Effectiveness of non-pharmacological Interventions For Fatigue in Long term conditions (EIFFEL)- systematic review and network meta-analysis

Joanna Leaviss Senior Research Fellow[1],
Andrew Booth, Professor in Evidence Synthesis[1],
David Coyle[2],
George Daly Research Associate [1],
Sarah Davis, Senior Lecturer[1],
Helen Dawes, Professor of Rehabilitation[3],
Vincent Deary, Professor of Pyschology[4],
Kritica Dwivedi, Academic Clinical Fellow[1],
Jessica Forsyth, Research Associate[1],
Kate Fryer, Research Fellow[1],
Samantha McCormick, patient representative[2],
Marissa Martyn-St James, research fellow[1],
Julia Newton, Medical Director[5],
Shijie Ren, Professor of Statistics[1],
Gillian Rooney, Research Fellow[1], Anthea Sutton, Senior Research Fellow[1],
Mon Mon-Yee, Research Associate[1],
Christopher Burton, Professor of Primary Medical Care[1]*

[1] Sheffield Centre for Health and Related Research, University of Sheffield, , UK

[2] Patient and public representative

[3] Medical School, University of Exeter, Exeter, United Kingdom

[4] Department of Psychology, Northumbria University, Newcastle, UK

[5] Academic Health Science Network for the North East and North Cumbria (AHSN NENC)

Abstract

Objective To assess the clinical effectiveness of non-pharmacological interventions for fatigue in adults with long term medical conditions.

Design Systematic review and network meta-analysis

Data sources All searches were performed on the following databases: MEDLINE, Embase, CINAHL, APA PsycINFO, Web of Science Core Collection and the Cochrane Central Register of Controlled Trials.

Methods Screening of eligible studies was performed independently and in duplicate, with data extraction and risk of bias assessments conducted by one of two reviewers and validated by the other. Random effects network meta-analyses were conducted for the primary analyses. The primary outcome was self-reported fatigue at end of treatment, short term (up to 3 months after end of treatment) and long term (more than 3 months). The primary network meta-analyses pooled data from all conditions for each time point; a secondary analysis was carried out for separate condition categories. Three rounds of focus groups of people with lived experience of fatigue informed decisions about aggregating data across interventions and conditions, and interpretation of the findings.

Eligibility criteria for selecting studies Randomised controlled trials of non-pharmacological interventions for fatigue in long term medical conditions where fatigue was either a criterion for inclusion, the primary target of the intervention, or the primary or co-primary outcome. We excluded studies of post-infectious, post-traumatic, cancer-related or idiopathic fatigue and limited inclusion to European-style healthcare systems.

Results 88 randomised controlled trials were included, comprising 6636 participants for end of treatment analyses, 1849 (short term) and 2322 (long term), allocated to one of 27 interventions. The most common condition studied was multiple sclerosis (51 studies). Compared to usual care, cognitive behavioural therapy (CBT) -based interventions showed statistically significant reductions in fatigue at end of treatment (standardised mean difference -0.63, 95% credible interval (CrI) -0.87 to -0.4, 17 studies) and long term follow up (-0.4, -0.63 to -0.21,9 studies). Physical activity promotion showed significant reduction in fatigue at all three time points: end of treatment (-0.32, -0.62 to -0.01,7 studies), short term (-0.51, -0.84 to -0.17, 1 study) and long term (-0.52, -0.86 to -0.18, 2 studies). Self-management focusing on energy conservation showed no statistically significant benefit at end of treatment (-0.2, -0.52 to 0.12, 10 studies), short term (-0.13, -0.51 to 0.25, 7 studies) or long term (-0.42, -0.9 to 0.09, 3 studies).

Conclusions - Interventions which support individuals to increase physical activity or that are based on cognitive behavioural are effective in reducing fatigue in people with long-term medical conditions. The strength of the evidence for these is moderate to low. Although there are relatively few studies in any condition other than multiple sclerosis, the magnitude of effect appears similar across different conditions. .

Systematic review registration - PROSPERO CRD42023440141

Introduction

Persistent fatigue is common in long-term medical conditions[1]. Alongside feelings of tiredness, fatigue includes a sense of needing to rest, or of difficulty in initiating or sustaining voluntary effort[2 3]. People with medical conditions typically describe their fatigue as “more than ordinary tiredness” [4] with impacts that go beyond the feeling of fatigue [5 6]. In addition to wanting their fatigue reduced, and a return to meaningful activities[7], patients want their experience of fatigue to be validated [8]. However, many patients report feeling that others, including clinicians, do not take fatigue seriously[9]

While fatigue is common in medical conditions, its presence correlates poorly with disease severity [10-13] and it commonly persists after the disease has been brought under control[14]. There appear to be similarities in fatigue across medical conditions, including similarities in experience and impairment [9]. Current models of fatigue include biological [15] and psychosocial factors[1 11], with increasing interest in the role of altered signalling between the brain and body[16-19]. There are currently no licensed drug treatments for fatigue in long-term conditions.

Non-pharmacological interventions have been developed to overcome fatigue in medical conditions. These include interventions focusing on physical activity (either managing or increasing activity), those that are more psychologically based, as well as a range of forms of non-invasive stimulation, body-mind practices and nutritional supplementation. In practice, many fatigue rehabilitation and self-management programmes contain multiple components. As fatigue is increasingly understood in terms of processes in the body, brain, and signalling between the two[16 18 19], these different types of non-pharmacological interventions described above are scientifically plausible. However, to many patients with fatigue this rationale is often not apparent. Thus, proposed interventions may be seen as illogical (physical exercise when they are already exhausted), stigmatising (psychological interventions implying fatigue is “all in the mind” or can be overcome just by thinking differently) or inappropriate (body-mind interventions being too “alternative”). These conceptual barriers to engagement with interventions are an important aspect of this problem[20].

We found two published network meta-analyses (NMA) of non-pharmacological interventions for fatigue in specific conditions: multiple sclerosis (113 studies) [21]and post-stroke (10 studies)[22] as well as one meta-analysis of physical activity interventions across multiple conditions[23] . We found no examples of NMA of the same intervention

type across different conditions, suggesting that generalisability across conditions is a largely unanswered question. We therefore conducted a systematic review and network meta-analysis to investigate the clinical effectiveness of non-pharmacological interventions for fatigue in long term conditions more generally. This study was conducted in response to a commissioned call from the UK National Institute of Health & Care Research and comprises one part of a larger evidence synthesis regarding fatigue in long term conditions that includes health economic and qualitative components; these have been submitted for publication separately.

Methods

This systematic review was conducted and reported in accordance with the Cochrane Handbook for Systematic Reviews of interventions [24] and the Preferred Reporting Items for Systematic review and Meta-Analysis guidelines. [25] The study eligibility criteria used the PICOS framework. The protocol for this review was registered with the CRD PROSPERO database CRD42023440141. The following alteration from the published protocol was applied: a limitation on included studies to countries with comparable healthcare systems to the UK.

Patient and public involvement

This review included extensive patient and public involvement (PPI). Two of the investigators were appointed on the basis of their lived experience of fatigue in long term medical conditions. In addition, we convened 5 focus groups involving 25 people with fatigue associated with long term conditions with the primary purpose of ensuring that any assumptions made about grouping interventions or conditions in the statistical analysis were compatible with patients' experiences.

Participants of focus groups were recruited by advertisement through national peer support organisations and community organisations in South Yorkshire. We invited and recruited purposively to obtain a diverse mixture of long-term conditions and ethnic heritage. Ethics approval was obtained for the focus group study (HRA and Health and Care Research Wales, reference 23/SC/0292).

Focus groups were co-led by PPI investigators (DC and SM) and KF, participants consented to participation and groups were recorded and transcribed for analysis. The focus groups explored important issues in relation to the conduct of the review, particularly the similarities and differences in experience of fatigue between conditions and between interventions. From this, focus groups discussed the appropriateness of combining studies across different conditions. Discussions also considered issues

around acceptability and feasibility of different interventions and guidance on framing and content of dissemination materials for patients and professionals.

Study eligibility criteria

To be eligible for inclusion, studies had to be randomised controlled trials that met the following criteria for population, intervention comparator, outcome and setting.

Population

Adults with a long-term condition, using the NHS definition as “an illness that cannot be cured but that can usually be controlled with medicines or other treatments”. The commissioning brief specifically excluded fatigue in people with cancer, in relation to or following from infection (HIV, Hepatitis C, Long Covid and ME/Chronic Fatigue Syndrome) or resulting from injuries or developmental disorders. It also excluded conditions in which symptoms, rather than observable pathology, were the defining features (e.g. fibromyalgia or irritable bowel syndrome).

Interventions

We included studies of any non-pharmacological intervention in which a stated explicit aim or primary outcome was to address fatigue. These included behavioural, exercise based, and nutritional interventions as well as a range of forms of non-invasive stimulation. We excluded interventions that were specific to a condition (e.g. pulmonary rehabilitation in lung disease) or to a problem other than fatigue (e.g. vestibular rehabilitation for balance problems in people with multiple sclerosis). Interventions could be delivered face-to-face or at a distance and included technology-assisted interventions.

Comparators

Comparators were “usual care”, waiting list control, sham or placebo (for stimulation or nutritional interventions), another non-pharmacological intervention or attentional control such as education or information.

Outcomes

Primary outcome: we required that studies reported an established measure for fatigue. We allocated three time points for follow up. These were end of treatment, short term (up to 3 months after the end of treatment), and long term (more than 3 months after the end of treatment). Where studies reported multiple long term time points, we extracted data for each of these, with the primary analysis using the longest follow up data.

Setting

Studies could be conducted in primary, secondary, or community-based settings, however we only included studies which could feasibly be delivered in an outpatient or community-based setting. We excluded studies set in countries with healthcare systems that are not comparable to the UK.

Information sources

A comprehensive search of bibliographic databases to identify randomised controlled trials (RCTs) was conducted in September-October 2023 and updated in September 2024. Search strategies combined free-text and thesaurus terms related to long-term conditions (both specific conditions and general terms such as “chronic disease” and “long-term illness”), and terms for fatigue measures (specifically named scales, and general terms for fatigue and assessment). Methodological search filters were used to identify RCTs. No date or language limits were applied to the search. All searches were performed on the following databases: Ovid MEDLINE, Embase (via Ovid), CINAHL (via EBSCO), APA Psycinfo (via Ovid), Web of Science Core Collection (Science Citation Index and Social Sciences Citation Index). Additionally, the Cochrane Central Register of Controlled Trials (CENTRAL) was searched for RCTs, and the Cochrane Database of Systematic Reviews (CDSR) was searched for systematic reviews. All databases were searched from inception to the respective search dates. There was no limit on date of study inclusion. Details of the search strategies are in Supplemental methods 1

Study selection and data collection

We carried out a two-stage sifting process for inclusion of studies, (title/abstract then full paper sift), using Covidence (Veritas Health Innovation) to manage the selection process. 3 reviewers initially reviewed 10% of titles and abstracts according to pre-specified inclusion and exclusion criteria. Issues relating to ambiguity of any criteria were resolved by team discussion. All remaining titles and abstracts were then scrutinised independently by two reviewers (Cohen’s kappa 0.58). Full texts of potentially eligible studies were then assessed for eligibility. Discrepancies were resolved by discussion between the two reviewers in consultation with a third investigator (CB) if required. The most common discrepancies were concerned with the cut-off criteria for inclusion where boundaries were blurred, for example whether the intervention focus was managing fatigue or whether fatigue was one of multiple secondary outcomes in a general condition self-management intervention. The update search was sifted using the same eligibility criteria.

Two reviewers (JL & GR) extracted the following data, with intervention characteristics using the 'Template for Intervention Description and Replication statement' (TIDieR) [26]. Data extraction aimed to reflect sources of complexity such as: population differences e.g. diagnostic criteria of the included long-term conditions; the use of multiple components within interventions; the expertise and skills of those delivering and receiving the intervention; the intervention context including method and intensity of delivery; settings; timepoints of outcome measurement; attrition. Results (estimates and corresponding standard errors (SE), standard deviations (SD), confidence intervals (CI) or inter quartile ranges (IQR)) were also extracted by one of two reviewers (JL & GR), and double checked by the other. Given the large numbers of included studies it was not feasible to contact the authors of included studies to enquire about missing or incomplete data or data that was only included graphically. Interventions were coded into categories using the method described below.

Risk of Bias Assessment of included studies

Risk of bias assessment of all studies included in the NMA of the present review was undertaken using an adapted version 2 of the Cochrane risk-of-bias tool (RoB2) for RCTs [27]. For pragmatic reasons relating to the volume of studies included in the NMA in the present review we adapted the RoB2 tool to facilitate quicker completion, reducing the number of signalling questions from 22 to 15 within five domains. A full description of these methods is presented in Supplemental methods 2.

GRADE assessment

Review findings were synthesised using an adaptation of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework[28] to assess the quality of the evidence (certainty in the evidence) for fatigue for each intervention compared to usual care, at each of the three timepoints analysed in the NMA. We adapted GRADE to incorporate elements of CINeMA,[29] a framework largely based on GRADE, modified to facilitate network meta-analysis. Whilst we adopted the assessment framework of CINeMA (e.g. methods of assessing heterogeneity and inconsistency), we used a Bayesian approach to analysis rather than the current CINeMA analysis platform. We used a framework based on risk of bias, inconsistency, imprecision and heterogeneity. We used a threshold of an SMD of 0.34 as clinically meaningful (see below for rationale). A full description of the methods used for the GRADE assessment is provided in Supplemental methods 3.

Classification of conditions

An initial description of the condition (checked against exclusion criteria) was generated for all extracted studies. These were aggregated into broad disease categories (e.g. musculoskeletal disorders). Within neurological disorders, multiple sclerosis and stroke were kept separate from other neurological disorders.

Classification of interventions

This followed an iterative inductive approach. First a simple description of the interventions in each arm was recorded by during data extraction. Next a clinical investigator reviewed these to generate an initial classification with draft criteria for each category. The same investigator then reviewed the full-text descriptions of interventions and classified them using the draft criteria: during this process the criteria were edited and refined following discussions with other clinical investigators. These criteria were then reviewed and tested (for a sample of behavioural interventions) by independent checking of categorisation. Differences were resolved by discussion. The final criteria (Supplemental methods 4) were then re-applied to all included studies. In parallel with this, we grouped the individual intervention categories into higher level groups to produce a hierarchical taxonomy. We took this approach as many interventions had multiple (often overlapping) components although in varying amounts.

Use of patient focus group and other qualitative data to inform our analysis

From the patient focus groups and a parallel qualitative evidence synthesis (Booth, personal communication) we identified three key observations to guide decisions about inclusion of interventions and conditions for analysis. These were: (1) The experience of fatigue is multifaceted and different for each individual; differences (and similarities) are as evident within conditions as between conditions, (2) while few focus group participants had experience of specific interventions for fatigue, none of those discussed was unacceptable to most participants, (3) personal circumstances and experience were important in valuing interventions. These observations informed our study design choices to carry out the primary analysis across conditions, to have no a priori restriction on interventions and to recognise the importance of personal context in recommendations arising from the analysis. Additional data relating to the focus groups is provided in Supplemental methods 5

Statistical Analysis

The primary analysis consisted of three separate NMAs, each corresponding to a different follow-up time point. We used standardised mean difference (SMD) of the change in fatigue outcomes from baseline as the measure of effect, evaluated using Hedge's correction for small studies. The detailed methodology is described in Supplemental methods 6. We generated networks of evidence at the three time points (end of treatment, short term and longer term) and conducted an NMA at each time point, using a random-effects model in view of the heterogeneity of study design, intervention and population[30]. Parameters of the random-effects model were estimated using a Bayesian framework, with non-informative parameter priors. All analyses were conducted using WinBUGS [31] via the R package, R2WinBUGS [32]. Results are presented as the posterior median treatment effects and 95% credible intervals (CrI). Study heterogeneity was assessed and interpreted using established categories [33]. Consistency was checked by comparing the posterior mean residual deviance from the unrelated mean effects model and the NMA model; and node-splitting analysis[34]

We conducted three secondary analyses. These were (1) to examine the sensitivity of the findings to different rules about preferred time point in longer term follow up studies; (2) to examine condition (or condition-group) specific networks and (3) to exclude studies identified as pilot or feasibility studies. Finally, in order to translate findings from the SMD into clinically meaningful values we took the estimated clinically important difference on the Fatigue Severity Scale (FSS) [35] and mapped it via an estimate of the baseline SD of studies within the EOT network which used FSS in order to calculate the corresponding clinically meaningful SMD.

Results

After de-duplication, 10108 titles and abstracts were reviewed. From these, 1068 full-text articles were assessed for eligibility, of which 118 studies reported in 120 manuscripts were eligible for inclusion. Of these, 88 studies, reported in 90 manuscripts, were included in the NMA (see figure 1 and Supplemental results 1). The 30 studies not included in the NMA are listed in Supplemental results 2 with reasons for non-inclusion in Supplemental results 3. Timepoints at which included studies reported results are in Supplemental results 4

Medical Conditions

The most common condition was multiple sclerosis (51 studies). There were 6 studies in stroke and 5 in other neurological conditions. 20 studies involved a range of musculoskeletal and connective tissue disorders ranging from osteoarthritis to systemic sclerosis. The remaining studies included inflammatory bowel disease (6) chronic kidney disease (3) and diabetes, hypothyroidism, heart disease and psoriasis (1 each).

Interventions

Table 1 shows the distribution of interventions by conditions. The most common intervention was CBT based interventions (19 studies). Other self-management interventions were energy conserving fatigue management (11), activating fatigue management (3) and general self-management (6). 28 interventions were focused on physical activity including supervised exercise (14), unsupervised exercise (7) and physical activity promotion (7). Other intervention categories were less common, often with single instances of distinct interventions within a category. Interventions were delivered to individuals and to groups, using in person, phone and online formats. Duration of the interventions ranged from three weeks to six months, although most behavioural interventions lasted between 6 and 12 weeks. More detailed descriptions of interventions content and delivery by study are provided in Supplemental results 5-7.

Risk of Bias

An overall summary of the risk of bias assessments is presented in Figure 2. Individual study risk of bias is reported in Supplemental results 6 and 7. Overall, whilst the body of evidence contains some larger trials, many of the studies are small, under-powered or pilot/feasibility studies. Furthermore, the large majority of trials involved at least one behavioural arm (e.g. physical activity or self-management) for which blinding was impossible because of the nature of the intervention, resulting in high risk of bias judgements in accordance with the RoB v2.0 guidance[27]. A summary of key findings by domain is presented below.

Risk of bias from the randomisation process:

Whilst all included studies described themselves as randomised controlled trials, nearly a quarter of the studies did not provide enough detail on the method of randomisation to make a judgement on whether there was a potential risk of bias. Of the studies that were judged to be at high risk of bias for randomisation, this was mostly due to the use of simple randomisation (alternate or manual). One study used a matched control group as a third arm, and another created an additional control arm after randomisation for participants who declined their allocated interventions.

Risk of bias due to blinding:

Blinding was rarely possible due to the nature of the interventions, most of which were behavioural. Whilst we acknowledge this practical restriction on study design, this still introduces a risk of bias. Lack of blinding of participants and care givers was the most common risk of bias across all studies. Where blinding was possible, e.g. studies of interventions with placebo or sham controls, it was not conducted in all cases.

Risk of bias due to missing outcome data:

The sample size in only half of the studies was based on a power calculation. Many of the studies that did not use a power calculation were reported by the authors to be underpowered. Around a quarter of studies reported high attrition (>20%), and for many of these, the withdrawals were not balanced between study arms.

Risk of bias from measurement of the outcome:

Around a half of the studies were at low risk of bias for measurement of outcome, due to blinding of outcome assessment. In the remaining studies, blinding of those conducting the outcome assessment was either specifically reported to have *not* been conducted, or did not provide details on the process.

Risk of bias from selective reporting:

The majority of studies were reported to be on trials registries, mostly NCT or ISRCTN. It was not possible to locate protocols for many studies within the time and resources of the review, and we therefore loosened our criteria, using the study plans on the trials registries to make our judgements where a full protocol was not readily accessible. Where there was a protocol or study plan identified, outcomes were mostly analysed as per the protocol.

Primary analysis

Network geometry

Network diagrams for the primary analysis at the different time points are shown in Figure 3. The networks contained 27 connected interventions (including control interventions) at the end of treatment, 16 at short term and 13 at long term follow up. They were evidenced from 84 studies (6636 participants), 24 studies (1849 participants) and 18 studies (2322 participants) respectively. To ensure connectivity of the networks, the “Control” node includes “Control”, “Placebo” and “Sham” interventions. “Information and education” is also included as a comparator rather than an intervention.

Synthesis of results

Figures 4 and 5 show the predicted SMDs for each intervention within the networks at each time point. A negative SMD indicates a reduction in fatigue relative to usual care. Within each of the forest plots, the final group ("Other") represents interventions typically included as comparator interventions. When assessing for inconsistency within the networks, no statistically significant inconsistency was detected within the primary analysis, (see Supplemental statistical data).

Relative to usual care, CBT-based interventions showed statistically significant reductions in fatigue at end of treatment (SMD -0.63, 95% CrI -0.87 to -0.4, 17 studies) and long term follow up (-0.4, -0.63 to -0.21,9 studies). The reduction at short term, with fewer studies was smaller and not statistically significant (-0.17, -0.42 to 0.06, 7 studies). Active fatigue management showed a statistically significant reductions in fatigue at end of treatment -0.77 (-1.2 to -0.32, 3 studies) but this was not sustained to short term (2 studies) and no studies reported long term follow up. Conservative self-management showed no statistically significant change in fatigue at end of treatment (-0.2, -0.52 to 0.12, 10 studies), short term (-0.13, -0.51 to 0.25, 7 studies) or long term (-0.42, -0.9 to 0.09, 3 studies). Mindfulness-based interventions showed statistically significant reductions in fatigue at end of treatment (-0.59, -0.99 to -0.18, 3 studies) and long term (-0.54, -0.99 to -0.11, 1 study).

Physical activity promotion showed significant reduction in fatigue at all three time points: end of treatment (-0.32, -0.62 to -0.01,7 studies), short term (-0.51, -0.84 to -0.17, 1 study) and long term (-0.52, -0.86 to -0.18, 2 studies). Supervised exercise showed statistically significant reductions in fatigue at end of treatment (-0.51, -0.74 to -0.28, 14 studies) but SMDs at short term (-0.44, -0.89 to 0.003, 3 studies) and long term (-0.41, -0.91 to 0.09, 2 studies), while of comparable magnitude, were not statistically significant.

Non-invasive stimulation studies were few in number and small in size (14 studies, 228 participants). While observed effects at end of treatment were large, only 5 studies (72 participants) reported effects at short term and 1 study (11 participants) reported longer term follow up. Nutritional studies reported end of treatment results only. Estimated effect sizes in the NMA for non-invasive stimulation and nutritional studies appear larger than reported in the original papers because SMDs are estimated relative to usual care, while these were compared to sham or placebo which in turn had a greater effect than usual care.

In each of the primary analyses, there was moderate heterogeneity indicating potentially varying treatment effects between studies. The standard deviation of the between study heterogeneity was greatest in the end of treatment analysis (0.256, 0.175 to 0.354) and comparable within the short and longer term networks (0.079, 0.004 to 0.308) and (0.096, 0.005 to 0.356) respectively. This suggests that there are generally smaller differences between the study design, interventions and populations in the short and longer term networks compared to the end of treatment network.

Sensitivity analysis:

Results of the sensitivity analysis are presented in Supplemental statistical data

Studies with multiple follow up time points after 3 months

Five studies included within the long-term analysis had data available from more than one time point after 3 months. Re-analysing the longer term data, instead using the shortest follow up point after 3 months had minimal impact on the results of the NMA

Sensitivity analysis: condition specific analyses

Due to the sparsity of evidence other than for multiple sclerosis, meaningful networks could only be constructed for the following conditions or condition groups: multiple sclerosis (at all three time points), musculoskeletal (end of treatment and long term), and inflammatory bowel disease, kidney disease and stroke (end of treatment only). The networks were small other than for multiple sclerosis so predicted treatment effects were generally associated with large uncertainty.

Sensitivity analysis: exclusion of pilot and feasibility studies

Reanalysis after removal of pilot and feasibility studies had minimal impact of the results of the NMA, although it did result in the exclusion of some interventions from the networks.

Clinically important difference

We estimated that a clinically important difference of 3.6 points on the Fatigue Severity Scale (range 9-63) [35] was equivalent to a SMD in the network meta-analysis of 0.34. This indicates that the effect sizes which reached statistical significance were also likely to be clinically meaningful.

The certainty of the evidence for the observed intervention effects using our adapted GRADE framework is summarised below for all timepoints.

The certainty of the evidence for the observed intervention effects at short term and long term follow up is summarised in table 2. In summary, at long term (more than 3

months after end of treatment) the evidence for physical activity promotion (interventions which supported individuals to increase physical activity) was rated as moderate. The evidence for CBT-based interventions and mindfulness was rated as low. The strength of evidence for all other interventions was rated as very low.

Discussion

Summary of main findings

Non-pharmacological interventions for fatigue in long term conditions other than multiple sclerosis have received relatively little attention in terms of large well conducted randomised studies, and have rarely been conducted across conditions. Nevertheless, we found evidence of effectiveness of interventions that increase physical activity or are based on cognitive behavioural therapy. We found no significant benefit from approaches to self-management in fatigue which focused on energy conservation. These findings appeared relatively consistent across conditions in keeping with other evidence of similarities in fatigue across conditions. The evidence generally carries high risk of bias, although this is at least due to taking a strict approach to judgement of risk of bias involving blinding.

Strengths and limitations

Strengths of this review include the broad scope both of eligible conditions and non-pharmacological interventions. This was underpinned by extensive patient and public involvement to ensure that assumptions made by researchers were concordant with the lived experience of people with fatigue in long term conditions. We used network meta-analysis to combine evidence across multiple conditions and interventions to maximise the available information in light of our focus groups and qualitative evidence synthesis that identified substantial similarities across conditions.

This review was limited by issues common to other reviews of complex interventions relating to eligibility of studies, choice of time points, categorisation of interventions and the large number of small studies. We identified many studies that included fatigue as one of multiple outcomes. Our inclusion criteria were restricted to studies where fatigue was the primary focus (in terms of either the population, the proposed mechanism of intervention, or the primary outcome). However, this created a grey area, particularly with self-management type interventions, where subjective judgement and resolution through discussion was often required. It is possible that another review team might have operationalised this differently. Although we took this relatively strict approach to inclusion, the small number of studies of general condition self-management which did

meet our inclusion criteria showed no significant effect, suggesting this approach was justified.

The timepoints at which outcomes were measured varied between studies. We anchored timepoints to the expected end of treatment rather than enrolment. In practice this meant that while the boundary between short term and long term treatment had a similar relationship to time of enrolment within studies with similar durations of intervention, this was not necessarily the case comparing across interventions. As the networks are sparse, results of the statistical analyses may be affected were the timepoint categories different. In particular, we considered that studies with longer follow up may be penalised relative to studies with shorter long term follow up due to attrition of effect or follow up, however the sensitivity analysis found no significant evidence of this.

The majority of studies were of behavioural interventions, often using pragmatic designs, and therefore blinding of participants was not possible. Risk of bias was therefore rated as high for almost all studies. The evidence base includes studies with heterogenous interventions, comparators and timepoints. Many interventions comprised of multiple components, some of which were common to interventions across categories. We were not able to conduct a component NMA due to limited data. Rather we developed a classification of interventions and applied a best-fit principle of allocation. In some cases, this may have obscured results – for instance the small category of Mind-body interventions included several studies where relaxation was used as a low intensity comparator intervention. Further, many different fatigue scales were used to measure outcomes across studies. This necessitated statistical standardisation and may have increased uncertainty due to the inherent differences between scales used due to the potential variability in focus of the different fatigue scales. Future trials in this area would benefit from more standardised methodology, to reduce the observed uncertainty and enable more confident interpretation of results across studies. Many studies were small, including pilot/feasibility studies, however excluding pilot and feasibility studies had little effect on the key findings. A few studies evaluated emerging treatments, in particular non-invasive transcranial and vagus nerve stimulation. These showed potentially large short term effects, and whilst they are still at an experimental stage they do appear to warrant further research.

Relationship to existing research

This was the first transdiagnostic review of multiple non-pharmacological interventions for long term conditions although we were aware of two previously published reviews in

multiple sclerosis [21]and stroke [22]. We applied stricter inclusion criteria in comparison to these reviews, in order to focus on fatigue outcomes. We identified one transdiagnostic review of physical activity promotion for fatigue which found sustained benefits with an estimated SMD slightly larger than those from our NMA[23]. We also restricted studies to those conducted within Western healthcare systems and culture to maximise transferability to those systems.

Implications for practice, policy and research

The review findings provide evidence for the effectiveness of interventions that promoted an increase in physical activity or were based on CBT. While effects were observed across different long-term conditions, all interventions were delivered within single conditions. We found some evidence for mindfulness based intervention and some forms of non-invasive stimulation which may warrant further research. We found no single clear best intervention and from our parallel focus group work and qualitative evidence synthesis recognise that offering patients a choice of interventions is better than aiming for a single best treatment for all. We recommend that further research focuses on delivery of interventions in a transdiagnostic format.

Conclusion

Interventions which support individuals to increase physical activity or that are based on cognitive behavioural are effective in reducing fatigue in people with long-term medical conditions. Strength of the evidence for these is moderate to low. Although there are relatively few studies in any condition other than multiple sclerosis, the magnitude of effect appears similar across different conditions.

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Conflict of Interest

The authors declare that they have o conflict of interests

Data-sharing statement

Search and data extraction tables from the systematic review will be made available on a public server at the University of Sheffield on publication of relevant studies.

Ethics statement

Ethics approval was obtained for the focus group study from HRA and Health and Care Research Wales, reference 23/SC/0292.

Table 1 Distribution of interventions by medical condition

		Long tern Condition								
	Intervention	MS	Stroke	Neuro	MSK	Kidney	IBD	Endo.	Other	Total
Exercise-based (N=30)	Exercise Supervised	12 [36-45]	-	1 [46]	1 [47]	-	-	-	2 [48 49]	16
	Exercise Unsupervised	4 [42 50-52]	-	-	3 [53-55]	-	-	-	-	7
	Physical activity promotion	3 [52 56 57]	-	-	4 [47 54 58 59]	-	-	-	-	7
Self - management (N=40)	CBT-based intervention	7 [60-66]	3 [67-69]	1 [70]	3 [20 58 71]	2 [72 73]	2 [74 75]	1 [76]	-	19
	Active Fatigue Self-Management	1 [77]	1 [78]	-	1 [79]	-	-	-	-	3
	Conservative Fatigue Self-Management	8 [80-87]	-	1 [88]	1 [89]	1 [90]	-	-	-	11
	General Self-Management	1 [86]	1 [78]	-	4 [91-94]	-	-	-	-	6
	Rehabilitation	1 [95]	-	-	-	-	-	-	-	1
Mind & Body (N=14)	Mind-Body	7 [65 84 87 96-98]	-	1 [99]	2 [55 100]	-	-	-	-	10
	Mindfulness based	2 [52 101]	-	-	-	-	1 [102]	-	-	3
	Other Psychological	-	1 [69]	-	-	-	-	-	-	1
Stimulation (N=14)	External stimulation	4 [103-106]	-	-	-	-	-	-	-	4
	Acupuncture-type	-	-	1 [107]	-	-	1 [108]	-	-	2
	Aromatheapy	-	-	-	-	-	-	1 [109]	-	1
	Transcranial Stimulation	4 [110-113]	-	-	-	-	-	-	-	4
	Vagal Nerve Stimulation	-	-	-	2 [114 115]	-	-	-	-	2
	Remote Ischaemic Conditioning	-	1 [116]	-	-	-	-	-	-	1
Nutritional (N=6)	Nutritional Supplement	1 [117]	-	-	1 [118]	-	2 [119 120]	-	-	4
	Diet	1 [121]	-	-	-	-	-	-	-	1
	Plant-based	1 [122]	-	-	-	-	-	-	-	1
	Total	57	7	5	22	3	6	2	2	104

Table 2 Summary of risk of GRADE evidence: fatigue as outcome at long term follow up (at least 13 weeks after end of treatment)

Intervention	Summary of findings	Quality of evidence	Reason for grading up or down
Behavioural			
Physical activity promotion	Evidence of a medium effect from 2 studies with 159 participants	Moderate	RoB - down 1
CBT based intervention	Evidence of a small effect from 9 studies with 640 participants	Low	RoB - down 1; Inconsistency - down 1
Mindfulness –based intervention	Evidence of a medium effect from 1 study with 76 participants	Low	RoB - down 1; Inconsistency - down 1
General self-management	Non significant evidence of a small effect from 3 studies with 231 participants	Very low	RoB - down 1; Inconsistency - down 1; Imprecision - down 1; Heterogeneity - down 1
Fatigue management (conservative)	Non significant evidence of a small effect from 3 studies with 175 participants	Very low	RoB - down 1; Inconsistency - down 1; Imprecision - down 1; Heterogeneity - down 1
Exercise (supervised)	Non significant evidence of a small effect from 2 studies with 79 participants	Very low	RoB - down 1; Inconsistency - down 1; Imprecision - down 1; Heterogeneity - down 1
Mind-body intervention	Non significant evidence of unsubstantial effect from 2 studies with 60 participants	Very low	RoB - down 1; Inconsistency - down 1; Imprecision - down 2; Heterogeneity - down 2
Other psychological	Non significant evidence of unsubstantial effect from 1 study with 45 participants	Very low	RoB - down 1; Inconsistency - down 1; Imprecision - down 2; Heterogeneity - down 2
Non-invasive Stimulation			
Remote ischaemic conditioning	Evidence of a large effect from 1 study with 11 participants	Very low	RoB - down 1; Inconsistency - down 1; Heterogeneity - down 1

Figure titles and Legends

Figure 1 PRISMA Flow Diagram

Figure 2 Summary of risk of bias for all included studies

Figure 3

Network geometry for A) end of treatment, B) short term, and C) long term analyses, respectively, indicating the number of participants who received each intervention (size of node) and the number of studies contributing to the direct evidence and comparisons between interventions (thickness of line). D) Key of intervention coding used in network geometry.

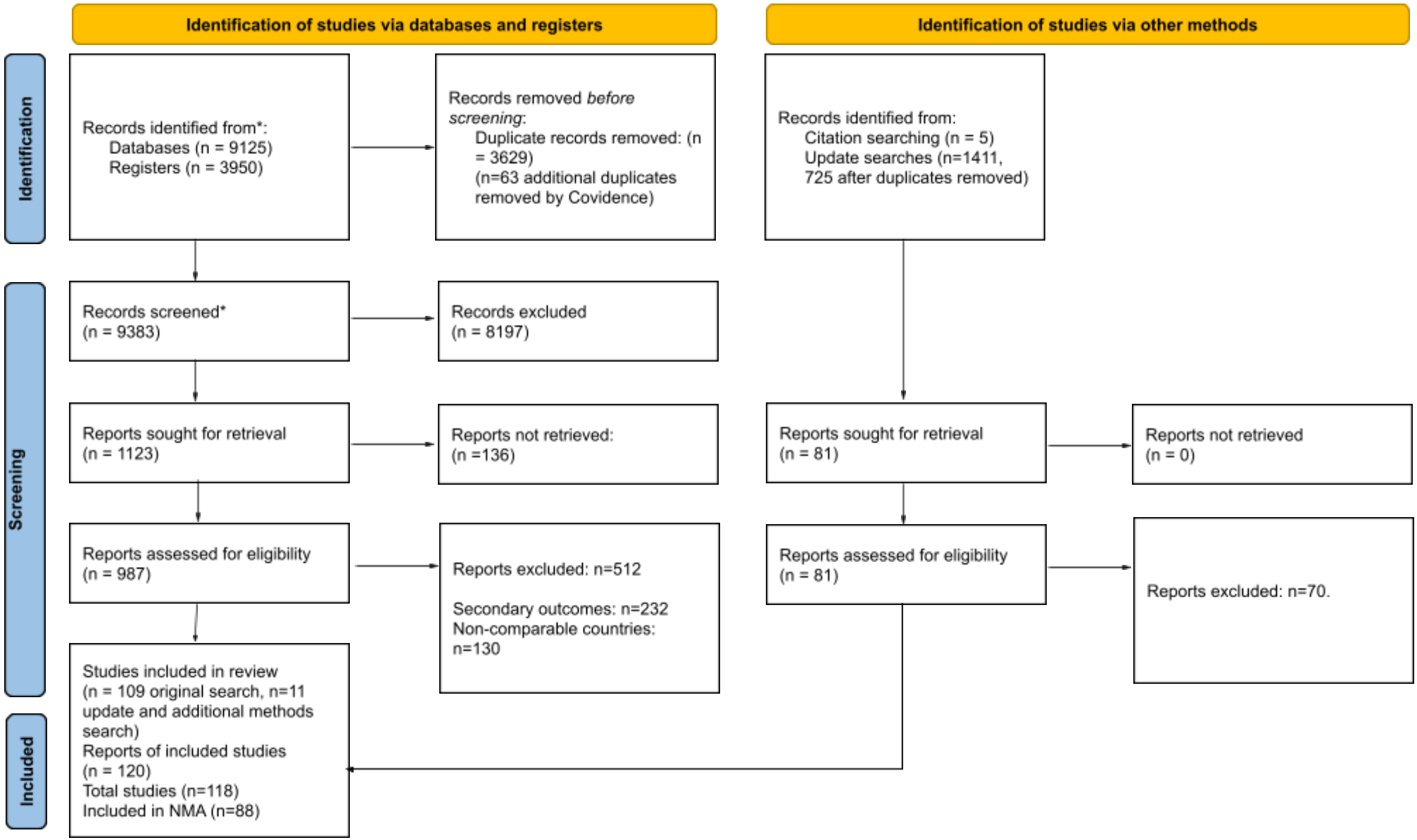
Figure 4

Predicted effects on fatigue outcomes of interventions, relative to usual care, at end of treatment, with 95% credible intervals (CrI). The number of participants (n) and the number of studies (N studies) are given for context. Broad intervention categorisation is also presented to aid interpretation (Behavioural, Stimulation, Nutritional, and Other). The “control” node is displayed as this functioned to ensure connectivity of the network, but this is not an active intervention for consideration/recommendation.

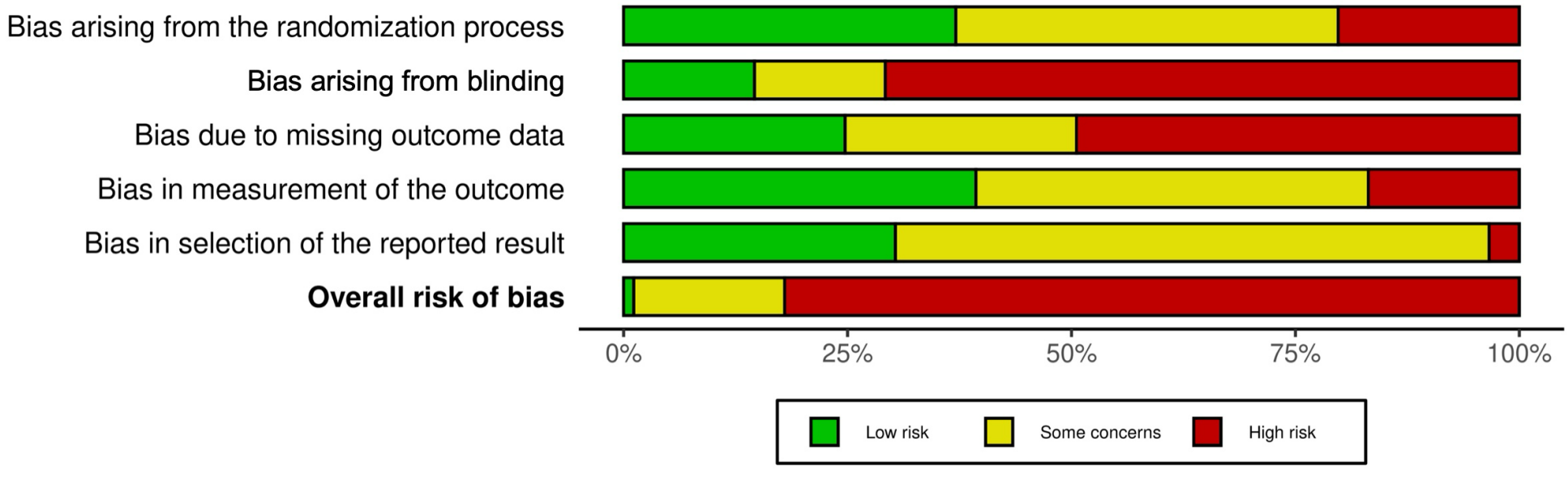
Figure 5

Predicted effects on fatigue outcomes of interventions, relative to usual care, at A) short term and B) long term follow up, with 95% credible intervals (CrI). The number of participants (n) and the number of studies (N studies) are given for context. The “control” node is displayed as this functioned to ensure connectivity of the network, but this is not an active intervention for consideration/recommendation.

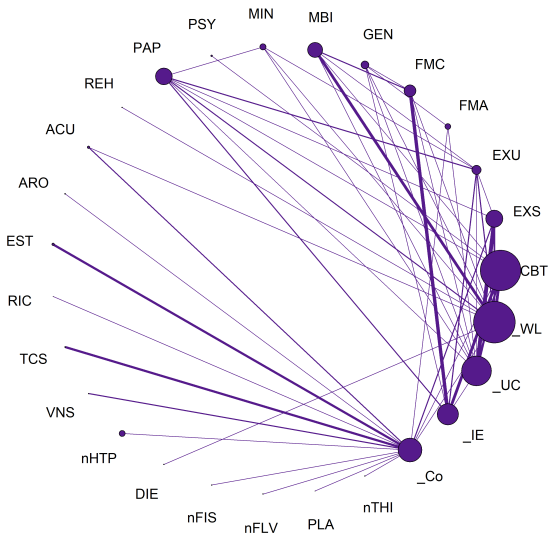
PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources



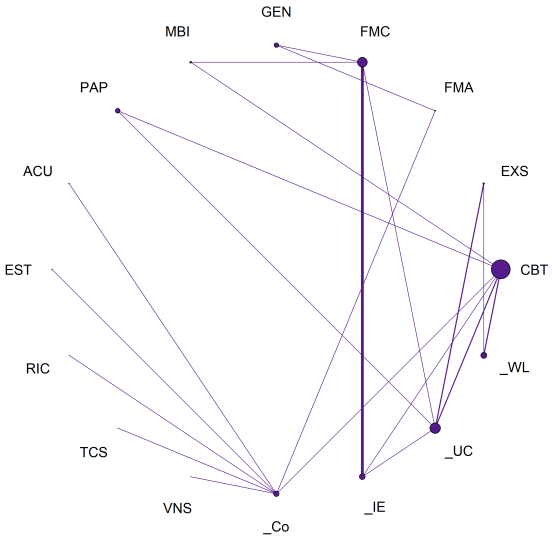
*Results for individual databases included in appendix; **Inter-rater Cohen's kappa for title/abstract 0.58, all records were double or triple sifted.
Source: Page MJ, et al. BMJ 2021;372:n71. doi: 10.1136/bmj.n71;


Bias arising from the randomization process
Bias arising from blinding
Bias due to missing outcome data
Bias in measurement of the outcome
Bias in selection of the reported result
Overall risk of bias
0%
25%
50%
75%
100%
Low risk
Some concerns
High risk

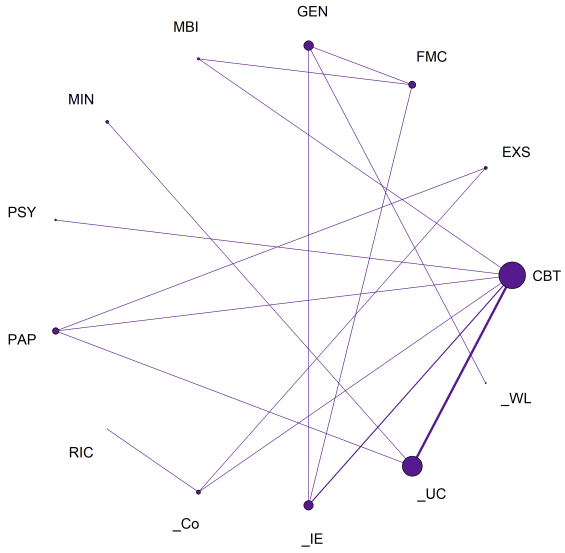
A



B



C

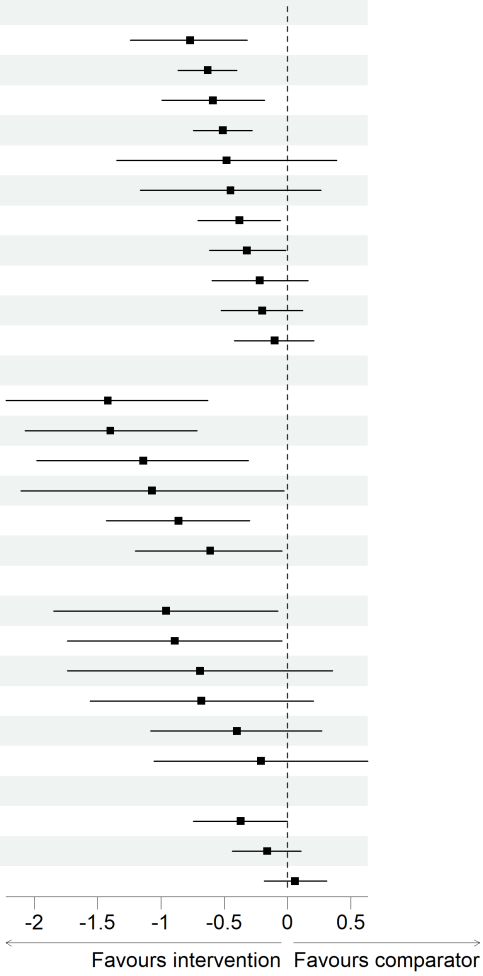


Code	Intervention
_Co	Control
_IE	Info/ Education
_UC	Usual care
_WL	Wait list
ACU	Acupuncture/ pressure
ARO	Aromatherapy
CBT	CBT-fatigue
DIE	Diet
EST	External stimulation
EXS	Exercise (supervised)
EXU	Exercise (unsupervised)
FMA	Fatigue management (active)
FMC	Fatigue management (conservative)
GEN	General self management
MBI	Mind-body intervention
MIN	Mindfulness based
nFIS	Fish Oil
nFLV	Flavenoid (Cocoa)
nHTP	5-HTP
nTHI	Thiamine
PAP	Physical activity promotion
PLA	Plant-based
PSY	Other psychological
REH	Non-specific rehabilitation
RIC	Remote Ischaemic Conditioning
TCS	Transcranial Stimulation
VNS	Vagal Stimulation

D

Treatment	SMD	95% CrI	n	(N studies)
Behavioural				
Fatigue management (active)	-0.77	-1.243 to -0.32	147	(3)
CBT-fatigue	-0.63	-0.865 to -0.402	995	(17)
Mindfulness based	-0.59	-0.994 to -0.182	155	(3)
Exercise (supervised)	-0.51	-0.744 to -0.281	424	(14)
Non-specific rehabilitation	-0.48	-1.351 to 0.388	18	(1)
Other psychological	-0.45	-1.164 to 0.263	45	(1)
Exercise (unsupervised)	-0.38	-0.71 to -0.058	230	(7)
Physical activity promotion	-0.32	-0.617 to -0.014	415	(7)
General self management	-0.22	-0.598 to 0.162	196	(5)
Fatigue management (conservative)	-0.2	-0.524 to 0.12	292	(10)
Mind-body intervention	-0.1	-0.421 to 0.209	373	(9)
Stimulation				
Vagal Stimulation	-1.42	-2.226 to -0.629	25	(2)
Transcranial Stimulation	-1.4	-2.075 to -0.716	34	(4)
Aromatherapy	-1.14	-1.982 to -0.309	27	(1)
Remote Ischaemic Conditioning	-1.07	-2.108 to -0.026	11	(1)
External stimulation	-0.86	-1.433 to -0.3	66	(4)
Acupuncture/ pressure	-0.61	-1.202 to -0.043	65	(2)
Nutritional				
Thiamine	-0.96	-1.849 to -0.076	20	(1)
Fish Oil	-0.89	-1.74 to -0.044	25	(1)
Plant-based	-0.69	-1.741 to 0.357	12	(1)
Flavenoid (Cocoa)	-0.68	-1.559 to 0.207	19	(1)
5-HTP	-0.4	-1.083 to 0.27	152	(1)
Diet	-0.21	-1.056 to 0.635	20	(1)
Other				
Control	-0.37	-0.745 to -0.001	590	(23)
Info/ Education	-0.16	-0.437 to 0.107	524	(15)
Waitlist control	0.06	-0.184 to 0.311	1022	(23)

Heterogeneity: between-study SD is 0.256 (95% CrI 0.175 to 0.354)



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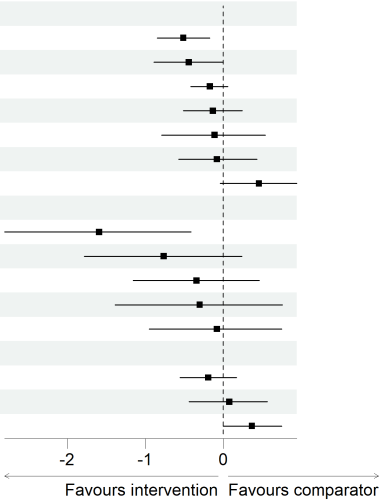
A

Treatment	SMD	95% CrI	n	(N studies)
Behavioural				
Physical activity promotion	-0.51	-0.844 to -0.171	121	(1)
Exercise (supervised)	-0.44	-0.888 to 0.003	48	(3)
CBT-fatigue	-0.17	-0.415 to 0.062	467	(7)
Fatigue management (conservative)	-0.13	-0.508 to 0.246	243	(7)
Fatigue management (active)	-0.11	-0.789 to 0.544	32	(2)
General self management	-0.08	-0.568 to 0.434	116	(2)
Mind-body intervention	0.46	-0.038 to 0.946	51	(2)
Stimulation				
Vagal Stimulation	-1.59	-2.803 to -0.409	12	(1)
Remote Ischaemic Conditioning	-0.76	-1.78 to 0.241	11	(1)
External stimulation	-0.34	-1.155 to 0.463	22	(1)
Transcranial Stimulation	-0.3	-1.384 to 0.763	9	(1)
Acupuncture/ pressure	-0.08	-0.949 to 0.751	18	(1)
Other				
Info/ Education	-0.19	-0.553 to 0.174	145	(6)
Control	0.08	-0.436 to 0.567	137	(7)
Waitlist control	0.37	0 to 0.752	153	(3)

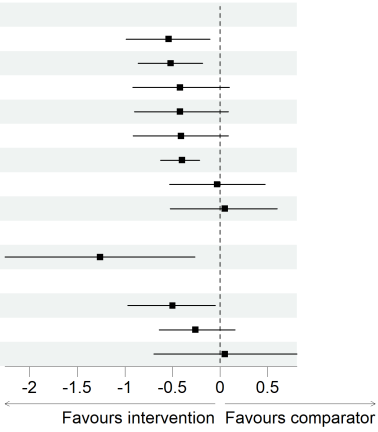
Heterogeneity: between-study SD is 0.079 (95% CrI 0.004 to 0.308)



B

Treatment	SMD	95% CrI	n	(N studies)
Behavioural				
Mindfulness based	-0.54	-0.99 to -0.105	76	(1)
Physical activity promotion	-0.52	-0.862 to -0.184	159	(2)
General self management	-0.42	-0.919 to 0.099	231	(3)
Fatigue management (conservative)	-0.42	-0.9 to 0.087	175	(3)
Exercise (supervised)	-0.41	-0.913 to 0.086	79	(2)
CBT-fatigue	-0.4	-0.627 to -0.214	640	(9)
Mind-body intervention	-0.03	-0.53 to 0.472	60	(2)
Other psychological	0.05	-0.525 to 0.602	45	(1)
Stimulation				
Remote Ischaemic Conditioning	-1.26	-2.261 to -0.264	11	(1)
Other				
Control	-0.5	-0.971 to -0.051	104	(3)
Info/ Education	-0.26	-0.642 to 0.156	229	(4)
Waitlist control	0.05	-0.697 to 0.808	34	(1)

Heterogeneity: between-study SD is 0.096 (95% CrI 0.005 to 0.356)



References

1. Goërtz YMJ, Braamse AMJ, Spruit MA, et al. Fatigue in patients with chronic disease: results from the population-based Lifelines Cohort Study. *Scientific Reports* 2021;11(1) doi: 10.1038/s41598-021-00337-z

2. Skau S, Sundberg K, Kuhn HG. A Proposal for a Unifying Set of Definitions of Fatigue. *Front Psychol* 2021;12:739764. doi: 10.3389/fpsyg.2021.739764 [published Online First: 20211013]

3. Chaudhuri A, Behan PO. Fatigue in neurological disorders. *Lancet* 2004;363(9413):978-88. doi: 10.1016/s0140-6736(04)15794-2

4. Jaime-Lara RB, Koons BC, Matura LA, et al. A Qualitative Metasynthesis of the Experience of Fatigue Across Five Chronic Conditions. *Journal of Pain and Symptom Management* 2020;59(6):1320-43. doi: 10.1016/j.jpainsymman.2019.12.358

5. Bootsma TI, Schellekens MPJ, Woezik RAM, et al. Experiencing and responding to chronic cancer-related fatigue: A meta-ethnography of qualitative research. *Psycho-Oncology* 2020;29(2):241-50. doi: 10.1002/pon.5213

6. Bloem AEM, Mostard RLM, Stoot N, et al. Perceptions of fatigue in patients with idiopathic pulmonary fibrosis or sarcoidosis. *Journal of Thoracic Disease* 2021;13(8):4872-84. doi: 10.21037/jtd-21-462

7. Askari S, Pappas C, De Smit C, et al. Comparison of goals set by people with multiple sclerosis during two fatigue management interventions. *Scandinavian Journal of Occupational Therapy* 2022:1-9. doi: 10.1080/11038128.2022.2051600

8. Power M, Arafa N, Wenz A, et al. Perceptions of fatigue and fatigue management interventions among people with multiple sclerosis: a systematic literature review and narrative synthesis. *International Journal of Therapy and Rehabilitation* 2021;28(6):1-21. doi: 10.12968/ijtr.2020.0144

9. Whitehead LC, Unahi K, Burrell B, et al. The Experience of Fatigue Across Long-Term Conditions: A Qualitative Meta-Synthesis. *Journal of Pain and Symptom Management* 2016;52(1):131-43.e1. doi: 10.1016/j.jpainsymman.2016.02.013

10. Goërtz YMJ, Spruit MA, Van 'T Hul AJ, et al. Fatigue is highly prevalent in patients with COPD and correlates poorly with the degree of airflow limitation. *Therapeutic Advances in Respiratory Disease* 2019;13:175346661987812. doi: 10.1177/1753466619878128

11. Druce KL, Basu N. Predictors of fatigue in rheumatoid arthritis. *Rheumatology* 2019;58(Supplement_5):v29-v34. doi: 10.1093/rheumatology/kez346

12. Kessing D, Denollet J, Widdershoven J, et al. Fatigue and self-care in patients with chronic heart failure. *European Journal of Cardiovascular Nursing* 2016;15(5):337-44. doi: 10.1177/1474515115575834

13. Boot EM, van de Camp S, Maaijwee NA, et al. Neuroimaging Parameters Are Not Associated With Chronic Post-stroke Fatigue in Young Stroke Patients. *Front Neurol* 2022;13:831357. doi: 10.3389/fneur.2022.831357 [published Online First: 20220428]

14. Druce KL, Bhattacharya Y, Jones GT, et al. Most patients who reach disease remission following anti-TNF therapy continue to report fatigue: results from the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis. *Rheumatology* 2016;55(10):1786-90. doi: 10.1093/rheumatology/kew241

15. Matura LA, Malone S, Jaime-Lara R, et al. A Systematic Review of Biological Mechanisms of Fatigue in Chronic Illness. *Biological Research for Nursing* 2018;20(4):410-21. doi: 10.1177/1099800418764326

16. Kuppuswamy A. The Neurobiology of Pathological Fatigue: New Models, New Questions. *The Neuroscientist* 2022;28(3):238-53. doi: 10.1177/1073858420985447

17. Bonaz B, Lane RD, Oshinsky ML, et al. Diseases, Disorders, and Comorbidities of Interoception. *Trends in Neurosciences* 2021;44(1):39-51. doi: 10.1016/j.tins.2020.09.009

18. Druce KL, McBeth J. Central sensitization predicts greater fatigue independently of musculoskeletal pain. *Rheumatology (Oxford)* 2019;58(11):1923-27. doi: 10.1093/rheumatology/kez028 [published Online First: 2019/03/01]

19. Gonzalez Campo C, Salamone PC, Rodríguez-Arriagada N, et al. Fatigue in multiple sclerosis is associated with multimodal interoceptive abnormalities. *Multiple Sclerosis Journal* 2020;26(14):1845-53. doi: 10.1177/1352458519888881

20. Hewlett S, Almeida C, Ambler N, et al. Group cognitive–behavioural programme to reduce the impact of rheumatoid arthritis fatigue: the RAFT RCT with economic and qualitative evaluations. *Health Technol Assess* 2019;23(57):1-130. doi: 10.3310/hta23570

21. Harrison AM, Safari R, Mercer T, et al. Which exercise and behavioural interventions show most promise for treating fatigue in multiple sclerosis? A network meta-analysis. *Multiple Sclerosis Journal* 2021;27(11):1657-78. doi: 10.1177/1352458521996002

22. Su Y, Yuki M, Otsuki M. Non-Pharmacological Interventions for Post-Stroke Fatigue: Systematic Review and Network Meta-Analysis. *J Clin Med* 2020;9(3):621. doi: 10.3390/jcm9030621

23. Barakou I, Sakalidis KE, Abonie US, et al. Effectiveness of physical activity interventions on reducing perceived fatigue among adults with chronic conditions: a systematic review and meta-analysis of randomised controlled trials. *Sci Rep* 2023;13(1):14582. doi: 10.1038/s41598-023-41075-8 [published Online First: 20230904]

24. Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of Interventions version 6.5 (updated August 2024): Cochrane, 2024.

25. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71 [published Online First: 20210329]

26. Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014;348(mar07 3):g1687-g87. doi: 10.1136/bmj.g1687

27. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019:l4898. doi: 10.1136/bmj.l4898

28. Schünemann H, Brożek J, Guyatt G, et al. GRADE handbook for grading quality of evidence and strength of recommendations. Updated October 2013. The GRADE Working Group, 2013, 2021.

29. Dias S, Sutton AJ, Ades AE, et al. Evidence Synthesis for Decision Making 2:A Generalized Linear Modeling Framework for Pairwise and Network Meta-

analysis of Randomized Controlled Trials. *Medical Decision Making* 2013;33(5):607-17. doi: 10.1177/0272989x12458724

30. Lunn DJ, Thomas A, Best N, et al. WinBUGS-a Bayesian modelling framework: concepts, structure, and extensibility. *Statistics and computing* 2000;10(4):325-37.

31. Sturtz S, Ligges U, Gelman A. R2WinBUGS: a package for running WinBUGS from R. *Journal of Statistical software* 2005;12:1-16.

32. Ren S, Oakley JE, Stevens JW. Incorporating Genuine Prior Information about Between-Study Heterogeneity in Random Effects Pairwise and Network Meta-analyses. *Medical Decision Making* 2018;38(4):531-42. doi: 10.1177/0272989x18759488

33. Dias S, Welton NJ, Sutton AJ, et al. NICE Decision Support Unit Technical Support Documents. NICE DSU Technical Support Document 4: Inconsistency in Networks of Evidence Based on Randomised Controlled Trials. London: National Institute for Health and Care Excellence (NICE)

34. Nordin Å, Taft C, Lundgren-Nilsson Å, et al. Minimal important differences for fatigue patient reported outcome measures-a systematic review. *BMC Med Res Methodol* 2016;16:62. doi: 10.1186/s12874-016-0167-6 [published Online First: 2016/07/09]

35. Dalgas U, Stenager E, Jakobsen J, et al. Fatigue, mood and quality of life improve in MS patients after progressive resistance training. *Mult Scler* 2010;16(4):480-90. doi: 10.1177/1352458509360040 [published Online First: 20100301]

36. Englund S, Piehl F, Kierkegaard M. High-intensity resistance training in people with multiple sclerosis experiencing fatigue: A randomised controlled trial. *Mult Scler Relat Disord* 2022;68:104106. doi: 10.1016/j.msard.2022.104106 [published Online First: 20220813]

37. Escudero-Uribe S, Hochsprung A, Heredia-Camacho B, et al. Effect of Training Exercises Incorporating Mechanical Devices on Fatigue and Gait Pattern in Persons with Relapsing-Remitting Multiple Sclerosis. *Physiother Can* 2017;69(4):292-302. doi: 10.3138/ptc.2016-19

38. Feys P, Moumdjian L, Van Halewyck F, et al. Effects of an individual 12-week community-located "start-to-run" program on physical capacity, walking, fatigue, cognitive function, brain volumes, and structures in persons with multiple sclerosis. *Mult Scler* 2019;25(1):92-103. doi: 10.1177/1352458517740211 [published Online First: 20171108]

39. Gervasoni E, Cattaneo D, Jonsdottir J. Effect of treadmill training on fatigue in multiple sclerosis: a pilot study. *Int J Rehabil Res* 2014;37(1):54-60. doi: 10.1097/MRR.0000000000000034

40. Heine M, Verschuren O, Hoogervorst EL, et al. Does aerobic training alleviate fatigue and improve societal participation in patients with multiple sclerosis? A randomized controlled trial. *Mult Scler* 2017;23(11):1517-26. doi: 10.1177/1352458517696596 [published Online First: 20170522]

41. Kratz AL, Atalla M, Whibley D, et al. Calling Out MS Fatigue: Feasibility and Preliminary Effects of a Pilot Randomized Telephone-Delivered Exercise Intervention for Multiple Sclerosis Fatigue. *J Neurol Phys Ther* 2020;44(1):23-31. doi: 10.1097/NPT.0000000000000296

42. Langeskov-Christensen M, Hvid LG, Jensen HB, et al. Efficacy of high-intensity aerobic exercise on common multiple sclerosis symptoms. *Acta Neurol Scand* 2022;145(2):229-38. doi: 10.1111/ane.13540 [published Online First: 20211022]

43. Louie J, Baquie K, Offerman J, et al. Maximising Abilities, Negotiating and Generating Exercise options (MANAGE) in people with multiple sclerosis: A feasibility randomised controlled trial. *Clin Rehabil* 2022;36(4):498-510. doi: 10.1177/02692155211064949 [published Online First: 20211209]

44. McCullagh R, Fitzgerald AP, Murphy RP, et al. Long-term benefits of exercising on quality of life and fatigue in multiple sclerosis patients with mild disability: a pilot study. *Clin Rehabil* 2008;22(3):206-14. doi: 10.1177/0269215507082283

45. Ortiz-Rubio A, Cabrera-Martos I, Torres-Sanchez I, et al. Effects of a resistance training program on balance and fatigue perception in patients with Parkinson's disease: A randomized controlled trial. *Med Clin (Barc)* 2018;150(12):460-64. doi: 10.1016/j.medcli.2017.10.022 [published Online First: 20171122]

46. Kucharski D, Lange E, Ross AB, et al. Moderate-to-high intensity exercise with person-centered guidance influences fatigue in older adults with rheumatoid arthritis. *Rheumatol Int* 2019;39(9):1585-94. doi: 10.1007/s00296-019-04384-8 [published Online First: 20190720]

47. Diaz AJ, Rosety MA, Armario JC, et al. Regular Exercise Improved Fatigue and Musculoskeletal Pain in Young Adult Psoriatic Patients without Psoriatic Arthritis. *Nutrients* 2023;15(21) doi: 10.3390/nu15214563 [published Online First: 20231027]

48. Pozehl B, Duncan K, Hertzog M. The effects of exercise training on fatigue and dyspnea in heart failure. *Eur J Cardiovasc Nurs* 2008;7(2):127-32. doi: 10.1016/j.ejcnurse.2007.08.002 [published Online First: 20070927]

49. Geddes EL, Costello E, Raivel K, et al. The effects of a twelve-week home walking program on cardiovascular parameters and fatigue perception of individuals with multiple sclerosis: a pilot study. *Cardiopulm Phys Ther J* 2009;20(1):5-12.

50. Maurer M, Schuh K, Seibert S, et al. A randomized study to evaluate the effect of exercise on fatigue in people with relapsing-remitting multiple sclerosis treated with fingolimod. *Mult Scler J Exp Transl Clin* 2018;4(1):2055217318756688. doi: 10.1177/2055217318756688 [published Online First: 20180214]

51. Torkhani E, Dematte E, Slawinski J, et al. Improving Health of People With Multiple Sclerosis From a Multicenter Randomized Controlled Study in Parallel Groups: Preliminary Results on the Efficacy of a Mindfulness Intervention and Intention Implementation Associated With a Physical Activity Program. *Front Psychol* 2021;12:767784. doi: 10.3389/fpsyg.2021.767784 [published Online First: 20211224]

52. Durcan L, Wilson F, Cunnane G. The effect of exercise on sleep and fatigue in rheumatoid arthritis: a randomized controlled study. *J Rheumatol* 2014;41(10):1966-73. doi: 10.3899/jrheum.131282 [published Online First: 20140815]

53. Katz P, Margaretten M, Gregorich S, et al. Physical Activity to Reduce Fatigue in Rheumatoid Arthritis: A Randomized Controlled Trial. *Arthritis Care Res (Hoboken)* 2018;70(1):1-10. doi: 10.1002/acr.23230 [published Online First: 20171206]

54. Tench CM, McCarthy J, McCurdie I, et al. Fatigue in systemic lupus erythematosus: a randomized controlled trial of exercise. *Rheumatology (Oxford)*

2003;42(9):1050-4. doi: 10.1093/rheumatology/keg289 [published Online First: 20030416]

55. Lutz C, Kersten S, Haas CT. Short-Term and Long-Term Effects of an Exercise-Based Patient Education Programme in People with Multiple Sclerosis: A Pilot Study. *Mult Scler Int* 2017;2017:2826532. doi: 10.1155/2017/2826532 [published Online First: 20170816]
56. Turner AP, Hartoonian N, Sloan AP, et al. Improving fatigue and depression in individuals with multiple sclerosis using telephone-administered physical activity counseling. *J Consult Clin Psychol* 2016;84(4):297-309. doi: 10.1037/ccp0000086 [published Online First: 20160225]
57. Bachmair EM, Martin K, Aucott L, et al. Remotely delivered cognitive behavioural and personalised exercise interventions for fatigue severity and impact in inflammatory rheumatic diseases (LIFT): a multicentre, randomised, controlled, open-label, parallel-group trial. *Lancet Rheumatol* 2022;4(8):e534-e45. doi: 10.1016/S2665-9913(22)00156-4 [published Online First: 20220627]
58. Callahan LF, Cleveland RJ, Shreffler J, et al. Evaluation of active living every day in adults with arthritis. *Journal of Physical Activity and Health* 2014;11(2):285-96.
59. Ehde DM, Elzea JL, Verrall AM, et al. Efficacy of a Telephone-Delivered Self-Management Intervention for Persons With Multiple Sclerosis: A Randomized Controlled Trial With a One-Year Follow-Up. *Arch Phys Med Rehabil* 2015;96(11):1945-58 e2. doi: 10.1016/j.apmr.2015.07.015 [published Online First: 20150806]
60. Gay MC, Cassedanne F, Barbot F, et al. Long-term effectiveness of a cognitive behavioural therapy (CBT) in the management of fatigue in patients with relapsing remitting multiple sclerosis (RRMS): a multicentre, randomised, open-label, controlled trial versus standard care. *J Neurol Neurosurg Psychiatry* 2024;95(2):158-66. doi: 10.1136/jnnp-2023-331537 [published Online First: 20240111]
61. Moss-Morris R, McCrone P, Yardley L, et al. A pilot randomised controlled trial of an Internet-based cognitive behavioural therapy self-management programme (MS Invigor8) for multiple sclerosis fatigue. *Behav Res Ther* 2012;50(6):415-21. doi: 10.1016/j.brat.2012.03.001 [published Online First: 20120313]
62. Pottgen J, Moss-Morris R, Wendebourg JM, et al. Randomised controlled trial of a self-guided online fatigue intervention in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2018;89(9):970-76. doi: 10.1136/jnnp-2017-317463 [published Online First: 20180316]
63. Thomas S, Thomas PW, Kersten P, et al. A pragmatic parallel arm multi-centre randomised controlled trial to assess the effectiveness and cost-effectiveness of a group-based fatigue management programme (FACETS) for people with multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2013;84(10):1092-9. doi: 10.1136/jnnp-2012-303816 [published Online First: 20130521]
64. Van Kessel K, Moss-Morris R, Willoughby E, et al. A randomized controlled trial of cognitive behavior therapy for multiple sclerosis fatigue. *Biopsychosocial Science and Medicine* 2008;70(2):205-13.
65. van den Akker LE, Beckerman H, Collette EH, et al. Cognitive behavioral therapy positively affects fatigue in patients with multiple sclerosis: Results of a randomized controlled trial. *Multiple Sclerosis Journal* 2017;23(11):1542-53.
66. Mead G, Gillespie D, Barber M, et al. Post stroke intervention trial in fatigue (POSITIF): Randomised multicentre feasibility trial. *Clin Rehabil*

2022;36(12):1578-89. doi: 10.1177/02692155221113908 [published Online First: 20220721]

67. Nguyen S, Wong D, McKay A, et al. Cognitive behavioural therapy for post-stroke fatigue and sleep disturbance: a pilot randomised controlled trial with blind assessment. *Neuropsychol Rehabil* 2019;29(5):723-38. doi: 10.1080/09602011.2017.1326945 [published Online First: 20170519]
68. Zedlitz AM, Rietveld TC, Geurts AC, et al. Cognitive and graded activity training can alleviate persistent fatigue after stroke: a randomized, controlled trial. *Stroke* 2012;43(4):1046-51. doi: 10.1161/STROKEAHA.111.632117 [published Online First: 20120202]
69. Okkersen K, Jimenez-Moreno C, Wenninger S, et al. Cognitive behavioural therapy with optional graded exercise therapy in patients with severe fatigue with myotonic dystrophy type 1: a multicentre, single-blind, randomised trial. *Lancet Neurol* 2018;17(8):671-80. doi: 10.1016/S1474-4422(18)30203-5 [published Online First: 20180619]
70. Hewlett S, Ambler N, Almeida C, et al. Self-management of fatigue in rheumatoid arthritis: a randomised controlled trial of group cognitive-behavioural therapy. *Ann Rheum Dis* 2011;70(6):1060-7. doi: 10.1136/ard.2010.144691
71. Jhamb M, Steel JL, Yabes JG, et al. Effects of Technology Assisted Stepped Collaborative Care Intervention to Improve Symptoms in Patients Undergoing Hemodialysis: The TACcare Randomized Clinical Trial. *JAMA Intern Med* 2023;183(8):795-805. doi: 10.1001/jamainternmed.2023.2215
72. Picariello F, Moss-Morris R, Norton S, et al. Feasibility Trial of Cognitive Behavioral Therapy for Fatigue in Hemodialysis (BReF Intervention). *J Pain Symptom Manage* 2021;61(6):1234-46 e5. doi: 10.1016/j.jpainsymman.2020.10.005 [published Online First: 20201014]
73. Artom M, Czuber-Dochan W, Sturt J, et al. Cognitive-behavioural therapy for the management of inflammatory bowel disease-fatigue: a feasibility randomised controlled trial. *Pilot Feasibility Stud* 2019;5:145. doi: 10.1186/s40814-019-0538-y [published Online First: 20191210]
74. Bredero QM, Fleer J, Smink A, et al. Mindfulness-based cognitive therapy for fatigue in patients with inflammatory bowel disease: results of a Randomized Controlled Trial. *Mindfulness* 2023;14(1):19-32.
75. Menting J, Tack CJ, van Bon AC, et al. Web-based cognitive behavioural therapy blended with face-to-face sessions for chronic fatigue in type 1 diabetes: a multicentre randomised controlled trial. *Lancet Diabetes Endocrinol* 2017;5(6):448-56. doi: 10.1016/S2213-8587(17)30098-0 [published Online First: 20170424]
76. Rietberg MB, van Wegen EE, Eyssen IC, et al. Effects of multidisciplinary rehabilitation on chronic fatigue in multiple sclerosis: a randomized controlled trial. *PLoS ONE* 2014;9(9):e107710. doi: 10.1371/journal.pone.0107710 [published Online First: 20140918]
77. Clarke A, Barker-Collo SL, Feigin VL. Poststroke fatigue: does group education make a difference? A randomized pilot trial. *Top Stroke Rehabil* 2012;19(1):32-9. doi: 10.1310/tsr1901-32
78. Murphy SL, Chen YT, Alore M, et al. Effects of a Resilience-Building Energy Management Program on Fatigue and Other Symptoms in Systemic Sclerosis: A Randomized Controlled Trial. *Arthritis Care Res (Hoboken)* 2024;76(3):318-27. doi: 10.1002/acr.25253 [published Online First: 20240112]

79. Abonie US, Hettinga FJ. Effect of a Tailored Activity Pacing Intervention on Fatigue and Physical Activity Behaviours in Adults with Multiple Sclerosis. *Int J Environ Res Public Health* 2020;18(1) doi: 10.3390/ijerph18010017 [published Online First: 20201222]

80. Askari S, Kessler D, Smyth P, et al. Evaluating occupational performance coaching to support fatigue management for people with multiple sclerosis: A feasibility study. *Clin Rehabil* 2022;36(9):1244-56. doi: 10.1177/02692155221107074 [published Online First: 20220607]

81. Blikman LJ, van Meeteren J, Twisk JW, et al. Effectiveness of energy conservation management on fatigue and participation in multiple sclerosis: A randomized controlled trial. *Mult Scler* 2017;23(11):1527-41. doi: 10.1177/1352458517702751 [published Online First: 20170522]

82. Garcia Jalon EG, Lennon S, Peoples L, et al. Energy conservation for fatigue management in multiple sclerosis: a pilot randomized controlled trial. *Clin Rehabil* 2013;27(1):63-74. doi: 10.1177/0269215512446495 [published Online First: 20120702]

83. Hersche R, Weise A, Michel G, et al. Development and Preliminary Evaluation of a 3-Week Inpatient Energy Management Education Program for People with Multiple Sclerosis-Related Fatigue. *Int J MS Care* 2019;21(6):265-74. doi: 10.7224/1537-2073.2018-058

84. Hugos CL, Copperman LF, Fuller BE, et al. Clinical trial of a formal group fatigue program in multiple sclerosis. *Mult Scler* 2010;16(6):724-32. doi: 10.1177/1352458510364536 [published Online First: 20100407]

85. Hugos CL, Chen Z, Chen Y, et al. A multicenter randomized controlled trial of two group education programs for fatigue in multiple sclerosis: Short- and medium-term benefits. *Mult Scler* 2019;25(2):275-85. doi: 10.1177/1352458517745723 [published Online First: 20171211]

86. Kos D, Duportail M, Meirte J, et al. The effectiveness of a self-management occupational therapy intervention on activity performance in individuals with multiple sclerosis-related fatigue: a randomized-controlled trial. *Int J Rehabil Res* 2016;39(3):255-62. doi: 10.1097/MRR.0000000000000178

87. Ghahari S, Leigh Packer T, Passmore AE. Effectiveness of an online fatigue self-management programme for people with chronic neurological conditions: a randomized controlled trial. *Clin Rehabil* 2010;24(8):727-44. doi: 10.1177/0269215509360648 [published Online First: 20100611]

88. Murphy SL, Lyden AK, Smith DM, et al. Effects of a tailored activity pacing intervention on pain and fatigue for adults with osteoarthritis. *Am J Occup Ther* 2010;64(6):869-76. doi: 10.5014/ajot.2010.09198

89. Farragher JF, Ravani P, Manns B, et al. A pilot randomised controlled trial of an energy management programme for adults on maintenance haemodialysis: the fatigue-HD study. *BMJ Open* 2022;12(2):e051475. doi: 10.1136/bmjopen-2021-051475 [published Online First: 20220210]

90. Austin JS, Maisiak RS, Macrina DM, et al. Health outcome improvements in patients with systemic lupus erythematosus using two telephone counseling interventions. *Arthritis Care Res* 1996;9(5):391-9. doi: 10.1002/1529-0131(199610)9:5<391::aid-anr1790090508>3.0.co;2-v

91. Feldthusen C, Dean E, Forsblad-d'Elia H, et al. Effects of Person-Centered Physical Therapy on Fatigue-Related Variables in Persons With Rheumatoid Arthritis: A Randomized Controlled Trial. *Arch Phys Med Rehabil*

2016;97(1):26-36. doi: 10.1016/j.apmr.2015.09.022 [published Online First: 20151016]

92. Hammond A, Bryan J, Hardy A. Effects of a modular behavioural arthritis education programme: a pragmatic parallel-group randomized controlled trial. *Rheumatology (Oxford)* 2008;47(11):1712-8. doi: 10.1093/rheumatology/ken380 [published Online First: 20080924]

93. Khan F, Granville N, Malkani R, et al. Health-Related Quality of Life Improvements in Systemic Lupus Erythematosus Derived from a Digital Therapeutic Plus Tele-Health Coaching Intervention: Randomized Controlled Pilot Trial. *Journal of medical Internet research* 2020;22(10):e23868. doi: 10.2196/23868 [published Online First: 20201020]

94. De Giglio L, De Luca F, Prosperini L, et al. A low-cost cognitive rehabilitation with a commercial video game improves sustained attention and executive functions in multiple sclerosis: a pilot study. *Neurorehabil Neural Repair* 2015;29(5):453-61.

95. Fleming KM, Coote SB, Herring MP. The feasibility of Pilates to improve symptoms of anxiety, depression, and fatigue among people with Multiple Sclerosis: An eight-week randomized controlled pilot trial. *Psychology of Sport and Exercise* 2019;45:101573.

96. Fleming KM, Coote SB, Herring MP. Home-based Pilates for symptoms of anxiety, depression and fatigue among persons with multiple sclerosis: An 8-week randomized controlled trial. *Mult Scler* 2021;27(14):2267-79. doi: 10.1177/13524585211009216 [published Online First: 20210419]

97. Sgoifo A, Bignamini A, La Mantia L, et al. Integrated Imaginative Distention Therapy to Cope with Fatigue. DIMMI SI Study: The First Randomized Controlled Trial in Multiple Sclerosis. *Neurol Ther* 2017;6(2):213-23. doi: 10.1007/s40120-017-0081-9 [published Online First: 20170809]

98. Walter AA, Adams EV, Van Puymbroeck M, et al. Changes in Nonmotor Symptoms Following an 8-Week Yoga Intervention for People with Parkinson's Disease. *Int J Yoga Therap* 2019;29(1):91-99. doi: 10.17761/2019-00025 [published Online First: 20190322]

99. Callahan LF, Cleveland RJ, Altpeter M, et al. Evaluation of Tai Chi Program Effectiveness for People with Arthritis in the Community: A Randomized Controlled Trial. *J Aging Phys Act* 2016;24(1):101-10. doi: 10.1123/japa.2014-0211 [published Online First: 20150618]

100. Grossman P, Kappos L, Gensicke H, et al. MS quality of life, depression, and fatigue improve after mindfulness training: a randomized trial. *Neurology* 2010;75(13):1141-9. doi: 10.1212/WNL.0b013e3181f4d80d

101. Goren G, Schwartz D, Friger M, et al. Randomized Controlled Trial of Cognitive-Behavioral and Mindfulness-Based Stress Reduction on the Quality of Life of Patients With Crohn Disease. *Inflamm Bowel Dis* 2022;28(3):393-408. doi: 10.1093/ibd/izab083

102. Granja-Dominguez A, Hochsprung A, Luque-Moreno C, et al. Effects of pulsed electromagnetic field therapy on fatigue, walking performance, depression, and quality of life in adults with multiple sclerosis: a randomized placebo-controlled trial. *Braz J Phys Ther* 2022;26(5):100449. doi: 10.1016/j.bjpt.2022.100449 [published Online First: 20221013]

103. Mostert S, Kesselring J. Effect of pulsed magnetic field therapy on the level of fatigue in patients with multiple sclerosis--a randomized controlled trial. *Mult Scler* 2005;11(3):302-5. doi: 10.1191/1352458505ms1156oa

104. Piatkowski J, Kern S, Ziemssen T. Effect of BEMER magnetic field therapy on the level of fatigue in patients with multiple sclerosis: a randomized, double-blind controlled trial. *J Altern Complement Med* 2009;15(5):507-11. doi: 10.1089/acm.2008.0501

105. Voggenberger L, Bock M, Moser D, et al. Bright light therapy as a non-pharmacological treatment option for multiple sclerosis-related fatigue: A randomized sham-controlled trial. *Mult Scler J Exp Transl Clin* 2022;8(4):20552173221133262. doi: 10.1177/20552173221133262 [published Online First: 20221107]

106. Kluger BM, Rakowski D, Christian M, et al. Randomized, Controlled Trial of Acupuncture for Fatigue in Parkinson's Disease. *Mov Disord* 2016;31(7):1027-32. doi: 10.1002/mds.26597 [published Online First: 20160329]

107. Horta D, Lira A, Sanchez-Lloansi M, et al. A Prospective Pilot Randomized Study: Electroacupuncture vs. Sham Procedure for the Treatment of Fatigue in Patients With Quiescent Inflammatory Bowel Disease. *Inflamm Bowel Dis* 2020;26(3):484-92. doi: 10.1093/ibd/izz091

108. Hawkins J, Hires CY, Dunne EW, et al. Aromatherapy reduces fatigue among women with hypothyroidism: A randomized placebo-controlled clinical trial. *J Complement Integr Med* 2019;17(1) doi: 10.1515/jcim-2018-0229 [published Online First: 20190822]

109. Cancelli A, Cottone C, Giordani A, et al. Personalized, bilateral whole-body somatosensory cortex stimulation to relieve fatigue in multiple sclerosis. *Mult Scler* 2018;24(10):1366-74. doi: 10.1177/1352458517720528 [published Online First: 20170731]

110. Charvet LE, Dobbs B, Shaw MT, et al. Remotely supervised transcranial direct current stimulation for the treatment of fatigue in multiple sclerosis: Results from a randomized, sham-controlled trial. *Mult Scler* 2018;24(13):1760-69. doi: 10.1177/1352458517732842 [published Online First: 20170922]

111. Tecchio F, Cancelli A, Cottone C, et al. Brain Plasticity Effects of Neuromodulation Against Multiple Sclerosis Fatigue. *Front Neurol* 2015;6:141. doi: 10.3389/fneur.2015.00141 [published Online First: 20150703]

112. Salemi G, Vazzoler G, Ragonese P, et al. Application of tRNS to improve multiple sclerosis fatigue: a pilot, single-blind, sham-controlled study. *J Neural Transm (Vienna)* 2019;126(6):795-99. doi: 10.1007/s00702-019-02006-y [published Online First: 20190503]

113. Aranow C, Atish-Fregoso Y, Lesser M, et al. Transcutaneous auricular vagus nerve stimulation reduces pain and fatigue in patients with systemic lupus erythematosus: a randomised, double-blind, sham-controlled pilot trial. *Annals of the Rheumatic Diseases* 2021;80(2):203-08. doi: 10.1136/annrheumdis-2020-217872

114. Tarn J, Legg S, Mitchell S, et al. The Effects of Noninvasive Vagus Nerve Stimulation on Fatigue and Immune Responses in Patients With Primary Sjögren's Syndrome. *Neuromodulation: Technology at the Neural Interface* 2019;22(5):580-85. doi: https://doi.org/10.1111/ner.12879

115. Moyle DB, Kudiersky MN, Totton MN, et al. Remote ischaemic conditioning for fatigue after stroke (RICFAST): A pilot randomised controlled trial. *J Stroke Cerebrovasc Dis* 2023;32(12):107420. doi: 10.1016/j.jstrokecerebrovasdis.2023.107420 [published Online First: 20231011]

116. Coe S, Cossington J, Collett J, et al. A randomised double-blind placebo-controlled feasibility trial of flavonoid-rich cocoa for fatigue in people with relapsing and remitting multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2019;90(5):507-13. doi: 10.1136/jnnp-2018-319496 [published Online First: 20190304]

117. Arriens C, Hynan LS, Lerman RH, et al. Placebo-controlled randomized clinical trial of fish oil's impact on fatigue, quality of life, and disease activity in Systemic Lupus Erythematosus. *Nutr J* 2015;14:82. doi: 10.1186/s12937-015-0068-2 [published Online First: 20150818]

118. Bager P, Hvas CL, Rud CL, et al. Randomised clinical trial: high-dose oral thiamine versus placebo for chronic fatigue in patients with quiescent inflammatory bowel disease. *Aliment Pharmacol Ther* 2021;53(1):79-86. doi: 10.1111/apt.16166 [published Online First: 20201118]

119. Truyens M, Lobaton T, Ferrante M, et al. Effect of 5-Hydroxytryptophan on Fatigue in Quiescent Inflammatory Bowel Disease: A Randomized Controlled Trial. *Gastroenterology* 2022;163(5):1294-305 e3. doi: 10.1053/j.gastro.2022.07.052 [published Online First: 20220806]

120. Chase E, Chen V, Martin K, et al. A low-fat diet improves fatigue in multiple sclerosis: Results from a randomized controlled trial. *Mult Scler* 2023;29(13):1659-75. doi: 10.1177/13524585231208330

121. Johnson SK, Diamond BJ, Rausch S, et al. The effect of Ginkgo biloba on functional measures in multiple sclerosis: a pilot randomized controlled trial. *Explore (NY)* 2006;2(1):19-24. doi: 10.1016/j.explore.2005.10.007

1. Goërtz YMJ, Braamse AMJ, Spruit MA, et al. Fatigue in patients with chronic disease: results from the population-based Lifelines Cohort Study. *Scientific Reports* 2021;11(1) doi: 10.1038/s41598-021-00337-z

2. Skau S, Sundberg K, Kuhn HG. A Proposal for a Unifying Set of Definitions of Fatigue. *Front Psychol* 2021;12:739764. doi: 10.3389/fpsyg.2021.739764 [published Online First: 20211013]

3. Chaudhuri A, Behan PO. Fatigue in neurological disorders. *Lancet* 2004;363(9413):978-88. doi: 10.1016/s0140-6736(04)15794-2

4. Jaime-Lara RB, Koons BC, Matura LA, et al. A Qualitative Metasynthesis of the Experience of Fatigue Across Five Chronic Conditions. *Journal of Pain and Symptom Management* 2020;59(6):1320-43. doi: 10.1016/j.jpainsymman.2019.12.358

5. Bootsma TI, Schellekens MPJ, Woezik RAM, et al. Experiencing and responding to chronic cancer-related fatigue: A meta-ethnography of qualitative research. *Psycho-Oncology* 2020;29(2):241-50. doi: 10.1002/pon.5213

6. Bloem AEM, Mostard RLM, Stoot N, et al. Perceptions of fatigue in patients with idiopathic pulmonary fibrosis or sarcoidosis. *Journal of Thoracic Disease* 2021;13(8):4872-84. doi: 10.21037/jtd-21-462

7. Askari S, Pappas C, De Smit C, et al. Comparison of goals set by people with multiple sclerosis during two fatigue management interventions. *Scandinavian Journal of Occupational Therapy* 2022:1-9. doi: 10.1080/11038128.2022.2051600

8. Power M, Arafa N, Wenz A, et al. Perceptions of fatigue and fatigue management interventions among people with multiple sclerosis: a systematic literature review and narrative synthesis. *International Journal of Therapy and Rehabilitation* 2021;28(6):1-21. doi: 10.12968/ijtr.2020.0144

9. Whitehead LC, Unahi K, Burrell B, et al. The Experience of Fatigue Across Long-Term Conditions: A Qualitative Meta-Synthesis. *Journal of Pain and Symptom Management* 2016;52(1):131-43.e1. doi: 10.1016/j.jpainsymman.2016.02.013

10. Goërtz YMJ, Spruit MA, Van 'T Hul AJ, et al. Fatigue is highly prevalent in patients with COPD and correlates poorly with the degree of airflow limitation. *Therapeutic Advances in Respiratory Disease* 2019;13:175346661987812. doi: 10.1177/1753466619878128

11. Druce KL, Basu N. Predictors of fatigue in rheumatoid arthritis. *Rheumatology* 2019;58(Supplement_5):v29-v34. doi: 10.1093/rheumatology/kez346

12. Kessing D, Denollet J, Widdershoven J, et al. Fatigue and self-care in patients with chronic heart failure. *European Journal of Cardiovascular Nursing* 2016;15(5):337-44. doi: 10.1177/1474515115575834

13. Boot EM, van de Camp S, Maaijwee NA, et al. Neuroimaging Parameters Are Not Associated With Chronic Post-stroke Fatigue in Young Stroke Patients. *Front Neurol* 2022;13:831357. doi: 10.3389/fneur.2022.831357 [published Online First: 20220428]

14. Druce KL, Bhattacharya Y, Jones GT, et al. Most patients who reach disease remission following anti-TNF therapy continue to report fatigue: results from the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis. *Rheumatology* 2016;55(10):1786-90. doi: 10.1093/rheumatology/kew241

15. Matura LA, Malone S, Jaime-Lara R, et al. A Systematic Review of Biological Mechanisms of Fatigue in Chronic Illness. *Biological Research for Nursing* 2018;20(4):410-21. doi: 10.1177/1099800418764326

16. Kuppuswamy A. The Neurobiology of Pathological Fatigue: New Models, New Questions. *The Neuroscientist* 2022;28(3):238-53. doi: 10.1177/1073858420985447

17. Bonaz B, Lane RD, Oshinsky ML, et al. Diseases, Disorders, and Comorbidities of Interoception. *Trends in Neurosciences* 2021;44(1):39-51. doi: 10.1016/j.tins.2020.09.009

18. Druce KL, McBeth J. Central sensitization predicts greater fatigue independently of musculoskeletal pain. *Rheumatology (Oxford)* 2019;58(11):1923-27. doi: 10.1093/rheumatology/kez028 [published Online First: 2019/03/01]

19. Gonzalez Campo C, Salamone PC, Rodríguez-Arriagada N, et al. Fatigue in multiple sclerosis is associated with multimodal interoceptive abnormalities. *Multiple Sclerosis Journal* 2020;26(14):1845-53. doi: 10.1177/1352458519888881

20. Hewlett S, Almeida C, Ambler N, et al. Group cognitive–behavioural programme to reduce the impact of rheumatoid arthritis fatigue: the RAFT RCT with economic and qualitative evaluations. *Health Technol Assess* 2019;23(57):1-130. doi: 10.3310/hta23570

21. Harrison AM, Safari R, Mercer T, et al. Which exercise and behavioural interventions show most promise for treating fatigue in multiple sclerosis? A network meta-analysis. *Multiple Sclerosis Journal* 2021;27(11):1657-78. doi: 10.1177/1352458521996002

22. Su Y, Yuki M, Otsuki M. Non-Pharmacological Interventions for Post-Stroke Fatigue: Systematic Review and Network Meta-Analysis. *J Clin Med* 2020;9(3):621. doi: 10.3390/jcm9030621

23. Barakou I, Sakalidis KE, Abonie US, et al. Effectiveness of physical activity interventions on reducing perceived fatigue among adults with chronic conditions: a systematic review and meta-analysis of randomised controlled trials. *Sci Rep* 2023;13(1):14582. doi: 10.1038/s41598-023-41075-8 [published Online First: 20230904]

24. Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of Interventions version 6.5 (updated August 2024): Cochrane, 2024.

25. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71 [published Online First: 20210329]

26. Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014;348(mar07 3):g1687-g87. doi: 10.1136/bmj.g1687

27. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019:l4898. doi: 10.1136/bmj.l4898

28. Schünemann H, Brożek J, Guyatt G, et al. GRADE handbook for grading quality of evidence and strength of recommendations. Updated October 2013. The GRADE Working Group, 2013, 2021.

29. Nikolakopoulou A, Higgins JPT, Papakonstantinou T, et al. CINeMA: An approach for assessing confidence in the results of a network meta-analysis. *PLoS Med* 2020;17(4):e1003082. doi: 10.1371/journal.pmed.1003082 [published Online First: 20200403]

30. Dias S, Sutton AJ, Ades AE, et al. Evidence Synthesis for Decision Making 2:A Generalized Linear Modeling Framework for Pairwise and Network Meta-analysis of Randomized Controlled Trials. *Medical Decision Making* 2013;33(5):607-17. doi: 10.1177/0272989x12458724

31. Lunn DJ, Thomas A, Best N, et al. WinBUGS-a Bayesian modelling framework: concepts, structure, and extensibility. *Statistics and computing* 2000;10(4):325-37.

32. Sturtz S, Ligges U, Gelman A. R2WinBUGS: a package for running WinBUGS from R. *Journal of Statistical software* 2005;12:1-16.

33. Ren S, Oakley JE, Stevens JW. Incorporating Genuine Prior Information about Between-Study Heterogeneity in Random Effects Pairwise and Network Meta-analyses. *Medical Decision Making* 2018;38(4):531-42. doi: 10.1177/0272989x18759488

34. Dias S, Welton NJ, Sutton AJ, et al. NICE Decision Support Unit Technical Support Documents. NICE DSU Technical Support Document 4: Inconsistency in Networks of Evidence Based on Randomised Controlled Trials. London: National Institute for Health and Care Excellence (NICE)

35. Nordin Å, Taft C, Lundgren-Nilsson Å, et al. Minimal important differences for fatigue patient reported outcome measures-a systematic review. *BMC Med Res Methodol* 2016;16:62. doi: 10.1186/s12874-016-0167-6 [published Online First: 2016/07/09]

36. Dalgas U, Stenager E, Jakobsen J, et al. Fatigue, mood and quality of life improve in MS patients after progressive resistance training. *Mult Scler* 2010;16(4):480-90. doi: 10.1177/1352458509360040 [published Online First: 20100301]

37. Englund S, Piehl F, Kierkegaard M. High-intensity resistance training in people with multiple sclerosis experiencing fatigue: A randomised controlled trial. *Mult Scler Relat Disord* 2022;68:104106. doi: 10.1016/j.msard.2022.104106 [published Online First: 20220813]

38. Escudero-Uribe S, Hochsprung A, Heredia-Camacho B, et al. Effect of Training Exercises Incorporating Mechanical Devices on Fatigue and Gait Pattern in Persons with Relapsing-Remitting Multiple Sclerosis. *Physiother Can* 2017;69(4):292-302. doi: 10.3138/ptc.2016-19

39. Feys P, Moumdjian L, Van Halewyck F, et al. Effects of an individual 12-week community-located "start-to-run" program on physical capacity, walking, fatigue, cognitive function, brain volumes, and structures in persons with multiple sclerosis. *Mult Scler* 2019;25(1):92-103. doi: 10.1177/1352458517740211 [published Online First: 20171108]

40. Gervasoni E, Cattaneo D, Jonsdottir J. Effect of treadmill training on fatigue in multiple sclerosis: a pilot study. *Int J Rehabil Res* 2014;37(1):54-60. doi: 10.1097/MRR.0000000000000034

41. Heine M, Verschuren O, Hoogervorst EL, et al. Does aerobic training alleviate fatigue and improve societal participation in patients with multiple sclerosis? A randomized controlled trial. *Mult Scler* 2017;23(11):1517-26. doi: 10.1177/1352458517696596 [published Online First: 20170522]

42. Kratz AL, Atalla M, Whibley D, et al. Calling Out MS Fatigue: Feasibility and Preliminary Effects of a Pilot Randomized Telephone-Delivered Exercise Intervention for Multiple Sclerosis Fatigue. *J Neurol Phys Ther* 2020;44(1):23-31. doi: 10.1097/NPT.0000000000000296

43. Langeskov-Christensen M, Hvid LG, Jensen HB, et al. Efficacy of high-intensity aerobic exercise on common multiple sclerosis symptoms. *Acta Neurol Scand* 2022;145(2):229-38. doi: 10.1111/ane.13540 [published Online First: 20211022]

44. Louie J, Baquie K, Offerman J, et al. Maximising Abilities, Negotiating and Generating Exercise options (MANAGE) in people with multiple sclerosis: A feasibility randomised controlled trial. *Clin Rehabil* 2022;36(4):498-510. doi: 10.1177/02692155211064949 [published Online First: 20211209]

45. McCullagh R, Fitzgerald AP, Murphy RP, et al. Long-term benefits of exercising on quality of life and fatigue in multiple sclerosis patients with mild disability: a pilot study. *Clin Rehabil* 2008;22(3):206-14. doi: 10.1177/0269215507082283

46. Ortiz-Rubio A, Cabrera-Martos I, Torres-Sanchez I, et al. Effects of a resistance training program on balance and fatigue perception in patients with Parkinson's disease: A randomized controlled trial. *Med Clin (Barc)* 2018;150(12):460-64. doi: 10.1016/j.medcli.2017.10.022 [published Online First: 20171122]

47. Kucharski D, Lange E, Ross AB, et al. Moderate-to-high intensity exercise with person-centered guidance influences fatigue in older adults with rheumatoid arthritis. *Rheumatol Int* 2019;39(9):1585-94. doi: 10.1007/s00296-019-04384-8 [published Online First: 20190720]

48. Diaz AJ, Rosety MA, Armario JC, et al. Regular Exercise Improved Fatigue and Musculoskeletal Pain in Young Adult Psoriatic Patients without Psoriatic

Arthritis. *Nutrients* 2023;15(21) doi: 10.3390/nu15214563 [published Online First: 20231027]

49. Pozehl B, Duncan K, Hertzog M. The effects of exercise training on fatigue and dyspnea in heart failure. *Eur J Cardiovasc Nurs* 2008;7(2):127-32. doi: 10.1016/j.ejcnurse.2007.08.002 [published Online First: 20070927]
50. Geddes EL, Costello E, Raivel K, et al. The effects of a twelve-week home walking program on cardiovascular parameters and fatigue perception of individuals with multiple sclerosis: a pilot study. *Cardiopulm Phys Ther J* 2009;20(1):5-12.
51. Maurer M, Schuh K, Seibert S, et al. A randomized study to evaluate the effect of exercise on fatigue in people with relapsing-remitting multiple sclerosis treated with fingolimod. *Mult Scler J Exp Transl Clin* 2018;4(1):2055217318756688. doi: 10.1177/2055217318756688 [published Online First: 20180214]
52. Torkhani E, Dematte E, Slawinski J, et al. Improving Health of People With Multiple Sclerosis From a Multicenter Randomized Controlled Study in Parallel Groups: Preliminary Results on the Efficacy of a Mindfulness Intervention and Intention Implementation Associated With a Physical Activity Program. *Front Psychol* 2021;12:767784. doi: 10.3389/fpsyg.2021.767784 [published Online First: 20211224]
53. Durcan L, Wilson F, Cunnane G. The effect of exercise on sleep and fatigue in rheumatoid arthritis: a randomized controlled study. *J Rheumatol* 2014;41(10):1966-73. doi: 10.3899/jrheum.131282 [published Online First: 20140815]
54. Katz P, Margaretten M, Gregorich S, et al. Physical Activity to Reduce Fatigue in Rheumatoid Arthritis: A Randomized Controlled Trial. *Arthritis Care Res (Hoboken)* 2018;70(1):1-10. doi: 10.1002/acr.23230 [published Online First: 20171206]
55. Tench CM, McCarthy J, McCurdie I, et al. Fatigue in systemic lupus erythematosus: a randomized controlled trial of exercise. *Rheumatology (Oxford)* 2003;42(9):1050-4. doi: 10.1093/rheumatology/keg289 [published Online First: 20030416]
56. Lutz C, Kersten S, Haas CT. Short-Term and Long-Term Effects of an Exercise-Based Patient Education Programme in People with Multiple Sclerosis: A Pilot Study. *Mult Scler Int* 2017;2017:2826532. doi: 10.1155/2017/2826532 [published Online First: 20170816]
57. Turner AP, Hartoonian N, Sloan AP, et al. Improving fatigue and depression in individuals with multiple sclerosis using telephone-administered physical activity counseling. *J Consult Clin Psychol* 2016;84(4):297-309. doi: 10.1037/ccp0000086 [published Online First: 20160225]
58. Bachmair EM, Martin K, Aucott L, et al. Remotely delivered cognitive behavioural and personalised exercise interventions for fatigue severity and impact in inflammatory rheumatic diseases (LIFT): a multicentre, randomised, controlled, open-label, parallel-group trial. *Lancet Rheumatol* 2022;4(8):e534-e45. doi: 10.1016/S2665-9913(22)00156-4 [published Online First: 20220627]
59. Callahan LF, Cleveland RJ, Shreffler J, et al. Evaluation of active living every day in adults with arthritis. *Journal of Physical Activity and Health* 2014;11(2):285-96.
60. Ehde DM, Elzea JL, Verrall AM, et al. Efficacy of a Telephone-Delivered Self-Management Intervention for Persons With Multiple Sclerosis: A Randomized Controlled Trial With a One-Year Follow-Up. *Arch Phys Med Rehabil*

2015;96(11):1945-58 e2. doi: 10.1016/j.apmr.2015.07.015 [published Online First: 20150806]

61. Gay MC, Cassedanne F, Barbot F, et al. Long-term effectiveness of a cognitive behavioural therapy (CBT) in the management of fatigue in patients with relapsing remitting multiple sclerosis (RRMS): a multicentre, randomised, open-label, controlled trial versus standard care. *J Neurol Neurosurg Psychiatry* 2024;95(2):158-66. doi: 10.1136/jnnp-2023-331537 [published Online First: 20240111]

62. Moss-Morris R, McCrone P, Yardley L, et al. A pilot randomised controlled trial of an Internet-based cognitive behavioural therapy self-management programme (MS Invigor8) for multiple sclerosis fatigue. *Behav Res Ther* 2012;50(6):415-21. doi: 10.1016/j.brat.2012.03.001 [published Online First: 20120313]

63. Pottgen J, Moss-Morris R, Wendebourg JM, et al. Randomised controlled trial of a self-guided online fatigue intervention in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2018;89(9):970-76. doi: 10.1136/jnnp-2017-317463 [published Online First: 20180316]

64. Thomas S, Thomas PW, Kersten P, et al. A pragmatic parallel arm multi-centre randomised controlled trial to assess the effectiveness and cost-effectiveness of a group-based fatigue management programme (FACETS) for people with multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2013;84(10):1092-9. doi: 10.1136/jnnp-2012-303816 [published Online First: 20130521]

65. Van Kessel K, Moss-Morris R, Willoughby E, et al. A randomized controlled trial of cognitive behavior therapy for multiple sclerosis fatigue. *Biopsychosocial Science and Medicine* 2008;70(2):205-13.

66. van den Akker LE, Beckerman H, Collette EH, et al. Cognitive behavioral therapy positively affects fatigue in patients with multiple sclerosis: Results of a randomized controlled trial. *Multiple Sclerosis Journal* 2017;23(11):1542-53.

67. Mead G, Gillespie D, Barber M, et al. Post stroke intervention trial in fatigue (POSITIF): Randomised multicentre feasibility trial. *Clin Rehabil* 2022;36(12):1578-89. doi: 10.1177/02692155221113908 [published Online First: 20220721]

68. Nguyen S, Wong D, McKay A, et al. Cognitive behavioural therapy for post-stroke fatigue and sleep disturbance: a pilot randomised controlled trial with blind assessment. *Neuropsychol Rehabil* 2019;29(5):723-38. doi: 10.1080/09602011.2017.1326945 [published Online First: 20170519]

69. Zedlitz AM, Rietveld TC, Geurts AC, et al. Cognitive and graded activity training can alleviate persistent fatigue after stroke: a randomized, controlled trial. *Stroke* 2012;43(4):1046-51. doi: 10.1161/STROKEAHA.111.632117 [published Online First: 20120202]

70. Okkersen K, Jimenez-Moreno C, Wenninger S, et al. Cognitive behavioural therapy with optional graded exercise therapy in patients with severe fatigue with myotonic dystrophy type 1: a multicentre, single-blind, randomised trial. *Lancet Neurol* 2018;17(8):671-80. doi: 10.1016/S1474-4422(18)30203-5 [published Online First: 20180619]

71. Hewlett S, Ambler N, Almeida C, et al. Self-management of fatigue in rheumatoid arthritis: a randomised controlled trial of group cognitive-behavioural therapy. *Ann Rheum Dis* 2011;70(6):1060-7. doi: 10.1136/ard.2010.144691

72. Jhamb M, Steel JL, Yabes JG, et al. Effects of Technology Assisted Stepped Collaborative Care Intervention to Improve Symptoms in Patients Undergoing

Hemodialysis: The TACcare Randomized Clinical Trial. *JAMA Intern Med* 2023;183(8):795-805. doi: 10.1001/jamainternmed.2023.2215

73. Picariello F, Moss-Morris R, Norton S, et al. Feasibility Trial of Cognitive Behavioral Therapy for Fatigue in Hemodialysis (BReF Intervention). *J Pain Symptom Manage* 2021;61(6):1234-46 e5. doi: 10.1016/j.jpainsymman.2020.10.005 [published Online First: 20201014]
74. Artom M, Czuber-Dochan W, Sturt J, et al. Cognitive-behavioural therapy for the management of inflammatory bowel disease-fatigue: a feasibility randomised controlled trial. *Pilot Feasibility Stud* 2019;5:145. doi: 10.1186/s40814-019-0538-y [published Online First: 20191210]
75. Bredero QM, Fleer J, Smink A, et al. Mindfulness-based cognitive therapy for fatigue in patients with inflammatory bowel disease: results of a Randomized Controlled Trial. *Mindfulness* 2023;14(1):19-32.
76. Menting J, Tack CJ, van Bon AC, et al. Web-based cognitive behavioural therapy blended with face-to-face sessions for chronic fatigue in type 1 diabetes: a multicentre randomised controlled trial. *Lancet Diabetes Endocrinol* 2017;5(6):448-56. doi: 10.1016/S2213-8587(17)30098-0 [published Online First: 20170424]
77. Rietberg MB, van Wegen EE, Eyssen IC, et al. Effects of multidisciplinary rehabilitation on chronic fatigue in multiple sclerosis: a randomized controlled trial. *PLoS ONE* 2014;9(9):e107710. doi: 10.1371/journal.pone.0107710 [published Online First: 20140918]
78. Clarke A, Barker-Collo SL, Feigin VL. Poststroke fatigue: does group education make a difference? A randomized pilot trial. *Top Stroke Rehabil* 2012;19(1):32-9. doi: 10.1310/tsr1901-32
79. Murphy SL, Chen YT, Alore M, et al. Effects of a Resilience-Building Energy Management Program on Fatigue and Other Symptoms in Systemic Sclerosis: A Randomized Controlled Trial. *Arthritis Care Res (Hoboken)* 2024;76(3):318-27. doi: 10.1002/acr.25253 [published Online First: 20240112]
80. Abonie US, Hettinga FJ. Effect of a Tailored Activity Pacing Intervention on Fatigue and Physical Activity Behaviours in Adults with Multiple Sclerosis. *Int J Environ Res Public Health* 2020;18(1) doi: 10.3390/ijerph18010017 [published Online First: 20201222]
81. Askari S, Kessler D, Smyth P, et al. Evaluating occupational performance coaching to support fatigue management for people with multiple sclerosis: A feasibility study. *Clin Rehabil* 2022;36(9):1244-56. doi: 10.1177/02692155221107074 [published Online First: 20220607]
82. Blikman LJ, van Meeteren J, Twisk JW, et al. Effectiveness of energy conservation management on fatigue and participation in multiple sclerosis: A randomized controlled trial. *Mult Scler* 2017;23(11):1527-41. doi: 10.1177/1352458517702751 [published Online First: 20170522]
83. Garcia Jalon EG, Lennon S, Peoples L, et al. Energy conservation for fatigue management in multiple sclerosis: a pilot randomized controlled trial. *Clin Rehabil* 2013;27(1):63-74. doi: 10.1177/0269215512446495 [published Online First: 20120702]
84. Hersche R, Weise A, Michel G, et al. Development and Preliminary Evaluation of a 3-Week Inpatient Energy Management Education Program for People with Multiple Sclerosis-Related Fatigue. *Int J MS Care* 2019;21(6):265-74. doi: 10.7224/1537-2073.2018-058

85. Hugos CL, Copperman LF, Fuller BE, et al. Clinical trial of a formal group fatigue program in multiple sclerosis. *Mult Scler* 2010;16(6):724-32. doi: 10.1177/1352458510364536 [published Online First: 20100407]

86. Hugos CL, Chen Z, Chen Y, et al. A multicenter randomized controlled trial of two group education programs for fatigue in multiple sclerosis: Short- and medium-term benefits. *Mult Scler* 2019;25(2):275-85. doi: 10.1177/1352458517745723 [published Online First: 20171211]

87. Kos D, Duportail M, Meirte J, et al. The effectiveness of a self-management occupational therapy intervention on activity performance in individuals with multiple sclerosis-related fatigue: a randomized-controlled trial. *Int J Rehabil Res* 2016;39(3):255-62. doi: 10.1097/MRR.0000000000000178

88. Ghahari S, Leigh Packer T, Passmore AE. Effectiveness of an online fatigue self-management programme for people with chronic neurological conditions: a randomized controlled trial. *Clin Rehabil* 2010;24(8):727-44. doi: 10.1177/0269215509360648 [published Online First: 20100611]

89. Murphy SL, Lyden AK, Smith DM, et al. Effects of a tailored activity pacing intervention on pain and fatigue for adults with osteoarthritis. *Am J Occup Ther* 2010;64(6):869-76. doi: 10.5014/ajot.2010.09198

90. Farragher JF, Ravani P, Manns B, et al. A pilot randomised controlled trial of an energy management programme for adults on maintenance haemodialysis: the fatigue-HD study. *BMJ Open* 2022;12(2):e051475. doi: 10.1136/bmjopen-2021-051475 [published Online First: 20220210]

91. Austin JS, Maisiak RS, Macrina DM, et al. Health outcome improvements in patients with systemic lupus erythematosus using two telephone counseling interventions. *Arthritis Care Res* 1996;9(5):391-9. doi: 10.1002/1529-0131(199610)9:5<391::aid-anr1790090508>3.0.co;2-v

92. Feldthusen C, Dean E, Forsblad-d'Elia H, et al. Effects of Person-Centered Physical Therapy on Fatigue-Related Variables in Persons With Rheumatoid Arthritis: A Randomized Controlled Trial. *Arch Phys Med Rehabil* 2016;97(1):26-36. doi: 10.1016/j.apmr.2015.09.022 [published Online First: 20151016]

93. Hammond A, Bryan J, Hardy A. Effects of a modular behavioural arthritis education programme: a pragmatic parallel-group randomized controlled trial. *Rheumatology (Oxford)* 2008;47(11):1712-8. doi: 10.1093/rheumatology/ken380 [published Online First: 20080924]

94. Khan F, Granville N, Malkani R, et al. Health-Related Quality of Life Improvements in Systemic Lupus Erythematosus Derived from a Digital Therapeutic Plus Tele-Health Coaching Intervention: Randomized Controlled Pilot Trial. *Journal of medical Internet research* 2020;22(10):e23868. doi: 10.2196/23868 [published Online First: 20201020]

95. De Giglio L, De Luca F, Prosperini L, et al. A low-cost cognitive rehabilitation with a commercial video game improves sustained attention and executive functions in multiple sclerosis: a pilot study. *Neurorehabil Neural Repair* 2015;29(5):453-61.

96. Fleming KM, Coote SB, Herring MP. The feasibility of Pilates to improve symptoms of anxiety, depression, and fatigue among people with Multiple Sclerosis: An eight-week randomized controlled pilot trial. *Psychology of Sport and Exercise* 2019;45:101573.

97. Fleming KM, Coote SB, Herring MP. Home-based Pilates for symptoms of anxiety, depression and fatigue among persons with multiple sclerosis: An 8-week

randomized controlled trial. *Mult Scler* 2021;27(14):2267-79. doi: 10.1177/13524585211009216 [published Online First: 20210419]

98. Sgoifo A, Bignamini A, La Mantia L, et al. Integrated Imaginative Distention Therapy to Cope with Fatigue. DIMMI SI Study: The First Randomized Controlled Trial in Multiple Sclerosis. *Neurol Ther* 2017;6(2):213-23. doi: 10.1007/s40120-017-0081-9 [published Online First: 20170809]

99. Walter AA, Adams EV, Van Puymbroeck M, et al. Changes in Nonmotor Symptoms Following an 8-Week Yoga Intervention for People with Parkinson's Disease. *Int J Yoga Therap* 2019;29(1):91-99. doi: 10.17761/2019-00025 [published Online First: 20190322]

100. Callahan LF, Cleveland RJ, Altpeter M, et al. Evaluation of Tai Chi Program Effectiveness for People with Arthritis in the Community: A Randomized Controlled Trial. *J Aging Phys Act* 2016;24(1):101-10. doi: 10.1123/japa.2014-0211 [published Online First: 20150618]

101. Grossman P, Kappos L, Gensicke H, et al. MS quality of life, depression, and fatigue improve after mindfulness training: a randomized trial. *Neurology* 2010;75(13):1141-9. doi: 10.1212/WNL.0b013e3181f4d80d

102. Goren G, Schwartz D, Friger M, et al. Randomized Controlled Trial of Cognitive-Behavioral and Mindfulness-Based Stress Reduction on the Quality of Life of Patients With Crohn Disease. *Inflamm Bowel Dis* 2022;28(3):393-408. doi: 10.1093/ibd/izab083

103. Granja-Dominguez A, Hochsprung A, Luque-Moreno C, et al. Effects of pulsed electromagnetic field therapy on fatigue, walking performance, depression, and quality of life in adults with multiple sclerosis: a randomized placebo-controlled trial. *Braz J Phys Ther* 2022;26(5):100449. doi: 10.1016/j.bjpt.2022.100449 [published Online First: 20221013]

104. Mostert S, Kesselring J. Effect of pulsed magnetic field therapy on the level of fatigue in patients with multiple sclerosis--a randomized controlled trial. *Mult Scler* 2005;11(3):302-5. doi: 10.1191/1352458505ms1156oa

105. Piatkowski J, Kern S, Ziemssen T. Effect of BEMER magnetic field therapy on the level of fatigue in patients with multiple sclerosis: a randomized, double-blind controlled trial. *J Altern Complement Med* 2009;15(5):507-11. doi: 10.1089/acm.2008.0501

106. Voggenberger L, Bock M, Moser D, et al. Bright light therapy as a non-pharmacological treatment option for multiple sclerosis-related fatigue: A randomized sham-controlled trial. *Mult Scler J Exp Transl Clin* 2022;8(4):20552173221133262. doi: 10.1177/20552173221133262 [published Online First: 20221107]

107. Kluger BM, Rakowski D, Christian M, et al. Randomized, Controlled Trial of Acupuncture for Fatigue in Parkinson's Disease. *Mov Disord* 2016;31(7):1027-32. doi: 10.1002/mds.26597 [published Online First: 20160329]

108. Horta D, Lira A, Sanchez-Lloansi M, et al. A Prospective Pilot Randomized Study: Electroacupuncture vs. Sham Procedure for the Treatment of Fatigue in Patients With Quiescent Inflammatory Bowel Disease. *Inflamm Bowel Dis* 2020;26(3):484-92. doi: 10.1093/ibd/izz091

109. Hawkins J, Hires CY, Dunne EW, et al. Aromatherapy reduces fatigue among women with hypothyroidism: A randomized placebo-controlled clinical trial. *J Complement Integr Med* 2019;17(1) doi: 10.1515/jcim-2018-0229 [published Online First: 20190822]

110. Cancelli A, Cottone C, Giordani A, et al. Personalized, bilateral whole-body somatosensory cortex stimulation to relieve fatigue in multiple sclerosis. *Mult Scler* 2018;24(10):1366-74. doi: 10.1177/1352458517720528 [published Online First: 20170731]

111. Charvet LE, Dobbs B, Shaw MT, et al. Remotely supervised transcranial direct current stimulation for the treatment of fatigue in multiple sclerosis: Results from a randomized, sham-controlled trial. *Mult Scler* 2018;24(13):1760-69. doi: 10.1177/1352458517732842 [published Online First: 20170922]

112. Tecchio F, Cancelli A, Cottone C, et al. Brain Plasticity Effects of Neuromodulation Against Multiple Sclerosis Fatigue. *Front Neurol* 2015;6:141. doi: 10.3389/fneur.2015.00141 [published Online First: 20150703]

113. Salemi G, Vazzoler G, Ragonese P, et al. Application of tRNS to improve multiple sclerosis fatigue: a pilot, single-blind, sham-controlled study. *J Neural Transm (Vienna)* 2019;126(6):795-99. doi: 10.1007/s00702-019-02006-y [published Online First: 20190503]

114. Aranow C, Atish-Fregoso Y, Lesser M, et al. Transcutaneous auricular vagus nerve stimulation reduces pain and fatigue in patients with systemic lupus erythematosus: a randomised, double-blind, sham-controlled pilot trial. *Annals of the Rheumatic Diseases* 2021;80(2):203-08. doi: 10.1136/annrheumdis-2020-217872

115. Tarn J, Legg S, Mitchell S, et al. The Effects of Noninvasive Vagus Nerve Stimulation on Fatigue and Immune Responses in Patients With Primary Sjögren's Syndrome. *Neuromodulation: Technology at the Neural Interface* 2019;22(5):580-85. doi: https://doi.org/10.1111/ner.12879

116. Moyle DB, Kudiersky MN, Totton MN, et al. Remote ischaemic conditioning for fatigue after stroke (RICFAST): A pilot randomised controlled trial. *J Stroke Cerebrovasc Dis* 2023;32(12):107420. doi: 10.1016/j.jstrokecerebrovasdis.2023.107420 [published Online First: 20231011]

117. Coe S, Cossington J, Collett J, et al. A randomised double-blind placebo-controlled feasibility trial of flavonoid-rich cocoa for fatigue in people with relapsing and remitting multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2019;90(5):507-13. doi: 10.1136/jnnp-2018-319496 [published Online First: 20190304]

118. Arriens C, Hynan LS, Lerman RH, et al. Placebo-controlled randomized clinical trial of fish oil's impact on fatigue, quality of life, and disease activity in Systemic Lupus Erythematosus. *Nutr J* 2015;14:82. doi: 10.1186/s12937-015-0068-2 [published Online First: 20150818]

119. Bager P, Hvas CL, Rud CL, et al. Randomised clinical trial: high-dose oral thiamine versus placebo for chronic fatigue in patients with quiescent inflammatory bowel disease. *Aliment Pharmacol Ther* 2021;53(1):79-86. doi: 10.1111/apt.16166 [published Online First: 20201118]

120. Truyens M, Lobaton T, Ferrante M, et al. Effect of 5-Hydroxytryptophan on Fatigue in Quiescent Inflammatory Bowel Disease: A Randomized Controlled Trial. *Gastroenterology* 2022;163(5):1294-305 e3. doi: 10.1053/j.gastro.2022.07.052 [published Online First: 20220806]

121. Chase E, Chen V, Martin K, et al. A low-fat diet improves fatigue in multiple sclerosis: Results from a randomized controlled trial. *Mult Scler* 2023;29(13):1659-75. doi: 10.1177/13524585231208330

122. Johnson SK, Diamond BJ, Rausch S, et al. The effect of Ginkgo biloba on functional measures in multiple sclerosis: a pilot randomized controlled trial. *Explore (NY)* 2006;2(1):19-24. doi: 10.1016/j.explore.2005.10.007

EIFFEL Supplementary Methods

Table of Contents

1 Supplementary Methods 1: Detailed search strategy

Search Strategies: RCT search
Ovid MEDLINE(R) ALL <1946 to September 27, 2023>

1 exp Chronic Disease/ 625076
2 ((chronic or long-term or long term) adj (condition* or disease* or illness*)).ti,ab. 129174
3 chronically ill.ti,ab. 6151
4 exp Rheumatic Diseases/ 261192
5 rheumati*.ti,ab. 63183
6 exp Diabetes Mellitus/ 511411
7 diabet*.ti,ab. 776423
8 exp Endocrine System Diseases/ 1133836
9 exp Thyroid Diseases/ 163788
10 exp Adrenal Gland Diseases/ or exp Adrenal Insufficiency/ 72739
11 exp Autoimmune Diseases/ 546702
12 ((endocrine or thyroid or adrenal or autoimmune or auto-immune or auto immune) adj1 (disorder* or disease* or condition*)).ti,ab. 122720
13 adrenal insufficiency.ti,ab. 7311
14 exp Heart Failure/ 148655
15 heart failure*.ti,ab. 209132
16 exp Coronary Disease/ 236955
17 coronary heart disease*.ti,ab. 55465
18 exp Renal Insufficiency, Chronic/ 135178
19 exp Kidney Failure, Chronic/ 101277
20 (chronic adj (renal or kidney) adj (insuffucien* or failure* or disease*)).ti,ab. 98172
21 exp Renal Dialysis/ 126720
22 dialysis.ti,ab. 122294
23 exp Transplants/ 31895
24 (transplant* adj3 (heart* or kidney* or liver* or lung*)).ti,ab. 180737
25 exp Multiple Sclerosis/ 70469
26 multiple sclerosis.ti,ab. 90255
27 exp Stroke/ 174658
28 stroke.ti,ab. 305418
29 exp Neurodegenerative Diseases/ 371816
30 ((neurodegenerative or neuro-degenerative or neuro degenerative) adj (disease* or disorder* or condition*)).ti,ab. 99788
31 exp Parkinson Disease/ 82813
32 (parkinson* adj disease).ti,ab. 116256
33 exp Arthritis, Rheumatoid/ 126357
34 rheumatoid arthritis.ti,ab. 120734
35 exp Osteoarthritis/ 78077
36 osteoarthritis.ti,ab. 84060
37 exp Lupus Erythematosus, Systemic/ 67452
38 lupus.ti,ab. 88490
39 exp Scleroderma, Systemic/ 23231
40 (systemic sclerosis or scleroderma).ti,ab. 28912
41 exp Inflammatory Bowel Diseases/ 97805
42 (inflammatory bowel disease* or IBD).ti,ab. 67194
43 exp Liver Cirrhosis, Biliary/ 8772
44 (primary biliary cirrhosis or PBS).ti,ab. 36509
45 exp Cholangitis, Sclerosing/ 4703
46 sclerosing cholangiti*.ti,ab. 7289
47 exp Lung Diseases/ 1236542
48 ((lung or pulmonary) adj (disease* or disorder* or condition*)).ti,ab. 142936
49 exp Pulmonary Disease, Chronic Obstructive/ 67441
50 ((chronic obstructive adj (pulmonary or lung or airway) adj (disease* or obstruction*)) or (COPD or COAD)).ti,ab. 83179
51 exp Asthma/ 143083
52 (asthma or asthmatic).ti,ab. 176832

53 exp Muscular Diseases/ 196410
54 (((muscle or muscular or myopathic) adj (disorder* or disease* or condition*)) or (myopathy or myopathies)).ti,ab. 36194
55 exp Muscular Dystrophies/ 30020
56 (muscular dystroph* or myodystroph*).ti,ab. 27210
57 or/1-56 5558763
58 "Fatigue Questionnaire".ti,ab. 382
59 "Fatigue Severity Scale".ti,ab. 1808
60 "Multidimensional Assessment of Fatigue".ti,ab. 139
61 "Short Form-36 Vitality".ti,ab. 34
62 ("Functional Assessment of Chronic Illness Therapy Fatigue" or FACIT F).ti,ab. 633
63 "Brief Fatigue Inventory".ti,ab. 472
64 "Numerical Rating Scale Fatigue".ti,ab. 7
65 ("Visual Analog Scale Fatigue" or VAS F).ti,ab. 105
66 "Checklist Individual Strength".ti,ab. 323
67 "Chalder Fatigue Scale".ti,ab. 201
68 "Multidimensional Fatigue Inventory Scale".ti,ab. 8
69 "Piper Fatigue Scale".ti,ab. 268
70 (PROMIS-29 or PROMIS 29 or PROMIS29).ti,ab. 235
71 Pittsburgh Fatigability Scale.ti,ab. 32
72 Fatigue Descriptive Scale.ti,ab. 10
73 Modified Fatigue Impact Scale.ti,ab. 517
74 ("40-item Fatigue Impact Scale" or "40 item Fatigue Impact Scale").ti,ab. 4
75 ("29-item Fatigue Assessment Instrument" or "29 item Fatigue Assessment Instrument").ti,ab. 1
76 ("Functional Assessment of Multiple Sclerosis" or FAMS).ti,ab. 172
77 or/58-76 4995
78 *Fatigue/ 16397
79 (fatigue adj7 (scale* or subscale* or sub-scale* or questionnaire* or assessment* or inventor* or measure* or tool*)).ti,ab. 17355
80 (scale or subscale or sub-scale or questionnaire or assessment or inventory or measure or measurement).ti,ab. 3456677
81 (fatigability or fatigable).ti,ab. 3406
82 78 or 81 19535
83 80 and 82 6761
84 79 or 83 19584
85 77 or 84 20135
86 57 and 85 8442
87 exp randomized controlled trial/ 602157
88 controlled clinical trial.pt. 95425
89 randomized.ab. 618304
90 placebo.ab. 241721
91 clinical trials as topic/ 201321
92 randomly.ab. 417343
93 trial.ti. 293560
94 or/87-93 1550631
95 exp animals/ not humans/ 5158236
96 94 not 95 1427530
97 86 and 96 1938

Embase <1974 to 2023 Week 38>

1 *chronic disease/ 32846
2 ((chronic or long-term or long term) adj (condition* or disease* or illness*)).ti,ab. 179677
3 chronically ill.ti,ab. 7536
4 *rheumatic disease/ 32096
5 rheumati*.ti,ab. 80760
6 *diabetes mellitus/ 242661
7 diabet*.ti,ab. 1174089
8 *endocrine disease/ 7079

9 *thyroid disease/ 13779
10 *adrenal disease/ 2041
11 *adrenal insufficiency/ 4392
12 *autoimmune disease/ 35243
13 ((endocrine or thyroid or adrenal or autoimmune or auto-immune or auto immune) adj1 (disorder* or disease* or condition*)).ti,ab. 182768
14 adrenal insufficiency.ti,ab. 10682
15 *heart failure/ 126614
16 heart failure*.ti,ab. 350732
17 *coronary artery disease/ 96075
18 coronary heart disease*.ti,ab. 75791
19 *chronic kidney failure/ 61974
20 (chronic adj (renal or kidney) adj (insuffucien* or failure* or disease*)).ti,ab. 155133
21 *hemodialysis/ 63019
22 dialysis.ti,ab. 181634
23 *transplantation/ 64169
24 (transplant* adj3 (heart* or kidney* or liver* or lung*)).ti,ab. 304389
25 *multiple sclerosis/ 102769
26 multiple sclerosis.ti,ab. 141053
27 *cerebrovascular accident/ 105016
28 stroke.ti,ab. 488091
29 *degenerative disease/ 18573
30 ((neurodegenerative or neuro-degenerative or neuro degenerative) adj (disease* or disorder* or condition*)).ti,ab. 131356
31 *Parkinson disease/ 121773
32 (parkinson* adj disease).ti,ab. 168860
33 *rheumatoid arthritis/ 127396
34 rheumatoid arthritis.ti,ab. 180981
35 *osteoarthritis/ 52154
36 osteoarthritis.ti,ab. 120269
37 *systemic lupus erythematosus/ 63341
38 lupus.ti,ab. 126358
39 *systemic sclerosis/ 22876
40 (systemic sclerosis or scleroderma).ti,ab. 44582
41 *inflammatory bowel disease/ 27489
42 (inflammatory bowel disease* or IBD).ti,ab. 119395
43 *biliary cirrhosis/ 2200
44 (primary biliary cirrhosis or PBS).ti,ab. 59132
45 *sclerosing cholangitis/ 1978
46 sclerosing cholangiti*.ti,ab. 12483
47 *lung disease/ 34450
48 ((lung or pulmonary) adj (disease* or disorder* or condition*)).ti,ab. 217538
49 *chronic obstructive lung disease/ 82916
50 ((chronic obstructive adj (pulmonary or lung or airway) adj (disease* or obstruction*)) or (COPD or COAD)).ti,ab. 143936
51 *asthma/ 152110
52 (asthma or asthmatic).ti,ab. 258285
53 *muscle disease/ 9985
54 (((muscle or muscular or myopathic) adj (disorder* or disease* or condition*)) or (myopathy or myopathies)).ti,ab. 51568
55 *muscular dystrophy/ 9507
56 (muscular dystroph* or myodystroph*).ti,ab. 36327
57 or/1-56 4496914
58 "Fatigue Questionnaire".ti,ab. 625
59 "Fatigue Severity Scale".ti,ab. 3460
60 "Multidimensional Assessment of Fatigue".ti,ab. 269
61 "Short Form-36 Vitality".ti,ab. 39
62 ("Functional Assessment of Chronic Illness Therapy Fatigue" or FACIT F).ti,ab. 1676
63 "Brief Fatigue Inventory".ti,ab. 881
64 "Numerical Rating Scale Fatigue".ti,ab. 11

65 ("Visual Analog Scale Fatigue" or VAS F).ti,ab. 163
66 "Checklist Individual Strength".ti,ab. 452
67 "Chalder Fatigue Scale".ti,ab. 310
68 "Multidimensional Fatigue Inventory Scale".ti,ab. 14
69 "Piper Fatigue Scale".ti,ab. 376
70 (PROMIS-29 or PROMIS 29 or PROMIS29).ti,ab. 617
71 Pittsburgh Fatigability Scale.ti,ab. 44
72 Fatigue Descriptive Scale.ti,ab. 17
73 Modified Fatigue Impact Scale.ti,ab. 1077
74 ("40-item Fatigue Impact Scale" or "40 item Fatigue Impact Scale").ti,ab. 4
75 ("29-item Fatigue Assessment Instrument" or "29 item Fatigue Assessment Instrument").ti,ab. 2
76 ("Functional Assessment of Multiple Sclerosis" or FAMS).ti,ab. 355
77 exp Fatigue Severity Scale/ or exp "Functional Assessment of Chronic Illness Therapy Fatigue Scale"/ or exp Multidimensional Fatigue Inventory/ or exp Chalder Fatigue Scale/ or exp Piper fatigue scale/ or exp "fatigue scale for motor and cognitive functions"/ or exp Fatigue Impact Scale/ 6541
78 or/58-77 12125
79 *fatigue/ 25859
80 (fatigue adj7 (scale* or subscale* or sub-scale* or questionnaire* or assessment* or inventor* or measure* or tool*)).ti,ab. 29052
81 (scale or subscale or sub-scale or questionnaire or assessment or inventory or measure or measurement).ti,ab. 4694159
82 (fatigability or fatigable).ti,ab. 5144
83 79 or 82 30552
84 81 and 83 12023
85 80 or 84 32495
86 78 or 85 35039
87 57 and 86 12690
88 exp randomized controlled trial/ 785235
89 controlled clinical trial/ 470992
90 random$.ti,ab. 1975440
91 randomization/ 98376
92 intermethod comparison/ 300743
93 placebo.ti,ab. 365413
94 (compare or compared or comparison).ti,ab. 7636197
95 ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. 2778695
96 (open adj label).ti,ab. 108778
97 ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab. 273962
98 double blind procedure/ 210736
99 parallel group$1.ti,ab. 32147
100 (crossover or cross over).ti,ab. 124632
101 ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant$1)).ti,ab. 415356
102 (assigned or allocated).ti,ab. 490792
103 (controlled adj7 (study or design or trial)).ti,ab. 450700
104 (volunteer or volunteers).ti,ab. 282605
105 human experiment/ 642664
106 trial.ti. 401617
107 or/88-106 10036592
108 (random$ adj sampl$ adj7 ("cross section$" or questionnaire$1 or survey$ or database$1)).ti,ab. not (comparative study/ or controlled study/ or randomi?ed controlled.ti,ab. or randomly assigned.ti,ab.) 9609
109 cross-sectional study/ not (exp randomized controlled trial/ or controlled clinical trial/ or controlled study/ or randomi?ed controlled.ti,ab. or control group$1.ti,ab.) 361562search
110 (((case adj control$) and random$) not randomi?ed controlled).ti,ab. 21555
111 systematic review.ti,ab. not (trial or study).ti. 325581
112 (nonrandom$ not random$).ti,ab. 18945
113 "random field$".ti,ab. 2966

114 (random cluster adj3 sampl$).ti,ab. 1583
115 (review.ab. and review.pt.) not trial.ti. 1131497
116 "we searched".ab. and (review.ti. or review.pt.) 49364
117 "update review".ab. 136
118 (databases adj4 searched).ab. 62550
119 (rat or rats or mouse or mice or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset$1).ti. and animal experiment/ 1220906
120 animal experiment/ not (human experiment/ or human/) 2564767
121 or/108-120 4382762
122 107 not 121 8767282
123 87 and 122 6538
124 limit 123 to "remove medline records" 4030

CINAHL via EBSCO
Monday, October 02, 2023 4:18:56 PM
S1 (MH "Chronic Disease+")
S2 TI ((chronic or long-term or long term) N1 (condition* or disease* or illness*)) OR AB ((chronic or long-term or long term) N1 (condition* or disease* or illness*))
S3 TI chronically ill OR AB chronically ill
S4 (MH "Rheumatic Diseases+")
S5 TI rheumati* OR AB rheumati*
S6 (MH "Diabetes Mellitus+")
S7 TI diabet* OR AB diabet*
S8 (MH "Endocrine Diseases+")
S9 (MH "Thyroid Diseases+")
S10 (MH "Adrenal Gland Diseases+")
S11 (MH "Adrenal Insufficiency+")
S12 (MH "Autoimmune Diseases+")
S13 TI ((endocrine or thyroid or adrenal or autoimmune or auto-immune or auto immune) N1 (disorder* or disease* or condition*)) OR AB ((endocrine or thyroid or adrenal or autoimmune or auto-immune or auto immune) N1 (disorder* or disease* or condition*))
S14 TI adrenal insufficiency OR AB adrenal insufficiency
S15 (MH "Heart Failure+")
S16 TI heart failure* OR AB heart failure*
S17 (MH "Coronary Disease+")
S18 TI coronary heart disease* OR AB coronary heart disease*
S19 (MH "Renal Insufficiency, Chronic+")
S20 (MH "Kidney Failure, Chronic+")
S21 TI (chronic adj (renal or kidney) N1 (insuffucien* or failure* or disease*)) OR AB (chronic adj (renal or kidney) N1 (insuffucien* or failure* or disease*))
S22 (MH "Dialysis Patients")
S23 TI dialysis OR AB dialysis
S24 TI (transplant* N3 (heart* or kidney* or liver* or lung*)) OR AB (transplant* N3 (heart* or kidney* or liver* or lung*))
S25 (MH "Multiple Sclerosis+")
S26 TI multiple sclerosis OR AB multiple sclerosis
S27 (MH "Stroke+")
S28 TI stroke OR AB stroke
S29 (MH "Neurodegenerative Diseases+")
S30 TI ((neurodegenerative or neuro-degenerative or neuro degenerative) N1 (disease* or disorder* or condition*)) OR AB ((neurodegenerative or neuro-degenerative or neuro degenerative) N1 (disease* or disorder* or condition*))
S31 (MH "Parkinson Disease")
S32 TI (parkinson* N1 disease) OR AB (parkinson* N1 disease)
S33 (MH "Arthritis, Rheumatoid+")
S34 TI rheumatoid arthritis OR AB rheumatoid arthritis
S35 (MH "Osteoarthritis+")
S36 TI osteoarthritis OR AB osteoarthritis
S37 (MH "Lupus Erythematosus, Systemic+")

S38 TI lupus OR AB lupus
S39 (MH "Scleroderma, Systemic+")
S40 TI (systemic sclerosis or scleroderma) OR AB (systemic sclerosis or scleroderma)
S41 (MH "Inflammatory Bowel Diseases+")
S42 TI (inflammatory bowel disease* or IBD) OR AB (inflammatory bowel disease* or IBD)
S43 (MH "Liver Cirrhosis+")
S44 TI (primary biliary cirrhosis or PBS) OR AB (primary biliary cirrhosis or PBS)
S45 (MH "Cholangitis, Sclerosing")
S46 TI sclerosing cholangiti* OR AB sclerosing cholangiti*
S47 (MH "Lung Diseases+")
S48 TI ((lung or pulmonary) N1 (disease* or disorder* or condition*)) OR AB ((lung or pulmonary) N1 (disease* or disorder* or condition*))
S49 (MH "Pulmonary Disease, Chronic Obstructive+")
S50 TI ((chronic obstructive N1 (pulmonary or lung or airway) N1 (disease* or obstruction*)) or (COPD or COAD)) OR AB ((chronic obstructive N1 (pulmonary or lung or airway) N1 (disease* or obstruction*)) or (COPD or COAD))
S51 (MH "Asthma+")
S52 TI (asthma or asthmatic) OR AB (asthma or asthmatic)
S53 (MH "Muscular Diseases+")
S54 TI (((muscle or muscular or myopathic) ADJ1 (disorder* or disease* or condition*)) or (myopathy or myopathies)) OR AB (((muscle or muscular or myopathic) ADJ1 (disorder* or disease* or condition*)) or (myopathy or myopathies))
S55 (MH "Muscular Dystrophy+")
S56 TI (muscular dystroph* or myodystroph*) OR AB (muscular dystroph* or myodystroph*)
S57 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56
S58 TI "Fatigue Questionnaire" OR AB "Fatigue Questionnaire"
S59 TI "Fatigue Severity Scale" OR AB "Fatigue Severity Scale"
S60 TI "Multidimensional Assessment of Fatigue" OR AB "Multidimensional Assessment of Fatigue"
S61 TI "Short Form-36 Vitality" OR AB "Short Form-36 Vitality"
S62 TI ("Functional Assessment of Chronic Illness Therapy Fatigue" or FACIT F) OR AB ("Functional Assessment of Chronic Illness Therapy Fatigue" or FACIT F)
S63 TI "Brief Fatigue Inventory" OR AB "Brief Fatigue Inventory"
S64 TI "Numerical Rating Scale Fatigue" OR AB "Numerical Rating Scale Fatigue"
S65 TI ("Visual Analog Scale Fatigue" or VAS F) OR AB ("Visual Analog Scale Fatigue" or VAS F)
S66 TI "Checklist Individual Strength" OR AB "Checklist Individual Strength"
S67 TI "Chalder Fatigue Scale" OR AB "Chalder Fatigue Scale"
S68 TI "Multidimensional Fatigue Inventory Scale" OR AB "Multidimensional Fatigue Inventory Scale"
S69 TI "Piper Fatigue Scale" OR AB "Piper Fatigue Scale"
S70 TI (PROMIS-29 or PROMIS 29 or PROMIS29) OR AB (PROMIS-29 or PROMIS 29 or PROMIS29)
S71 TI Pittsburgh Fatigability Scale OR AB Pittsburgh Fatigability Scale
S72 TI Fatigue Descriptive Scale OR AB Fatigue Descriptive Scale
S73 TI Modified Fatigue Impact Scale OR AB Modified Fatigue Impact Scale
S74 TI ("40-item Fatigue Impact Scale" or "40 item Fatigue Impact Scale") OR AB ("40-item Fatigue Impact Scale" or "40 item Fatigue Impact Scale")
S75 TI ("29-item Fatigue Assessment Instrument" or "29 item Fatigue Assessment Instrument") OR AB ("29-item Fatigue Assessment Instrument" or "29 item Fatigue Assessment Instrument")
S76 TI ("Functional Assessment of Multiple Sclerosis" or FAMS) OR AB ("Functional Assessment of Multiple Sclerosis" or FAMS)
S77 S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76
S78 (MM "Fatigue")
S79 TI (fatigue N7 (scale* or subscale* or sub-scale* or questionnaire* or assessment* or inventor* or measure* or tool*)) OR AB (fatigue N7 (scale* or subscale* or sub-scale* or questionnaire* or assessment* or inventor* or measure* or tool*))

S80 TI (scale or subscale or sub-scale or questionnaire or assessment or inventory or measure or measurement) OR AB (scale or subscale or sub-scale or questionnaire or assessment or inventory or measure or measurement)
S81 TI (fatigability or fatigable) OR AB (fatigability or fatigable)
S82 S78 OR S81
S83 S80 AND S82
S84 S79 OR S83
S85 S77 OR S84
S86 S57 AND S85
S87 MH "Clinical Trials+"
S88 PT Clinical trial S89 TX clinic* n1 trial*
S90 TX ((singl* n1 blind*) or (singl* n1 mask*)) or TX ((doubl* n1 blind*) or (doubl* n1 mask*)) or TX ((tripl* n1 blind*) or (tripl* n1 mask*)) or TX ((trebl* n1 blind*) or (trebl* n1 mask*))
S91 TX randomi* control* trial*
S92 MH "Random Assignment" S93 TX random* allocat*
S94 TX placebo*
S95 MH "Placebos"
S96 MH "Quantitative Studies"
S97 TX allocat* random*
S98 S87 OR S88 OR S89 OR S90 OR S91 OR S92 OR S93 OR S94 OR S95 OR S96 OR S97
S99 S86 AND S98 Results 1905

APA PsycInfo <1806 to September Week 4 2023>
1 exp Chronic Illness/ 34600
2 ((chronic or long-term or long term) adj (condition* or disease* or illness*)).ti,ab. 29719
3 chronically ill.ti,ab. 3184
4 exp Rheumatoid Arthritis/ 2100
5 rheumati*.ti,ab. 1112
6 exp Diabetes Mellitus/ 10460
7 diabet*.ti,ab. 36523
8 exp Thyroid Disorders/ 1539
9 exp Adrenal Gland Disorders/ 422
10 exp Immunologic Disorders/ 53042
11 ((endocrine or thyroid or adrenal or autoimmune or auto-immune or auto immune) adj1 (disorder* or disease* or condition*)).ti,ab. 3899
12 adrenal insufficiency.ti,ab. 148
13 exp Heart Disorders/ 16450
14 heart failure*.ti,ab. 4536
15 exp Cardiovascular Disorders/ 72080
16 coronary heart disease*.ti,ab. 4403
17 exp Kidney Diseases/ 2674
18 (chronic adj (renal or kidney) adj (insuffucien* or failure* or disease*)).ti,ab. 1543
19 exp Dialysis/ 2247
20 dialysis.ti,ab. 2381
21 exp Organ Transplantation/ 5421
22 (transplant* adj3 (heart* or kidney* or liver* or lung*)).ti,ab. 2086
23 exp Multiple Sclerosis/ 14366
24 multiple sclerosis.ti,ab. 17136
25 exp Cerebrovascular Accidents/ 24837
26 stroke.ti,ab. 37683
27 exp Neurodegenerative Diseases/ 95903
28 ((neurodegenerative or neuro-degenerative or neuro degenerative) adj (disease* or disorder* or condition*)).ti,ab. 19229
29 (parkinson* adj disease).ti,ab. 32763
30 exp Rheumatoid Arthritis/ 2100
31 rheumatoid arthritis.ti,ab. 2806
32 exp Arthritis/ 4810
33 osteoarthritis.ti,ab. 2288
34 exp Lupus/ 883
35 lupus.ti,ab. 1629

36 (systemic sclerosis or scleroderma).ti,ab. 219
37 exp Colon Disorders/ 5096
38 (inflammatory bowel disease* or IBD).ti,ab. 1201
39 exp Liver Disorders/ 5073
40 (primary biliary cirrhosis or PBS).ti,ab. 1564
41 sclerosing cholangiti*.ti,ab. 19
42 exp Lung Disorders/ 5469
43 ((lung or pulmonary) adj (disease* or disorder* or condition*)).ti,ab. 3973
44 exp Chronic Obstructive Pulmonary Disease/ 1788
45 ((chronic obstructive adj (pulmonary or lung or airway) adj (disease* or obstruction*)) or (COPD or COAD)).ti,ab. 3014
46 exp Asthma/ 5266
47 (asthma or asthmatic).ti,ab. 8470
48 exp Muscular Disorders/10761
49 (((muscle or muscular or myopathic) adj (disorder* or disease* or condition*)) or (myopathy or myopathies)).ti,ab. 1828
50 exp Muscular Dystrophy/ 1524
51 (muscular dystroph* or myodystroph*).ti,ab. 1629
52 or/1-51 380568
53 "Fatigue Questionnaire".ti,ab. 128
54 "Multidimensional Assessment of Fatigue".ti,ab. 35
55 "Short Form-36 Vitality".ti,ab. 7
56 ("Functional Assessment of Chronic Illness Therapy Fatigue" or FACIT F).ti,ab. 75
57 "Brief Fatigue Inventory".ti,ab. 105
58 "Numerical Rating Scale Fatigue".ti,ab. 4
59 ("Visual Analog Scale Fatigue" or VAS F).ti,ab. 21
60 "Checklist Individual Strength".ti,ab. 110
61 "Chalder Fatigue Scale".ti,ab. 73
62 "Multidimensional Fatigue Inventory Scale".ti,ab. 0
63 "Piper Fatigue Scale".ti,ab. 74
64 (PROMIS-29 or PROMIS 29 or PROMIS29).ti,ab. 54
65 Pittsburgh Fatigability Scale.ti,ab. 8
66 Fatigue Descriptive Scale.ti,ab. 1
67 Modified Fatigue Impact Scale.ti,ab. 139
68 ("40-item Fatigue Impact Scale" or "40 item Fatigue Impact Scale").ti,ab. 2
69 ("29-item Fatigue Assessment Instrument" or "29 item Fatigue Assessment Instrument").ti,ab. 1
70 ("Functional Assessment of Multiple Sclerosis" or FAMS).ti,ab. 62
71 or/52-70 380976
72 exp Fatigue/ 11615
73 (fatigue adj7 (scale* or subscale* or sub-scale* or questionnaire* or assessment* or inventor* or measure* or tool*)).ti,ab. 5324
74 (scale or subscale or sub-scale or questionnaire or assessment or inventory or measure or measurement).ti,ab. 1060391
75 (fatigability or fatigable).ti,ab. 536
76 72 or 75 11998
77 74 and 76 4608
78 73 or 77 7340
79 52 and 78 2359
80 (double-blind or random: assigned or control).tw. 554265
81 79 and 80 497

Web of Science Core Collection (Science and Social Sciences Citation Indexes – SCI-EXPANDED, SSCI)
TS=(((chronic) NEAR/1 (condition* or disease* or illness*))) — 3,672,386
TS=(((long-term) NEAR/1 (condition* or disease* or illness*))) — 16,292
TS=(chronically ill) — 6,072
TS=(rheumati*) — 54,425
TS=(diabet*) — 879,022
TS=(((endocrine) NEAR/1 (disorder* or disease* or condition*))) — 8,914

TS=(((thyroid) NEAR/1 (disorder* or disease* or condition*))) — 20,043
TS=(((adrenal) NEAR/1 (disorder* or disease* or condition*))) — 1,557
TS=(((autoimmune) NEAR/1 (disorder* or disease* or condition*))) — 106,203
TS=(((auto-immune) NEAR/1 (disorder* or disease* or condition*))) — 1,931
TS=(((auto immune) NEAR/1 (disorder* or disease* or condition*))) — 3,507
TS=adrenal insufficiency — 8,383
TS=heart failure* — 326,475
TS=coronary heart disease* — 192,572
TS=(chronic NEAR/1 (renal or kidney) NEAR/1 (insuffucien* or failure* or disease*)) — 121,026
TS=dialysis — 131,347
TS=(transplant* NEAR/3 (heart* or kidney* or liver* or lung*)) — 257,475
TS=multiple sclerosis — 146,702
TS=stroke — 409,574
TS=((neurodegenerative) NEAR/1 (disease* or disorder* or condition*)) — 106,263
TS=((neuro-degenerative) NEAR/1 (disease* or disorder* or condition*)) — 786
TS=((neuro degenerative) NEAR/1 (disease* or disorder* or condition*)) — 996
TS=(parkinson* NEAR/1 disease) — 176,729
TS=rheumatoid arthritis — 192,358
TS=osteoarthritis — 111,937
TS=lupus — 123,376
TS=(systemic sclerosis or scleroderma) — 45,897
TS=(inflammatory bowel disease* or IBD) — 113,244
TS=(primary biliary cirrhosis or PBS) — 55,103
TS=sclerosing cholangiti* — 11,277
TS=((lung or pulmonary) NEAR/1 (disease* or disorder* or condition*)) — 167,964
TS=((chronic obstructive NEAR/1 (pulmonary or lung or airway) NEAR/1 (disease* or obstruction*)) or (COPD or COAD)) — 104,320
TS=(asthma or asthmatic) — 225,022
TS=(((muscle or muscular or myopathic) NEAR/1 (disorder* or disease* or condition*)) or (myopathy or myopathies)) — 49,529
TS=(muscular dystroph* or myodystroph*) — 38,613
#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 – 4,071,294
TS=("Fatigue Questionnaire") — 349
TS=("Fatigue Severity Scale") — 1,806
TS="Multidimensional Assessment of Fatigue" — 126
TS="Short Form-36 Vitality" — 34
TS=("Functional Assessment of Chronic Illness Therapy Fatigue" or FACIT F) — 598
TS="Brief Fatigue Inventory" — 438
TS=("Visual Analog Scale Fatigue" or VAS F) — 1,168
TS="Checklist Individual Strength" — 318
TS="Chalder Fatigue Scale" — 189
TS="Multidimensional Fatigue Inventory Scale" — 6
TS="Piper Fatigue Scale" — 234
TS=(PROMIS-29 or PROMIS 29 or PROMIS29) — 464
TS=Pittsburgh Fatigability Scale — 35
TS=Fatigue Descriptive Scale — 785
TS=Modified Fatigue Impact Scale — 852
TS=("40-item Fatigue Impact Scale" or "40 item Fatigue Impact Scale") — 4
TS=("29-item Fatigue Assessment Instrument" or "29 item Fatigue Assessment Instrument") — 1
TS=("Functional Assessment of Multiple Sclerosis" or FAMS) — 266
TS=(fatigue NEAR/7 (scale* or subscale* or sub-scale* or questionnaire* or assessment* or inventor* or measure* or tool*)) — 26,432
TS=(scale or subscale or sub-scale or questionnaire or assessment or inventory or measure or measurement) — 10,552,202
TS=(fatigue or fatigability or fatigable) — 260,526
#56 AND #57 — 7,113
#55 OR #58 — 93,806

#32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 -7,673
TI=(randomi?ed controlled trial) — 153,872
#36 AND #60 AND #61 - 756

Cochrane
Date Run: 03/10/2023 15:24:43

ID	Search	Hits
#1	MeSH descriptor: [Chronic Disease] explode all trees	38848
#2	((chronic or long-term or long term) NEXT (condition* or disease* or illness*)):ti OR ((chronic or long-term or long term) NEXT (condition* or disease* or illness*)):ab	14796
#3	chronically ill:ti OR chronically ill:ab	553
#4	MeSH descriptor: [Rheumatic Diseases] explode all trees	21037
#5	rheumati*:ti OR rheumati*:ab	4521
#6	MeSH descriptor: [Diabetes Mellitus] explode all trees	46685
#7	diabet*:ti OR diabet*:ab	109423
#8	MeSH descriptor: [Endocrine System Diseases] explode all trees	61968
#9	MeSH descriptor: [Thyroid Diseases] explode all trees	2994
#10	MeSH descriptor: [Adrenal Gland Diseases] explode all trees	755
#11	MeSH descriptor: [Adrenal Insufficiency] explode all trees	327
#12	MeSH descriptor: [Autoimmune Diseases] explode all trees	25146
#13	((endocrine or thyroid or adrenal or autoimmune or auto-immune or auto immune) NEAR/1 (disorder* or disease* or condition*)):ti OR ((endocrine or thyroid or adrenal or autoimmune or auto-immune or auto immune) NEAR/1 (disorder* or disease* or condition*)):ab	6114
#14	adrenal insufficiency:ti OR adrenal insufficiency:ab	517
#15	MeSH descriptor: [Heart Failure] explode all trees	14623
#16	heart failure*:ti OR heart failure*:ab	38262
#17	MeSH descriptor: [Coronary Disease] explode all trees	18489
#18	coronary heart disease*:ti OR coronary heart disease*:ab	21575
#19	MeSH descriptor: [Renal Insufficiency, Chronic] explode all trees	8653
#20	MeSH descriptor: [Kidney Failure, Chronic] explode all trees	5550
#21	(chronic NEXT (renal or kidney) NEXT (insuffucien* or failure* or disease*)):ti OR (chronic NEXT (renal or kidney) NEXT (insuffucien* or failure* or disease*)):ab	12353
#22	MeSH descriptor: [Renal Dialysis] explode all trees	6578
#23	dialysis:ti OR dialysis:ab	13972
#24	MeSH descriptor: [Transplantation] explode all trees	16684
#25	(transplant* NEAR/3 (heart* or kidney* or liver* or lung*)):ti OR (transplant* NEAR/3 (heart* or kidney* or liver* or lung*)):ab	13405
#26	MeSH descriptor: [Multiple Sclerosis] explode all trees	5959
#27	multiple sclerosis:ti OR multiple sclerosis:ab	11695
#28	MeSH descriptor: [Stroke] explode all trees	15152
#29	stroke:ti OR stroke:ab	63149
#30	MeSH descriptor: [Neurodegenerative Diseases] explode all trees	14828
#31	((neurodegenerative or neuro-degenerative or neuro degenerative) NEXT (disease* or disorder* or condition*)):ti OR ((neurodegenerative or neuro-degenerative or neuro degenerative) NEXT (disease* or disorder* or condition*)):ab	2697
#32	MeSH descriptor: [Parkinson Disease] explode all trees	6233
#33	(parkinson* NEXT disease):ti OR (parkinson* NEXT disease):ab	11158
#34	MeSH descriptor: [Arthritis, Rheumatoid] explode all trees	7374
#35	rheumatoid arthritis:ti OR rheumatoid arthritis:ab	17496
#36	MeSH descriptor: [Osteoarthritis] explode all trees	10596
#37	osteoarthritis:ti OR osteoarthritis:ab	19163
#38	MeSH descriptor: [Lupus Erythematosus, Systemic] explode all trees	1448
#39	lupus:ti OR lupus:ab	3797
#40	MeSH descriptor: [Scleroderma, Systemic] explode all trees	731
#41	(systemic sclerosis or scleroderma):ti OR (systemic sclerosis or scleroderma):ab	2068
#42	MeSH descriptor: [Inflammatory Bowel Diseases] explode all trees	4872

#43 (inflammatory bowel disease* or IBD):ti OR (inflammatory bowel disease* or IBD):ab 4800
#44 MeSH descriptor: [Liver Cirrhosis, Biliary] explode all trees 368
#45 (primary biliary cirrhosis or PBS):ti OR (primary biliary cirrhosis or PBS):ab 1704
#46 MeSH descriptor: [Cholangitis, Sclerosing] explode all trees 135
#47 sclerosing cholangiti*:ti OR sclerosing cholangiti*:ab 365
#48 MeSH descriptor: [Lung Diseases] explode all trees 58875
#49 ((lung or pulmonary) NEXT (disease* or disorder* or condition*)):ti OR ((lung or pulmonary) NEXT (disease* or disorder* or condition*)):ab 20401
#50 MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees 7303
#51 ((chronic obstructive NEXT (pulmonary or lung or airway) NEXT (disease* or obstruction*)) or (COPD or COAD)):ti OR ((chronic obstructive NEXT (pulmonary or lung or airway) NEXT (disease* or obstruction*)) or (COPD or COAD)):ab 22726
#52 MeSH descriptor: [Asthma] explode all trees 15046
#53 (asthma or asthmatic):ti OR (asthma or asthmatic):ab 34442
#54 MeSH descriptor: [Muscular Diseases] explode all trees 11960
#55 (((muscle or muscular or myopathic) NEXT (disorder* or disease* or condition*)) or (myopathy or myopathies)):ti OR (((muscle or muscular or myopathic) NEXT (disorder* or disease* or condition*)) or (myopathy or myopathies)):ab 1361
#56 MeSH descriptor: [Muscular Dystrophies] explode all trees 595
#57 (muscular dystroph* or myodystroph*):ti OR (muscular dystroph* or myodystroph*):ab 1101
#58 {OR #1-#57} 494013
#59 "Fatigue Questionnaire":ti OR "Fatigue Questionnaire":ab 240
#60 "Fatigue Severity Scale":ti OR "Fatigue Severity Scale":ab 1152
#61 "Multidimensional Assessment of Fatigue":ti OR "Multidimensional Assessment of Fatigue":ab 56
#62 "Short Form-36 Vitality":ti OR "Short Form-36 Vitality":ab 8
#63 ("Functional Assessment of Chronic Illness Therapy Fatigue" or FACIT F):ti OR ("Functional Assessment of Chronic Illness Therapy Fatigue" or FACIT F):ab 954
#64 "Brief Fatigue Inventory":ti OR "Brief Fatigue Inventory":ab 412
#65 "Numerical Rating Scale Fatigue":ti OR "Numerical Rating Scale Fatigue":ab 4
#66 ("Visual Analog Scale Fatigue" or VAS F):ti OR ("Visual Analog Scale Fatigue" or VAS F):ab 2248
#67 "Checklist Individual Strength":ti OR "Checklist Individual Strength":ab 167
#68 "Chalder Fatigue Scale":ti OR "Chalder Fatigue Scale":ab 190
#69 "Multidimensional Fatigue Inventory Scale":ti OR "Multidimensional Fatigue Inventory Scale":ab 3
#70 "Piper Fatigue Scale":ti OR "Piper Fatigue Scale":ab 205
#71 (PROMIS-29 or PROMIS 29 or PROMIS29):ti OR (PROMIS-29 or PROMIS 29 or PROMIS29):ab 258
#72 Pittsburgh Fatigability Scale:ti OR Pittsburgh Fatigability Scale:ab 10
#73 Fatigue Descriptive Scale:ti OR Fatigue Descriptive Scale:ab 493
#74 Modified Fatigue Impact Scale:ti OR Modified Fatigue Impact Scale:ab 700
#75 ("40-item Fatigue Impact Scale" or "40 item Fatigue Impact Scale"):ti OR ("40-item Fatigue Impact Scale" or "40 item Fatigue Impact Scale"):ab 1
#76 ("29-item Fatigue Assessment Instrument" or "29 item Fatigue Assessment Instrument"):ti OR ("29-item Fatigue Assessment Instrument" or "29 item Fatigue Assessment Instrument"):ab 1
#77 ("Functional Assessment of Multiple Sclerosis" or FAMS):ti OR ("Functional Assessment of Multiple Sclerosis" or FAMS):ab 50
#78 {OR #59-#77} 6577
#79 MeSH descriptor: [Fatigue] this term only 8377
#80 (fatigue NEXT/7 (scale* or subscale* or sub-scale* or questionnaire* or assessment* or inventor* or measure* or tool*)):ti OR (fatigue NEXT/7 (scale* or subscale* or sub-scale* or questionnaire* or assessment* or inventor* or measure* or tool*)):ab 7123
#81 (scale or subscale or sub-scale or questionnaire or assessment or inventory or measure or measurement):ti OR (scale or subscale or sub-scale or questionnaire or assessment or inventory or measure or measurement):ab 512278
#82 (fatigability or fatigable):ti OR (fatigability or fatigable):ab 393
#83 #79 OR #82 8708

#84 #81 AND #83 3579
#85 #80 OR #84 9134
#86 #58 AND #85 3981

Search Strategies: Systematic Reviews search
Ovid MEDLINE(R) Epub Ahead of Print and In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <November 27, 2024>
1 exp Chronic Disease/ 654158
2 ((chronic or long-term or long term) adj (condition* or disease* or illness*)).ti,ab. 141815
3 chronically ill.ti,ab. 6323
4 exp Rheumatic Diseases/ 272346
5 rheumati*.ti,ab. 66215
6 exp Diabetes Mellitus/ 538090
7 diabet*.ti,ab. 834172
8 exp Endocrine System Diseases/ 1181269
9 exp Thyroid Diseases/ 168992
10 exp Adrenal Gland Diseases/ or exp Adrenal Insufficiency/ 74467
11 exp Autoimmune Diseases/ 570667
12 ((endocrine or thyroid or adrenal or autoimmune or auto-immune or auto immune) adj1 (disorder* or disease* or condition*)).ti,ab. 132811
13 adrenal insufficiency.ti,ab. 7868
14 exp Heart Failure/ 157212
15 heart failure*.ti,ab. 226915
16 exp Coronary Disease/ 242628
17 coronary heart disease*.ti,ab. 57626
18 exp Renal Insufficiency, Chronic/ 141810
19 exp Kidney Failure, Chronic/ 103657
20 (chronic adj (renal or kidney) adj (insuffucien* or failure* or disease*)).ti,ab. 107957
21 exp Renal Dialysis/ 130524
22 dialysis.ti,ab. 127861
23 exp Transplants/ 33321
24 (transplant* adj3 (heart* or kidney* or liver* or lung*)).ti,ab. 191883
25 exp Multiple Sclerosis/ 73877
26 multiple sclerosis.ti,ab. 96133
27 exp Stroke/ 186713
28 stroke.ti,ab. 330970
29 exp Neurodegenerative Diseases/ 394228
30 ((neurodegenerative or neuro-degenerative or neuro degenerative) adj (disease* or disorder* or condition*)).ti,ab. 111431
31 exp Parkinson Disease/ 88202
32 (parkinson* adj disease).ti,ab. 126026
33 exp Arthritis, Rheumatoid/ 130626
34 rheumatoid arthritis.ti,ab. 126907
35 exp Osteoarthritis/ 82888
36 osteoarthritis.ti,ab. 92680
37 exp Lupus Erythematosus, Systemic/ 69932
38 lupus.ti,ab. 93222
39 exp Scleroderma, Systemic/ 24020
40 (systemic sclerosis or scleroderma).ti,ab. 30500
41 exp Inflammatory Bowel Diseases/ 103655
42 (inflammatory bowel disease* or IBD).ti,ab. 73818
43 exp Liver Cirrhosis, Biliary/ 9010
44 (primary biliary cirrhosis or PBS).ti,ab. 38807
45 exp Cholangitis, Sclerosing/ 4920
46 sclerosing cholangiti*.ti,ab. 7766
47 exp Lung Diseases/ 1312727
48 ((lung or pulmonary) adj (disease* or disorder* or condition*)).ti,ab. 154066
49 exp Pulmonary Disease, Chronic Obstructive/ 70946
50 ((chronic obstructive adj (pulmonary or lung or airway) adj (disease* or obstruction*)) or (COPD or COAD)).ti,ab. 89722

51 exp Asthma/ 147301
52 (asthma or asthmatic).ti,ab. 184955
53 exp Muscular Diseases/ 203180
54 (((muscle or muscular or myopathic) adj (disorder* or disease* or condition*)) or (myopathy or myopathies)).ti,ab. 38290
55 exp Muscular Dystrophies/ 30943
56 (muscular dystroph* or myodystroph*).ti,ab. 28443
57 or/1-56 5874536
58 "Fatigue Questionnaire".ti,ab. 421
59 "Fatigue Severity Scale".ti,ab. 2067
60 "Multidimensional Assessment of Fatigue".ti,ab. 144
61 "Short Form-36 Vitality".ti,ab. 34
62 ("Functional Assessment of Chronic Illness Therapy Fatigue" or FACIT F).ti,ab. 752
63 "Brief Fatigue Inventory".ti,ab. 517
64 "Numerical Rating Scale Fatigue".ti,ab. 7
65 ("Visual Analog Scale Fatigue" or VAS F).ti,ab. 120
66 "Checklist Individual Strength".ti,ab. 352
67 "Chalder Fatigue Scale".ti,ab. 240
68 "Multidimensional Fatigue Inventory Scale".ti,ab. 10
69 "Piper Fatigue Scale".ti,ab. 289
70 (PROMIS-29 or PROMIS 29 or PROMIS29).ti,ab. 335
71 Pittsburgh Fatigability Scale.ti,ab. 43
72 Fatigue Descriptive Scale.ti,ab. 11
73 Modified Fatigue Impact Scale.ti,ab. 606
74 ("40-item Fatigue Impact Scale" or "40 item Fatigue Impact Scale").ti,ab. 4
75 ("29-item Fatigue Assessment Instrument" or "29 item Fatigue Assessment Instrument").ti,ab. 1
76 ("Functional Assessment of Multiple Sclerosis" or FAMS).ti,ab. 193
77 or/58-76 5751
78 *Fatigue/ 17037
79 (fatigue adj7 (scale* or subscale* or sub-scale* or questionnaire* or assessment* or inventor* or measure* or tool*)).ti,ab. 19310
80 (scale or subscale or sub-scale or questionnaire or assessment or inventory or measure or measurement).ti,ab. 3753921
81 (fatigability or fatigable).ti,ab. 3630
82 78 or 81 20385
83 80 and 82 7203
84 79 or 83 21678
85 77 or 84 22367
86 57 and 85 9455
87 (MEDLINE or systematic review).tw. or meta analysis.pt. 500343
88 86 and 87 325

Embase <1974 to 2024 Week 47>

1 *chronic disease/ 34954
2 ((chronic or long-term or long term) adj (condition* or disease* or illness*)).ti,ab. 196339
3 chronically ill.ti,ab. 7801
4 *rheumatic disease/ 33333
5 rheumati*.ti,ab. 86414
6 *diabetes mellitus/ 255008
7 diabet*.ti,ab. 1266395
8 *endocrine disease/ 7508
9 *thyroid disease/ 14564
10 *adrenal disease/ 2112
11 *adrenal insufficiency/ 4871
12 *autoimmune disease/ 37088
13 ((endocrine or thyroid or adrenal or autoimmune or auto-immune or auto immune) adj1 (disorder* or disease* or condition*)).ti,ab. 199767
14 adrenal insufficiency.ti,ab. 12291

15 *heart failure/ 136001
16 heart failure*.ti,ab. 381715
17 *coronary artery disease/ 100373
18 coronary heart disease*.ti,ab. 79147
19 *chronic kidney failure/ 69844
20 (chronic adj (renal or kidney) adj (insuffucien* or failure* or disease*)).ti,ab. 172600
21 *hemodialysis/ 67261
22 dialysis.ti,ab. 193744
23 *transplantation/ 64725
24 (transplant* adj3 (heart* or kidney* or liver* or lung*)).ti,ab. 329022
25 *multiple sclerosis/ 108475
26 multiple sclerosis.ti,ab. 149971
27 *cerebrovascular accident/ 115826
28 stroke.ti,ab. 529463
29 *degenerative disease/ 20667
30 ((neurodegenerative or neuro-degenerative or neuro degenerative) adj (disease* or disorder* or condition*)).ti,ab. 145110
31 *Parkinson disease/ 129695
32 (parkinson* adj disease).ti,ab. 181036
33 *rheumatoid arthritis/ 133978
34 rheumatoid arthritis.ti,ab. 191238
35 *osteoarthritis/ 55895
36 osteoarthritis.ti,ab. 131490
37 *systemic lupus erythematosus/ 67671
38 lupus.ti,ab. 135191
39 *systemic sclerosis/ 24539
40 (systemic sclerosis or scleroderma).ti,ab. 47556
41 *inflammatory bowel disease/ 33488
42 (inflammatory bowel disease* or IBD).ti,ab. 131258
43 *biliary cirrhosis/ 2407
44 (primary biliary cirrhosis or PBS).ti,ab. 62982
45 *sclerosing cholangitis/ 2054
46 sclerosing cholangiti*.ti,ab. 13366
47 *lung disease/ 35911
48 ((lung or pulmonary) adj (disease* or disorder* or condition*)).ti,ab. 237743
49 *chronic obstructive lung disease/ 88575
50 ((chronic obstructive adj (pulmonary or lung or airway) adj (disease* or obstruction*)) or (COPD or COAD)).ti,ab. 155701
51 *asthma/ 157738
52 (asthma or asthmatic).ti,ab. 271814
53 *muscle disease/ 10264
54 (((muscle or muscular or myopathic) adj (disorder* or disease* or condition*)) or (myopathy or myopathies)).ti,ab. 55279
55 *muscular dystrophy/ 9781
56 (muscular dystroph* or myodystroph*).ti,ab. 38669
57 or/1-56 4825307
58 "Fatigue Questionnaire".ti,ab. 685
59 "Fatigue Severity Scale".ti,ab. 3809
60 "Multidimensional Assessment of Fatigue".ti,ab. 278
61 "Short Form-36 Vitality".ti,ab. 41
62 ("Functional Assessment of Chronic Illness Therapy Fatigue" or FACIT F).ti,ab. 1940
63 "Brief Fatigue Inventory".ti,ab. 951
64 "Numerical Rating Scale Fatigue".ti,ab. 11
65 ("Visual Analog Scale Fatigue" or VAS F).ti,ab. 181
66 "Checklist Individual Strength".ti,ab. 500
67 "Chalder Fatigue Scale".ti,ab. 365
68 "Multidimensional Fatigue Inventory Scale".ti,ab. 18
69 "Piper Fatigue Scale".ti,ab. 401
70 (PROMIS-29 or PROMIS 29 or PROMIS29).ti,ab. 804
71 Pittsburgh Fatigability Scale.ti,ab. 56

72 Fatigue Descriptive Scale.ti,ab. 18
73 Modified Fatigue Impact Scale.ti,ab. 1198
74 ("40-item Fatigue Impact Scale" or "40 item Fatigue Impact Scale").ti,ab. 4
75 ("29-item Fatigue Assessment Instrument" or "29 item Fatigue Assessment Instrument").ti,ab. 2
76 ("Functional Assessment of Multiple Sclerosis" or FAMS).ti,ab. 374
77 exp Fatigue Severity Scale/ or exp "Functional Assessment of Chronic Illness Therapy Fatigue Scale"/ or exp Multidimensional Fatigue Inventory/ or exp Chalder Fatigue Scale/ or exp Piper fatigue scale/ or exp "fatigue scale for motor and cognitive functions"/ or exp Fatigue Impact Scale/ 7913
78 or/58-77 13999
79 *fatigue/ 27870
80 (fatigue adj7 (scale* or subscale* or sub-scale* or questionnaire* or assessment* or inventor* or measure* or tool*)).ti,ab. 31993
81 (scale or subscale or sub-scale or questionnaire or assessment or inventory or measure or measurement).ti,ab. 5085498
82 (fatigability or fatigable).ti,ab. 5536
83 79 or 82 32922
84 81 and 83 13199
85 80 or 84 35785
86 78 or 85 38984
87 57 and 86 14155
88 exp review/ 3355072
89 (literature adj3 review$).ti,ab. 494495
90 exp meta analysis/ 338595
91 exp "Systematic Review"/ 496268
92 88 or 89 or 90 or 91 3753315
93 (medline or medlars or embase or pubmed or cinahl or amed or psychlit or psyclit or psychinfo or psycinfo or scisearch or cochrane).ti,ab. 523890
94 RETRACTED ARTICLE/ 14987
95 93 or 94 538405
96 92 and 95 424367
97 (systematic$ adj2 (review$ or overview)).ti,ab. 458236
98 (meta?anal$ or meta anal$ or meta-anal$ or metaanal$ or metanal$).ti,ab. 411264
99 96 or 97 or 98 771746
100 87 and 99 519
101 limit 100 to "remove medline records" 247

CINAHL via EBSCO
S1 (MH "Chronic Disease+")
S2 TI ((chronic or long-term or long term) N1 (condition* or disease* or illness*)) OR AB ((chronic or long-term or long term) N1 (condition* or disease* or illness*))
S3 TI chronically ill OR AB chronically ill
S4 (MH "Rheumatic Diseases+")
S5 TI rheumati* OR AB rheumati*
S6 (MH "Diabetes Mellitus+")
S7 TI diabet* OR AB diabet*
S8 (MH "Endocrine Diseases+")
S9 (MH "Thyroid Diseases+")
S10 (MH "Adrenal Gland Diseases+")
S11 (MH "Adrenal Insufficiency+")
S12 (MH "Autoimmune Diseases+")
S13 TI ((endocrine or thyroid or adrenal or autoimmune or auto-immune or auto immune) N1 (disorder* or disease* or condition*)) OR AB ((endocrine or thyroid or adrenal or autoimmune or auto-immune or auto immune) N1 (disorder* or disease* or condition*))
S14 TI adrenal insufficiency OR AB adrenal insufficiency
S15 (MH "Heart Failure+")
S16 TI heart failure* OR AB heart failure*
S17 (MH "Coronary Disease+")
S18 TI coronary heart disease* OR AB coronary heart disease*

S19 (MH "Renal Insufficiency, Chronic+")
S20 (MH "Kidney Failure, Chronic+")
S21 TI (chronic adj (renal or kidney) N1 (insuffucien* or failure* or disease*)) OR AB (chronic adj (renal or kidney) N1 (insuffucien* or failure* or disease*))
S22 (MH "Dialysis Patients")
S23 TI dialysis OR AB dialysis
S24 TI (transplant* N3 (heart* or kidney* or liver* or lung*)) OR AB (transplant* N3 (heart* or kidney* or liver* or lung*))
S25 (MH "Multiple Sclerosis+")
S26 TI multiple sclerosis OR AB multiple sclerosis
S27 (MH "Stroke+")
S28 TI stroke OR AB stroke
S29 (MH "Neurodegenerative Diseases+")
S30 TI ((neurodegenerative or neuro-degenerative or neuro degenerative) N1 (disease* or disorder* or condition*)) OR AB ((neurodegenerative or neuro-degenerative or neuro degenerative) N1 (disease* or disorder* or condition*))
S31 (MH "Parkinson Disease")
S32 TI (parkinson* N1 disease) OR AB (parkinson* N1 disease)
S33 (MH "Arthritis, Rheumatoid+")
S34 TI rheumatoid arthritis OR AB rheumatoid arthritis
S35 (MH "Osteoarthritis+")
S36 TI osteoarthritis OR AB osteoarthritis
S37 (MH "Lupus Erythematosus, Systemic+")
S38 TI lupus OR AB lupus
S39 (MH "Scleroderma, Systemic+")
S40 TI (systemic sclerosis or scleroderma) OR AB (systemic sclerosis or scleroderma)
S41 (MH "Inflammatory Bowel Diseases+")
S42 TI (inflammatory bowel disease* or IBD) OR AB (inflammatory bowel disease* or IBD)
S43 (MH "Liver Cirrhosis+")
S44 TI (primary biliary cirrhosis or PBS) OR AB (primary biliary cirrhosis or PBS)
S45 (MH "Cholangitis, Sclerosing")
S46 TI sclerosing cholangiti* OR AB sclerosing cholangiti*
S47 (MH "Lung Diseases+")
S48 TI ((lung or pulmonary) N1 (disease* or disorder* or condition*)) OR AB ((lung or pulmonary) N1 (disease* or disorder* or condition*))
S49 (MH "Pulmonary Disease, Chronic Obstructive+")
S50 TI ((chronic obstructive N1 (pulmonary or lung or airway) N1 (disease* or obstruction*)) or (COPD or COAD)) OR AB ((chronic obstructive N1 (pulmonary or lung or airway) N1 (disease* or obstruction*)) or (COPD or COAD))
S51 (MH "Asthma+")
S52 TI (asthma or asthmatic) OR AB (asthma or asthmatic)
S53 (MH "Muscular Diseases+")
S54 TI (((muscle or muscular or myopathic) ADJ1 (disorder* or disease* or condition*)) or (myopathy or myopathies)) OR AB (((muscle or muscular or myopathic) ADJ1 (disorder* or disease* or condition*)) or (myopathy or myopathies))
S55 (MH "Muscular Dystrophy+")
S56 TI (muscular dystroph* or myodystroph*) OR AB (muscular dystroph* or myodystroph*)
S57 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56
S58 TI "Fatigue Questionnaire" OR AB "Fatigue Questionnaire"
S59 TI "Fatigue Severity Scale" OR AB "Fatigue Severity Scale"
S60 TI "Multidimensional Assessment of Fatigue" OR AB "Multidimensional Assessment of Fatigue"
S61 TI "Short Form-36 Vitality" OR AB "Short Form-36 Vitality"
S62 TI ("Functional Assessment of Chronic Illness Therapy Fatigue" or FACIT F) OR AB ("Functional Assessment of Chronic Illness Therapy Fatigue" or FACIT F)
S63 TI "Brief Fatigue Inventory" OR AB "Brief Fatigue Inventory"
S64 TI "Numerical Rating Scale Fatigue" OR AB "Numerical Rating Scale Fatigue"

S65 TI ("Visual Analog Scale Fatigue" or VAS F) OR AB ("Visual Analog Scale Fatigue" or VAS F)
S66 TI "Checklist Individual Strength" OR AB "Checklist Individual Strength"
S67 TI "Chalder Fatigue Scale" OR AB "Chalder Fatigue Scale"
S68 TI "Multidimensional Fatigue Inventory Scale" OR AB "Multidimensional Fatigue Inventory Scale"
S69 TI "Piper Fatigue Scale" OR AB "Piper Fatigue Scale"
S70 TI (PROMIS-29 or PROMIS 29 or PROMIS29) OR AB (PROMIS-29 or PROMIS 29 or PROMIS29)
S71 TI Pittsburgh Fatigability Scale OR AB Pittsburgh Fatigability Scale
S72 TI Fatigue Descriptive Scale OR AB Fatigue Descriptive Scale
S73 TI Modified Fatigue Impact Scale OR AB Modified Fatigue Impact Scale
S74 TI ("40-item Fatigue Impact Scale" or "40 item Fatigue Impact Scale") OR AB ("40-item Fatigue Impact Scale" or "40 item Fatigue Impact Scale")
S75 TI ("29-item Fatigue Assessment Instrument" or "29 item Fatigue Assessment Instrument") OR AB ("29-item Fatigue Assessment Instrument" or "29 item Fatigue Assessment Instrument")
S76 TI ("Functional Assessment of Multiple Sclerosis" or FAMS) OR AB ("Functional Assessment of Multiple Sclerosis" or FAMS)
S77 S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76
S78 (MM "Fatigue")
S79 TI (fatigue N7 (scale* or subscale* or sub-scale* or questionnaire* or assessment* or inventor* or measure* or tool*)) OR AB (fatigue N7 (scale* or subscale* or sub-scale* or questionnaire* or assessment* or inventor* or measure* or tool*))
S80 TI (scale or subscale or sub-scale or questionnaire or assessment or inventory or measure or measurement) OR AB (scale or subscale or sub-scale or questionnaire or assessment or inventory or measure or measurement)
S81 TI (fatigability or fatigable) OR AB (fatigability or fatigable)
S82 S78 OR S81
S83 S79 AND S80
S84 (S82 OR S83)
S85 (TI (systematic* n3 review*)) or (AB (systematic* n3 review*)) or (TI (systematic* n3 bibliographic*)) or (AB (systematic* n3 bibliographic*)) or (TI (systematic* n3 literature)) or (AB (systematic* n3 literature)) or (TI (comprehensive* n3 literature)) or (AB (comprehensive* n3 literature)) or (TI (comprehensive* n3 bibliographic*)) or (AB (comprehensive* n3 bibliographic*)) or (TI (integrative n3 review)) or (AB (integrative n3 review)) or (JN “Cochrane Database of Systematic Reviews”) or (TI (information n2 synthesis)) or (TI (data n2 synthesis)) or (AB (information n2 synthesis)) or (AB (data n2 synthesis)) or (TI (data n2 extract*)) or (AB (data n2 extract*)) or (TI (medline or pubmed or psyclit or cinahl or (psycinfo not “psycinfo database”) or “web of science” or scopus or embase)) or (AB (medline or pubmed or psyclit or cinahl or (psycinfo not “psycinfo database”) or “web of science” or scopus or embase)) or (MH “Systematic Review”) or (MH “Meta Analysis”) or (TI (meta-analy* or metaanaly*)) or (AB (meta-analy* or metaanaly*)) 319,272
S86 (S84 AND S85) 266

APA PsycInfo <1806 to November 2024 Week 4>

1 exp Chronic Illness/ 38747
2 ((chronic or long-term or long term) adj (condition* or disease* or illness*)).ti,ab. 31815
3 chronically ill.ti,ab. 3266
4 exp Rheumatoid Arthritis/ 2191
5 rheumati*.ti,ab. 1171
6 exp Diabetes Mellitus/ 10907
7 diabet*.ti,ab. 38686
8 exp Thyroid Disorders/ 1601
9 exp Adrenal Gland Disorders/ 434
10 exp Immunologic Disorders/ 62844
11 ((endocrine or thyroid or adrenal or autoimmune or auto-immune or auto immune) adj1 (disorder* or disease* or condition*)).ti,ab. 4101
12 adrenal insufficiency.ti,ab. 152
13 exp Heart Disorders/ 17285
14 heart failure*.ti,ab. 4886
15 exp Cardiovascular Disorders/ 75870

16 coronary heart disease*.ti,ab. 4513
17 exp Kidney Diseases/ 2855
18 (chronic adj (renal or kidney) adj (insuffucien* or failure* or disease*)).ti,ab. 1678
19 exp Dialysis/ 2398
20 dialysis.ti,ab. 2467
21 exp Organ Transplantation/ 5681
22 (transplant* adj3 (heart* or kidney* or liver* or lung*)).ti,ab. 2172
23 exp Multiple Sclerosis/ 14944
24 multiple sclerosis.ti,ab. 17760
25 exp Cerebrovascular Accidents/ 26271
26 stroke.ti,ab. 39801
27 exp Neurodegenerative Diseases/ 102451
28 ((neurodegenerative or neuro-degenerative or neuro degenerative) adj (disease* or disorder* or condition*)).ti,ab. 20837
29 (parkinson* adj disease).ti,ab. 34494
30 exp Rheumatoid Arthritis/ 2191
31 rheumatoid arthritis.ti,ab. 2904
32 exp Arthritis/ 5077
33 osteoarthritis.ti,ab. 2449
34 exp Lupus/ 922
35 lupus.ti,ab. 1691
36 (systemic sclerosis or scleroderma).ti,ab. 232
37 exp Colon Disorders/ 6783
38 (inflammatory bowel disease* or IBD).ti,ab. 1324
39 exp Liver Disorders/ 5368
40 (primary biliary cirrhosis or PBS).ti,ab. 1666
41 sclerosing cholangiti*.ti,ab. 21
42 exp Lung Disorders/ 6793
43 ((lung or pulmonary) adj (disease* or disorder* or condition*)).ti,ab. 4200
44 exp Chronic Obstructive Pulmonary Disease/ 1930
45 ((chronic obstructive adj (pulmonary or lung or airway) adj (disease* or obstruction*)) or (COPD or COAD)).ti,ab. 3223
46 exp Asthma/ 5507
47 (asthma or asthmatic).ti,ab. 8811
48 exp Muscular Disorders/11266
49 (((muscle or muscular or myopathic) adj (disorder* or disease* or condition*)) or (myopathy or myopathies)).ti,ab. 1877
50 exp Muscular Dystrophy/ 1575
51 (muscular dystroph* or myodystroph*).ti,ab. 1679
52 or/1-51 403622
53 "Fatigue Questionnaire".ti,ab. 135
54 "Multidimensional Assessment of Fatigue".ti,ab. 36
55 "Short Form-36 Vitality".ti,ab. 8
56 ("Functional Assessment of Chronic Illness Therapy Fatigue" or FACIT F).ti,ab. 85
57 "Brief Fatigue Inventory".ti,ab. 112
58 "Numerical Rating Scale Fatigue".ti,ab. 4
59 ("Visual Analog Scale Fatigue" or VAS F).ti,ab. 26
60 "Checklist Individual Strength".ti,ab. 121
61 "Chalder Fatigue Scale".ti,ab. 84
62 "Multidimensional Fatigue Inventory Scale".ti,ab. 0
63 "Piper Fatigue Scale".ti,ab. 76
64 (PROMIS-29 or PROMIS 29 or PROMIS29).ti,ab. 83
65 Pittsburgh Fatigability Scale.ti,ab. 14
66 Fatigue Descriptive Scale.ti,ab. 1
67 Modified Fatigue Impact Scale.ti,ab. 151
68 ("40-item Fatigue Impact Scale" or "40 item Fatigue Impact Scale").ti,ab. 2
69 ("29-item Fatigue Assessment Instrument" or "29 item Fatigue Assessment Instrument").ti,ab. 1
70 ("Functional Assessment of Multiple Sclerosis" or FAMS).ti,ab. 62
71 or/52-70 404079

72 exp Fatigue/ 12644
73 (fatigue adj7 (scale* or subscale* or sub-scale* or questionnaire* or assessment* or inventor* or measure* or tool*)).ti,ab. 5752
74 (scale or subscale or sub-scale or questionnaire or assessment or inventory or measure or measurement).ti,ab. 1120968
75 (fatigability or fatigable).ti,ab. 558
76 72 or 75 13033
77 74 and 76 5113
78 73 or 77 8002
79 52 and 78 2577
80 (meta-analysis or search:).tw. 169257
81 79 and 80 93

Web of Science Core Collection (Science and Social Sciences Citation Indexes – SCI-EXPANDED, SSCI)
TS=(((chronic) NEAR/1 (condition* or disease* or illness*))) Results: 359541
(TS=(((long-term) NEAR/1 (condition* or disease* or illness*)))) Results: 18258
TS=(chronically ill) Results: 6642
TS=(rheumati*) Results: 60176
TS=(diabet*) Results: 950365
TS=(((endocrine) NEAR/1 (disorder* or disease* or condition*))) Results: 10304
TS=(((thyroid) NEAR/1 (disorder* or disease* or condition*))) Results: 22399
TS=(((adrenal) NEAR/1 (disorder* or disease* or condition*))) Results: 1817
TS=(((autoimmune) NEAR/1 (disorder* or disease* or condition*))) Results: 116974
TS=(((auto-immune) NEAR/1 (disorder* or disease* or condition*))) Results: 2123
TS=(((auto immune) NEAR/1 (disorder* or disease* or condition*))) Results: 3843
TS=adrenal insufficiency Results: 9764
TS=heart failure* Results: 358758
TS=coronary heart disease* Results: 204650
TS=(chronic NEAR/1 (renal or kidney) NEAR/1 (insuffucien* or failure* or disease*)) Results: 133763
TS=dialysis Results: 149587
TS=(transplant* NEAR/3 (heart* or kidney* or liver* or lung*)) Results: 275387
TS=multiple sclerosis Results: 156702
TS=stroke Results: 450117
TS=((neurodegenerative) NEAR/1 (disease* or disorder* or condition*)) Results: 117914
TS=((neuro-degenerative) NEAR/1 (disease* or disorder* or condition*)) Results: 826
TS=((neuro degenerative) NEAR/1 (disease* or disorder* or condition*)) Results: 1058
TS=(parkinson* NEAR/1 disease) Results: 190306
TS=rheumatoid arthritis Results: 205223
TS=osteoarthritis Results: 123264
TS=lupus Results: 132734
TS=(systemic sclerosis or scleroderma) Results: 49435
TS=(inflammatory bowel disease* or IBD) Results: 123692
TS=(primary biliary cirrhosis or PBS) Results: 60151
TS=sclerosing cholangiti* Results: 12099
TS=((lung or pulmonary) NEAR/1 (disease* or disorder* or condition*)) Results: 185254
TS=((chronic obstructive NEAR/1 (pulmonary or lung or airway) NEAR/1 (disease* or obstruction*)) or (COPD or COAD)) Results: 112767
TS=(asthma or asthmatic) Results: 239662
TS=(((muscle or muscular or myopathic) NEAR/1 (disorder* or disease* or condition*)) or (myopathy or myopathies)) Results: 54161
TS=(muscular dystroph* or myodystroph*) Results: 41449
#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 Results: 3991303
TS=(fatigue or fatigability or fatigable) Results: 288108
TS=(fatigue NEAR/7 (scale* or subscale* or sub-scale* or questionnaire* or assessment* or inventor* or measure* or tool*)) Results: 29495

TS=(scale or subscale or sub-scale or questionnaire or assessment or inventory or measure or measurement) Results: 11727743
#37 AND #39 Results: 103757
#38 OR #40 Results: 104634
#36 AND #41 Results: 17495
TI=(systematic NEAR/3 (review OR overview)) OR TI=(methodologic NEAR/3 (review OR overview)) OR TI=(quantitative NEAR/3 (review OR overview OR synthesis)) OR TI=(research NEAR/3 (integrative OR overview)) OR TI=(integrative NEAR/3 (review OR overview)) OR TI=(collaborative NEAR/3 (review OR overview)) Results: 316800
#42 AND #43 Results: 627

Cochrane Database of Systematic Reviews
Issue 11 of 12, November 2024
ID Search
#1 MeSH descriptor: [Chronic Disease] explode all trees
#2 ((chronic or long-term or long term) NEXT (condition* or disease* or illness*)):ti OR ((chronic or long-term or long term) NEXT (condition* or disease* or illness*)):ab
#3 chronically ill:ti OR chronically ill:ab
#4 MeSH descriptor: [Rheumatic Diseases] explode all trees
#5 rheumati*:ti OR rheumati*:ab
#6 MeSH descriptor: [Diabetes Mellitus] explode all trees
#7 diabet*:ti OR diabet*:ab
#8 MeSH descriptor: [Endocrine System Diseases] explode all trees
#9 MeSH descriptor: [Thyroid Diseases] explode all trees
#10 MeSH descriptor: [Adrenal Gland Diseases] explode all trees
#11 MeSH descriptor: [Adrenal Insufficiency] explode all trees
#12 MeSH descriptor: [Autoimmune Diseases] explode all trees
#13 ((endocrine or thyroid or adrenal or autoimmune or auto-immune or auto immune) NEAR/1 (disorder* or disease* or condition*)):ti OR ((endocrine or thyroid or adrenal or autoimmune or auto-immune or auto immune) NEAR/1 (disorder* or disease* or condition*)):ab
#14 adrenal insufficiency:ti OR adrenal insufficiency:ab
#15 MeSH descriptor: [Heart Failure] explode all trees
#16 heart failure*:ti OR heart failure*:ab
#17 MeSH descriptor: [Coronary Disease] explode all trees
#18 coronary heart disease*:ti OR coronary heart disease*:ab
#19 MeSH descriptor: [Renal Insufficiency, Chronic] explode all trees
#20 MeSH descriptor: [Kidney Failure, Chronic] explode all trees
#21 (chronic NEXT (renal or kidney) NEXT (insuffucien* or failure* or disease*)):ti OR (chronic NEXT (renal or kidney) NEXT (insuffucien* or failure* or disease*)):ab
#22 MeSH descriptor: [Renal Dialysis] explode all trees
#23 dialysis:ti OR dialysis:ab
#24 MeSH descriptor: [Transplantation] explode all trees
#25 (transplant* NEAR/3 (heart* or kidney* or liver* or lung*)):ti OR (transplant* NEAR/3 (heart* or kidney* or liver* or lung*)):ab
#26 MeSH descriptor: [Multiple Sclerosis] explode all trees
#27 multiple sclerosis:ti OR multiple sclerosis:ab
#28 MeSH descriptor: [Stroke] explode all trees
#29 stroke:ti OR stroke:ab
#30 MeSH descriptor: [Neurodegenerative Diseases] explode all trees
#31 ((neurodegenerative or neuro-degenerative or neuro degenerative) NEXT (disease* or disorder* or condition*)):ti OR ((neurodegenerative or neuro-degenerative or neuro degenerative) NEXT (disease* or disorder* or condition*)):ab
#32 MeSH descriptor: [Parkinson Disease] explode all trees
#33 (parkinson* NEXT disease):ti OR (parkinson* NEXT disease):ab
#34 MeSH descriptor: [Arthritis, Rheumatoid] explode all trees
#35 rheumatoid arthritis:ti OR rheumatoid arthritis:ab
#36 MeSH descriptor: [Osteoarthritis] explode all trees
#37 osteoarthritis:ti OR osteoarthritis:ab
#38 MeSH descriptor: [Lupus Erythematosus, Systemic] explode all trees
#39 lupus:ti OR lupus:ab

#40 MeSH descriptor: [Scleroderma, Systemic] explode all trees
#41 (systemic sclerosis or scleroderma):ti OR (systemic sclerosis or scleroderma):ab
#42 MeSH descriptor: [Inflammatory Bowel Diseases] explode all trees
#43 (inflammatory bowel disease* or IBD):ti OR (inflammatory bowel disease* or IBD):ab
#44 MeSH descriptor: [Liver Cirrhosis, Biliary] explode all trees
#45 (primary biliary cirrhosis or PBS):ti OR (primary biliary cirrhosis or PBS):ab
#46 MeSH descriptor: [Cholangitis, Sclerosing] explode all trees
#47 sclerosing cholangiti*:ti OR sclerosing cholangiti*:ab
#48 MeSH descriptor: [Lung Diseases] explode all trees
#49 ((lung or pulmonary) NEXT (disease* or disorder* or condition*)):ti OR ((lung or pulmonary) NEXT (disease* or disorder* or condition*)):ab
#50 MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees
#51 ((chronic obstructive NEXT (pulmonary or lung or airway) NEXT (disease* or obstruction*)) or (COPD or COAD)):ti OR ((chronic obstructive NEXT (pulmonary or lung or airway) NEXT (disease* or obstruction*)) or (COPD or COAD)):ab
#52 MeSH descriptor: [Asthma] explode all trees
#53 (asthma or asthmatic):ti OR (asthma or asthmatic):ab
#54 MeSH descriptor: [Muscular Diseases] explode all trees
#55 (((muscle or muscular or myopathic) NEXT (disorder* or disease* or condition*)) or (myopathy or myopathies)):ti OR (((muscle or muscular or myopathic) NEXT (disorder* or disease* or condition*)) or (myopathy or myopathies)):ab
#56 MeSH descriptor: [Muscular Dystrophies] explode all trees
#57 (muscular dystroph* or myodystroph*):ti OR (muscular dystroph* or myodystroph*):ab
#58 {OR #1-#57}
#59 "Fatigue Questionnaire":ti OR "Fatigue Questionnaire":ab
#60 "Fatigue Severity Scale":ti OR "Fatigue Severity Scale":ab
#61 "Multidimensional Assessment of Fatigue":ti OR "Multidimensional Assessment of Fatigue":ab
#62 "Short Form-36 Vitality":ti OR "Short Form-36 Vitality":ab
#63 ("Functional Assessment of Chronic Illness Therapy Fatigue" or FACIT F):ti OR ("Functional Assessment of Chronic Illness Therapy Fatigue" or FACIT F):ab
#64 "Brief Fatigue Inventory":ti OR "Brief Fatigue Inventory":ab
#65 "Numerical Rating Scale Fatigue":ti OR "Numerical Rating Scale Fatigue":ab
#66 ("Visual Analog Scale Fatigue" or VAS F):ti OR ("Visual Analog Scale Fatigue" or VAS F):ab
#67 "Checklist Individual Strength":ti OR "Checklist Individual Strength":ab
#68 "Chalder Fatigue Scale":ti OR "Chalder Fatigue Scale":ab
#69 "Multidimensional Fatigue Inventory Scale":ti OR "Multidimensional Fatigue Inventory Scale":ab
#70 "Piper Fatigue Scale":ti OR "Piper Fatigue Scale":ab
#71 (PROMIS-29 or PROMIS 29 or PROMIS29):ti OR (PROMIS-29 or PROMIS 29 or PROMIS29):ab
#72 Pittsburgh Fatigability Scale:ti OR Pittsburgh Fatigability Scale:ab
#73 Fatigue Descriptive Scale:ti OR Fatigue Descriptive Scale:ab
#74 Modified Fatigue Impact Scale:ti OR Modified Fatigue Impact Scale:ab
#75 ("40-item Fatigue Impact Scale" or "40 item Fatigue Impact Scale"):ti OR ("40-item Fatigue Impact Scale" or "40 item Fatigue Impact Scale"):ab
#76 ("29-item Fatigue Assessment Instrument" or "29 item Fatigue Assessment Instrument"):ti OR ("29-item Fatigue Assessment Instrument" or "29 item Fatigue Assessment Instrument"):ab
#77 ("Functional Assessment of Multiple Sclerosis" or FAMS):ti OR ("Functional Assessment of Multiple Sclerosis" or FAMS):ab
#78 {OR #59-#77}
#79 MeSH descriptor: [Fatigue] this term only
#80 (fatigue NEXT/7 (scale* or subscale* or sub-scale* or questionnaire* or assessment* or inventor* or measure* or tool*)):ti OR (fatigue NEXT/7 (scale* or subscale* or sub-scale* or questionnaire* or assessment* or inventor* or measure* or tool*)):ab
#81 (scale or subscale or sub-scale or questionnaire or assessment or inventory or measure or measurement):ti OR (scale or subscale or sub-scale or questionnaire or assessment or inventory or measure or measurement):ab
#82 (fatigability or fatigable):ti OR (fatigability or fatigable):ab
#83 #79 OR #82
#84 #81 AND #83

#85	#80 OR #84
#86	#58 AND #85

2 Supplementary Methods 2 risk of bias assessment

2.1 Detailed description of methods

Risk of bias assessment of all studies included in the network meta-analysis (NMA) of the present review was undertaken by two experienced reviewers (MMSJ and JL). Any disagreements were resolved through discussion.

Version 2 of the Cochrane risk-of-bias tool (RoB2) for randomised trials (RCTs) [(Sterne et al. 2019] is the recommended tool to assess the risk of bias in RCTs included in Cochrane Reviews. We selected RoB2 as this provides a domain-based approach to identifying biases in RCTs. The tool is structured into five domains through which bias might be introduced into an RCT's results:

Domain1: bias arising from the randomisation process,

Domain 2: bias due to deviations from intended interventions,

Domain 3: bias due to missing outcome data,

Domain 4: bias in measurement of the outcome; and

Domain 5: bias in selection of the reported result.

The judgment for each domain (high risk, low risk, some concerns) is then used to inform an overall risk of bias judgement for each RCT (high risk, low risk, some concerns).

These domains focus on different aspects of trial design, conduct, and reporting. Within each domain, a series of questions ('signalling questions') aim to elicit information about features of the RCT that are relevant to risk of bias. On the RoB2 tool, each signalling question has up to six possible responses - yes, partial yes, no, partial no, not applicable, no information.

There are 22 signalling questions in total in RoB2, which means that the completion rate for each RCT included in a review can be lengthy. We estimate ≤4 RCT reports per day. For pragmatic reasons relating the volume of studies included in the NMA in the present review, we adapted the RoB2 tool to facilitate quicker completion, whilst still capturing the issues with methodological conduct, reporting and other potential biases we observed in some of the RCTs (independent, small-scale, unregistered, minimally reported) that were included in the present NMA.

Two reviewers with RoB2 experience adapted the RoB2 tool so that some signalling questions that would be redundant for the RCTs included in the present NMA were omitted. The remaining signalling questions (n=15) responses were still yes, no, or unclear. We then adapted the RoB2 algorithms to be able to still judge each domain as low risk, high risk, or some concerns. We also retained the overall RoB2 tool risk of bias judgement algorithm for each RCT as follows:

All domains judged as 'low risk' = overall low risk,

Any domain judged as 'high risk' = overall high risk,

All domains judged as 'some concerns' = overall some concerns

Some domains 'low risk' and some domains 'unclear risk' = some concerns

Through the adaptation process we were also able to combine some domains resulting in four assessment domains, with a total of 15 signalling questions, as follows:

Domain1: bias arising from the randomisation process – three signalling questions,

Domain 2: bias due to blinding– three signalling questions,

Domain 3: bias due to missing outcome data– five signalling questions; and

Domain 4: Selection of the reported result and analysis of the outcome– four signalling questions

Agreement of the domains and signalling questions to be included in the adapted RoB2 tool was reached through discussion. We developed the adapted RoB2 tool in Excel and the two reviewers independently piloted this on 10 of the RCTs included in the NMA. Any amendments needed to the tool were discussed and agreed through discussion. As a result of this process, a key adjustment was made to the criteria used for risk of bias judgements for 'attrition'. In consultation with the subject experts on the team we amended our prior threshold of >10% attrition to equal high risk of bias to >20%, due to this level of attrition being within the bounds of normal expectations for behavioural interventions. A copy of the adapted RoB2 tool is presented below.

Reference:

Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng H-Y, Corbett MS, Eldridge SM, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019; 366: l4898.

2.2 Adapted Risk of Bias 2 assessment criteria

Domain	Signalling questions	Responses	Domain judgement
Domain 1: Risk of bias arising from the randomization process	Is randomisation unbiased	Yes – e.g., computer generated No – e.g., alternate allocation Unclear – e.g., 1:1 ratio or method not reported	All 'yes' = low risk All 'no' = high risk 1 or 2 'unclear' = unclear risk 1 or 2 'no' = high risk
	Is allocation concealed	Yes – e.g., sequential, opaque sealed envelopes, interactive voice No – e.g., staff aware of assignment Unclear – method not reported	
	Are groups balanced at baseline	Yes – balanced in the publication No – balanced in the publication Unclear -not reported	
Domain 2: Risk of bias due to blinding	Are participants blind	Yes – reported as blind No – reported as unblinded or impossible that intervention could be blind from participants Unclear -not reported (where intervention could be blinded)	All 'yes' = low risk All 'no' = high risk All 'unclear' = unclear risk Any 'no' = high risk
	Are care-givers blind	Yes – reported as blind No – reported as unblinded or impossible that intervention could be blind from caregivers Unclear -not reported (where intervention could be blinded)	
	Are outcome assessors blind	Yes – reported as blind No – reported as unblinded or impossible that group allocation could be blind from outcome assessors Unclear -not reported (where group allocation could be blinded)	
Domain 3: Missing outcome data	Is sample size based on power	Yes – sample sized based on power calculation No – reported as underpowered Unclear -not reported	All 'yes' = low risk All 'no' = high risk All 'unclear' = unclear risk 2, 3, 4, 'yes', 5 'no' = low risk 2, 3, 4, or 5 'no' = high risk
	Is number recruited and completed reported	Yes – both n allocation and n completed reported No – only reports n allocated or only reports n completed Unclear -unclear if n is n allocated or n completed	
	Is attrition <20%	Yes – attrition <20% in all study groups No – attrition ≥20% in any study group Unclear -attrition not reported or unclear	

Domain	Signalling questions	Responses	Domain judgement
	Are withdrawals balanced across groups	Yes – attrition balanced across groups No – attrition imbalanced across groups Unclear -not reported or unclear	
	Is ITT used to include withdrawals	Yes – reported as analysed as ITT and ns in flowcharts and tables support this No – reported as completer analysis only Unclear - reported as analysed as ITT but ns in flowcharts and tables do not support this or unclear if ITT and ns not reported	
Domain 4: Selection of the reported result and analysis of the outcome	Is the study on a trials register (reported in the paper)?	Yes – trial register and number reported No – reports that it is not on a trials register or unable to find on one	All 'yes' = low risk All 'no' = high risk All 'unclear' = unclear risk 3 or 4 'no' = high risk
	Is there a pre-defined protocol that can be obtained (i.e., as a supplement not just a trials register record)?	Yes – full study protocol available No – reports there is a study protocol, but no details of how to obtain it Unclear – not reported if there is a protocol or not	
	Is the outcome and its analysis pre-specified in the protocol	Yes – in the protocol No – not in the protocol Unclear – unable to assess (no protocol)	
	Is the outcome analysed as per the protocol	Yes – matches the protocol No – difference between what is in the publication and the protocol Unclear – unable to assess (no protocol)	
Overall Risk of Bas Judgment			
			All domains 'low' = low risk
			Any domain 'high' = high risk
			All domains 'unclear' = some concerns
			Some domains 'low' and some domains 'unclear' = some concerns

3 Supplementary Methods 3 GRADE Classification

3.1 Adapted GRADE methods.

We assessed the certainty of the effect estimates of non-pharmacological interventions for fatigue compared to usual care using an adaption of GRADE and CINeMA methodology. Methods are described in detail below, and were designed to be appropriate for interpreting results from the body of evidence identified in this review, with judgements based on the data generated by the analyses of our network meta-analysis. The CINeMA framework is largely based on the GRADE framework, with modifications to facilitate assessment of network meta-analyses. As part of the introduction of CINeMA, a web application has been developed, which enables the conduct of network meta-analyses via the netmeta package in R within the application. As our analyses were conducted using a Bayesian approach and the R2WinBUGS package, we were unable to utilise the CINeMA web application for assessment of the network. Therefore, we used a modified GRADE assessment, incorporating elements of the CINeMA framework for assessment of heterogeneity and inconsistency.

All evidence was derived from randomised controlled trials (RCTs), which were considered to be high quality as a starting point. As per GRADE methodology, the quality of evidence was to be upgraded for large effect size (up one or two levels depending on the magnitude of the effect size) and dose response (up one level). Quality was downgraded for high risk of bias, imprecision, inconsistency and heterogeneity. Number of participants given in the summary tables refers to total N in the relevant intervention arm, not the total in the studies. This is due to inclusion of indirect evidence which may be categorised in another intervention arm (not usual care). The evidence for each outcome was assessed using this framework by JL (RoB, publication bias) and JF (inconsistency, heterogeneity) and validated by the other, or independently in duplicate by JL and JF (imprecision). Disagreements were resolved through discussion. Any uncertainties were discussed with CB. Effect sizes were graded using Cohen's categories; not substantial (SMD<0.2), small (0.2<=SMD<0.5), medium (0.5<=SMD<0.8), large (0.8<=SMD) (J. Cohen, *Statistical power analysis for the behavioral sciences*. Academic press, 2013). Final ratings were high, moderate, low or very low.

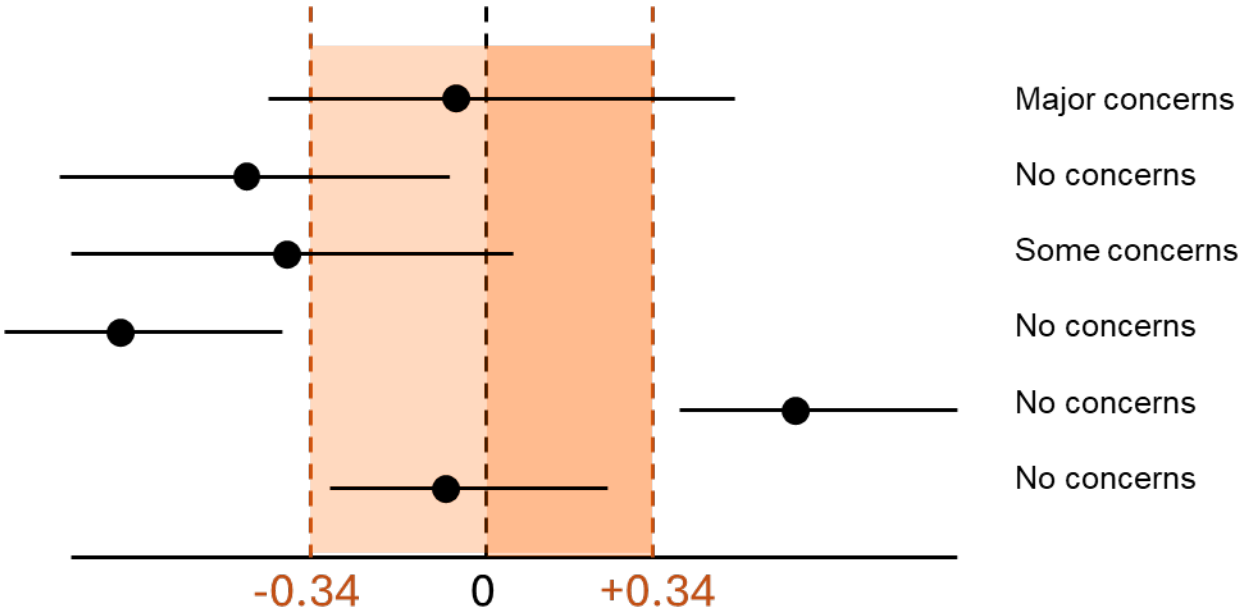
GRADE judgements were based on the following domains of the GRADE book (Neumann et al. 2024):

Limitations in the design or execution of randomized trials (RoB): Individual studies were assessed using Cochrane RoB v2.0 tool. Overall ratings were then clustered by intervention group, as analysed in the NMA. For a variety of reasons, outlined in our detailed RoB section, the evidence included in most intervention groups was rated as high risk of bias and was downgraded by 1. The reason for an overall high RoB rating in many studies was for 'blinding', which may not be possible in behavioural interventions. Lack of blinding is more problematic with outcomes that

have a subjective component, and as the fatigue measures in the included studies were self-reported and were administered in situations where participants or investigators could influence the probability of the outcomes, studies of these interventions were judged to be at high risk of bias as per the RoB v 2.0 handbook. The few studies with overall 'some concerns' were judged to also be at risk of bias and were also downgraded by 1.

Inconsistency: For the purpose of applying the GRADE rating, inconsistency was interpreted as any meaningful differences between the direct evidence (provided by the study data used within the NMA) and indirect evidence (resulting from indirect comparisons within the network). Comparisons of interventions relative to usual care were assessed as these are the primary results presented within forest plots. Other comparisons within the network may exhibit potential inconsistencies but not have been within this assessment. Agreement of indirect and direct evidence was assessed via node-splitting, if any of the predicted treatment effects from direct evidence were statistically significantly different from indirect estimates or no direct evidence was available, the comparison was downgraded by 1. If the difference between the two estimates (direct and indirect) differed by an amount greater than 0.34, chosen as a clinically meaningful SMD, the comparison was downgraded by one. At all three timepoints, the majority of interventions could not be assessed for inconsistency of evidence relative to usual care, due to other comparators being used and connecting within the network.

Imprecision: Ratings were based around thresholds for the minimal important difference for fatigue. In consultation with subject experts, we used a threshold of an SMD of 0.34 as clinically meaningful, as described in the methods section. Imprecision was judged on whether the credible intervals of predicted treatment effects spanned both the lower and upper bounds of the clinically meaningful SMD, i.e. -0.34 and +0.34. If a credible interval spanned both -0.34 and +0.34, we rated down by 2 levels (major concerns), if the 95% credible interval spanned SMD=0 and one clinically meaningful threshold, we rated down by 1 (serious imprecision) and if the 95% credible interval was entirely included within the shaded region we did not downgrade.



Values which do not clinically meaningfully favour the intervention or usual care. Darker region indicates interval between null effect and clinically important effect in opposite direction to observed effect.

Heterogeneity: The 95% prediction intervals were compared to the clinically meaningful thresholds. The predicted intervals capture the uncertainty in the modelled treatment effect but also the heterogeneity between studies. The prediction intervals were graded as for the 95% credible intervals for the imprecision domain, as shown in the figure above.

Publication bias: Funnel plots were not created due to too few studies comparing the same two interventions. Any remaining assessments regarding publication bias are by necessity based on subjective judgements around the likelihood that evidence has been missed, for example: non-inclusion of conference abstracts or grey literature; non-publication of negative studies without an external funder; non-publication of negative studies in novel/emerging interventions. We decided therefore not to include publication bias as a formal domain in our overall assessment. Instead we offer the following observations: The body of evidence for non-pharmacological interventions comes from studies that are generally small in nature. These were not always externally funded or published on trials registries and it is therefore possible that other, similar studies with negative results may not have been published. This is also possible for some emerging interventions, for example the stimulation interventions, where there is a risk of publication bias due to studies with negative results potentially remaining unpublished. It is also important to note that just under half of the intervention groups consist of only one study - in fact all of those included in the nutritional group are single study interventions. Because of the small, exploratory nature of some of these single study interventions, we chose not to upgrade for large effect size where a large effect was observed.

References

Schünemann H, Brożek J, Guyatt G, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendations. Updated October 2013. The GRADE Working Group, 2013. Available from guidelinedevelopment.org/handbook.

Nikolakopoulou, A., Higgins, J. P., Papakonstantinou, T., Chaimani, A., Del Giovane, C., Egger, M., & Salanti, G. (2020). CINeMA: an approach for assessing confidence in the results of a network meta-analysis. *PLoS medicine*, *17*(4), e1003082.

4 Supplementary Methods 4 : Intervention classification criteria

4.1 Physical activity-oriented interventions

4.1.1 Exercise Supervised.

Multiple sessions involving physical activity in a supervised / observed environment. Can include familiarisation with exercise, addressing barriers to exercise in addition to PA aimed at increasing exercise capacity / strength or fitness. May include recommendations to continue between sessions. May be delivered in groups or 1:1. May be in a gym, community resource, or outdoors. May include advice to repeat at home. Excludes specific forms of activity around training e.g. balance.

4.1.2 Exercise Home.

Unsupervised exercise at home aimed at increasing exercise capacity / strength or fitness. May involve initial explanation of physical activity and addressing barriers to exercise. Includes ongoing contact / review to adapt exercise through the programme. May include initial or occasional observed sessions. May take place at home or at other personally relevant location.

4.1.3 Physical activity promotion

One or more sessions aimed at increasing physical activity by addressing barriers to exercise, goal setting, and encouraging greater physical activity. May involve motivational techniques, cognitive / behavioural features, reporting and feedback, or the use of activity sensors. Less focused on structured exercise regimen than Exercise-Home,

4.1.4 Active Recreational

Engage in physical activity generally used as recreation – includes hippotherapy, dance and Interventions involving specific therapeutic environment. Combine body based activity with indirect positive mental well-being.

4.2 Self-management interventions

4.2.1 CBT-based fatigue intervention

Multiple sessions, focused on reducing and adapting to fatigue. May include other symptoms or aspects of the condition. Content includes (1) discussion of helpful / unhelpful thoughts and beliefs (2) behavioural activation - this may include increasing physical activity, management of time / resources, and body/emotion regulating activities (3) tasks / homework between sessions. May be 1:1 or in groups, in person or online. May include second generation features such as Acceptance and Commitment. Can include mindfulness as long as clearly meets CBT definition

4.2.2 Fatigue-self-management-activation

One or more sessions focused on adapting to fatigue and increasing overall activity / engagement. Has only limited emphasis on energy conservation. Includes encouragement to increase activity – either social (behavioural activation) or physical (explicitly increasing physical activity). May include isolated CBT component such as thought challenges but does not meet sufficient criteria for CBT

4.2.3 Fatigue self-management – energy conservation

One or more sessions focused on adapting to fatigue. Primary focus is on energy conservation and prudent allocation. Does not explicitly encourage increase in overall physical or social activity or set out to challenge thoughts. Includes activity pacing and other energy conservation concepts

4.2.4 General / condition specific self-management

Multiple sessions focused on self-management of specific medical condition / disability. May include condition-related fatigue but that is not the primary focus (see Fatigue Self-Management). Includes condition monitoring / specific self-care.

4.2.5 Rehabilitation

Multiple sessions focused on rehab from medical condition / disability. Has specific focus on either function or condition.

4.3 Mind / Mind-body interventions

4.3.1 Body-Mind

Multiple sessions at least partly supervised which use approaches to maximise body-mind connection. Can involve traditional methods (yoga, tai-chi) or “scientific” methods e.g. neurofeedback. Emphasises control of the body (contrast with mindfulness which emphasises control of the mind). Also includes Pilates and Exercise-Breathing where slow movement and controlled breathing are combined.

4.3.2 Mind-Body

Interventions focused on mental relaxation / control (contrast with body-mind). Includes relaxation, imagery etc

4.3.3 Mindfulness based stress reduction

Multiple contacts focusing on learning and applying mindfulness-based techniques (meditation / breathwork). May include general guidance on living within energy resources, sleep, mental health and social interaction. Main focus is on applying mindfulness to daily life (rather than explicitly on addressing fatigue – which would be categorised as CBT with mindfulness)

4.3.4 Psychosocial adaptation to condition

Psychosocial intervention focused on adapting to emotional consequences of medical condition. Less explicit structure and content than CBT, more focus on emotional consequences and less on other behavioural factors than Living Well / rehabilitation.

4.3.5 Other specific psychological therapy

Multiple sessions, focused adapting to medical condition without specific focus on fatigue. Includes condition focused cognitive therapy and problem solving

4.4 Non-invasive stimulation

4.4.1 CNS Stimulation

Use of one or more sessions of external stimulation of the nervous system either transcranially or via peripheral nerves.

4.4.2 External stimulation

Application of detectable or undetectable external stimulation of the body (includes vibration, heat, light, electromagnetic force

4.4.3 Aromatherapy

Intervention defined as aromatherapy

4.4.4 Touch-based

Therapies that involve the direct (or indirect) use of human touch / interaction. Includes massage, reiki etc. Typically delivered in CAMH settings. May include passive movement.

4.4.5 Acupuncture-type

Interventions using traditional chinese anatomical framework to deliver stimulation - acupuncture, acupressure etc.

4.5 Oral Interventions

4.5.1 Plant based

Non-pharmacological supplement described by source rather than ingredient (e.g. paeony extract, ginseng)

4.5.2 Nutritional supplement

Non-pharmacological supplement described by ingredient rather than source (l-carnitine, vitamins)

4.5.3 Diet

Specific dietary intervention (e.g. low-GI, anti-inflammatory)

4.6 Education / information

4.6.1 Information

Provision of written / digital information with no more than one session of personal contact

4.6.2 Education

Provision and discussion / tailoring of written / digital information with more than one session of personal contact

4.7 Control definitions

4.7.1 Usual care

Usual care or equivalent term either explicit or clearly implied.

4.7.2 Waiting list control

Use of wait list control. Note can include both cross-over design (where arms cross over and all followed to final FU and parallel with no follow up of 2nd arm active intervention.

4.7.3 Placebo

Use of inert ingested substance

4.7.4 Sham

Use of inert external procedure

4.7.5 Control

Includes attentional control (presumed inert activity to adjust for time / attention), unfocused discussion meetings and activities (e.g. writing). Also used as default term if not sufficiently clear

5 Supplementary Methods 5: Focus Groups

5.1 Patient focus groups

We recruited 5 focus groups in order to reflect diversity of participants, clinical conditions, and location. Each group met on three occasions during the study, in early and mid 2024 and in early 2025. We conducted the focus groups using participatory approaches that we had previously found effective in PPI work with diverse patient groups, including using concise information summaries to inform interactive discussion and activities such as preference sorting. Ethics approval was obtained from the NHS Health Research Authority (23/SC/0292). The focus groups were co-led by an academic researcher (KF) and patient-researchers (DC & SM).

5.1.1 Participants and recruitment

Inclusion and exclusion criteria matched those of the systematic review. We used multiple approaches to ensure a diverse sample involving contacting patients through specialist clinics and recruitment through patient and other community organisations with a focus of ethnic minority heritage. We recruited through the patient organisations and community groups, particularly in communities of minority ethnic heritage. Invitations were sent as posters / flyers as organisations permitted with the opportunity to respond via email or by a dedicated phone number. Individuals who expressed an interest were then contacted and received further information prior to enrolment. Participants provided written consent before the first focus group and this was verbally confirmed at the start of each focus group.

5.1.2 Focus Groups

Focus groups were held online (3) and in community settings (2). The first round of focus groups gave participants the opportunity to describe their experiences of fatigue and to compare and contrast experiences across conditions. The second round focused on potential interventions and involved both description of experiences and discussion about a set of vignettes of potential fatigue interventions. The third round focused on communicating results of the evidence synthesis. The content of the groups was audio-recorded and transcribed before analysis which used thematic analysis. Developing findings were discussed within the study team.

5.2 Participant characteristics

The focus groups were recruited through patient organisations and community groups, specifically targeted non-white ethnic heritage. From 44 respondents, we recruited 25 (18 women 7 men) who were able to attend focus group which were held in person (2 groups) and online (3 groups) each on three separate occasions. While some individuals missed one of the series of three groups, none actively withdrew. Although we intended that people stay in the same group allowed people to move between groups and were struck that people were keen to continue their engagement.

Ages of participants ranged from under 30 to over 70, with the most represented age group being 50-59 years. We recruited from diverse ethnic heritages, with 10 identifying as South Asian, 8 as White, 5 as African-Caribbean and 2 others. Long term medical conditions reported included kidney or liver disease (6 participants), arthritis (5) diabetes (5) diabetes, heart conditions and neurological disorders (3 each).

5.3 Focus group findings informing the clinical effectiveness analysis

We drew on three themes in framing our analysing and reporting of clinical effectiveness.

1. Fatigue is an invisible problem. Few people had talked constructively about their fatigue with peers or with clinicians. There was little common language or models for explanation about fatigue and few people were aware that interventions for fatigue had been developed.

2. The experience of fatigue crosses diagnostic boundaries. Each individual's experience of fatigue was personal to them. Where similarities occurred with others, these were as much across conditions as within. Nonetheless, certain features of conditions affected the experience of fatigue or constrained the approaches that might be taken to reduce it.

3. There is no one-size-fits-all solution. Differences in the experience of fatigue extended to differences in what people had found helpful for them (or saw as appropriate to try). There were some instances of scepticism, particularly where an intervention conflicted with prior experiences or beliefs, however in general people were open to considering new information and to trying interventions if these were made available. Participants often ranked availability or accessibility as more important than the particular name or content of an intervention.

6 Supplementary Methods 6 - additional statistical analysis methods

6.1 Multiple fatigue measures

Some studies reported multiple measures of fatigue. The scale “FSS” was prioritised, following input from the clinical experts on the team, followed by “MFIS”. Therefore, if a study reported multiple fatigue outcomes using different scales, and if one of the outcomes was reported using the “FSS” scale, this data was selected and used for the network meta-analysis (NMA). However, if they did not use the “FSS” scale but used the “MFIS” scale, the data reported using the MFIS scale was selected for the NMA. This ruling resolved most cases, however in cases where there were multiple scales not including “FSS” or “MFIS”, clinical experts were consulted to obtain the most appropriate scale for inclusion within the NMA.

6.2 Evaluation of the SMD

As mentioned above, fatigue outcomes were measured using different scoring methods across studies. To facilitate the analysis of studies using different scoring methods within a single NMA, standardised mean differences (SMDs) of the change from baseline of fatigue, were calculated for each study. The use of SMDs is based on the assumption that all scoring scales are quantifying the same treatment effect and can be transformed onto a common scale by dividing the mean difference in change from baseline between the intervention and comparator within each study by the standard deviation of the difference.[1]

Raw data extracted from study results in the form of means, standard deviations, standard errors, inter quartile ranges and confidence intervals were used to evaluate the SMD and subsequently the standard error (SE) of the SMD for each study using Hedge’s correction.[1] In some studies, change from baseline was reported as opposed to pre and post intervention data, where available this data was extracted and used within the network.

Using intervention 1 as the reference treatment (for most analyses in this work, this corresponds to “usual care”), the SMD for the interventions in arm t, at follow-up f is given by

$$SMD_{t,f} = c \cdot \frac{\mu_{f,t} - \mu_{f,1}}{S},$$

$$S = \sqrt{\frac{(n_1 - 1)SD_1^2 + (n_t - 1)SD_t^2}{n_1 + n_t - 2}},$$

$$c = 1 - \frac{3}{4(n_1 + n_t) - 9}$$

where $\mu_{f,t}$ and $\mu_{f,1}$ is the change in fatigue score before and after treatment in arm t and arm 1 at follow-up f, respectively; S is the within group standard deviation pooled across arms, SD_t and SD_1 are the standard deviations in arm t and arm 1, respectively; n_t and n_1 are the number of participants at baseline in arm t and arm 1, respectively; and c is Hedges’ correction factor. The standard error (SE) of the SMD is given by

$$SE(SMD_{t,f}) = \sqrt{c^2\left(\frac{n_1 + n_t}{n_1 n_t} + \frac{SMD_{t,f}^2}{2(n_1 + n_t)}\right)}.$$

For studies where only the 95% confidence interval was presented alongside the mean instead of the standard deviation, the standard deviation was evaluated using

$$SD_t = \sqrt{n_t}\ \frac{CI_{t_{upper}} - CI_{t_{lower}}}{3.92},$$

where n_t is the number of participants in study arm t, $CI_{t_{upper}}$ and $CI_{t_{lower}}$ are the upper and lower 95% confidence intervals. For cases where only the inter-quartile range was recorded, the standard deviation was evaluated as

$$SD_t = \frac{IQR_{t_{upper}} - IQR_{t_{lower}}}{1.349},$$

where $IQR_{t_{upper}}$ and $IQR_{t_{lower}}$ are the upper and lower quartiles.[2] In most cases, fatigue scores were presented at baseline and then post-treatment, the mean change from baseline was therefore evaluated and the standard deviation of the mean change from baseline calculated using

$$SD_{change} = \sqrt{SD_{f,1}^2 + SD_{f,t}^2 - \left(2 \times corr \times SD_{f,1} \times SD_{f,t}\right)}$$

where the correlation coefficient ($corr$) was assumed to be equal to 0.5 as a conservative estimate.[3-5]

For studies where multiple arms presented data for the same intervention, according to the intervention classification conducted by the clinical experts, the data were combined. The mean change from baseline was evaluated as a weighted average, according to the number of participants in the arms being combined. The standard deviation was then evaluated as

$$SD = \sqrt{\frac{\left(N_{f,1} - 1\right)SD_{f,1}^2 + \left(N_{f,t} - 1\right)SD_{f,t}^2 + \frac{n_1 n_t}{n_1 + n_t}\left(M_{f,1}^2 + M_{f,t}^2 - 2M_{f,1}M_{f,t}\right)}{n_1 + n_t - 1}},$$

where $M_{f,t}$ is the weighted average of the mean change from baseline in arm t at follow-up f.[5]

In the case where no available data were available to evaluate the mean and standard deviation of the change from baseline of the fatigue score for each arm, the study was not included within the NMA. No studies which only presented data graphically were included within the NMA due to the high number of studies.

6.3 Statistical model for the NMA

A random-effects NMA model was used to account for between study heterogeneity.[6] Let y_{ik} denote the standardised mean difference (SMD) of arm k of trial i, where $k = 1, \ldots, na$ and $i = 1, \ldots, ns$, with variance V_{ik}. Here, na and ns correspond to the number of arms and the number of studies respectively. We assume that the treatment effects are normally distributed according to

$$y_{ik} \sim \mathcal{N}(\theta_{ik}, V_{ik}),$$

where $\boldsymbol{\theta}$ are the parameters of interest. The individual θ_{ik} are modelled using the identity link function as they are continuous on the entire real line

$$\theta_{ik} = \delta_{i,1k},$$

where $\delta_{i,1k}$ is the individual study treatment effect of intervention k relative to intervention 1 in study i. To allow for heterogeneity of treatment effects across studies, a random-effects model was assumed. The random-effects model was structured such that all individual study treatment effects arise from a common normal distribution centred about a mean population treatment effect, with some variance τ^2

$$\delta_{i,1k} \sim \mathcal{N}\left(d_{t_{i1},t_{ik}}, \tau^2\right),$$

where $d_{t_{i1},t_{ik}}$ is the mean effect of the intervention in arm k of study i (t_{ik}) compared to the intervention in arm 1 of study i (t_{i1}).

In the case of studies with more than two arms, adjustment to the likelihood (function) was necessary to account for the correlation between multiple comparisons to arm 1 and was included via the assumption that the covariance between two comparisons relative to treatment 1 can be approximated as $1/n_{i,1}$, where $n_{i,1}$ is the number of participants in arm 1 of study i at baseline.[7]

6.4 Definition of priors

Parameters were estimated using a Bayesian framework, as such, non-informative priors were chosen for the between-study variance of treatment effects

$$\tau \sim \mathcal{U}(0,5) \cdot \frac{\sqrt{3}}{\pi}.$$

The $\sqrt{3}/\pi$ factor is included to account for the transformation of τ between the odds-ratio scale and the SMD scale.[8] An informative prior, a truncated log-normal prior on τ^2 was used in cases where there were less than 5 studies within the connected network.[8]

$$\tau^2 \sim \text{lognormal}(-2.56, 0.33) \cdot I(0,1).$$

The prior on the mean treatment effects were defined as

$$d_{t_{i1},t_{ik}} \sim \mathcal{N}(0, 100^2)$$

6.5 Implementation

All analyses were conducted using the freely available software package WinBUGS[9] and R, via the R2Winbugs[10] interface package. Model code was modified from NICE technical support document 2.[11] Convergence to the target posterior distributions was assessed using the Gelman-Rubin statistic, as modified by Brooks and Gelman, for three chains with different initial values.[12] The autocorrelation of samples from the burn-in period was also assessed for any significant autocorrelation which requires sample thinning. A burn-in period of 50,000 samples was implemented, with a further 1,000,000 samples after the burn-in period. The samples after the burn-in were subject to a thinning by a factor of 10.

Results are presented using the posterior median treatment effects and 95% credible intervals (CrI).

The validity of the inconsistency assumption was assessed by comparing the posterior mean residual deviance from the unrelated mean effects model and the NMA model; and node-splitting analysis. The posterior means of the deviance contributions for the unrelated mean effects model and the NMA model were plotted, cases where the posterior means lie across the $y = x$ line, demonstrated that the inconsistency assumption held. Cases where the posterior deviance contributions deviated from this line (indicating an improvement greater than 0.5 points in the unrelated mean effects model) were investigated using node-splitting via the gemtc package in R.[13]

6.6 References

1. Higgins JPT, Altman DG, Sterne JAC (editors). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Churchill R, Chandler J, Cumpston MS (editors), Cochrane Handbook for Systematic Reviews of Interventions version 5.2.0 (updated June 2017), Cochrane, 2017. Available from www.training.cochrane.org/handbook.

EIFFEL Supplementary Results

Table of Contents

Supplemental Results 1
Studies included in Network Meta-analysis

Study	Condition	Diagnostic Criteria	Selected for fatigue	Fatigue selection criteria
Dalgas 2010	Multiple Sclerosis	Physician diagnosis + Expanded Disability Status Scale (EDSS) score between 3.0 and 5.5	Y	Significant fatigue with a Fatigue Severity Scale (FSS) score above 4
Englund 2022	Multiple Sclerosis	Physician diagnosis	Y	Fatigue Scale for Motor and Cognitive Functions (FSMC), with a score of ≥53
Escudero-Uribe 2017	Multiple Sclerosis – relapsing remitting	Physician diagnosis	Y	Fatigue Severity Scale (FSS) ≥4 and fatigue as one of the most disabling symptoms
Feys 2019	Multiple Sclerosis	N/R	Y	Fatigue Scale for Motor and Cognitive Functions (FSMC)N/R
Gervasoni 2014	Multiple Sclerosis	Expanded Disability Status Scale (EDSS) < 8	Y	N/R
Heine 2017	Multiple Sclerosis	Physician diagnosis and Expanded Disability Status Scale (EDSS) ≤ 6.0	Y	Checklist Individual Strength (CIS20r) fatigue subscale - severe fatigue⩾35
Kratz 2020	Multiple Sclerosis	Physician diagnosis	Y	N/R
Langeskov-Christensen 2022	Multiple Sclerosis	N/R	Y	N/R
Louie 2022	Multiple Sclerosis	Physician diagnosis and Expanded Disability Status Scale (EDSS) ≤ 6.5	Y	N/R
McCullagh 2008	Multiple Sclerosis	Relapsing -remitting or secondary progressive type multiple sclerosis only	Y	Modified Fatigue Impact Scale (MFIS), cut-off value of 38 to discriminate fatigued from non-fatigued participants.
Kucharski 2019	Rheumatoid Arthritis	Physician Diagnosis (ACR criteria)	Y	N/R
Ortiz-Rubio 2018	Parkinsons Disease	UK Brain Bank Criteria in the II-III Hoehn & Yahr stages	Y	N/R
Diaz 2023	Psoriasis	Physician diagnosis, without PsA and dermatology life quality index scores < 7	N	N/A
Pozehl 2008	Heart Failure	New York Heart Association class II, III or IV	Y	N/R
Geddes 2009	Multiple Sclerosis	Diagnosis of MS greater than 1 year	Y	N/R
Maurer 2018	Multiple Sclerosis	Physician diagnosis of RRMS	Y	N/R
Torkhani 2021	Multiple Sclerosis	Physician diagnosis at least 12 months prior and relapse free in previous 90 days	N	N/A
Durcan 2014	Rheumatoid Arthritis	Physician Diagnosis (ACR critiera)i	Y	N/R
Katz 2018	Rheumatoid Arthritis	Physician-diagnosed RA	Y	N/R

Tench 2003	Systemic Lupus Erythematosus	Physician Diagnosis (ACR)	Y	N/R
Lutz 2017	Multiple Sclerosis	Physician diagnosis	Y	N/R
Turner 2016	Multiple Sclerosis	Physician diagnosis	Y	Reporting fatigue (Modified Fatigue Impact Scale [MFIS] score greater than or equal to 20).
Bachmair 2022	Inflammatory arthritis	Inflammatory rheumatic disease diagnosed by specialist	Y	Reported fatigue to be a problem that was persistent (>3 months) with score(>6/10 on NRS for average fatigue over past 7 days)
Callahan 2014	Arthritis	Self-report any type of doctor diagnosed arthritis or join pain /stiffness with associated limitation.	N	N/A
Ehde 2015	Multiple Sclerosis	self-reported physician diagnosis	Y/N	Either pain, depression or significant fatigue symptoms.(score ³10 on the 5-item MFIS Short Form)
Gay 2023	Multiple Sclerosis – relapsing remitting	Physician diagnosis	Y	Fatigue at screening visit MFIS score >45
Moss-Morris 2012	Multiple Sclerosis	Physician diagnosis	Y	Significant fatigue indicated by a score of >4 on the Fatigue Scale
Pottgen 2018	Multiple Sclerosis	Self-reported diagnosis verified by a clinician letter in 50% random sample	Y	Fatigue indicated by >43 on the FSMC
Thomas 2013	Multiple Sclerosis	Physician diagnosis	Y	Fatigue impacting on daily life (FSS total score >4)
van den Akker 2017	Multiple Sclerosis	Physician diagnosis	Y	Experience of severe fatigue (CIS20r fatigue ≥35)
van Kessel 2008	Multiple Sclerosis	Physician diagnosis	Y	A fatigue score of 4 or greater on the Fatigue Scale
Mead 2022	Stroke	Any stroke between three months and two years previously	Y	Answered 'Yes' to both the Greater Manchester Stroke Assessment Tool fatigue questions
Nguyen 2019	Stroke	History of stroke	Y	Clinically significant self-reported fatigue (FSS ≥4) and/or poor sleep
Zedlitz 2012	Stroke	Any stroke >4 months before treatment	Y	Severe fatigue (CIS-fatigue ≥40)
Okkersen 2018	Myotonic Dystrophy (type 1)	Physician diagnosis	Y	Severely fatigued CIS20r subscale fatigue ≥35
Hewlett 2011	Rheumatoid Arthritis	Physician diagnosis	Y	Scoring ≥6 for fatigue in the past week (VAS)
Hewlett 2019a	Rheumatoid Arthritis	Physician diagnosis	Y	Fatigue severity ≥6/10 on an NRS
Jhamb 2023	Kidney Disease	Receiving in-centre treatment	Y/N	Cutoffs for a clinically significant level for fatigue, pain or depression
Picariello 2021	End-stage Kidney Failure	Physician diagnosis	Y	Experiencing Physician levels of fatigue, ≥18 on the Chalder Fatigue Scale
Artom 2019	Inflammatory Bowel Disease	Physician diagnosis	Y	Self-reported fatigue
Bredero 2023	Inflammatory Bowel Disease	Physician diagnosis	Y	Scoring ≥27 on the subjective fatigue scale of the CIS-20
Menting 2017	Type 1 Diabetes	Diagnosed for at least 1 year	Y	Score ³35 on the fatigue severity subscale of the CIS, with duration of more than 6 months
Rietberg 2014	Multiple Sclerosis	Physician diagnosis	Y	Chronic fatigue according to the MSCCPG definition
Clarke 2012	Stroke	Hospital stroke clinic or known to the local Stroke Foundation	Y	Experiencing fatigue FSS >3.9
Murphy 2024	Systemic Sclerosis	Physician diagnosis	Y	Moderate to severe fatigue (average score >4 AC on the FSS

Abonie 2020	Multiple Sclerosis	Physician diagnosis	N	N/A
Askari 2022	Multiple Sclerosis	Physician diagnosis	Y	Having a score >5.4 on the FSS
Blikman 2017	Multiple Sclerosis	Physician diagnosis	Y	Severely fatigued CIS20r subscale fatigue >35
Garcia Jalon 2013	Multiple Sclerosis	Physician diagnosis	Y	Scoring 4 or more on the FSS
Hersche 2019	Multiple Sclerosis	Physician diagnosis	Y	Fatigue Severity Scale score > 4
Hugos 2010	Multiple Sclerosis	Physician diagnosis	N	N/A
Hugos 2019	Multiple Sclerosis	Physician diagnosis	Y	Moderate to severe fatigue (scores>25 on the MFIS)
Kos 2016	Multiple Sclerosis	Physician diagnosis	Y	A high impact of fatigue (VAS score of at least 60)
Ghahari 2010		Self-reported diagnosis	Y	Minimum FSS score of 4
Murphy 2010	Osteoarthritis	Knee or hip OA>= 3 months with radiographic evidence	N	N/A
Farragher 2022	Kidney	Undergoing haemodialysis for ≥3 months	Y	Scored an average of ≥4 on items 5,7,8 and 9 on FSS
Austin 1996	Systemic Lupus Erythematosus	Physician diagnosis	Y	Moderate to severe fatigue due to SLE >2.5 FSS score
Feldthusen 2016	Rheumatoid Arthritis	Physician diagnosis	Y	Fatigue >50 on VAS
Hammond 2008	Inflammatory Arthritis	Rheumatoid or other inflammatory arthritis	N	N/A
Khan 2020	Systemic Lupus Erythematosus	Physician diagnosis	N	N/A
DeGiglio 2015	Multiple Sclerosis	Physician diagnosis	N	N/A
Callahan 2016	Arthritis	Self-reported doctor diagnosed arthritis of any type	N	N/A
Fleming 2019	Multiple Sclerosis	Self-reported physician diagnosis of MS	Y	MFISN/R
Fleming 2021	Multiple Sclerosis	Self-reported, physician diagnosed	Y	21-item Modified Fatigue impact Scale (MFIS)N/R
Sgoifo 2017	Multiple Sclerosis	Cliical diagnosis with at least one month free of relapses	N	N/A
Walter 2019	Parkinsons Disease	Physician diagnosis; score of 1.5 on the Modified Hoehn and Yahr Scale	N	N/A
Goren 2022	Crohns Disease	Physician diagnosis, Harvey-Bradshaw Index (HBI) between 5 and 16	N	N/A
Grossman 2010	Multiple Sclerosis	Relapsing -remitting or secondary progressive type multiple sclerosis only	N	N/A
Granja-Dominguez 2022	Multiple Sclerosis	McDonald Criteria	Y	FSS ≥ 4
Mostert 2005	Multiple Sclerosis	MS as defined by Poser	Y	FSS ≥ 3.5
Piatkowski 2009	Multiple Sclerosis	Clinically definite, relapsing-remitting MS	N	N/A
Voggenberger 2022	Multiple Sclerosis	McDonald Criteria	Y	FSS ≥ 36
Kluger 2016	Parkinsons Disease	UK Brain Bank criteria for PD	Y	Moderate/severe fatigue using International Parkinson & Movement Disorder Society UPDRS fatigue item
Horta 2020	Inflammatory bowe disease	IBD diagnosis (Harvey-Bradshaw score <5 and modified Mayo score ≤2)	Y	FACIT-FS score <40
Hawkins 2019		Clinically diagnosed with hypothyroidism.	N	N/A

Cancelli 2018	Multiple Sclerosis	Physician diagnosis	Y	mFIS >35
Charvet 2018	Multiple Sclerosis	Physician diagnosis	N	N/A
Salemi 2019	Multiple Sclerosis	Physician diagnosis	Y	MFIS >20
Tecchio 2015	Multiple Sclerosis	N/R	Y	MFIS >15
Aranow 2021	Systemic Lupus Erythematosus	Physican diagnosis (Revised ACR or SLICC)	N	N/A
Tarn 2023	Sjogrens Syndrome	Physician Diagnosis	N	N/A
Moyle 2023	Stroke	Any stroke .	Y	FSS-7 ≥ 4) for at least 4 weeks
Coe 2019	Multiple Sclerosis	RRMS (<10 year since diagnosis),	Y	FSS> 4/7
Arriens 2015	Systemic Lupus Erythematosus	SLE according to the 1997 revised ACR criteria	N	N/A
Bager 2021	Inflammatory Bowel Disease	Physician Diagnosis (Crohn's Disease or Ulcerative Colitis)		
Truyens 2022	Inflammatory Bowel Disease	N/R	Y	VAS ≥ 5
Chase 2023		N/R	N	N/A
Johnson 2006	Multiple Sclerosis	Physician Diagnosis		

Systemic Lupus Erythematosus	Systemic Lupus Erythematosus	ACR criteria for diagnosis	Y	Fatigue Severity Scale ≥ 3.7
Callahan 2008	arthritis	Self-reported arthritis	N	N/R
Chalah 2020	MS	McDonald criteria	Y	FSS/MFIS
Coe 2022	Parkinsons Disease	Clinical diagnosis; between 1-2 on Hoehn and Yahr scale	N	N/A
Coghe 2018	MS	Diagnosis based on the 2010 McDonald criteria	N	N/R
Daltroy 1995	Rheumatoid Arthritis	American College of Rheumatology criteria	N	N/R
DeCarvalho 2012	MS	McDonald Criteria	Y	FSS > 27
DeDoncker 2021	Stroke	Stroke > 3 months ago	Y	A score of FSS ≥4
Drory 2001	ALS	Revised El Escorial criteria	N	N/R
Finlayson 2011	MS	Self-reported diagnosis	Y	Fatigue score of 4 or greater (moderate to severe fatigue)
Gaede 2018	MS	Diagnosis based on 2005 revised McDonald criteria	Y/N	Either a score of ≥4 on the Fatigue Severity Scale or ≥12 Beck Depression Inventory
Hidding 2017	Parkinsons Disease	Advanced idiopathic PD Hoehn and Yahr stage: 2.2 ±	N	N/A
Irish 2017	Relapsing-remitting MS	Neurologist diagnosis (McDonald criteria)	N	N/A
Kim 2011	MS	Mcdonald criteria	Y	Fatigue for > two months (Fatigue Severity Scale (FSS) score >=4)
Kos 2007	MS	Physician diagnosis of MS	Y	High impact of fatigue score
Lee 2021	MS	N/R	Y	Severe fatigue (MFIS score 38)
Mateen 2020	MS	McDonald Criteria	Y	FSS ≥36

Mathiowetz 2005	MS	Phsycician diagnosis of MS	Y	FSS score of 4 or greater
McNelly 2016	IBD	Crohn's disease or ulcerative colitis in remission, clinically and biochemically	Y	Self-reported fatigue
O'Connor 2019	IBD	Quiescent IBD (clinical & biochemical)	Y	Scoring 1 or more on Section I of the Crohn's and Colitis UK IBD fatigue self-assessment scale.
Palsdottir 2020	Stroke	Acute stroke =- CHECK****	N	N/A
Plow 2022	MS	Physician confirmed diagnosis of MS	Y	Moderate to severe fatigue.
Robb-Nicholson 1989	Systemic Lupus Erythematosus	N/R	Y	N/R
Saoite 2014	MS	Diagnosed by physician	Y	FSS ≥4
Theander 2002	Sjogren's syndrome	Copenhagen criteria	N	N/A
van Kessel 2016	MS	neurologist diagnosis of MS	Y	Chalder fatigue score of 4 or greater
Voet 2014	Neuromuscular disorder	Known to study team or registered on neuromuscular database	Y	Severe fatigue (CIS-fatigue ≥35)
Vogelaar 2011	Crohns Disease	Phsycician diagnosis	Y	A high fatigue score (≥ 35 on the CIS dimension 1)

Supplemental Results 2

Characteristics of potentially eligible studies, not included in network meta-analysis

Avaux 2016	Systemic Lupus Eythematosus	ACR criteria for diagnosis	Y	Fatigue Severity Scale ≥ 3.7
Callahan 2008	arthritis	Self-reported arthritis	N	N/R
Chalah 2020	MS	McDonald criteria	Y	FSS/MFIS
Coe 2022	Parkinsons Disease	Clinical diagnosis; between 1-2 on Hoehn and Yahr scale	N	N/A
Coghe 2018	MS	Diagnosis based on the 2010 McDonald criteria	N	N/A
Daltroy 1995	Rheumatoid Arthritis	American College of Rheumatology criteria	N	N/A
DeCarvalho 2012	MS	McDonald Criteria	Y	FSS > 27
DeDoncker 2021	Stroke	Stroke > 3 months ago	Y	A score of FSS ≥4
Drory 2001	ALS	Revised El Escorial criteria	N	N/R
Finlayson 2011	MS	Self-reported diagnosis	Y	Fatigue score of 4 or greater (moderate to severe fatigue)
Gaede 2018	MS	Diagnosis based on 2005 revised McDonald criteria	Y/N	Either a score of ≥4 on the Fatigue Severity Scale or ≥12 Beck Depression Inventory
Hidding 2017	Parkinsons Disease	Advanced idiopathic PD Hoehn and Yahr stage: 2.2 ±	N	N/A
Irish 2017	Relapsing-remitting MS	Neurologist diagnosis (McDonald criteria)	N	N/A
Kim 2011	MS	Mcdonald criteria	Y	Fatigue for > two months (Fatigue Severity Scale (FSS) score >=4)
Kos 2007	MS	Physician diagnosis of MS	Y	High impact of fatigue score
Lee 2021	MS	N/R	Y	Severe fatigue (MFIS score 38)
Mateen 2020	MS	McDonald Criteria	Y	FSS ≥36
Mathiowetz 2005	MS	Phsycician diagnosis of MS	Y	FSS score of 4 or greater
McNelly 2016	IBD	Crohn's disease or ulcerative colitis in remission, clinically and biochemically	Y	Self-reported fatigue
O'Connor 2019	IBD	Quiescent IBD (clinical & biochemical)	Y	Scoring 1 or more on Section I of the Crohn's and Colitis UK IBD fatigue self-assessment scale.
Palsdottir 2020	Stroke	Admitted to hospital with acute stroke or in the chronic phase (1 year post stroke)	N	N/A
Plow 2022	MS	Physician confirmed diagnosis of MS	Y	Moderate to severe fatigue.
Robb-Nicholson 1989	Systemic Lupus Erythematosus	N/R	Y	N/R
Sabapathy 2011	MS	N/R	N	N/A
Saoite 2014	MS	Diagnosed by physician	Y	FSS ≥4
Theander 2002	Sjogren's syndrome	Copenhagen criteria	N	N/A
van Kessel 2016	MS	Neurologist diagnosis of MS	Y	Chalder fatigue score of 4 or greater

Voet 2014	Neuromuscular disorder	Known to study team or registered on neuromuscular database	Y	Severe fatigue (CIS-fatigue ≥35)
Vogelaar 2011	Crohns Disease	Phsycician diagnosis	Y	A high fatigue score (≥ 35 on the CIS dimension 1)
Vogelaar 2014	IBD	Diagnosis of IBD of at least 6 months	Y	CIS-fatigue score of ≥35

References:

Avaux, M., Hoellinger, P., Nieuwland-Husson, S., Fraselle, V., Depresseux, G., & Houssiau, F. A. (2016). Effects of two different exercise programs on chronic fatigue in lupus patients. *Acta Clinica Belgica*, *71*(6), 403-406.

Callahan, L. F., Mielenz, T., Freburger, J., Shreffler, J., Hootman, J., Brady, T., ... & Schwartz, T. (2008). A randomized controlled trial of the people with arthritis can exercise program: symptoms, function, physical activity, and psychosocial outcomes. *Arthritis Care & Research: Official Journal of the American College of Rheumatology*, *59*(1), 92-101.

Chalah, M. A., Grigorescu, C., Padberg, F., Kümpfel, T., Palm, U., & Ayache, S. S. (2020). Bifrontal transcranial direct current stimulation modulates fatigue in multiple sclerosis: a randomized sham-controlled study. *Journal of Neural Transmission*, *127*, 953-961.

Coe, S., Andreoli, D., George, M., Collett, J., Reed, A., Cossington, J., ... & Dawes, H. (2022). A feasibility study to determine whether the daily consumption of flavonoid-rich pure cocoa has the potential to reduce fatigue and fatigability in people with Parkinson's (pwP). *Clinical Nutrition ESPEN*, *48*, 68-73.

Coghe, G., Corona, F., Marongiu, E., Fenu, G., Frau, J., Lorefice, L., ... & Cocco, E. (2018). Fatigue, as measured using the Modified Fatigue Impact Scale, is a predictor of processing speed improvement induced by exercise in patients with multiple sclerosis: data from a randomized controlled trial. *Journal of Neurology*, *265*, 1328-1333.

Daltroy, L. H., Robb-Nicholson, C., Iversen, M. D., Wright, E. A., & Liang, M. H. (1995). Effectiveness of minimally supervised home aerobic training in patients with systemic rheumatic disease. *Rheumatology*, *34*(11), 1064-1069.

de Carvalho, M. L. L., Motta, R., Konrad, G., Battaglia, M. A., & Brichetto, G. (2012). A randomized placebo-controlled cross-over study using a low frequency magnetic field in the treatment of fatigue in multiple sclerosis. *Multiple Sclerosis Journal*, *18*(1), 82-89.

De Doncker, W., Ondobaka, S., & Kuppuswamy, A. (2021). Effect of transcranial direct current stimulation on post-stroke fatigue. *Journal of neurology*, *268*, 2831-2842.

Drory, V. E., Goltsman, E., Reznik, J. G., Mosek, A., & Korczyn, A. D. (2001). The value of muscle exercise in patients with amyotrophic lateral sclerosis. *Journal of the neurological sciences*, *191*(1-2), 133-137.

Finlayson, Marcia, et al. "Randomized trial of a teleconference-delivered fatigue management program for people with multiple sclerosis." *Multiple Sclerosis Journal* 17.9 (2011): 1130-1140.

Gaede, G., Tiede, M., Lorenz, I., Brandt, A. U., Pfueller, C., Dörr, J., ... & Paul, F. (2017). Safety and preliminary efficacy of deep transcranial magnetic stimulation in MS-related fatigue. *Neurology: Neuroimmunology & Neuroinflammation*, *5*(1), e423.

Hidding, U., Gulberti, A., Horn, A., Buhmann, C., Hamel, W., Koeppen, J. A., ... & Pötter-Nerger, M. (2017). Impact of combined subthalamic nucleus and substantia nigra stimulation on neuropsychiatric symptoms in Parkinson's disease patients. *Parkinson's Disease*, *2017*(1), 7306192.

Irish, A. K., Erickson, C. M., Wahls, T. L., Snetselaar, L. G., & Darling, W. G. (2017). Randomized control trial evaluation of a modified Paleolithic dietary intervention in the treatment of relapsing-remitting multiple sclerosis: a pilot study. *Degenerative neurological and neuromuscular disease*, 1-18.

Kim, E., Cameron, M., Lovera, J., Schaben, L., Bourdette, D., & Whitham, R. (2011). American ginseng does not improve fatigue in multiple sclerosis: a single center randomized double-blind placebo-controlled crossover pilot study. *Multiple Sclerosis Journal*, *17*(12), 1523-1526.

Kos, D., Duportail, M., D'hooghe, M. B., Nagels, G., & Kerckhofs, E. (2007). Multidisciplinary fatigue management programme in multiple sclerosis: a randomized clinical trial. *Multiple Sclerosis Journal*, *13*(8), 996-1003.

Lee, J. E., Titcomb, T. J., Bisht, B., Rubenstein, L. M., Louison, R., & Wahls, T. L. (2021). A modified MCT-based ketogenic diet increases plasma β-hydroxybutyrate but has less effect on fatigue and quality of life in people with multiple sclerosis compared to a modified paleolithic diet: a waitlist-controlled, randomized pilot study. *Journal of the American College of Nutrition*, *40*(1), 13-25.

Mateen, F. J., Vogel, A. C., Kaplan, T. B., Hotan, G. C., Grundy, S. J., Holroyd, K. B., ... & Videnovic, A. (2020). Light therapy for multiple sclerosis-associated fatigue: a randomized, controlled phase II trial. *Journal of Neurology*, *267*, 2319-2327.

Mathiowetz, V. G., Finlayson, M. L., Matuska, K. M., Chen, H. Y., & Luo, P. (2005). Randomized controlled trial of an energy conservation course for persons with multiple sclerosis. *Multiple Sclerosis Journal*, *11*(5), 592-601.

McNelly, A., Nathan, I., Monti, M., Grimble, G., Norton, C., Bredin, F., ... & Forbes, A. (2016). Inflammatory bowel disease and fatigue: the effect of physical activity and/or omega-3 supplementation.

O'Connor, A., Ratnakumaran, R., Warren, L., Pullen, D., Errington, A., Gracie, D. J., ... & Ford, A. C. (2019). Randomized controlled trial: a pilot study of a psychoeducational intervention for fatigue in patients with quiescent inflammatory bowel disease. *Therapeutic advances in chronic disease*, *10*, 2040622319838439.

Pálsdóttir, A. M., Andersson, G., Grahn, P., Norrving, B., Kyrö Wissler, S., Petersson, I. F., & Pessah-Rasmussen, H. (2015). A randomized controlled trial of nature-based post-stroke fatigue rehabilitation. *International Journal of Stroke*, *10*(S1).

Plow, M., Motl, R. W., Finlayson, M., & Bethoux, F. (2022). Response heterogeneity in a randomized controlled trial of telerehabilitation interventions among adults with multiple sclerosis. *Journal of telemedicine and telecare*, *28*(9), 642-652.

Robb-Nicholson, L. C., DALTROY, L., EATON, H., GALL, V., WRIGHT, E., Hartley, L. H., ... & Liang, M. H. (1989). Effects of aerobic conditioning in lupus fatigue: a pilot study. *Rheumatology*, *28*(6), 500-505.

Sabapathy, N. M., Minahan, C. L., Turner, G. T., & Broadley, S. A. (2011). Comparing endurance-and resistance-exercise training in people with multiple sclerosis: a randomized pilot study. *Clinical rehabilitation*, *25*(1), 14-24.

Saiote, C., Goldschmidt, T., Timäus, C., Steenwijk, M. D., Opitz, A., Antal, A., ... & Nitsche, M. A. (2014). Impact of transcranial direct current stimulation on fatigue in multiple sclerosis. *Restorative neurology and neuroscience*, *32*(3), 423-436.

Theander, E., Horrobin, D. F., Jacobsson, L. T., & Manthorpe, R. (2002). Gammalinolenic acid treatment of fatigue associated with primary Sjögren's syndrome. *Scandinavian journal of rheumatology*, *31*(2), 72-79.

Van Kessel, K., Wouldes, T., & Moss-Morris, R. (2016). A New Zealand pilot randomized controlled trial of a web-based interactive self-management programme (MSInvigor8) with and without email support for the treatment of multiple sclerosis fatigue. *Clinical Rehabilitation*, *30*(5), 454-462.

Voet, N., Bleijenberg, G., Hendriks, J., de Groot, I., Padberg, G., van Engelen, B., & Geurts, A. (2014). Both aerobic exercise and cognitive-behavioral therapy reduce chronic fatigue in FSHD: an RCT. *Neurology*, *83*(21), 1914-1922.

Vogelaar, L., Van't Spijker, A., Vogelaar, T., van Busschbach, J. J., Visser, M. S., Kuipers, E. J., & der Woude, C. J. V. (2011). Solution focused therapy: A promising new tool in the

management of fatigue in Crohn's disease patients: Psychological interventions for the management of fatigue in Crohn's disease. *Journal of Crohn's and Colitis*, *5*(6), 585-591.

Vogelaar, L., van't Spijker, A., Timman, R., van Tilburg, A. J., Bac, D., Vogelaar, T., ... & van der Woude, C. J. (2014). Fatigue management in patients with IBD: a randomised controlled trial. *Gut*, *63*(6), 911-918.

Supplemental Results 3
Reasons for non-inclusion of studies in NMA

Studies not included in NMA	
Study	**Reason for exclusion from NMA**
Avaux 2016	Graphical only
Callahan 2008	No SDs for EOT, means only
Chalah 2020	No Ns for each intervention group
Coe 2022	Graphical data only
Coghe 2018	Wilcoxon test statistics only, no means
Daltroy 1995	Means only or group difference no SDs
De Carvelho 2012	Graphical only
De Doncker 2021	Graphical only
Drory 2001	Graphical only
Finlayson 2011	Between group t-test only, no means only Cohen's D
Gaede 2018	No means and SDs, graphs and reduction numbers
Hidding 2017	Individual patient data only
Irish 2017	Graphs and percentage increases only
Kim 2011	Graphical only, means only for baseline
Kos 2007	Change scores compares groups
Lee 2021	Graphical only
Mateen 2020	No SDs
Mathiowetz 2005	Data is difference between groups
McNelly 2016	4 x 4 factorial with merged groups
O'Connor 2019	No SDs
Palsdottir 2020	No SDs
Plow 2022	Beta coefficients or graphical only
Robb-Nicholson 1987	Correlations plus baseline data only
Sabapathy	Intervention arms the same category
Saiote 2014	Fatigue scores graphical or means by responders/non responders
Theander 2002	Correlations only
van Kessel 2016	2 arms same intervention category
Voet 2014	Median and ranges only
Vogelaar 2011	No Means, % of participants with decreased fatigue
Vogelaar 2014	No Means, % of participants with decreased fatigue

Supplemental Results 4
Timing of outcome measures

4.1 Self-management interventions

Behavioural Interventions						
Study	**Population**	**Intervention duration (EOT)**	**Short term**	**Long term**	**Short Long term (if any)**	
Self-Management						
Fatigue self-management - conservative						
Abonie 2020	MS	4 weeks				
Askari 2022	MS	12 weeks				
Blikman 2017	MS	4 months	10 weeks	36 weeks		
Farragher 2022	Kidney	8 weeks	12 weeks			
Finlayson 2011	MS	6 weeks	3 months	3 months		
GarciaJalon 2013	MS	5 weeks	3 months			
Ghahari 2010	Chronic	7 weeks	3 months			
Hersche 2019	MS	3 weeks	3 months			
Hugos 2010	MS	6 weeks				
Hugos 2019a	MS	6 weeks	3 months	6 months		
Kos 2016	MS	3 weeks	3 months			
Mathiowetz 2005						
Murphy 2010	OA	2 weeks	10 weeks			

Fatigue self-management - active						
Clarke 2012	Stroke	6 weeks	3 months			
Murphy 2024	Sys. Sclerosis	12 weeks				
O'Connor 2019	IBD	6 months				
Rietberg 2014	MS	12 weeks	12 weeks			
Vogelaar 2014	IBD	3 months		3 months		
General self-management						
Austin 1996	SLE	6 months				
Feldthusen 2016	RA	12 weeks		6 months		
Hammond 2008	RA			12 months	6 months	
Khan 2020	SLE	16 weeks				
CBT – fatigue						
Artom 2019	IBD	8 weeks		10 months	4 months	
Bredero 2023	IBD	8 weeks				
Ehde 2015	MS			10 months	4 months	
Gay 2023	MS	6 weeks		12 months	6 months	
Hewlett 2011	RA	6 weeks				
Hewlett 2019a	RA	6 weeks		46 weeks	20 weeks	
Jhamb 2023	Kidney	12 weeks				
Mead 2022	Stroke	4 months	2 months			
Menting 2017	T1 Diabetes	5 months				
Moss-Morris 2012	MS	10 weeks				
Nguyen 2019	Stroke	2 months	2 months			

Okkersen 2018	MD	10 months				
Picariello 2021	Kidney	12 weeks				
Pottgen 2018	MS	12 weeks	12 weeks			
Thomas 2013	MS	6 weeks		1 month	4 months	
van Kessel 2008	MS	8 weeks	3 months	6 months		
Van Kessel 2016	MS	10 weeks				
van den Akker 2017	MS	4 months	10 weeks	36 weeks		
Zedlitz 2012	Stroke	12 weeks		6 months		
Physical Activity						
Physical activity promotion						
Bachmair 2022	Inflammatory	22 weeks	6 weeks	34 weeks		
Callahan 2014	Arthritis	20 weeks				
Lutz 2017	MS	6 weeks				
Turner 2016	MS	6 months				
Exercise – supervised						
Dalgas 2010	MS	12 weeks	12 weeks			
Diaz 2023	PsO	16 weeks				
Englund 2022	MS	12 weeks				
Escudero-Uribe 2017	MS	12 weeks				
Heine 2017	MS	16 weeks		36 weeks		
Feys 2019	MS	12 weeks				
Gervasoni 2014	MS	2 weeks				
Kratz 2020	MS	8 weeks				

Kucharski 2019	RA	20 weeks		12 months		
Langeskov-Christensen 2022	MS	24 weeks				
Louie 2022	MS	12 weeks	12 weeks			
McCullagh 2008	MS	12 weeks	3 months			
Ortiz-Rubio 2018	PD	8 weeks				
Pozehl 2008	HF	24 weeks				
Exercise – unsupervised						
Durcan 2014	Arthritis	12 weeks				
Geddes 2009	MS	12 weeks				
Katz 2018	RA	21 weeks				
Maurer 2018	MS	6 months				
Tench 2003	SLE	12 weeks				
Active recreational						
Rehabilitation						
DeGiglio 2015	MS	8 weeks				
Mindbody						
Callahan 2016	Arthritis	8 weeks				
Fleming 2019	MS	8 weeks				
Fleming 2021	MS	8 weeks				
Walter 2019	PD	8 weeks				
Sgoifo 2017	MS	8 weeks				
Mindfulness						

Goren 2022	Crohn's	3 months				
Grossman 2010	MS	8 weeks		6 months		
Torkhani 2021	MS	8 weeks				

4.2 Stimulation interventions

Study	Population	Intervention duration (EOT)	Short term	Long term	Short Long term (if any)	
Vagal stimulation						
Aranow 2021	SLE	5 days	1 week			
Tarn 2023	Sjogren's	54 days				
Trans Cranial stimulation						
Cancelli 2018	MS	5 days				
Chalah 2020	MS	5 days				
Charvet 2018	MS	4 weeks				
Salemi 2019	MS	2 weeks	1 month			
Tecchio 2015	MS	5 days				
External stimulation						
Granja-Dominguez 2022	MS	4 weeks	3 months			
Mostert 2005	MS	4 weeks				
Piatkowski 2009	MS	12 weeks				
Voggenberger 2022	MS	2 weeks				
Aromatherapy						
Hawkins 2019	Hypothyroidism	14 days				

Acupuncture/acupressure						
Horta 2020	IBD	8 weeks	8 weeks			
Kluger 2016	PD	6 weeks				
RIC						
Moyle 2023	Stroke	6 weeks	6 weeks	18 weeks		

4.3 Nutritional Interventions

Study	Population	Intervention duration (EOT)	Short term	Long term	Short Long term (if any)	
Fish oil						
Arriens 2015	SLE	6 months				
Thiamine HD						
Bager 2021	IBD	4 weeks				
5-HTP						
Truyens 2022	IBD	8 weeks				
Flavenoid - cocoa						
Coe 2019	MS	6 weeks				
Diet						
Chase 2023	MS	16 weeks				
Plant						
Johnson 2006	MS	4 weeks				

Supplemental Results 5
Intervention content: studies included in NMA
5.1 Behavioural Interventions

Tables of intervention characteristics for studies in the NMA

Behavioural Interventions						
Study/ Population	**Pop.**	**Study N**	**Intervention (as named in study)**	**Intervention description**	**Intervention aim**	
Self-Management						
Fatigue self-management - conservative						
1.Abonie 2020	MS	21	Tailored activity pacing	Tailored pacing based on data from an accelerometer and logbook. Personalised report based on symptom-activity relationship - physical activity, fatigue, physical activity patterns. Develop strategies to develop graded consistent physical activity or increase rest as necessary.	Individual tailoring of intervention should improve the success of activity pacing interventions	
			Control	No intervention	Control.	
2.Askari 2022	MS	26	MSInform	Information about fatigue, fatigue rating and monitoring fatigue. Goal setting for fatigue management. Occupational performance coaching to reflect on meaningful activities affected by MS fatigue. Problem solving.	Improve performance in personally valued activities whilst building skills to address future challenges.	
			Control	Access to the control section of the MSInform website.	Control.	
3.Blikman 2017	MS	86	Energy Conservation Management (TREFAMs)	Aerobic training; Cognitive Behavioural Therapy; Energy Conservation Management	Teaching people to identify and modify their activities to reduce the impact of fatigue on daily life	

			Information only	Nurse consultations providing standardised information about MS fatigue	To control for attention and information about fatigue	
4.Farragher 2022	Kidney	30	Personal Energy Management Programme (PEP)	Energy management strategies e.g. simplifying tasks, pacing, using assistive devices, organising home environments. Structured energy management problem-solving strategies. Assisted application of the principals.	To improve life participation by helping identify energy management strategies to facilitate individual life participation goals.	
			General Disease Self-Management Programme	General information about kidney disease management.	Control.	
5.GarciaJalon 2013	MS	23	Energy Conservation Programme	A group based Energy Conservation Programme, educating people with multiple sclerosis on how to analyse and modify their own activity patterns in order to cope with their fatigue.	To modify unhelpful behaviours to manage fatigue	
			Peer support group	Peer support consisting of education and discussion of common topics for people with multiple sclerosis as recommended by the MS Society, the MS Trust and Action MS	Active control	
6.Ghahari 2010	Neuro	95	Online fatigue self-management programme	Importance of rest, communication, body mechanics, rearranging activity stations, setting priorities and standards, balancing a schedule.	N/R	
			Information only fatigue self-management programme	Information as intervention group, but no activities	N/R	
			Control	Routine care	N/R	

7.Hersche 2019	MS	47	Inpatient Energy Management Education + RAU	Learning how to manage available energy in order to achieve a satisfying and meaningful daily routine. Participants acquire knowledge and understanding about factors that influence energy and the consequences of fatigue on their habits and lifestyle. Identifying and implementing tailored behavior modification + rehabilitation as usual	To ensure that participants learn how to manage available energy in order to achieve a satisfying and meaningful daily routine.	
			Progressive Muscle Relaxation +RAU	A standardized series of relaxation exercises (involving 11 large muscle groups) combined with deep breathing + rehabilitation as usual	To achieve enhanced mental relaxation by reducing muscle tension	
8.Hugos 2010	MS	41	Fatigue Take Control formal group fatigue program	DVD viewing, topic focused discussion, individual goal setting, homework assignments. Identification of treatable or secondary causes of fatigue such as depression, sleep disturbance, deconditioning. Setting goals and priorities, environmental modification, managing mobility, energy effectiveness strategies, importance of exercise.	Fatigue can be reduced by guiding individuals to make the environmental, behavioural and lifestyle changes necessary to manage MS fatigue	
			Wait list	Usual activities	A control	
9.Hugos 2019a	MS	204	Fatigue Take Control group education program	DVD viewing, topic discussion, individual goal setting. Aspects of MS fatigue e.g. depression, sleep disturbance, heat sensitivity, deconditioning. Setting goals and priorities, managing mobility problems, energy conservation strategies.	Based on belief that fatigue can be reduced by guiding individuals to make environmental, behavioural and lifestyle changes necessary to manage fatigue	
			MS Take Control group program	Educational pamphlets and group discussion around: MS and your emotions; solving cognitive	No DVDs or goal setting activities	

				problems; taming stress, food for thought, MS and Nutrition, urinary dysfunction, Vitamins, minerals and herbs in MS.		
10.Kos 2016	MS	31	SMOoTH self management occupational, therapy programme	Strategies to support clients to take control over the performance of activities within the limits of their available energy, raising self-efficacy.	Based on principles of the Energy Conservation/Enveloped Theory	
			Stress management and relaxation	Education about the role of stress in MS, practicing relaxation techniques.	To alleviate stress which may play an important factor in persistence of fatigue	
11.Murphy 2010	OA	32	Tailored activity pacing	Accelerometer data to measure physical activity, symptom log, diary of daily activities. Study specific education module on activity pacing, tailored activity recommendations based on personalised report.	To use tailored activity pacing to address symptoms that interfere with activity engagement	
			General activity pacing	Accelerometer data to measure physical activity, symptom log, diary of daily activities. Study specific education module on activity pacing. No tailored recommendations.	To control for tailoring of activity pacing.	
Fatigue self-management - active						
12.Clarke 2012	Stroke	19	Fatigue Management Group	Psychoeducation aimed at alleviating fatigue symptoms. Fatigue diary (tracking fatigue and activities) and homework. Group brainstorming to find solutions to problems identified. Sharing individual experiences and individual assistance.	To evaluate the benefits of educational fatigue management	
			General Stroke Education	Psychoeducation not particularly aimed at alleviating fatigue. Information presented in a didactic format with illustrations from daily life. Sharing individual experiences and individual assistance.	A control	

13.Murphy 2024	SS	173	Resilience- Building Energy Management Program (RENEW)	Focuses on wellness through bolstering self-efficacy, positive experiences, and emotions as opposed to focusing on reducing symptom burden or suffering. Positive activity interventions encourage behavioral activation by inviting patients to engage in pleasant activities. Physical activity, pacing activities, relaxation techniques, practicing adaptive (positive) thoughts, taking care of one's body, healthy diet, and sleep.	Theoretical grounding in self-efficacy theory and positive psychology, which teaches people to more optimally respond to stressors to build resiliency	
			Wait list	Usual routine	Control	
14.Rietberg 2014	MS	48	Multidisciplinary rehabilitation	An individually tailored programme focused on optimising self-management behaviour in daily life activities on the domains of physical fitness, behaviours or cognitions that perpetuate fatigue, and energy conservation. Physical therapy; occupational therapy; social work	To investigate the effects of an individually tailored multidisciplinary outpatient rehabilitation programme on MS fatigue	
			MS Nurse consultation	Nurse consultation to set goals and evaluated in a follow-up session	A mono-disciplinary programme as control	
General self-management						
15.Austin 1996	SLE	58	Telephone Counselling	Counselling targeting six behaviours: self-care activities in managing fatigue; patient's communication skills; removing barriers to medical care; medication self-management; symptom monitoring; stress control methods.	To assist patients in decreasing fatigue, physical function and improving psychological function.	
			Symptom monitoring	A review of fatigue; physical function; self-care activities; social activity; support from family; flare ups; joint pain; mood and tension.	To assist patients in decreasing fatigue, physical function and improving psychological function.	

16.Feldthusen 2016	RA	70	Person-centred Physical Therapy	Self-care plan to manage fatigue focused on tailoring health-enhancing physical activity and balancing life activities.	To devise a mutually agreed care plan	
			Control	Usual activities	Control.	
17.Hammond 2008	RA or PsA	218	Modular Behavioural Arthritis Education Programme	Looking after your joints; keeping mobile and managing pain and mood; advice, goal setting and action planning towards recommended frequency targets. Behavioural joint protection programme, health beliefs, personal impact of arthritis, understanding factors affecting symptoms, attitudes, self management methods, motivation to change.	A modular structure is proposed to promote sustained behavioural change	
			Standard information focused education programme	What is arthritis, how it affects the joints and body; drug treatments; managing arthritis. Exercise: 30 minute stretching program, rest, posture pain management. Joint protection, managing fatigue, healthy diet.	A control	
18. Khan 2020	SLE	50	Digital Therapeutic Intervention	Tracking of lifestyle activities (e.g. diet, sleep habits, physical activity, bowel movements); analysis and organisation of data; presentation of data to health coach. Telehealth coaching sessions based on individual data.	To identify and intervene on dietary and other lifestyle factors	
			Usual Care	Usual care as recommended by treating physician	Control.	
CBT – fatigue						
19. Artom 2019	IBD	31	Cognitive Behavioural Therapy	IBD-fatigue explained; CBT for IBD-fatigue; activity scheduling; improving your sleep; understanding IBD symptoms; changing your thinking; managing stress; determining a sense of control and coping	Disease-related factors trigger fatigue. The ways in which people respond cognitively, emotionally and behaviourally to their fatigue may then	

				with emotions; social support; preparing for the future. CBT manual.	contribute to the perpetuation or worsening of symptoms. The targeting of cognitions, emotions and behaviour related to fatigue through (CBT) may improve clinical and psychosocial outcomes	
			Information	CCUK 'Fatigue in IBD' Information Sheet to use without therapist help	Control	
20. Bredero 2023	IBD	113	Mindfulness-Based Cognitive Therapy	A structured group intervention. Group meditation, cognitive-behavioural exercises, psycho-education (fatigue symptoms and management, stress management), daily homework. Helping patients to develop more non-judgemental awareness of fatigue experiences, to learn to de-centre from negative feelings and perceptions of fatigue, to become more aware of unhelpful automatic reactions, and to make conscious choices about doing physical activity.	To focus away from unhelpful reactions to fatigue and physical activity	
			Wait List	Usual activities	A control	
21. Ehde 2015	MS	163	Self-management telehealth	Evidenced-based cognitive-behavioural and positive psychology strategies for helping participants self-manage pain,	To help adults with MS effectively manage fatigue, chronic pain, and/or depression.	
			MS education telehealth	Telephone-delivered MS education intervention, educational material on additional topics such as fatigue and nutrition	A rigorous active control	

22. Gay 2023	MS	105	CBT FACETS+	Management of MS-related fatigue, incorporating elements of cognitive-behavioural, energy effectiveness, self-efficacy therories. To help people normalise their experience of fatigue, learn to change the way they think about fatigue to a more adaptive perspective and make more effective use of their energy.	To challenge and modifying dysfunctional beliefs and thoughts related to fatigue that can contribute to its onset, maintenance and amplification.	
			Standard care	Local standard care comprising general advice and information about MS-related fatigue, including its characteristics, contributory factors and ways to reduce its impact. Information booklet and tips for fatigue management.	A control	
23. Hewlett 2011	RA	168	Cognitive Behavioural Therapy	Topic likely to improve fatigue: thoughts, feelings and behaviours related to fatigue were addressed using Socratic questioning and guided discovery to enable patients to work out links themselves. Problem-solving; goal setting; self-monitoring or activity/rest and energy management.	To help patients turn cognitive and behavioural changes into improved well-being	
			Information only	Arthritis Research UK leaflets 'Fatigue and RA' and fatigue excerpts from 'Looking after your joints'. A session covering fatigue symptoms, consequences, causes	Control	
24.Hewlett 2019a	RA	333	Cognitive behavioural approach RAFT	RAFT course uses CBT approaches to address behaviours likely to be related to fatigue and their underpinning thoughts and feelings. Exploratory questioning, goal setting, peer support to enhance self-efficacy, prompting changes in self-management	Enhancing self-efficacy prompts changes in fatigue self-management	
			Usual Care	Arthritis Research UK fatigue self management booklet based on the original RAFT intervention.	A control	

				Group session covering fatigue symptoms, consequences, causes and self-management suggestions.		
25.Jhamb 2023	Kidney	160	Collaborative care	Targeted at 1 or more symptoms (fatigue,pain, and/or depression) based on patients' reported levels of each symptom and preference. Using an individualized and shared decision-making approach, pharmacotherapy, and/or CBT were offered. A stepped approach to treatment intensification allowed for monitoring patient adherence, treatment response, preferences, and outcomes, and modifying the treatment to achieve the best possible outcome for each patient. The CBT strategies were contextualized to address the unique challenges and needs of each patient receiving hemodialysis.	Treatment of symptom clusters may be more effective given that many of the physical and mental symptoms frequently coexist, are highly correlated, can exacerbate each another, and may share similar biologic and psychologic pathogenesis.	
			Health education	ESKD-relevant education on relevant topics - kidney transplantation, heart health, immunizations, diet, travel per patient preference via telemedicine delivered in the dialysis units or at home.	Attention control	
26.Mead 2022	Stroke	76	Cognitive Behavioural Intervention	Focused on the potentially reversible nature of fatigue, teaches (a) overcome fears about physical activity, (b) increase physical activity using diary monitoring and activity scheduling, (c) achieve a balance between activities, rest and sleep and (d) address unhelpful thoughts related to fatigue and low mood if present.	Symptoms, feelings and behaviours are interconnected and that identifying unhelpful thoughts, and challenging them, e.g. through the use of behavioural experiments, can lead to changes.	

			Information only	Patient information leaflet provided by the Stroke Association	Control	
27.Menting 2017	T1D	120	CBT	Dia-Fit CBT. Goal setting; regulation of sleep-wake pattern; formulation of helpful fatigue-related beliefs; activity regulation and graded activity; coping with pain; optimisation of social support and interactions; reduction of diabetes-related distress; step-by-step realisation of goals.	Assumes that disease-specific elements trigger fatigue, which is maintained by cognitive behavioural factors. CBT aims to address these perpetuating factors.	
			Wait list	Care as usual	A control.	
28.Moss-Morris 2012	MS	45	MS Invigor8	Website based on a CBT programme containing modules on MS fatigue; a fatigue diary; rest and activity patterns; improving sleep; understanding MS symptoms; recording thoughts; managing stress; emptions, support and the future.	To test a behavioural approach to MS fatigue with a clear conceptualisation of fatigue.	
			Standard care	Usual activities	A control	
29.Nguyen 2019	Stroke	15	CBT	CBT addressing fatigue and sleep encompassing principles of psychoeducation, behavioural activation, behavioural experiments, cognitive restructuring, problem-solving, relapse prevention, plus suitable exercise guidelines to encourage physical exercise to improve energy, sleep and mood	To investigate the efficacy of individual CBT targeting fatigue and insomnia with exercise to improve energy, sleep and mood	
			Wait list	Treatment as usual	Control.	
30.Okkersen 2018	MD	255	CBT with optional graded exercise	Cognitive behavioural therapy customised to individual participants by selecting from modules including regulating sleep/wake pattern; compensating for reduced patient initiative;	Patient reported HRQoL can be improved by addressing reduced patient initiative,	

				formulating helpful beliefs about fatigue and myotonic dystrophy type 1; optimising social interactions; coping with pain. Optional graded exercise where available.	optimising physical activity, and alleviating fatigue	
			Standard care	Standard care applicable to the patient's home country	Control.	
31.Picariello 2021	Kidney	24	CBT (BReF)	CBT based self-management intervention aimed specifically at fatigue. Targets fatigue thoughts, emotions and behaviours by creating consistent activity and rest routine, graded increase of daily activity, and identifying and managing unhelpful thoughts in relation to fatigue.	To target the perpetuators of fatigue which is likely to lead to improvements	
			Wait list	Usual renal care	Control.	
32.Pottgen 2018	MS	275	Self-guided online fatigue intervention	ELEVIDA programme: based on CBT strategies conveyed through simulated dialogue.	To test a web-based version of CBT for MS fatigue to improve accessibility.	
			Wait list	Usual activities	A control	
33.Thomas 2013	MS	164	FACETS group based fatigue management programme	A conceptual framework integrating elements from cognitive behavioural, social-cognitive, energy effectiveness, self-management and self-efficacy theories.	To normalise fatigue experiences, learn helpful ways of thinking about fatigue and use available energy more efficiently.	
			Usual care	Current local practice alone	A control	
34.van Kessel 2008	MS	72	CBT	Manual based of a cognitive behaviour model of fatigue. Socratic questioning. Individually tailored to focus on aspects that were important to participants. Goal setting according to specific issues; development of behavioural and cognitive strategies.	To challenge and behavioural, cognitive, emotional and external factors that may be contributing to MS fatigue.	

			Relaxation training	Participants taught a range of relaxation techniques including diaphramatic breathing, progressive muscle relaxation, visualisation, cue-controlled relaxation, rapid relaxation.	To control for therapist contact and support	
35.van den Akker 2017	MS		CBT TREFAMS-CBT	Cognitive behavioural therapy protocol with modules on formulating goals; regulating sleep/wake pattern; changing beliefs regarding MS; changing beliefs regarding fatigue; reducing the focus on fatigue; regulation of physical, social and mental activity, addressing the role of the environment; handling pain.	Disease-related factors trigger fatigue in MS, and cognitive, emotional and behavioural factors determine the extent to which fatigue interferes with daily life. CBT aims to address these factors if dysfunctional.	
			Control treatment	Written and oral information about MS fatigue; discussion of personal experiences in coping with fatigue and other fatigue-related issues	Attention control	
36.Zedlitz 2012	Stroke	83	Cognitive Therapy and Graded Activity Training COGRAT	Cognitive treatment emphasising pacing and relaxation to mange fatigue and psychological distress, plus graded activity including walking on a treadmill, strength training, and homework assignments	To test whether adding graded activity to cognitive therapy is effective at alleviating fatigue and fatigue like symptoms in stroke patients	
			Cognitive Therapy only CO	Cognitive treatment emphasising pacing and relaxation to mange fatigue and psychological distress	To test the effectiveness of CO alone	
Physical Activity						
Physical activity promotion						
37.Bachmair 2022	IRD	367	Cognitive behavioural approach	LIFT CBA - psychological intervention targeting unhelpful beliefs and behaviours and aiming to replace them with more adaptive ones	Aimed to replace unhelpful behaviours with more adaptive ones	

			Personalised exercise programme	LIFT PEP - exercise programme individually tailored and combined with graded exposure behavioural therapy aimed to normalise misperceptions of effort and enhance exercise tolerance	Aimed to normalise misperceptions of effort and enhance exercise tolerance	
			Usual Care	VERSUS arthritis education booklet for fatigue	Control.	
38.Callahan 2014	RA	354	Behavioural Lifestyle Intervention ALED	Instructor-led group discussion session covering topics such as setting goals, enlisting support, and managing time. Group discussions reinforce material in the ALED Workbook.	Behavioral theory–based lifestyle program teaches appropriate cognitive and behavioral skills to identify and overcome barriers to physical activity participation.	
			Wait List	Usual daily activities	Control	
39.Lutz 2017	MS	14	EG-I	Participants were taught neurophysiological essentials in MS disease, (neuro) physiological effects of sports, and physical exercises in general and specific for MS, MS-specific recommendations of exercise training, training principles, and the importance of resting periods. In order to guarantee a comprehensive treatment, various types of exercise training (cardiorespiratory, strength, coordination/reflex-based, and flexibility) were offered based on individual performance abilities.	Evaluate the effects of the revised six-week ePEP on self-regulated and long-term exercise behaviour	
			EG-W	Instructed not to change their daily routines	Control	
40.Turner 2016	MS	64	Physical Activity Counseling	Telephone-Administered Physical Activity Counseling. Telephone counseling and home-based telehealth monitoring. Education as control arm plus mailed graphic feedback, 6 telephone counseling sessions using	MI encourages behavior change by contrasting current behavior, such as physical inactivity, with	

				principles of motivational interviewing, and telehealth home monitoring to track progress on physical activity goals.	desired goals and values, such as physical fitness, good self-care, and quality of life, in a manner that is empathetic, evocative, collaborative and intended to promote self-efficacy.	
			Physical activity education	Self-directed physical activity education. Advice to increase physical activity and a DVD with examples of in-home exercises for multiple physical ability levels.	Control	
Exercise – supervised						
41.Dalgas 2010	MS	38	Progressive resistance training [PRT]	Intervention to improve muscular strength, functional capacity, and reduce fatigue	N/R	
			Usual care	Continued previous daily activity level	Control	
42.Diaz 2023	PsO	118	Aerobic training program	Aerobic training program on a conventional motorized treadmill, consisting of a warm-up, treadmill exercise at a work intensity of 50–65% of peak heart rate (increasing by 5% every four weeks) measured during a previous maximal treadmill test, cool-down.	Sedentary lifestyle may influence the natural course of psoriasis natural and the existence of comorbidities	
			Control	N/R	Control	

43.Englund 2022	MS	140	High-Intensity Resistance Training (HIRT) - Group A	Resistance training	To compare the effects of high-intensity resistance training (HIRT) on self-reported fatigue	
			High-Intensity Resistance Training (HIRT) - Group B	Resistance training	As above with fewer sessions	
			Control	No intervention	Control.	
44.Escudero-Uribe 2017	MS	55	Whole Body Vibration	Exercises (amplitude 1⁄4 3 mm, average frequency 1⁄4 4 Hze1 Hz/sec) using a Zeptor Med System. Vibrations transmitted to the body stimulate the participants' muscle spindles, generating subconscious muscle contractions.		
			Balance Trainer System	Dynamic balance with the BT system, a mechanical device that provides a fall-safe balancing environment. The BT software (Balance-Soft version 01.04.02) includes different types of exercises and games that force a person's centre of gravity to be shifted in different directions, thereby activating their leg, pelvis, and trunk muscles.		
			Wait List	Usual activities	Control	
45.Heine 2017	MS	89	Aerobic training	Aerobic interval training	To test the effectiveness of aerobic training on MS-related fatigue	
			Usual care	Consultations with an MS nurse including reliable information on MS-related fatigue and guidance from the experienced MS nurse	Education control	

46.Feys 2019	MS	42	Group exercise	Remotely supervised community-located “start-to-run” program	To test the effectiveness of physical activity on Fatigue	
			Waiting List Control Group (WLC)	No intervention	Control.	
47.Gervasoni 2014	MS	22	Arm cycling and task-oriented exercises	Aerobic training and task-oriented rehabilitation programme	Aerobic activity will improve fatigue and fatiguability in people with MS	
			Wait list	Crossed over to intervention group after 8 weeks	Control	
48.Kratz 2020	MS	20	Exercise therapy	Weekly educational modules and resources, and equipment for a range of exercises (yoga mat, 1 set of 5 resistance bands attached to a carabiner, 1 leg strap with carabiner, a door anchor for securing resistance bands); weekly exercise logs, and a wrist-worn pedometer/HR monitor.	To test the benefits of exercise in improving fatigue	
			Telephone exercise intervention	A weekly phone call	Control	
49.Kucharski 2019	RA	74	Aerobic and resistance exercise	Moderate-to-high intensity, aerobic and resistance exercise in the gym with person-centred guidance	Moderate to high intensity exercise will improve fatigue	
			Home exercise	Performed light home-based exercise for mobility, lower body strength and balance, but no gym-based exercise	Control	
50.Langeskov-Christensen 2022	MS	86	High intensity aerobic exercise	High-intensity progressive aerobic exercise (PAE).	High-intensity aerobic exercise leads to cardioprotective benefits and may be superior in ameliorating secondary	

					MS fatigue through a higher increase in fitness and motor efficiency	
			Wait List	Habitual lifestyle (including ongoing physiotherapy treatment).	Control	
51.Louie 2022	MS	33	Exercise and education programme	Program incorporating behaviour change education, exercise and community integration		
			Usual care	Usual daily activities	Control.	
52.McCullagh 2008	MS	30	Exercise	3 months' exercise programme	To determine if exercise benefits patients with multiple sclerosis	
			Usual care	Usual daily activities	Control	
53.Ortiz-Rubio 2018	PD	46	Resistance training program	Training structure included 5 to 10min warm up, core activities and 5-min cool-down, lower-extremity exercises focused on strengthening all major muscle groups of lower limbs with the aid of elastic bands in a seated position. Exercises at lower loads (elastic bands resistance of 1.5 kg), then exercises performed in 1–3 sets with 10–15 repetitions in each and using a band with a resistance of 2.7 kg. The rate of progression was modified and adapted according to specific physical limitations.	Examine the effects of a twice-a-week resistance training program using elastic bands during 8 weeks on dynamic balance and fatigue in patients with PD.	
			Low intensity exercise	Weak low-intensity exercise program in order to introduce similar social interaction, enjoyment and physical activity levels. This program included breathing, stretching and relaxation activities, with the activities performed in a seated position.	Control	

54.Pozehl 2008	HF	21	Exercise programme	Four different aerobic modalities (treadmills, stationary bikes, rowers, and arm ergometers) were utilized according to individual tolerance during the aerobic phase. Intensity of this phase was set at 60–85% maximum VO2 obtained from the baseline cardiopulmonary exercise test and a rating of 12–14 of perceived exertion (RPE) on the Borg scale. The strength/resistance training consisted of subjects performing light upper-body exercises (military press, biceps curl, and lateral deltoid raises) and lower-body exercises (knee extension, side hip raise, and hip extension) with 1–10 lb hand and ankle weights. Wall push-ups, abdominal curl-ups, and/or pelvic tilts were also included in the 20-minute strength/ resistance training.	Aerobic exercise will improve fatigue in people with heart failure	
			Usual care	Usual daily activities	Control	
Exercise – unsupervised						
			Usual	Instructed not to perform any physical activity besides their usual daily life requirements. Every 14 days they also received a phone call.	Control	
55.Durcan 2014	RA	80	Home-based exercise	Specific exercises were prescribed to target the individual deficiencies identified. Cardiovascular Exercise: 5 days of moderate intensity cardiovascular exercise, based on a walking program. Resistance Training: Each major muscle group to be trained 2–3 days per week 40–50% of 1 RM. In addition, functional exercises were prescribed according to deficiency identified in HAQ. Flexibility and Neuromotor Conditioning: A daily stretching regimen was devised for each	Evaluate the effect of an exercise program on self-reported sleep quality and fatigue in RA.	

				patient. Timed 1 leg stands were prescribed for neuromotor health. These were advised 2–3 days per week.		
56.Geddes 2009	MS	12	Exercise programme	An individualised home walking program. Participants adjusted their walking speed to stay within their prescribed HR range using a home Heart Rate Monitor. The exercise group subjects were instructed to walk 3 times per week for 12 weeks. For the first 2 weeks, the subjects walked 5 minutes below the lower limits of their THR range, followed by 15 minutes of walking within their THR range, and then a 5-minute cool down below their THR range. During weeks 3 through 12, training time increased in the THR range to 20 to 30 minutes. Weekly exercise log including RPE values and received biweekly telephone calls to monitor their exercise compliance.	To investigate the effects of a convenient 12-week home exercise walking program on cardiovascular parameters, energy expenditure, and fatigue perception in individuals with mild to moderate MS.	
			No regular exercise	The control group was asked to refrain from any regular exercise during the period.	Control	
57.Katz 2018	RA	96	Pedometer + step log	Educational booklet and discussion, plus a pedometer and a diary to record daily step counts from the pedometer. The step diary with prewritten dates and space to record each day's steps and notes about other activities, problems with the activity monitor, injuries, or other relevant issues.	To test the comparative effectiveness of exercise with the additional of step targets.	
			Pedometer + step log + step targets	Educational booklet and discussion, pedometer and step diary, and individualized daily step targets. Step targets were based on the week of activity monitoring between the baseline and randomization visits, and were calculated to	As above.	

				increase participants' average daily step counts by 10% for every 2 weeks of the intervention period.		
			Education only	Received an educational brochure (Be Active Your Way: A Guide for Adults). Guided discussion of simple ways to increase physical activity in daily life based on the booklet. The brochure was available in English and Spanish.	Control	
58.Maurer 2018	178	MS	Exercise	The individual exercise schedules comprised strengthening exercises twice a week and endurance training once a week. Balance or core stability exercise could be added. The personal exercise schedule and the comprised exercises were explained in a two-day on-site introductory group session at the beginning of the intervention period. Participants documented each exercise session via a web-based application (duration, type of exercises, number of repetitions, and sets, perceived exertion) and used an electronic exercise diary that could be supervised by the exercise therapist.	Evaluated the effect of an exercise intervention on fatigue in relapsing–remitting MS patients receiving fingolimod.	
			Wait List	No intervention	Control	
59.Tench 2003	SLE	93	Aerobic exercise therapy	Asked to exercise at home at least three times a week for between 30 and 50 min for a period of 12 weeks at a heart rate corresponding to 60% of peak oxygen consumption. The main exercise was walking but patients were encouraged to take other forms of exercise, such as cycling and swimming, and were seen every 2 weeks for a supervised exercise session.	To compare aerobic exercise therapy with relaxation therapy	

			Relaxation therapy	Asked to listen to a 30-min relaxation audiotape a minimum of three times a week in a darkened, warm and quiet room and were seen every 2 weeks for a supervised relaxation session.	To compare aerobic exercise therapy with relaxation therapy	
			No intervention	Asked to continue with their normal daily activity pattern and specifically asked to avoid doing any extra physical activities. They were reviewed at follow-up but not seen at other times.	Control	
Active recreational						
Rehabilitation						
60.DeGiglio 2015	MS	35	Cognitive rehabilitation with commercial video game	Training in games of memory, attention and visuospatial processing, and calculations	N/R	
			Wait list	Wait list control	Control.	
Mindbody						
61.Callahan 2016	RA	343	Tai Chi	12 tai chi movements	Reduce arthritis symptoms	
			Control	Usual activities	Control.	
62.Fleming 2019	MS	17	Home-based pilates	Pilates following a DVD	Effect of pilates on anxiety, depression and fatigue in people with MS	
			Supervised pilates	Certified pilates instructor supervises pilates exercises	Effect of pilates on anxiety, depression and fatigue in people with MS	
			Wait list control	Maintain pre-trial activity level	Control.	

63.Fleming 2021	MS	80	Pilates	Home-based pilates guided by DVD	To improve anxiety, depression and fatigue through pilates	
			Wait list control	Pre-intervention physical activity levels and contacted by email or telephone to ensure completion of biweekly outcome assessments	Control.	
64.Walter 2019	PD	27	Yoga	Progressive yoga for PD, focused on balance, strength and mobility. Meditation, physical postures, breathwork.	Non-motor symptoms e.g. pervasive fatigue can lead to decreased HRQoL. Physical activity can alleviate non-motor symptoms.	
			Wait List	Usual care	Control	
65.Sgoifo 2017	MS	48	Integrated Imaginative Distention Therapy	A selection of Jacobson relaxation exercises with breath awareness, motor imaging, body imaginative scan, imaginative experience. After the practice, the participants were invited to a group discussion, managed by the psychotherapist. Participants were invited to repeat the IID steps at home.	Joins interventions previously proven effective on MS fatigue: relaxation, self-awareness, and psychotherapy	
			Wait List	Usual activities	Control	
Mindfulness						
66.Goren 2022	CD	116	COBMINDEX	COBMINDEX (Cognitive Behavioural and Mindfulness-based stress reduction with Daily Exercise) is a psychological intervention including techniques such as breathing awareness, body scanning, muscle relaxation, and mindfulness	To improve the quality of life by reducing psychological distress and fatigue in patients with Crohn's Disease	
			Wait list control	No form of psychological instruction during the study period	Control.	

67.Grossman 2010	MS	150	Mindfulness-Based Intervention (MBI)	Specific exercises and topics within the context of mindfulness training, i.e., practices during lying, sitting, and dynamic yoga postures, as well as during everyday life, e.g., stressful situations and social interactions. Mindfulness exercises included observation of sensory, affective, and cognitive domains of perceptible experience.	Proposes that non-judgmental awareness of moment-to-moment experience (i.e., mindfulness) may positively affect accuracy of perception, acceptance of intractable health-related changes, realistic sense of control, and appreciation of available life experiences.	
			Usual care (UC)	Received regular, currently optimal medical care during the duration of the study	Control.	
68.Torkhani 2021	MS	35	Mindfulness-Based Intervention (MBI)	Daily mindfulness training associated with a Physical Activity program, delivered via internet	To compare with Implementation Intention in reducing Multiple Sclerosis symptoms	
			Implementation Intention	If-then plan associated with a Physical Activity program, delivered via internet	To with mindfulness in reducing Multiple Sclerosis symptoms	
			Control group	Not guided to develop if-then plans and they did not receive any mindfulness training, however, they received the same PA program	Control	

Stimulation Interventions						
Study	**Population**	**Study N**	**Intervention (as named in study)**	**Intervention description**	**Intervention aim**	
Vagal stimulation						
69.Aranow 2021	SLE	18	VNS	Vagus Nerve Stimulation	The inflammatory	

					reflex is a physiological mechanism that attenuates the innate inflammatory response. Stimulation of the vagus nerve results in the reduction of inflammatory mediators	
			Sham Stimulation	Sham VNS	Control	
70.Tarn 2023	Sjögren's Syndrome	40	VNS	VAGUS NERVE STIMULATION	Reduce fatigue & pain	
			Sham	Sham VNS	Control	
Trans Cranial stimulation						
71.Cancelli 2018	MS	10	tDCS	Cross over transcranial direct current stimulation (tDCS)	Reduce fatigue symptoms	
			Sham			
72.Charvet 2018	MS	42	(Study 2) tDCS	To evaluate whether tDCS can reduce fatigue in individuals with MS.	Reduce fatigue	
			Sham		Control	
73.Salemi 2019	MS	17	tRNS	Transcranial direct current stimulation	Stimulate motor cortex to improve fatigue	
			Sham tRNS	Sham	Control	
74.Tecchio 2015	MS	21	Transcranial direct current stimulation whole body	Cross-over bilateral whole body S1 anodal tDCS/ hand treatment/ sham	Reduce fatigue and assess whether it also induces changes in the excitability of	

					sensorimotor cortical areas	
			tDCS hand & sham			
External stimulation						
75.Granja-Dominguez 2022	MS	44	Pulsed electromagnetic field therapy	PEMF	Effects of PEMF therapy on the self-reported level of fatigue in people with RRMS.	
			Placebo	Sham	Control	
76.Mostert 2005	MS	24	Pulsed Magnetic field therapy	Pulsed magnetic therapy	Reduce fatigue	
			Sham	Sham pulsed magnetic therapy	Control	
77.Piatkowski 2009	MS	37	Bio-Electro-Magnetic- Energy-Regulation (BEMER)	8 minutes twice every day at home. In the treatment group (verum), the BEMER mattress was activated BEMER pulsed electromagnetic fields	To evaluate the long-term effects of BEMER therapy in MS patients with significant fatigue	
			Sham	As above but no magnetic field was generated although there was the typical BEMER sound.		
78.Voggenberger 2022	MS	26	Bright light therapy (BLT)	Light box positioned at a height aligned with eyes at a distance of 30 cm, at which 10 000 lux were achieved. Participants were instructed to keep their eyes open during the whole 30 min of light therapy.	Improve fatigue	
			Dim red light therapy (DRL)	As above The light boxes were identical in both groups, with the only difference	Placebo	

				that we installed a filter that dimmed the light to 200 lux and tinted it red		
Aromatherapy						
79.Hawkins 2019	Hypothyroidism	54	Peppermint aromatherapy	Essential oil blend was primarily composed of peppermint (Mentha x piperita) essential oil. In addition to the peppermint essential oil, small amounts of black pepper (Piper nigrum) essential oil, clove bud (Eugenia caryophyllus) essential oil, white grapefruit (Citrus x paradisii) essential oil, and bergamot (Citrus Aran- tium bergamia)	Peppermint essential oil is traditionally used to reduce fatigue by aromatherapists	
			Avocado vegetable oil	A bottle of avocado vegetable oil with disposable paper inhaler sticks. This oil was selected due to its light green hue which resembles the color of the essential oil blend used for the intervention group, and for its lack of an aroma.	Placebo	
Acupuncture/ acupressure						
80.Horta 2020	IBD	46	EAc	Electroacupuncture	Evaluate effect on fatigue	
			ShEAc	Sham electroacupuncture	Placebo effect	
			Wait List	Waiting list	Control	
81.Kluger 2016	PD	94	Acupuncture	Acupuncture needles inserted at 10 points	Improve fatigue	
			Sham	Toothpicks used on sham points	Control	

RIC						
82.Moyle 2023	Stroke	24	Remote Ischaemic Conditioning RICFAST	Inflating a blood pressure cuff around the participant's upper arm to 200 mmHg for 5 min and then deflating for 5 min.	RIC can preserve mitochondrial function, improve tissue perfusion and may mitigate PSF.	
			Sham RIC	As above, inflation pressure 20 mmHg	Control	

Nutritional Interventions						
Study	**Population**	**Study N**	**Intervention (as named in study)**	**Intervention description**	**Intervention aim**	
Fish oil						
83.Arriens 2015	SLE	50	Fish oil	Fish oil (6 capsules/day equaling 2.25 g EPA and 2.25 g DHA)	Reduced omega-3 fatty acids, which are powerful anti-oxidants observed in SLE. This deficiency may be causally related to oxidative stress, inflammation, disease activity, and fatigue in SLE.	
			Placebo	Visually identical capsules	Control	
Thiamine HD						
84.Bager 2021	IBD	40	Thiamine	High-dose oral thiamine for 4 weeks (containing 300 mg thiamine hydrochloride), 4 weeks of	Most interventions are of behavioural or	

				washout, 4 weeks of oral placebo Daily dose depended on gender and body weight (BW) according to the following scheme: Females: BW < 60 kg: 600 mg (2 tablets), BW 60-70 kg: 900 mg (3 tablets), BW 71-80 kg: 1200 mg (4 tablets), and BW > 80 kg: 1500 mg (5 tablets) Males: BW < 60 kg: 900 mg (3 tablets), BW 60-70 kg: 1200 mg (4 tablets), BW 71-80 kg: 1500 mg (5 tablets), and BW > 80 kg: 1800 mg (6 tablets)	psychological character not on pharmacological treatments. Therefore, high-dose oral thiamine versus placebo for chronic fatigue in patients with quiescent inflammatory bowel disease	
			Placebo	Oral placebo for 4 weeks, 4 weeks of washout, 4 weeks of high-dose oral thiamine (containing 300 mg thiamine hydrochloride). Daily dose depended on gender and body weight (BW) according to the following scheme: Females: BW < 60 kg: 600 mg (2 tablets), BW 60-70 kg: 900 mg (3 tablets), BW 71-80 kg: 1200 mg (4 tablets), and BW > 80 kg: 1500 mg (5 tablets), Males: BW < 60 kg: 900 mg (3 tablets), BW 60-70 kg: 1200 mg (4 tablets), BW 71-80 kg: 1500 mg (5 tablets), and BW > 80 kg: 1800 mg (6 tablets).	To test high-dose oral thiamine as an alternative to behavioural or pharmacological interventions	
5-HTP						
85.Truyens 2022	IBD	166	5-HTP	Oral 5-HTP (100 mg) twice daily for 8 weeks (then crossover - no washing out period given placebo twice daily for 8 weeks)	Effect of 5-Hydroxytryptophan on Fatigue in Quiescent Inflammatory Bowel Disease	

			Placebo	Placebo twice daily for 8 weeks (then crossover - no washing out period then given oral 5-HTP (100 mg) twice daily for 8 weeks)	Effect of 5-Hydroxytryptophan on Fatigue in Quiescent Inflammatory Bowel Disease	
Flavenoid - cocoa						
86.Coe 2019	MS	40	High-flavanol cocoa drink	Consume one sachet with heated rice milk (after an overnight fast) at the same time each morning. Wait 30 minutes before consuming any other food or beverage and/or take their medication. Usual diet followed for the rest of the day. High flavanoid content.	Investigate whether flavanoid rich cocoa will improve fatigue in people with RRMS	
			Low-flavanol cocoa drink	As above but with low flavanoid content.	Control	
Diet						
87.Chase 2023	MS	39	Low fat diet	Nutrition counselling + low fat diet. A low-fat diet (fat total daily calories⩽20%) with saturated fat<7% of daily caloric intake and the rest of caloric breakdown consisting of 20% protein and 60% carbohydrate (primarily complex).	There is a possible association between weight loss and fatigue.	
			Wait List	Usual diet	Control	
			Usual diet	Consume their pre-study vitamins, supplements, and/or medications.	Control	
Plant-based						
88.Johnson 2006	MS	21	Ginko	Four 60mg tablets of EGb-761 (ginko extract) per day	Will ginko extract improve functional performance	

			Placebo	Placebo	Control	

Supplemental Results 6
Intervention delivery characteristics for studies in the NMA
6.1 Behavioural Interventions

Study/ Population	Individual/ group	Setting	Number of sessions	Duration of sessions	Total duration of intervention	Intervention provider
Self-Management						
Fatigue self-management - conservative						
Abonie 2020	I	Home monitoring	1	30 minutes intervention session after 7 days home monitoring	4 weeks	N/R
	N/A	N/A	N/A	N/A	4 weeks	N/A
Askari 2022	I	Web-based plus telephone sessions	6 telephone calls	30-60 minutes	12 weeks	Web + registered occupational therapist
	I	Web-based	N/A	N/A	12 weeks	Web only
Blikman 2017	I	Outpatient rehabilitation department	12	45 minutes	4 months	Occupational therapist
	I	Outpatient rehabilitation department	3	45 minutes	4 months	Nurse
Farragher 2022	I	Web-based + one-to-one training	3 web modules + 4-6 face-to-face sessions	Web modules: 20-30 minutes; one-to-one sessions: 30 minutes	7-9 weeks	Occupational therapist

	I	Web-based one-to-one sessions	6 to 8 sessions	N/R	7-9 weeks	Trained study coordinator
GarciaJalon 2013	G	Face to face	5	2 hours	5 weeks	Therapist
	G	Face to face	5	2 hours	5 weeks	Therapist
Ghahari 2010	G	Online	6	2-3 hours	7 weeks	Occupational therapist
	I	Online	6	N/R	7 weeks	Group facilitator for technical queries only
	I	N/A	N/A	N/A	7 weeks	N/A
Hersche 2019	G	Rehab centre	6 x 1 hour + 1 x 0.5 hours	1 hour or 0.5 hours	3 weeks	Occupational therapist
	G	Rehab centre	6	1 hour	3 weeks	Physical therapist
Hugos 2010	G	N/R	6	2 hours	6 weeks	MS healthcare professionals via DVD
	N/A	N/A	N/A	N/A	6 weeks	N/A
Hugos 2019a/2017	G	N/R	6	2 hours	6 weeks	MS professionals
	G	N/R	6	2 hours	6 weeks	MS professionals
Kos 2016	I	Face to face	3	60-90 minutes	3 weeks	Occupational therapist
	I	Face to face	3	60-90 minutes	3 weeks	Occupational therapist
Murphy 2010	I	Home and face to face	2	1.5 hours	4 weeks	Occupational therapist
	I	Home and face to face	2	1.5 hours	4 weeks	Occupational therapist
Fatigue self-management - active						
Clarke 2012	G	Face to face	6	60 minutes	6 weeks	Researcher
	G	Face to face	6	60 minutes	6 weeks	Researcher

Murphy 2024	G	Online	9	15-30 minutes	12 weeks	Health coaches
	N/A	N/A	N/A	N/A	12 weeks	N/A
Rietberg 2014	I	Outpatient	PT 24; minimum 2 session for other treatments	PT 45 minutes; 1 hour other treatments	12 weeks	Multi-diciplinary
	I	Outpatient	2	1 hour	12 weeks	Nurse
General self-management						
Austin 1996	I	Telephone	N/A	N/A	6 months	Certified reality therapy counselor
	I	Telephone	N/A	N/A	6 months	Trained staff member
Feldthusen 2016	I	Face to face	According to preferences	According to preferences	12 weeks	Physical therapist
	I	N/A	N/A	N/A	12 weeks	N/A
Hammond 2008	G	District or community hospitals	8	2.5 hours	3-4 weeks	Experienced therapists
	G	District or community hospitals	5	2 hours	3-4 weeks	Experienced therapists
Khan 2020	I	Telehealth	16	20-30 minutes	16 weeks	Health coach
	I	N/A	N/A	N/A	16 weeks	Usual physician
CBT – fatigue						
Artom 2019	I	Telephone	1 x 1 hour and 7 x 30 minutes	1 x 1 hour and 7 x 30 minutes	8 weeks	Therapist
	I	Home	N/A	N/A	8 weeks	N/A

Bredero 2023	G	Outpatient	8	2.5 hours	8 weeks	3 licensed and experienced mindfulness trainers.
	N/A	N/A	N/A	N/A	8 weeks	N/A
Ehde 2015	I	Telehealth	8 + 2 follow-up calls	45-60 minutes	8 weeks + follow up call at 4 and 8 weeks post treatment	Study therapist
	I	Telehealth	8 + 2 follow-up calls	45-60 minutes	8 weeks + follow up call at 4 and 8 weeks post treatment	Study therapist
Gay 2023	G	Face to face	6 + 4 booster sessions	90 minutes	6 weeks + booster sessions	Occupational therapists, physiotherapists, MS nurses
	I	Face to face	N/A	N/A	6 weeks	Usual clinician
Hewlett 2011	G	Face to face	6	2 hours	6 weeks	Clinical psychologist + occupational therapist
	G	Face to face	1	1 hour	6 weeks	Rheumatology nurse
Hewlett 2019a	G	Face to face	7	2 hours for first 6 weeks, 1 hour consolidation session	6 weeks	Nurses, occupational therapists
	N/A	N/A	N/A	N/A	6 weeks	N/A
Jhamb 2023	I	Telemedicine at home	12	45-60 minutes	12 weeks	Therapist with counselling qualification
	G	Face to face	6	20-30 minutes	12 weeks	Research coordinator

Mead 2022	I	Telephone	6	1 hour	12 weeks	Stroke nurses + physiotherapist + psychologist
	I	Home	N/A	N/A	12 weeks	N/A
Menting 2017	I	Web-based with face to face	5 to 8	50 minutes	5 months	Therapist
	N/A	N/A	N/A	N/A	5 months	N/A
Moss-Morris 2012	I	Web-based	8	25 to 50 minutes	8 weeks	Assistant psychologist
	N/A	Standard care	N/A	N/A	8 weeks	N/A
Nguyen 2019	I	Face to face with homework	8	N/R	2 months	Licensed psychologists and exercise physiologist
	N/A	N/A	N/A	N/A	2 months	N/A
Okkersen 2018	I	Face to face	10 to 14	N/R	10 months	Therapists experienced in CBT
	N/A	N/A	N/A	N/A	10 months	N/A
Picariello 2021	I	Face to face and telephone	3 to 5	2 session of 1 hour + 1 to 3 sessions of 30 minutes	3 months	Researcher with background in health psychology
	N/A	N/A	N/A	N/A	3 months	N/A
Pottgen 2018	I	Web-based	Average access 14.5 times	N/R	12 weeks	Web-site
	N/A	N/A	N/A	N/A	12 weeks	N/A
Thomas 2013	G	Face to face	6	90 minutes	6 weeks	Health professionals

	N/A	N/A	N/A	N/A	6 weeks	N/A
van Kessel 2008	I	Face to face or telephone	8	50 minutes	8 weeks	Therapist
	I	Face to face or telephone	8	50 minutes	8 weeks	Therapist
van den Akker 2017	I	Face to face	12	N/R	16 weeks	MS nurse
	I	Face to face	3	45 minutes	16 weeks	MS nurse
	N/A	N/A	N/A	N/A	16 weeks	N/A
Zedlitz 2012	G	Face to face	24	2 hours	12 weeks	Neuropsychologists, physiotherapists
	G	Face to face	12	2 hours	12 weeks	Neuropsychologists
Physical Activity						
Physical activity promotion						
Bachmair 2022	I	Telephone delivery	7	45 minutes	14 weeks + booster at 22 weeks	Therapist
	I	Telephone delivery	7	45 minutes	14 weeks + booster at 22 weeks	Therapist
	N/A	N/A	N/A	N/A	14 weeks	N/A
Callahan 2014	G	Face to face	20	1 hour	20 weeks	ALED instructors
	I	N/A	N/A	N/A	20 weeks	N/A
Lutz 2017	I	Home-based	N/R	N/R	12 weeks	N/R
	I	Home-based	N/R	N/R	12 weeks	N/R
Turner 2016	I	Telephone delivery	6	30 to 60 minutes	6 months (3 months counseling + 3 months telehealth monitoring)	Study therapist

	I	Home based	N/A	N/A	6 months	N/A
Exercise – supervised						
Dalgas 2010	G	Training facility (gym)	24 sessions	60-75 minutes	2 sessions per week for 12 weeks	Principal investigator
	N/A	N/A	N/A	N/A	12 weeks	N/R
Diaz 2023	I	N/R	48	1 hour	16 weeks	N/R
	N/R	N/R	N/R	N/R	16 weeks	N/R
Englund 2022	G	Karolinska University Hospital, Stockholm, Sweden	24 sessions	60 minutes	2 sessions per week for 12 weeks	Physiotherapist
	G	Karolinska University Hospital, Stockholm, Sweden	12 sessions	60 minutes	1 sessions per week for 12 weeks	Physiotherapist
	N/A	N/A	N/A	N/A	N/A	N/A
Escudero-Uribe 2017	G	Face to face	24	60 to 100 minutes	12 weeks	Neurologic physical therapist.
	G	Face to face	24	60 to 100 minutes	12 weeks	Neurologic physical therapist.
	N/A	N/A	N/A	N/A	12 weeks	N/A
Heine 2017	I	Outpatient clinic for supervised sessions, home-based for the rest	48 sessions (12 supervised, 36 home-based)	30 minutes	16 weeks	Physiotherapists
	I	Outpatient clinic	3 sessions	45 minutes	16 weeks	MS nurse
Feys 2019	G	Running track at KULeuven	36 sessions	N/R	3 sessions per week for 12 weeks	Research assistant

	N/A	N/A	N/A	N/A	N/A	N/A
Gervasoni 2014	I	Hospital-based rehabilitation setting	20 sessions	60 minutes (30 minutes of arm cycling, 30 minutes of task-oriented exercises)	16 weeks (8-week active period and an 8-week resting period)	Physical therapists
	N/A	N/A	N/A	N/A	16 weeks	N/A
Kratz 2020	I	Home-based + physical therapist	8 sessions	30 mins (endurance), 30 mins (strength)	8 weeks	N/R
	I	Home-based + physical therapist	8 sessions	N/R	8 weeks	N/R
Kucharski 2019	G	Gym-based exercise and home-based exercise	60 sessions	27 minutes	3 sessions per week for 20 weeks	Physiotherapists
	I	Home-based	N/R	N/R	20 weeks	N/A
Langeskov-Christensen 2022	G	N/R	48 sessions	30 to 60 minutes	2 sessions per week for 24 weeks	N/R
	N/A	N/A	N/A	N/A	24 weeks	N/A
Louie 2022	G	Outpatient rehabilitation facility	20 sessions (14 exercise and 6 education)	60 minutes	Twice weekly exercise and once weekly education sessions for 12 weeks	Physiotherapist and an exercise physiologist
	N/A	N/A	N/A	N/A	12 weeks	N/A
McCullagh 2008	G	At home and also attended exercise classes	36 sessions	50 minutes	Twice-weekly supervised exercise	Physiotherapists

		held in a hospital physiotherapy gym			sessions for 12 weeks, and one home exercise session per week.	
	N/A	N/A	N/A	N/A	12 weeks	N/A
Ortiz-Rubio 2018	I	N/R	16 sessions	60 mins	8 weeks	N/R
	I	N/R	16 sessions	60 mins	8 weeks	N/R
Pozehl 2008	I	Standard cardiac rehabilitation setting	72 sessions	60 mins	24 weeks	N/R
	I	Standard cardiac rehabilitation setting	N/R	N/R	24 weeks	N/R
Exercise – unsupervised						
Durcan 2014	I	Home-based	N/R	N/R	12 weeks	N/R
	I	N/A	N/A	N/A	12 weeks	N/A
Geddes 2009	I	Home-based	36 sessions	30 mins	12 weeks	N/R
	I	N/A	N/A	N/A	12 weeks	N/A
Katz 2018	I	Home-based	N/R	Daily	21 weeks	N/R
	I	Home-based	N/R	Daily	21 weeks	N/R
	I	N/A	N/A	N/A	21 weeks	N/A
Maurer 2018	I	Home-based	N/R	N/R	12 months	N/R
	I	N/A	N/A	N/A	12 months	N/A
Tench 2003	I	Home-based	3 sessions/week	30-50 mins	12 weeks	N/R
	I	Home-based	3 sessions/week	30 mins	12 weeks	N/R
	I	N/A	N/A	N/A	12 weeks	N/A

Active recreational						
Rehabilitation						
DeGiglio 2015	I	Home	40	30 minutes	8 weeks	Psychologist
	N/A	N/A	N/A	N/A	8 weeks	N/A
Mindbody						
Callahan 2016	G	20 community locations in North Carolina and New Jersey	16 sessions	60 minutes	2 sessions per week for 8 weeks	Instructors trained by AF master tai chi trainers
	N/A	N/A	N/A	N/A	N/A	N/A
Fleming 2019	I	Home-based	16 sessions	60 minutes	2 sessions per week for 8 weeks	DVD instructions and weekly telephone call
	G	University of Limerick	16 sessions	60 minutes	2 sessions per week for 8 weeks	Pilates instructor
	N/A	N/A	N/A	N/A	N/A	N/A
Fleming 2021	I	Home-based	16 sessions	60 minutes	2 sessions per week for 8 weeks	Pilates instructor
	N/A	N/A	N/A	N/A	N/A	N/A
Walter 2019	G	Face to face	16 sessions	60 minutes	8 weeks	Yoga therapist
	N/A	N/A	N/A	N/A	8 weeks	N/A
Sgoifo 2017	G	Healthcare facility	8 sessions	60 minutes	Once a week for 2 months	Skilled psychotherapist
	N/A	N/A	N/A	N/A	N/A	N/A
Mindfulness						

Goren 2022	I	Online video conferences	7 sessions	60 minutes	3 months	Clinical social workers who underwent special training in cognitive-behavioral and mindfulness-based stress reduction
	N/A	N/A	N/A	N/A	N/A	N/A
Grossman 2010	G	In-person sessions at a clinic	9 sessions	2.5 hours per session with one 7 hour session	8 weekly sessions, plus 1 full-day session	Certified mindfulness teachers with at least 9 years of experience
	N/A	N/A	N/A	N/A	N/A	N/A
Torkhani 2021	I	Remote (TailorBuilder tool)	48 sessions	10 minutes	8 weeks	Pre-recorded sessions
	I	Remote (TailorBuilder tool)	8 sessions	Variable	8 weeks	Plans approved by trainer; weekly telephone call follow up
	N/A	N/A	N/A	N/A	N/A	N/A

6.2 Stimulation Interventions

Study/ Population	Individual/ group	Setting	Number of sessions	Duration of sessions	Total duration of intervention	Intervention provider
Vagal stimulation						
Aranow 2021	I	Feinstein Institutes for Medical Research	4	5 minutes	4 days	N/R

	I	Feinstein Institutes for Medical Research	4	5 minutes	4 days	N/R
Tarn 2023	I	Hospital	108	120 seconds	54 days	N/R
	I	Hospital	108	120 seconds	54 days	N/R
Trans Cranial stimulation						
Cancelli 2018	I	Hospital	5	15 mins	5 days	N/R
	I	Hospital				
Charvet 2018	I	Home	10	20 mins	2 weeks	N/R
	I	Home	10	20 mins	2 weeks	N/R
	I		20	20 mins	4 weeks	N/R
Salemi 2019	I	N/R	10	15 mins	2 weeks	N/R
	I					
Tecchio 2015	I	Hospital	5	15 mins	5 days	N/R
	I					
Granja-Dominguez 2022	I	Hospital	20	45 mins	4 weeks	N/R
	I					
Mostert 2005	I	Hospital	10 per week	16 mins	3-4 weeks	N/R
	I					
Piatkowski 2009	I	Home	24	8 mins	12 weeks	N/R
	I	Home	24	8 mins	12 weeks	N/R
Voggenberger 2022	I	Home	Daily	30 minutes	30 days	N/R

	I	Home	Daily	30 minutes	30 days	
Aromatherapy						
Hawkins 2019	I	Home	Daily	15 minutes	14 days	N/R
	I	Home	Daily	15 minutes	14 days	N/R
Acupuncture/ acupressure						
Horta 2020	I	N/R	9	20 mins	7 weeks	3 senior acupuncturists
	I	N/R	9	20 mins	7 weeks	3 senior acupuncturists
Kluger 2016	I	Clinic	12	30 mins	6 weeks	Licensed acupuncturist
	I	Clinic	12	30 mins	6 weeks	N/A
RIC						
Moyle 2023	I	Hospital or home	18	40 minutes	6 weeks	Researcher, self, or carer
	I	Hospital or home	18	40 minutes	6 weeks	Researcher, self, or carer

6.3 Nutritional Interventions

Study/ Population	**Individual/ group**	**Setting**	**Number of sessions**	**Duration of sessions**	**Total duration of intervention**	**Intervention provider**
Fish oil						

Arriens 2015	I	Home	6 capsules per days	N/A	6 months	N/A
	I	Home	6 capsules per days	N/A	6 months	N/A
Thiamine HD						
Bager 2021	I	Home-based	N/A	N/A	12 weeks	Herlev Hospital Pharmacy
	I	Home-based	N/A	N/A	12 weeks	Herlev Hospital Pharmacy
5-HTP						
Truyens 2022	I	Home-based	N/A	N/A	16 weeks	University Hospital Ghent Clinical Trial Unit
	I	Home-based	N/A	N/A	16 weeks	University Hospital Ghent Clinical Trial Unit
Flavenoid - cocoa						
Coe 2019	I	Home-based with an optional home visit in week 3	N/A	N/A	6 weeks	N/R
	I	Home-based with an optional home visit in week 4	N/A	N/A	6 weeks	N/R
Diet						
Chase 2023	I	Home	Daily diet. Plus 2 to 3 diet counselling sessions.	N/R	12 weeks	Dieticians
	N/A	N/A	N/A	N/A	12 weeks	N/A

Plant						
Johnson 2006	I	Home-based	N/A	N/A	4 weeks	Dr. Wilmar P. Schwabe Company, Gmb, Germany
	I	Home-based	N/A	N/A	4 weeks	Dr. Wilmar P. Schwabe Company, Gmb, Germany

Supplemental Results 7
Intervention characteristics, studies not included in NMA
7.1 Intervention content

Behavioural Interventions						
Study/ Population	**Pop.**	**Study N**	**Intervention (as named in study)**	**Intervention description**	**Intervention aim**	
Self-Management						
Fatigue self-management - conservative						
Finlayson 2011	MS	190	Teleconference Fatigue Management Program	Discussions about fatigue; how to communicate about fatigue; body mechanics; activity analysis - evaluating priorities; living a balanced life - taking control of your day; goal setting.	To teach behavioural changes that will lead to improvement in fatigue severity and HRQoL	
			Wait List	Usual daily activities	Control	
			Progressive Muscle Relaxation +RAU	A standardized series of relaxation exercises (involving 11 large muscle groups) combined with deep breathing + rehabilitation as usual	To achieve enhanced mental relaxation by reducing muscle tension	
Kos 2007	MS	51	Multidisciplinary Fatigue Management Programme	Information concerning possible strategies to manage fatigue and reduced energy levels, ie, pharmacological treatment, diet, informing and involving the social environment, regular sleep, exercise, relaxation, cooling, assistive devices, adaptation of home or work environment and energy saving methods	To reduce the impact of MS fatigue on daily life	

			Placebo Intervention Programme	Information on topics that did not concern themes directly related to fatigue (ie, car adaptations and driving abilities, communication skills, lift techniques for back protection and general information about MS)	Active control	
Mathiowetz 2005	MS	169	Energy Conservation Course	Based on theory of psychoeducational group development. Long and short term goal setting; practice activities and homework. Importance of rest throughout the day, positive and effective communication; proper body mechanisms; ergonomic principles; modification of the environment; changing standards; setting priorities; activity analysis and modification; living a balanced lifestyle.	To determine whether energy conservation education can reduce the impact of fatigue in persons with MS	
			Wait list	Usual activities	A control	
Fatigue self-management - active						
O'Connor 2019	IBD	23	Psychoeducation	Structured around psychological and physical interventions, which were geared towards understanding fatigue, energy conservation, management strategies and improving relaxation techniques tailored to the specific needs of patients with IBD.	To test whether or not fatigue, energy and quality of life indices could be improved	
			Usual care	Standard medical care	Control	
Vogelaar 2014	IBD	98	Solution Focused Therapy	Solution-focused course, focussing on coping styles for fatigue. Psychoeducation about IBD and fatigue and SFT. Focus is on the existing adequate coping abilities of patients, rather than on their problems.	To develop coping skills to enhance fatigue management	
			Usual care	Received care as usual	Control	

CBT – fatigue						
van Kessel 2016	MS	39	MSInvigor8 + support	Interactive CBT self-management programme with email support from a clinical psychologist. Explanation of MS fatigue and the CBT approach; topics such as activity scheduling, improving sleep, altering unhelpful thinking and patterns and behaviour, managing stress, coping with emotions, social support, preparing for the future.	To test the addition of email support to the MSINVIGOR8 programme	
			MSInvigor8	Interactive CBT self-management programme as above with no email support	Control.	
Voet 2014	FSHD	57	CBT	Modules based on known fatigue perpetuating factors. Directed at insufficient coping with their disease; dysfunctional cognitions regarding fatigue, activity, pain or other symptoms; fatigue catastrophising; dysregulation of sleep or activity; poor social support; negative social interactions.	To alleviate individually relevant fatigue-perpetuating factors.	
			Aerobic exercise	Cycling exercises on an ergometer, with cardiovascular monitoring. Aim to achieve 50%-60% increase in heart rate reserve.	To increase exercise which plays a central role in perpetuating fatigue	
Physical Activity						
Physical activity promotion						
McNelly 2016	IBD	52	Omega-3 and exercise	Individual consultation with a personal trainer provided at week 1. Advice consisted of personalised goal-setting using the treatment paradigm of treat-to-target to initiate an increase in physical activity levels of at least 30%.	To compare the effectiveness of individual advice to increase physical activity (PA) and/or ementation with omega-3 fatty acids on fatigue in patients with inactive IBD	

			Placebo and exercise	A 15-minute conversation with the researcher about the participant's dietary habits and general health was undertaken at week 1, including questions such as: 'Can you tell me about your current dietN/R', 'Did you have to change your diet following the diagnosis of IBDN/R' and 'In what way has IBD affected your general healthN/R' No advice was given by the researcher regarding exercise.	As above	
			Omega-3 and no exercise	A total daily oral dose comprised 2970mg of pharmaceutical-grade omega-3 fatty acids — 2250mg of EPA and 150mg of DHA (takeOmega3, Edinburgh, UK)—in three capsules. Guidelines suggest that doses of up to 3g per day of marine-derived omega-3 fatty acids are safe, and a high EPA:DHA ratio is thought to be preferable.	As above	
			Placebo and no exercise	Capsules with a similar appearance to the omega-3 supplement capsules, but which contained a placebo: capric and caprylic acid.	Control	
Callahan 2008	RA	346	PACE exercise programme	A land-based exercise programme to promote self-management of arthritis through exercise	Exercise programs of moderate intensity are proposed to improve HRQoL in individuals with rheumatoid arthritis	
			Wait list	Usual activities	Control	
Exercise – supervised						
Avaux 2016	SLE	45	Supervised exercise	Endurance exercises (walking or bicycle) with the aim of achieving between	SLE patients have a lower cardiovascular capacity and a lower muscle strength compared	

				60 and 80% of the theoretical maximal heart rate; and (ii): strengthening exercises (with elastoband or weights for both upper and lower limbs). Plus education about benefits of exercise.	to controls, suggesting that fatigue could be improved by exercise	
			Home exercise	As above but unsupervised	To test benefits of supervision	
			Control	No training (participants who declined to train or refused their allocation)	Control	
Coghe 2018	MS	22	Physical activity	Supervised training program	To improve processing speed, fatigue, and motor performance in patients with multiple sclerosis	
			Usual care	Usual daily activities	Control.	
			Control	N/R	Control	
Englund 2022	MS	140	High-Intensity Resistance Training (HIRT) - Group A	Resistance training	To compare the effects of high-intensity resistance training (HIRT) on self-reported fatigue	
			High-Intensity Resistance Training (HIRT) - Group B	Resistance training	As above with fewer sessions	
			Control	No intervention	Control.	
			Usual care	Usual daily activities	Control.	
Exercise – unsupervised						
Daltroy 1995	RA and SLE	71	Home cardiopulmonary	Stationary bicycles were provided for the exercisers. Each subject was asked to	Stimulating longer-term compliance by providing	

			conditioning programme	exercise to achieve a heart rate of 60-80% of the maximum heart rate achieved on the ETT. Pulse meters were provided to help patients monitor their heart rates and as a compliance-enhancing strategy. The physical therapist instructed the patient at home when setting up the bike, and made a second visit 2-3 weeks later at an exercise session to check the patient's ability to follow the regimen correctly.	patients with initial gains in endurance and self-confidence, but without the costs associated with long-term, supervised training.	
			Control	Encouraged to maintain current level of activity during the programme and as an attention control the physical therapist would ring in weekly.	Control	
Drory 2001	ALS	25	Exercise	Received list of exercises involving most muscle groups of the four limbs and trunk. The exercise program was developed for each patient, individually taking into account his general health, neurological status and actual fitness level. The main purpose of the exercise program was to improve muscle endurance, having the muscles work against only modest loads but undergo significant changes in length. The exercise program was demonstrated to each patient individually and reviewed at each clinic visit.	To determine the effect of moderate regular exercise under professional guidance on various parameters of HRQoL	
			Usual	Instructed not to perform any physical activity besides their usual daily life requirements. Every 14 days they also received a phone call.	Control	
Plow 2022	MS	170	Physical activity plus fatigue self-management	Group teleconference sessions + individually tailored phone calls. Taught how to engage in a pedometer-based walking programme, set goals, overcome obstacles, and self-monitor progress. Additional content adapted from the	N/R	

				Managing Fatigue programme.		
			Physical activity only	Group teleconference sessions + individually tailored phone calls. Taught how to engage in a pedometer-based walking programme, set goals, overcome obstacles, and self-monitor progress.	N/R	
			Contact control	Generic health information (e.g. healthy eating and preventive screening).	Control	
Robb-Nicholson 1989	SLE	23	Aerobic conditioning	Exercise at home for 30 min three times per week for 8 weeks to attain 60-80% of their maximum heart rate achieved during the exercise tolerance test (the target range). Walking, cycling or jogging were permitted.	To determine the effects of aerobic conditioning in SLE	
			Non-aerobic exercise	Non-aerobic stretching exercises	Control	
Active recreational						
Palsdottir 2020	Stroke	101	Nature-based rehabilitation	Daily themed sessions: morning gathering with a cup of herbal tea, allowing participants to feel at ease after travelling from their homes; physical activities, such as a garden walk, tricycling, or “on the spot” exercises, which were held indoors in the greenhouses when the weather was not favourable; garden and horticultural occupation, in a group or on their own, or “just being” (i.e. mental recovery on their own enjoying the garden); and gathering for “closure for the day”, with some light refreshments harvested from the garden, fresh or preserved.	Offering an enriched environment and multiple sensory stimuli through meaningful nature-based occupations has been shown to improve general health and wellbeing.	

			Usual care	Usual daily activities	Control	
Other psychological						
Vogelaar 2011	CD	29	Solution-Focused Therapy	The solution-focused model offers a wide range of interventions that channel the attention of patients towards constructing possible solutions. SFT was modified to focus on fatigue management.	Fatigue contributes to impairment of HRQoL. No problem exists - the solution to a problem is finding the exception when no problem exists. Patients learn to be in the moment and the problem disappears.	
			Problem-solving Therapy	Based on a general model of problem solving, adjusted for the purpose of patients with Crohn's Disease.	To increase the capabilities of the patients to deal with the daily stressful problems caused by CD	
			Usual care	Standard medical care and no additional psychological interventions.	Control	

Stimulation Interventions						
Study	**Population**	**Study N**	**Intervention (as named in study)**	**Intervention description**	**Intervention aim**	
Trans Cranial stimulation						
Chalah 2020	MS	11	Tdcs & shAM	Active transcranial direct current stimulation (tDCS) and Sham	Brain stimulation to relieve fatigue	
DeDoncker 2021	Stroke	33	tDCS	Increase cortical excitability using anodal transcranial direct current stimulation (tDCS).	Increase cortical excitability to ease fatigue	
			Sham	Sham	Control	
Gaede 2018	MS	33	rTMS - left PFC	H6 coil rTMS over the left prefrontal cortex	PFC stimulation is effective for depression - potential use for fatigue is supported by the high overlap between fatigue and depressive symptoms. Stimulates circuits implicated in fatigue	
			rTMS - MC	H10 coil rTMS over the primary motor cortex bilaterally	PFC and MC stimulation directly targets circuits for which alterations in fatigue were reported	
			Sham stimulation	Sham rTMS over the left prefrontal cortex	Control	

Hidding 2017	PD	12	Conventional subthalamic nucleus stimulation	High frequency stimulation of the Subthalamic Nucleus Stimulation	LC might therefore represent an important structure in the pathogenesis of certain neuropsychiatric symptoms such as apathy, fatigue, or depression.	
			Combined subthalamic nucleus and substantia nigra stimulation	High frequency Stimulation of the subthalamic nucleus and substantia nigra stimulation	LC might therefore represent an important structure in the pathogenesis of certain neuropsychiatric symptoms such as apathy, fatigue, or depression.	
Saoite 2014	MS	14	Transcranial direct current stimulation (tDCS)	Cross over one block real tDCS, one block sham	To assess whether fatigue symptoms can be reduced by excitability-enhancing anodal transcranial direct current stimulation (tDCS).	
			Sham			
External stimulation						
DeCarvalho 2012	MS	50	Magnetic field therapy	Pulsed low frequency magnetic field	Beneficial effects of magnetic fields may improve fatigue	

			Sham	Sham	Control	
Mateen 2020	MS	35	Bright White Light Therapy (BWLT)	Light box with instructions. Participants were instructed to sit in front of the light box with eyes approximately 36″ from the light source to achieve desired LT exposure, aligned with their eyes and at a distance of 30 cm, at which 10 000 lux were achieved. Participants were instructed to keep their eyes open during the whole 30 min of light therapy.		
			Dim Red light therapy (DRLT)	As above with the only difference that a filter was installed that dimmed the light to 200 lux and tinted it red.		

Nutritional Interventions						
Study	**Population**	**Study N**	**Intervention (as named in study)**	**Intervention description**	**Intervention aim**	
American Ginseng						
Kim 2011	MS	56	Ginseng	100mg capsules/day week 1; 2 capsules/day week 2; 4 capsules/day week 3-6	Drug treatments available for MS fatigue are limited in their efficacy. Herbal treatments may help	
			Placebo	Placebo	Control	
GLA						

Theander 2002	Sjorgen's syndrome	87	GLA	800mg of GLA (Gammalinolenic acid) given daily	To evaluate GLA's efficacy on treating Sjorgen's syndrome with fatigue	
			GLA	1600mg of GLA (Gammalinolenic acid) given daily	To evaluate GLA's efficacy at a higher dose on treating Sjorgen's syndrome with fatigue	
			Placebo	Containing mainly corn oil and no GLA given daily	Control	
Flavenoid - cocoa						
Coe 2022	PD	30	High-flavanol cocoa drink	Intervention taken following an overnight fast, at the same time each morning. 1 sachet containing 18g of cocoa powder (high flavanoid cocoa (10.79mg/g), contained in silver air tight sachets (identical in appearance to the control) consumed with 200ml of rice milk each morning on an empty stomach, at least 15-30 minutes before any food or drink consumption. Followed usual medication and diet.	To test whether daily consumption of flavanoid reduce fatigue in those with Parkinson's	
			Low-flavanol cocoa drink	As above but with 1 sachet containing 18g of cocoa powder (low flavanoid cocoa (1.02mg/g)), contained in silver air tight sachets (identical in appearance to the intervention).	Control	
Diet						
Irish 2017	MS	34	Modified Paleolithic dietary intervention	Diet consists mainly of fish, grass fed and pasture-raised meats, vegetables, fruits,	Evaluation of a modified Paleolithic	

				fungi, roots, and nuts; excludes grains, legumes, and dairy products; and limits refined sugars, starches, processed foods, and oils. The Paleo diet is relatively high in vitamins B, D, E, and K, polyunsaturated fatty acids, coenzyme Q10, α-lipoic acid, polyphenols, carotenoids, zinc, and selenium.	dietary intervention in the treatment of relapsing-remitting multiple sclerosis. One symtom includes fatigue, so this was one of the major topics they based the study on	
			Usual care (control)	Typical physician recommendations for MS	Control	
Lee 2021	MS	15	Modified Paleolithic diet	The modified Paleolithic diet (Wahls PaleoTM Diet) includes: 1) nine daily recommended servings of vegetables comprised of leafy green vegetables, sulfur rich vegetables, and deeply coloured fruits and vegetables; 2) encourages plant and animal protein, seaweed, nutritional yeast, non-dairy milks; and 3) excludes gluten-containing grains, eggs, casein. Participants were given the Whole Life Nutrition Cookbook	Used as a comparator to the other 2 groups tested	
			Medium-chain triglyceride (MCT)-based ketogenic diet	A ketogenic version of the modified Paleolithic diet with these additional requirements: 1) no starchy vegetables or fruit; 2)reduce vegetable consumption to 6 servings daily; and 3)increase fat intake with additional MCTs to achieve a daily goal of 70% of total calories from fat	Investigate the feasibility of a modified MCT-based ketogenic diet and its impact on plasma b-hydroxybutyrate and MS	
			Usual diet	Consume their pre-study vitamins, supplements, and/or medications.	Control	

7.2 Intervention delivery

Behavioural Interventions						
Study/ Population	**Individual/ group**	**Setting**	**Number of sessions**	**Duration of sessions**	**Total duration of intervention**	**Intervention provider**
Self-Management						
Fatigue self-management - conservative						
Finlayson 2011	G	Teleconference	6	70 minutes	6 weeks	Licensed occupational therapist
	I	N/A	N/A	N/A	6 weeks	N/A
Kos 2007	G	Face to face	4	2 hours	4 weeks	Occupational therapist
	G	Face to face	4	2 hours	4 weeks	Occupational therapist
Mathiowetz 2005	G	Community	6	2 hours	6 weeks	Occupational therapists
	N/A	N/A	N/A	N/A	6 weeks	N/A
Fatigue self-management - active						
O'Connor 2019	G	Face to face	3	1 hour	6 months	Occupational therapist
	N/A	N/A	N/A	N/A	6 months	N/A
Vogelaar 2014	G	Face to face	6 + booster at month 6	1.5 hours	3 months	N/R
	N/A	N/A	N/A	N/A	3 months	N/A

CBT – fatigue						
van Kessel 2016	I	Web-based	8	25 to 50 minutes	8 weeks	Web-site with email support from a skilled clinical psychologist
	I	Web-based	8	25 to 50 minutes	8 weeks	Web-site with no therapeutic contact
Voet 2014	I	Face to face	Minimum 3 sessions	50 minutes	16 weeks	Cognitive behaviour therapist
	I	Home and supervised	3 supervised sessions and minimum 40 home sessions	30 minutes	16 weeks	Physical therapist
	N/A	N/A	N/A	N/A	16 weeks	N/A
Physical Activity						
Physical activity promotion						
McNelly 2016	I	Home-based	N/R	N/R	12 weeks	N/R
	I	Home-based	N/R	N/R	12 weeks	N/R
	I	Home-based	N/R	N/R	12 weeks	N/R
	I	Home-based	N/R	N/R	12 weeks	N/R
Callahan 2008	G	Community	At least one class	N/R	8 weeks	Exercise and health professionals
	N/A	N/A	N/A	N/A	8 weeks	N/A
Exercise – supervised						
Avaux 2016	I	Hospital validation centre	Individualised	3 hours per week	12 weeks	Multidisciplinary team

	I	Home	Individualised	3 hours per week	12 weeks	Unsupervised
	N/A	N/A	N/A	N/A	12 weeks	N/A
Coghe 2018	G	N/R	72 sessions	60 minutes	3 sessions per week for 24 weeks	Two coaches specializing in physical activity
	N/A	N/A	N/A	N/A	24 weeks	N/A
Englund 2022	G	Karolinska University Hospital, Stockholm, Sweden	24 sessions	60 minutes	2 sessions per week for 12 weeks	Physiotherapist
	G	Karolinska University Hospital, Stockholm, Sweden	12 sessions	60 minutes	1 sessions per week for 12 weeks	Physiotherapist
	N/A	N/A	N/A	N/A	N/A	N/A
Exercise – unsupervised						
Daltroy 1995	I	Home-based + physical therapist	36 sessions	30 mins	12 weeks	N/R
	I	Home-based + physical therapist	N/R	N/R	12 weeks	N/R
Drory 2001	I	Home-based	2 sessions/day	15 mins	12 months	N/R
	I	N/A	N/A	N/A	12 months	N/A
Plow 2022	G	Telephone	10	N/R	12 weeks	Occupational therapist + research assistant
	G	Telephone	10	N/R	12 weeks	Occupational therapist + research assistant

	G	Telephone	10	N/R	12 weeks	Occupational therapist + research assistant
Robb-Nicholson 1989	I	Home-based	24	30 minutes	8 weeks	Unsupervised
	I	Home-based	24	30 minutes	8 weeks	N/A
Active recreational						
Palsdottir 2020	G	Alnarp Rehabilitation garden	20	3.5 hours	10 weeks	Occupational therapist; horticulturalist; psychologist; physiotherapist
		N/A	N/A	N/A	10 weeks	Individualised multidisciplinary care
Other psychological						
Vogelaar 2011	N/R	Outpatients	5 sessions	N/R	3 months	Experienced psychotherapist
	N/R	Outpatients	10 sessions	N/R	3 months	Experienced psychotherapist
	N/A	N/A	N/A	N/A	3 months	N/A

Stimulation Interventions						
Study/ Population	**Individual/ group**	**Setting**	**Number of sessions**	**Duration of sessions**	**Total duration of intervention**	**Intervention provider**
Transcranial Stimulation						

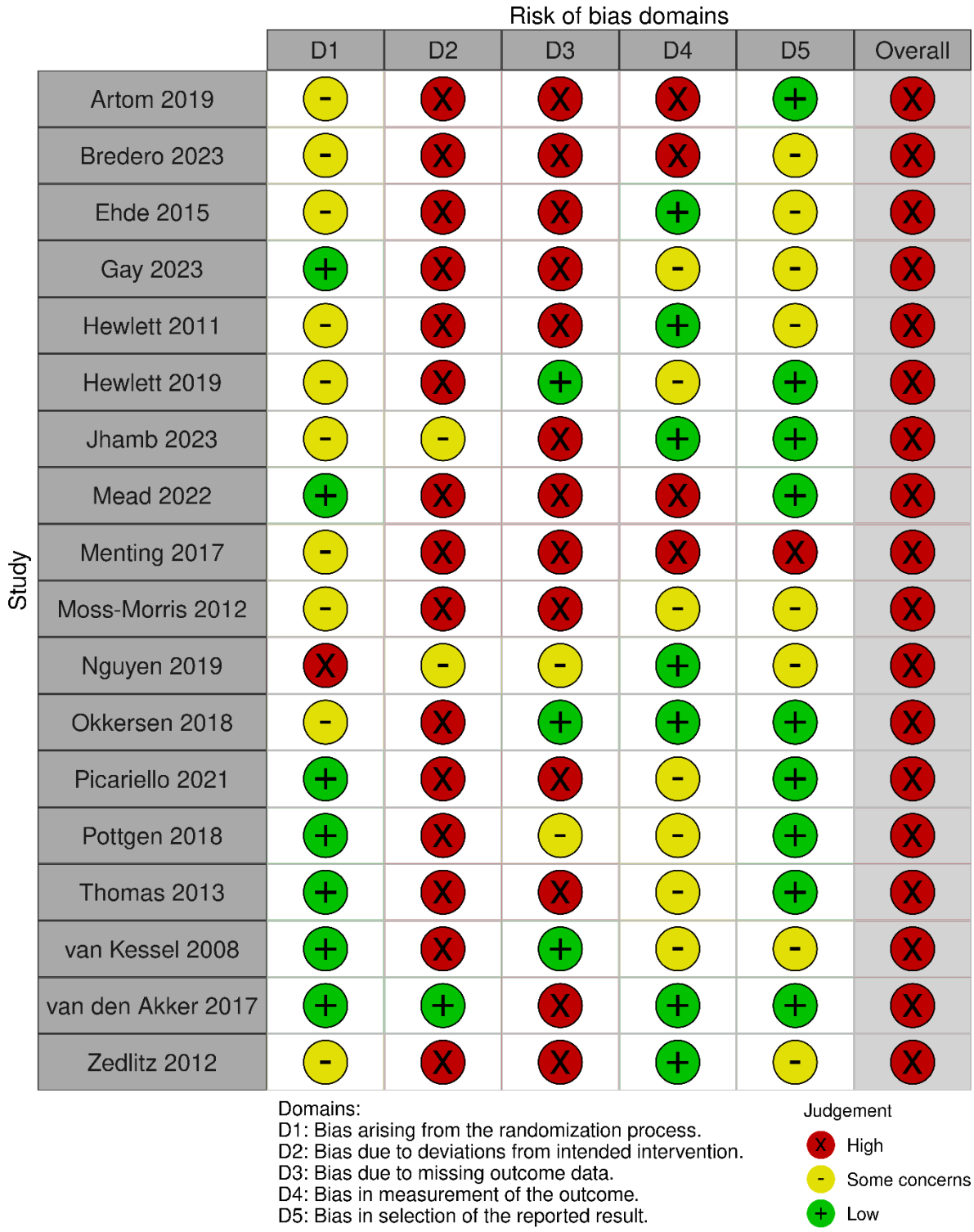
Chalah 2020	I	Hospital	5 real, 5 sham	20 mins	5 days of each with 3 week washout period in-between	
DeDoncker 2021	I		2	20 mins	1 day	
	I		2	20 mins	1 day	
Gaede 2018	I	Clinic	3 sessions per week	16 minutes	6 weeks	N/R
	I	Clinic	3 sessions per week	16 minutes	6 weeks	N/R
	I	Clinic	3 sessions per week	16 minutes	6 weeks	N/R
Hidding 2017	I	Clinic	N/R	N/R	3 weeks	N/R
	I	Clinic	N/R	N/R	3 weeks	N/R
Saoite 2014	I	Clinic	5	20 minutes	5 days/ 2 weeks wash-out/ 5 days	
	I					
External stimulation						
DeCarvalho 2012	I	Outpatient dept.	24	24 mins	8 weeks	
	I					
Mateen 2020	I	Clinic/Home	15	30 mins	15 days	
	I					

Nutritional Interventions						
Study/ Population	**Individual/ group**	**Setting**	**Number of sessions**	**Duration of sessions**	**Total duration of intervention**	**Intervention provider**
American Ginseng						

Kim 2011	I	Home-based	N/A	N/A	6 weeks	Afexa Life Sciences, Edmonton, Canada
	I	Home-based	N/A	N/A	6 weeks	Afexa Life Sciences, Edmonton, Canada
GLA						
Theander 2002	I	Home-based	N/A	N/A	6 months	Scotia Pharmaceutical Ltd., Guilford, Surrey, UK
	I	Home-based	N/A	N/A	6 months	Scotia Pharmaceutical Ltd., Guilford, Surrey, UK
	I	Home-based	N/A	N/A	6 months	Scotia Pharmaceutical Ltd., Guilford, Surrey, UK
Flavanoid - cocoa						
Coe 2022	I	A hotel	N/A	N/A	6 days	OBU in the Oxford Brookes Centre for Nutrition and Health (OxBCNH) kitchen

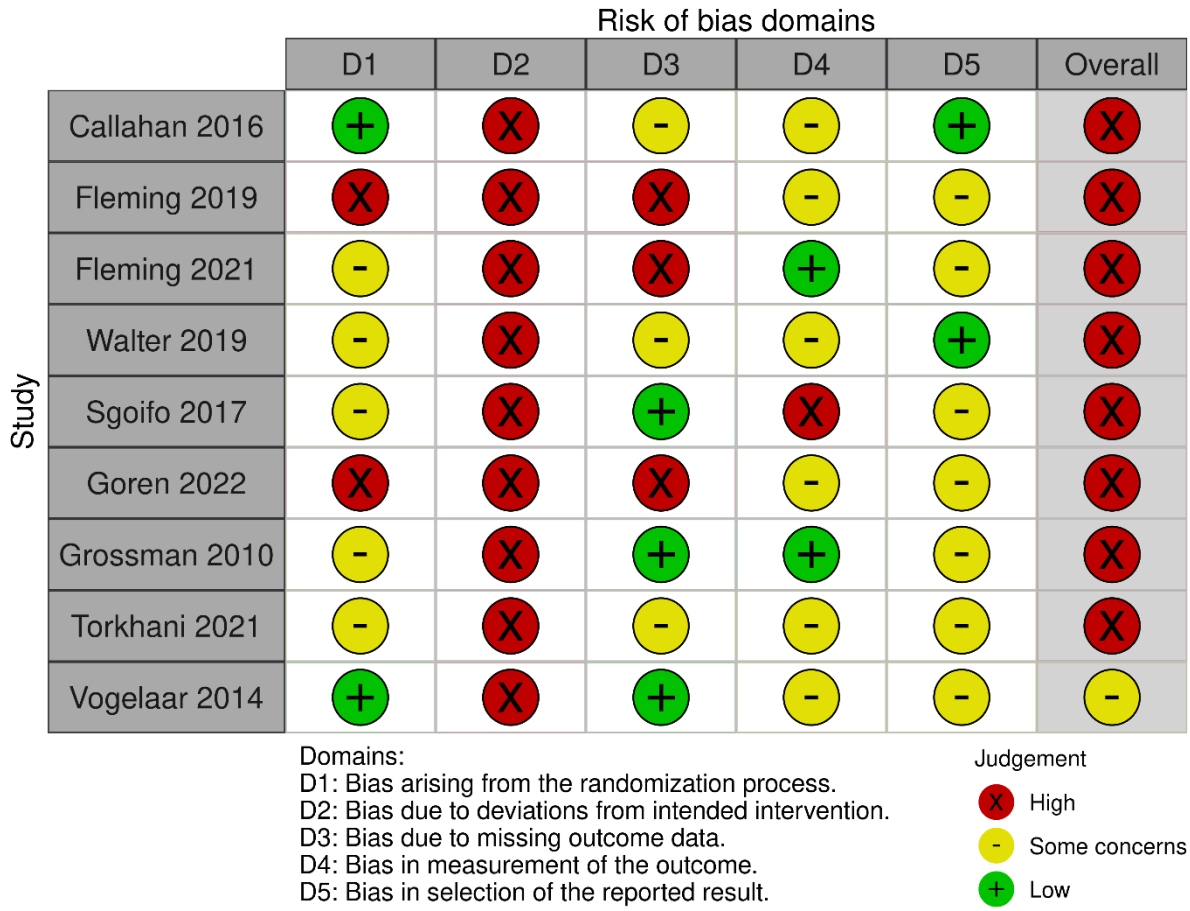
	I	A hotel	N/A	N/A	6 days	OBU in the Oxford Brookes Centre for Nutrition and Health (OxBCNH) kitchen
Diet						
Irish 2017	I	Home-based plus visit every 2 weeks	Visit every 2 weeks visit	N/R	3 months	N/R
	I	Home-based plus visit every 2 weeks	Visit every 2 weeks visit	N/R	3 months	N/R
Lee 2021	I	Home based	Nutritional ketosis monitoring every 4 weeks	N/R	12 weeks	Wahls Paleo Diet + dietician
	I	Home based	Nutritional ketosis monitoring every 4 weeks	N/R	12 weeks	Wahls Paleo Plus + dietician
	I	Home based	Nutritional ketosis monitoring every 4 weeks	N/R	12 weeks	Dietician

Supplemental Results 8
Risk of Bias summary plots by intervention group
8.1 CBT-based interventions

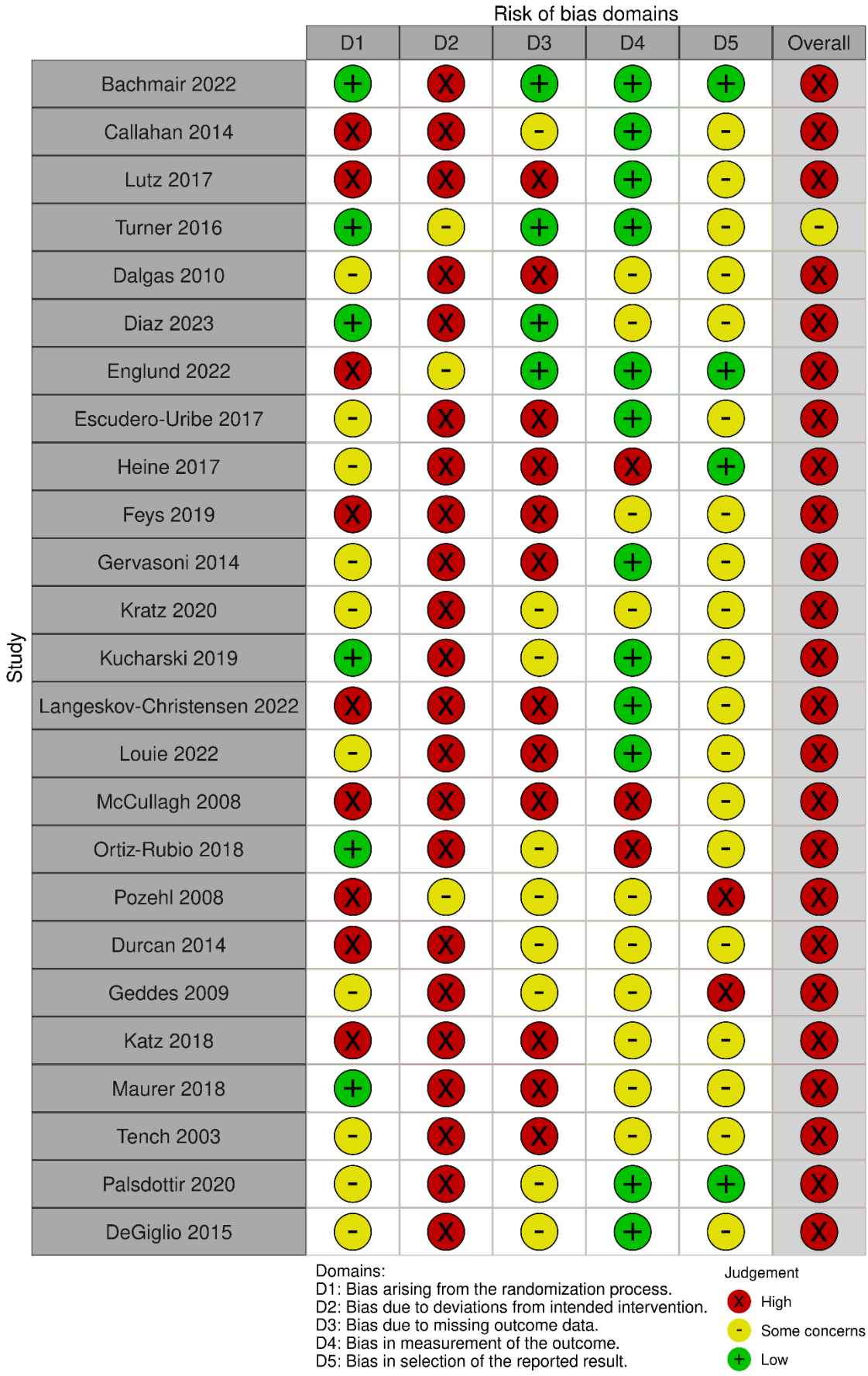


8.2 Fatigue self-management interventions

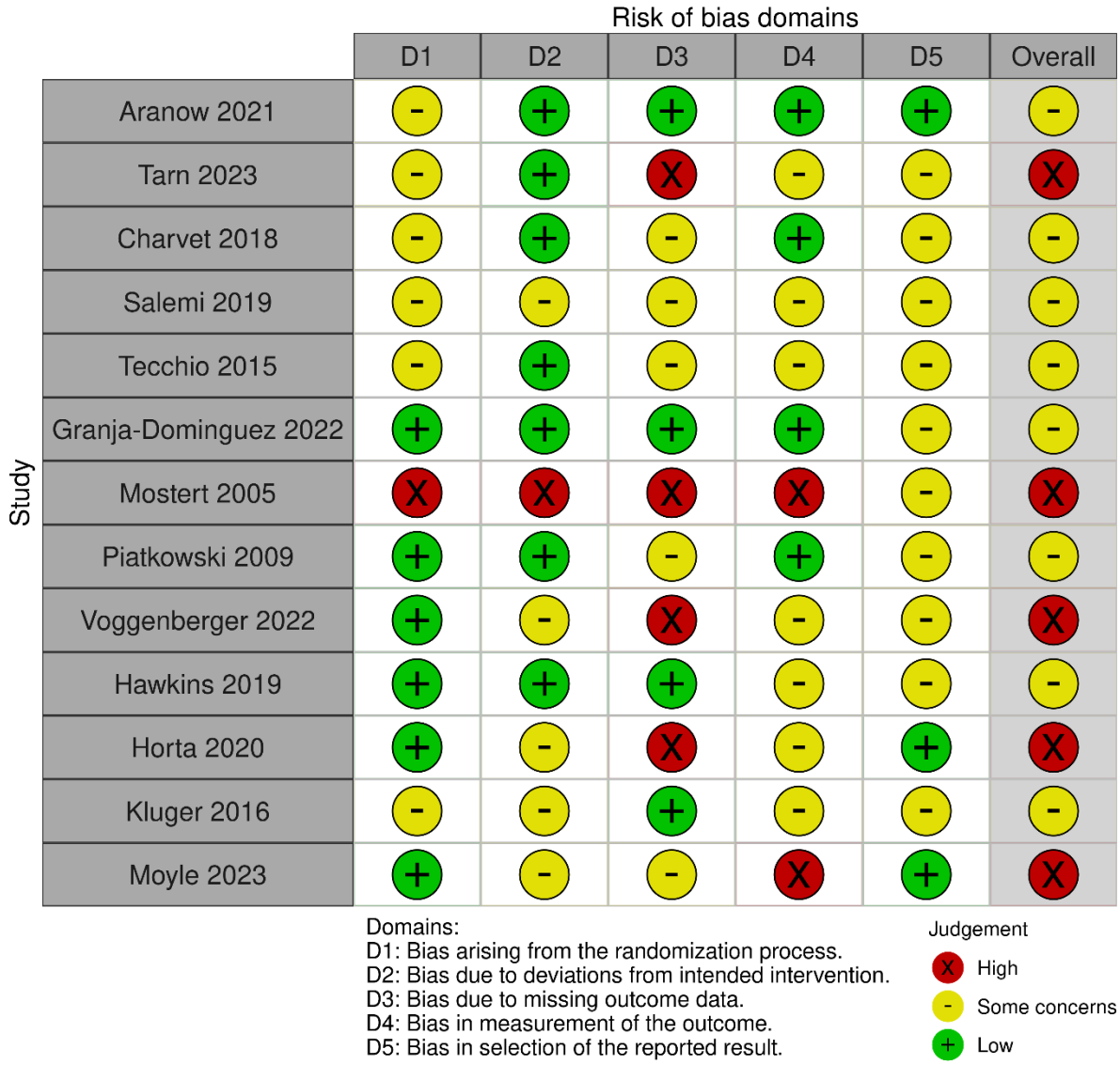
8.3 Mind-body interventions



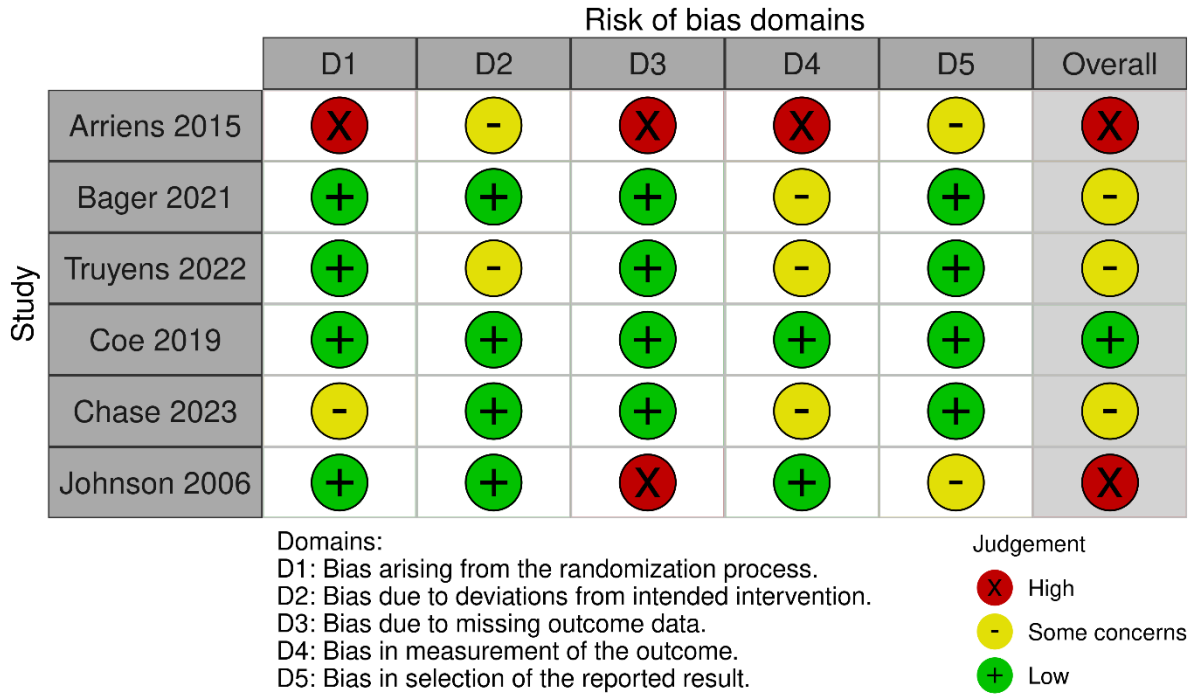
8.4 Physical Activity Promotion Interventions



8.5 External stimulation interventions



8.6 Nutritional and other supplement interventions



EIFFEL Supplementary Statistical Analysis Results

Contents

All network diagrams were labelled with three letter intervention identifiers, as summarized in Table 1.

Table 1 Three letter intervention identifier codes included within network diagrams.

Code	Intervention	Code	Intervention
_Co	Control	MBI	Mind-body intervention
_IE	Info/ Education	MIN	Mindfulness based
_UC	Usual care	nFIS	Fish Oil
_WL	Wait list	nFLV	Flavenoid (Cocoa)
ACU	Acupuncture/ pressure	nHTP	5-HTP
ARO	Aromatherapy	nTHI	Thiamine
CBT	CBT-fatigue	PAP	Physical activity promotion
DIE	Diet	PLA	Plant-based
EST	External stimulation	PSY	Other psychological
EXS	Exercise (supervised)	REH	Non-specific rehabilitation
EXU	Exercise (unsupervised)	RIC	Remote Ischaemic Conditioning
FMA	Fatigue management (active)	TCS	Transcranial Stimulation
FMC	Fatigue management (conservative)	VNS	Vagal Stimulation
GEN	General self management	MBI	Mind-body intervention

Primary analysis: inconsistency checks

End of treatment (EOT)

The mean posterior residual deviances were compared between the unrelated mean effects model and NMA models, Figure 1. The following studies were identified as being below the $y = x$ line indicating potential inconsistency within the network; Louie 2022[1], Fleming 2021[2] Menting 2017[3], Langeskov-Christensen 2022[4], Turner 2016[5] and Horta 2020[6]. The studies were checked for any errors in data extraction or noticeable population differences, but none were identified. Node-splitting was subsequently used to assess whether there was any statistically significant inconsistency within the network, none was identified and thus no further action was taken.

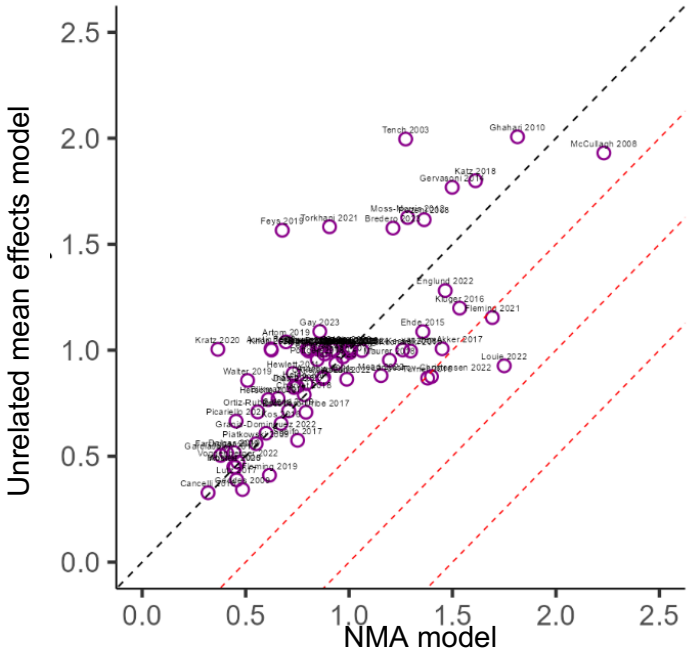


Figure 1 Mean posterior residual deviances according to the unrelated mean effects model and the NMA model, at end of treatment. Black dashed line is given by $y = x$, red dashed lines represent contours separated by differences of 0.5 between the two models. Any studies below the first red dashed line indicative of potential inconsistency.

Short term (ST)

The mean posterior residual deviances were compared between the unrelated mean effects model and NMA models, Figure 2. The following study was identified as being below the $y = x$ line; Clarke 2012[7] The study was inspected for any errors that may have occurred during data extraction or noticeable population differences, but none were found. Node-splitting was subsequently used to assess whether there was any statistically significant inconsistency within the network, none was identified and thus no further action was taken.

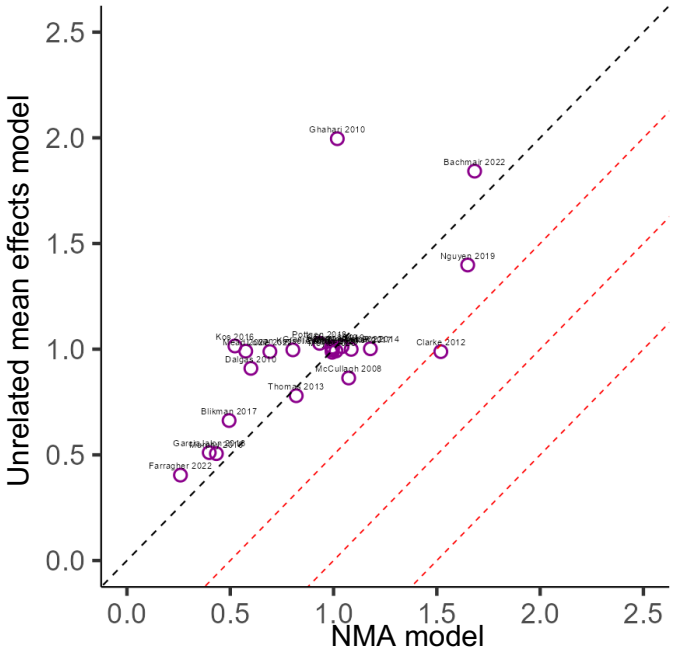


Figure 2 Mean posterior residual deviances according to the unrelated mean effects model versus the NMA model, at short term. Black dashed line is given by $y = x$, red dashed lines represent contours separated by differences of 0.5 between the two models. Any studies below the first red dashed line indicative of potential inconsistency.

Longer term (LT)

The mean posterior residual deviances were compared between the inconsistency and consistency models, Figure 3. No studies were identified as being below the $y = x$ line, suggesting that there is no evidence of inconsistency within the network.

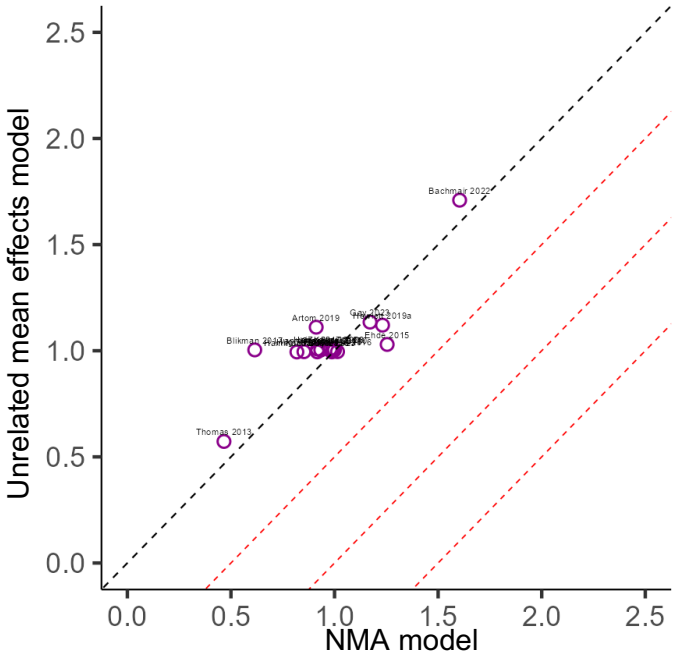


Figure 3 Mean posterior residual deviances according to the unrelated mean effects model and NMA model, at long term. Black dashed line is given by $y = x$ red dashed lines represent contours separated by differences of 0.5 between the two models. Any studies below the first red dashed line indicative of potential inconsistency.

NMA scenario analysis: use of alternative data to inform the LT analysis

Data were available from 18 studies presenting a graded fatigue outcome at LT follow up. Five studies (Artom 2019[8], Ehde 2015[9], Gay 2023[10], Hammond 2008[11] and Hewlett 2019a[12]) presented alternative data for the LT follow-up at a time point closer to 3 months. These studies in the primary analysis had a follow up time of 10 months, 10 months, 12 months, 12 months and 46 weeks respectively. Within this scenario analysis, data collected at 4 months, 4 months, 6 months, 6 months and 20 weeks was instead used for each study in order to assess the potential impact of our decision to extract the longest available time points for the LT analysis. The network of evidence remains the same as that presented in Figure 2 of the main text.

The figure below shows the updated forest plot for the scenario analysis using alternative data for these five studies. There were no changes to which interventions were identified as statistically significant, though some minor differences were observed in the 95% credible intervals (CrIs). The between study heterogeneity was slightly increased in this analysis, compared with the LT primary analysis; 0.137 [95% CrI 0.009, 0.436] versus 0.096 [95% CrI 0.005, 0.356]. Both indicate moderate heterogeneity, but the slight increase is likely due to the inclusion of more variable follow-up times within this scenario.

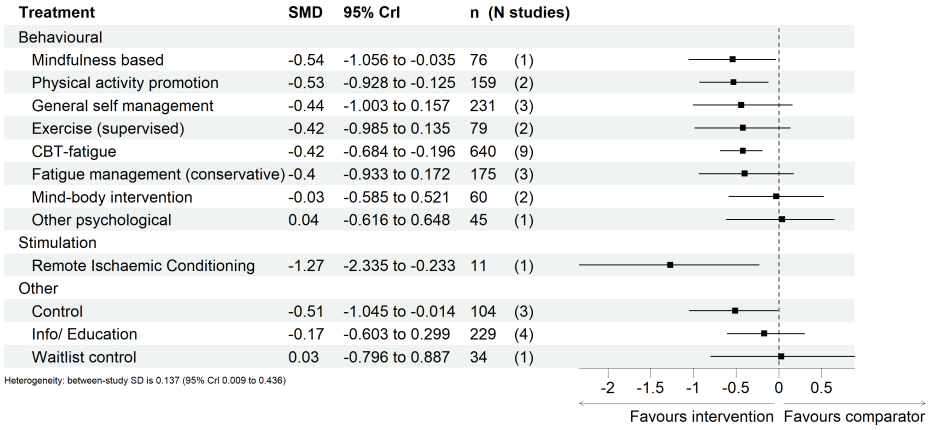


Figure 4 Predicted effects on fatigue outcomes of interventions, relative to usual care, at long term†, with 95% credible intervals (CrI). The number of participants (n) and the number of studies (N studies) are given for context. Broad intervention categorisation is also presented to aid interpretation (Behavioural, Stimulation, Nutritional, and Other). The "control" node is displayed as this functioned to ensure connectivity of the network, but this is not an active intervention for consideration/recommendation. †Data for five studies changed to use earlier follow-up data within the long-term analysis time window.

NMA scenario analysis: relaxation of the transdiagnostic assumption

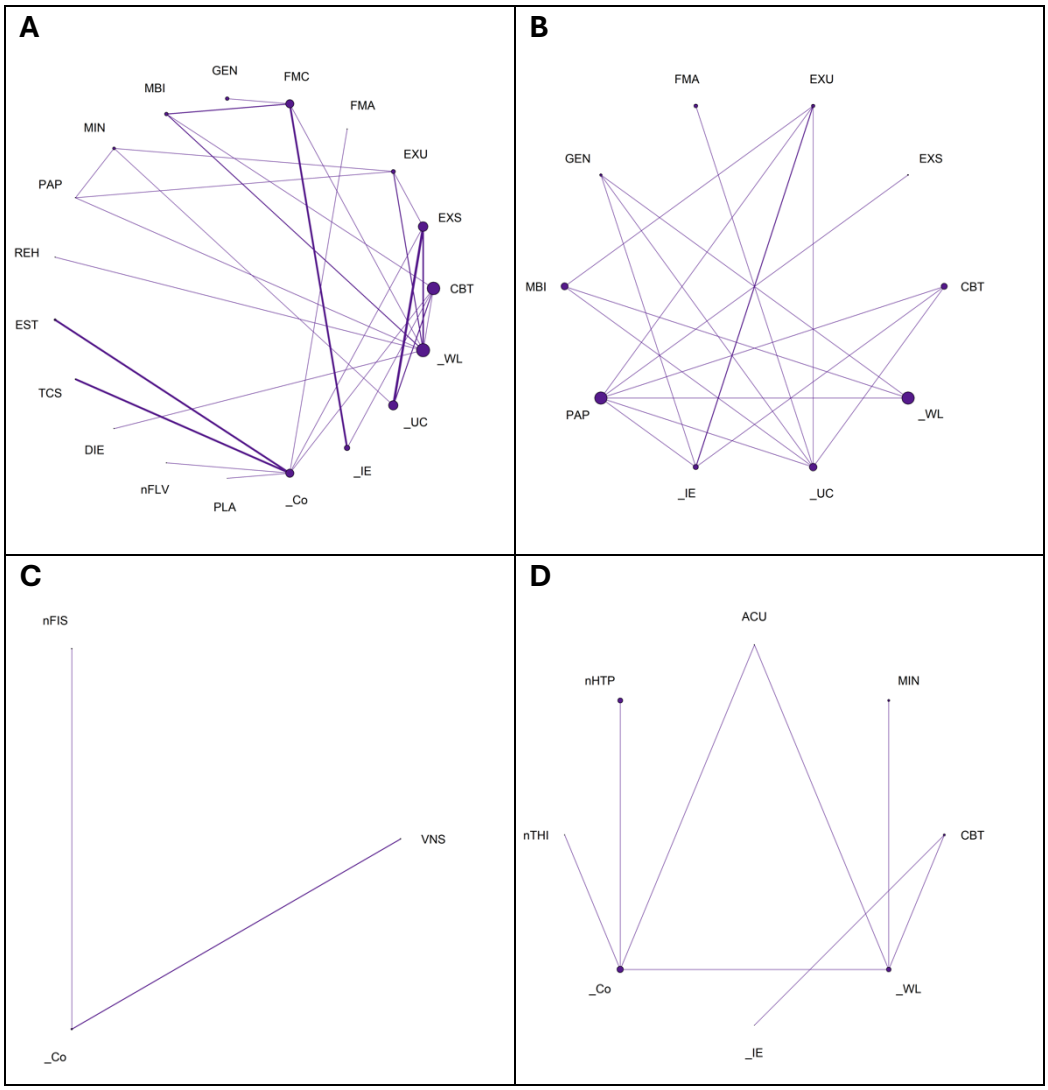
Condition group specific networks were constructed to help assess any potential differences in treatment effects across different condition groups. Due to the sparsity of evidence, networks could only be constructed using: EOT data for multiple sclerosis (MS), musculoskeletal conditions (MSK), inflammatory bowel disease (IBD), Kidney-related and Stroke-related conditions; ST for MS; and LT for MS and MSK. The results for each of these networks are presented below.

EOT

For the EOT condition-specific networks, Figure 5, there were 6 viable networks relating to the following condition groups: MS, MSK (two disconnected networks), IBD, Kidney, and

Stroke. The largest EOT network was for MS with 19 interventions across 44 studies; the network originally included 46 studies, but statistically significant inconsistency was detected via node-splitting, which led to the removal of two studies, Fleming (2021)[2] and Turner (2016)[5] which provided direct evidence for the interventions flagged with statistically significant inconsistency. Two disconnected EOT networks were constructed for MSK: the first, “MSK #1”, included 10 interventions over 12 studies; the second, “MSK #2”, included 3 interventions over 3 studies. The EOT network for IBD included 8 interventions over 6 studies. Whilst the EOT networks for Kidney and Stroke each contained 4 interventions across 3 studies. Note that no inconsistency checking via node-splitting was not feasible for the following networks: MSK #2, Kidney, and Stroke, because the networks contained no closed loops of evidence.

The point estimates and 95% CrIs for the EOT condition-specific networks are shown in Figures 6-11; the treatment effect is relative to usual care unless otherwise stated. Several differences can be seen between the primary analysis where the transdiagnostic assumption is upheld and the condition group specific networks – these are detailed below.



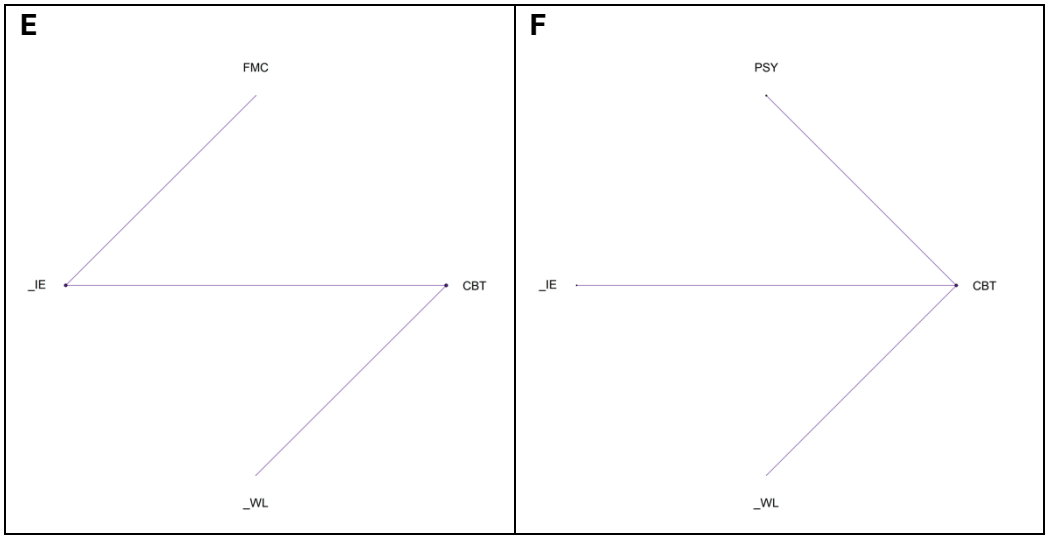


Figure 5 Network geometry for A) MS, B) MSK #1, C) MSK #2, D) IBD, E) Kidney, and F) Stroke condition-specific analyses, at end of treatment, respectively, indicating the number of participants who received each intervention (size of node) and the number of studies contributing to the direct evidence and comparisons between interventions (thickness of line).

In the EOT MS-specific network, all behavioural interventions (except physical activity promotion) were found to have beneficial, statistically significant effects on fatigue outcomes. Transcranial and external stimulation were also shown to have beneficial predicted effects. Of the nutritional interventions, only Flavenoid (cocoa) supplements were shown to have a potentially beneficial, statistically significant effect on fatigue outcomes, but as in the primary analysis, this was only evidenced by one study and should be interpreted with caution.
A number of treatments were found to have statistically significant effects which were not identified in the primary analysis, these included: non-specific rehabilitation, fatigue management (conservative), general self management, mind-body intervention and Flavenoid (Cocoa), suggesting these interventions may have improved effects on fatigue for individuals with MS. Conversely, physical activity promotion is not shown to have a statistically significant beneficial effect on fatigue outcomes. Furthermore, the treatment effect of waitlist control relative to usual care was non-beneficial for fatigue outcomes within the primary analysis but within the MS-specific network was shown to have a statistically significant, beneficial effect. Generally, treatment effects observed in the MS-specific network were indicative of greater treatment effects on fatigue outcomes when compared to the primary analysis, however, the evidence base of the MS-specific network is approximately half of that analysed within the primary analysis (44 vs. 84 studies) and results should therefore be interpreted with appropriate caution.
The between study heterogeneity was found to be 0.12 [95% CrI 0.007, 0.312] which indicates moderate heterogeneity within the network.

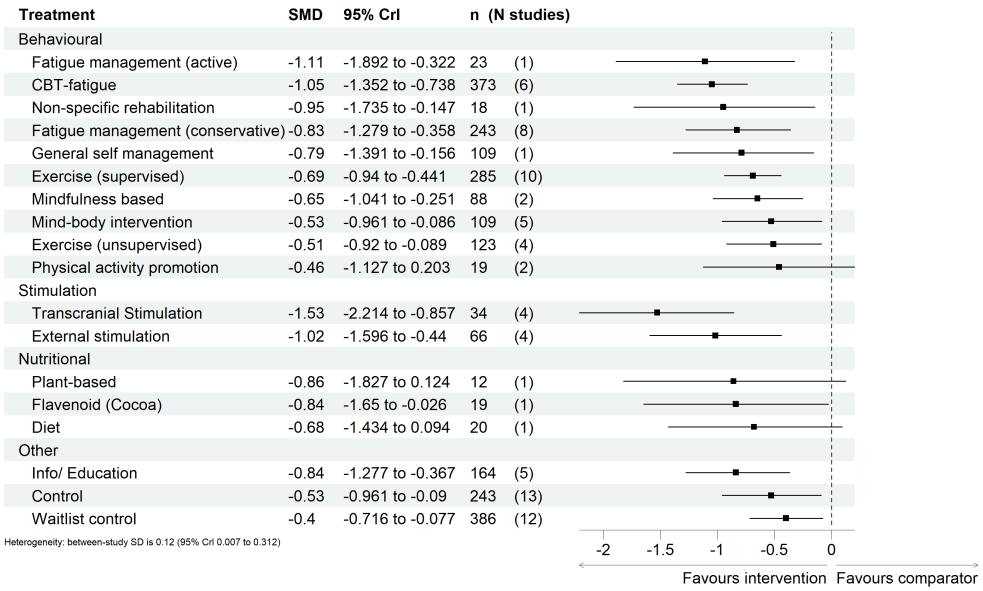


Figure 6 Predicted effects on fatigue outcomes of interventions within the MS-specific network, relative to usual care, at end of treatment, with 95% credible intervals (CrI). The number of participants (n) and the number of studies (N studies) are given for context. Broad intervention categorisation is also presented to aid interpretation (Behavioural, Stimulation, Nutritional, and Other). The "control" node is displayed as this functioned to ensure connectivity of the network, but this is not an active intervention for consideration/recommendation.

In the EOT MSK #1 network, exercise (supervised) and fatigue management (active) had statistically significant, beneficial effects on fatigue outcomes, as in the primary analysis. However, although CBT-fatigue and physical activity promotion were found to be statistically significantly beneficial in the primary analysis, in the MSK #1 analysis, they were no longer found to be statistically significant. The evidence base of the MSK #1 network is however much smaller than the primary analysis network (12 vs 84 studies) and therefore the treatment effects presented should be interpreted with caution as no intervention featured across more than 4 MSK studies.

The between study heterogeneity was 0.138 [95% CrI 0.007, 0.498], which indicates a moderate study heterogeneity within the network.

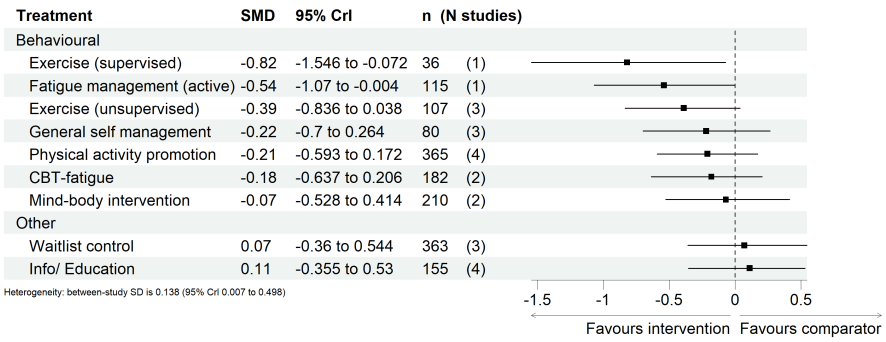


Figure 7 Predicted effects on fatigue outcomes of interventions within the MSK-specific network (#1), relative to usual care, at end of treatment, with 95% credible intervals (CrI). The number of participants (n) and the number

of studies (N studies) are given for context. Broad intervention categorisation is also presented to aid interpretation (Behavioural, Stimulation, Nutritional, and Other).

The EOT MSK #2 network treatment effects are presented relative to control and only included comparison of vagal stimulation and fish oil, Figure 8. As there were fewer than 5 studies within the 2nd network for MSK-related conditions, an informative prior on the between study heterogeneity was used. Vagal stimulation was found to be statistically significant with a positive effect on fatigue outcomes, however, this network only consisted of 3 studies, two of which influenced the vagal stimulation node, results should therefore be interpreted with caution. The between study heterogeneity was predicted to be 0.14 [95%CrI 0.027, 0.477] indicating moderate heterogeneity.

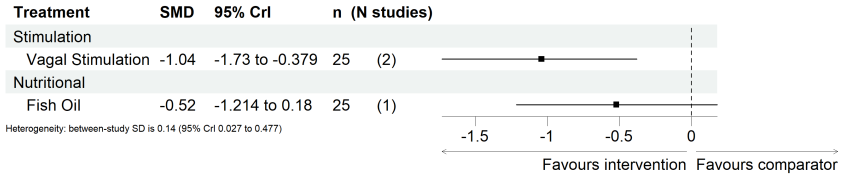


Figure 8 Predicted effects on fatigue outcomes of interventions within the MSK-specific network (#2), relative to control, at end of treatment, with 95% credible intervals (CrI). The number of participants (n) and the number of studies (N studies) are given for context. Broad intervention categorisation is also presented to aid interpretation (Behavioural, Stimulation, Nutritional, and Other).

The EOT analysis for IBD conditions showed that none of the interventions were identified to have statistically significant effects relative to waitlist control. However, these interventions were informed by a maximum of 2 studies and thus have minimal evidence. In addition to the low number of studies, the between study heterogeneity standard deviation was found to be 1.385 [95% CrI 0.071, 2.694], which indicates extremely high heterogeneity amongst the 6 studies included within the network, and therefore these results should be interpreted accordingly.

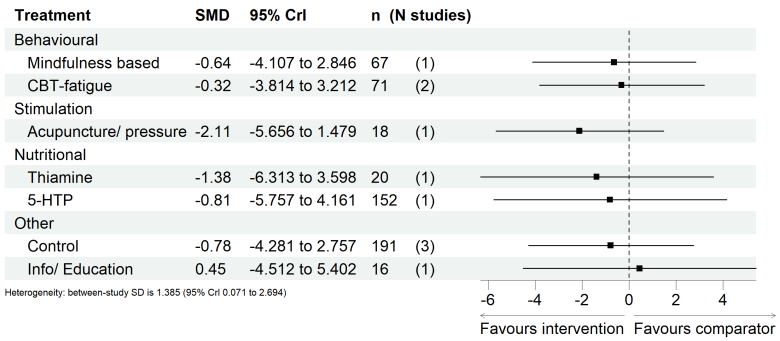


Figure 9 Predicted effects on fatigue outcomes of interventions within the IBD-specific network, relative to wait list, at end of treatment, with 95% credible intervals (CrI). The number of participants (n) and the number of studies (N studies) are given for context. Broad intervention categorisation is also presented to aid interpretation (Behavioural, Stimulation, Nutritional, and Other). The "control" node is displayed as this functioned to ensure connectivity of the network, but this is not an active intervention for consideration/recommendation.

As there were fewer than 5 studies within the network for Kidney-related conditions, an informative prior on the between study heterogeneity was used. The analysis showed that neither CBT-fatigue nor fatigue management (conservative) were found to be statistically significantly beneficial for fatigue outcomes relative to wait list controls. This network was

informed by only four studies and is likely underinformed. The between study heterogeneity was found to be moderate (0.143 [95%CrI 0.027, 0.483]).

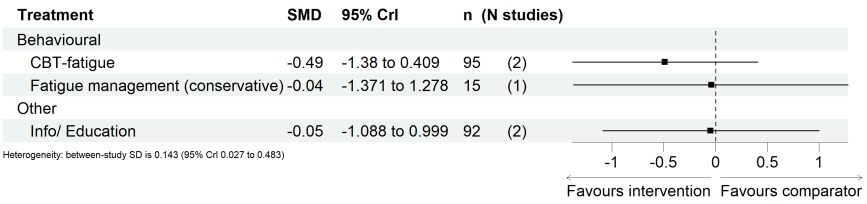


Figure 10 Predicted effects on fatigue outcomes of interventions within the Kidney-specific network, relative to wait list, at end of treatment, with 95% credible intervals (CrI). The number of participants (n) and the number of studies (N studies) are given for context. Broad intervention categorisation is also presented to aid interpretation (Behavioural, Stimulation, Nutritional, and Other).

Finally, the analysis of Stroke-related conditions had again less than 5 studies informing the network and thus the informative prior was used. Three studies provided evidence for CBT-fatigue, for which a statistically significant beneficial effect was identified relative to wait list control. A statistically significant, beneficial effect was also identified for “other psychological” interventions. Due to the low numbers of studies, these results should be interpreted with caution. The between study heterogeneity was again found to be moderate, with the standard deviation equal to 0.143 [95% CrI 0.027, 0.484].

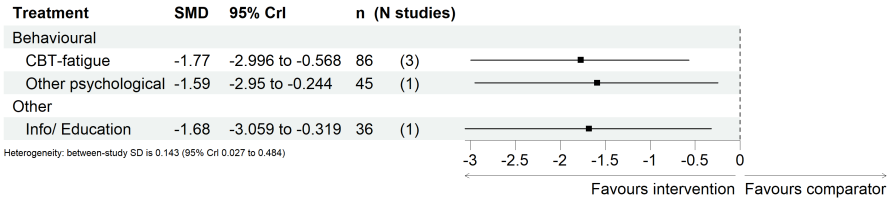


Figure 11 Predicted effects on fatigue outcomes of interventions within the Stroke-specific network, relative to wait list, at end of treatment, with 95% credible intervals (CrI). The number of participants (n) and the number of studies (N studies) are given for context. Broad intervention categorisation is also presented to aid interpretation (Behavioural, Stimulation, Nutritional, and Other).

Inconsistency was assessed for the EOT condition-specific networks with closed loops using the posterior mean residual deviances, followed by node-splitting, Figure 12. Following removal of Fleming (2021)[2] and Turner (2016)[5] from the EOT MS-specific network, no statistically significant inconsistency was detected in the EOT analyses.

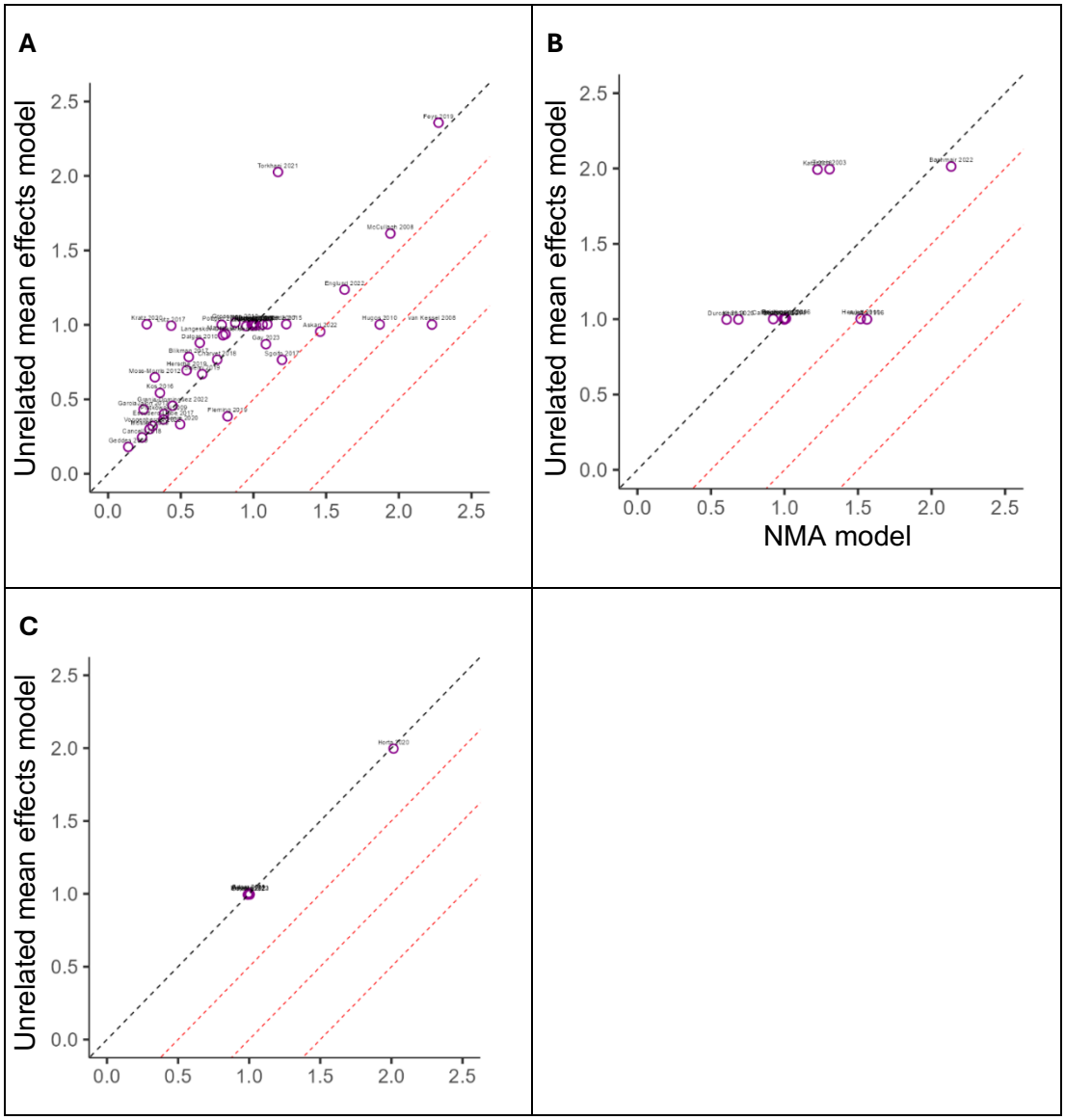


Figure 12 Mean posterior residual deviances according to the unrelated mean effects model versus the NMA model for A) MS, B) MSK #1, and C) IBD condition-specific analyses, at end of treatment, respectively. Black dashed line is given by $y = x$, red dashed lines represent contours separated by differences of 0.5 between the two models. Any studies below the first red dashed line indicative of potential inconsistency.

ST

For the ST condition-specific analysis, only one viable network could be constructed which summarised evidence for studies in MS, shown in Figure 13 A. This network included 12 interventions across 14 studies. The point estimates and 95% CrIs for the ST MS network are shown in Figure 13 B where the treatment effect is relative to usual care. Inconsistency was assessed for the ST MS network via comparison of the posterior mean residual deviances from the unrelated mean effects model and NMA model, followed by node-splitting, Figure 13 C; no statistically significant inconsistency was detected.

In the ST MS-specific network, no treatment was identified to have a statistically significant effect on fatigue outcomes, however, none of the included treatments were found to be statistically significant in the ST primary analysis. Additionally, the evidence base of the MS-specific network is smaller than the evidence within the primary analysis (14 vs. 24 studies).

In general, the treatment effects should be interpreted with caution as no intervention featured in more than 4 studies.

The between study heterogeneity standard deviation was 0.243 [95% CrI 0.01, 1.528] which indicates moderate heterogeneity within the network.

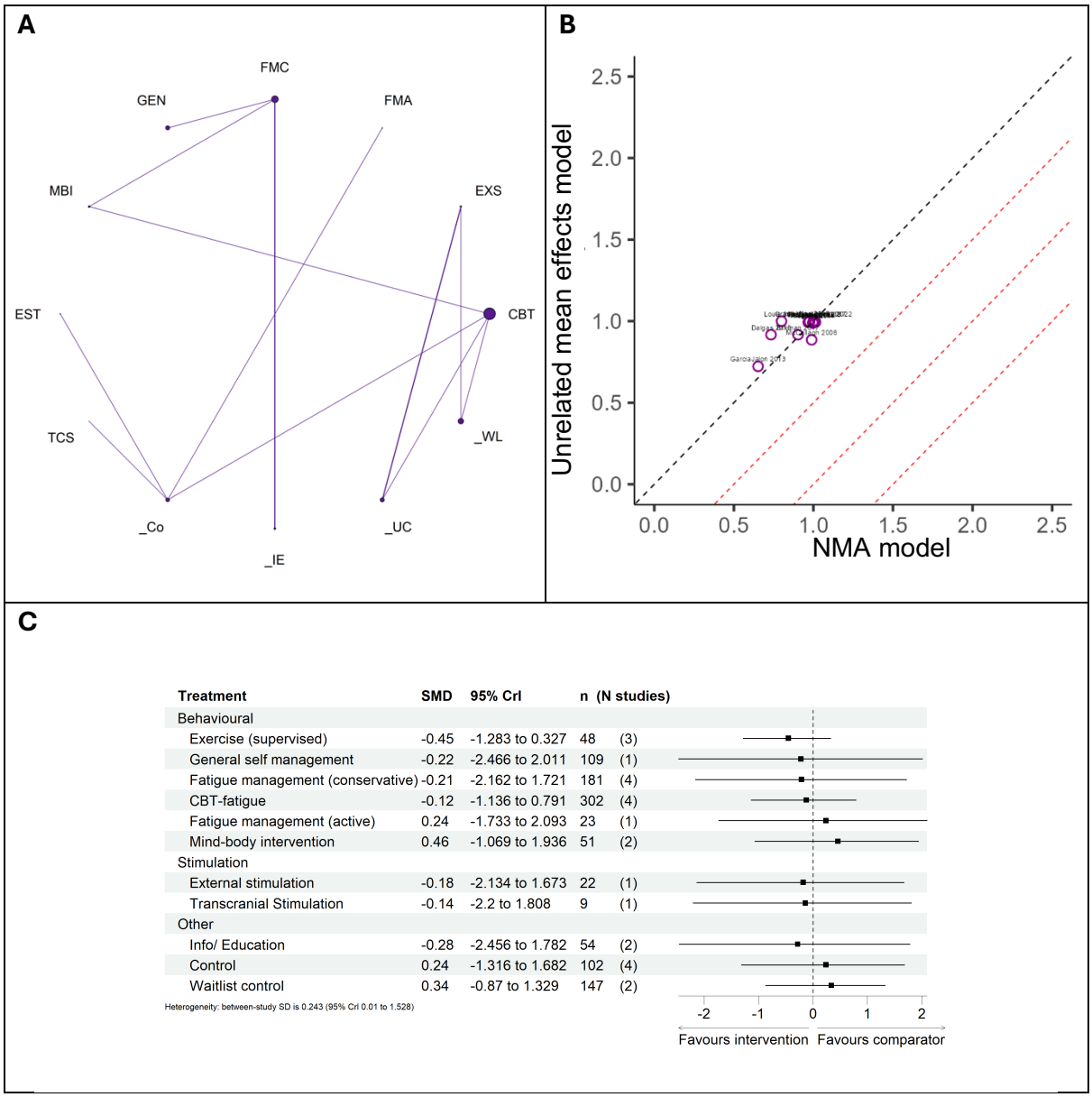


Figure 13 A) Network geometry, B) posterior residual deviances according to the unrelated mean effects model and the NMA model, and C) predicted effects on fatigue outcomes of interventions, relative to usual care, with 95% credible intervals (CrI); for the MS condition-specific analysis, at short term, respectively. The number of participants (n) and the number of studies (N studies) are given for context. The "control" node is displayed as this functioned to ensure connectivity of the network, but this is not an active intervention for consideration/recommendation.

LT

For the LT condition-specific analysis, there were two viable networks relating to: MS, shown in Figure 14 A, and MSK, shown in Figure 15 A. These networks included: 9 interventions across 10 studies, and 4 interventions across 3 studies, respectively. The point estimates and 95% CrIs for the LT networks are shown in Figure 14 B and 15 B, respectively; the treatment effects are relative to usual care. Inconsistency was assessed for the LT networks

by comparing the posterior mean residual deviances from the unrelated mean effects model and the NMA model, followed by node-splitting, Figure 14 C and 15 C; no statistically significant inconsistency was detected in either network.

In the LT MS-specific network, no treatment was shown to have a statistically significant effect on fatigue outcomes. In the LT primary analysis, mindfulness and CBT-fatigue were shown to have statistically significant, beneficial effects on fatigue outcomes, but this was not mirrored in the MS-specific analysis. As for the MS-specific EOT and ST networks, the evidence base is approximately half of the transdiagnostic case (10 vs. 18 studies); though there is some consensus between treatment effects seen in the MS-specific network and the primary analysis, however the broadening of the 95% CrIs resulted in non-significance.

The between study heterogeneity standard deviation was 0.317 [95% CrI 0.015, 2.119], indicating moderate to high heterogeneity within the network.

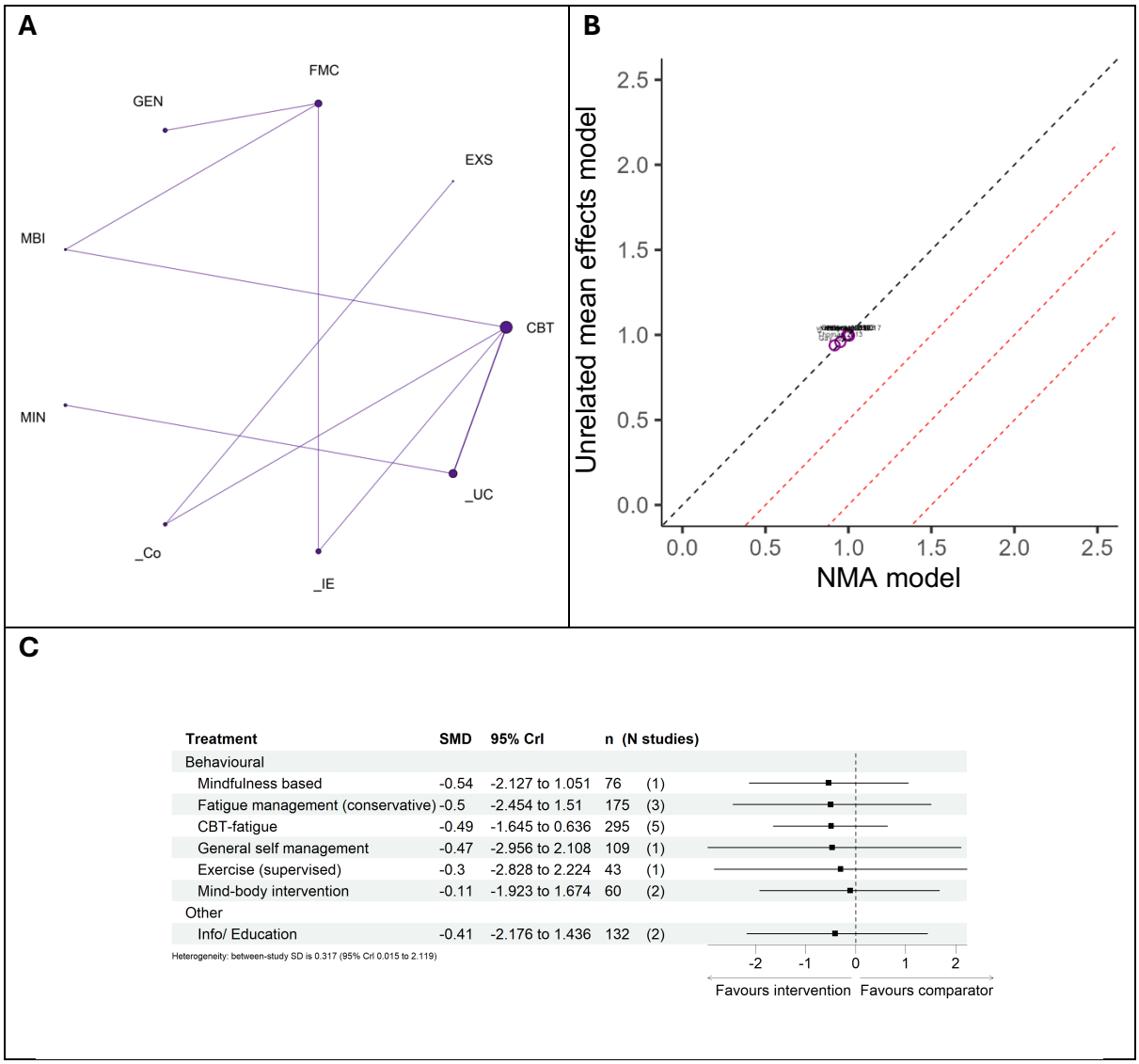


Figure 14 A) Network geometry, B) posterior residual deviances according to the unrelated model effects model and the NMA model, and C) predicted effects on fatigue outcomes of interventions, relative to usual care, with 95% credible intervals (CrI); for the MS condition-specific analysis, at long term, respectively. The number of participants (n) and the number of studies (N studies) are given for context. The "control" node is displayed as this functioned to ensure connectivity of the network, but this is not an active intervention for consideration/recommendation.

In the LT MSK-specific network, two treatments were shown to have statistically significant treatment effects relative to usual care: physical activity promotion and CBT-fatigue. Exercise (supervised) was found not to be statistically significant – these results are consistent with the LT primary analysis.

The between study heterogeneity standard deviation was moderate, 0.121 [95% CrI 0.025, 0.435].

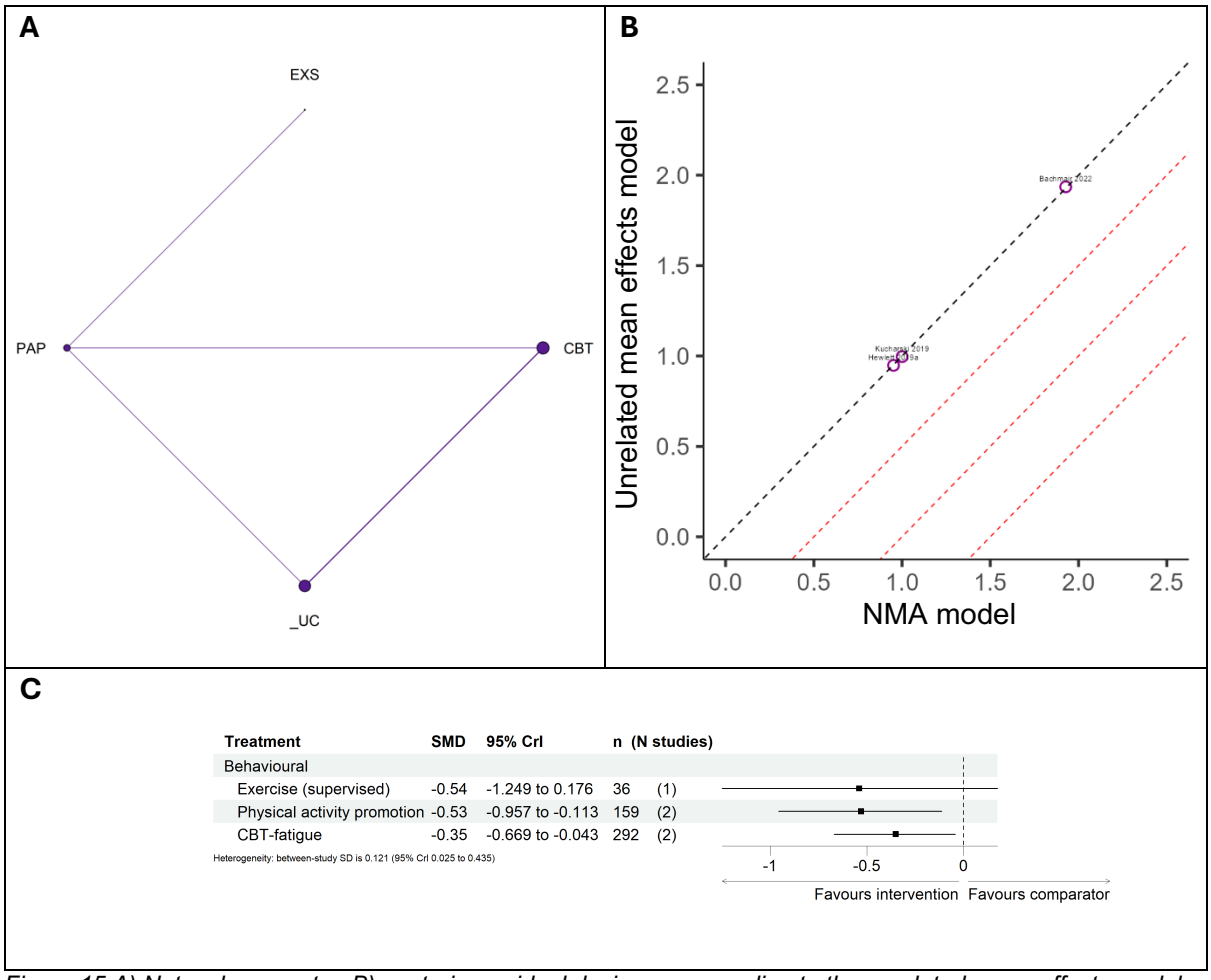


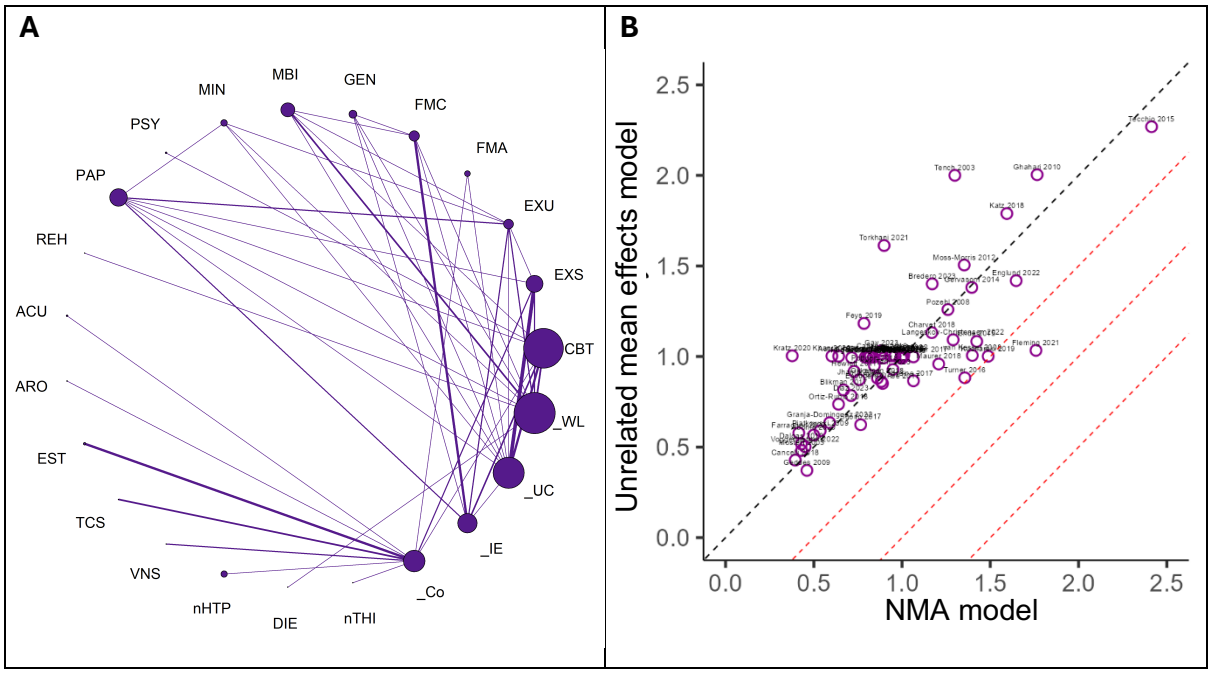
Figure 15 A) Network geometry, B) posterior residual deviances according to the unrelated mean effects model and the NMA model, and C) predicted effects on fatigue outcomes of interventions, relative to usual care, with 95% credible intervals (CrI); for the MSK condition-specific analysis, at long term, respectively. The number of participants (n) and the number of studies (N studies) are given for context. The "control" node is displayed as this functioned to ensure connectivity of the network, but this is not an active intervention for consideration/recommendation.

NMA scenario analysis: exclusion of pilot and feasibility studies

The evidence base for the primary analysis consists of studies reporting results from RCTs as well as pilot and feasibility trials. To assess the potential impact of the inclusion of pilot and feasibility studies within the NMAs, we re-constructed the networks for EOT, ST and LT follow up, omitting any pilot or feasibility studies. This resulted in networks with 23, 13 and 12 connected interventions, informed by 65, 15 and 15 studies.

EOT

Generally, the NMA results when excluding pilot/feasibility studies were similar to the primary analysis. Four interventions were no longer included in the network; remote ischaemic conditioning, fish oil supplements, plant based supplements, and flavonoid (cocoa) derived supplements. In the primary analysis, acupuncture was shown to exhibit statistically significant beneficial effects for fatigue outcomes, this was however only directly informed by two studies. In this scenario analysis, one of these studies was excluded and the treatment effect of acupuncture was no longer shown to be statistically significant. Similarly, thiamine-based supplements in this scenario analysis were directly informed by two fewer studies than the primary analysis and no longer found to be statistically significant. The between study variance was comparable between this analysis and the primary analysis. Other than the changes listed above, there was generally a minor impact on treatment effect estimates and the associated 95% CrIs at EOT.



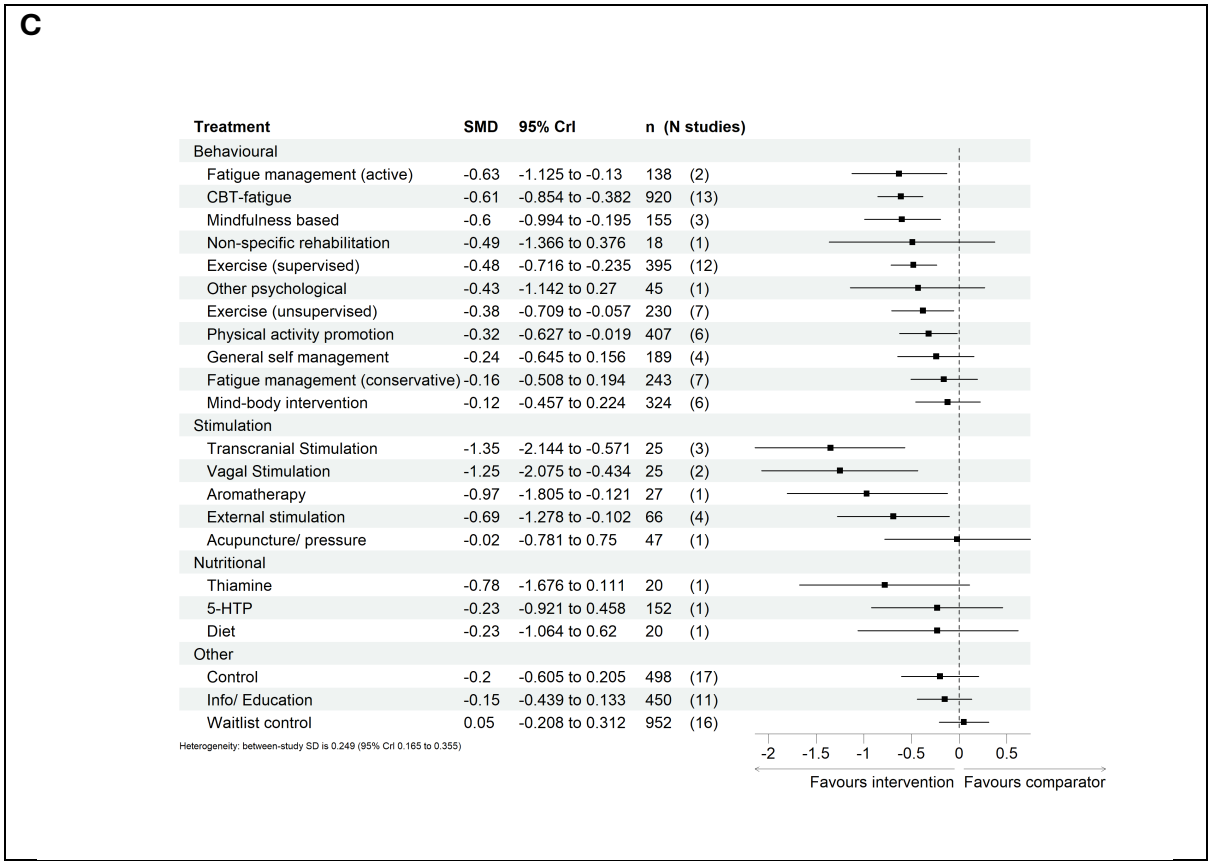


Figure 16 A) Network geometry, B) posterior residual deviances according to the unrelated mean effects model and NMA model, and C) predicted effects on fatigue outcomes of interventions, relative to usual care, with 95% credible intervals (CrI); for the end of treatment analysis†, respectively. The number of participants (n) and the number of studies (N studies) are given for context. The "control" node is displayed as this functioned to ensure connectivity of the network, but this is not an active intervention for consideration/recommendation. †Data from pilot/feasibility studies were excluded in this analysis.

ST

The SMDs and 95% credible intervals were similar at ST follow-up when pilot and feasibility studies were excluded with the primary analysis, with no changes in statistical significance for the included interventions. Three interventions were however no longer included in the network including: remote ischaemic conditioning, transcranial stimulation, and acupuncture/pressure based interventions. Between study variance was comparable between the two analyses.

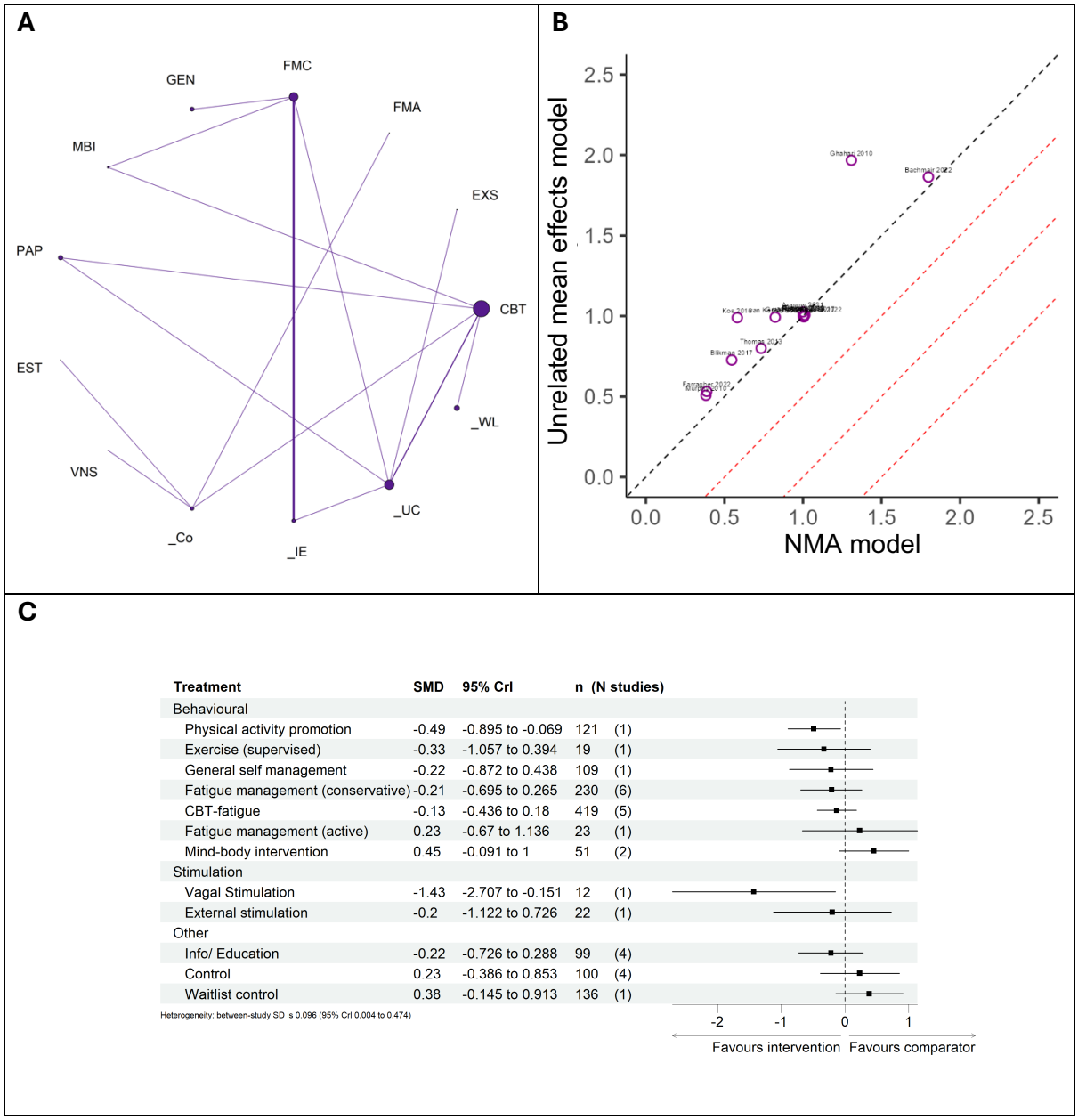


Figure 17 A) Network geometry, B) posterior residual deviances according to the unrelated mean effects model versus the NMA model, and C) predicted effects on fatigue outcomes of interventions, relative to usual care, with 95% credible intervals (CrI); for the short term analysis†, respectively. The number of participants (n) and the number of studies (N studies) are given for context. The "control" node is displayed as this functioned to ensure connectivity of the network, but this is not an active intervention for consideration/recommendation. †Data from pilot/feasibility studies were excluded in this analysis.

LT

In the LT follow-up analysis, when pilot studies were not included, broader 95% CrIs were evident for the majority of interventions compared to the primary analysis. Despite this, two interventions were found to exhibit statistically significant, beneficial effects for fatigue, which were not found to be statistically significant in the primary analysis, including: conservative fatigue management approaches, and general self management. Only one study directly evidencing conservative fatigue management was a pilot study in the primary analysis, and thus the changes in the scenario analysis results appear to be an indirect effect resulting from changes to other interventions within the network. Despite this, other intervention treatment effect point estimates, appear to be similar to the primary analysis. As in the EOT and ST follow-up analyses, remote ischaemic conditioning was no longer included within the

network. As with the other time points, between study variance was comparable to that observed in the primary analyses.

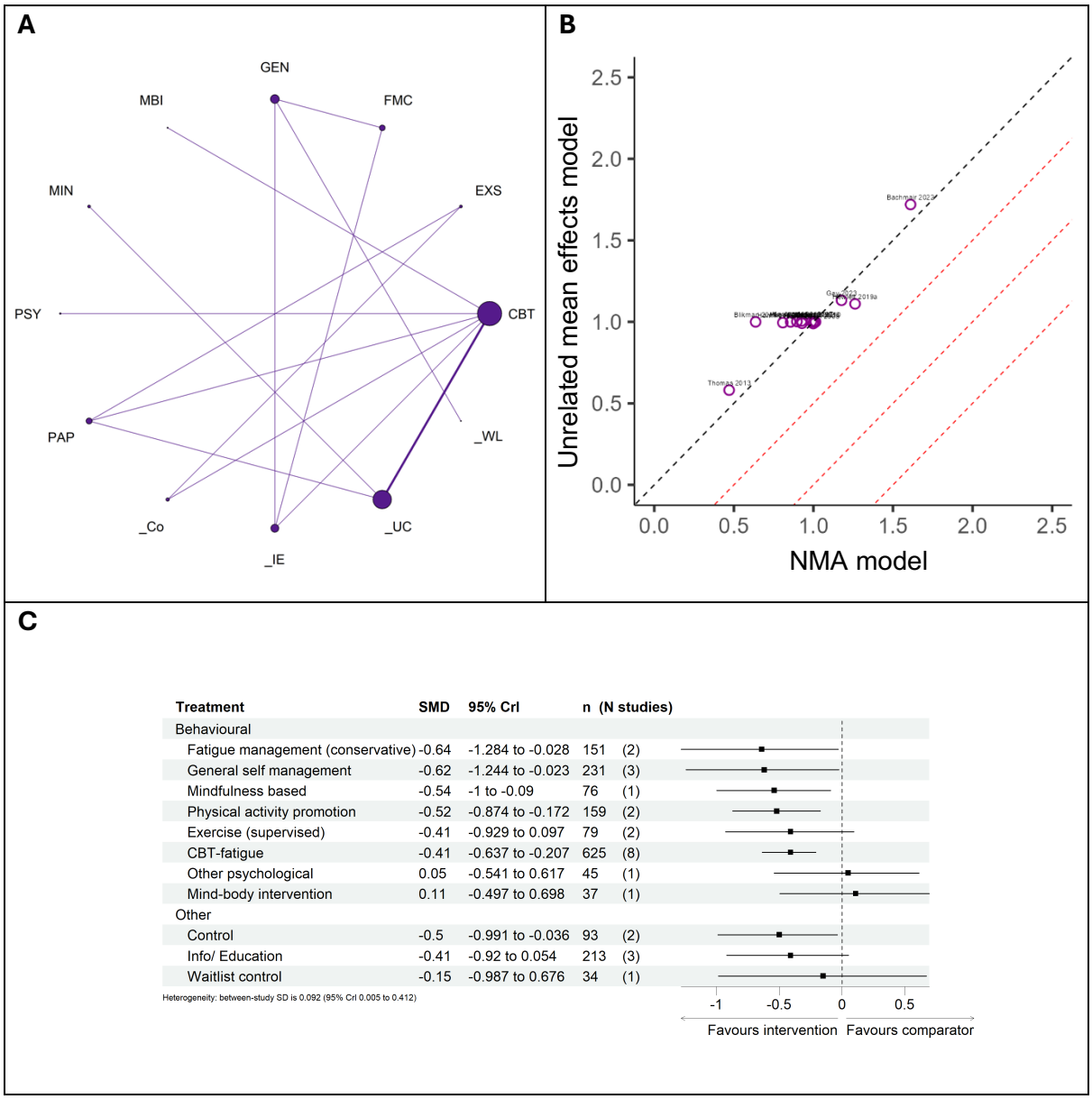


Figure 18 A) Network geometry, B) posterior residual deviances according to the unrelated mean effects model and the NMA model, and C) predicted effects on fatigue outcomes of interventions, relative to usual care, with 95% credible intervals (CrI); for the long term analysis†, respectively. The number of participants (n) and the number of studies (N studies) are given for context. The "control" node is displayed as this functioned to ensure connectivity of the network, but this is not an active intervention for consideration/recommendation. †Data from pilot/feasibility studies were excluded in this analysis.

References

1. Louie, J., Baquie, K., Offerman, J., Granger, C. L., Khan, F., & Bower, K. J. (2022). Maximising Abilities, Negotiating and Generating Exercise options (MANAGE) in people with multiple sclerosis: A feasibility randomised controlled trial. *Clinical Rehabilitation*, *36*(4), 498-510.

2. Fleming, K. M., Coote, S. B., & Herring, M. P. (2021). Home-based Pilates for symptoms of anxiety, depression and fatigue among persons with multiple sclerosis: An 8-week randomized controlled trial. *Multiple Sclerosis Journal*, *27*(14), 2267-2279.
3. Menting, J., Tack, C. J., van Bon, A. C., Jansen, H. J., van den Bergh, J. P., Mol, M. J., ... & Knoop, H. (2017). Web-based cognitive behavioural therapy blended with face-to-face sessions for chronic fatigue in type 1 diabetes: a multicentre randomised controlled trial. *The lancet Diabetes & endocrinology*, *5*(6), 448-456.
4. Langeskov-Christensen, M., Hvid, L. G., Jensen, H. B., Nielsen, H. H., Petersen, T., Stenager, E., & Dalgas, U. (2022). Efficacy of high-intensity aerobic exercise on common multiple sclerosis symptoms. *Acta Neurologica Scandinavica*, *145*(2), 229-238.
5. Turner, A. P., Hartoonian, N., Sloan, A. P., Benich, M., Kivlahan, D. R., Hughes, C., ... & Haselkorn, J. K. (2016). Improving fatigue and depression in individuals with multiple sclerosis using telephone-administered physical activity counseling. *Journal of Consulting and Clinical Psychology*, *84*(4), 297.
6. Horta, D., Lira, A., Sanchez-Lloansi, M., Villoria, A., Teggiachi, M., García-Rojo, D., ... & Calvet, X. (2020). A prospective pilot randomized study: electroacupuncture vs. sham procedure for the treatment of fatigue in patients with quiescent inflammatory bowel disease. *Inflammatory Bowel Diseases*, *26*(3), 484-492.
7. Clarke, A., Barker-Collo, S. L., & Feigin, V. L. (2012). Poststroke fatigue: does group education make a difference? A randomized pilot trial. *Topics in stroke rehabilitation*, *19*(1), 32-39.
8. Artom, M., Czuber-Dochan, W., Sturt, J., Proudfoot, H., Roberts, D., & Norton, C. (2019). Cognitive-behavioural therapy for the management of inflammatory bowel disease-fatigue: a feasibility randomised controlled trial. *Pilot and feasibility studies*, *5*(1), 1-20.
9. Ehde, D. M., Arewasikporn, A., Alschuler, K. N., Hughes, A. J., & Turner, A. P. (2018). Moderators of treatment outcomes after telehealth self-management and education in adults with multiple sclerosis: a secondary analysis of a randomized controlled trial. *Archives of physical medicine and rehabilitation*, *99*(7), 1265-1272.
10. Gay, M. C., Cassedanne, F., Barbot, F., Vaugier, I., Thomas, S., Manchon, E., ... & Heinzlef, O. (2024). Long-term effectiveness of a cognitive behavioural therapy (CBT) in the management of fatigue in patients with relapsing remitting multiple sclerosis (RRMS): a multicentre, randomised, open-label, controlled trial versus standard care. *Journal of Neurology, Neurosurgery & Psychiatry*, *95*(2), 158-166.
11. Hammond, A., Bryan, J., & Hardy, A. (2008). Effects of a modular behavioural arthritis education programme: a pragmatic parallel-group randomized controlled trial. *Rheumatology*, *47*(11), 1712-1718.
12. Hewlett, S., Almeida, C., Ambler, N., Blair, P. S., Choy, E. H., Dures, E., ... & RAFT Study Group. (2019). Reducing arthritis fatigue impact: two-year randomised controlled trial of cognitive behavioural approaches by rheumatology teams (RAFT). *Annals of the rheumatic diseases*, *78*(4), 465-472.

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	7
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supp Methods 1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	8
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	8
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	8
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	8 and supp methods 2
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	8
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	10 and supp methods 6
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	10 and Supp methods 6
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	10 and Supp methods 6
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	10 and Supp methods 6
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	10 and

Section and Topic	Item #	Checklist item	Location where item is reported
			Supp methods 6
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Supp methods 6
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Supp methods 3
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Supp methods 3
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	10 and supp appendix
Study characteristics	17	Cite each included study and present its characteristics.	Table 2 and supp results
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supp results
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Supp results
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	11 & 12
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	13 & 14, 21, 22, 23 and supp results
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	14, 21, 22, 23 and supp results
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	14, 21, 22, 23 and supp results
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	14 & table 2 & supp results
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	15
	23b	Discuss any limitations of the evidence included in the review.	15 & 16
	23c	Discuss any limitations of the review processes used.	15 & 16

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
	23d	Discuss implications of the results for practice, policy, and future research.	17
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	5
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	5
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	5
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	5
Competing interests	26	Declare any competing interests of review authors.	
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	N/A

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.