


REVIEW

Online pain management programs for chronic, widespread musculoskeletal conditions: A systematic review with meta-analysis

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Abstract

Face-to-face pain management programs demonstrate positive clinical outcomes in the chronic pain population by improving pain intensity and attitudes, depression, and functional disability scores. The effects of this modality carried out online is less known, particularly in subgroups of chronic pain. This systematic review assessed the effects of online pain management programs in chronic, widespread musculoskeletal conditions on pain measurements (intensity, interference, coping, and catastrophizing), health-related quality of life, depression, and anxiety scores immediately post-intervention. Five electronic databases (Embase, Medline, CINAHL, Scopus, and PEDro) were searched with 3546 studies identified. Eighteen randomized controlled trials fulfilled the inclusion criteria. Included studies had moderate methodological quality (using the Effective Public Health Practice Project (EPHPP) quality assessment tool) but high risk of bias (using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2)). There were significant improvements in pain intensity (11 studies, 1397 participants, SMD -0.30 , 95% CI -0.50 to -0.10 , $p=0.004$), health-related quality of life (eight studies, 1054 participants, SMD 0.41 , 95% CI 0.08 to 0.75 , $p=0.02$), and depression (nine studies, 1283 participants, SMD -0.32 , 95% CI -0.55 to -0.08 , $p=0.008$). However, effect sizes were small and did not meet their respective measure's minimal clinically important change score. Guided interventions (regular interaction with an instructor) appeared to be superior to self-completed interventions. Future research should standardize outcome measures for assessing pain, use active control groups, and analyze other outcome measures such as cost and long-term effects. This study was registered with Prospero on August 15, 2021 (CRD42021267565).

KEYWORDS

arthritis, fibromyalgia, musculoskeletal diseases, pain, telehealth

INTRODUCTION

Chronic pain describes pain persisting beyond the expected healing times, a duration usually exceeding 3 months.¹ People with chronic, non-cancer pain report poorer health-related quality of life,^{2,3} affecting sleep, exercise, housework, and social relationships.⁴ Unsurprisingly, they often experience higher rates of

depression and anxiety.^{5,6} From an individual financial perspective, the median cost of care for a person with chronic pain waiting for treatment at multidisciplinary pain treatment facilities in Canada was ~US\$1377/month in 2010.⁷ On a societal level, the total financial cost of chronic and non-chronic pain, which includes medical and loss of productivity costs, ranged from US\$560 billion to \$635 billion in America in 2010 dollars.⁸ With

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these costs predicted to rise, there is urgent need for high-value and effective management options for chronic pain.

Recognizing that pain is contributed by physiological, psychological, and social factors, management approaches need to be interdisciplinary and adopt a patient-centered biopsychosocial model.^{9,10} Pain management programs involving pain education and/or skills-based training is one approach that incorporates this model and is increasingly being implemented. This encompasses a wide range of interventions such as cognitive behavioral therapies, pain coping skills training, and pain neuroscience education. These interventions individually may have different focuses. For example, pain neuroscience focuses on the biological processes of pain, while cognitive behavioral therapy and pain coping skills training focus on changing thoughts and behaviors. A comprehensive biopsychosocial pain management program should include all these aspects of the biopsychosocial model focuses. Previous systematic reviews of face-to-face behavioral change interventions (in rheumatoid arthritis), cognitive behavioral therapy (in fibromyalgia), and pain neuroscience education (in chronic musculoskeletal pain such as chronic neck and back pain) have shown improvements in some pain outcome measures (such as pain attitudes), and healthcare use and functional disability.^{11–14} Biopsychosocial approaches combining biological and psychosocial education of pain was found to be more effective than education and advice in improving function and pain for people with chronic low back pain.¹⁵

Remote delivery of healthcare is increasingly accepted and adopted.^{16,17} The global COVID-19 pandemic greatly expedited the uptake of these services. In Australia, government subsidized medical telehealth services rose from 8% in March 2020, to 20% by June 2021.¹⁸ America experienced a 154% increase in telehealth use in March 2020.¹⁹ Importantly, people who require regular pain management may benefit from remote healthcare delivery, which may be cost-effective^{20,21} and improves access to specialist health care professionals.²²

There is paucity of high-quality studies investigating the effectiveness and acceptability of online pain management. Moderate quality studies indicate the potential of online cognitive behavioral therapy to improve pain in a mixed chronic pain population.²³ In site-specific populations, such as adults with chronic back pain, three systematic reviews reported minimal evidence for online interventions in reducing pain and disability.^{24–26} Conversely, for hip and knee osteoarthritis, online pain education reduced pain^{27,28} and improved physical function.²⁸ This inconclusive data may be explained by the heterogenous populations and relatively low quality of studies incepted in existing secondary evidence.

The recent ICD-11 classification²⁹ provides greater clarity in the different subgroups of chronic pain. This reduces heterogeneity, permits better identification of

specific pain presentations and increases translatability of the evidence into clinical practice through more careful treatment selection for a targeted subgroup. As defined by the ICD-11, one subgroup is chronic primary pain and includes conditions such as fibromyalgia. Another subgroup is chronic secondary musculoskeletal pain syndromes such as rheumatoid arthritis, juvenile idiopathic arthritis, and heritable disorders of connective tissue such as the Ehlers-Danlos syndromes.^{30–33} In this systematic review, we combine these subgroups as chronic widespread musculoskeletal conditions. The rationale for this is that in addition to chronic widespread pain, these conditions impact non-musculoskeletal systems, such as the skin, eyes, lungs, and gastrointestinal systems. Affected individuals commonly require regular pain management.

The main objective of this systematic review was to identify current literature investigating pain, health-related quality of life, depression, and anxiety outcomes following online pain management programs for people with chronic widespread musculoskeletal conditions. We critically appraised the quality of identified studies and summarized the effectiveness, acceptability, and components of online pain management resources implemented by researchers, presenting meta-analyses results where possible.

METHODS

The protocol for this systematic review was registered with PROSPERO on August 15, 2021 (CRD42021267565). This review followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement which sets out a checklist of items for reporting.³⁴

Databases and search strategies

The search terms were developed prior to the database search using the Population, Intervention, Comparator, and Outcome (PICO) format,³⁵ which is further detailed in the next section (eligibility criteria). Five electronic databases were searched: Embase, Medline, CINAHL, Scopus, and PEDro. Our search strategy contained two sets of keywords, one set for population (medical condition in our case) and one set for interventions. We used medical subject headings (MeSH) terms where they were allowed and our Boolean search strategy 'OR' was used to combine within each set, and 'AND' for combining the two sets. An example of our full search terms for each database is shown in Appendix SI. A search of Google Scholar was performed with search year starting from 2011, sorted by relevance. The top 300 search results that appeared were included for screening. Handsearching was performed by checking reference lists of final selected papers and by searching through

relevant online clinical trial registries. The first search was completed in July 2021 and a final search was completed in December 2021.

Eligibility criteria

Full-text, peer-reviewed, and published quantitative studies without language restriction from the earliest record were included. Randomized controlled trials, case, and cohort studies were eligible. We included studies of people with chronic pain (more than 3 months) relating to widespread musculoskeletal conditions that affect multiple areas of the body. Management programs that included pain education (eg, education on pain neuroscience, pain management, pain acceptance, cognitive behavioral therapy, or mindfulness) and were carried out online were included. Studies with a control group of either standard care, waitlist with usual care, or other generic, non-structured online interventions (eg, a collection of publicly available websites) were included.

We excluded systematic reviews/review papers, qualitative trials, and unpublished or non-peer-reviewed sources such as books and conference papers. Trials enrolling participants without chronic widespread conditions (eg, low back pain or single-joint osteoarthritis), trauma-related disorders, post-surgical pain, non-musculoskeletal pain (eg, cancer pain, somatic symptom disorder, and neurological conditions) were excluded. We also excluded interventions not delivered in an online or standardized/replicable format (eg, purely telephone call interventions, social media posts or fully individualized interventions), and studies utilizing interventions without pain education as a standalone comparator and/or a pain outcome measure.

Outcomes of interest

The primary outcome was pain-related measurements, and four components of pain measures were included: intensity/severity, interference (how pain interferes with daily life), coping (how often or how well do participants use coping strategies), and catastrophizing (extent of exaggeration about the pain experience). Secondary outcomes were health-related quality of life measures, depression, and anxiety measures. Adverse events, completion rates and participant feedback, and knowledge/skills acquisitions results were included where available.

Screening process and selection of studies

Database search results were imported into EndNote X9 (Clarivate, Philadelphia, United States) and Covidence (Veritas Health Innovation, Melbourne, Australia). All studies were independently screened against the inclusion

and exclusion criteria. Abstract and title screening, and full-text screening were undertaken by the main author (MTC) and one other co-author. Disagreements were discussed between the authors involved and conflicts that could not be resolved were brought to a third author for resolution. Where only abstracts were available or further information was required from full-text papers, we attempted to contact the corresponding authors via email to retrieve the full-text article or any necessary information. A repeat search for any additional literature was performed in December 2021, and screening and resolution procedures were again undertaken by two authors (MTC and CC).

Data extraction

Data were extracted into a customized Microsoft Excel (Version 16.58, Washington, United States) spreadsheet. Data collection was performed independently by two authors (MTC and LN) with disagreements resolved through discussion and consensus. Data extracted included authorship information, population, sample data, type of intervention, type of control, outcome measures, program parameters, and statistical analyses performed in each study.

Methodological quality assessment

The quality of each study was assessed independently by two authors (MTC and SK) using the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies, which is a tool used for assessing public health articles.^{36,37} The EPHPP scores the quality of studies on six domains: selection bias, study design, confounders, blinding, data collection method, and withdrawals, and dropouts. Based on the user dictionary, each component was rated as “strong,” “moderate,” or “weak.” A global rating was derived based on the number of weak ratings. A study was rated as “strong” if there were no weak ratings, “moderate” if they were allocated one weak rating, and “weak” if they received 2 or more weak ratings. Disagreements were discussed, and final consensus was reached between the two authors.

Risk of bias assessment

To assess risk of bias, the revised Cochrane risk-of-bias tool for randomized trials (RoB 2) was utilized.³⁸ The RoB 2 has 5 bias domains: randomization process, deviations from the intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Responses to each question were “yes,” “probably yes,” “probably no,” “no,” or “no information.” Each domain yielded a judgment of “low

risk,” “some concerns,” or “high risk” and in combination they provide an overall risk of bias judgment. Two authors (MTC and CC) performed the assessments independently, and disagreements were resolved by discussion and consensus.

Meta-analyses and data interpretation

Meta-analyses were performed for outcome measures that could be pooled from at least three studies. These included pain, health-related quality of life, depression, and anxiety. All trials included in the meta-analyses were randomized controlled trials and there were no significant baseline differences between control groups and intervention groups based on the RoB 2 assessment. Therefore, post-intervention means and standard deviations were used for the meta-analyses using a random effects analysis model with 95% confidence interval. Standardized mean differences (SMD) were used for comparison due to the different scales used across studies for each outcome measure. We standardized all outcome measure scales to point in the same direction (eg, for health-related quality of life scores, a higher score reflects better health-related quality of life). We performed subgroup analysis on individual health conditions where the results showed significant difference and where there were at least three conditions in the meta-analysis. All statistical calculations were completed using Review Manager (RevMan 5.4) software

(Cochrane Collaboration, London, United Kingdom). Since all our outcomes were continuous measures, the SMD was used as effect size (Cohen's *d*), where 0.2 reflects small, 0.5 medium, and 0.8 large effect sizes.³⁹ Heterogeneity was determined using the I^2 value. The following ranges classify the extent of the heterogeneity: 0%–40% not important, 30%–60% moderate, 50%–90% substantial, and 75%–100% considerable heterogeneity.⁴⁰ Due to overlap in these, a conservative estimate (higher range) was used when the I^2 value fell into two categories (eg, 80% heterogeneity was classified as considerable). Publication bias was assessed by analyzing funnel plot asymmetry and performing an Egger's test if there were sufficient data.

RESULTS

Study selection and characteristics of included studies.

There were 3546 articles identified from the database searches with an additional seven from other methods. A final 18 articles were included and the selection process with exclusion reasons detailed in the PRISMA flowchart (Figure 1).^{41–58} Characteristics of the included studies are detailed in Table 1. Majority of participants were female (average 83%). Eight studies were performed in the USA, five in Canada, three in the Netherlands, and one each in Brazil and Sweden, and these results represent countries

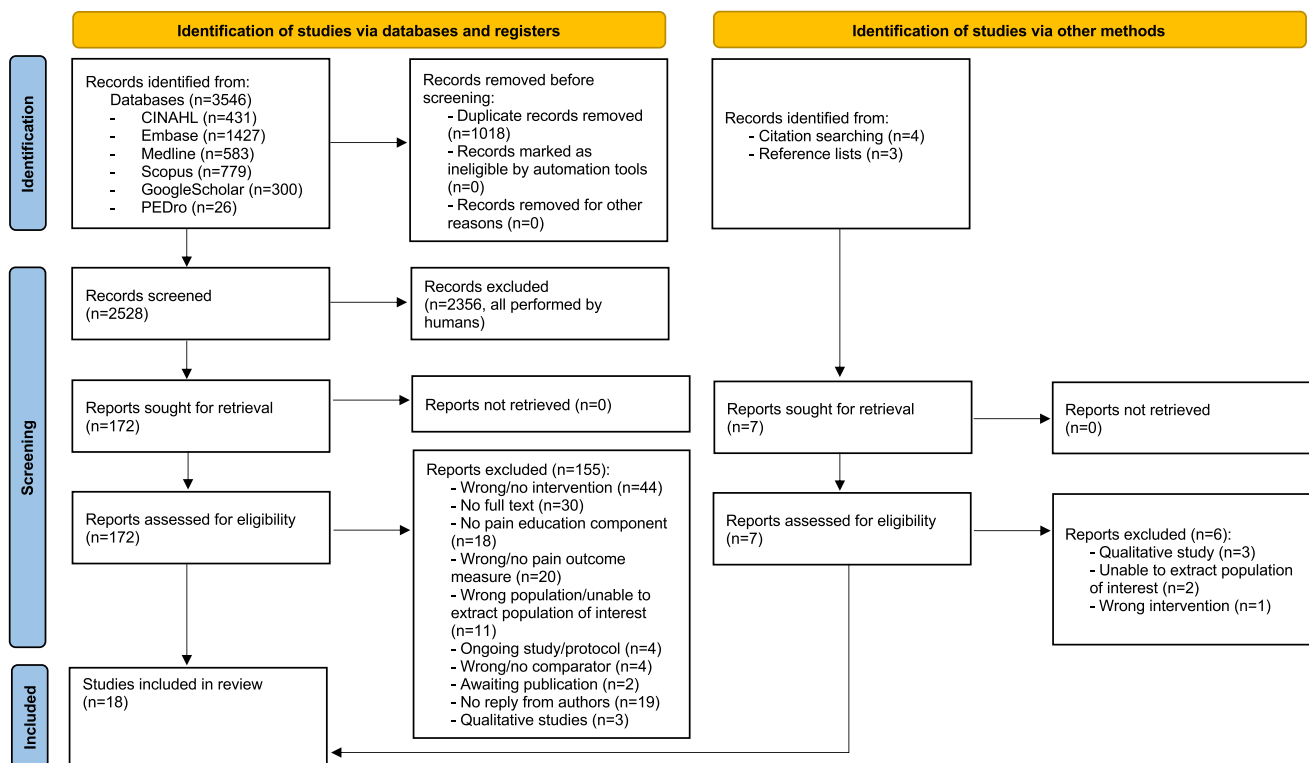


FIGURE 1 PRISMA flow chart with reasons for exclusion and other sources.

TABLE 1 Characteristics of included studies ($n=18$).

Authors, year of publication	Country	Sample N, age in years, sex (% female)	Condition	Control description	Intervention description	Intervention parameters	Quality rating (EPHPP)
Allen et al., 2021 ⁴¹	USA	<ul style="list-style-type: none"> Control $N=30$, age M 47 (SD 12), 93% Intervention $N=30$, age M 51 (SD 14), 97% 	SLE	Waitlist usual care	painTRAINER	<p>Eight modules, 8 weeks.</p> <p>Internet version of Pain Coping Skills Training (involving education on pain management, coping strategies, problem solving, pacing etc.).</p> <p>Self-completed</p>	<p>Strong ●●●●</p> <p>Moderate ●●○</p> <p>Weak ●○○</p>
Armbrust et al., 2017 ⁴²	NLD	<ul style="list-style-type: none"> Control $N=21$, age Mdn 10.2 (IQR 9.0–10.8), 57% Intervention $N=28$, age Mdn 9.7 (IQR 8.7–11.3), 75% 	JIA	Waitlist standard care	Rheumates@Work (R@W)	<p>14 modules, 14 weeks.</p> <p>Cognitive behavioral program (involving education on condition, symptom management, goal setting, coping strategies, activity performance, social interaction etc.)</p> <p>Included a combination of internet-based and individual instruction; four group sessions and one chat session with staff member</p>	●○○
Connelly et al., 2019 ⁴³	USA	<ul style="list-style-type: none"> Control $N=145$, age M 14.5 (SD 1.7), 77% Intervention $N=144$, age 14.6 (SD 1.8), 68% 	JIA	Online education control (websites about JIA but no CBT coping skills or social interaction), health coach phone calls but only about control websites	Teens taking charge	<p>12 modules, weekly.</p> <p>Online self-management program using multimedia-based modules (comprising education on condition, psychoeducation, training in cognitive-behavioral coping skills, stress management, self-management topics etc.).</p> <p>Included three phone calls (monthly), <30-min duration by trained health coaches</p>	●●●
Davis et al., 2019 ⁴⁴	USA	<ul style="list-style-type: none"> Control $N=40$ Intervention $N=39$ Overall age M 46.14 (range 22–81), 98% 	FM	Health tips (health behavior information but no instruction on how to implement health behavior)	Mindful socioemotional regulation intervention (MSER)	<p>12 modules, 6 weeks.</p> <p>Mindfulness program (including awareness of emotions and pain, regulation of emotions through awareness and acceptance using meditation, mindful living with pain, use of mindful awareness skills to build social bonds, increase sense of belonging and enjoyment of relationships etc.).</p> <p>Self-completed</p>	●●○

TABLE 1 (Continued)

Authors, year of publication	Country	Sample N, age in years, sex (% female)	Condition	Control description	Intervention description	Intervention parameters	Quality rating (EPHPP)
Ferwerda et al., 2017 ³⁸	NLD	<ul style="list-style-type: none"> Control $N=71$, age M 57.14 (SD 9.36), 66% Intervention $N=62$, age M 55.45 (SD 10.69), 61% 	RA	Standard care	Internet-based cognitive behavioral intervention	<p>Four modules, 9–65 weeks.</p> <p>Four modules: Pain and functional disability, Fatigue, Negative mood, Social functioning (All included cognitive strategies, problem solving skills and goal setting specific to each module). Patients completed at least one of four.</p> <p>Included therapists selecting relevant texts and assignments within each treatment module based on the treatment goal and patient characteristics.</p> <p>Also included weekly to biweekly contact with the patients through a secure e-mail messaging service</p>	<p>Strong ●●●●</p> <p>Moderate ●●○</p> <p>Weak ●○○</p>
Friesen et al., 2017 ⁴⁵	CAN	<ul style="list-style-type: none"> Control $N=30$, age M 46 (range 20–67), 97% Intervention $N=30$, age, 49 (range 28–65), 93% 	FM	Waitlist treatment as usual	Pain course	<p>Five lessons, 8 weeks.</p> <p>Pain Course, adapted for FM from the Pain Course developed by eCentreClinic. (Includes information about chronic pain and skills to manage impact of pain on daily activities and emotions).</p> <p>Included standardized automated emails weekly and a guide (a doctorate-level clinical psychology student) contacted participants weekly via telephone for 5–10 min</p>	●●○
Hedman-Lagerlof et al., 2018 ⁴⁶	SWE	<ul style="list-style-type: none"> Control $N=70$, age M 49.3 (SD 10.0), 99% Intervention $N=70$, age M 51.8 (SD 10.7), 97% 	FM	Waitlist control	Internet delivered exposure treatment (iExp)	<p>Eight modules, 10 weeks.</p> <p>Internet delivered exposure treatment with exposure to stimuli that triggers pain-related distress (including education on condition, psychoeducation, exposure, overcoming challenges, coping with setbacks etc.)</p> <p>Included monitoring by therapist (psychologists or graduate psychology students), regular contact (one to three times/week) through text messaging</p>	●○○

(Continues)

TABLE 1 (Continued)

Authors, year of publication	Country	Sample N, age in years, sex (% female)	Condition	Control description	Intervention description	Intervention parameters	Quality rating (EPHPP)
Khanna et al., 2019 ⁴⁷	USA	<ul style="list-style-type: none"> Control $N=133$, age M 52.9 (SD 13.1), 90.2% Intervention $N=134$, age M 54.3 (SD 10.1), 91.8% 	SSc	Book control ("The Scleroderma Book: A guide for Patients and Families" by Dr Maureen Mayes)	Internet-based self-management program	<p>15 modules, 16 weeks.</p> <p>Internet-based self-management program. (Including coping skills, exercise, symptom management, activity management, tips for family and caregivers, clinical trials and emergencies etc.).</p> <p>Included weekly questions regarding the modules posted on Discussion Board and moderated by the investigators. Also included phone calls or email contact at 4-, 8-, and 12-weeks.</p>	<p>Strong ●●●●</p> <p>Moderate ●●○</p> <p>Weak ●○○</p>
Kohms et al., 2020 ⁴⁸	USA	<ul style="list-style-type: none"> Control $N=53$ (FM $N=27$), age M 44.34 (SD 14.69), 77.4% Intervention $N=51$ (FM $N=23$), age M 44.35 (SD 14.87), 68.6% 	Subgroup FM	Health behaviors (video and exercises but does not address pain nor its causes)	Pain Psychology and Neuroscience (PPN)	<p>1 video (education about neural pathways, pain perception, pain as a learned response no longer due to injury or damage but is driven by psychological factors. Education that brain can cause pain, but this can be "unlearned") and self-assessment exercises.</p> <p>Self-completed</p>	●○
Lalloo et al., 2021 ⁴⁹	CAN	<ul style="list-style-type: none"> Control $N=31$, age M 15.1 (SD 1.6), 77.4% Intervention $N=29$, age M 14.9 (SD 1.7), 79.3% 	JIA	Attention control (smartphone based symptom tracking features only)	iCanCope mobile app	<p>8 weeks, daily check in.</p> <p>App included symptom tracking, goal setting, library of disease education and pain coping strategies (about 100 articles, each article was focused on JIA disease education, pain coping strategies, or disease self-management) pushed to participants based on their reports.</p> <p>Included community forum for "question for the week" monitored by the research team</p>	●○
Lorig et al., 2008 ⁵⁰	USA	<p>Control $N=422$ (FM $N=46$, RA $N=72$), age M 52.5 (SD 12.2), 90.5%</p> <p>Intervention $N=433$ (FM $N=40$, RA $N=72$), age M 52.2 (SD 10.9), 89.8%</p>	Subgroup RA and FM	Usual care	Internet-based Arthritis Self-Management Program (ASMP)	<p>16 topics, 6 weeks.</p> <p>Focused on reducing pain and improving function (including symptom management, interaction with healthcare providers, evaluation of treatment plan etc.).</p> <p>Included weekly workshops led by moderators, bulletin boards, email reminders, exercises suggested via automated algorithms</p>	●○○

TABLE 1 (Continued)

Authors, year of publication	Country	Sample N, age in years, sex (% female)	Condition	Control description	Intervention description	Intervention parameters	Quality rating (EPHP)
Shigaki et al., 2013 ⁵¹	USA	<ul style="list-style-type: none"> Control $N=53$, age M 49.3 (SD 12.3), 92% Intervention $N=55$, age M 50.3 (SD 11.6), 93% 	RA	Waitlist control	RAHelp	<p>10 modules, 10 weeks.</p> <p>Educational modules that encourage positive coping strategies (including education on condition, coping, goals, symptom management, relationships and community participation etc.).</p> <p>Included weekly phone calls (15–30 min) with clinician leaders, personalized to-do lists, “homework,” discussion board, secured messaging system between participants</p>	<p>●○○</p> <p>Strong ●●●●</p> <p>Moderate ●●○</p> <p>Weak ●○○</p>
Simister et al., 2018 ⁵²	CAN	<ul style="list-style-type: none"> Control $N=34$ Intervention $N=33$ Overall age M 39.7 (SD 9.36), 95% 	FM	Waitlist treatment as usual	Acceptance and Commitment Therapy (ACT)	<p>Seven modules, eight weeks.</p> <p>Guided by relational frame theory, aiming to develop psychological flexibility (including education on condition, psychoeducation, symptom management, cognitive and mindfulness strategies communication strategies etc.).</p> <p>Included weekly email reminders, written assignments with feedback provided by one of the authors</p>	●○○
Stinson et al., 2020 ⁵⁴	CAN	<ul style="list-style-type: none"> Control $N=169$, age M 14.5 (SD 1.7), 69.5% Intervention $N=88$, age M 14.0 (SD 1.5), 72.0% 	JIA	Web-based education (12 publicly available education websites but no self-management strategies or social support), monthly phone call (health coach) but discussed “own best efforts” and minimal interaction	Teens taking charge	<p>12 modules, 12 weeks.</p> <p>Multicomponent treatment (consisting of JIA-specific education, self-management strategies, and social support etc.).</p> <p>Included monthly telephone with trained health coaches (non-healthcare professional), weekly email reminders and two caregiver modules</p>	●○○
Stinson et al., 2010 ⁵³	CAN	<ul style="list-style-type: none"> Control $N=24$, age M 14.8 (SD 1.7), 66.7% Intervention $N=22$, age M 14.4 (SD 1.3), 68.2% 	JIA	Waitlist and attention control (weekly phone call with research assistant to discuss “own best efforts” at managing JIA)	Teens taking charge	<p>12 sessions, 12 weeks.</p> <p>Multicomponent treatment (including self-management strategies, disease-specific information and social support etc.).</p> <p>Included weekly phone calls by a coach (non-healthcare professional with an undergraduate degree in psychology), discussion board, personal journals/goals. Included two caregiver modules</p>	●○○

(Continues)

TABLE 1 (Continued)

Authors, year of publication	Country	Sample N, age in years, sex (% female)	Condition	Control description	Intervention description	Intervention parameters	Quality rating (EPHPP)
Williams et al., 2010 ⁵⁵	USA	<ul style="list-style-type: none"> Control N = 59, age M 50.75 (SD 10.58), 95% Intervention N = 59, age M 50.17 (SD 12.34), 95% 	FM	Standard care	Web-Enhanced Behavioral Self-Management (WEB-SM)	13 modules, 6 months. "Living well with Fibromyalgia" program (consisting of background knowledge on condition, behavioral and cognitive skills for symptom management, behavioral and cognitive skills for adaptive lifestyle changes etc.). Self-completed	<p>Strong ●●●●</p> <p>Moderate ●●○</p> <p>Weak ●○○</p>
Yuan et al., 2021 ⁵⁶	BRA	<ul style="list-style-type: none"> Control N = 20, age M 42.1 (SD 11.8), 100% Intervention N = 20, age M 43.3 (SD 8.4), 95% 	FM	Book control (book version of the app)	ProfFibro mobile app	6 weeks. Patient education (including self-monitoring, sleep hygiene and strategies, stimulus control therapy, planning the day, graded exercise program, gratitude diary, family adjustments etc.) Self-completed	●●○
Zuidema et al., 2019 ⁵⁷	NLD	<ul style="list-style-type: none"> Control N = 79, age M 62.9 (SD 10.2), 66% Intervention N = 78, age M 61.0 (SD 11.3), 65% 	RA	Usual care	Web-based Self-Management Enhancing Program	Nine modules, 6 months. Using theory of planned behavior and behavioral change techniques (including coping strategies, pacing, social interaction, symptom management, communicating with health professionals etc.). Included email and nurse reminder during consultations	●●○

Abbreviations: BRA, Brazil; CAN, Canada; FM, fibromyalgia; IQR, interquartile range; JIA, juvenile idiopathic arthritis; M, mean; Mdn, median; NLD, the Netherlands; RA, rheumatoid arthritis; SD, standard deviation; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; SWE, Sweden; USA, the United States of America.

with different socio-economic status. Seven studies included participants with fibromyalgia, five with juvenile idiopathic arthritis, three with rheumatoid arthritis, one study with both fibromyalgia and rheumatoid arthritis subgroups, and one study each with systemic lupus erythematosus and systemic sclerosis. Sixteen studies used online web-based interventions, and the remaining two were mobile phone applications. Sixteen studies divided their intervention into modules which participants completed at their own pace (ranging from weekly to monthly), one intervention comprised of a video, and five self-assessment exercises, while the final intervention provided a phone application that participants were encouraged to use daily. Five of the 18 interventions were purely self-completed (no interaction with instructors or researchers and no online community groups as part of the intervention). Ten of the studies used non-educative control groups such as usual or standard care (with or without being on a waitlist), while the other eight utilized some form of non-structured educative control (eg, book control or publicly available online health information).

The duration for intervention completion ranged from 6 weeks to 6 months.

Methodological quality assessment

Most of the included studies were of at least moderate methodological quality. Seven were rated as weak, 10 as moderate, and one received a strong rating (Table 1). A descriptive table of the EPHPP quality assessment is included in Appendix S2.

Risk of bias analysis

Twelve studies were assessed as having an overall high risk of bias, two had moderate risk while four were rated as low risk of bias using the RoB 2 tool (Figure 2). Ten of the studies were rated high risk in one of the domains (measurement of outcome domain) due to their use of passive control groups (ie, usual care with or without



FIGURE 2 Cochrane risk of bias assessment.

being on a waitlist) instead of active controls (ie, a book). This means that the participants had higher likelihood of knowing which group they were allocated to, which may have influenced their patient-reported outcome measures.

Publication bias

We were unable to perform statistical tests of publication bias due to insufficient studies and the level of heterogeneity in our meta-analyses. One of our meta-analyses included 11 studies but performing statistical analysis on only one meta-analysis would not provide an accurate representation of all included studies. Therefore, we chose to assess overall publication bias for all included studies using descriptive analysis.⁵⁹ Our search spanned five major databases and yielded ongoing, unpublished trials and published trials in different languages (Mandarin, German, and Spanish). These suggest that our search was wide enough to minimize publication bias due to language or small database searches. To check for selective non-reporting, we cross-checked each trial using either clinicaltrials.org, trialsearch.who.int, trialregister.nl or isrctn.com. Seventeen were registered prior to implementation and one was registered retrospectively.⁴⁵ Of the 17, only two revealed differences between protocol and published outcomes. One study proposed to measure outcomes at 16 weeks and 6 months,

but the 6 months results were not published.⁴⁷ However, we found the results on the trial registry reporting no significant difference at the two time points. Another trial proposed measuring outcomes at 3, 6, 9, and 12 months but in their published paper, results (which were significant improvements in health-related quality of life) were only reported for 3 and 9 months.⁵¹ The authors did not state reasons for non-reporting on 6- and 12-month results. As such, there may be some reporting bias in this paper. All 18 studies declared their funding sources and conflicts of interest, and we deemed there to be low risk of non-publication bias. Overall, our qualitative analysis of publication bias suggests low or acceptable levels of bias.

Outcome measures

Pain intensity/severity

Eleven studies (1397 participants) reported pain intensity data (Figure 3). A 0–10 visual analog or numeric rating scale was used for all except one study.⁵⁸ Not all studies reported the timing of the pain rating (eg, worst pain over a week or pain at time of assessment) and those that did are summarized in Appendix S3. As there was no standard time point of measuring pain across the studies, we chose to use pain intensity measured over at least 7 days if this was an option (as majority of the

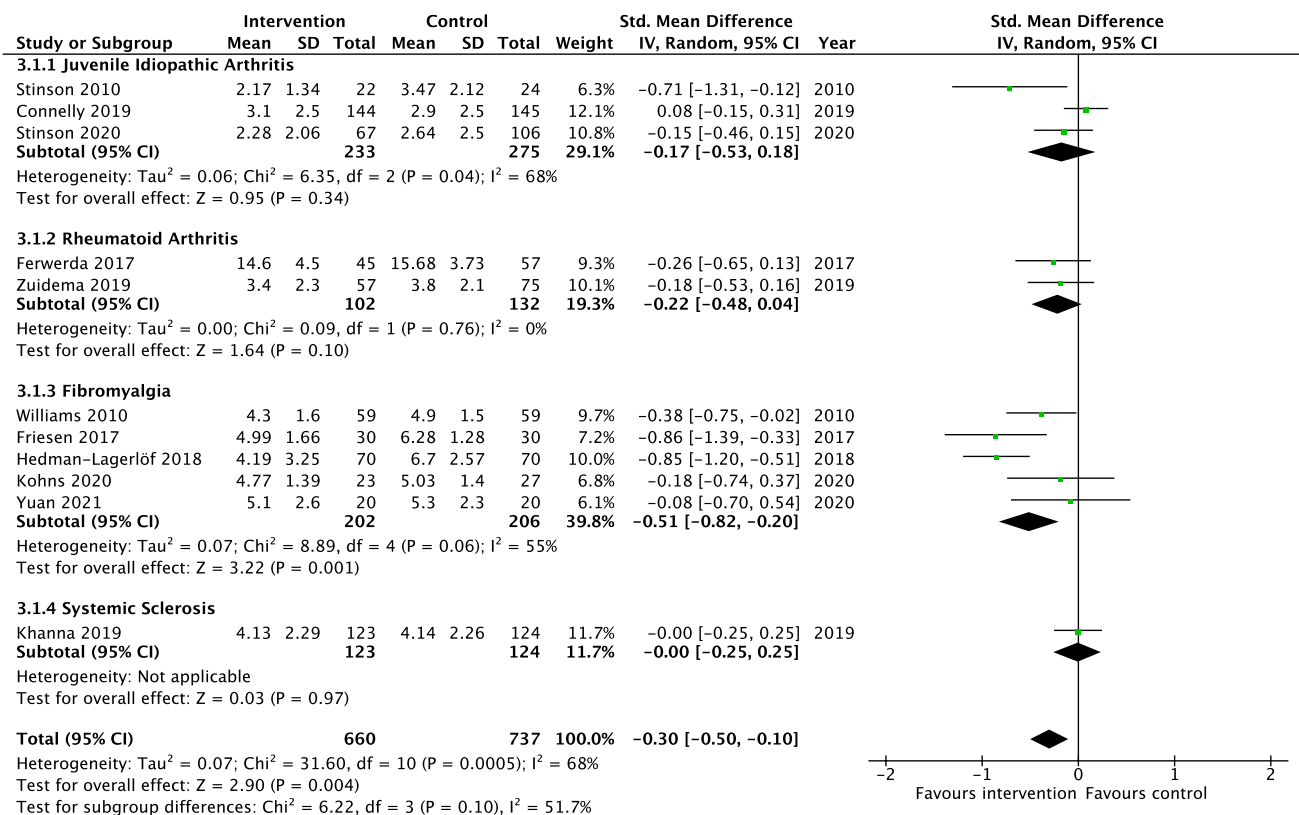


FIGURE 3 Pain intensity forest plot with subgroup by condition.

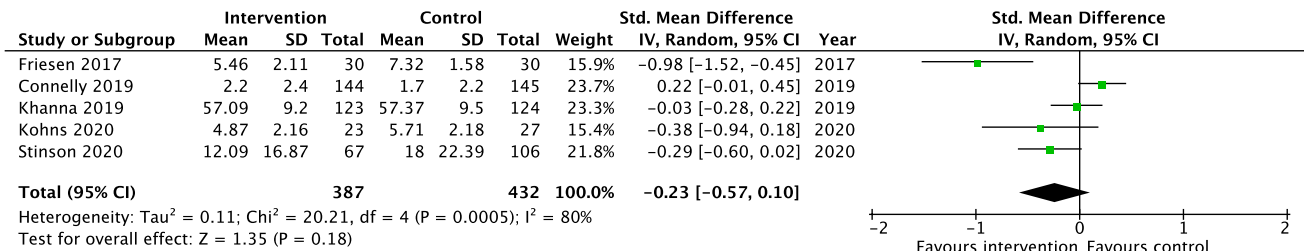


FIGURE 4 Pain interference forest plot.

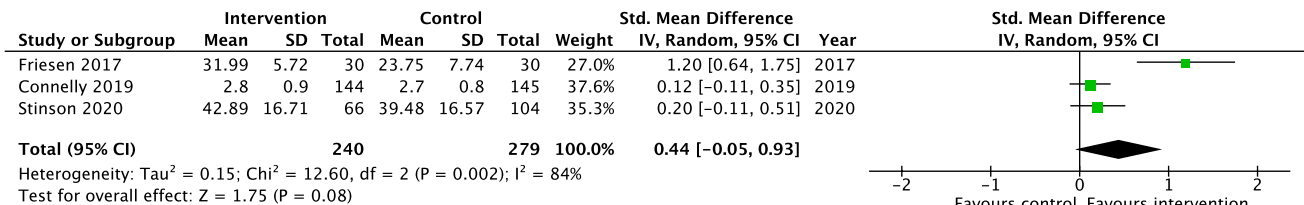


FIGURE 5 Pain coping forest plot.

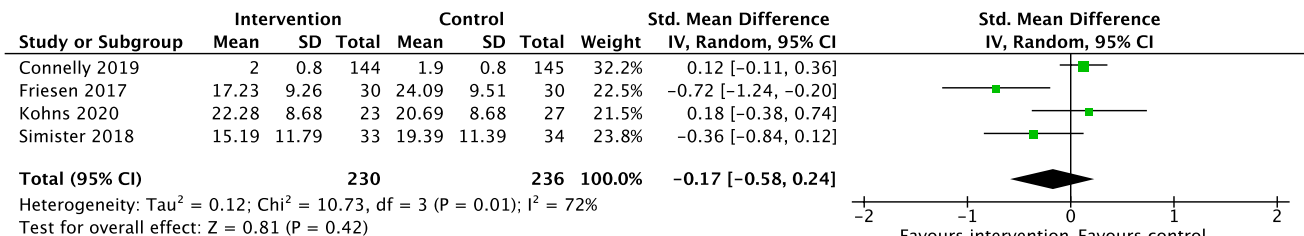


FIGURE 6 Pain catastrophizing forest plot.

studies included in our pain intensity meta-analysis used average pain over at least 7 days) and composite pain severity scores (such as the BPI or pain subscale of the FIQ). We expected the heterogeneity to be reflected in the results. Meta-analysis determined that online pain management significantly reduced pain intensity at post-intervention, compared with control (SMD -0.30 , 95% CI -0.50 to -0.10 , $p=0.004$) with small effect size. There was substantial between-study heterogeneity ($I^2=68\%$). Subgroup analysis by condition revealed significant improvements for the fibromyalgia group (SMD -0.51 , 95% CI -0.82 to -0.20 , $p=0.001$) but not for other conditions.

Pain interference

Five studies included measures of pain interference ($n=432$) (Figure 4). Meta-analysis revealed no difference between groups (SMD -0.23 , 95% CI -0.57 to 0.10 , $p=0.18$). Considerable between-study heterogeneity was identified for this outcome measure ($I^2=80\%$).

Pain coping

Three studies ($n=279$) included outcome measures of pain coping (Figure 5). No difference was found when

comparing online pain interventions to the control conditions (SMD -0.01 , 95% CI -1.21 to 1.20 , $p=0.99$). Considerable heterogeneity ($I^2=97\%$) was found between studies.

Pain catastrophizing

Four studies measured pain catastrophizing ($n=236$) and analysis revealed no difference between the groups (SMD -0.17 , 95% CI -0.58 to 0.24 , $p=0.42$) (Figure 6). Substantial between-group heterogeneity was identified ($I^2=72\%$). Several studies reported other types of pain-related measures (Appendix S3), but we did not analyze these results as they were beyond the scope of our aims.

Health-related quality of life

Eight studies reported on health-related quality of life ($n=1054$). A significant between-group difference favoring online pain management was found in the meta-analysis (SMD 0.41 , 95% CI 0.08 to 0.75 , $p=0.02$), with small effect size and considerable heterogeneity between studies ($I^2=85\%$) (Figure 7). Subgroup analysis revealed a significant improvement following the online pain management in the fibromyalgia group (SMD 0.71 , 95% CI

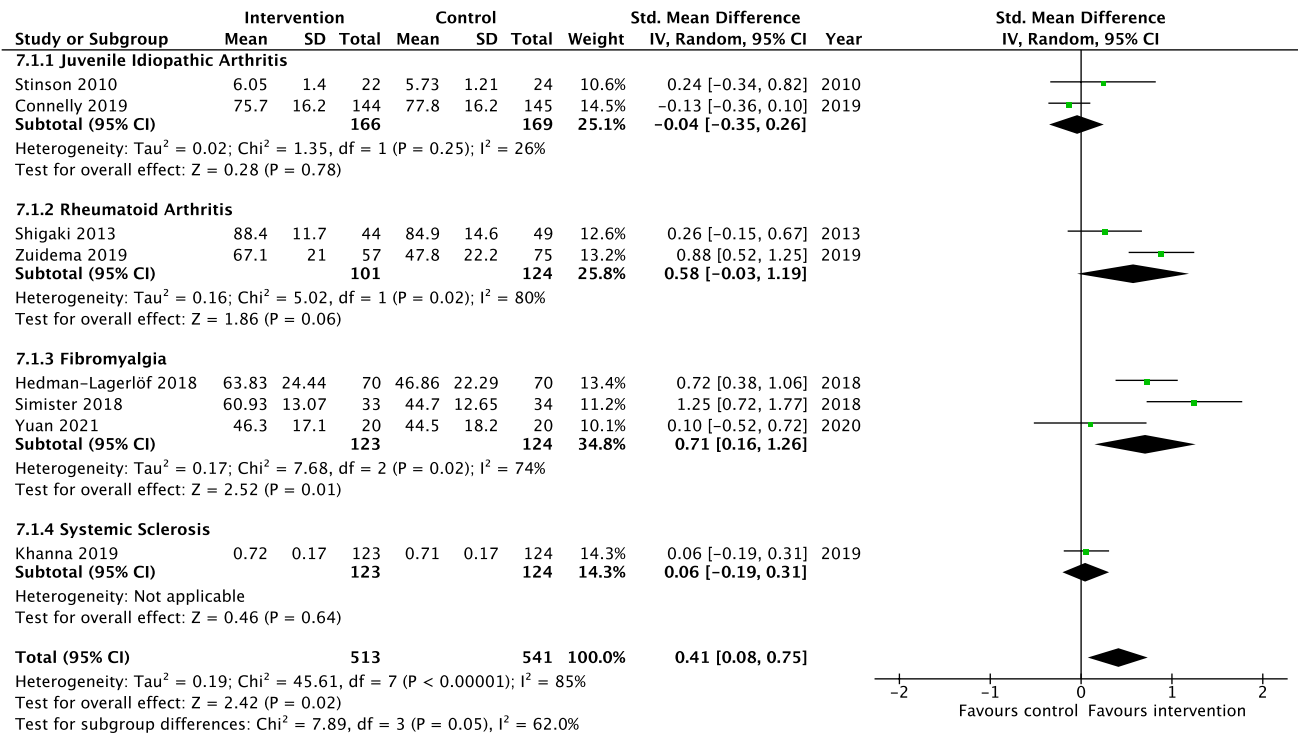


FIGURE 7 Health-related quality of life forest plot with subgroup by condition.

0.16 to 1.26, $p=0.01$). We excluded one study in this meta-analysis as their data and reported results were conflicting.⁵⁸ The authors used a composite score to estimate the overall impact of rheumatoid arthritis on daily life (comprising four scales: the self-care and mobility scales of the Impact of Rheumatic diseases on General Health and Lifestyle, and the RAND-36 role limitations due to physical health problems and emotional problems). The means of each of the individual scales revealed improvements in the intervention group, but the final composite score did not reflect this, which is counterintuitive. The authors did not report how they calculated the composite score and did not respond to our efforts to contact them. Consequently, we were unable to include their results in our analysis.

Depression and anxiety

Nine studies reported on the effect of the interventions on depression ($n=1283$) (Figure 8). Meta-analysis revealed a significant reduction in depression scores following online pain management compared with control (SMD -0.32, 95% CI -0.55 to -0.08, $p=0.008$). The effect size was small. There was considerable heterogeneity between studies ($I^2=76%$). Subgroup analysis revealed significant difference between intervention and control in only the fibromyalgia group (SMD -0.55, 95% CI -0.90 to -0.21, $p=0.002$).

Anxiety scores were reported in seven studies ($n=1125$) (Figure 9). Meta-analysis did not reveal any

between-group differences (SMD -0.19, 95% CI -0.43 to 0.05, $p=0.12$). There was substantial between-group heterogeneity ($I^2=73%$).

Type of intervention

To explore which type of intervention contributed to the significant findings in the above meta-analyses (pain intensity, health-related quality of life, depression, and anxiety), we performed a post-hoc analysis by subgrouping included papers by types of intervention. These subgroups were cognitive-behavioral therapy (CBT) only, cognitive-behavioral with disease education and/or pain neuroscience education (CBT with DE and/or PE), behavioral therapy only, disease education (DE) only, pain neuroscience education (PE) only, and other combined psychological therapy approaches (CBT with DE and mindfulness and exposure therapy; Acceptance and commitment therapy with DE). This analysis showed a significant reduction in pain intensity but only for the CBT with DE and/or PE intervention subgroup (SMD -0.34, 95% CI -0.67 to -0.01, $p=0.04$). The effect size was small. Even though there was significant effect of CBT with DE and/or PE, there was high level of heterogeneity ($I^2=74%$). This may be due to variability in age group and conditions that were studied. All other subgroup analyses did not show significant results or there were insufficient studies (less than 3) to pool the types of intervention together for subgroup analysis.

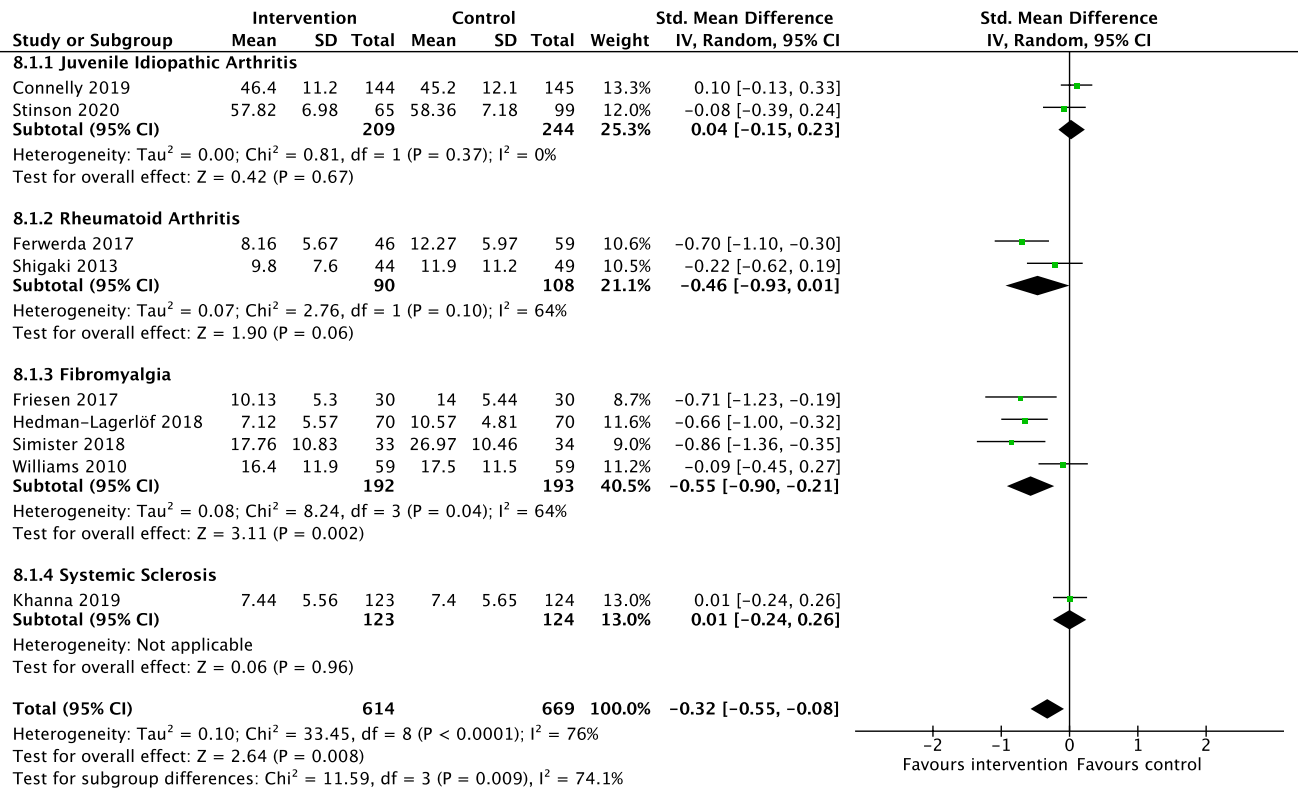


FIGURE 8 Depression forest plot with subgroup by condition.

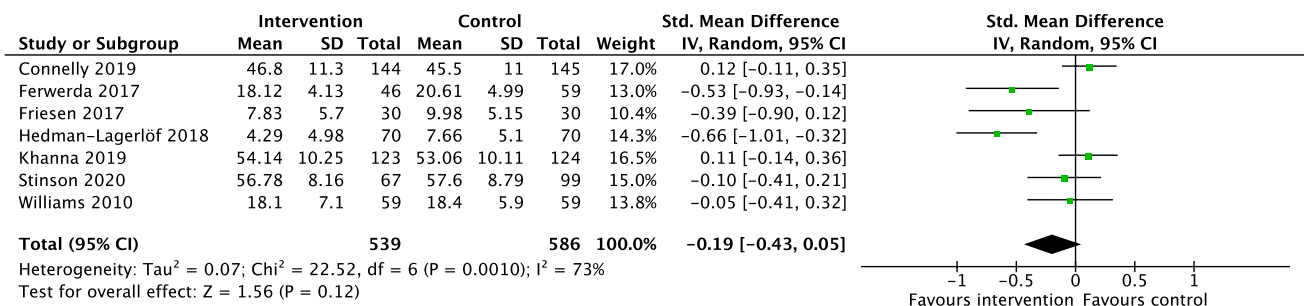


FIGURE 9 Anxiety forest plot.

Other outcomes

Adverse events

Three studies reported on adverse events experienced during their study.^{43,46,58} In arthritic conditions, adverse events included infections, arthritis flares (some requiring specialized treatment) and suicidal thoughts that were low in incidence and comparable between groups.^{43,58} In the fibromyalgia population, one study reported higher incidence of adverse events in the intervention group (34% versus 6% in the control group).⁴⁶ Their adverse events included increased pain (most common), sleep disturbance, increased fatigue, migraine, swelling, and weight loss. Four (out of 70 in the intervention group) had increased stress,

anxiety, depressive symptoms, and suicidal thoughts. Most of these side effects were reported as short-term, and however, two participants in the intervention group had ongoing increased pain at 12 months follow-up.

Completion rates

Completion rates (defined as finishing all or a pre-determined percentage of modules) were reported across six studies.^{44,45,48,52,53,58} Intervention group completion rates ranged from 49% to 100%, while the control groups ranged from 63% to 100% completion.^{44,48} Overall, completion rates varied, but were comparable between on-line pain management and control groups.

Participant feedback (acceptability, satisfaction, and helpfulness)

Participant feedback was measured diversely with helpfulness, satisfaction, and acceptability most commonly reported. Using helpfulness rating scales, majority of participants in two studies rated their online pain management intervention as helpful (one used 0–10 rating scale and one used a 4-item Likert scale).^{41,47} Two studies measured satisfaction with one reporting a 7.4/10 rating⁵⁸ and the other reporting 86% of their participants being satisfied or very satisfied.⁴⁵ One study rated their acceptability as high using their own Likert scale based questionnaire.⁵³ Two studies compared results between intervention and control groups. One used a validated tool (Acceptability E-scale form with scores from 8 to 40) reporting the mean score for the intervention and control groups as similar (34.7 and 34.6 respectively).⁴⁹ The other study used a modified Client Satisfaction Questionnaire reporting higher general satisfaction (91%) and helpfulness (78%) for the online intervention compared with the standard care control group (73% and 44% respectively).⁵⁵

Knowledge or skills acquisition

Three studies reported outcomes on knowledge or skills acquisition. Two studies of juvenile idiopathic arthritis participants used the Medical Issues, Exercise, Pain, and Social Support Questionnaire (MEPS).^{53,54} Both studies reported improvements in disease knowledge following online pain management, although only one was significant ($p=0.001$).⁵³ The third study utilized open-ended questions and reported that 86% of the intervention group improved their self-management skills, 77% had increase in self-management skill usage and 76% experienced behavioral change (compared with 42%, 33%, and 29% in the control group respectively).⁵⁵

Self-completed versus guided

There were insufficient data to perform a meta-analysis comparing self-completed versus guided interventions (such as email reminders and online interaction with health coaches or psychologists). Overall, guided interventions appear to be more effective. Of the four studies^{45,46,54,55} that reported improvements in pain intensity, three were guided (Figure 3). All studies with significant improvements in health-related quality of life^{46,52,57} (Figure 7), depression^{45,46,52,58} (Figure 8), and anxiety^{46,58} (Figure 9) utilized guided interventions. There is a strong indication to suggest that guided online pain interventions are superior to self-completed interventions.

Differences between protocol and review

Several modifications were made while we conducted the systematic review and meta-analyses and as such, there are some differences between our registered protocol and final review.

- Omission of physical outcomes measures and qualitative data. During our article screening stage, we realized that there were many diverse physical outcome measures. This would potentially complicate the analysis and interpretation of our results in addressing our aims. After registering and commencing database searching for our systematic review, we found another registered review with a similar research question focused specifically on qualitative studies.
- Exclusion of case studies, cohort studies, and systematic reviews. Our initial protocol included randomized controlled trials, case studies, or cohort studies. During the title and abstract screening stage, most of the search yielded randomized controlled trials and we made the decision to only include these, since they would yield stronger conclusions and recommendations. We expected to exclude other systematic reviews from the onset of the study but neglected to state this.
- Increasing minimum number of studies required for meta-analysis from 2 to 3 as the ratio between RCTs to meta-analysis was too high.⁶⁰
- Change in quality assessment and risk of bias tools. Given that our final 18 studies were all randomized controlled trials with quantitative outcome measures, we chose to use the RoB 2 which is specific for such trials. After registering our protocol on PROSPERO, we were made aware of some of the challenges in using the GRADE approach for public health systematic reviews.⁶¹ This led us to the EPHPP quality assessment tool, which is used for assessments of public health articles.³⁷

DISCUSSION

Main findings and clinical implications

The findings of our systematic review show that online pain management is effective in reducing pain intensity, improving health-related quality of life, and reducing depression particularly in those with fibromyalgia. These are encouraging results and validate the use of online pain management for improving pain and certain psychosocial outcomes for people in this chronic pain subgroup.

In our review, the online interventions demonstrating significant improvements in pain intensity all adopted

the biopsychosocial model to varying extents.^{45,46,53,55} Their programs included education about the condition, symptom management, behavioral coping skills, and social/lifestyle skills. Indeed, our post hoc analysis provided additional justification for the use of cognitive-behavioral therapy with disease education and/or pain neuroscience education. This suggests that the biopsychosocial model of pain management programs may be effective in reducing pain intensity for people with widespread chronic musculoskeletal conditions and can be successfully delivered online.

Despite the finding that online pain management reduced pain intensity, we recommend caution when translating this into clinical practice. Firstly, the effect size was small and using the recommended minimal clinically important change score of 2/10 for pain intensity,⁶² only one study came close with a reduction of 1.8 in their intervention group compared with an increase of 0.4 in their control group.⁴⁶ This study uniquely included exposure therapy (repeated contact with pain provoking stimuli and learning skills to overcome avoidance). There is room for more research into this method as it may benefit those with hypervigilance or fear avoidance. Secondly, more than half the studies in our pain intensity meta-analysis had high risk of bias in the RoB 2 measurement of outcome domain. Most of these studies did not have active control groups (eg, waitlisted with usual care); therefore, biasing participants self-reported outcome measures. With these in mind, clinicians should be aware that online pain management may not result in clinically useful improvements in pain intensity and recognize that reduction in pain intensity is not the only indicator of success of an intervention.

Reduction in pain intensity does not necessarily equate to improvements in ones' perception of well-being, and therefore, our additional findings of improved health-related quality of life and depression increase the value of online pain management in improving multiple aspects of life for patients with a chronic widespread musculoskeletal condition. Due to the different conditions and various health-related quality of life scales used, we are unable to make an overall clinical recommendation using a minimal clinically important change score. With respect to depression, the two most used outcome measures in our trials were the Center for Epidemiologic Studies Depression Scale (CES-D) and the Patient Health Questionnaire (PHQ-9). We are unable to find an accepted minimal clinically important change score for the CES-D. However, a paper suggested that a 20% reduction in Patient Health Questionnaire score can be used to indicate clinical improvement for moderately severe depression symptoms.⁶³ Two studies in our depression meta-analysis used the PHQ-9, with all participants starting with depression scores in the severe range.^{45,46} Both studies reported greater than 20% reductions in mean score (pre versus post) for their intervention

participants, with less than 5% mean reduction in their control participants. From our analysis, online pain management is efficacious in improving depression in this population. Interestingly, all but one of the trials included in our depression meta-analysis included external interaction and guidance. Individuals with depression have less social interaction and difficulty with social functioning.^{64,65} Therefore, having a trainer engage with them during remote treatment may be more beneficial than a self-guided program. With our results showing improvements in pain intensity, quality of life, and depression for individuals with chronic widespread musculoskeletal conditions, this trifecta supports possible clinical use of online pain management. Future research into the minimal clinically important changes for commonly used outcome measures for different conditions is needed to assist researchers in translating their research evidence into clinical recommendations.

Our systematic review yielded eight out of 18 studies incepted participants with fibromyalgia and the meta-analyses revealed most positive effects in this subgroup compared with others (juvenile idiopathic arthritis, rheumatoid arthritis, systemic sclerosis, and systemic lupus erythematosus). Indeed, our overall results were influenced by a high proportion of fibromyalgia studies. These findings are supported by another systematic review of a mix of face-to-face and remotely delivered psychoeducation (education and psychotherapeutic approaches such as cognitive behavioral therapy) for fibromyalgia and found significant reduction in both pain intensity and depression.⁶⁶ However, our preliminary results showing that different conditions seem to respond differently to online pain management are interesting. Compared with the other conditions in our study, the etiology of fibromyalgia is currently undetermined and people often face difficult and prolonged journeys to diagnosis and treatment.⁶⁷ As a result, we postulate that they may be more inclined to seek information themselves and be more receptive to potential education sources, both of which may also help in validating their medical experience. Furthermore, the participants of this group were predominantly female (~83%). There is some research to suggest that women may have higher health literacy and women with long-term illnesses were more likely to use the internet for health information than men.^{68,69} Therefore, we are unable to generalize our findings to males with chronic widespread musculoskeletal conditions.

Completion rates and feedback pertaining to online pain management programs based on our review indicated that this mode of delivery was generally well accepted, although there is possibility of more serious adverse effects such as an increase in depression, anxiety, and suicidal thoughts. Treatments such as exposure therapy may trigger a higher incidence of these severe adverse events and is something for future researchers to consider. Guided interventions appear additionally

advantageous, consistent with another review which reported that guided internet-based interventions provided better management of depression, anxiety, social interaction anxiety, and social phobia in adults with a mental disorder including depression.⁷⁰ In contrast, a recent randomized controlled trial in a chronic pain population compared guided versus self-completed acceptance and commitment therapy (ACT) on pain interference and acceptance reported no difference between self-completed and guided treatment.⁷¹ We postulate that their results differ from ours because they used a broad cohort of chronic pain population (pain more than 6 months, stratified by type and location of pain). More high-quality trials and reviews are needed to conclude if guided online pain management is more effective and whether people with different conditions respond differently.

Limitations

There were some limitations in our study. Pain is complex and requires a multi-dimensional measurement approach to accurately represent one's pain experience. As can be seen from our review, the array of pain measures, timing of pain ratings, and types of scales used were greatly variable. Online pain management programs do not have a fixed set of components, and this can be seen by the post hoc analysis in our systematic review where some included only CBT, some included disease education or pain neuroscience education, and some utilized other psychological approaches such as mindfulness and exposure therapy. This diversity in the different types of education and/or psychological approaches may have also contributed to heterogeneity. Also, the combination of standard care and active controls as a comparator group aimed to reflect what participants would have received in their local context. Though we narrowed down our population to subgroups of chronic pain, there was still variability in the resultant conditions in our study. These factors contributed to the high heterogeneity in our results even after utilizing standardization methods. Lastly, we did not include any physical outcome measures, long-term results, or cost analysis due to the potential scale of the study.

Strengths and future recommendations

Our systematic review aimed to provide evidence of the efficacy of online pain management for people with chronic widespread musculoskeletal conditions. This was achieved firstly by including only randomized controlled trials, the highest level of primary evidence available. Secondly, these studies included only specific subgroups of chronic pain participants, allowing clearer translation of this evidence to these clinical populations.

This is exemplified by the improvements in pain intensity, health-related quality of life and depression for participants with fibromyalgia more so than those diagnosed with other chronic widespread musculoskeletal conditions. More research is needed to confirm our findings in other chronic, widespread musculoskeletal conditions such as heritable disorders of connective tissue.

Another strength was our ability to perform meta-analyses for several outcome measures. Sufficient studies measuring the more common components of pain (ie, intensity, interference, coping, and catastrophizing) allowed us to pool data and rigorously investigate the aspects of pain most affected by online pain management. This may help direct future studies on what components to include in online pain management programs.

We recommend the implementation of common data elements in the assessment of chronic widespread musculoskeletal pain with consensus on which outcome measures possess the best clinimetrics for the task. In addition, standardizing length of time to follow-up will improve comparison across future studies. Long-term follow-up will determine whether the immediate positive effects of online pain management are maintained. Similar issues and recommendations apply for measuring completion and participant feedback of online pain management programs. Another trial component we recommend is the use of active control groups to minimize the risk of bias, especially when using patient-reported outcome measures which can be biased by unblinded standard care control groups. Some other recommendations for future reviews are to include physical outcome measures and cost analysis of online pain management programs. These additional areas are extremely relevant to the individual and to society as they affect healthcare planning and expenditure. Future studies could investigate these areas to determine whether online pain management has any effect on these outcome measures and on the cost-efficacy of implementing online programs.

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CONFLICT OF INTEREST STATEMENT

The authors of this systematic review declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data are available upon request to the author listed in the correspondence.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

Appendix S1

Appendix S2

Appendix S3

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