burnout compared to the control group (MD –0.50; 95% CI –0.89, –0.11; p = 0.01) (*GRADE: Low*). In the absence of an MCID, this is considered a small change (i.e. MD < 10% of the scale). After treatment, both the yoga and control groups had SMBQ mean scores lower than the proposed cut-off of 4.00, suggesting neither group was experiencing clinically significant burnout. Adjusting for baseline SMBQ score, the single study contributing data reported no difference in burnout between the yoga and control groups.

No sensitivity analysis was conducted that examined the impact of RCTs judged to be at high risk of bias, as only one study was included in this comparison.

Sleep Quality

Three studies (179 participants) reported sleep quality measured with the Insomnia Severity Index (ISI) at the end of treatment (range: 5 to 16 weeks) (Daukantaitė 2018, Köhn 2013, Maddux 2018)

The ISI is a 7-item questionnaire assessing the nature, severity and impact of insomnia, with the focus being on subjective feelings about insomnia symptoms. Each question is summed to give a total score that ranges from 0 to 28. Scores are categorised as follows: 0 to 7, no clinical insomnia; 8 to 14, subclinical insomnia; 15 to 21, clinical insomnia (moderate); 22 to 28, clinical insomnia (severe). A cut-off score of 10 has been found to maximise sensitivity and specificity in a community sample (68). In a clinical sample of people seeking treatment for insomnia, an improvement of 8.4 points corresponded to a moderate improvement in insomnia (68).

The pooled results suggests an effect that favours the yoga group when compared with the control group (MD –2.58; 95% CI –5.93, 0.77; p = 0.13; I^2 = 69%) (*GRADE: Low*), however there is significant statistical heterogeneity and the MCID is not reach.

In a sensitivity analysis that examined the effect of 2 RCTs at high risk of bias (Daukantaitė 2018, Maddux 2018), the size of the effect estimate increased (MD –6.10; 95% CI –9.81, –2.39; p = 0.001) but did not meet the proposed MCID of –8.4 points. Adjusting for baseline ISI score, the single study contributing data reported no difference in sleep quality between the yoga and control groups.

Comparison 2 (vs other intervention)

There were 5 studies comparing Yoga with ‘other’ interventions in people with elevated perceived stress that were eligible for this comparison(Daukantaite 2018, Granath 2006, Grensman 2018, Kumar 2016, Smith 2007). Data from these studies are present in Appendix F2 Supplementary outcome .

There were 3 ongoing studies (total 650+ participants) and no studies awaiting classification that compared yoga with 'other' interventions in people with elevated perceived stress.

Appendix E Risk of bias forms

This appendix documents the risk of bias judgements made on studies that met the prespecified inclusion criteria for a systematic review on the effect of yoga for preventing and treating any health condition.

The risk of bias of included RCTs was assessed using the Revised Cochrane Risk of Bias tool v2.0 (266, 267) (see www.riskofbias.info). Assessments were based on the primary outcome for that study (or for which the study was powered).

Appendix E (see attachment) lists the included RCTs and quasi-RCTs (for priority populations) in order of ICD-11 category. Studies within the ICD-11 category are then ordered by the prioritised condition and listed alphabetically. For each study there are two columns: column one is the judgement applied to each signalling question associated with each risk of bias domain (answered as yes, partial yes, no, partial no, no information or not applicable); column two is a comment that briefly explains the reasoning that underpins the judgement.

Appendix F Characteristics of included studies

This appendix documents the data extracted from studies that met the prespecified inclusion criteria for a systematic review on the effect of yoga for preventing and treating any health condition and were conducted in populations prioritised for inclusion in the evidence synthesis.

All extracted data is presented, including that which was not synthesised in the main report.

F1 Study details

Appendix F1 (see attachment F1) lists the characteristics of each included study (for priority populations) in order of ICD-11 category. Studies within the ICD-11 category are then ordered by the prioritised condition and listed alphabetically.

For each study, the data extraction has included (but was not limited to) the following characteristics: study design, year conducted, setting and location, participant inclusion criteria, intervention and comparator characteristics (including number of treatment sessions, program duration, co-interventions), outcomes (including measurement method and timing), and funding sources.

Outcome domains and measures considered critical or important for inclusion in the review are highlighted with a blue box. Conversely, outcome domains and measures that were of limited importance are not highlighted.

F2 Supplementary outcome data

Appendix F2 (see separate spreadsheet attachment F2) lists the data extracted for critical or important outcomes identified in each included study (for priority populations) in order of ICD-11 category. Studies within the ICD-11 category are then ordered by the prioritised condition. Within each sheet, studies are listed by comparison (Yoga vs control or Yoga vs 'other') with the study results per outcome reported (critical or important outcome measures) that includes (but is not limited to) the following: outcome domain, timing, outcome measure, measure details, number of included participants, point estimates, p-value, direction of effect.

Data extracted is that reported by the study authors at the end of treatment (where possible) with footnotes included if further explanation was required (e.g., authors do not provide end-of treatment results therefore the mean change from baseline data are reported). The final column lists the risk of bias assessment for that outcome as made by the review authors (see Appendix E).

Appendix G Differences between protocol & review

G1 Methods not implemented

Search for NRSIs and assessment of bias within studies

The protocol stated that NRSIs were eligible for inclusion under certain circumstance. Specifically, for certain populations or outcomes that may be more appropriately or more feasibly evaluated with a non-randomised study design. After the identification and evaluation of eligible RCTs, population-specific search terms were to be added to the search to identify NRSIs for populations and/or outcomes specified by the NTWC.

A search for NRSIs was not conducted as there were no priority populations or critical or important outcomes nominated by the NTWC that would have been more appropriately or more feasibly evaluated with a non-randomised study design. Given NRSIs was not included in the evidence evaluation, the ROBINS-I risk of bias tool was not used.

Requests for data

Eligible primary studies not published in English, ongoing trials and studies published as conference abstracts with incomplete results were identified for inclusion and listed as either '*Ongoing*' or within the '*Studies Awaiting Classification*'. It was intended that study authors would be contacted through an open-ended request for further information, and, if available, the study would be included in the evidence appraisal. Given time and resource constraints, we did not contact study authors for additional information regarding missing data.

Quantitative synthesis

Prior to provision of the first draft evaluation report, the NTWC could request that data comparing Yoga with 'other' (active) intervention be synthesised, where:

i. at least two studies compare the effect of yoga with the same active comparator, and the comparator is sufficiently homogenous across studies to support synthesis, and

ii. at least two of these studies are at low or moderate risk of bias, and

iii. the comparator represents an accepted, evidence-based 'gold standard' of care for the population in question.

No such cases were identified or requested.

Subgroup analyses and investigations of heterogeneity

We did not plan to undertake any subgroup analyses of subsets of participants within or across studies, unless there was substantial inconsistency between effect estimates. Any subgroup analysis was intended to explore possible sources of heterogeneity relating to delivery of the intervention. Studies were to be grouped according to intervention characteristics (i.e. intensity, duration, mode of delivery, or who delivers) and a standard test for heterogeneity across the subgroups was to be reported. Due to time and resource constraints, we did not undertake a subgroup analysis of intervention characteristics; noting that most conditions did not meet the recommended number of studies (at least 10 studies) that are needed for subgroup analysis (268).

Summary of findings and certainty of the evidence

We had specified that the evidence from RCTs and NRSIs would be evaluated separately in the summary of findings table. Given there were no NRSIs included in the evidence synthesis, this was not implemented.

G2 Changes from protocol

There were some differences between the protocol and review relating to the following sections:

Types of participants

Additional clarification on what constitutes an 'at-risk' healthy population was made prior to data extraction and evidence synthesis, to avoid ambiguity regarding eligibility and to establish a minimum threshold requirement for inclusion. The NTWC agreed that, where a study could provide sufficient evidence of the individual participant being 'at-risk' then it was eligible for inclusion. This meant that studies that enrolled participants at a population level were not eligible unless there was some form of prespecified enrolment criteria for the otherwise healthy participants or there were baseline data that indicated all participants met a certain criterion.

For example, a study that enrolled generally healthy women to examine the effects of a yoga program on mood was excluded, unless the study participants had been enrolled based on help-seeking behaviour (e.g. referral after visit to medical practitioner), the participants had been screened for elevated stress, anxiety or depression prior to study entry (e.g. enrolment based on a certain perceived stress score [PSS]), or baseline data suggested all participants met a preclinical condition (e.g. participants had elevated markers for obesity or heart disease). A similar example would be a study that examined age-related mental decline in otherwise healthy older adults (aged over 60 years), with eligible studies being those in which the participants had been judged by a clinician prior to study entry to be at risk of cognitive impairment (e.g. via mini-mental state exam) or enrolled participants had family history of dementia. Where there was ambiguity, information on participants and the aim of the study was provided to the NTWC for a decision about eligibility.

Comparators

Additional clarification on what constitutes an 'inactive' or 'active' control was made prior to data extraction and evidence synthesis. Comparators that provided minimal intervention or change to the participants day-to-day activities were judged to be 'inactive', whereas comparators that required the participants involvement over the course of the study were judged to be 'active'.

For example, an education booklet or handout providing health advice given to participants at the study start was judged 'inactive', whereas education in the form of weekly group sessions that tended to mimic the yoga program was judged 'active'. Similarly, a control group that received a weekly phone call was judged 'inactive', but if the control group received a weekly health check-up including clinical advice (either at home or requiring site visits), then this was judged to be 'active'.

Outcome measures and timepoints of interest

It was intended that outcomes reported at different timepoints were to be grouped and considered as either: short term, intermediate term, long-term (or not specified); with the NTWC to decide during outcome prioritisation as to whether evidence reported at multiple timepoints would be considered critical or important for decision-making (to be considered and reported separately). To maximise the available data eligible for inclusion, and for consistency with the reports for Pilates and Tai Chi, it was determined that 'end-of-treatment' outcomes would be the sole timepoint of interest to be considered in the evidence synthesis (unless there was good rationale for selecting an alternative timeframe). While most studies in yoga focused on change from baseline scores at the end of treatment, it is noted that several studies also reported mid-treatment or follow-up results after completion of the yoga program.

Studies identified in the literature search

It was intended that the lead reviewer would reinspect a random 20% sample of articles marked as excluded to ensure adherence to the *a priori* exclusion criteria. In fact, the lead reviewer (MJ) screened approximately 35% of articles marked for exclusion, but the selection of articles screened in duplicate was not random, rather it was targeted towards studies excluded for the following reasons: population out of scope, comparator out of scope and non-randomised study.

Appendix H How comments from methodological review were addressed

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

For reporting, the methodological review assessed the systematic review against the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) Checklist (2020) and where applicable, the MECIR (Methodological Expectations of Cochrane Intervention Reviews) manual.

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

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

The ROBIS assessment included specification and application of criteria for considering studies for the review and synthesis, search methods, data extraction and analysis, assessment of risk of bias of studies, assessment of the certainty of evidence using GRADE, and the interpretation and summary of findings.

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

- Clarification of the list of priority populations and conditions included in the evidence synthesis, including separation of fibromyalgia from other chronic pain conditions (osteoarthritis, rheumatoid arthritis).
- Clarification of the reporting of methods, including those related to the assessment of bias due to missing results from each synthesis, contacting of authors for missing information.
- Edits to Summary of Findings tables and the addition of a footnote to forest plots to avoid misinterpretation of results relating to the direction of the measure of effect, particularly when SMD analysis was used.

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

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