The Influence of Exercise Intensity on Psychosocial Outcomes in Musculoskeletal Disorders: A Systematic Review

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Context: Psychosocial parameters play an important role in the onset and persistence of chronic musculoskeletal disorders (CMSDs). Exercise therapy is a valuable therapeutic modality as part of CMSD rehabilitation. Hereby, exercise intensity is an important factor regarding changes in pain and disability in multiple CMSDs. However, the impact of exercise intensity on psychosocial outcomes remains poorly explored.

Objective: To identify the effects of different modes of exercise intensity on psychosocial outcomes in persons with CMSDs.

Data Sources: A systematic search was conducted up to November 2020 using the following databases: PubMed/MEDline, PEDro, Cochrane Library, and Web of Science.

Study Selection: Studies reporting exercise therapy in CMSDs with a predefined display of exercise intensity and an evaluation of at least 1 psychosocial outcome were included.

Study Design: Systematic review.

Level of Evidence: Level 2a.

Data Extraction: Data regarding demographics, exercise intensity, and psychosocial outcomes were included in a descriptive analysis. Methodological quality was assessed using the PEDro scale and Critical Appraisal Skills Programme (CASP) checklist.

Results: A total of 22 studies, involving 985 participants (with fibromyalgia, chronic low back pain, knee osteoarthritis, psoriatic arthritis, and axial spondyloarthritis) were included (mean PEDro score = 5.77/10). The most common psychosocial outcomes were quality of life (QoL) (n = 15), depression (n = 10), and anxiety (n = 9). QoL improved at any exercise intensity in persons with fibromyalgia. However, persons with fibromyalgia benefit more from exercising at low to moderate intensity regarding anxiety and depression. In contrast, persons with chronic low back pain benefit more from exercising at a higher intensity regarding QoL, anxiety, and depression. Other CMSDs only showed limited or conflicting results regarding the value of certain exercise intensities.

Conclusion: Psychosocial outcomes are influenced by the intensity of exercise therapy in fibromyalgia and chronic low back pain, but effects differ across other CMSDs. Future research is necessary to determine the exercise intensity that yields optimal exercise therapy outcomes in specific CMSDs.

Keywords: chronic musculoskeletal disorder; exercise therapy; intensity; psychosocial parameters

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Chronic musculoskeletal disorders (CMSDs) are common at all ages and across all sociodemographic strata of society.[88] Their point prevalence averages approximately 30%.[15] As such, CMSDs account for the most common cause of disability and severe long-lasting pain.[88] Globally, this translates to 21.3% of the total years lived with disability.[47] Unfortunately, prevalence of CMSDs is predicted to increase by more than 50% by 2050,[11] highlighting the need to optimize management.

To interpret disability levels in CMSDs appropriately, a biopsychosocial perspective should be used. Besides the often-restricted impact of biomedical factors in CMSDs in explaining disability, it is therefore important to consider the role that psychological and social factors play. Indeed, psychosocial factors have been identified as important predictors for the persistence and level of disability of CMSDs.[3,5,10,85,89] For example, perceived self-efficacy (ie, a person's own judgment of capability to perform a certain activity to attain a certain outcome[91]) relates to pain and disability in chronic low back pain as well as to disability in arthritis, fibromyalgia, and shoulder pain.[1,17,20,52] Higher levels of pain catastrophizing predict development of long-term pain, increase disability, and yield higher health care costs among persons with chronic low back pain and peripheral joint pain. Symptoms of depression and anxiety contribute to impaired long-term outcomes such as physical disability and work disability in several CMSDs. Likewise, movement-related fear often predicts progression of pain intensity, quality of life (QoL), and disability.[46]

Exercise therapy is advised as a primary treatment modality for CMSDs.[43] It significantly improves physical fitness and consequently decreases disability and pain levels.[27] The most frequently applied modes of exercise therapy are cardiorespiratory training, muscular strength training, or a multimodal protocol in which the previous modes are combined.[68] But, even though exercise therapy is frequently applied for CMSDs, overall treatment success rates remains modest.[36,76] Two distinct reasons are suggested in literature. First, exercise therapy research in CMSDs so far has predominantly focused on improving physical function.[36,76] However, there is ambiguity concerning the relationship between changes in physical function targeted by the treatment (eg, flexibility, strength, endurance) and changes in clinical outcome (eg, pain, disability).[74] It is conceivable that other mechanisms elicited by exercise therapy, such as improvements on psychosocial outcomes, play an important role in the effect size of treatment success.[74] This line of thought is supported by a recent review on exercise therapy in chronic low back pain which showed that 36% of studies propose at least 1 working mechanism of the therapy to have a psychosocial basis.[81] Moreover, while it was initially hypothesized that impact of psychosocial factors was dependent on specifics of each musculoskeletal disorder, psychosocial correlates of several disabling CMSDs have actually been found to be quite comparable.[81,86] Second, an exercise program should be described using FITT principles, which includes the modalities Frequency, Intensity, Time, and Type or mode of exercise.[12] But, for a variety of CMSDs, these modalities of exercise therapy to optimize treatment efficacy have not yet been evaluated or displayed properly.[11,33] This contributes to considerate heterogeneity between study protocols and ultimately results in difficulties with comparing data and making practical guideline statements.

To maximize the impact of exercise therapy, exercise intensity is one of the most important factors to provide the correct physiological response.[25] For CMSDs specifically, recent research in exercise therapy has shown that the magnitude of exercise intensity is determinative for the effect size of improvements in disability and pain intensity.[13,77,82] However, there is no consensus concerning optimal FITT principles to affect psychosocial outcomes.[2,56,72] This is particularly relevant because the impact of exercise intensity on psychosocial outcomes can be explained by both psychological and neurophysiological mechanisms. With regard to psychological mechanisms, training at a higher intensity might provide persons with more pronounced mastery experiences, which in turn can lead to improved self-efficacy and psychosocial well-being.[6,44,62] For example, Jung et al[37] already showcased that in healthy persons high-intensity interval training increases self-efficacy beliefs as it breaks down exercise sessions into short, surmountable bursts, potentially allowing for multiple successful experiences. Likewise, Bilberg et al[7] found that in axial spondyloarthritis, a combined high-intensity cardiorespiratory and resistance training program was perceived as challenging for both body and mind and described as a positive experience, with rapid bodily effects that strengthened respondents' faith in their own bodies. The latter also changed the respondents' attitude and motivation for exercise and made them start taking charge of their health by challenging the disease.[7] With regard to neurophysiological mechanisms, exercise intensity can influence the inflammatory response[19] and the response of stress-related biomarkers such as brain-derived neurotrophic factor, opioids, and cortisol,[65,66] which in turn affect pain experience and affective response.[55,66] Therefore, this systematic review investigated the effects of different modes of exercise intensity on psychosocial outcomes in adult persons with CMSDs.

METHODS

This review was reported according to the (PRISMA) Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[53] It was submitted to the international prospective register of systematic reviews (PROSPERO) with ID 197575. The systematic search, screening process, assessment of methodological quality, and data extraction were all performed by 2 reviewers independently.

Literature Search

The following electronic databases were searched until November 28, 2020: PubMed/MEDline, PEDro, Cochrane Library, and Web of Science. Database-specific search terms or keywords in title/abstract were used to find clinical trials studying the effects of different modes of exercise intensity on psychosocial outcomes in adult persons with CMSDs. A varying combination of the following search terms and their derivatives was used: *chronic musculoskeletal disorders*, *pain*, *rehabilitation*, and *psychosocial factors*. Details of the literature search for each database are displayed in Appendix 1 (available in the online version of this article). Boolean operators "OR" and "AND" were used to combine search terms. Reference lists of the eligible studies and gray literature were screened to identify remaining potentially relevant studies.

Eligibility Criteria

Studies were included that involved (1) persons with a CMSD (ie, ongoing pain felt in the bones, joints, and/or soft tissues that persists for longer than 3 months[11]); (2) exercise therapy of at least 8 weeks as sole intervention in at least 1 of the study groups; (3) evaluation of 1 or more psychosocial outcomes, including affective, perceptual-cognitive, behavioral factors, or general mental health factors; (4) English or Dutch language; (5) adults between 18 and 65 years of age; (6) objective measures of exercise intensity defined as $\%VO_{2max}$ (maximal oxygen uptake), $\%HR_{max}$ (maximum heart rate), %HRR (heart rate reserve), or %1RM (1-repetition maximum); and (7) a randomized clinical trial or longitudinal cohort study design. Exclusion criteria were (1) (systematic) reviews, (2) case studies, (3) replies to research results, (4) interviews, (5) and research protocols.

Study Selection

After duplicate removal, all titles, abstracts, and full texts of the articles were screened in a blinded manner according to the eligibility criteria. Disagreement was solved by discussion and consensus.

Assessment of Methodological Quality

Methodological quality was assessed using the 11-item PEDro scale for randomized controlled trails and the 12-item Critical Appraisal Skills Programme (CASP) checklist for cohort studies. For PEDro, the following scoring criteria were applied: a score from 9 to 10 = excellent quality, 6 to 8 = good quality, 4 to 5 = fair quality, and below 4 = poor quality.[22] CASP does not provide a scoring grid and was evaluated in a qualitative manner only. After initial screening, a consensus meeting was held between the 2 reviewers. First, Cohen kappa coefficient was calculated to assess the agreement between reviewers.[50] Then, disagreement was solved by discussion and consensus.

Data Extraction

The following data were extracted from the included studies according to a template that was agreed on in advance: (1) author names, (2) year of publication, (3) participant characteristics (pathology, n, mean age, sex); (4) exercise intensity (as a percentage of HR_{max}, HRR, or 1RM), (5) intervention type (cardiorespiratory, resistance, or combined training), (6) intervention duration (in weeks), (7) exercise frequency (in days/week), (8) psychosocial outcome measures (categorized into affective factors, perceptual-cognitive factors, behavioral factors, or general mental health[80]), and (9) within-group baseline to postintervention therapy results on psychosocial outcome measures. Data extraction is summarized in Table 1. For further data extraction of the main outcome of interest, exercise intensity was divided into 3 categories (low, moderate, high).[25,75] A detailed overview of intensity ranges in each category is shown in Table 2. Studies with changes in exercise intensity across different categories during the study protocol were discussed separately. A detailed overview of which psychosocial outcomes belong to the predefined categories is shown in Table 3. A calculation of effect sizes (Cohen *D* or Hedge *g*) was attempted through evaluation of within-group outcomes. When means and standard deviations were not provided in the article, respective authors were contacted by email and data were requested. However, insufficient data were obtained from a vast majority of the source articles. Hence, no effect sizes were displayed in this review and results were evaluated descriptively.

RESULTS

Results Study Selection

A flowchart of the study selection process is displayed in Figure 1. The search strategy resulted in 7403 articles. Based on the eligibility criteria, 19 articles were included. The most frequent reason (40.1%) for exclusion by abstract screening was lack of exercise therapy as the sole intervention in one of the groups. The most frequent reason (40.9%) for excluding full-text studies was the lack of an objective description of exercise intensity. An overview of studies excluded based on full-text screening is displayed in Appendix 2 (available online). Screening of reference lists of eligible studies resulted in 3 extra relevant studies. A total of 22 studies were found eligible to be included. Patient data from 2 studies—namely, Ericsson et al[23] and Larsson et al[45]—were extracted together, as they evaluated the same patient sample. This also applied to the 2 studies of Smeets et al.[69,70] Finally, data involving 985 participants were used.

Results: Quality Assessment

Results of the quality assessment of the included studies are presented in Appendix 3 (available online). Mean score of the PEDro scale was 5.77 (SD, ±1.70; range, 2-8). Therefore, overall quality was rated as fair. More specifically, 13 studies were classified as good quality,[14,18,23,31,32,34,35,45,54,64,69,70,77] 7 as fair,[8,13,26,28,38,39,67] and 2 as poor.[41,51] Criteria 1 (eligibility criteria), 10 (between-group comparisons), and 11 (point measures and measures of variability) of the PEDro scale were fulfilled in more than 90% of the studies. Criteria 5 (blinding of patients) and 6 (blinding of therapists) were not satisfied in any study. These criteria are often not feasible in studies involving exercise therapy.[4] Only 1 longitudinal study[41] was included. It scored 9/12 on the CASP checklist. It lost points because of lacking transparent information on possible confounding factors and

Table 1. Results of data extraction

Reference	Patients (n; Mean Age; Sex)	Dropouts, n (% Rate)	Exercise Intensity Value	Intervention Type	Intervention Period	Exercise Frequency	Exercise Intensity Description	Psychosocial Outcome Measures	Results of Psychosocial Outcomes
LIT									
Gavi et al, 2014	Fibromyalgia (80; 46.5 y; 0 M)	14 (18)	45%	Resistance exercises (IG1)	16 weeks	2×/week	% 1RM	QoL (FIQ and SF-36), depression (BDI), anxiety (STAI)	FIQ scale: PP = ↗ in IG1 BDI scale: PP = ↗ in IG1 STAI scale: PP = ↗ in IG1 SF-36 functional capacity: PP = ↗ in IG1 SF-36 physical aspects: PP = ↗ in IG1 SF-36 pain: PP = ↗ in IG1 SF-36 general state of health: PP = ↗ in IG1 SF-36 vitality: PP = ↗ in IG1 SF-36 social aspects: PP = ↗ in IG1
Harts et al, 2008	CLBP (21; 42 y; 21 M)	2 (10)	20% (LI)	Resistance exercises LI (IG1)	8 weeks	Week 1-2: 2×/week Week 3-8: 1×/week	%1RM	QoL (SF-36) and fear of movement (TSK)	SF-36 overall scores: PP = ? in IG1 TSK scale: PP = ? in IG1
Helmhout et al, 2004	CLBP (40; 40 y; 4 0 M)	4 (10)	20% (LI)	Resistance exercises LI (IG1)	12 weeks	Week 1-2: 2×/week Week 3-12: 1×/week	%1RM	QoL (SF-36) and fear of movement (TSK)	SF-36 overall scores: PP = ? in IG1 TSK scale: PP = ? in IG1
MIT									
Bircan et al, 2008	Fibromyalgia (26; 47.2y; 0 M)	4 (13)	60%-70%	Aerobic exercises (IG1) Resistance exercises (IG2)	8 weeks	3×/week	HR_{max}	Anxiety, depression (HADS) and QoL (SF-36)	HADS-depression scale: PP = ↗ in IG1, ↗ in IG2 HADS-anxiety scale: PP = NS in IG1, NS in IG2 SF-36 bodily scale: PP = ↗ in IG1, ↗ in IG2 SF-36 social functioning: PP = ↗ in IG1
Glasgow et al, 2017	Fibromyalgia (26; 50.5 y; 0 M)	1 (4)	50%-60%	Resistance exercises (IG1)	8 weeks	2×/week	%1RM	QoL (FIQ) and pain catastrophizing (PCS)	FIQ scale: PP = ↗ in IG1 PCS scale: PP = NS in IG1

(continued)

Table 1. (continued)

Reference	Patients (n; Mean Age; Sex)	Dropouts, n (% Rate)	Exercise Intensity Value	Intervention Type	Intervention Period	Exercise Frequency	Exercise Intensity Description	Psychosocial Outcome Measures	Results of Psychosocial Outcomes
Gowans et al, 2001	Fibromyalgia (51; 47.2 y; 3 M)	20 (39)	60%-75%	Aerobic exercises (IG1)	24 weeks	3×/week	$\%HR_{max}$	Depression (BDI), anxiety (STAI), general mental health (MHI), QoL (FIQ) and self-efficacy (ASES)	BDI total score: PP = ↗ in IG1 BDI-cognitive scale: PP = ↗ in IG1 BDI-affective scale: PP = ↗ in IG1 STAI scale: PP = ↗ in IG1 MHI total score = NS in IG1 MHI positive affect scale: PP = ↗ in IG1 MHI depression scale: PP = ↗ in IG1 MHI behavioural scale: PP = ↗ in IG1 MHI emotional control scale: PP = ↗ in IG1 FIQ total scores: PP = ↗ in IG1 ASES all subscales: PP = ↗ in IG1
Gowans et al, 2004	Fibromyalgia (18; 47.3 y; 2 M)	8 (22)	60%-75%	Aerobic exercises (IG1)	24 weeks	3×/week	$\%HR_{max}$	Depression (BDI), anxiety (STAI), QoL (FIQ) and self-efficacy (ASES)	BDI total score: PP = ↗ in IG1 (6 and 12 months) BDI-cognitive scale: PP = ↗ in IG1 (12 months) BDI-affective scale: PP = ↗ in IG1 (12 months) STAI scale: PP = ↗ in IG1 (6 months) FIQ total scores: PP = ↗ in IG1 (6 and 12 months) ASES-pain scale: PP = ↗ in IG1 (6 and 12 months) ASES function-scale: PP = ↗ in IG1 (6 and 12 months)
Harts et al, 2008	CLBP (23; 44 y; 23 M)	3 (13)	50% (HI)	Resistance exercises HI (IG2)	8 weeks	Week 1-2: 2×/week Week 3-8: 1×/week	%1RM	QoL (SF-36) and fear of movement (TSK)	SF-36 overall scores: PP = ? in IG2 TSK scale: PP = ? in IG2

(continued)

Table 1. (continued)

Reference	Patients (n; Mean Age; Sex)	Dropouts, n (% Rate)	Exercise Intensity Value	Intervention Type	Intervention Period	Exercise Frequency	Exercise Intensity Description	Psychosocial Outcome Measures	Results of Psychosocial Outcomes
Helmhout et al, 2004	CLBP (41; 41 y; 41 M)	2 (5)	50%-70% (HI)	Resistance exercises HI (IG2)	12 weeks	Week 1-2: 2×/week Week 3-12: 1×/week	%1RM	QoL (SF-36) and fear of movement (TSK)	SF-36 overall scores: PP = ? in IG2 TSK scale: PP = ? in IG2
Kell and Asmundson, 2009	CLBP (18; 38.4 y; 15 M, 7 F)	nd	53%-72%	Resistance exercises (IG1) Aerobic exercises (IG2)	16 weeks	3×/week	%1RM	QoL (SF-36)	SF-36 mental scale: WG = ↗ in IG1, WG = ↗ in IG2 SF-36 physical scale: WG = ↗ in IG1
King et al, 2008	KOA (14; 48.4 y; 12 M, 2 F)	0 (0)	60%	Resistance exercises (IG1)	12 weeks	3×/week	%1RM	Self-efficacy (ASES)	ASES scale: PP = NS in IG1
Roger-Silva et al, 2018	PA (20; 54.2 y; 10 M, 21 F)	0 (0)	60%	Resistance exercises (IG1)	12 weeks	2×/week	%1RM	QoL (SF-36)	SF-36 pain scale: PP = ↗ in IG1 SF-36 general health scale: PP = ↗ in IG1
HIT									
Chatzitheodorou et al, 2007	CLBP (10; 42.4 y; 10 M, 5 F)	0 (0)	60%-85%	Aerobic exercises (IG1)	12 weeks	3×/week	%HRR	Anxiety and depression (HADS)	HADS-depression scale: PP = ↗ in IG1
Chatzitheodorou et al, 2008	CLBP (64; 40.1 y; 26 M)	3 (5)	60%-85%	Aerobic exercises (IG1)	12 months	3×/week	%HRR	Anxiety and depression (HADS)	HADS-depression scale: PP = ↗ in IG1
Murtezani et al, 2011	CLBP (58; 50 y; 26 M)	8 (14)	70%-85%	Aerobic exercises (IG1)	12 weeks	3×/week	$\%HR_{max}$	Anxiety and depression (HADS)	HADS-depression scale: PP = ↗ in IG1 HADS-anxiety scale: PP = ↗ in IG1
Smeets et al, 2006	CLBP (53; 42.7 y; 31 M)	1 (2)	65%-80% 70%	Aerobic exercises and resistance exercises (IG1)	10 weeks	3×/week	$\%HR_{max}$ %1RM	Depression (BDI)	BDI total score: PP = ↗ in IG1

(continued)

Table 1. (continued)

Reference	Patients (n; Mean Age; Sex)	Dropouts, n (% Rate)	Exercise Intensity Value	Intervention Type	Intervention Period	Exercise Frequency	Exercise Intensity Description	Psychosocial Outcome Measures	Results of Psychosocial Outcomes
Smeets et al, 2006								Pain catastrophizing (PCL)	PCL-catastrophizing: PP = ↗ in IG1
Sveaas et al, 2018	ASA (13; 48.5 y; 2 M)	3 (23)	90%-95%	Aerobic and resistance exercises (IG1)	12 weeks	2×/week	$\%HR_{max}$	Emotional distress (GHQ-12)	GHQ-12 scale: PP = ↗ in IG1
Progression through different categories									
Da Costa et al, 2005	Fibromyalgia (39; 49.2 y; 0 M)	0 (0)	60%/70% to 75%/85%	Aerobic exercises (IG1)	12 weeks		$\%HR_{max}$	QoL (FIQ) and psychological distress (SCL-90-R)	FIQ scale: PP = ↗ in IG1 SCL-90-R psychological distress scale: PP = ↗ in IG1
Ericsson et al, 2016	Fibromyalgia (67; 22-64 y; 0 M)	17 (26)	40%-80%	Resistance exercises (IG1)	15 weeks	2×/week	%1RM	Fatigue (MFI and FIQ-fatigue), pain catastrophizing (PCS), anxiety and depression (HADS)	MFI-20 general fatigue scale: PP = ↗ in IG1 MFI-20 physical fatigue scale: PP = ↗ in IG1 MFI-20 mental fatigue scale: PP = ↗ in IG1 FIQ-fatigue scale: PP = ↗ in IG1 PCS-rumination scale: PP = ↗ in IG1 PCS-magnification scale: PP = ↗ in IG1 PCS-helplessness scale: PP = ↗ in IG1 PCS total score: PP = ↗ in IG1 HADS-depression scale: PP = NS in IG1 HADS-anxiety scale: PP = NS in IG1
Larsson et al, 2015	Fibromyalgia (67; 22-64 y; 0 M)	17 (26)	40%-80%	Resistance exercise (IG1)	15 weeks	2×/week	%1RM	QoL (FIQ and SF-36), pain-related acceptance (CPAQ) and fear avoidance beliefs (FAB-Q)	FIQ total scores: WG = ↗ in IG1 SF-36 mental scale: PP = ↗ in IG1 SF-36 physical scale: PP = ↗ in IG1 CPAQ scale: PP = ↗ in IG1 FAB-Q scale: PP = NS in IG1

(continued)

Table 1. (continued)

Reference	Patients (n; Mean Age; Sex)	Dropouts, n (% Rate)	Exercise Intensity Value	Intervention Type	Intervention Period	Exercise Frequency	Exercise Intensity Description	Psychosocial Outcome Measures	Results of Psychosocial Outcomes
Kell et al, 2011	CLBP (180; 42.3 y; 119 M, 84 F)	nd	50%-80%	Resistance exercises 2×/w (IG1) Resistance exercises 3×/w (IG2) Resistance exercises 4×/w (IG3)	13 weeks	2, 3, or 4×/ week	%1RM	QoL (SF-36)	SF-36 scale: PP = ↗ in IG1, ↗ in IG2, ↗ in IG3
Meyer and Lemley, 2000	Fibromyalgia (16; 49.5 y; 0 M)	8 (50)	25%-60% (LI)	Aerobic exercises LI (IG1)	12 weeks (LI)	3×/week (HI)	%HRR	QoL (FIQ), depression (BDI) and anxiety (STAI)	FIQ total scores: PP = ↗ in IG1, NS in IG2 BDI scale: PP = NS in IG1, NS in IG2 STAI scale: PP = NS in IG1, NS in IG2
			40%-85% (HI)	Aerobic exercises HI (IG2)	24 weeks (HI)	Week 1-2: 2×/week; Week 3-12: 1×/week			
Schachter et al, 2003	Fibromyalgia (107; 41.6 y; 0 M)	36 (34)	40%/50% to 655/75%	Aerobic exercises (IG1) Aerobic exercise (IG2)	16 weeks	5×/week + 1×/day (SBE) 5×/week + 2×/day (LBE)	%HRR	QoL (FIQ), self-efficacy (CPSS) and psychological well-being (AIMS2)	FIQ-disease severity scale: PP = ↗ in IG1, ↗ in IG2 FIQ-symptoms scale: PP = ↗ in IG2 CPSS scale: PP = ↗ in IG1, ↗ in IG2 AIMS2 scale: PP = ↗ in IG2

1RM, 1-repetition maximum; AIMS2, Arthritis Impact Measurement Scales 2; ASA, axial spondylarthritis; ASES, Arthritis Self-Efficacy Scale; BDI, Beck Depression Inventory; CLBP, chronic low back pain; CPAQ, Chronic Pain Acceptance Questionnaire; CPSS, Chronic Pain Self-Efficacy Scale; F, female; FAB-Q, Fear Avoidance Beliefs Questionnaire; FIQ, Fibromyalgia Impact Questionnaire; GHQ-12, General Health Questionnaire–1; HADS, Hospital Anxiety and Depression Scale; HI, high intensity; HIT, high-intensity training; HR_{max}, maximum heart rate; HRR, heart rate reserve; IG1, intervention group 1; IG2, intervention group 2; IG3, intervention group 3; KOA, knee osteoarthritis; LBE, long bout exercise; LI, low intensity; LIT, low-intensity training; M, male; MFI, Multidimensional Fatigue Inventory; MHI, Mental Health Inventory; MIT, moderate-intensity training; nd, no or insufficient data; NS, nonsignificant result; PA, psoriatic arthritis; PCL, Pain Cognition List; PCS, Pain Catastrophizing Scale; PP, pre-post within-group analysis; QoL, quality of life; SBE, short bout exercise; SCL-90-R, Symptom Checklist 90–Revised; SF-36, 36-item Short Form Health Survey; STAI, State-Trait Anxiety Inventory; TSK, Tampa Scale Kinesiophobia; WG, between group delta analysis; ↗, improvement; ↘ = deterioration; ? = information on significance was lacking.

Table 2. Exercise intensity categories

	VO_2max, %	HRR, %	HR_{max}, %	1RM, %
LIT	0-44	0-44	0-49	0-49
MIT	45-59	45-59	50-69	50-69
HIT	60-100	60-100	70-100	70-100

1RM, 1-repetition maximum; HIT, high-intensity training; HR_{max}, maximum heart rate; HRR, heart rate reserve; LIT, low-intensity training; MIT, moderate-intensity training; VO_{2max}, maximum rate of oxygen consumption.

Table 3. Psychosocial outcome categorization

Category	Psychosocial outcome
Affective factors	Anxiety Depression Emotional distress Psychological distress Psychological well-being Kinesiophobia
Perceptual-Cognitive factors	Self-efficacy Quality of life Pain catastrophizing Fear avoidance beliefs Mental fatigue
Behavioral factors	Pain-related acceptance
Mental health	General mental health

unclear generalizability. Agreement between the 2 reviewers was "almost perfect" (κ = 0.87).

Results: Data Extraction

Study Population Characteristics

The CMSDs studied in the included studies are shown in Table 1. Ten studies reported on training effects of exercise therapy in fibromyalgia (FM; n = 430)[8,18,23,26,28,31,32,45,51,67]; 9 on chronic low back pain (CLBP; n = 508)[13,14,34,35,38,39,54,69,70]; 1 on knee osteoarthritis (KOA; n = 14)[41], 1 on psoriatic arthritis (PA; n = 20)[64]; and 1 on axial spondylarthritis (ASA; n = 13).[77]

Exercise Modality Characteristics

An overview of the intervention characteristics is shown in Table 1. In total, data from 28 intervention groups were evaluated. In terms of exercise intensity, 3 studies used low-intensity training (LIT),[26,34,35] 9 used moderate-intensity training (MIT),[8,28,31,32,34,35,38,41,64] and 6 used high-intensity training (HIT).[13,14,54,69,70,77] Six studies[18,23,39,45,51,67] made a progression through different exercise intensity categories and could not be

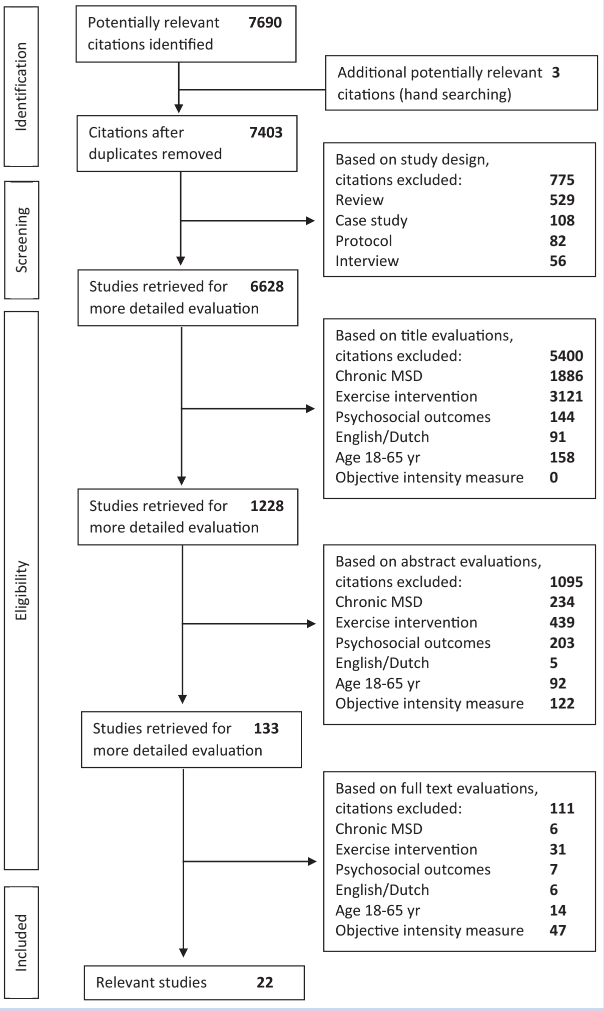

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart diagram. MSD, musculoskeletal disorder.

categorized in the LIT, MIT, or HIT group. In terms of exercise type, 12 intervention groups performed a cardiorespiratory protocol,[8,13,14,18,31,32,38,51,54,67] 14 interventions performed a resistance protocol,[8,23,26,28,34,35,38,39,41,64] and 2 performed a combined protocol.[69,70,77] In terms of intervention duration, trials ranged 8 and 24 weeks. In terms of exercise frequency, trials ranged between 1 and 4 times per week.

Psychosocial Outcome Characteristics

An overview of the psychosocial outcomes is shown in Table 1. A total of 13 different psychosocial outcomes were evaluated in the included studies, most often in terms of QoL (n = 15),[8,18,23,26,28,31,32,34,35,38,39,45,51,64,67] depression (n = 10),[8,13,14,23,26,28,32,51,54,69] anxiety (n = 9),[8,13,14,23,26,28,32,51,54] and self-efficacy (n = 4).[8,28,41,67] Pain catastrophizing[18,31,70] was evaluated in 3 studies and kinesiophobia[34,35] in 2 studies. Fear avoidance beliefs,[45] general mental health,[8] emotional distress,[77] psychological well-being,[67] psychological distress,[18] mental fatigue,[23] and pain-related acceptance[45] were each only evaluated in 1 study.

Effect of Different Modes of Exercise Intensity on Psychosocial Outcomes

A simple matrix of the effects of different modes of exercise intensity on psychosocial outcomes per CMSD is provided in Table 4. A detailed overview of all results can be found in Table 1.

Low-intensity training. Affective and perceptual-cognitive factors were evaluated in 3 studies.[26,34,35] In FM, LIT improved anxiety, depression, and QoL.[26] In CLBP, LIT showed a percentage improvement of 7.4%[34] and 4.2%[35] in kinesiophobia and a percentage improvement of 4.0%[34] and 6.4%[35] in QoL from baseline to study completion, respectively, in 2 studies; however, information on statistical significance was lacking.

Moderate-intensity training. Affective factors were evaluated in 5 studies.[8,31,32,34,35] in FM, MIT improved depression.[8,31,32] With regard to anxiety, results were conflicting. Two studies found an improvement,[31,32] whereas 1 study found no improvement.[8] In CLBP, MIT showed a percentage improvement of 2.9%[34] and 3.0%[35] in kinesiophobia from baseline to study completion, respectively, in 2 studies; however, information on statistical significance was lacking.

Perceptual-cognitive factors were evaluated in 9 studies.[8,28,31,32,34,35,38,41,64] MIT was effective for improving QoL in several CMSDs such as FM,[28,32] CLBP,[38] and PA.[64] In CLBP, MIT showed a percentage improvement of 10.0%[34] and 5.2%[35] in QoL from baseline to study completion in 2 studies; however, information on statistical significance was lacking. In FM, MIT improved self-efficacy.[31] Furthermore, MIT was not effective for pain catastrophizing.[28] In KOA, only the subscale "function" of the Arthritis Self-Efficacy Scale improved with no improvement in the total score.[41]

General mental health was evaluated in 1 study.[32] MIT was not effective for general mental health in FM.[32]

High-intensity training. Affective factors were evaluated in 5 studies using HIT.[13,14,54,69,77] In CLBP, HIT improved both anxiety and depression.[13,14,54] In ASA, HIT improved emotional distress.[77]

Perceptual-cognitive factors were evaluated in 1 study using HIT.[70] HIT improved pain catastrophizing in CLBP.[70]

Progressive intensity training. Affective factors were evaluated in 4 studies.[18,23,51,67] In FM, 2 exercise programs that progressed from LIT to HIT improved neither anxiety nor depression.[23,51] However, in the same population, exercise programs that progressed from LIT[67] or MIT[18] to HIT improved, respectively, psychological well-being and psychological distress.

Perceptual-cognitive factors were evaluated in 6 studies.[18,23,39,45,51,67] In FM, exercise programs that progressed from LIT[23,45,51,67] or MIT[18] to HIT improved QoL,[18,45,51,67] self-efficacy,[67] pain catastrophizing,[23] and mental fatigue.[23] However, Meyer and Lemley[51] reported conflicting results as one intervention group showed an improvement in QoL, whereas the other intervention group showed a deterioration. Furthermore, an exercise program that progressed from LIT to HIT did not improve fear avoidance beliefs about physical activity and work.[45,59] In CLBP, exercise programs that progressed from MIT to HIT improved QoL.[39]

Behavioral factors were evaluated in 1 study.[45] An exercise program that progressed from LIT to HIT improved pain-related acceptance in FM.[45]

DISCUSSION

The aim of this systematic review was to summarize current evidence regarding the influence of exercise intensity on psychosocial outcomes in persons with CMSDs. Twenty-two studies reporting on 5 different CMSDs were found. Based on the analysis of these studies, this review shows that changes in psychosocial outcomes, elicited by exercise therapy, can be affected by exercise intensity. However, the impact of exercise intensity seems to differ between patient groups and sufficient information is lacking in certain CMSDs.

The majority of studies in this review reported on 2 CMSDs; namely, FM and CLBP. For these disorders, some specific outcomes are displayed. In persons with FM, QoL improved with exercise programs of any intensity, suggesting that exercise intensity is not the determining factor for QoL in this population. Only 1 study[51] with an intervention program that progressed to exercising at high intensity found a deterioration of QoL. But this result should be evaluated with caution, as this study had a high probability of bias due to low study quality (PEDro = 2/10). Also, this was the only study with a prolonged exposure to HIT showing the potential impact of program duration. High exercise intensity was reached at week 3 and lasted up until the last week of the program (week 24). In comparison, the other studies applied an average of only 5 weeks of HIT.[18,23,45,59,67] The authors of the study hypothesized that HIT might only be tolerated for a limited amount of time, which explains that a prolonged exposure to HIT may have

Table 4. Simple matrix of the effects of exercise intensity on psychosocial outcomes

AF						P-CF					BF	MH	
Anxiety	Depression	Emotional Distress	Psychological Distress	Psychological Well-Being	Kinesiophobia	Self-Efficacy	Quality of Life	Pain Catastrophizing	Fear Avoidance Beliefs	Mental Fatigue	Pain-Related Acceptance	General Mental Health	MSK disorder
LIT													
+	+						+						FM[26]
					?		?						CLBP[34]
					?		?						CLBP[35]
MIT													
–	+						+						FM[8]
							+	–					FM[28]
+	+					+	+					–	FM[32]
+	+					+	+						FM[31]
					?		?						CLBP[34]
					?		?						CLBP[35]
							+						CLBP[38]
							+						CLBP[38]
						–							KOA[41]
							+						PA[64]
HIT													
+	+												CLBP[13]
+	+												CLBP[14]
+	+												CLBP[54]
	+												CLBP[69]
								+					CLBP[70]
		+											ASA[77]

(continued)

Table 4. (continued)

AF						P-CF					BF	MH	
Anxiety	Depression	Emotional Distress	Psychological Distress	Psychological Well-Being	Kinesiophobia	Self-Efficacy	Quality of Life	Pain Catastrophizing	Fear Avoidance Beliefs	Mental Fatigue	Pain-Related Acceptance	General Mental Health	MSK disorder
Progression through different categories													
			+				+						FM[18]
–	–						+	+		+			FM[23]
							+		–		+		FM[45]
–	–						+						FM[51]
–	–						–						FM[51]
				+		+	+						FM[67]
							+						CLBP[39]
							+						CLBP[39]
							+						CLBP[39]

AF, affective factors; ASA, axial spondylarthritis; BF, behaviorial factors; CLBP, chronic low back pain; FM, fibromyalgia; HIT, high-intensity training; KOA, knee osteoarthritis; LIT, low-intensity training; MH, mental health; MIT, moderate-intensity training; PA, psoriatic arthritis; P-CF, perceptual-cognitive factors; +, significant improvement; –, no improvement; ?, information on statistical significance is lacking.

reverse effects on QoL in persons with FM.[51] Indeed, in healthy persons, prolonged exposure to HIT can lead to overtraining, which can manifest itself in a deterioration in psychosocial outcomes such as depression, anxiety, and sleep disturbances.[29] Anxiety and depression decreased after both LIT[26] and MIT[31,32] programs in persons with FM. However, when persons with FM participate in programs that progress from MIT to HIT, no decreases were observed in these outcomes.[23,51] The lesser ability to withstand higher intensity exercise protocols in this population might be linked to altered central pain processing mechanisms and the perception of considerate muscle fatigue or cardiorespiratory exertion during HIT protocols as an abnormal peripheral input.[30,83] However, dropout rates were fairly high throughout exercise programs of all intensities (with 5 of 10 studies scoring a dropout rate of >20%). As such, results seem comparable with recommendations for exercise therapy in FM to improve outcomes such as physical fitness, pain, and fatigue, where mostly low- to moderate-intensity protocols are recommended. Nonetheless, often information is also lacking here and calls for more high-quality data to provide conclusions have been made.[2]

In contrast to persons with FM, persons with CLBP clearly benefit from exercising at a higher intensity for improving anxiety and depression.[13,14,54] Multiple causes for this potential benefit have been stated. On one hand, in terms of neurophysiology, LIT is not sufficient to induce significant changes in the nervous system, as it doesn't exceed the intensity threshold to activate the hypothalamus-pituitary-adrenal hormonal axis to improve anxiety and depression.[60] On the other hand, although HIT is more physically demanding than LIT or MIT, healthy persons report greater enjoyment after HIT compared with MIT and LIT.[78] In that way, a high-intensity exercise protocol may contribute to obtaining psychosocial results that are better than a LIT or MIT exercise protocol.[73,78] Moreover, HIT is beneficial for QoL in persons with CLBP,[39] whereas LIT has no obvious effects for QoL as the studies did not report improvements.[51] Furthermore, HIT is also beneficial for pain catastrophizing in persons with CLBP.[70] Results of Sveaas et al[77] concerning persons with ASA are in line with the results of CLBP, as an improvement in emotional distress was found after a 3-month HIT program. While kinesiophobia is a well-known psychosocial factor related to persistence of CLBP and disability in this population,[48,61] no significant improvement on this outcome was displayed in any exercise program. Possibly, these programs should be designed to be more specific to the activities that incite fear of movement such as bending or lifting. While studies have already shown a task-specific approach to be effective,[9,57] they lack clear description and supportive evidence of exact modalities that are needed to produce results. Besides, for persons with CLBP, only studies using LIT or MIT are available and no studies with a HIT program or progression of intensity evaluating fear of movement could be identified. Hence, it is not yet clear whether this modality produces better results on this outcome.

For other common CMSDs such as chronic neck pain and rheumatoid arthritis, no studies meeting the inclusion criteria were found. This was mainly because of the lack of reporting outcome measures related to psychosocial factors. Nonetheless, these factors have been found to interact with the onset and persistence of these disorders.[40,49,58,79] Furthermore, similar to the results found in CLBP, differences in exercise intensity seem to affect results on pain intensity and disability, with better results in HIT protocols.[21,90] Therefore, the authors argue the importance of including psychosocial outcome measures in future exercise therapy protocols in these and other CMSDs.

Despite the fact that all studies included in this review described the exercise intensity objectively, 6 studies could not be classified into LIT, MIT, or HIT because they used a combination of exercise intensity modes, more specifically progression from LIT or MIT toward HIT.[18,23,39,45,51,67] This might be due to recommendations to not immediately start with high-intensity exercises but progressively increase the intensity of exercises in certain CMSDs.[71] By making a gradual progression in exercise intensity and thus an increasing exposure to loaded movements, one's physiological and psychosocial treatment outcomes could improve as the person with the CMSD can tolerate higher demands placed on the body and has a gradual exposure of pain-related fear,[84] without triggering the previous experience of pain and pain-related fear.[42,71] Because of this advantage, it is plausible to use a gradual progression in exercise intensity. However, it is important that a correct representation of the progression model and adaptations throughout the exercise protocol are added in the methods of these studies. Only in this way can an analysis be made of the influence of different exercise intensities.

The results of this review need to be interpreted in the context of a number of specific limitations. First, previous studies already reported high variability and unclear protocols in the description of exercise therapy.[2,56,72] Indeed, many studies did not objectively reflect exercise intensity in their protocol, which was the main reason (40.9%) for exclusion. Moreover, variety in pathology, outcome measure, type of intervention, and follow-up period prevented pooling of the data. Hence, no meta-analysis could be performed. Also, differences in underlying working mechanisms of either cardiorespiratory or strength-training protocols might have an impact on whether exercise intensity is a factor in those specific training modes. While in this review, data were insufficient to evaluate results of subgrouping therapy modes, this should be an analysis in future research. Moreover, current studies are investigating possible mediating effects of a wide variety of other factors related to the onset and persistence of CMSDs that were not yet sufficiently inventoried in earlier research such as inflammation,[24] body composition,[87] and nociceptive processing.[16] Potentially, these factors also have a significant impact on how exercise intensity can be managed by a patient. Progressing insights on these factors and their influence on CMSDs might direct subgrouping even more. Second, no studies were included comparing 2 groups where an exercise program of different exercise intensity was applied. As such, this review could not evaluate whether these results differ from a control group performing other exercise programs or even no exercise. Third, as many studies failed to provide sufficient data for evaluating effect sizes, the authors decided not to include it. However, this limits this review to only providing descriptive information. Fourth, widely used psychosocial patient-reported outcome measures, such as the 36-item Short Form Health Survey, Pain Catastrophizing Scale, and Tampa Scale for Kinesiophobia, might not be responsive enough and not able to distinguish a clinically important change from measurement error in persons with CMSD.[63] As such, results might be underestimated and must be interpreted carefully.

The current systematic review shows that there is a need for future high-quality studies using a clear description of exercise intensity to enable comparison of effects of different modes of exercise intensity on psychosocial outcomes in CMSDs. Future studies should include different groups undergoing exercise therapy with the sole difference between groups being the intensity level of exercise therapy. Furthermore, there is a need to compare the outcomes of exercise therapy programs to other therapy modalities such as psychological or even multimodal programs.

CONCLUSION

Changes in psychosocial outcomes, elicited by exercise therapy, can be affected by exercise intensity. However, there seems to be a difference between CMSDs in how they respond to exercise intensity. Persons with fibromyalgia benefit more from low to moderate exercise intensity, whereas persons with CLBP benefit more from moderate to high exercise intensity. For other CMSDs, outcomes are contradictory. However, pooling of data and comparison of the studies was obstructed because of heterogeneity of study designs, and some studies showed considerable risk of bias. Therefore, more high-quality research is needed to justify the influence of exercise intensity on psychosocial outcomes in persons with CMSDs.

REFERENCES

1. Ahlstrand I, Vaz S, Falkmer T, Thyberg I, Björk M. Self-efficacy and pain acceptance as mediators of the relationship between pain and performance of valued life activities in women and men with rheumatoid arthritis. *Clin Rehabil.* 2017;31:824-834.
2. Andrade A, Dominski FH, Sieczkowska SM. What we already know about the effects of exercise in patients with fibromyalgia: an umbrella review. *Semin Arthritis Rheum.* 2020;50:1465-1480.
3. Ang DC, Bair MJ, Damush TM, Wu J, Tu W, Kroenke K. Predictors of pain outcomes in patients with chronic musculoskeletal pain co-morbid with depression: results from a randomized controlled trial. *Pain Med.* 2010;11:482-491.
4. Armijo-Olivo S, Fuentes J, da Costa BR, Saltaji H, Ha C, Cummings GG. Blinding in physical therapy trials and its association with treatment effects: a meta-epidemiological study. *Am J Phys Med Rehabil.* 2017;96:34-44.
5. Bailey KM, Carleton RN, Vlaeyen JW, Asmundson GJ. Treatments addressing pain-related fear and anxiety in patients with chronic musculoskeletal pain: a preliminary review. *Cogn Behav Ther.* 2010;39:46-63.
6. Barnett F. The effect of exercise on affective and self-efficacy responses in older and younger women. *J Phys Act Health.* 2013;10:97-105.
7. Bilberg A, Sveaas SH, Dagfinrud H, Mannerkorpi K. How do patients with axial spondyloarthritis experience high-intensity exercise? *ACR Open Rheumatol.* 2020;2:207-213.
8. Bircan C, Karasel SA, Akgun B, El O, Alper S. Effects of muscle strengthening versus aerobic exercise program in fibromyalgia. *Rheumatol Int.* 2008;28:527-532.
9. Boersma K, Linton S, Overmeer T, Jansson M, Vlaeyen J, de Jong J. Lowering fear-avoidance and enhancing function through exposure in vivo. A multiple baseline study across six patients with back pain. *Pain.* 2004;108:8-16.
10. Boonstra AM, Reneman MF, Waaksma BR, Schiphorst Preuper HR, Stewart RE. Predictors of multidisciplinary treatment outcome in patients with chronic musculoskeletal pain. *Disabil Rehabil.* 2015;37:1242-1250.
11. Booth J, Moseley GL, Schiltenwolf M, Cashin A, Davies M, Hübscher M. Exercise for chronic musculoskeletal pain: a biopsychosocial approach. *Musculoskeletal Care.* 2017;15:413-421.
12. Bushman BA. Determining the I (intensity) for a FITT-VP aerobic exercise prescription. *ACSM Health Fitness J.* 2014;18(3):4-7.
13. Chatzitheodorou D, Kabitsis C, Malliou P, Mougios V. A pilot study of the effects of high-intensity aerobic exercise versus passive interventions on pain, disability, psychological strain, and serum cortisol concentrations in people with chronic low back pain. *Phys Ther.* 2007;87:304-312.
14. Chatzitheodorou D, Mavromoustakos S, Milioti S. The effect of exercise on adrenocortical responsiveness of patients with chronic low back pain, controlled for psychological strain. *Clin Rehabil.* 2008;22:319-328.
15. Cimmino MA, Ferrone C, Cutolo M. Epidemiology of chronic musculoskeletal pain. *Best Pract Res Clin Rheumatol.* 2011;25:173-183.
16. Coppieters I, Meeus M, Kregel J, et al. Relations between brain alterations and clinical pain measures in chronic musculoskeletal pain: a systematic review. *J Pain.* 2016;17:949-962.
17. Costa Lda C, Maher CG, McAuley JH, Hancock MJ, Smeets RJ. Self-efficacy is more important than fear of movement in mediating the relationship between pain and disability in chronic low back pain. *Eur J Pain.* 2011;15:213-219.
18. Da Costa D, Abrahamowicz M, Lowensteyn I, et al. A randomized clinical trial of an individualized home-based exercise programme for women with fibromyalgia. *Rheumatology (Oxford).* 2005;44:1422-1427.
19. da Cruz Fernandes IM, Pinto RZ, Ferreira P, Lira FS. Low back pain, obesity, and inflammatory markers: exercise as potential treatment. *J Exerc Rehabil.* 2018;14:168-174.
20. De Baets L, Matheve T, Meeus M, Struyf F, Timmermans A. The influence of cognitions, emotions and behavioral factors on treatment outcomes in musculoskeletal shoulder pain: a systematic review. *Clin Rehabil.* 2019;33:980-991.
21. de Jong Z, Munneke M, Zwinderman AH, et al. Is a long-term high-intensity exercise program effective and safe in patients with rheumatoid arthritis? Results of a randomized controlled trial. *Arthritis Rheum.* 2003;48:2415-2424.
22. de Morton NA. The PEDro scale is a valid measure of the methodological quality of clinical trials: a demographic study. *Aust J Physiother.* 2009;55:129-133.
23. Ericsson A, Palstam A, Larsson A, et al. Resistance exercise improves physical fatigue in women with fibromyalgia: a randomized controlled trial. *Arthritis Res Ther.* 2016;18:176.
24. Gallo J, Raska M, Kriegova E, Goodman SB. Inflammation and its resolution and the musculoskeletal system. *J Orthop Translat.* 2017;10:52-67.
25. Garber CE, Blissmer B, Deschenes MR, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc.* 2011;43:1334-1359.
26. Gavi MB, Vassalo DV, Amaral FT, et al. Strengthening exercises improve symptoms and quality of life but do not change autonomic modulation in fibromyalgia: a randomized clinical trial. *PLoS One.* 2014;9:e90767.
27. Geneen LJ, Moore RA, Clarke C, Martin D, Colvin LA, Smith BH. Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews. *Cochrane Database Syst Rev.* 2017;1:CD011279.
28. Glasgow A, Stone TM, Kingsley JD. Resistance exercise training on disease impact, pain catastrophizing and autonomic modulation in women with fibromyalgia. *Int J Exerc Sci.* 2017;10:1184-1195.
29. Gottschall JS, Davis JJ, Hastings B, Porter HJ. Exercise time and intensity: how much is too much? *Int J Sports Physiol Perform.* 2020;15:808-815.
30. Goubert D, Danneels L, Graven-Nielsen T, Descheemaeker F, Meeus M. Differences in pain processing between patients with chronic low back pain, recurrent low back pain, and fibromyalgia. *Pain Physician.* 2017;20:307-318.
31. Gowans SE, Dehueck A, Voss S, Silaj A, Abbey SE. Six-month and one-year followup of 23 weeks of aerobic exercise for individuals with fibromyalgia. *Arthritis Rheum.* 2004;51:890-898.

32. Gowans SE, deHueck A, Voss S, Silaj A, Abbey SE, Reynolds WJ. Effect of a randomized, controlled trial of exercise on mood and physical function in individuals with fibromyalgia. *Arthritis Rheum*. 2001;45:519-529.
33. Hagen KB, Dagfinrud H, Moe RH, et al. Exercise therapy for bone and muscle health: an overview of systematic reviews. *BMC Med*. 2012;10:167.
34. Harts CC, Helmhout PH, de Bie RA, Staal JB. A high-intensity lumbar extensor strengthening program is little better than a low-intensity program or a waiting list control group for chronic low back pain: a randomised clinical trial. *Aust J Physiother*. 2008;54:23-31.
35. Helmhout PH, Harts CC, Staal JB, Candel MJ, de Bie RA. Comparison of a high-intensity and a low-intensity lumbar extensor training program as minimal intervention treatment in low back pain: a randomized trial. *Eur Spine J*. 2004;13:537-547.
36. Hurley M, Dickson K, Hallett R, et al. Exercise interventions and patient beliefs for people with hip, knee or hip and knee osteoarthritis: a mixed methods review. *Cochrane Database Syst Rev*. 2018;4:CD010842.
37. Jung ME, Bourne JE, Little JP. Where does HIT fit? An examination of the affective response to high-intensity intervals in comparison to continuous moderate- and continuous vigorous-intensity exercise in the exercise intensity-affect continuum. *PLoS One*. 2014;9:e114541.
38. Kell RT, Asmundson GJ. A comparison of two forms of periodized exercise rehabilitation programs in the management of chronic nonspecific low-back pain. *J Strength Cond Res*. 2009;23:513-523.
39. Kell RT, Risi AD, Barden JM. The response of persons with chronic nonspecific low back pain to three different volumes of periodized musculoskeletal rehabilitation. *J Strength Cond Res*. 2011;25:1052-1064.
40. Kim R, Wiest C, Clark K, Cook C, Horn M. Identifying risk factors for first-episode neck pain: a systematic review. *Musculoskelet Sci Pract*. 2018;33:77-83.
41. King LK, Birmingham TB, Kean CO, Jones IC, Bryant DM, Giffin JR. Resistance training for medial compartment knee osteoarthritis and malalignment. *Med Sci Sports Exerc*. 2008;40:1376-1384.
42. Kraemer WJ, Ratamess NA. Fundamentals of resistance training: progression and exercise prescription. *Med Sci Sports Exerc*. 2004;36:674-688.
43. Kroll HR. Exercise therapy for chronic pain. *Phys Med Rehabil Clin N Am*. 2015;26:263-281.
44. Kwan BM, Bryan AD. Affective response to exercise as a component of exercise motivation: attitudes, norms, self-efficacy, and temporal stability of intentions. *Psychol Sport Exerc*. 2010;11:71-79.
45. Larsson A, Palstam A, Löfgren M, et al. Resistance exercise improves muscle strength, health status and pain intensity in fibromyalgia—a randomized controlled trial. *Arthritis Res Ther*. 2015;17:161.
46. Luque-Suarez A, Martinez-Calderon J, Falla D. Role of kinesiophobia on pain, disability and quality of life in people suffering from chronic musculoskeletal pain: a systematic review. *Br J Sports Med*. 2019;53:554-559.
47. March L, Smith EU, Hoy DG, et al. Burden of disability due to musculoskeletal (MSK) disorders. *Best Pract Res Clin Rheumatol*. 2014;28:353-366.
48. Martinez-Calderon J, Flores-Cortes M, Morales-Asencio JM, Luque-Suarez A. Pain-related fear, pain intensity and function in individuals with chronic musculoskeletal pain: a systematic review and meta-analysis. *J Pain*. 2019;20:1394-1415.
49. Martinez-Calderon J, Meeus M, Struyf F, Luque-Suarez A. The role of self-efficacy in pain intensity, function, psychological factors, health behaviors, and quality of life in people with rheumatoid arthritis: a systematic review. *Physiother Theory Pract*. 2020;36:21-37.
50. McHugh ML. Interrater reliability: the kappa statistic. *Biochem Med (Zagreb)*. 2012;22:276-282.
51. Meyer BB, Lemley KJ. Utilizing exercise to affect the symptomology of fibromyalgia: a pilot study. *Med Sci Sports Exerc*. 2000;32:1691-1697.
52. Miró E, Martínez MP, Sánchez AI, Prados G, Medina A. When is pain related to emotional distress and daily functioning in fibromyalgia syndrome? The mediating roles of self-efficacy and sleep quality. *Br J Health Psychol*. 2011;16:799-814.
53. Moher D, Liberati A, Tetzlaff J, Altman DG; the PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA statement. *PLoS Med*. 2009;6:e1000097.
54. Murtezani A, Hundozi H, Orovcanec N, Sllamniku S, Osmani T. A comparison of high intensity aerobic exercise and passive modalities for the treatment of workers with chronic low back pain: a randomized, controlled trial. *Eur J Phys Rehabil Med*. 2011;47:359-366.
55. Naugle KM, Naugle KE, Fillingim RB, Samuels B, Riley JL 3rd. Intensity thresholds for aerobic exercise-induced hypoalgesia. *Med Sci Sports Exerc*. 2014;46:817-825.
56. O'Dwyer T, O'Shea F, Wilson F. Exercise therapy for spondyloarthritis: a systematic review. *Rheumatol Int*. 2014;34:887-902.
57. Ogston JB, Crowell RD, Konowalchuk BK. Graded group exercise and fear avoidance behavior modification in the treatment of chronic low back pain. *J Back Musculoskelet Rehabil*. 2016;29:673-684.
58. Ortego G, Villafañe JH, Doménech-García V, Berjano P, Bertozzi L, Herrero P. Is there a relationship between psychological stress or anxiety and chronic nonspecific neck-arm pain in adults? A systematic review and meta-analysis. *J Psychosom Res*. 2016;90:70-81.
59. Palstam A, Larsson A, Lofgren M, et al. Decrease of fear avoidance beliefs following person-centered progressive resistance exercise contributes to reduced pain disability in women with fibromyalgia: secondary exploratory analyses from a randomized controlled trial. *Arthritis Res Ther*. 2016;18:116.
60. Paolucci EM, Loukov D, Bowdish DME, Heisz JJ. Exercise reduces depression and inflammation but intensity matters. *Biol Psychol*. 2018;133:79-84.
61. Picavet HS, Vlaeyen JW, Schouten JS. Pain catastrophizing and kinesiophobia: predictors of chronic low back pain. *Am J Epidemiol*. 2002;156:1028-1034.
62. Pickett, K., Yardley, L., & Kendrick, T. (2012). Physical activity and depression: A multiple mediation analysis. *Mental Health and Physical Activity*, 5(2):125-134.
63. Pulles A, Koke AJA, Strackke RP, Smeets R. The responsiveness and interpretability of psychosocial patient-reported outcome measures in chronic musculoskeletal pain rehabilitation. *Eur J Pain*. 2020;24:134-144.
64. Roger-Silva D, Natour J, Moreira E, Jennings F. A resistance exercise program improves functional capacity of patients with psoriatic arthritis: a randomized controlled trial. *Clin Rheumatol*. 2018;37:389-395.
65. Ross RE, Saladin ME, George MS, Gregory CM. High-intensity aerobic exercise acutely increases brain-derived neurotrophic factor. *Med Sci Sports Exerc*. 2019;51:1698-1709.
66. Saanijoki T, Tuominen L, Tuulari JJ, et al. Opioid release after high-intensity interval training in healthy human subjects. *Neuropsychopharmacology*. 2018;43:246-254.
67. Schachter CL, Busch AJ, Peloso PM, Sheppard MS. Effects of short versus long bouts of aerobic exercise in sedentary women with fibromyalgia: a randomized controlled trial. *Phys Ther*. 2003;83:340-358.
68. Searle A, Spink M, Ho A, Chuter V. Exercise interventions for the treatment of chronic low back pain: a systematic review and meta-analysis of randomised controlled trials. *Clin Rehabil*. 2015;29:1155-1167.
69. Smeets RJ, Vlaeyen JW, Hidding A, et al. Active rehabilitation for chronic low back pain: cognitive-behavioral, physical, or both? First direct post-treatment results from a randomized controlled trial [ISRCTN22714229]. *BMC Musculoskelet Disord*. 2006;7:5.
70. Smeets RJ, Vlaeyen JW, Kester AD, Knottnerus JA. Reduction of pain catastrophizing mediates the outcome of both physical and cognitive-behavioral treatment in chronic low back pain. *J Pain*. 2006;7:261-271.
71. Smith BE, Hendrick P, Bateman M, et al. Musculoskeletal pain and exercise-challenging existing paradigms and introducing new. *Br J Sports Med*. 2019;53:907-912.
72. Smith C, Grimmer-Somers K. The treatment effect of exercise programmes for chronic low back pain. *J Eval Clin Pract*. 2010;16:484-491.
73. Smith C, Kozlowski D, Provost SC. Stress. Anxiety. Pleasure. *Front Psychol Conference Abstract: Southern Cross University 14th Annual Honours Psychology Research Conference*. 2017:1. doi:10.3389/conf.fpsyg.2017.72.00009
74. Steiger F, Wirth B, de Bruin ED, Mannion AF. Is a positive clinical outcome after exercise therapy for chronic non-specific low back pain contingent upon a corresponding improvement in the targeted aspect(s) of performance? A systematic review. *Eur Spine J*. 2012;21:575-598.
75. Strath SJ, Kaminsky LA, Ainsworth BE, et al. Guide to the assessment of physical activity: clinical and research applications: a scientific statement from the American Heart Association. *Circulation*. 2013;128:2259-2279.
76. Sundstrup E, Jakobsen MD, Brandt M, Jay K, Aagaard P, Andersen LL. Strength training improves fatigue resistance and self-rated health in workers with chronic pain: a randomized controlled trial. *Biomed Res Int*. 2016;2016:4137918.
77. Sveaas SH, Berg IJ, Fongen C, Provan SA, Dagfinrud H. High-intensity cardiorespiratory and strength exercises reduced emotional distress and fatigue in patients with axial spondyloarthritis: a randomized controlled pilot study. *Scand J Rheumatol*. 2018;47:117-121.
78. Thum J, Parsons G, Whittle T, Astorino T. High-intensity interval training elicits higher enjoyment than moderate intensity continuous exercise. *PLoS One*. 2017;12:e0166299.
79. Treharne GJ, Kitas GD, Lyons AC, Booth DA. Well-being in rheumatoid arthritis: the effects of disease duration and psychosocial factors. *J Health Psychol*. 2005;10:457-474.
80. Van Houdenhove B, Luyten P. Customizing treatment of chronic fatigue syndrome and fibromyalgia: the role of perpetuating factors. *Psychosomatics*. 2008;49:470-477.

81. Vargas-Prada S, Coggon D. Psychological and psychosocial determinants of musculoskeletal pain and associated disability. *Best Pract Res Clin Rheumatol*. 2015;29:374-390.
82. Verbrugghe J, Agten A, Stevens S, et al. Exercise intensity matters in chronic nonspecific low back pain rehabilitation. *Med Sci Sports Exerc*. 2019;51:2434-2442.
83. Vierck CJ Jr. Mechanisms underlying development of spatially distributed chronic pain (fibromyalgia). *Pain*. 2006;124:242-263.
84. Vlaeyen JW, de Jong J, Geilen M, Heuts PH, van Breukelen G. Graded exposure in vivo in the treatment of pain-related fear: a replicated single-case experimental design in four patients with chronic low back pain. *Behav Res Ther*. 2001;39(2):151-166.
85. Vlaeyen JWS, Linton SJ. Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. *Pain*. 2000;85:317-332.
86. Vranceanu AM, Barsky A, Ring D. Psychosocial aspects of disabling musculoskeletal pain. *J Bone Joint Surg Am*. 2009;91:2014-2018.
87. Walsh TP, Arnold JB, Evans AM, Yaxley A, Damarell RA, Shanahan EM. The association between body fat and musculoskeletal pain: a systematic review and meta-analysis. *BMC Musculoskelet Disord*. 2018;19:233.
88. Woolf AD, Erwin J, March L. The need to address the burden of musculoskeletal conditions. *Best Pract Res Clin Rheumatol*. 2012;26:183-224.
89. Yi TI, Kim BK, Ha SA, Lim JY. The relationships between determination of treatment success and emotional factors in patients with chronic musculoskeletal pain. *Ann Rehabil Med*. 2014;38:77-83.
90. Zebis MK, Andersen LL, Pedersen MT, et al. Implementation of neck/shoulder exercises for pain relief among industrial workers: a randomized controlled trial. *BMC Musculoskelet Disord*. 2011;12:205.
91. Zulkosky K. Self-efficacy: a concept analysis. *Nurs Forum*. 2009;44:93-102.