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A systematic review on the effects of non-pharmacological interventions for fatigue among people with upper and/or lower limb osteoarthritis

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Abstract

Objectives: To identify non-pharmacological fatigue interventions and determine the effectiveness of these non-pharmacological interventions in reducing fatigue immediately and over time in OA.

Methods: A review protocol (CRD42020163730) was developed and registered with the PROSPERO database. Included studies comprised peer-reviewed randomized controlled trials (RCTs) that examined the effects of conservative interventions on fatigue in people with upper and lower limb OA. Cochrane Collaboration's tool for assessing the risk of bias (ROB-2) was used to assess the quality of evidence of studies. Narrative synthesis was used to summarize the effectiveness of identified fatigue interventions.

Results: Out of 2644 citations identified from databases, 32 reports were included after screening for titles, abstracts and full texts. Of these reports, 30 parallel RCTs, one cluster and one cross-over RCT were included. 13 RCTs were of low ROB, 6 had some concerns and 13 had high ROB. The narrative synthesis identified interventions for fatigue including exercise, activity pacing, cognitive behavioural therapy, telerehabilitation and complementary alternative therapies. Exercise interventions showed the most significant beneficial effects on fatigue.

Conclusions: Diverse interventions for fatigue management among individuals with upper and lower limb OA were identified. Of these, exercise interventions appear to be the most promising with the majority of these interventions favouring fatigue improvement. While cognitive behavioural therapy has limited evidence of beneficial effects, there is insufficient evidence regarding the effectiveness of other identified interventions, including complementary and alternative therapies, and telerehabilitation.

Lay Summary

What does this mean for patients?

Fatigue, a feeling of tiredness or exhaustion, is a common symptom reported by people with OA which may lead to impairment of physical function and quality of life. There is a need to identify non-drug treatments that can be used to reduce fatigue immediately and over time among individuals with OA. This review found twelve treatments for fatigue for osteoarthritis. These include activity pacing, cognitive behavioural therapy, yoga, exercise, acupuncture, moxibustion, pain-coping skills, BEMER therapy, modified shoes, massage/aromatherapy, education and thermotherapy. Of these, exercise interventions appear to be the most promising treatment for fatigue improvement. Other treatments that may require further studies include cognitive behaviour therapy, complementary and alternative therapies, and telerehabilitation.

Keywords: OA, fatigue, vitality, non-pharmacological interventions.

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Key messages

- Diverse non-pharmacological interventions are available for the management of fatigue among individuals with upper limb and lower limb OA.
- Exercise interventions appear to be the most promising of these interventions.
- There is insufficient and conflicting evidence to ascertain the effects of other identified interventions on fatigue.

Introduction

OA is a musculoskeletal condition affecting an estimated 303 million people globally [1], and it is the single most common cause of disability in older adults [2]. OA presents with a long-term health challenge leading to global impact and the burden of disease [3]. According to the World Health Organisation (WHO), OA is a leading cause of disability among musculoskeletal conditions, globally [4]. Knee OA is highlighted as the most common form of OA [5]. An estimated 10% to 13% of old people aged ≥60 years have some degree of OA, with the disease being more common in women than in men [6].

OA, also known as degenerative arthritis or degenerative joint disease, commonly affects joints of the shoulder, hip, knee and the hand [7]. It is characterized by pain, stiffness, tenderness, loss of flexibility, crepitation, presence of bone spurs, swelling, depression and fatigue. The risk of occurrence of OA in a person can be increased by some modifiable and non-modifiable factors, including, older age, being female, obesity, joint injuries, repeated stress on the joint, genetics, bone disease, certain metabolic diseases and smoking [8–10].

An important symptom of OA that has received little research attention is fatigue, despite evidence showing fatigue to be a significant component of OA experience [11]. People with OA report fatigue as an important symptom negatively impacting their daily functional performance and QoL [11]. The prevalence of clinically-relevant fatigue in OA ranges from 41–56% [12, 13] similar to those found in other rheumatic conditions such as RA [14, 15] and higher than those found in older adults without OA (13–25%) [16].

There is currently no universally adopted definition for fatigue [17], but it can be defined as a subjective symptom that ranges from tiredness to total exhaustion leading to an unrelenting feeling that negatively impacts daily functional capacity. Equally, fatigue in OA has been identified as a research priority that should be considered a top priority in clinical practice [14]. Fatigue has been found to worsen physical functional abilities more than pain in OA [18], highlighting the need for an effective fatigue intervention in OA. The impact of fatigue may worsen the pre-existing disability in individuals with upper limb and/or lower limb OA. In other rheumatic conditions including RA, SLE, there is strong evidence for the effectiveness of physical activity and psychoeducational interventions in relieving fatigue symptoms [19]. However, this finding may not be extrapolated to individuals with OA. Therefore, there is a need to determine and identify effective fatigue interventions in those with OA, especially given that the OA management plan aims to alleviate symptoms and improve quality of life (QoL).

There is currently no specific recommendation for fatigue management in OA, although; there are indications that fatigue could be managed with both pharmacological and non-pharmacological modalities in rheumatic conditions [20]. To our knowledge, there is no systematic review currently available on the effects of non-pharmacological interventions that can reduce fatigue in people with upper limb and lower limb OA. Bridging this gap may provide preliminary insight into the potential effects of current approaches used to reduce fatigue in OA. The aim of this study was to identify non-pharmacological interventions for fatigue among individuals with upper limb and lower limb OA and to determine the effect of the identified fatigue interventions.

Methodology

Review

This review adhered to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines [21]. A review protocol was developed and registered with the PROSPERO database in April 2020 (CRD42020163730).

Search strategy

The following electronic databases Cochrane Library, MEDLINE (via OVID) AMED and CINAHL (via EBSCOhost); ProQuest (Health and Medical Collections, Nursing and Allied Health database, PsycINFO) and Web of Science core collections were searched from inception to 26th November 2021. The search was updated from November 2021 to 27th January 2023 using the Web of Science core collections database. The search strategy was reviewed by an experienced researcher in a systematic review methodology. The search strategy included a combination of subject headings, words in subject headings and keywords which were modified as needed in each database. Where possible, proximity searches were used to ensure that search terms (e.g. 'fatigue' and 'osteoarthritis') were mentioned in one sentence of the abstract. The following keywords, medical headings in combination with specific database search syntax, filters, limiters and Boolean operators were used: 'fatigue' OR 'fatigue severity' OR 'vitality' OR 'tiredness' OR 'physical fatigue' OR 'mental fatigue' OR 'general fatigue' OR 'fatigue impact' AND 'osteoarthritis' OR 'OA' 'knee osteoarthritis' OR 'knee OA' OR 'hip osteoarthritis' OR 'hip OA' OR 'ankle osteoarthritis' OR 'ankle OA' OR 'foot osteoarthritis' OR 'foot OA' OR 'shoulder osteoarthritis' OR 'shoulder OA' OR 'elbow osteoarthritis' OR 'elbow OA' OR 'hand osteoarthritis' OR 'hand OA' (Supplementary Table S1, available at *Rheumatology Advances in Practice* online).

Study criteria and selection

Population, intervention, study types, settings, comparators and outcomes

The population of interest of this review was individuals with upper or lower limb OA, or a mixed population reporting subgroup analysis on individuals with upper or lower limb OA. We included all physical interventions used to address fatigue in individuals with OA but not pharmacological interventions. We included all types of randomized controlled

trials (RCTs) and quasi-experimental studies from all settings. The comparison interventions included standard care, placebo, usual care or no intervention. The primary outcome of the review was fatigue using a self-reported instrument.

Inclusion criteria

Studies included comprised full-text and peer-reviewed RCTs, non-randomized controlled trials, uncontrolled pre-post intervention studies, quasi-experimental studies, pre and post studies and cross-over studies that examined the effects of any intervention in the management of fatigue in people with upper limb and lower limb OA.

Exclusion criteria

Articles were excluded if they were thesis reports and abstracts or studies not published in the English Language. Studies that used spiritual, pharmacological or surgical interventions to manage fatigue in patients with upper limb and lower limb OA were excluded.

Study selection

Two reviewers, OO and MI, independently screened identified studies for titles and abstracts. Thereafter, both reviewers screened eligible full texts against the inclusion criteria. In cases of disagreement, both reviewers discussed and reach a consensus. Where a consensus cannot be reached, two authors, OI and HF were consulted for the final decision. All the articles found from the databases were exported into the Endnote reference manager where duplicates were removed. Thereafter articles were exported to Rayyan (https://rayyan.ai) for titles and abstract screening based on inclusion and exclusion criteria, and to manage all the retrieved records.

Data extraction

Three reviewers (OO, MI and MO) extracted the following information independently from all included studies using a pre-piloted data extraction form: study population, participant characteristics, OA type, fatigue outcome tool, intervention type, intervention description, intervention mode, findings and implications. OI and HF reconciled any discrepancies.

Three authors (MI, MO, & OO) independently assessed the risk of bias (ROB) for studies using the Cochrane Collaboration's tool for assessing the risk of bias (ROB-2) for parallel, cluster or cross-over randomised controlled trials [22]. In cases where the three reviewers were unable to reach a consensus after discussions, three other authors (OI, HF and OA) were consulted and a unanimous agreement was reached. The reviewers independently pilot-tested the risk of bias assessment to familiarize themselves with the tool and to ensure consistency.

Data synthesis

Characteristics of the included studies and any important questions related to the aim of this systematic review are summarized in tables. The results are presented using narrative synthesis based on the type of intervention. We could not perform a meta-analysis because the interventions identified were heterogeneous.

Results

Study characteristics

Out of the 2644 citations identified, we included 32 reports (see Fig. 1). Two of the studies Yip *et al.* [23, 24] and Diracolgu *et al.* [25, 26] were reported twice due to follow-up studies. A total of 32 studies are presented. Thirty were

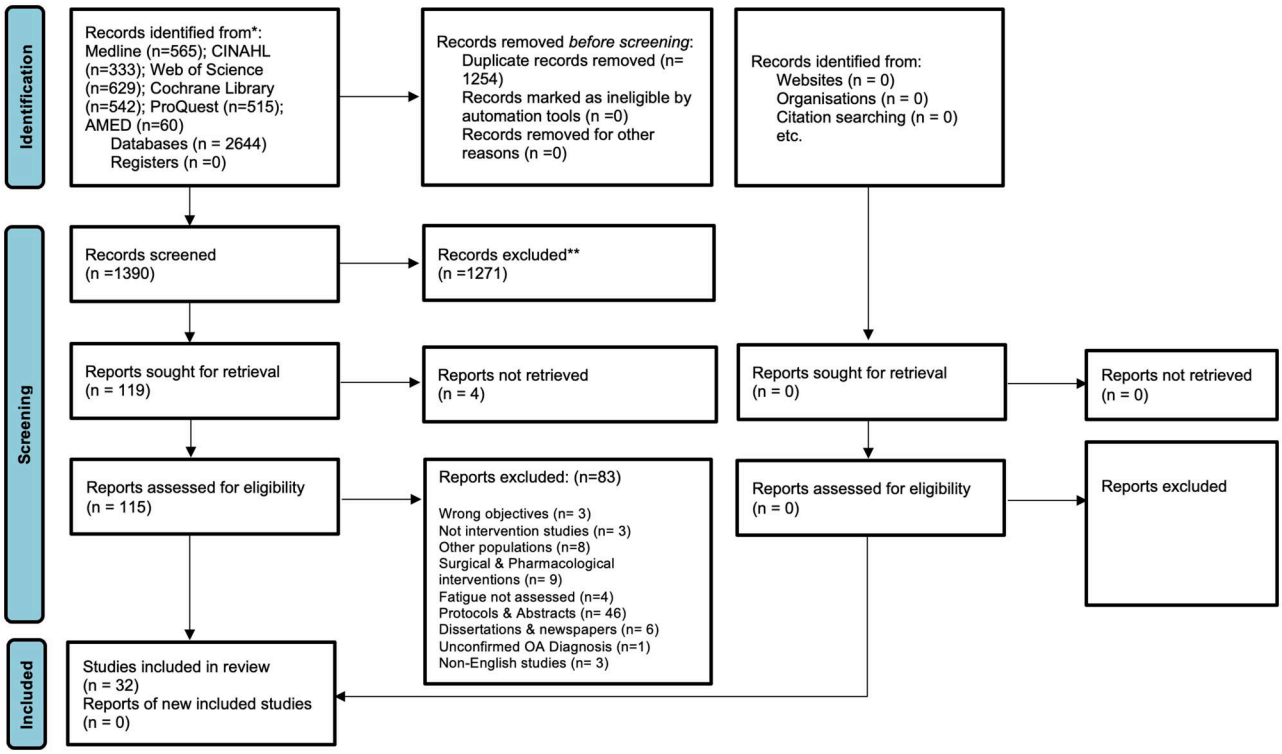

Figure 1. PRISMA flow diagram

parallel RCTs, one was a cluster RCT [27] and one was a cross-over RCT [28]. The sample size of the included studies ranged from 27 to 291. Of these studies, four studies were conducted in the United States [29–32], four from Brazil [33–36], four from Turkey [25, 26, 37–39], four from [28, 40–42], three from China [23, 24, 43, 44], two from Norway [45, 46], two from The Netherlands [27, 47], and one each from India [48], Spain [49], Taiwan [50], South Korea [51], Germany [52], Hungary [53], as well as Bosnia and Herzegovina [54] (Table 1).

In the selected studies, fatigue was assessed with ten different tools. The Short-form 36 vitality subscale (SF-36 scale) was used in thirteen of the studies [25, 26, 33, 34, 35, 37, 42, 43, 44, 48, 51, 52, 54], Visual Analogue Scale was used in three studies [27, 28, 49], Brief Fatigue Inventory was used in three studies [29, 30, 31] Numerical Rating Scale was used in four studies [23, 24, 45, 46, 47], Facit Fatigue Scale [38, 53], and the Multidimensional Fatigue Inventory [40, 50] were each used in two studies. Other fatigue tools include the PROMIS Fatigue-V 1.0 SF-8a [32], Short-form 12 [41], WHO quality of life questionnaire (WHOQoL) [36] and Fatigue severity scale (FSS) [39] (Table 1).

There were four types of OA included in this study: knee, knee and hip, hip, and hand OA. There were 24 knee OA studies [23–26, 28, 30, 33, 34–40, 42, 43, 44, 46, 48, 49, 50, 51, 53, 54], one study had participants with hip OA only [52], five studies recruited participants with hip and knee OA [27, 30, 31, 41, 47]; one with hand OA [45], and one with any of the lower limb joints (ie, hip, knee, foot or ankle OA) [32] (Table 1).

Fatigue intervention types

We identified various forms of interventions ranging from exercise to behavioural interventions. The interventions utilized include: exercise [23, 24, 25, 26, 32–36, 45, 49, 52, 53, 54], yoga [48], footwear modification [28], activity pacing [29], mobile app-based instructions [42], thermotherapy [41], moxibustion therapy [43, 51], pain-coping skills [31], multidisciplinary intervention [46], cognitive behavioural therapy [30], planned behaviour-based intervention [41], balneotherapy and physiotherapy [38], Bio-electromagnetic energy regulation (BEMER) therapy, a subtype of pulsed electromagnetic field therapy which uses micro-circulation in the muscles to facilitate blood circulation [53], mud-pack [37], active video games [50], acupuncture and usual care [44], tele-rehabilitation [39, 47], massage plus aromatherapy and electrotherapy [40]. The exercises included strengthening, balance, kinaesthesia, and mobilization, hand-based, stretching, aquatic dance-based and web-based exercises.

Narrative synthesis

Effects of exercise on fatigue

Of the eleven studies that used exercise interventions, five reported an immediate statistically significant reduction in fatigue [25, 26, 34, 45, 49]. In addition, exercise significantly improved vitality compared with control [54] or motor training [35]. Conversely, two studies showed no statistically significant effect of exercise interventions on fatigue, compared with the control groups among older adults [36, 50]. Yoga had a significant improvement in fatigue relative to exercise intervention [48], while the effectiveness of exercise could not be ascertained in the study by Park *et al.* [32] as the baseline data for the control group was not given (Table 2).

Effects of cognitive behavioural therapy (CBT) on fatigue

CBT was found to be clinically effective in reducing fatigue immediately [30, 31] and at 12 months follow-up [31]. Contrastingly, Saffari *et al.* [41] found no significant effect of planned behaviour-based intervention on fatigue at follow-up relative to the control intervention (Table 1). Veenhof *et al.* [27] found behavioural-graded activity to significantly improve fatigue scores compared with usual care.

Effects of alternative and complementary therapies on fatigue

Relative to TENS, both massage therapy and aromatherapy had reductive effects on fatigue levels immediately and after the 10th session although the effect after massage therapy was not clinically significant [40]. Acupuncture, electroacupuncture, and usual care (i.e. analgesics) had reductive effects on fatigue; however, the effects were significantly higher for acupuncture and electroacupuncture [42]. In comparison to hot packs, mature mud packs had a significant reductive effect on fatigue immediately and at 6 months follow-up [37]. Balneotherapy plus physiotherapy was more effective in reducing fatigue compared with physiotherapy alone [38]. Modified shoes decreased fatigue than no shoes in the cross-over study by Navali *et al.* [28]. BEMER therapy plus physiotherapy significantly improved fatigue and vitality than placebo BEMER therapy plus physiotherapy immediately and at three months follow-up [53]. Two studies reported a non-statistically significant effect of moxibustion on fatigue compare with control group [43, 51].

Effects of activity pacing, telerehabilitation and multidisciplinary group-based interventions on fatigue

Activity pacing significantly reduced fatigue severity at 10 weeks follow-up in comparison to the control intervention [29]. Telerehabilitation had a significant beneficial effect on fatigue levels immediately [39]. Web-based physical activity program had statistically significant difference on fatigue relative to usual care three months post intervention and at 12 months follow-up [47]. Multi-disciplinary based education intervention showed no clinically relevant improvement in fatigue [46] whilst mobile-based instruction improved vitality compared with routine medical care and education [42].

Quality appraisal

Of the 32 RCT studies (Fig. 2), 30 were parallel RCTs, one cluster RCT (Supplementary Fig. S1, available at *Rheumatology Advances in Practice* online) and one cross-over RCT (Supplementary Fig. S2, available at *Rheumatology Advances in Practice* online). The ROB-2 plots showed that these studies mostly had: challenges in their randomization process, deviations from intended interventions and measurement of the outcome. Figure 3 shows the summary of the overall risk of bias for parallel RCTs. Following a quality appraisal of all RCTs, 13 studies (41.0%) were found to be of low ROB [24, 27, 29, 32, 35, 36, 37, 39, 40, 45, 49, 52, 53], six (18.0%) were adjudicated as having some concern [23, 28, 30, 31, 43, 44]. Furthermore, 13 studies (41.0%) were found to have a high risk of bias [25, 26, 33, 34, 38, 41, 42, 46, 47, 48, 50, 51, 54] (Fig. 2).

Discussion

In this systematic review, our aim was to synthesize the evidence on non-pharmacological fatigue-management interventions

Table 1. Characteristics of included studies, ordered by year of publication

Authors/Country	OA type	Participant characteristic	Fatigue outcome tool	Intervention type	Intervention description	Control description	Baseline fatigue scores: Mean (SD), median [IQR]	Post-intervention fatigue scores: Mean (SD), median [IQR]	Findings & implications
Dias *et al.*, 2003 [33]/Brazil	Knee OA	*n* = 50 (IG = 24 CG = 23) M = 6 F = 44 Drop out = 3	SF-36 vitality subscale	Exercise + walking	Exercise protocol: Participants had exercise sessions twice a week comprising stretching exercises, concentric and eccentric isotonic progressive resistance exercises to the muscles of the lower limb, and closed kinetic chain weight-bearing exercises, for 12 weeks. Walking protocol: Participants also completed a 40-min walking programme thrice a week while walking at a self-selected pace.	Participants in this group were given instructions in the educational session which consisted of a lecture about disease characteristics, joint protection, pain management and strategies to overcome difficulties in activities of daily living.	Vitality **Intervention group:** Median = 90 [NR] **Control group:** Median = 85 [NR]	Vitality **Intervention group:** Median: 90[NR]; 6 months FU = 93 [NR] **Control group:** Median: 90 [NR]; 6 months FU = 87 [NR]	Participants in the experimental group showed a significant statistical reduction in fatigue levels compared with those in the control group.
Diracoglu *et al.*, 2005 [25]/Turkey	Knee OA	*N* = 66 (IG = 32 CG = 32) Drop out = 6 All females	SF-36 vitality subscale	Exercise	Kinesthesia/balance and strengthening exercises three times a week for 8 weeks.	Strengthening exercises were done three times a week for 8 weeks.	Vitality **Intervention group:** 45 (16.5) **Control group:** 42.14 (17.66)	Vitality **Intervention group:** 54 (19.5) **Control group:** 43.5 (18.3)	SF-36 scores for vitality post-exercise were found to be higher in the kinesthesia group.
Veenhof *et al.*, 2006 [27]/The Netherlands (Cluster RCT)	Hip and knee OA	*n* = 200 (IG = 97 CG = 103) All females Drop out = 21	Visual analogue scale	Behavioural graded activity	The treatment consisted of a 12-week period with a maximum of 18 sessions, followed by 5 pre-set booster moments with a maximum of 7 sessions (in weeks 18, 25, 34, 42, and 55, respectively).	Usual care: Participants were treated for 18 sessions over 12 weeks, according to the Dutch physiotherapy guidelines for patients with hip and/or knee OA. This guideline consists of education, exercise therapy and advice.	Fatigue **Intervention group:** 5.3 (2.4) **Control group:** 4.9 (2.3)	Fatigue **Intervention group:** Mean = 1.28; 39 weeks FU = 0.59; 65 weeks FU = 2.13 **Control group:** Mean = 0.84; 39 weeks FU = 0.31; 65 weeks FU = 1.12	The change in fatigue reduction was small and in favour of the BGA group relative to the usual care group. However, both interventions showed beneficial long term results.
Yip *et al.*, 2006 [23]/China	Knee OA	*n* = 182 (IG = 88 CG = 94) M = 29 F = 153 Drop out = 62	100mm horizontal visual analogue fatigue scale	Arthritis self-management program (ASMP) + exercise	ASMP: Participants received a 2-h class held once a week for 6 weeks, where they learnt how to manage the consequences of knee osteoarthritis. Exercise: The participants were coached on stretching, walking and tai chi.	Participants received only orthopaedic treatments prescribed by an orthopaedist or an outpatient doctor.	Fatigue **Intervention group :** 52.50 (21.17) **Control group:** 51.65 (19.60)	Fatigue **Intervention group:** 43.47 922.03); 16 weeks FU = 44.77 (22.64) **Control group:** 50.48 (19.41); 16 weeks FU = 49.41 (19.67)	The intervention was found to have a short term effect in reduction of fatigue.
Diracolgu *et al.*, 2008 [26]/Turkey	Knee OA	*n* = 66 (IG = 32 CG = 28) All females Drop out = 6	SF-36 vitality subscale	Exercise	Kinesthesia/balance and strengthening exercises 3 days a week and for a period of 8 weeks.	Range of motion exercises, strengthening exercises for the quadriceps, hamstrings, abductor and adductor muscles of the hip joint and knee extension exercises, three times a week or 8 weeks.	Vitality **Intervention group:** 45 (16.53) **Control group:** 42.14 (17.66)	Vitality **Intervention group:** 54.00 (19.58); 1 year FU = 51.07 (15.4) **Control group:** 45.52 (18.33); 1 year FU = 43.82 (11.93)	Strengthening exercise alone provided only a short-term benefit. However, the addition of kinesthesia/balance exercises produced a long-term result.

(continued)

Table 1. (continued)

Authors/Country	OA type	Participant characteristic	Fatigue outcome tool	Intervention type	Intervention description	Control description	Baseline fatigue scores: Mean (SD), median [IQR]	Post-intervention fatigue scores: Mean (SD), median [IQR]	Findings & implications
Yip *et al.*, 2008 [24]/China	Knee OA	*n* = 95 (IG = 45 CG = 50) M = 11 F = 81	100mm visual analogue scale- fatigue subscale	Arthritis self-management programme (ASMP) + exercise	ASMP: Participants received a 2-h class held once a week for 6 weeks, where they learnt how to manage the consequences of knee osteoarthritis. Exercise: The participants were coached on stretching, walking and tai chi.	Participants received only orthopaedic treatments prescribed by an orthopaedist or an out-patient doctor.	**Fatigue** **Intervention group:** 52.50 (21.17) **Control group:** 51.65 (19.60)	**Fatigue** **Intervention group:** 45.51 (19.89); 3 months FU = 46.28 (21.66); 1 year FU = 44.74 (21.15) **Control group:** 47.03 (20.22); 3 months FU = 46.62 (20.79); 1 year FU = 48.24 (20.52)	The intervention group recorded a decrease in fatigue compared with those in the control group.
Murphy *et al.*, 2010 [29]/USA	Hip or knee OA	*n* = 42 (IG = 17 CG = 15) KOA = 21 HOA = 11 Drop out = 10	Brief fatigue inventory (BFI)	Tailored activity pacing	Participants met with an occupational therapist for 1 h 30 min, twice a week for 2 weeks. They received an education module on general principles of activity pacing, as well as OT-tailored recommendations that were personalized for each participant.	Participants also met with an occupational therapist for 1 h 30 min, twice a week for 2 weeks. They only received an education module on general principles of activity pacing.	**Fatigue** **Intervention group**: 4.1 (2.1) **Control group**: 4.3 (2.3)	**Fatigue** **Intervention group**: 3.3 (1.8) **Control group**: 4.8 (3.1)	Fatigue severity on the BFI decreased in the intervention group compared with the general activity group. This shows that specific activities recommended based on the recent symptoms and general activity of each patient will help reduce fatigue.
Ebnezar *et al.*, 2011 [48]/India	Knee OA	*n* = 250 (IG = 125 CG = 125) M = 174 F = 76	SF-36 vitality subscale	Yoga + physiotherapy	Physiotherapy: Application of TENS and ultrasound to the affected knees for 20 min. Yoga: 40 min daily yoga therapy for 2 weeks consisting of shithilikaranavyayama (loosening and strengthening), asanas, relaxation techniques, pranayama, meditation and lectures on yama, niyama, jnana yoga, bhakti yoga, and karma yoga.	Physiotherapy: Application of TENS and ultrasound to the affected knees for 20 min. Exercise: Participants in this group carried out therapeutic exercises for 40 min, which included loosening and strengthening all the joints of the upper and lower limbs, and specific knee practices.	**Vitality** **Intervention group**: 66.6 (36) **Control group**: 64.91 (5.41)	**Vitality** **Intervention group:** 50.10 (6.30); 90 days FU = 36.35(6.08) **Control group:** 58.97 (5.63); 90 days FU = 53.20 (6.86)	The vitality level increased significantly in both groups, but with a better result in the yoga group.
Sarsan *et al.*, 2012 [37]/Turkey	Knee OA	*n* = 27 (IG =15 CG =12)	SF-36 vitality subscale	Mature mud pack + home exercise programme versusssss hot pack + home exercise programme	The two intervention groups used: Mud pack: Mud packs were applied directly on both knees at 42 degree Celsius for 20 min, 5 days a week, for a total of 10 sessions. Hot pack: Hot packs were applied directly on both knees at 42 degree Celsius for 20 min, 5 days a week, for a total of 10 sessions. Home exercise programme:	No control group	**Vitality** **Mud pack:** 43 (22.2) **Hot pack**: 59.5 (20.9)	**Vitality** **Mud pack**: 48.60 (14.0); 3 months FU = 54.0 (19.5); 6 months FU = 51.0 (18.0) **Hot pack**: 62.1 (20.8); 3 months FU = 56.6 (29.1); 6 months FU = 48 (25.5)	Significant long term improvements were found in fatigue level of patients who used the mud pack over those who used the hot pack.

(continued)

Table 1. (continued)

Authors/Country	OA type	Participant characteristic	Fatigue outcome tool	Intervention type	Intervention description	Control description	Baseline fatigue scores: Mean (SD), median [IQR]	Post-intervention fatigue scores: Mean (SD), median [IQR]	Findings & implications
					Home exercises consisting of isometric quadriceps contraction, knee ROM exercises and quadriceps strengthening exercises were carried out by all patients, with 10 repetitions of each exercise, 3 times a day for 12 weeks.				
Bossen *et al.*, 2013 [47]/The Netherlands	Hip and knee OA	$n = 199$ (IG = 100 CG = 99)	10-point numerical rating scale	Web-based physical activity programme	Participants were registered on the Join2move intervention platform where they received 8 tailored physical activity modules each week for 8 weeks. The intensity of each person's physical activity was increased based on the answers given in the questionnaire at the end of each week.	Participants were also registered on the Join2move intervention, but the intensity of their physical activity remained the same throughout.	**Fatigue** **Intervention group:** Mean = 5.6 (95% CI = 4.3, 6.9) **Control group:** Mean = 5.5 (95% CI = 4.3, 6.8)	**Fatigue** **Intervention group:** Mean = 3.2 (95% CI = 4.3, 6.8); 12 months FU = 3 (95% CI = 1.9, 4.2) **Control group:** Mean = 4.1 (95% CI = 2.9,5.3); 12 months FU = 4.1 (95% CI = 3, 5.2)	The intervention proved effective in reducing fatigue overtime in people with OA.
Kim *et al.*, 2014 [51]/ South Korea	Knee OA	$n = 212$ (IG = 102 CG = 110) M = 33 F = 179	SF-36 vitality subscale	Moxibustion (burning mugwort devices over acupuncture and Ashi (tender)points) + exercise	Moxibustion therapy on the affected knee(s) was offered at six standard acupuncture points (ST36, ST35, ST34, SP9, ExLE04 and SP10) alongside 2 points of ashi if need be, three times a week for 4 weeks. They were also instructed on exercises to stretch and strengthen the hamstrings and calf muscles.	Exercises to stretch and strengthen the hamstrings and calf muscles	**Vitality** **Intervention group:** 48.35 (10.46) **Control group:** 46.55 (9.72)	**Vitality** **Intervention group:** 50.12 (10.29); 13 weeks FU = 50.41 (10.82) **Control group:** 47.39 (10.63); 13 weeks FU = 48.30 (10.97)	The intervention did not prove effective for reducing fatigue
Kraub *et al.*, 2014 [52]/Germany	Hip OA	$n = 218$ (IG = 71 Placebo group = 70 Ultrasound group- = 8 CG = 69) M = 130 F = 88	SF-36 vitality subscale	Exercise + Education	THuKo exercise therapy that included a once weekly group intervention (education and strengthening exercises) of 60–90 min and a 30–40 min home exercise programme twice a week, for 12 weeks. Placebo ultrasound group: A 15-min placebo ultrasound treatment on the hip once a week.	No intervention	**Vitality** **Placebo Ultrasound group:** 62 (16) **Exercise group:** 64 (17) **Control group:** 63 (17)	**Vitality** **Placebo Ultrasound group:** 1 (15) **Exercise group:** −1 (15) **Control group:** 0 (12)	There was no statistical significance in vitality symptoms in the exercise therapy group, placebo ultrasound group and the control group.
Broderick *et al.*, 2014 [31]/USA	Hip or knee 0A	$n = 257$ (IG = 129 CG = 128) M = 60 F = 197 Dropout = 74	Brief fatigue inventory (BFI)	Pain-coping skills training (PCST)	Participants were taught cognitive and behavioural skills to manage their pain and enhance their perception of pain control. The skills taught include: relaxation	Participants were given OA informational brochure from the Arthritis Foundation and information on programs (support groups, arthritis education, and aquatic exercise	**Fatigue** **Intervention group:** 5.14 (SE: 2.01) **Control group:** 5.06 (SE: 1.90)	**Fatigue** **Intervention group:** 0.82 (0.16); 6 months FU = −0.24 (0.21); 12 months FU = 0.29 (SE : 0.18)	PCST decreased the fatigue level in participants.

(continued)

Table 1. (continued)

Authors/Country	OA type	Participant characteristic	Fatigue outcome tool	Intervention type	Intervention description	Control description	Baseline fatigue scores: Mean (SD), median [IQR]	Post-intervention fatigue scores: Mean (SD), median [IQR]	Findings & implications
					response, attention diversion techniques, altering activity and rest patterns as a way of increasing activity level, and reducing negative pain-related thoughts and emotions. This lasted 30–45 minutes for 20 weeks.	classes) offered in the community.		**Control group:** −0.07 (SE: 0,17) 6 months FU = 0.16 (SE: 0.18) 12 months FU = −0.29 (SE: 0.18)	
Hennig *et al.*, 2015 [45]/Norway	Hand OA	$n = 80$ (IG = 40 CG = 40) All females Drop out = 9	11 point Numeric rating scale	Home exercise	A rubber ball made of polyethylene with a diameter of 7 cm was used to provide resistance in the grip strengthening exercise, while rubber bands were used to provide resistance to the thumb abduction/extension exercise.	Education on OA which includes symptoms of OA, alternative working methods for better ease and comfort.	**Fatigue** **Intervention group:** Median = 6.0 [range = 0,9] **Control group:** Median = 6.0 [range = 0,10]	**Fatigue** **Intervention group:** mean: -.0.7 (3.4) **Control group:** mean change: 0.5 (1.9)	The hand exercises were well tolerated by the patients and it greatly reduced fatigue.
Ren *et al.*, 2015 [43]/China	Knee OA	$n = 136$ (IG = 69 CG = 67) M = 43 F = 93	SF-36 vitality subscale	Moxibustion (which is burning mugwort devices over acupuncture and Ashi (tender) points)	Participants were treated at three local points, ST 35, EX-LE4, and an Ashi point on the most painful part of the affected knee.	Participants received sham moxibustion from a device that provided insulation from the heat.	**Vitality** **Intervention group:** 53.55 (18.19) **Control group:** 52.99 (18.55)	**Vitality** **Intervention group:** 56.16 (16.50) : 6 weeks FU = 59.42 (15.87); 12 weeks FU = 61.30 (16.22) **Control group:** 56.87 (14.40); 6 weeks FU = 56.49 (14.62); 12 weeks FU = 55.52 (16.68)	Participants in the true moxibustion group experienced great improvement in vitality.
Da Silva *et al.*, 2015 [34]/Brazil	Knee OA	$n = 30$ (IG = 19 CG = 22) M = 4 F = 26 Drop out = 11	SF-36 vitality subscale	Exercise	Members participated in a group rehabilitation programme that lasted 60 min, twice a week for 8 weeks. 15 min from this time was used to educate them about KOA.	Participants received booster education on how to improve quality of life and function through leaflets for 8 weeks	**Vitality** **Intervention group**: 56.0 (19.2) **Control group:** 60 (12.64)	**Vitality** **Intervention group**: 72.0 (16.56) **Control group:** 58.3 (16.22)	The intervention proved effective in reducing fatigue.
Gyulai *et al.*, 2015 [53]/Hungary	Knee OA	$n = 50$ (IG = 25 CG = 25)	Facit fatigue scale	BEMER therapy + physiotherapy	Physiotherapy: Individual and group exercises (30 min), underwater whirlpool massage (10 min), TENS therapy on the low back or knee (15 min every day), aqua gym (30 min every other day). BEMER therapy: Mattress applicator (B. Body Pro): 7–35 microTesla, intensive	Physiotherapy treatment as received by the intervention group and placebo BEMER treatment.	**Fatigue** **Intervention group:** Difference: 6.03 (6.08) **Control group:** Difference: 4.96 (9.57)	**Fatigue** **Intervention group:** Difference : 3 months FU: 4.22 (8.54) **Control group:** Difference: 3 months FU: −3.30 (8.52)	BEMER therapy was found to be effective in reducing fatigue over time.

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Table 1. (continued)

Authors/Country	OA type	Participant characteristic	Fatigue outcome tool	Intervention type	Intervention description	Control description	Baseline fatigue scores: Mean (SD), median [IQR]	Post-intervention fatigue scores: Mean (SD), median [IQR]	Findings & implications
					applicator (B. PAD): 60–100 microTesla and using vascular motion signal configuration (BEMER signal). This session lasted 20 min and was done for 3 months.				
Moe *et al.*, 2016 [46]/Norway	Knee OA	*n* = 391 (CG = 197 IG = 194) M = 53 F = 338	11-point Numerical rating scale	Multidisciplinary intervention	Participants received a multidisciplinary group-based education about OA, immediately followed by individual consultations with a rheumatologist and members of the multidisciplinary team as needed (orthopaedic surgeon, physical therapists, occupational therapists, pharmacists or dieticians).	Participants only received usual individual outpatient care where a nurse received and a rheumatologist examined the patient. The rheumatologist referred the patient to other health professionals according to individual needs.	**Fatigue** **Intervention group**: 4.24 (2.9) **Control group**: 4.11 (2.8)	**Fatigue** **Intervention group:** Mean = 4.6; 4 months FU = 4.41 (95% CI = 4.01, 4.81); 12 months FU = 4.6 (95% CI = 4.91, 5) **Control group:** Mean = 4.05; 4 months FU = 4.26 (95% CI = 3.87, 4.66); 12 months FU = 5.34 (95% CI = 3.63, 4.46)	Patients receiving multidisciplinary intervention care were more satisfied that those who received usual care. However, there were no clinically relevant improvements in health outcome.
Casilda-Lopez *et al.*, 2017 [49]/Spain	Knee OA	*n* = 34 (IG = 17 CG = 17) All females	Visual analogue scale	A dance-based aquatic exercise programme	The dance-based exercise had the rhythm of 5 min of slow rhythm music, 3 min of fast rhythm music, 5 min of slow rhythm, 3 min of fast rhythm, 5 min of slow rhythm, all a total of 21 min. This was done 3 times a week for 8 weeks.	They received a 12-min aerobic warm-up, followed by a 21-min cardiovascular training programme. The 12 min cool down period included breathing exercises and stretching of the main muscles used.	**Fatigue** **Intervention group**: 2.85 (1.57) **Control group**: 2.75 (2.06)	**Fatigue** **Intervention group**: 2.07 (1.58)) ; 3 months FU = 2.16 (1.15) **Control group**: 3.84 (2.03)) ; 3 months FU = 4.03(2.56)	This program significantly decreased fatigue in patients with knee OA.
Park *et al.*, 2017 [32]/USA	Hip, knee, ankle or foot OA	*n* = 112 (CG = 63 IG = 49) M = 27 F = 85 Drop out = 19	PROMIS Fatigue-V 1.0 SF-8a	Chair yoga	Participants received a 45 min session, twice a week comprising of physical postures, breathing, deep relaxation, and meditation using a chair as support, for 8 weeks.	Participants received a manual containing yoga instructions and pictures (health education programme).	**Fatigue** **Intervention group**: 20 (NR) **Control group**: Not presented	**Fatigue** **Intervention group**: 19.5 (NR); 8 weeks FU = 17.8 (NR); 1 month FU = 18.1 (6.5); 3 months FU = 17.8 (NR) **Control group:** 1 month FU = 19.2 (7.4)	There was a significantly greater decrease in fatigue for the yoga group over 8 weeks.
Kapetanovic *et al.*, 2018 [54]/Bosnia and Herzegovina	Knee OA	*n* = 60 (IG = 30 CG- 30) M = 6 F = 54	SF-36 vitality subscale	Exercise	Participants performed strength, stretching, and balance exercises of moderate intensity, once daily, 5 times a week, for 8 weeks (6 weeks at home), after the 2 weeks training in the hospital.	Participants in this group only performed the 2 weeks training, in hospital, on how to implement the exercise program at home but did not carry out the programme.	**Vitality** **Intervention group**: 44.83 (11.02) **Control group**: 45.66 (10.14)	**Vitality** **Intervention group**: difference = 36.50 (7.21) **Control group:** difference = −2.50 (5.84)	At the end of the treatment program, vitality score significantly improved in the intervention group relative to control group.
Kabiri *et al.*, 2018 [40]/Iran	Knee OA	*n* = 93 (ATG = 31 MTG = 31	Multidimensional Fatigue	Massage therapy or aroma	Massage therapy: 3 ml of oil was used to conduct 10 massage sessions,	The participants received routine physiotherapy alone.	**Fatigue** **Aroma therapy group**: 12.61 (3.19)	**Fatigue** **Aroma therapy group**: 12.58 (3.16); after 10th	A great decrease in the fatigue scores of those in the aroma therapy group

(continued)

Table 1. (continued)

Authors/Country	OA type	Participant characteristic	Fatigue outcome tool	Intervention type	Intervention description	Control description	Baseline fatigue scores: Mean (SD), median [IQR]	Post-intervention fatigue scores: Mean (SD), median [IQR]	Findings & implications
		CG = 31) M = 30 F = 63	Inventory (MFI).	therapy + physiotherapy	with each session lasting 20 min, 3 times a week. Aroma therapy: Participants in this group were referred for physiotherapy in the morning. Then, two drops of Lavender essential oil embedded in a 3 ml dropper was put on a cotton ball and then the cotton ball was attached to the collar from 10:00 pm to 7:00 am at home every other day for one month. Physiotherapy: TENS and Faradic current at 50 Hz.		**Massage therapy group**: 13.03 (1.97) **Control group**: 12.71 (2.51)	session = 12.39 (3.24) **Massage therapy group**: 12.38 (1.80); after 10th session = 11.97 (1.49) **Control group**: 12.84 (2.53); after 10th session = 13.10 (2.48)	was noticed, in comparison to the scores of those in the control group. There was however no significant difference between the fatigue scores of those in the control group and those in the massage therapy group.
Murphy *et al.*, 2018 [30]/USA	Knee OA	*n* = 46 (IG = 38 CG = 19) All female	Brief fatigue inventory	Cognitive behavioural therapy (CBT)	Participants had occupational therapy sessions every 2 to 3 weeks for 6 months. The meetings consisted of education about cognitive behavioural principles, discussion of individual treatment sessions, and review of responses to completed homework by participants.	Participants continued with their usual osteoarthritis care.	**Fatigue** **Intervention group:** 2.5 (2.5) **Control group**: 2.7 (2.3)	**Fatigue** **Intervention group**: 2.3 (2.3) **Control group**: 2.8 (2.1)	The participants in the control group had statistically significant improvement in the quality of life.
Saffari *et al.*, 2018 [41]/Iran	Hip and knee OA	*n* = 120 (IG = 60 CG = 60)	SF-12	Planned behaviour-based intervention	Participants received an educational program based on theory of planned behaviour-based intervention that was administered over 1 month.	Participants continued with their routine treatment of OA in the hospital.	**Vitality** **Intervention group:** 40 (20) **Control group**: 41 (20.1)	**Vitality** **Intervention group**: 54.7 (15.1) **Control group**: 54.3 (18.1)	There was no significant difference between the fatigue scores for both groups.
Gomiero *et al.*, 2018 [35]/Brazil	Knee OA	*n* = 64 (RTG = 32 SMTG = 32) M = 3 F = 61 Drop out = 2	SF-36 vitality subscale	Sensory-motor training or resistance training	Resistance training: This group received a 16-week exercise program twice a week, which included warm-up on a stationary bicycle for 10 min, quadriceps and hamstring strengthening exercises using ankle weights, isometric exercises for the quadriceps muscle and stretching for the lower limbs (stretching of the quadriceps, hamstrings and triceps). Sensory-motor training: Participants received the	No control group	**Vitality** **Resistance training group:** Mean = 46.4 (95% CI = 38.72, 54.08) **Sensory-motor training**: Mean = 55.6 (95% CI = 47.99, 63.21)	**Vitality** **Resistance training group:** Mean = 60.3 (95% CI = 53.13, 67.47) **Sensory-motor training:** Mean = 64.5 (95% CI = 58.41, 70.59)	Vitality increased in the resistance training group compared with the sensory-motor group.

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Table 1. (continued)

Authors/Country	OA type	Participant characteristic	Fatigue outcome tool	Intervention type	Intervention description	Control description	Baseline fatigue scores: Mean (SD), median [IQR]	Post-intervention fatigue scores: Mean (SD), median [IQR]	Findings & implications
					same warm-up and stretching program as the RT group, with the same duration and frequency of treatment, but with replacement of the strengthening program with: walking in different directions following verbal commands from the therapist; crossing steps while walking; crossing steps while walking backwards; implementing sudden changes of direction; walking on several types of surfaces (including mattresses); maintaining posture during use of a balance board; and using a minitrampoline to expose individuals to potentially destabilizing loads.				
Dilekci *et al.*, 2019 [38]/Turkey	Knee OA	$n = 305$ (IG = 159 CG = 146)	FACIT-F scale (version 4)	Balneotherapy + physiotherapy	Balneotherapy: 20 min of 38–40 °C mineral water bath (containing calcium bicarbonate, sulphate, carbon dioxide, and fluoride), in the curative pool after physiotherapy. This was done daily for 3 weeks. Physiotherapy: 20 min of 45 °C local heat pack, 30 min of 80 Hz frequency TENS and 6 min of therapeutic continuous ultrasound with frequency: 1 MHz, intensity: 1.5 W/cm2. All participants were also given home exercises for joint movement angles, stretching, and isometric strengthening.	This group received no intervention after physiotherapy.	**Fatigue** **Intervention group**: 38.04 (9.45) **Control group**: 35.62 (8.85)	**Fatigue** **Intervention group**: Not presented **Control group:** Not presented	Balneotherapy and physical therapy is a better intervention than physical therapy alone in the reduction of fatigue in patients with KOA.
Zhang *et al.*, 2019 [44]/China	Knee OA	$n = 90$ (IG = 60 CG = 30)	SF-36 vitality subscale	Acupuncture/electro acupuncture + usual care	Acupuncture: Acupuncture on ipsi-lateral acupoints of Neixiyan (EXLE 5), Dubi (ST 35), Zusanli	Participants in this group received only usual care.	**Vitality** **AP + UC**: 184 (46) **EA+ UC**: 187 (55) **Control group**: 183 (46)	**Vitality** **AP + UC**: 295 (56); 2 weeks FU = 331 (53); **EA+ UC**: 294 (65);	Fatigue showed better results following the treatment of AP + UC at 1st week ($p < 0.05$), and

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Table 1. (continued)

Authors/Country	OA type	Participant characteristic	Fatigue outcome tool	Intervention type	Intervention description	Control description	Baseline fatigue scores: Mean (SD), median [IQR]	Post-intervention fatigue scores: Mean (SD), median [IQR]	Findings & implications
		M = 47 F = 43			(ST 36), Yinlingquan (SP 9), Ququan (LV 8), Liangqiu (ST 34), Xuehai (SP 10) and Ashi point (pain point) once a day for 30 min. Electro acupuncture: Direct current and dilatational wave were delivered with a medical Hwato Electronic Acupuncture Treatment Instrument (SDZ-II, Suzhou, China), at 2/100 Hz frequency and 0.2 ms pulse width for 30 min. Usual care: Use of analgesics and drugs for activating blood circulation.			2 weeks FU = 337 (56) **Control group**: 265 (49); 2 weeks FU = 307 (51)	EA + UC at 2nd weeks ($p < 0.05$).
Lin *et al.*, 2020 [50]/Taiwan	Knee OA	$n = 80$ (AVG Group = 40 Exercise Group = 40) M = 39 F = 41 Drop out = 1	Multidimensional Fatigue Inventory	Active video games (AVGs) or exercise	AVG: Participants received hot packs on the knees for 20 min followed by TENS for 20 min, after which they played active video games for 20 min that required them to move their trunk and lower limbs as fast as possible to tread on the step-sensing pad placed on the floor. They had 3 sessions a week for 4 weeks. Exercise: This group participated in therapeutic exercises comprising of a stretching warm up, stabilization exercises, weight-shift training, cycling for 10 min and a stretching cooling down. This totalled 20 min.	No control group	**Fatigue** **AVG group**: Not presented **Exercise Group**: Not presented	**Fatigue** **AVG group**: Not presented **Exercise Group**: Not presented	AVGs improved physical functional performance, (which may include fatigue scores) more than therapeutic exercises did.
Gomes *et al.*, 2020 [36]/Brazil	Knee OA	$n = 100$ (IG = 80 CG = 20) M = 8 F = 92 Dropout = 0	World Health Organization Quality questionnaire of Life (WHOQOL)	Exercise program combined with electro physical modalities	Exercise only: Warm up on a treadmill for 10mins, supine bridge, straight leg raise in supine position, seated knee extension (90° to 45° of knee flexion), prone knee flexion, wall	Exercise+ placebo: At the end of the exercise protocol intervention, an ultrasound device was used to perform the placebo therapy for 20 min.	**Fatigue** **Exercise only**: 3.05 (0.6) **Exercise + ICT**: 3.0 (0.65) **Exercise + SDT**: 3.25 (0.55) **Exercise + photo**: 3.10	**Fatigue** **Exercise only**: 2.15 (0.58) **Exercise + ICT**: 2.05 (0.60) **Exercise + SDT**: 2.35 (0.59)	All the interventions were found to significantly decrease fatigue.

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Table 1. (continued)

Authors/Country	OA type	Participant characteristic	Fatigue outcome tool	Intervention type	Intervention description	Control description	Baseline fatigue scores: Mean (SD), median [IQR]	Post-intervention fatigue scores: Mean (SD), median [IQR]	Findings & implications
					squat (0° to 60° of knee flexion), hip abduction/lateral rotation/extension in side-lying position, hip abduction in standing position, isometric contraction hip extension/lateral rotation in prone position. Exercise +ICT: At the end of each exercise session, participants in this group received ICT four electrodes (8 × 6 cm) were placed around the affected knee joint. The intensity of the stimulator was kept at a level considered strong, but comfortable, throughout the treatment time which was 40 min. Exercise + SDT: A thermo-pulse device set to continuous mode, 27.12-MHz frequency and 150-W input was used for 20 min, and the intensity was defined based on each participant reporting a warm sensation. A standard size malleable electrode (16 × 20 cm) was applied to the anterior area of the thigh, 5 cm above the upper border of the patella, and a second electrode was applied on the posterior area of the leg. Exercise + photo: This group underwent photo bio-modulation therapy using a laser pulse device. Treatment was administered in contact with the skin using a dose of 6J/cm2 applied on eight points, with a total dose of 48J/cm2, each session.		(0.55) **Exercise+ placebo:** 3.05 (0.68)	**Exercise + photo:** 2.10 (0.55) **Exercise+ placebo:** 2.05 (0.75)	
Arfaei Chitkar *et al.*, 2021 [42]/Iran	Knee OA	$n = 64$ (IG = 32	SF-36 vitality subscale	Mobile app-based instruction	Participants received routine medical care. They also had education about OA and its	Participants received routine medical care and education about OA and its causes, OA	**Vitality** **Intervention group:** 50.96 (13.50)	**Vitality** **Intervention group:** 67.09 (11.74)	The use of mobile app-based instructions may improve the vitality of

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Table 1. (continued)

Authors/Country	OA type	Participant characteristic	Fatigue outcome tool	Intervention type	Intervention description	Control description	Baseline fatigue scores: Mean (SD), median [IQR]	Post-intervention fatigue scores: Mean (SD), median [IQR]	Findings & implications
		CG = 32) Dropout =4			causes, OA risk factors, the healthy diet and nutrients, treatment modalities, and the exercises for OA patients, only through the app.	risk factors, the healthy diet and nutrients, treatment modalities, and the exercises for OA patients via 2 face to face sessions.	**Control group:** 49.82 (11.21)	**Control group:** 56.72 (10.46)	patients suffering from KOA.
Tore *et al.*, 2022 [39]/Turkey	Knee OA	*n* = 48 (IG = 25 CG = 25) F = 43 M = 5 Dropout = 2	Fatigue severity scale (FSS)	Tele rehabilitation	Participants performed their exercises via video conference simultaneously, accompanied by a physiotherapist. This was carried out 3 times weekly, for 45- 60 min for 8 weeks.	Participants were given a brochure showing exercises and explaining how to do each exercise.	**Fatigue** **Intervention group:** 5.07 (1.01) **Control group:** 5.26 (1.44)	**Fatigue** **Intervention group :** 2.95 (1.28) **Control group:** 4.87 (1.16)	Fatigue was significantly lower in the tele rehabilitation group in comparison to the control group, post-exercise.
Navali *et al.*, 2012 [28]/Iran (Cross over)	Knee OA	*n* = 99 (Group 1 = 44 Group 2 = 50) M = 12 F = 87 Drop outs = 5	100 mm Visual analogue fatigue scale	New pair of shoes with one pair half the height of the stairs.	The patients were asked to ascend and descend the stairs with and without the shoes. There was a 20 min rest time between the stages.	Cross over design Group 1 = (1^{st} activity—without shoe, 2^{nd} activity—with shoe) Group 2 = (1^{st} activity—with shoe, 2^{nd} activity—without shoe)	**Fatigue** Group 1 **Without shoe** Before ascending = 0.12 (0.33) After ascending = 0.61 (0.99) Before descending = 0.18 (0.44) After descending = 0.91 (1.09) **With shoe** Before ascending = 0.20 (0.53) After ascending = 1.06 (1.40) Before descending = 0.28(0.61) After descending = 1.30 (1.44)	**Fatigue** Group 2 **With shoe** Before ascending = 0.04 (0.20) After ascending = 0.60 (1.07) Before descending = 0.06 (0.25) After descending = 0.64 (0.98) **Without shoe** Before ascending = 0.13 (0.34) After ascending = 0.75 (1.19) Before descending = 0.24 (0.48) After descending = 1.20 (1.42)	A new shoe decreased fatigue during descending and ascending of the stairs.

Table 2. Effects of Exercise interventions on fatigue or vitality

	Interventions		
Author/Year	**Intervention**	**Control**	**Effectiveness of exercise versusssss control**
Outcome			
Diracolgu *et al.* [25] (2005) *SF-36 Vitality subscale*	Baseline 45 (16.5) Post 54 (19.5) Change 9 (3)	Baseline 42.14 (17.66) Post 43.5 (18.3) Change 1.36 (0.64)	Exercise interventions favoured fatigue or vitality
Diracolgu *et al.* [26] (2008) *SF-36 Vitality subscale*	Baseline 45(16.53) Post 51.07 (15.4) Change 6.07 (−1.13)	Baseline 42.14 (17.66) Post 43.82 (11.93) Change 1.68 (−5.73)	Exercise interventions favoured fatigue or vitality
Ebnezar *et al.* [48] (2011)[a] *SF-36 Vitality subscale*	Baseline 66.6 (36) Post 36.35 (6.08) Change 30.25 (−29.92)	Baseline 64.91 (5.41) Post 63.20 (6.86) Change −1.71 (1.45)	Control interventions favoured fatigue or vitality
Hennig *et al.* [45] (2015) *11point Numeric rating scale*	Baseline NA Post −0.7 (3.4) Change −0.7	Baseline NA Post NA Change 0.5 (1.9)	Exercise interventions favoured fatigue or vitality
Da Silva *et al.* [34] (2015) *SF-36 Vitality subscale*	Baseline 56.0 (19.2) Post 72.0 (16.56) Change 16 (−2.64)	Baseline 60 (12.64) Post 58.3 (16.22) Change −1.7 (3.58)	Exercise interventions favoured fatigue or vitality
Kraub *et al.* [52] (2014)[d] *SF-36 Vitality subscale*	Baseline 63 (17) Post −1 (15) Change −63 (−2)	Baseline 63 (17) Post 0 (12) Change −63 (−5)	No differences between exercise and control interventions
Casilda-Lopez *et al.* [49] *(2017)* *Visual analogue scale*	Baseline 2.58 (1.57) Post 2.07 (1.58) Change −0.51 (0.01)	Baseline 2.75 (2.06) Post 3.84 (2.03) Change 1.09 (−0.03)	Exercise interventions favoured fatigue or vitality
Park *et al.* [32] (2017)[b] *PROMIS Fatigue-V 1.0 SF-8a*	Baseline 20 (NR) Post 18.1 (6.5) at 1 month follow-up Change −1.9 (NR)	Baseline NR Post 19.2 (7.4) at 1 month follow-up Change NR	No differences between exercise and control interventions
Kapetanovic *et al.* [54] (2018)[c] *SF-36 Vitality subscale*	Baseline 44.83 (11.02) Post NR Change 36.50 (7.21)	Baseline 45.66 (10.14) Post NR Change −2.50 (5.84)	No differences between exercise and control interventions

(continued)

Table 2. (continued)

Author/Year	Interventions		Effectiveness of exercise versusssss control
	Intervention	Control	
Gomiero *et al.* [35] (2018)	Baseline	Baseline	Exercise interventions favoured fatigue or vitality
	46.4 (NR)	60.3 (NR)	
	Post	Post	
	55.6 (NR)	64.5 (NR)	
	Change	Change	
	9.2 (NR)	4.2 (NR)	
Gomes *et al.* [36] (2020) *World Health Organisation Quality of Life Questionnaire*	Baseline	Baseline	No differences between exercise and control interventions
	3.05 (0.6)	Exercise + ICT: 3.0 (0.65) Exercise + SDT: 3.25 (0.55) Exercise + photo: 3.10 (0.55) Exercise + placebo: 3.05 (0.68)	
	Post	Post	
	2.15 (0.58)	Exercise + ICT: 2.05 (0.60) Exercise + SDT: 2.35 (0.59) Exercise + photo: 2.10 (0.55) Exercise+ placebo: 2.05 (0.75)	
	Change	Change	
	−0.9 (−0.2)	Exercise + ICT: −0.95 (−0.05) Exercise + SDT: −0.95 (0.04) Exercise + photo: −1 0 Exercise + placebo: −1 (0.07)	

[a] Intervention group used yoga and control group used exercise.
[b] Incomplete baseline information for control group.
[c] Incomplete data.
[d] Exercise plus additional intervention; NR: not reported.

with respect to short- and long-term effectiveness among people diagnosed with upper and/or lower limb OA. Intervention identified for the management of fatigue in OA include; exercise, activity pacing, yoga, CBT, BEMER therapy, aroma therapy, as well as wearing modified shoes. Most of the included studies (73.3%) focused on knee OA. Nineteen studies showed improvement in fatigue outcomes, however for studies that utilized exercises, six ($n = 11$) reported a positive improvement on fatigue.

In the current review, we found six out of eleven studies to be effective in reducing fatigue immediately [25, 26, 34, 45, 49, 54]. Previous studies have shown that exercise improves fatigue [55]. A recent meta-analysis by Labie *et al.* [55] reported exercise and other physical activity interventions to be effective in reducing fatigue symptoms in people with OA in the short term (Standardized mean difference = -0.22; 95% confidence interval was −0.43 to −0.01). The three studies included in the meta-analysis reported different interventions. Also, exercises have been shown to improve fatigue in other chronic conditions such as RA, HIV, multiple sclerosis, chronic fatigue syndrome, and SLE [56]. In a recent systematic review, physical activity was found to be effective in reducing fatigue symptoms in a variety of inflammatory rheumatic and musculoskeletal diseases such as RA, SLE, spondyloarthritis, systemic sclerosis and Sjogren's syndrome [19]. An examination of the 49 studies encompassed in the review by Hulme *et al.* [56] shed light on the pivotal role of exercise as an effective intervention for mitigating fatigue in individuals grappling with RA, multiple sclerosis, chronic fatigue syndrome, and HIV. Evidence indicates that regular low to moderate intensity exercise boosts energy [57]. A proposed mechanism is through the release of epinephrine and norepinephrine. Although, being stress-related hormones, epinephrine and norepinephrine increase energy levels when released in small quantities during exercise [58]. Puetz *et al.* [59] found that low to moderate intensity exercise performed three times a week reduced fatigue symptoms by 65%. Further, their findings showed that exercise intensity predicted fatigue levels, with low- and moderate-intensity being protective of fatigue [59]. Relatedly, higher intensity of exercise can increase the release of stress hormones in higher amounts which can be a deterrent to the energy levels of individuals [57].

CBT is an evidence-based psychological approach to self-management that can help people with chronic pain improve psychological and physical functioning and prevent disability [30]. For people with OA, CBT alleviates symptoms of pain, anxiety, depression and physical function [60]. The study by Murphy *et al.* [30] identified in this review has added fatigue to the existing symptoms improved by CBT, although more studies are needed in this area.

Our review found conflicting evidence on the effects of complementary and alternative medicine interventions on fatigue. These current findings contrast the findings of Hulme *et al.* [56] which reported beneficial effects of complementary and alternative medicine interventions such as acupuncture, phototherapy, and massage on fatigue in chronic conditions. The majority of interventions had reductive effects on fatigue across the spectrum of long-term health conditions, with the exception of acupuncture which did not yield substantial fatigue reduction among individuals with RA. While the Hulme *et al.* review [56] reported that acupuncture was not effective, our current review found evidence of the beneficial effect of acupuncture on fatigue within one week and after two weeks in people with OA [44]. A likely discrepancy in the findings of these two reviews may be due to an improved quality of

Figure 2. ROB plot for parallel RCTs

evidence in the current review. Also, activity pacing, which is generally considered a strategy to conserve energy and to modify activities for people with chronic conditions [61], was reported by Murphy *et al.* [30] to significantly reduce fatigue levels both immediately and overtime in a 10-week follow-up. Activity pacing aims to reduce the fluctuation between high and low energy levels, in order to improve function and reduce the presence of overwhelming symptoms [62, 63]. However, it is important to note that activity pacing is mostly effective when individualized [29]. Kabiri *et al.* [40] reported clinically non-significant reductions in fatigue scores after massage therapy. However, Ozdemir *et al.* [64] found that massage therapy significantly decreased fatigue in end-stage renal disease patients. Similarly, Sakamoto *et al.* [65] reported a decrease in fatigue following massage therapy among post-partum women. Hou *et al.* [66], echoing the conflicting nature of the evidence on the effect of massage on fatigue, reported that some studies showed significant improvement (decrease) in fatigue while others failed to show such improvement. These conflicting findings could be attributed to the diverse methodologies employed in these studies. For instance, there is a challenge in determining the appropriate classification of dosage that is deemed therapeutic. To gain a comprehensive understanding of the effectiveness of massage in addressing fatigue among individuals with upper and lower limb osteoarthritis OA, future studies should focus on determining the optimal dosage of massage therapy, such as duration and frequency of treatment.

It is important to note that only six studies considered fatigue or vitality as a primary outcome. This shows how little attention fatigue has received as a symptom in OA, in comparison to pain and physical function, despite being flagged as an OA research priority by Outcome Measures in Rheumatoid Arthritis Clinical Trials-Osteoarthritis Research Society International (OMERACT-OARSI) [67].

Strengths and limitations of the study

To our knowledge, this represents the first systematic review designed to identify non-pharmacological fatigue interventions among individuals with upper and lower limb OA and assess the effects of these identified interventions. Some of the studies in this review did not include sufficient data such as mean and standard deviation of outcome scores at follow-up. The majority of the studies were only in the knee OA

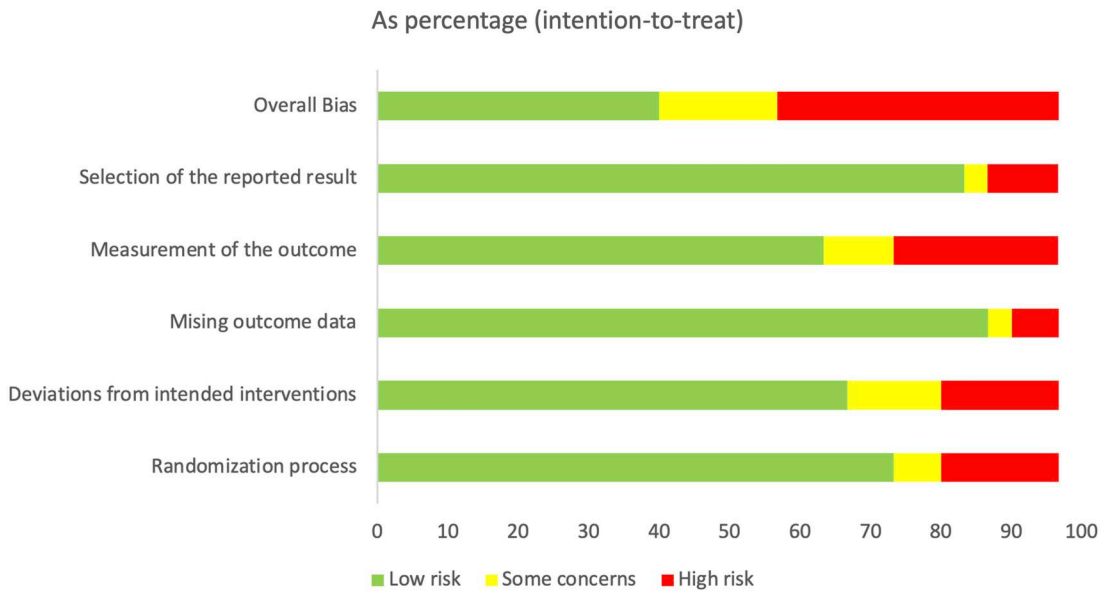

Figure 3. Summary of risk of bias for parallel RCTs

population which is not representative of the upper and lower limb OA populations. In addition, different fatigue interventions and fatigue outcomes were used in these studies, limiting the ability to conduct a meta-analysis or directly compare results. Only six studies used fatigue as primary outcomes and these studies did not include participants with pre-existing clinically significant fatigue at baseline. In addition, varied RCT designs were included which led to the presentation of our findings with a narrative synthesis.

Recommendations

More experimental investigations should be conducted on other recently suggested non-pharmacological interventions (ie, activity pacing, CBT, telerehabilitation, complementary and alternative therapies) for managing fatigue in OA as this may provide a broader horizon for fatigue management. Education of individuals with OA on symptoms and management should be made a priority in the clinical setting. Clinicians should discuss evidence-based fatigue treatment options with their patients. In addition, patients' needs, preferences, disease status and other contextual factors regarding fatigue management should be considered during management [68]. Public health advocates should be adequately equipped with the knowledge to educate community-dwelling individuals on OA and its management. Policymakers and educationists should consider fatigue as a core symptom of OA in line with OMERACT-OARSI [67] and more so as it has been shown to have significant effects on the productivity of individuals affected [11].

Conclusion

In this systematic review, diverse non-pharmacological interventions for fatigue management among individuals with upper and lower limb OA were identified. However, most interventions were targeted at lower limb OA, particularly knee OA. Exercise interventions appear to be the most promising intervention for fatigue with the majority favouring fatigue improvement. In addition, CBT has limited evidence of beneficial effects. Currently, there is insufficient evidence regarding the effectiveness of the majority of the identified interventions, including complementary and alternative therapies, telerehabilitation, and activity pacing examined in this review. Large-scale RCTs are needed to ascertain the effects of these interventions on fatigue in individuals with upper and lower limb OA.

Supplementary material

Supplementary material is available at *Rheumatology Advances in Practice* online.

Data availability

Data are available upon reasonable request to the corresponding author. All data relevant to this study are included in the article.

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Systematic Review and Meta-Analysis