BMJ Open

Community-Deliverable Exercise and Anxiety in Adults with Arthritis and other Rheumatic Diseases: A Systematic Review with Meta-Analysis of Randomized Controlled Trials

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-019138
Article Type:	Research
Date Submitted by the Author:	16-Aug-2017
Complete List of Authors:	Kelley, George; West Virginia University, Biostatistics Kelley, Kristi; West Virginia University, Biostatistics Callahan, Leigh F; Thurston Arthritis Research Center, Department of Medicine
Primary Subject Heading:	Public health
Secondary Subject Heading:	Sports and exercise medicine, Evidence based practice
Keywords:	exercise, anxiety, arthritis, systematic review, meta-analysis

Title: Community-Deliverable Exercise and Anxiety in Adults with Arthritis and other Rheumatic Diseases: A Systematic Review with Meta-Analysis of Randomized Controlled Trials

Authors: Corresponding author: *George A. Kelley*, DA, FACSM, School of Public Health, Department of Biostatistics, West Virginia University, Morgantown, WV, USA, 26506-9190, Office Phone: 304-293-6279, Fax: 304-293-5891,E-mail: gkelley@hsc.wvu.edu

Co-author: *Kristi S. Kelley*, M.Ed., Research Instructor, School of Public Health, Department of Biostatistics, Robert C. Byrd Health Sciences Center, West Virginia University, PO Box 9190, Morgantown, WV, USA, 26506-9190, Office Phone: 304-293-6280, Fax: 304-293-5891, E-mail: kskelley@hsc.wvu.edu

Co-author: *Leigh F. Callahan*, PhD, Mary Link Briggs Distinguished Professor of Medicine, Professor, Departments of Social Medicine and Orthopaedics, Adjunct Professor, Department of Epidemiology, 3300 Thurston Bldg, Campus Box 7280, University of North Carolina, Chapel Hill, NC 27599-7280, Office Phone: 919-966-0564, E-mail: leigh callahan@med.unc.edu

Keywords: exercise, anxiety, arthritis, systematic review, meta-analysis

Abstract: 300 words

Introduction, Methods, Results, Conclusions: 7,729 words

ABSTRACT

Background/Purpose: Given conflicting findings, the purpose of this study was to use the meta-analytic approach to examine the effects of exercise (aerobic, strength training or both) on anxiety in adults with arthritis and other rheumatic diseases (AORD).

Methods: Randomized controlled exercise intervention trials ≥ 4 weeks in adults ≥ 18 years of age with osteoarthritis, rheumatoid arthritis or fibromyalgia were included. Studies were located by searching 8 electronic databases, cross-referencing and expert review. Dual selection and data abstraction of studies were performed. Hedge's standardized effect size (ES) was calculated for each result and pooled using the recently developed inverse-heterogeneity (IVhet) model. Two-tailed *z*-alpha values ≤ 0.05 and non-overlapping 95% confidence intervals (CI) were considered statistically significant. Heterogeneity was estimated using Q and I^2 with alpha values ≤ 0.10 for Q considered statistically significant. Small-study effects were examined using funnel plots and Egger's regression test. In addition, the number-needed-to-treat (NNT), percentile improvement and meta-regression were conducted. **Results:** Of the 639 citations screened, 14 studies representing 926 initially enrolled participants (539 exercise, 387 control) met the criteria for inclusion. Length of training averaged 15.8 ± 6.7 weeks, frequency 3.3 ± 1.3 times per week and duration 28.8 ± 14.3 minutes per session. Overall, statistically significant exercise minus control reductions in anxiety were found (ES = -0.40, 95% CI, -0.65, -0.15, tau^2 = 0.14; Q = 40.3, p = 0.0004; I^2 = 62.8%). The NNT was 6 with a percentile improvement of 15.5% and an estimated 5.3 million inactive US adults with AORD improving their anxiety if they started exercising regularly. Statistically significant small-study effects were observed (p < 0.0001).

Conclusions: Exercise is associated with reductions in anxiety among adults with selected types of AORD. However, a need exists for additional, well-designed, randomized controlled trials on this topic. **Trial registration number:** PROSPERO (CRD42016048728)

STRENGTHS AND LIMITATIONS OF THIS STUDY

- To the best of the investigative team's knowledge, this is the first systematic review with meta-analysis to examine the effects of exercise on anxiety as a primary outcome in adults with AORD.
- The use of the recently developed IVhet model appears to provide more robust estimates than those derived from other models.
- Common to all aggregate data meta-analyses, the possibility of ecological fallacy exists and the meta-regression analyses conducted do not allow for causal inferences.
- Given that no adjustments for multiple testing were made because of concerns about missing possibly important findings that could be tested in original trials, the possibility of chance findings exist.

INTRODUCTION

Rationale

Arthritis and other rheumatic diseases (AORD) are major public health problems in the United States (US). Based on combined 2013-2015 data from the National Health Interview Survey, the annual prevalence of doctor-diagnosed arthritis in the civilian, non-institutionalized US population aged 18 years or older was 22.7% (54.4 million), with prevalence higher among women (23.5%) than men (18.1%).[1] By 2040, it is estimated that 78.4 million (25.9%) US adults 18 years of age and older will have doctor-diagnosed arthritis.[2] Compared to combined 2013-2015 data,[1] this represents an increase of approximately 24 million adults. Not surprisingly, the financial costs associated with AORD in the United States are high. In 2003, the total costs attributable to AORD were estimated to be approximately $128 billion, $80.8 billion in direct costs (medical expenditures) and $47 billion in indirect costs (lost earnings).[3] This represents an increase of 24% between 1997 and 2003 and was primarily the result of an increase in the number of people with AORD.[3]

Elevated and sustained levels of anxiety can result in a number of deleterious consequences. These include, but are not limited to, (1) an increased risk for coronary heart disease as a result of heightened arousal leading to an increased risk for hypertension and a pro-inflammatory state,[4-6] (2) an increased risk for cardiac death,[5] and (3) poorer health-related quality-of-life.[7] While it is well-recognized that depression is a common comorbidity among adults with AORD, recent research suggests that the prevalence of anxiety among US adults with arthritis is approximately twice as high as depression.[8] Using data from the Arthritis Conditions Health Effects Survey, the

prevalence of anxiety and depression among US adults with doctor-diagnosed arthritis was estimated to be almost twice as high for anxiety (30.5%) versus depression (17.5%), with US population estimates of 11.5 million for anxiety and 6.6 million for depression.[8] Given the prevalence of anxiety, it was recommended that health care providers screen people with arthritis for anxiety.[8]

Exercise is an intervention that is generally safe and appropriate for most persons with various types of AORD.[9 10] Recent meta-analytic work has shown that community-deliverable exercise interventions reduce depressive symptoms in adults, with an estimated 3.1 million inactive US adults with AORD improving their depressive symptoms if they began and maintained a regular exercise program.[11] However, the effects of community-deliverable exercise on anxiety as a primary outcome are not known given a plethora of conflicting randomized controlled trials on this topic as well as a lack of studies that assess both depression and anxiety within the same study (only 44.8% based on a previous meta-analysis).[11] Most importantly, a recent systematic review of previous meta-analyses, not to be confused with an original systematic review with meta-analyses, found that no meta-analysis of randomized controlled trials has examined the effects of community-deliverable exercise on anxiety as a primary outcome in adults with AORD.[12] Clearly, it is critically important to develop a better understanding of the overall magnitude of effect, as well as factors associated with, exercise for improving anxiety in adults with AORD.

Objective

The primary objective of this study was to conduct a systematic review with an aggregate data meta-analysis of randomized controlled trials to determine the effects of

community-deliverable exercise interventions on anxiety in adults with AORD.

METHODS

Overview

This study followed the guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement for meta-analyses of health care interventions.[13] The protocol for this study is registered in PROSPERO (trial registration number CRD42016048728) and has been previously published in BMJ Open.[14]

Eligibility criteria

Studies that met the following criteria were included: (1) randomized controlled trials with the unit of assignment at the participant level, (2) community-deliverable exercise-only intervention group (aerobic, strength training, or both), (3) interventions ≥ 4 weeks, (4) comparative control group (non-intervention, wait-list control, usual care, attention control), (5) adults ≥ 18 years of age with doctor-diagnosed osteoarthritis, rheumatoid arthritis or fibromyalgia, (6) studies (published and unpublished in the form of Master's theses and dissertations) in any language, assuming an English-language abstract was available, from January 1, 1981 forward, and (7) data for anxiety, as defined by the authors of the original studies. Studies were limited to those with osteoarthritis, rheumatoid arthritis or fibromyalgia based on previous meta-analytic research showing a lack of exercise intervention studies for other types of AORD.[11] Studies were limited to randomized trials because it is the only way to control for confounders that are not known or measured as well as the observation that nonrandomized controlled trials tend to overestimate the effects of healthcare interventions.[15 16] Aerobic and progressive resistance (strength training)

exercise were defined according to section C2 of the 2008 Physical Activity Guidelines Advisory Committee Report.[17] Specifically, aerobic exercise is defined as any 'exercise that primarily uses the aerobic energy-producing systems, can improve the capacity and efficiency of these systems, and is effective for improving cardiorespiratory endurance,' while strength training is defined as 'exercise training primarily designed to increase skeletal muscle strength, power, endurance, and mass'.[17]

For this proposed project, community-deliverable exercise interventions were considered to be those that could be performed, or have the potential to be adapted and performed, by persons in a community setting (recreation or senior centers, in the home or neighborhood, etc.) and meet the implementation guidelines for physical activity interventions recently recommended by the Arthritis Program at the Centers for Disease Control and Prevention: (1) no academic degree required for a leader/implementer but leader training available, if needed, (2) no special facilities beyond a community room (except a warm pool for aquatic exercise), (3) inexpensive equipment, (4) cost to participants less than $50.00, (5) implementation guide available, (6) supporting structures judged to be adequate to support widespread implementation.[18] An exercise duration of at least 4 weeks was chosen based on previous research in which statistically significant improvements in anxiety occurred as a result of as little as 4 weeks of exercise training.[19] There was no maximum limit on the length of any interventions for the studies included in our proposed project. We limited our studies to adults ages 18 and older because the inclusion of children and adolescents pose additional confounding problems congruent with the many

developmental changes that occur during this period. In addition, the prevalence of AORD is more common in adults than children and adolescents. We restricted our studies to published articles, dissertations and master's theses and examined for potential small-study effects such as publication bias when limited to published articles in peer-reviewed journals. The year 1981 was chosen as the starting point for eligibility based on a preliminary PubMed search in which it was found that this was the first year that a randomized controlled trial on exercise and arthritis was published.[20] Studies from both English and non-English-language sources were included with the latter translated into English by the second author using the freely available web-based Babelfish and Bing translators. Finally, while acknowledging that the mechanisms for changes in anxiety may differ for different types of AORD, for example fibromyalgia versus osteoarthritis and rheumatoid arthritis, the purpose of the current systematic review with meta-analysis was to determine whether exercise reduces anxiety in adults with AORD, not why it reduces anxiety.

Information sources

Eight electronic databases were searched for potentially eligible studies in any language published from January 1, 1981 forward. The last searches were conducted on January 6, 2017. Databases searched included (1) PubMed, (2) SPORTDiscus, (3) Cochrane Central Register of Controlled Clinical Trials (CENTRAL), (4) Cumulative Index to Nursing and Allied Health Literature (CINAHL), (5) PsycINFO, (6) Web of Science, (7) Scopus and (8) ProQuest (Master's theses and dissertations). In addition, cross-referencing from retrieved studies was conducted. Furthermore, the third author, an expert on physical activity and AORD, reviewed the reference list for completeness.

Search strategy

Search strategies were developed using text words as well as medical subject headings (MeSH) associated with the effects of exercise on anxiety in adults with AORD. The second author conducted all electronic database searches. A copy of the search strategy for one of the databases searched (PubMed) is shown in Supplementary file 1.

Study records

Study selection

All studies to potentially be screened were imported into EndNote (EndNote, Version X8. New York, NY: Thomson Reuters, 2016). Duplicates were then removed both electronically and manually by the second author. A copy of the database was then provided to the first author for duplicate screening. The first two authors selected all studies, independent of each other. The full report for each article was obtained for all titles and abstracts that appeared to meet the inclusion criteria or where there was any uncertainty. Multiple reports of the same study were handled by including the most recently published article as well as drawing from previous reports, assuming similar methods and sample sizes. Neither of the screeners were blinded to the journal titles or to the study authors or institutions. Reasons for exclusion were coded as one or more of the following: (1) inappropriate population, (2) inappropriate intervention, (3) inappropriate comparison(s), (4) inappropriate outcome(s), (5) inappropriate study design, (6) other. Upon completion, the first two authors met and reviewed their selections. Discrepancies were resolved by consensus. If consensus could not be reached, the third author provided a recommendation. Using Cohen's kappa statistic (κ),[21] the overall agreement rate prior to correcting disagreements was 0.90. After

identifying the final number of studies to be included, the overall precision of the searches was calculated by dividing the number of studies included by the total number of studies screened after removing duplicates.[22] The number needed-to-read (NNR) was then calculated as the inverse of the precision.[22]

Data abstraction

Prior to the abstraction of data, a codebook that could hold more than 200 items per study was developed using Microsoft Excel (Microsoft Excel, Version 2010, Redmond, WA). The codebook was developed by the first two authors with input from the third author. The major categories of variables coded included (1) study characteristics (author, journal, year, etc.), (2) participant characteristics (age, height, body weight, etc.), (3) intervention characteristics (type, length, frequency, intensity, duration, compliance, etc.), and (4) outcome characteristics for anxiety (sample sizes, baseline and post-exercise means and standard deviations, etc.). The first two authors abstracted data from all studies, independent of each other, using separate codebooks in Microsoft Excel. Upon completion of coding, the codebooks were merged into one primary codebook for review. Both authors then met and reviewed every item for agreement. Discrepancies were resolved by consensus. If consensus could not be reached, the third author provided a recommendation. Using Cohen's kappa statistic (κ),[21] the overall agreement rate prior to correcting disagreements was 0.95.

Outcomes and prioritization

The primary outcome in this study was changes in anxiety. Secondary outcomes included changes in physical function, pain, depression, quality of life, body mass index

(BMI in $kg \cdot m^{-2}$), maximum oxygen consumption ($VO2_{max}$ in $ml \cdot kg^{-1} \cdot min^{-1}$), and muscular strength.

Risk of bias assessment in individual studies

Risk of bias was assessed at the study level using the Cochrane Risk of Bias instrument,[23] with a focus on the primary outcome of interest, changes in anxiety. Bias was evaluated across six domains: (1) random sequence generation, (2) allocation concealment, (3) blinding of participants and personnel, (4) blinding of outcome assessment, (5) incomplete outcome data, (6) selective reporting and (7) whether participants were exercising regularly, as defined by the original study authors, prior to taking part in the study. Each item was classified as having either a high, low, or unclear risk of bias. Because it's virtually impossible to blind participants to group assignment in exercise intervention protocols, all studies were classified as high risk with respect to the category "blinding of participants and personnel". Based on previous research, no study was excluded based on the results of the risk of bias assessment.[24] The first two authors conducted all assessments, independent of each other. Both authors then met and reviewed all selections for agreement. Discrepancies were resolved by consensus, and if necessary, consultation with the third author. Using Cohen's kappa statistic (κ),[21] the overall agreement rate for risk of bias assessment prior to correcting disagreements was 0.71.

Data Synthesis

Calculation of effect sizes

The primary outcome for this proposed project was changes in anxiety, calculated as Hedge's standardized mean difference effect size (ES), adjusted for small-sample

bias.[25] This was calculated by subtracting the change outcome difference in the exercise group minus the change outcome difference in the control group, and then dividing by the pooled standard deviation of the change outcome for the exercise and control groups. If change score standard deviations were not available, they were calculated from reported change outcomes, treatment effect 95% confidence intervals (CI), or pre and post standard deviation values according to procedures developed by Follmann et al.[26] Secondary outcomes (physical function, pain, quality of life, depression, muscular strength) were calculated using the same procedures as for the primary outcome while BMI and $VO2_{max}$ were calculated using the original metric. For studies in which outcomes were assessed at multiple time points, differences between baseline values and the final time point closest to cessation of the exercise intervention were used.

Pooled estimates for changes in outcomes

Effect size changes in anxiety and all secondary outcomes were pooled using the recently developed inverse heterogeneity (IVhet) model.[27] The IVhet model is a quasi-likelihood model that is computed by (1) calculating weights that sum to 1 from each study, (2) pooling effects from all the studies, and (3) calculating the variance of the pooled ES. The IVhet model has been shown to be superior to the original random-effects, method-of-moments model of Dersimonian and Laird,[28] the most common random-effects model used to pool aggregate data meta-analytic results.[29] Specifically, simulation studies have shown that the IVhet model retains correct coverage probabilities as well as a lower observed variance than the random-effects

model, regardless of heterogeneity.[27] Two-tailed z-alpha values ≤ 0.05 and non-overlapping 95% confidence intervals were considered statistically significant.

Heterogeneity and *inconsistency* for each pooled outcome were estimated using the Q[30] and I^2 statistic,[31] respectively. An alpha level of ≤ 0.10 for Q was considered to represent statistically significant heterogeneity while inconsistency was categorized as very low (<25%), low (25% to <50%), moderate (50% to <75%) or large (≥ 75%).[31] To improve practical relevance with respect to potential improvements in anxiety and all secondary outcomes, percentile gain in the exercise groups was calculated using Cohen's U_3 index[32] In addition, the number-needed-to treat (NNT) was estimated using the approach suggested by the Cochrane Collaboration[23] and a control group risk of 30% based on previous research on anxiolytics.[33] This was accomplished by converting the standardized mean differences into a log odds ratio, odds ratio, assumed control risk (30%) and then NNT. Extending the NNT, estimates of the number of US adults with AORD who could improve their anxiety levels but were not currently meeting physical activity recommendations were calculated. These were based on the reciprocal of the NNT multiplied by the number of adults in the United States with doctor-diagnosed arthritis who were not currently meeting exercise guidelines, currently approximately 31.6 million.[1 34] *Influence analysis* was conducted with each study deleted from the model once while *cumulative meta-analysis*, ranked by year, was used to examine the accumulation of results over time.

The primary pooling of results was based on group level findings. However, findings were also examined by collapsing results so that only one ES represented each study. In addition, for those outcomes that were assessed using multiple instruments, results

from these instruments were pooled into one ES. The rationale for this was based on the lack of consensus regarding the most valid and reliable instrument for the outcome and population of interest as well as the need to maintain as much independence as possible. For those studies that reported both per protocol and intention-to-treat analyses, results were also pooled into one ES.

Exploratory m*eta-regression* based on the IVhet model was used to examine the relationship between changes in our primary outcome (anxiety) and selected covariates.[27] This was accomplished by (1) conducting simple meta-regression for statistically significant associations between selected covariates and changes in anxiety, (2) examining for multicollinearity between covariates ($r > 0.80$), and (3) building a multiple meta-regression model. These models used a multiplicative versus additive component for residual heterogeneity. To achieve matching error variances, robust Huber-Ecker-White-sandwich error variances were used to account for the underestimated dispersion. Such errors were expected to calculate the correct standard errors for heterogeneous data that are traditionally heteroskedastic. Because of the small sample size, a post hoc decision was made to include the three potential predictors with the largest R^2 values as a result of simple regression analyses. However, since the investigative team felt that total minutes of training per week was more appropriate than total minutes of training over the entire duration of the study, the former was included in the regression. Multiple imputation was used to impute missing values for minutes of training per week so that the maximum sample size could be achieved.

Based on the recommendations of Rothman,[35] no adjustments for multiple testing were made because of concerns about missing possibly important findings that could be pursued in future randomized controlled trials. While this could be viewed as a 'fishing expedition', such analyses are important for providing investigators with potential direction for future randomized controlled trials, one of the very reasons for conducting a systematic review with meta-analysis.[36] This approach is especially appropriate for meta-analysis since covariates are not randomly assigned in meta-analysis and thus, such analyses are considered to be observational in nature.[37] As a result, causal inferences cannot be derived from meta-regression. However, any observed associations can provide direction for future research.

Meta-biases

Small-study-effects (publication bias, etc.) for primary and secondary outcomes were assessed following current guidelines.[38] This included qualitative analysis using funnel plots as well as quantitative analysis using Egger's regression-intercept test for continuous data.[38] An alpha level $\leq$ 0.05 and 95% CI that did not include zero (0) was considered to represent statistically significant small-study effects.

Confidence in cumulative evidence

Strength of findings for our primary outcome (anxiety) was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) for meta-analysis.[39] The quality of evidence was assessed across the domains of risk of bias, consistency, directness, precision and publication bias. Quality was judged as high (further research is very unlikely to change our confidence in the estimate of effect), moderate (further research is likely to have an important impact on our confidence in the

estimate of effect and may change the estimate), low (further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate), or very low (very uncertain about the estimate of effect).

Software used for data synthesis

All data was analyzed using Stata (V.14.1; Stata/SE for Windows (Version 14.1). College Station, Texas: Stata Corporation LP, 2015), Microsoft Excel 2010 (Microsoft Excel (Version 2010)), and three add-ins for Excel, Meta XL (V.5.3; Meta XL (Version 5.3). 2016), SSC-Stat (V.2.18; SSC-Stat (Version 2.18). University of Reading, UK: Statistical Services Center, 2007), and EZ-Analyze (V.3.0; EZ Analyze (Version 3.0). Boston, MA: Tim Poynton, 2007).

RESULTS

Study Characteristics

A flow diagram that depicts the search process for study selection is shown in Figure 1. After initially identifying 639 citations and removing 240 duplicates both electronically and manually, 399 citations were screened. Of these, 14 studies representing 30 groups (16 exercise, 14 control) and 926 initially enrolled participants (539 exercise, 387 control) met the criteria for inclusion.[40-53] Two studies included more than one intervention group.[48 51] One included a pool and walking group[48] while the other included a long and short bout exercise group.[51] The major reasons for exclusion were (1) inappropriate intervention (47.8%), (2) inappropriate study design (32.2%), (3) inappropriate population (11.9%), (4) inappropriate comparison group (4.7%), and (5) inappropriate outcome (3.4%). The precision of the search, excluding duplicates, was

3.5% while the NNR was 29. A list of excluded studies, including the reasons for exclusion, can be found in Supplementary File 2.

With respect to source, 1 study (7.1%) was published as a dissertation[41] while the remaining 13 (92.9%) were published in peer-reviewed journals.[40 42-53] For the 12 studies (85.7%) in which data were available, the 5-year impact factor of the journals in which studies were published ranged from 1.7 to 7.9 ($\bar{x} \pm$ SD, 4.1 $\pm$ 2.4, median = 2.9). Five studies (35.7%) were published in the United States,[41 42 46-48] 2 each in either Canada,[45 51] Portugal[52 53] or Spain,[49 50] and 1 each in either Australia,[43] Brazil,[40] or Ireland.[44] Thirteen of the 14 studies (92.9%) were published in English-language journals[40-52] while 1 (7.1%) was published in Spanish.[53] With respect to types of control groups, 4 studies used either a wait-list control[40 41 43 44] or what appeared to be some type of attention control group,[42 46 48 51] while three each used either a non-intervention[45 47 52] or usual care group.[49 50 53] Three studies (21.4%) reported using matching procedures according to either sex,[45] age, sex and BMI,[46] or type of arthritis (rheumatoid or osteoarthritis).[48] None of the studies reported using any type of crossover design.[40-53] For data analysis, 7 studies (50.0%) reported using the per-protocol approach,[41 46-48 50 52 53] 4 (28.6%) used intention-to-treat,[40 42-44] while the remaining 3 (21.4%) used both.[45 49 51] Eight studies (57.1%) provided sample size estimates.[40 42-44 46 50 51 53] With respect to funding, 12 studies (85.7%), reported receiving funding from government, university, or private sources for their work.[40 42-52]

Participant Characteristics

A description of the physical characteristics of participants for those studies that reported data is shown in Tables 1 and 2. On average, participants were overweight

and had low cardiorespiratory fitness. The majority of participants were women, although 7 studies (50.0%) also included a small number of men.[42-48] Nine studies (64.3%) were limited to participants with fibromyalgia,[40 41 45 46 49-53] 3 (21.4%) with osteoarthritis,[42-44] 1 with rheumatoid arthritis[47] and 1 with either rheumatoid arthritis or osteoarthritis.[48] For those studies in which data were available, the number of years in which rheumatic symptoms were present ranged from 3 to 24 ($\bar{x} \pm$ SD, 13.1 $\pm$ 7.0, median = 12.0),[44-46 49 51-53] while years since diagnosis ranged from 3 to 7 ($\bar{x} \pm$ SD, 4.1 $\pm$ 2.0, median = 3).[45 51-53] Nine of the 14 studies (64.3%) reported that one or more participants were taking some type of medication for their condition.[41 43-45 47-49 52 53] These included, but were not necessarily limited to, non-steroidal anti-inflammatory drugs (NSAIDS), analgesics, narcotics and non-narcotics for pain, muscle relaxants, antidepressants, and anxiolytics. One study reported cigarette smoking in some of the participants.[51] Participant withdrawals or removal in the exercise groups ranged from 0% to 50% ($\bar{x} \pm$ SD, 17.4 $\pm$ 13.4, median = 17.0) while withdrawals or removal in the control groups ranged from 0% to 41% ($\bar{x} \pm$ SD, 11.5 $\pm$ 12.7, median = 6.3). Reasons for withdrawals or removal included such things as family issues, pain from exercising, injuries, personal issues, time, unhappiness with group assignment, transportation issues, moving, employment commitments, boredom with exercise routine, not enough room or privacy to perform exercise, failure to complete lab assessments, not attending a specific percentage of the exercise sessions, or changing medications that could affect mood.

Exercise Intervention Characteristics

Exercise intervention characteristics for each group from each study are shown in Tables 1 and 3. Intensity of training, categorized according to American College of Sports Medicine[54] and limited to aerobic exercise only, included very light, light, moderate and vigorous exercise for the 9 (64.3%) studies that reported such information.[41 45 46 48-53] For mode of training, 6 studies (42.9%) focused on aerobic types of exercise,[40 41 45 48 50 51] 1 (7.1%) on weight training,[47] and 7 (50.0%) on both.[42-44 46 49 52 53] Specific types of aerobic activities included such things as aquatic exercise, walking, jogging, exercising to music and cycling. For the few studies that provided detailed information on resistance training, the number of sets ranged from 1 to 3,[47 49] the number of repetitions from 8 to 15,[47 49] and the number of exercises from 2 to 10 or more.[46 47 49] One study reported a rest period for 30 seconds between sets.[47] For those studies that reported data, the equipment used for resistance training included free weights and elastic bands.[42 46 47 52 53] Seven studies (50.0%) reported supervised exercise,[45 46 48-50 52 53] 5 (35.7%) reported both supervised and unsupervised exercise,[40-44] while the remaining 2 (14.3%) reported unsupervised exercise.[47 51] Three of the 14 studies (21.4%) reported some type of adverse event.[41 42 51] Reasons included 1 participant dropping out due to pain after the first exercise session,[41] 2 participants because of a history of a herniated disk and low back and leg pain,[42] and 1 participant because of a metatarsal fracture.[51] Another study reported that 1 participant withdrew because of the exacerbation of back pain[43] while a final study reported the exclusion of 2 participants because of severe coronary artery disease.[47] None of the studies provided data on the costs associated with conducting the intervention.[40-53]

Risk of Bias Assessment

Results for risk of bias assessment using the Cochrane Risk of Bias Assessment Instrument are shown in Figure 2 and Supplementary file 3. As can be seen, greater than 50% of the studies were at an unclear or high risk of bias with respect to (1) incomplete outcome reporting (78.6%), (2) allocation concealment (78.6%), and (3) blinding of outcome assessors (57.1%). Given the inability to truly blind participants in exercise intervention trials, all studies (100%) were considered to be at a high risk of bias for the category 'blinding of participants and personnel'.

Data Synthesis

Overall results for primary outcome (anxiety). Overall results for changes in anxiety for the 14 included studies[40-53] are shown in Table 4 and Figure 3. As can be seen, statistically significant (p = 0.002) reductions in anxiety were observed. In addition, statistically significant heterogeneity was observed while overall inconsistency was categorized as moderate, (range = low to large). The NNT was 6 with a percentile improvement of 15.5% and an estimated 5.3 million inactive US adults with AORD improving their anxiety if they started exercising regularly. Statistically significant small-study effects were observed (p < 0.0001) (Figure 4). With each result deleted from the model once, results remained statistically significant across all deletions, ranging from -0.44 (95% CI, -0.71 to -0.18) to -0.35 (-0.57 to -0.12). Cumulative meta-analysis, ranked by year, demonstrated that results have been statistically significant since the first study was conducted in 1989,[48] but with a trend towards smaller improvements in anxiety with each accumulating year (Figure 5). Reductions in anxiety were similar to group-level results when collapsed so that only one ES represented each study (ES, -0.40, 95% CI, -0.67 to -0.13, p = 0.004; Q = 39.6, p = 0.0002; I^2 = 67.2%, 95% CI, 42.6% to 81.3%,

tau^2 = 0.15). With six outliers deleted from the model, overall reductions in anxiety were similar but heterogeneity was no longer statistically significant and overall inconsistency was reduced to a level categorized as small (ES, -0.40, 95% CI, -0.62 to -0.18, p = 0.0004; Q = 11.8, p =0.22; I^2 = 24.0%, 95% CI, 0% to 63.1%, tau2 = 0.03).

Meta-regression results for anxiety. Simple meta-regression results are shown in Supplementary File 4. For study characteristics, greater reductions in anxiety were associated with (1) earlier publication year, (2) studies at an unclear versus low risk of bias, (3) studies in which sample size estimates were not provided, (4) trials in which a larger percentage of participants initially agreed to participate in, and (5) studies that were not funded versus funded. For participant characteristics, greater improvements were associated with a larger percent dropout in the exercise groups as well as younger age. For exercise intervention characteristics, greater reductions were associated with (1) aerobic/strength training versus aerobic and strength training combined, (2) fewer minutes of exercise per session, (3) minutes of exercise per week, and (4) total minutes of exercise for the entire intervention period. Greater reductions were also associated with (1) supervised and unsupervised exercise versus both, (2) facility and home-based exercise versus both and (3) group and self-exercise versus both.

Results for the final multiple regression model are shown in Table 5. The overall model was statistically significant (F = 17.2, p = 0.0005). Earlier year of publication and studies at an unclear versus low risk of bias for incomplete outcome data were statistically significant predictors for greater reductions in anxiety. However, minutes of exercise per week was no longer statistically significant.

GRADE findings for changes in anxiety. An evidence profile for changes in anxiety is shown in Supplementary file 5. As can be seen, the outcome (anxiety) was considered critical and the overall strength of the finding was considered high, with future additional studies unlikely to have an effect on the overall direction of findings.

Results for secondary outcomes. Overall results for changes in secondary outcomes are shown in Table 4. *Physical function* was assessed in 10 studies[40 42-45 47 48 51-53] using the 10 meter walk test, 50 foot walk, 6 minute walk, Arthritis Impact and Measurement Scale (AIMS), Fibromyalgia Impact Questionnaire (FIQ), Short Physical Performance Battery, sit-to-stand test, stairclimbing test, up and go test, and the Western Ontario and McMaster Osteoarthritis Index (WOMAC). As can be seen, statistically significant ($p < 0.001$) improvements in *physical function* were observed. Statistically significant heterogeneity was observed while inconsistency was categorized as moderate, (range = low to large). The NNT was 4 with a percentile improvement of 24.5% and an estimated 9 million inactive US adults with AORD improving their physical function if they started exercising regularly. No statistically significant small-study effects were observed ($p = 0.17$). With each result deleted from the model once, results remained statistically significant across all deletions, ranging from 0.54 (95% CI, 0.30 to 0.78) to 0.73 (95% CI, 0.39 to 1.06). Cumulative meta-analysis, ranked by year, demonstrated that results have been statistically significant since the first study was conducted in 1989,[48] but with a trend towards smaller improvements in physical function with each accumulating year (from 0.86 in 1989 to 0.66 in 2016). Improvements in physical function were similar to group-level results when collapsed so that only one ES represented each study (ES, 0.66, 95% CI, 0.31 to 1.01, $p = 0.0002$; $Q = 35.6$, $p < 0.001$; $I^2 = 74.7\%$, 95% CI, 52.8%

to 86.5%, tau^2 = 0.21). With four outliers deleted from the model, overall improvements in physical function were statistically significant but slightly smaller, heterogeneity was no longer statistically significant, and overall inconsistency was reduced to a level categorized as very low (ES, 0.57, 95% CI, 0.36 to 0.78, p <0.001; Q = 7.2, p =0.41; I^2 = 2.7%, 95% CI, 0% to 68.5%, tau^2 = 0.003).

For *pain,* assessment was conducted in 13 studies[40-44 46-53] using the AIMS, FIQ, numerical rating scale, tender point count, visual analog scale and the WOMAC. As can be seen in Table 4, statistically significant (p = 0.017) decreases in pain were found. Statistically significant heterogeneity was observed while inconsistency was categorized as large, including both CIs. The NNT was 6 with a percentile improvement of 23.1% and an estimated 5.6 million inactive US adults with AORD decreasing their pain if they started exercising regularly. No statistically significant small-study effects were observed (p = 0.34). With each result deleted from the model once, results remained statistically significant across all deletions, ranging from -0.70 (95% CI, -1.21 to -0.19) to -0.47 (95% CI, -0.80 to -0.15). Cumulative meta-analysis, ranked by year, demonstrated that results have been statistically significant, and remained statistically significant, since only 2013. Decreases in pain were similar to group-level results when collapsed so that only one ES represented each study (ES, -0.62, 95% CI, -1.16 to -0.07, p = 0.03; = 123.7, p <0.001; I^2 = 90.3%, 95% CI, 85.3% to 93.6%, tau^2 = 0.75). With ten outliers deleted from the model, decreases in pain remained statistically significant but smaller, heterogeneity was no longer statistically significant, and overall inconsistency was reduced to a level categorized as very low (ES, -0.44, 95% CI, -0.70 to -0.18, p = 0.001; Q = 1.5, p =0.68; I^2 = 0%, 95% CI, 0% to 69.5%, tau^2 = 0).

Depression was assessed in 13 studies[40-48 50-53] using the AIMS, Beck Depression Inventory (BDI), Center for Epidemiologic Studies Depression Scale (CES-D), Depression, Anxiety and Stress Scale (DASS21), FIQ, HADS, MHI, and VAS. As can be seen in Table 4, statistically significant (p = 0.009) decreases in depression were found. Statistically significant heterogeneity was observed while inconsistency was categorized as moderate (95% CI = low to large). The NNT was 6 with a percentile improvement of 15% and an estimated 5.1 million inactive US adults with AORD reducing their depression if they started exercising regularly. Small-study effects were not statistically significant (p = 0.08). With each result deleted from the model once, results remained statistically significant across all deletions, ranging from -0.52 (95% CI, -0.68 to -0.37) to -0.32 (95% CI, -0.61 to -0.0.3). Cumulative meta-analysis, ranked by year, demonstrated that improvements have been statistically significant and remained stable since 2013. Decreases in depression were similar to group-level results when collapsed so that only one ES represented each study (ES, -0.38, 95% CI, -0.70 to -0.07, p = 0.02; Q = 45.6, p < 0.001; I^2 = 73.7%, 95% CI, 54.3% to 84.8%, tau^2 = 0.21). With three outliers deleted from the model, improvements in depression remained statistically significant, slightly larger, but with non-significant heterogeneity and overall inconsistency categorized as very low (ES, -0.43, 95% CI, -0.60 to -0.26, p < 0.001; Q = 5.7, p =0.89; I^2 = 0%, 95% CI, 0% to 19.3%, tau^2 = 0).

Quality-of-life was assessed in 12 studies[40-47 49 51-53] using the FIQ, Health Assessment Questionnaire (HAQ), Quality of Life Scale (QOLS), SF-12, and SF-36. As shown in Table 4, statistically significant (p < 0.0001) improvements in quality-of-life were found. Statistically significant heterogeneity was observed while inconsistency was categorized

as large (95% CI = low to large). The NNT was 4 with a percentile improvement of 23.1% and an estimated 8.6 million inactive US adults with AORD improving their quality-of-life if they started exercising regularly. Statistically significant small-study effects were observed ($p < 0.001$). With each result deleted from the model once, results remained statistically significant across all deletions, ranging from 0.58 (95% CI, 0.35 to 0.81) to 0.70 (95% CI, 0.41 to 0.99). Cumulative meta-analysis, ranked by year, demonstrated that improvements have been statistically significant since 2001, but with a trend towards a decrease in the magnitude of effect. Increases in quality-of-life were similar to group-level results when collapsed so that only one ES represented each study (ES, 0.63, 95% CI, 0.34 to 0.92, $p < 0.001$; $Q = 30.9$, $p = 0.001$; $I^2 = 64.3\%$, 95% CI, 33.9% to 80.8%, $tau^2 = 0.14$). With four outliers deleted from the model, improvements in quality-of-life remained statistically significant, similar in magnitude, but with non-significant heterogeneity and overall inconsistency categorized as low (ES, 0.64, 95% CI, 0.39 to 0.90, $p < 0.001$; $Q = 11.4$, $p = 0.18$; $I^2 = 29.8\%$, 95% CI, 0% to 67.5%, $tau^2 = 0.04$).

Maximum oxygen consumption ($VO2_{max}$ in $ml \cdot kg^{-1} \cdot min^{-1}$) was assessed in 5 studies[46-48] [51 52] using various maximal treadmill tests while one study used a submaximal step test (Canadian Aerobic Fitness Test). As can be seen in Table 4, statistically significant ($p = 0.001$) improvements in $VO2_{max}$ were observed. Statistically significant heterogeneity was observed while inconsistency was categorized as moderate (95% CI = low to large). The NNT was 3 with a percentile improvement of 25.7% and an estimated 9.5 million inactive US adults with AORD improving their relative $VO2_{max}$ if they started exercising regularly. No statistically significant small-study effects were observed ($p =$

0.18). With each result deleted from the model once, results remained statistically significant across all deletions, ranging from 1.80 $ml \cdot kg^{-1} \cdot min^{-1}$ (95% CI, 0.58 to 3.01) to 2.47 $ml \cdot kg^{-1} \cdot min^{-1}$ (95% CI, 1.25 to 3.69). Cumulative meta-analysis, ranked by year, demonstrated that improvements have been statistically significant since 2003, but with a trend towards a decrease in the magnitude of effect over time. Increases in $VO2_{max}$ were similar to group-level results when collapsed so that only one ES represented each study (ES, 2.01 $ml \cdot kg^{-1} \cdot min^{-1}$, 95% CI, 0.59 to 3.44, p = 0.01; Q = 19.4, p = 0.001; I^2 = 79.4%, 95% CI, 51.2% to 91.3%, tau^2 = 1.7). With outliers deleted from the model, improvements in $VO2_{max}$ were smaller, with non-significant heterogeneity and overall inconsistency categorized as low (ES, 1.93 $ml \cdot kg^{-1} \cdot min^{-1}$, 95% CI, 0.83 to 3.02, p = 0.001; Q = 0.03, p =0.86; I^2 = 0%, 95% CI, 0% to 0%, tau^2 = 0).

Upper and lower body *muscular strength* was assessed in five studies[45 47-49 52] using free weights, grip strength, isokinetic strength and the sit-to-stand test with free weights. As shown in Table 4, statistically significant (p < 0.001) improvements in strength were observed. No statistically significant heterogeneity or mean inconsistency was observed (95% CI = none to moderate). The NNT was 4 with a percentile improvement of 22.2% and an estimated 8 million inactive US adults with AORD improving their strength if they started exercising regularly. No statistically significant small-study effects were observed (p = 0.65). With each result deleted from the model once, results remained statistically significant across all deletions, ranging from 0.50 (95% CI, 0.21 to 0.79) to 0.68 (95% CI, 0.39 to 0.96). Cumulative meta-analysis, ranked by year, demonstrated that improvements in strength have been statistically significant since the first included study in 1989.[48] Changes in strength were similar to group-level results when collapsed

so that only one ES represented each study (ES, 0.59, 95% CI, 0.33 to 0.85, p < 0.001; Q = 3.5, p = 0.48; I^2 = 0%, 95% CI, 0% to 76.2%, tau^2 = 0). There were no outliers.

Insufficient data were available to analyze *BMI*. The one study that did provide change outcome results for BMI reported no statistically significant changes.[46]

DISCUSSION

Overall Findings

The primary purpose of the current systematic review with meta-analysis was to examine the effects of exercise (aerobic, strength training, or both) on anxiety in adults with AORD. The overall findings, a primary purpose of meta-analysis,[55] suggest that exercise results in both statistically significant and practically important reductions in anxiety among adults with selected types of AORD. These findings are supported by (1) a magnitude of effect comparable to or greater than anxiolytics,[56] (2) a large percentile improvement (15.5), (3) low NNT (6), large number of physically inactive US adults with AORD who could benefit from exercising regularly (5.3 million), (4) similar findings when examined at the study versus group level, (5) continued existence of a statistically significant effect when each result was deleted from the analysis once, (6) similar findings when outliers were deleted and statistical heterogeneity was reduced to a non-significant effect and overall inconsistency to zero, and (7) a consistent finding of improvements in anxiety since the first included study was reported in 1989.[48] Based on GRADE, it was concluded that anxiety was a critical outcome and that further research would unlikely change the direction of effect.

While the current findings are encouraging, it is interesting to note that cumulative meta-analysis revealed a distinct trend for a reduction in the pooled ES over time (from -

1.47 in 1989 to -0.40 in 2016) and based on meta-regression, a statistically significant association between greater reductions in anxiety with older versus more recent studies. While the specific reasons for this could not be determined, it may be that the experimental design and conduct of studies have improved over time. However, from the investigative team's perspective, it is highly unlikely that the results will become non-significant in future years. The former notwithstanding, the general conclusion that exercise reduces anxiety in adults with selected types of AORD may need to be viewed with some caution given that the majority of included studies consisted of participants with fibromyalgia[40 41 45 46 49-53] while the remaining studies included those with osteoarthritis and/or rheumatoid arthritis.[42-44 47 48] While meta-regression revealed no statistically significant association between type of AORD and changes in anxiety, such analyses may have been underpowered to detect such an association. In addition, since other types of AORD such as systemic lupus erythematosus were not included, generalizing to populations with other types of AORD may not be appropriate.

The final meta-regression model resulted in two statistically significant variables being included with earlier year of publication and studies at an unclear versus low risk of bias for incomplete outcome data associated with greater reductions in anxiety. These findings further reinforce the influence of year of publication on changes in anxiety in the current systematic review with meta-analysis, a potential reason for such having been previously mentioned. The greater reductions observed for studies at an unclear versus low risk of bias suggests that more poorly reported, and possibly conducted, studies may have led to inflated findings.

In addition to statistically significant and practically important improvements in anxiety, similar improvements were also observed for all secondary outcomes assessed (physical function, pain, depression, quality of life, $VO2_{max}$ in $ml \cdot kg^{-1} \cdot min^{-1}$, muscular strength). These findings are important because unlike pharmacologic interventions that are usually targeted to address one condition, exercise has the potential to improve multiple physiological and psychological outcomes. Given the former, it would seem plausible to suggest that continued efforts be made to increase the exercise and physical activity levels of adults with AORD.

Implications for Research

There are at least four implications for the conduct and reporting of future research on exercise and anxiety in adults with AORD. First, since only five of the studies included participants with osteoarthritis and/or rheumatoid arthritis, future randomized controlled trials on exercise and anxiety in these populations appear warranted. Second, exercise was performed indoors in the majority of included studies. Given that previous research has suggested the exercise performed outdoors may have better mood-enhancing effects than indoor exercise,[57 58] future research examining this phenomenon with respect to anxiety as well as other outcomes in adults with AORD seems appropriate. Third, future studies should focus on examining the dose-response effects of exercise on anxiety in adults with AORD and report complete information on the characteristics of the intervention, including intervention fidelity.[59] Such information is critical for the development of evidence-based recommendations aimed at practitioners. Fourth, since more than half of the studies were considered to be at high or unclear risk of bias with respect to allocation concealment, blinding of outcome assessors, and incomplete

outcome reporting, future studies should address these issues in their experimental design and report such information. Notably, while all included studies were considered to be at a high risk of bias with respect to blinding of participants, this is difficult for researchers to address since unlike pharmacologic studies, it is almost impossible to blind intervention participants to group assignment in exercise intervention studies.

Implications for Practice

The results of this study appear to have important implications for practice. First, since changes in both anxiety and secondary outcomes resulted in statistically significant and practically important improvements, exercise may be more vital than any other intervention given the apparent multiple benefits of such. While the current systematic review with meta-analysis was unable to establish with any degree of certainty the dose-response effects of exercise on anxiety in adults with AORD, it would appear prudent to adhere to the Active Adult or Active Older Adult Guidelines from the Physical Activity Guidelines for Americans Physical Activity Guidelines[17] as recommended by the Centers for Disease Control and Prevention.[60] Broadly, this includes aerobic activities on most, if not all, days of the week, muscle strengthening activities at least 2 days per week, balance exercises at least 3 days per week, and flexibility exercises on a daily basis.

Strengths and Limitations

There are at least four apparent *strengths* of the current study. First, to the best of our knowledge, this is the first systematic review with meta-analysis to examine, as a primary outcome, the effects of exercise on anxiety in adults with AORD. This is important given (1) the prevalence of AORD,[1] (2) the expected future increase in the

prevalence of AORD,[2] (3) the financial costs associated with AORD,[3] and (4) the previously reported finding that the prevalence of anxiety is almost twice that of depression.[8] Second, a novel and recently developed approach, the IVhet model, was used to pool findings.[27] This resulted in more robust estimates than those derived from the traditional random-effects model.[28] This is noteworthy given the need to provide the most accurate results possible when examining the effects of an intervention on selected outcome(s). Third, the statistically significant and practically relevant improvements in anxiety as well as selected secondary outcomes observed in the current systematic review with meta-analysis should be useful to practitioners and policy-makers for making informed decisions about the role of exercise in the treatment of anxiety among adults with selected types of AORD. Fourth, the current findings as well as gaps in the reviewed literature provide researchers with direction for the conduct and reporting of future research on this topic.

While there are several strengths to this study, there are also at least four potential *limitations*. First, similar to any aggregate data meta-analysis, the potential for ecological fallacy exists. Thus, it may be that the observed findings in the current study would not apply at the individual participant level. Second, and also common to any type of aggregate data meta-analysis, meta-regression results do not support causal inferences because the included studies are not randomly assigned to covariates.[37] Therefore, the associations observed in the current investigation would need to be assessed in appropriately powered randomized trials. Third, while a large number of statistical tests were conducted, no adjustments were made for such. Thus, some findings could have been nothing more than the play of chance. However, common to

most aggregate data meta-analyses, no adjustments for multiple testing were made because of concerns about missing possibly important findings that could be tested in original trials.[35] Fourth, since anxiety was assessed using self-report instruments,[40-53] the possibility of reporting bias in the original studies existed.

CONCLUSIONS

Exercise is associated with reductions in anxiety among adults with selected types of AORD. However, a need exists for additional, well-designed, randomized controlled trials on this topic.

CONTRIBUTORS

GAK was responsible for the conception and design, acquisition of data, analysis and interpretation of data, drafting the initial manuscript and revising it critically for important intellectual content. KSK was responsible for the conception and design, acquisition of data, drafting the initial manuscript, and revising all drafts critically for important intellectual content. LFC was responsible for the conception and design, acquisition of data, drafting the initial manuscript, and revising all drafts critically for important intellectual content. All authors read and approved the final manuscript.

REGISTRATION

In accordance with Primary Reporting Items for Systematics Reviews and Meta-Analyses, our systematic review with network meta-analysis was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on October 4, 2016 (registration number CRD42016048728).

COMPETING INTERESTS

None.

FUNDING

This meta-analysis was funded by the National Institutes of Health, National Institute for Arthritis, Musculoskeletal and Skin Diseases, grant number R01AR061346 (GAK, Principal Investigator).

DATA SHARING STATEMENT

All data are available upon request from the corresponding author.

REFERENCES

1. Barbour KE, Helmick CG, Boring M*, et al.* Vital signs: Prevalence of doctor-diagnosed arthritis and arthritis-attributable activity limitation — United States, 2013–2015. *Morb Mortal Wkly Rep* 2017;66(9):8.
2. Hootman JM, Helmick CG, Barbour KE*, et al.* Updated projected prevalence of self-reported doctor-diagnosed arthritis and arthritis-attributable activity limitation among us adults, 2015-2040. *Arthritis Rheumatol* 2016;68(7):1582-7.
3. Yelin E, Murphy L, Cisternas MG*, et al.* Medical care expenditures and earnings losses among persons with arthritis and other rheumatic conditions in 2003, and comparisons with 1997. *Arthritis Rheum* 2007;56(5):1397-407.
4. Player MS, Peterson LE. Anxiety disorders, hypertension, and cardiovascular risk: a review. *Int J Psychiatry Med* 2011;41(4):365-77.
5. Roest AM, Martens EJ, de JP*, et al.* Anxiety and risk of incident coronary heart disease: a meta-analysis. *J Am Coll Cardiol* 2010;56(1):38-46.
6. Janszky I, Ahnve S, Lundberg I*, et al.* Early-onset depression, anxiety, and risk of subsequent coronary heart disease: 37-year follow-up of 49,321 young Swedish men. *J Am Coll Cardiol* 2010;56(1):31-37.
7. Blakemore A, Dickens C, Guthrie E*, et al.* Depression and anxiety predict health-related quality of life in chronic obstructive pulmonary disease: systematic review and meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2014;9:501-12.
8. Murphy LB, Sacks JJ, Brady TJ*, et al.* Anxiety and depression among US adults with arthritis: Prevalence and correlates. *Arthritis Care Res* 2012;64(7):968-76.

9. Busch AJ, Schachter CL, Overend TJ*, et al.* Exercise for fibromyalgia: a systematic review. *J Rheumatol* 2008;35(6):1130-44.

10. Hurkmans E, van der Giesen FJ, Vliet Vlieland TP*, et al.* Dynamic exercise programs (aerobic capacity and/or muscle strength training) in patients with rheumatoid arthritis. *Cochrane Database Syst Rev* 2009(4):CD006853.

11. Kelley GA, Kelley KS, Hootman JM. Effects of exercise on depression in adults with arthritis: a systematic review with meta-analysis of randomized controlled trials. *Arthritis Res Ther* 2015;17:21.

12. Kelley GA, Kelley KS. Effects of exercise on anxiety in adults with arthritis and other rheumatic disease: A systematic review of meta-analyses. *J Nov Physiother* 2014;4(4):1-5.

13. Liberati A, Altman DG, Tetzlaff J*, et al.* The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Ann Intern Med* 2009;151(4):W65-W94.

14. Kelley GA, Kelley KS, Callahan LF. Community-deliverable exercise and anxiety in adults with arthritis and other rheumatic diseases: a protocol for a systematic review and meta-analysis of randomised controlled trials. *BMJ Open* 2017;7(3):e014957.

15. Sacks HS, Chalmers TC, Smith H. Randomized versus historical controls for clinical trials. *Am J Med* 1982;72:233-40.

16. Schulz KF, Chalmers I, Hayes R*, et al.* Empirical evidence of bias: Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *J Am Med Assoc* 1995;273:408-12.

17. Physical Activity Guidelines Advisory Committee. *Physical Activity Guidelines Advisory Report*. Washington, DC: U.S. Department of Health and Human Services, 2008

18. Brady TJ, Jernick SL, Hootman JM*, et al.* Public health interventions for arthritis: expanding the toolbox of evidence-based interventions. *J Womens Health (Larchmt)* 2009;18(12):1905-17.

19. Ide MR, Laurindo IMM, Rodrigues AL*, et al.* Effect of aquatic respiratory exercise-based program in patients with fibromyalgia. *Int J Rheum Dis* 2008;11(2):131-40.

20. Waggoner CD, LeLieuvre RB. A method to increase compliance to exercise regimens in rheumatoid arthritis patients. *J Behav Med* 1981;4(2):191-201.

21. Cohen J. Weighted kappa: nominal scale agreement with provision for scaled disagreement or partial credit. *Psychol Bull* 1968;70:213-20.

22. Lee E, Dobbins M, DeCorby K*, et al.* An optimal search filter for retrieving systematic reviews and meta-analyses. *BMC Med Res Methodol* 2012;12:51.

23. Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]*: The Cochrane Collaboration, 2011.

24. Ahn S, Becker BJ. Incorporating quality scores in meta-analysis. *J Educ Behav Stat* 2011;36(5):555-85.

25. Hedges LV, Olkin I. *Statistical methods for meta-analysis*. San Diego, CA: Academic Press, 1985.

26. Follmann D, Elliot P, Suh I*, et al.* Variance imputation for overviews of clinical trials with continuous response. *J Clin Epidemiol* 1992;45:769-73.

27. Doi SA, Barendregt JJ, Khan S*, et al.* Advances in the meta-analysis of heterogeneous clinical trials I: The inverse variance heterogeneity model. *Contemp Clin Trials* 2015;45(Pt A):130-38.

28. Dersimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;7:177-88.

29. Dersimonian R, Laird N. Meta-analysis in clinical trials revisited. *Contemp Clin Trials* 2015;45(Pt A):139-45.

30. Cochran WG. The combination of estimates from different experiments. *Biometrics* 1954;10:101-29.

31. Higgins JPT, Thompson SG, Deeks JJ*, et al.* Measuring inconsistency in meta-analyses. *Br Med J* 2003;327(7414):557-60.

32. Cohen J. *Statistical power analysis for the behavioral sciences*. New York: Academic Press, 1988.

33. Khan A, Khan S, Brown WA. Are placebo controls necessary to test new antidepressants and anxiolytics? *Int J Neuropsychopharmacol* 2002;5(3):193-7.

34. Murphy LB, Hootman JM, Boring MA*, et al.* Leisure time physical activity among U.S. adults with arthritis, 2008-2015. *Am J Prev Med* 2017

35. Rothman KJ. No adjustments are needed for multiple comparisons. *Epidemiology* 1990;1:43-46.

36. Sacks HS, Berrier J, Reitman D*, et al.* Meta-analysis of randomized controlled trials. *N Engl J Med* 1987;316:450-55.

37. Littell JH, Corcoran J, Pillai V. *Systematic reviews and meta-analysis*. New York: Oxford University Press, 2008:1-202.

38. Sterne JA, Sutton AJ, Ioannidis JP*, et al.* Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *Br Med J* 2011;343:d4002.

39. Guyatt G, Oxman AD, Akl EA*, et al.* GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;64(4):383-94.

40. Baptista AS, Villela AL, Jones A*, et al.* Effectiveness of dance in patients with fibromyalgia: a randomized, single-blind, controlled study. *Clin Exp Rheumatol* 2012;30(6 Suppl 74):18-23.

41. Beltran R. The effects of a supervised group aerobic exercise program and a chronobiologicary oriented treatment protocol on symptomotatogy and mood in women with fibromyalgia [Dissertation]. Alliant University, 2003.

42. Cheung C, Wyman JF, Bronas U*, et al.* Managing knee osteoarthritis with yoga or aerobic/strengthening exercise programs in older adults: a pilot randomized controlled trial. *Rheumatol Int* 2017;37(3):389-98.

43. Fransen M, Nairn L, Winstanley J*, et al.* Physical activity for osteoarthritis management: a randomized controlled clinical trial evaluating hydrotherapy or Tai Chi classes. *Arthritis Rheum* 2007;57(3):407-14.

44. French HP, Cusack T, Brennan A*, et al.* Exercise and manual physiotherapy arthritis research trial (EMPART) for osteoarthritis of the hip: a multicenter randomized controlled trial. *Arch Phys Med Rehabil* 2013;94(2):302-14.

45. Gowans SE, deHueck A, Voss S*, et al.* Effect of a randomized, controlled trial of exercise on mood and physical function in individuals with fibromyalgia. *Arthritis Rheum* 2001;45(6):519-29.

46. Jones KD, Burckhardt CS, Deodhar AA*, et al.* A six-month randomized controlled trial of exercise and pyridostigmine in the treatment of fibromyalgia. *Arthritis Rheum* 2008;58(2):612-22.

47. Komatireddy GR, Leitch RW, Cella K*, et al.* Efficacy of low load resistive muscle training in patients with rheumatoid arthritis functional class II and III. *J Rheumatol* 1997;24(8):1531-39.

48. Minor MA, Hewett JE, Webel RR*, et al.* Efficacy of physical conditioning exercise in patients with rheumatoid arthritis and osteoarthritis. *Arthritis Rheum* 1989;32(11):1396-405.

49. Munguia-Izquierdo D, Legaz-Arrese A. Assessment of the effects of aquatic therapy on global symptomatology in patients with fibromyalgia syndrome: a randomized controlled trial. *Arch Phys Med Rehabil* 2008;89(12):2250-7.

50. Sanudo B, Carrasco L, de Hoyo M*, et al.* Vagal modulation and symptomatology following a 6-month aerobic exercise program for women with fibromyalgia. *Clin Exp Rheumatol* 2015;33(1 Suppl 88):S41-5.

51. Schachter CL, Busch AJ, Peloso PM*, et al.* Effects of short versus long bouts of aerobic exercise in sedentary women with fibromyalgia: a randomized controlled trial. *Phys Ther* 2003;83(4):340-58.

52. Tomas-Carus P, Gusi N, Hakkinen A*, et al.* Eight months of physical training in warm water improves physical and mental health in women with fibromyalgia: a randomized controlled trial. *J Rehabil Med* 2008;40(4):248-52.

53. Tomas-Carus P, Gusi N, Leal A*, et al.* [The fibromyalgia treatment with physical exercise in warm water reduces the impact of the disease on female patients' physical and mental health]. *Rheumatol Clin* 2007;3(1):33-37.

54. Garber CE, Blissmer B, Deschenes MR*, et al.* 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(7):1334-59.

55. Glass GV, McGaw B, Smith ML. *Meta-analysis in social research*. Newbury Park, California: Sage, 1981.

56. Hidalgo RB, Tupler LA, Davidson JR. An effect-size analysis of pharmacologic treatments for generalized anxiety disorder. *J Psychopharmacol* 2007;21(8):864-72.

57. Rogerson M, Gladwell VF, Gallagher DJ*, et al.* Influences of green outdoors versus indoors environmental settings on psychological and social outcomes of controlled exercise. *Int J Environ Res Public Health* 2016;13(4):363.

58. Pasanen TP, Tyrvainen L, Korpela KM. The relationship between perceived health and physical activity indoors, outdoors in built environments, and outdoors in nature. *Appl Psychol Health Well Being* 2014;6(3):324-46.

59. Resnick B, Inguito P, Orwig D*, et al.* Treatment fidelity in behavior change research - A case example. *Nurs Res* 2005;54(2):139-43.

60. CDC. Physical activity for arthritis Atlanta, Georgia: Centers for Disease Control and Prevention; 2017 [updated April 18, 2017. Available from: https://www.cdc.gov/arthritis/basics/physical-activity-overview.html accessed July 5 2017.

Table 1. Study characteristics.

Study and Year	Country	Participants	Exercise Intervention	Anxiety Assessment
Baptista et al., 2012[40]	Brazil	Women (N = 80) 18-65 yrs of age with FM assigned to exercise (n = 40, age, $\bar{x}$ = 49.5 yrs) or control (n = 40, age, $\bar{x}$ = 49.1 yrs) group	Dance exercise 2 x/wk, 60 min/session, for 12 wks	STAI
Beltran, 2003[41]	United States	Women (N = 21) 22-65 yrs of age with FM assigned exercise (n = 11, age, $\bar{x}$ ± SD = 50.1 ± 12.6 yrs) or control (n = 10, age, $\bar{x}$ ± SD = 53.7 ± 6.9 yrs) group	Aerobic aquatic exercise, 3 x/wk, 25 min/session, 60-85% MHR, for 10 wks	AIMS
Cheung et al., 2017 [42]	United States	Men and women (N=51) ≥ 65 yrs of age with knee OA assigned to exercise (n = 28, age, $\bar{x}$ ± SD = 74.4 ± 7.5 yrs), or control (n = 23, age, $\bar{x}$ ± SD = 71.8 ± 8.0 yrs) group	Aerobic exercise, 5 x/wk, 20-30 min/session for 8 wks, and strength exercise 3 x/wk, 30 min/session for 8 wks (10+ exercises)	HADS
Fransen et al., 2007[43]	Australia	Men and women (N=96) 59-85 yrs of age with hip or knee OA assigned to hydrotherapy (n = 55, age, $\bar{x}$ ± SD = 70 ± 6.3 yrs), or wait-list control (n = 41, age, $\bar{x}$ ± SD = 69.6 ± 6.1 yrs) group	Hydrotherapy exercises in warm water, 2 x/wk, 60 min/session, for 12 wks	DASS21
French et al., 2013[44]	Ireland	Men and women (N = 88) 40-80 yrs of age with hip OA assigned to exercise (n = 45, age, $\bar{x}$ ± SD =	Aerobic & strength training, 30 min/session, for 8 wks, up to 5 strength	HADS

		61.8 ± 9.7 yrs), or control (n = 43, age, $\bar{x}$ ± SD = 60.8 ± 9.7 yrs) group	exercises	
Gowans et al., 2001[45]	Canada	Men and women (N = 57) with FM assigned to an exercise (n = 30, age, $\bar{x}$ ± SD = 44.6 ± 8.7 yrs), or control (n = 27, age, $\bar{x}$ ± SD = 49.8 ± 7.3 yrs) group	Aerobic exercise (2 walking/jogging classes in a gym, 1 pool class), 3 x/wk, 30 min/session, 60-75% MHR, for 23 wks	MHI, STAI
Jones et al., 2008[46]	United States	Men and women (N = 101) 18-65 yrs of age with FM assigned to an exercise (n = 47, age, $\bar{x}$ ± SD = 49.6 ± 7.7 yrs), or control (n = 54, age, $\bar{x}$ ± SD = 49.8 ± 7.9 yrs) group	Aerobic exercise 3 x/wk, 30 min/session, 40-50% MHR & strength exercise, 3 x/wk, 10 min/session, for 24 wks	FIQ (Anxiety)
Komatireddy et al.[47]	United States	Men and women (n = 49), 35-76 yrs of age with RA assigned to exercise (n = 25, $\bar{x}$ ± SD = 57.7 ± 9.8 yrs of age, range 40–72 yrs) or control (n = 24, $\bar{x}$ ± SD = 60.5 ± 11 yrs of age, range 35–76 yrs) group	Circuit weight training with light loads and high repetitions, 7 exercises, 2–3 circuits/session, 12–15 reps, 30-second rest between sets, 20–27 min/session, $\geq$ 3 x/wk, RPE of 3–4, for 12 wks	AIMS
Minor et al., 1989[48]	United States	Men and women (N = 115) 21–83 yrs of age with RA or OA assigned to a pool (n = 47), walking (n = 36) or control group (n = 32)	Aerobic aquatics or walking group, 3 x/wk, 60 min/session (30 min of this was aerobic), 60-80% MHR, for 12 wks	AIMS
Munguia-Izquieerdo & Legaz-Arrese,	Spain	Men and women (N = 60) 18-60 yrs of age with FM assigned to exercise (n = 35, $\bar{x}$ ± SD = 50.0 ± 7.0 yrs) or control (n = 25 $\bar{x}$ ± SD = 46.0 ± 8.0 yrs)	Aerobic aquatic exercise, 3 x/wk, 20-30 min/session, 50-80% MHR, & strength exercise 3 x/wk, 8-20 min/session, 1-3	STAI

2008[49]		group	sets, 8-15 reps, for 16 wks	
Sanudo et al., 2015[50]	Spain	Women (N = 32) with FM assigned to exercise (n = 16, $\bar{x}$ ± SD = 55.0 ± 8.0 yrs of age), or control (n = 16, $\bar{x}$ ± SD = 58.0 ± 6.9 yrs of age) group	Aerobic/interval training, 2 x/wk, 30-35 min/session, 60-80% MHR, for 24 weeks	VAS
Schachter et al., 2003[51]	Canada	Women (N = 143) 20–55 yrs of age with FM assigned to a short bout (n = 56, $\bar{x}$ ± SD = 41.9 ± 8.6 yrs of age), long bout (n = 51, $\bar{x}$ ± SD = 41.3 ± 8.7 yrs of age), or control group (n = 36, $\bar{x}$ ± SD = 42.5 ± 6.7 yrs of age)	Low impact, videotape-based, aerobic exercise to music. Short bout, 2 x/d, 7.1 x/wk, 12.3 min/session, 60% HRR; Long-bout group: 1 x/d, 3.6 x/wk, 24.5 min/session, 60% HRR, for 16 wks	FIQ (Anxiety)
Tomas-Carus et al., 2008[52]	Portugal	Women with FM (N = 33) assigned to aquatic exercise (n = 17, $\bar{x}$ ± SD = 50.7 ± 10.6 yrs of age) or control group (n = 16, $\bar{x}$ ± SD = 50.9 ± 6.7 yrs of age)	Pool exercises performed in warm water, 3 x/wk, 20 min, aerobic phase, 60-65% MHR, strength exercise, 20 min, 4 sets, 10 reps, for 32 wks	FIQ (Anxiety), STAI
Tomas-Carus et al., 2007[53]	Portugal	Women with FM (N = 34) assigned to aquatic exercise (n = 17, $\bar{x}$ ± SD = 51 ± 10.0 yrs of age) or control group (n = 17, $\bar{x}$ ± SD = 51 ± 9.0 yrs of age)	Pool exercises performed in warm water, 3 x/wk, 20 min, aerobic phase, 60-65% MHR, strength exercises, 20 min, 4 sets, 10 reps, for 12 wks	FIQ (Anxiety)

Notes: Description of groups from each study limited to those that met the criteria for inclusion; $\bar{x}$ ± SD, mean ± standard deviation; AIMS, Arthritis Measurement Impact Scale; DASS21, Depression, Anxiety and Stress Scale; FIQ, Fibromyalgia Impact Questionnaire; FM, fibromyalgia; HADS, Hospital Anxiety & Depression Scale; HRR, heart rate reserve; MHI, Mental Health Inventory; min, minutes; MHR, maximum heart rate; STAI,

State-Trait Anxiety Inventory; MHR, maximum heart rate; OA, osteoarthritis; RA, rheumatoid arthritis; reps, repetitions; RPE, rating of perceived exertion; VAS, Visual Analog Scale; wk(s), week(s); yrs, years;

Table 2. Baseline characteristics of participants.

	Exercise				Control			
Variable	Groups/Participants	$\bar{x} \pm$ SD	Median	Range	Groups/Participants	$\bar{x} \pm$ SD	Median	Range
Age (years)	14/458	53.4 ± 9.7	50	41 – 74	13/349	54.9 ± 8.8	50	43 - 72
BMI ($kg \cdot m^2$)	7/204	29.0 ± 1.5	29	27 - 31	7/170	28.4 ± 1.7	28	27 – 31
VO_{2max} ($ml \cdot kg^{-1} \cdot min^{-1}$)	7/245	21.3 ± 2.3	21	19 – 24	5/101	20.7 ± 2.7	21	17 – 24

Notes: Groups represents number of exercise and control groups reporting data; $\bar{x} + SD$, mean ± standard deviation; BMI, body mass index; $VO_{2max,}$ maximum oxygen consumption.

Table 3. Exercise program characteristics.

Variable	Groups/Participants	$\bar{x} \pm$ SD	Median	Range
Length (weeks)	16/514	16 ± 7	14	8 - 32
Frequency (times/week)	14/469	3.3 ± 1.3	3	2 – 7
Duration (min/session)	14/450	28.8 ± 14.3	30	10 – 60
Minutes per week	11/407	85.5 ± 21.2	88	60 – 120
Minutes per week (adj)	7/277	61.3 ± 22.7	58	33 – 99
Compliance (%)	8/312	74.3 ± 19	80	38 - 97

Notes: Groups represents number of exercise groups reporting data; $\bar{x} \pm$ SD, mean ± standard deviation; min, minutes; adj, adjusted for compliance.

Table 4. Results for primary and secondary outcomes (data reported as standardized effect size unless otherwise noted).

Variable	ES (#)	Participants (#)	$\bar{x}$ (95% CI)	Q (p)	I^2 (95% CI)	τ^2
Primary outcome						
- Anxiety	16	883	-0.40 (-0.65, -0.15)*	40.3 (<0.001)**	62.8 (36.2, 78.3	0.14
Secondary outcomes						
- Physical function	12	677	0.66 (0.34, 0.97)*	36.0 (0.0002)**	69.4 (44.5, 83.1)	0.19
- Pain	15	803	-0.62 (-1.12, -0.11)*	128.6 (<0.001)**	89.1 (83.7, 92.7)	0.75
- QOL	13	730	0.63 (0.35, 0.91)*	32.4 (0.001)**	63.0 (32.7, 79.7)	0.15
- Depression	15	813	-0.38 (-0.67, -0.10)*	46.3 (<0.001)**	69.7 (48.6, 82.2)	0.20
- VO2max ($ml \cdot kg^{-1} \cdot min^{-1}$)	7	346	2.01 (0.85, 3.2)*	20.2 (0.003)**	70.3 (35.0, 86.4)	1.40
- Muscular strength	6	261	0.59 (0.33, 0.85)*	3.9 (0.6)	0 (0, 67.1)	0

Notes: ES, effect size; #, number; $\bar{x}$ (95% CI), mean effect size and 95% confidence interval; Q (p), Cochran Q statistic and alpha value for Q; I^2 (95% CI), I-squared and 95% confidence interval; τ^2, tau-squared; *, statistically significant (two-tailed alpha value $\leq$ 0.05 and non-overlapping 95% confidence intervals); **, statistically significant (alpha value $\leq$ 0.10);

Table 5. Final multiple regression model for changes in anxiety (N = 16).

Variable	Coefficient ± SE	*t* (p)	95% CI
Year of publication	0.031 ± 0.009	3.58 (0.01)	0.010 to 0.051
Incomplete data	-0.448 ± 0.139	-3.23 (0.01)	-0.763 to -.0134
Minutes of training per week	0.007 ± 0.004	1.71 (0.13)	-0.002 to 0.016
Intercept	-61.940 ± 17.152	-3.61 (0.01)	-103.17 to -20.71

Notes: SE, standard error; *t*, t-value; p, alpha value for *t*; CI, confidence interval.

FIGURE LEGEND

Figure 1. Flow diagram depicting the search process.

Figure 2. Risk of bias results using the Cochrane Risk of Bias Assessment Instrument.

Figure 3. Forest plot for changes in anxiety.

Figure 4. Funnel plot for changes in anxiety.

Figure 5. Cumulative meta-analysis for changes in anxiety.

SUPPLEMENTARY FILES

Supplementary File 1. Search strategy for PubMed.

Supplementary file 2. List of excluded studies, including reasons for exclusion.

Supplementary file 3. Study-level risk of bias results using the Cochrane Risk of Bias Assessment Instrument.

Supplementary file 4. Simple meta-regression results with changes in anxiety as the outcome.

Supplementary file 5. Evidence profile for changes in anxiety based on GRADE.

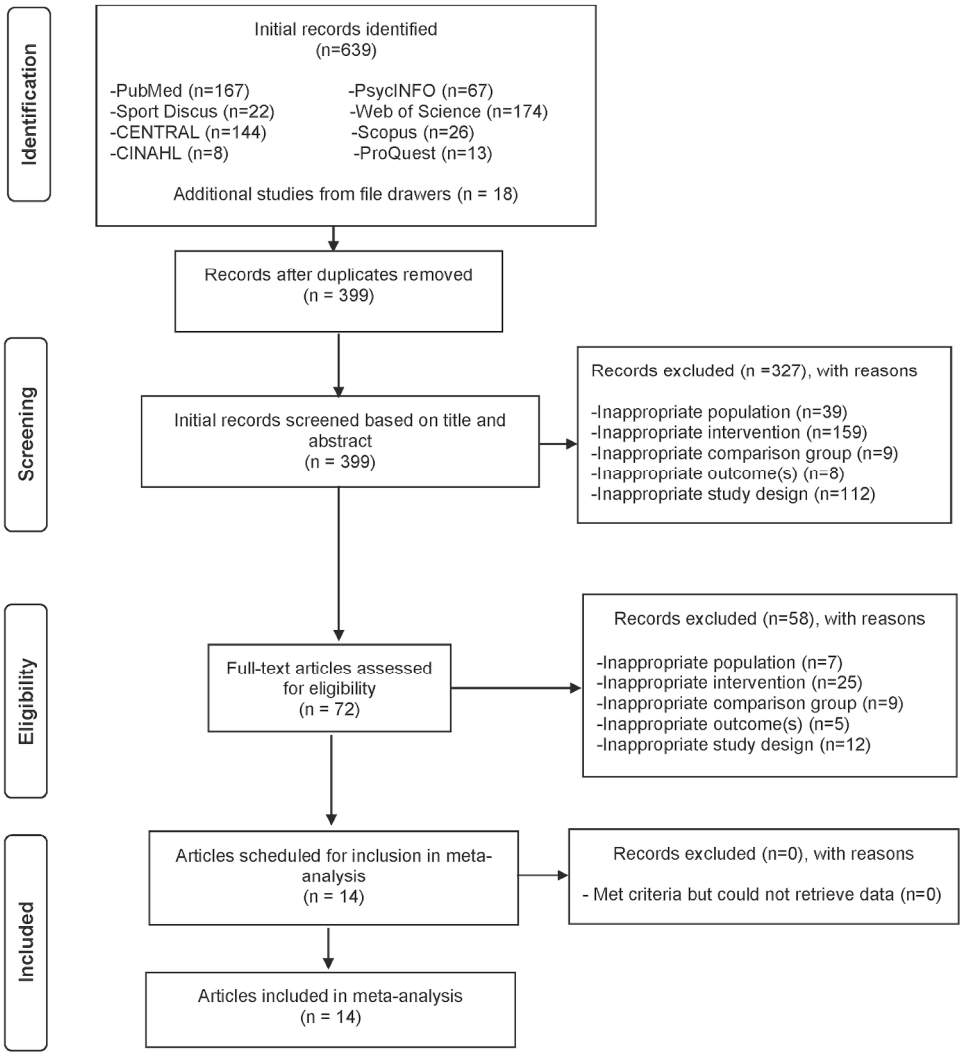


Figure 1. Flow diagram depicting the search process.

173x192mm (300 x 300 DPI)

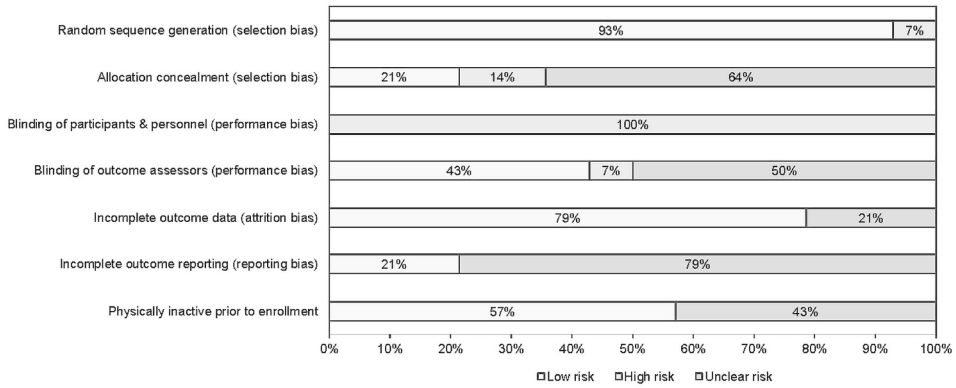


Figure 2. Risk of bias results using the Cochrane Risk of Bias Assessment Instrument.

173x77mm (300 x 300 DPI)

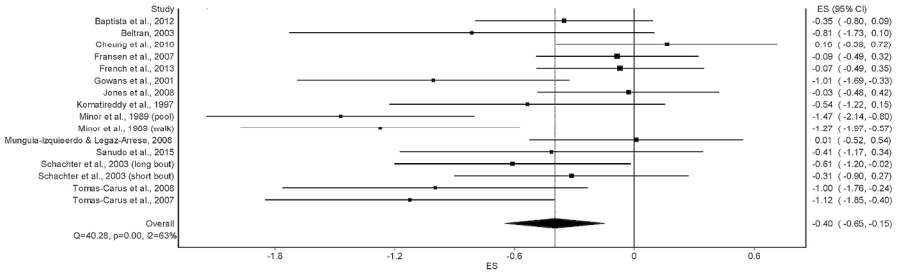


Figure 3. Forest plot for changes in anxiety.

173x57mm (300 x 300 DPI)

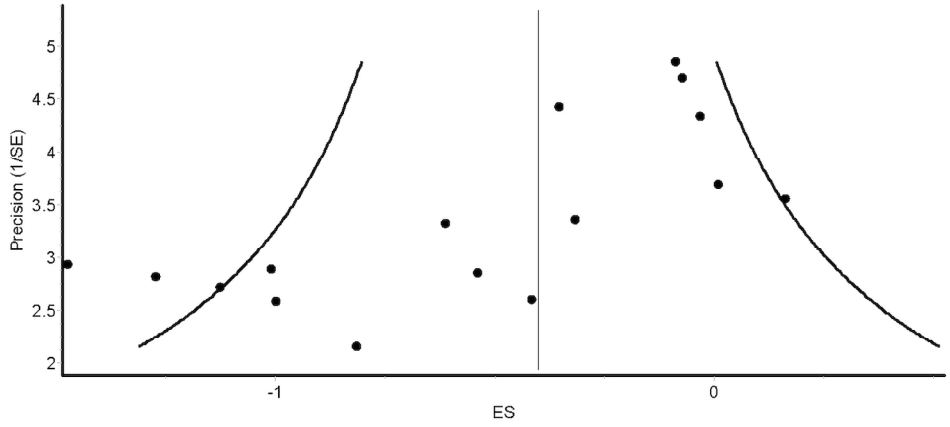


Figure 4. Funnel plot for changes in anxiety.

165x74mm (300 x 300 DPI)

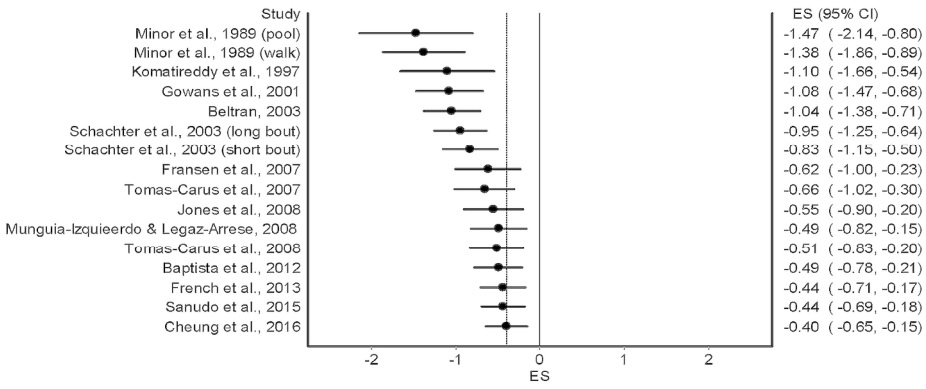
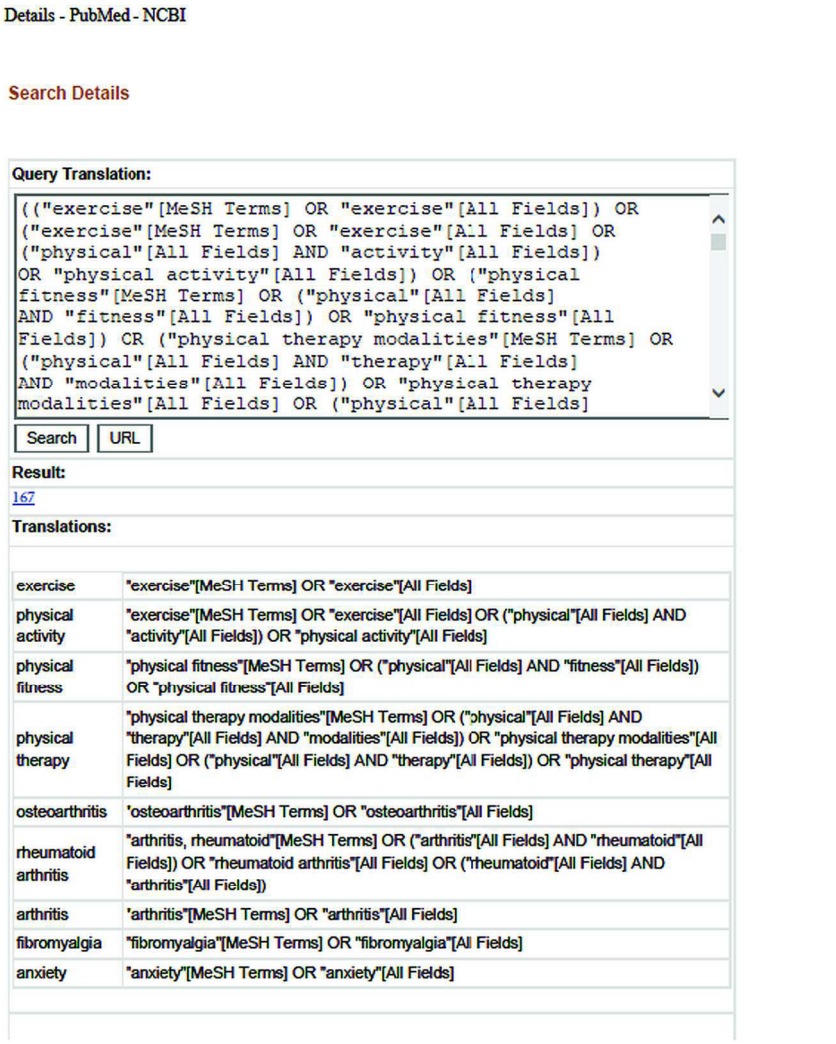


Figure 5. Cumulative meta-analysis for changes in anxiety.

173x87mm (300 x 300 DPI)



Details - PubMed - NCBI

Search Details

Query Translation:

```
(("exercise"[MeSH Terms] OR "exercise"[All Fields]) OR
("exercise"[MeSH Terms] OR "exercise"[All Fields] OR
("physical"[All Fields] AND "activity"[All Fields])
OR "physical activity"[All Fields]) OR ("physical
fitness"[MeSH Terms] OR ("physical"[All Fields]
AND "fitness"[All Fields]) OR "physical fitness"[All
Fields]) CR ("physical therapy modalities"[MeSH Terms] OR
("physical"[All Fields] AND "therapy"[All Fields]
AND "modalities"[All Fields]) OR "physical therapy
modalities"[All Fields] OR ("physical"[All Fields]
```

Search URL

Result:

167

Translations:

exercise	"exercise"[MeSH Terms] OR "exercise"[All Fields]
physical activity	"exercise"[MeSH Terms] OR "exercise"[All Fields] OR ("physical"[All Fields] AND "activity"[All Fields]) OR "physical activity"[All Fields]
physical fitness	"physical fitness"[MeSH Terms] OR ("physical"[All Fields] AND "fitness"[All Fields]) OR "physical fitness"[All Fields]
physical therapy	"physical therapy modalities"[MeSH Terms] OR ("physical"[All Fields] AND "therapy"[All Fields] AND "modalities"[All Fields]) OR "physical therapy modalities"[All Fields] OR ("physical"[All Fields] AND "therapy"[All Fields]) OR "physical therapy"[All Fields]
osteoarthritis	"osteoarthritis"[MeSH Terms] OR "osteoarthritis"[All Fields]
rheumatoid arthritis	"arthritis, rheumatoid"[MeSH Terms] OR ("arthritis"[All Fields] AND "rheumatoid"[All Fields]) OR "rheumatoid arthritis"[All Fields] OR ("rheumatoid"[All Fields] AND "arthritis"[All Fields])
arthritis	"arthritis"[MeSH Terms] OR "arthritis"[All Fields]
fibromyalgia	"fibromyalgia"[MeSH Terms] OR "fibromyalgia"[All Fields]
anxiety	"anxiety"[MeSH Terms] OR "anxiety"[All Fields]

https://www.ncbi.nlm.nih.gov/pubmed/details?querykey=9 1/5/2017

153x187mm (300 x 300 DPI)

Supplementary File 2. Excluded Studies, including reasons for exclusion.

1. 12th Commonwealth International Sport conference, 19-23 July 2002, Manchester, United Kingdom: abstract book. London;: Association of Commonwealth Universities 2002. *inappropriate study design*
2. ABSTRACTS. *Journal of Orthopaedic & Sports Physical Therapy* 2005;35(6):389-96. *inappropriate study design*
3. Fibromyalgia: poorly understood; treatments are disappointing. *Prescrire international* 2009;18(102):169-73. [published Online First: 2009/09/15] *inappropriate study design*
4. A Controlled Examination of Medical and Psychosocial Factors Associated With Low Back Pain in Combination With Widespread Musculoskeletal Pain. *Physical therapy* 2009;89(8):786-803. *inappropriate study design*
5. Acupuncture. *Focus on Alternative and Complementary Therapies* 2010;15(2):163-69. doi: 10.1211/fact.15.2.0065 *inappropriate intervention*
6. 2013 SYR Accepted Poster Abstracts. *International journal of yoga therapy* 2013;23 Suppl:32-53. [published Online First: 2013/01/01] *inappropriate study design*
7. Abbott R, Whear R, Nikolaou V, et al. Tumour necrosis factor-alpha inhibitor therapy in chronic physical illness: A systematic review and meta-analysis of the effect on depression and anxiety. *Journal of psychosomatic research* 2015;79(3):175-84. doi: 10.1016/j.jpsychores.2015.04.008 [published Online First: 2015/05/04] *inappropriate study design*
8. Adachi T, Nakae A, Maruo T, et al. Validation of the Japanese Version of the Pain Self-Efficacy Questionnaire in Japanese Patients with Chronic Pain. *Pain Medicine* 2014;15(8):1405-17. doi: 10.1111/pme.12446 *inappropriate study design*
9. Akhavan J. The effect of a dyadic intervention on self-efficacy, physical functioning, and anxiety/depression in older adults post joint replacement surgery [Ph.D.]. University of California, Los Angeles, 2008. *inappropriate study design*
10. Akman-Demir G, Saip S, Siva A. Behçet's disease. *Current Treatment Options in Neurology* 2011;13(3):290-310. doi: 10.1007/s11940-011-0120-2 *inappropriate study design*
11. Alamo MM, Moral RR, de Torres LAP. Evaluation of a patient-centred approach in generalized musculoskeletal chronic pain/fibromyalgia patients in primary care. *Patient education and counseling* 2002;48(1):23-31. doi: 10.1016/S0738-3991(02)00095-2 *inappropriate intervention*
12. Alayli G, Kuru O, Bilgici A. The effects of aerobic exercise and home exercise on pain and disability in patients with knee osteoarthritis. [Turkish]. *Journal of Rheumatology and Medical Rehabilitation* 2007; 18(2). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/761/CN-00707761/frame.html. *inappropriate comparison group*
13. Alipour B, Homayouni-Rad A, Vaghef-Mehrabany E, et al. Effects of Lactobacillus casei supplementation on disease activity and inflammatory cytokines in rheumatoid arthritis patients: a randomized double-blind clinical trial. *International journal of rheumatic diseases* 2014;17(5):519-27. doi: 10.1111/1756-185X.12333 *inappropriate intervention*

14. Ambrose KR, Golightly YM. Physical exercise as non-pharmacological treatment of chronic pain: Why and when. *Best Practice & Research in Clinical Rheumatology* 2015;29(1):120-30. doi: 10.1016/j.berh.2015.04.022 *inappropriate study design*
15. Andrews NE, Strong J, Meredith PJ. Activity Pacing, Avoidance, Endurance, and Associations With Patient Functioning in Chronic Pain: A Systematic Review and Meta-Analysis. *Archives of physical medicine and rehabilitation* 2012;93(11):2109-21. doi: 10.1016/j.apmr.2012.05.029 *inappropriate study design*
16. Ang D, Jensen M, Steiner J, et al. Combining cognitive-behavioral therapy and milnacipran for fibromyalgia: a feasibility randomized-controlled trial. *The Clinical journal of pain* 2013; 29(9). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/880/CN-00918880/frame.html. *inappropriate study design*
17. Appelbaum KA, Blanchard EB, Hickling EJ, et al. Cognitive behavioral treatment of a veteran population with moderate to severe rheumatoid arthritis. *Behavior Therapy* 1988;19(4):489-502. doi: 10.1016/S0005-7894(88)80019-4 *inappropriate intervention*
18. Archer T, Josefsson T, Lindwall M. Effects of Physical Exercise on Depressive Symptoms and Biomarkers in Depression. *Cns & Neurological Disorders-Drug Targets* 2014;13(10):1640-53. *inappropriate study design*
19. Arcos-Carmona IM, Castro-Sanchez AM, Mataran-Penarrocha GA, et al. [Effects of aerobic exercise program and relaxation techniques on anxiety, quality of sleep, depression, and quality of life in patients with fibromyalgia: a randomized controlled trial]. *Medicina clinica* 2011;137(9):398-401. doi: 10.1016/j.medcli.2010.09.045 [published Online First: 2011/02/25] *inappropriate intervention*
20. Arends RY, Bode C, Taal E, et al. A goal management intervention for polyarthritis patients: rationale and design of a randomized controlled trial. *BMC musculoskeletal disorders* 2013;14:239. doi: 10.1186/1471-2474-14-239 [published Online First: 2013/08/15] *inappropriate intervention*
21. Arne M, Janson C, Janson S, et al. Physical activity and quality of life in subjects with chronic disease: chronic obstructive pulmonary disease compared with rheumatoid arthritis and diabetes mellitus. *Scandinavian journal of primary health care* 2009;27(3):141-7. doi: 10.1080/02813430902808643 [published Online First: 2009/03/24] *inappropriate study design*
22. Arnold L, Wang F, Ahl J, et al. Improvement in multiple dimensions of fatigue in patients with fibromyalgia treated with duloxetine: secondary analysis of a randomized, placebo-controlled trial. *Arthritis research & therapy* 2011; 13(3). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/474/CN-00843474/frame.html. *inappropriate intervention*
23. Arnold L, Zlateva G, Sadosky A, et al. Correlations between Fibromyalgia Symptom and Function Domains and Patient Global Impression of Change: A Pooled Analysis of Three Randomized, Placebo-Controlled Trials of Pregabalin. *Pain medicine (Malden, Mass)* 2011; 12(2). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/608/CN-01016608/frame.html. *inappropriate study design*

24. Arnold LM. Strategies for managing fibromyalgia. *The American journal of medicine* 2009;122(12 Suppl):S31-43. doi: 10.1016/j.amjmed.2009.09.009 [published Online First: 2010/01/09] *inappropriate study design*
25. Arnold LM, Arsenault P, Huffman C, et al. Once daily controlled-release pregabalin in the treatment of patients with fibromyalgia: A phase III, double-blind, randomized withdrawal, placebo-controlled study. *Current Medical Research and Opinion* 2014;30(10):2069-83. doi: 10.1185/03007995.2014.928275 *inappropriate intervention*
26. Arnold LM, Clauw D, Wang F, et al. Flexible dosed duloxetine in the treatment of fibromyalgia: a randomized, double-blind, placebo-controlled trial. *The Journal of rheumatology* 2010;37(12):2578-86. doi: 10.3899/jrheum.100365 [published Online First: 2010/09/17] *inappropriate intervention*
27. Arnold LM, Crofford LJ, Martin SA, et al. The effect of anxiety and depression on improvements in pain in a randomized, controlled trial of pregabalin for treatment of fibromyalgia. *Pain Medicine* 2007;8(8):633-38. doi: 10.1111/j.1526-4637.2007.00332.x *inappropriate intervention*
28. Arnold LM, Russell IJ, Diri EW, et al. A 14-week, randomized, double-blinded, placebo-controlled monotherapy trial of pregabalin in patients with fibromyalgia. *The Journal of Pain* 2008;9(9):792-805. doi: 10.1016/j.jpain.2008.03.013 *inappropriate intervention*
29. Arnold LM, Wang F, Ahl J, et al. Improvement in multiple dimensions of fatigue in patients with fibromyalgia treated with duloxetine: secondary analysis of a randomized, placebo-controlled trial. *Arthritis research & therapy* 2011;13(3):R86. doi: 10.1186/ar3359 [published Online First: 2011/06/15] *inappropriate intervention*
30. Arnold LM, Williams DA, Hudson JI, et al. Development of responder definitions for fibromyalgia clinical trials. *Arthritis and rheumatism* 2012;64(3):885-94. doi: 10.1002/art.33360 [published Online First: 2011/09/29] *inappropriate outcomes*
31. Arnold LM, Zhang S, Pangallo BA. Efficacy and safety of duloxetine 30 mg/d in patients with fibromyalgia: A randomized, double-blind, placebo-controlled study. *The Clinical journal of pain* 2012;28(9):775-81. doi: 10.1097/AJP.0b013e3182510295 *inappropriate outcomes*
32. Arnold LM, Zlateva G, Sadosky A, et al. Correlations between fibromyalgia symptom and function domains and patient global impression of change: a pooled analysis of three randomized, placebo-controlled trials of pregabalin. *Pain medicine (Malden, Mass)* 2011;12(2):260-7. doi: 10.1111/j.1526-4637.2010.01047.x [published Online First: 2011/01/27] *inappropriate study design*
33. Assis MR, Silva LE, Alves AM, et al. A randomized controlled trial of deep water running: clinical effectiveness of aquatic exercise to treat fibromyalgia. *Arthritis and rheumatism* 2006;55(1):57-65. doi: 10.1002/art.21693 *inappropriate comparison group*
34. Ayral X, Gicquere C, Duhalde A, et al. Effects of video information on preoperative anxiety level and tolerability of joint lavage in knee osteoarthritis. *Arthritis and rheumatism* 2002;47(4):380-2. doi: 10.1002/art.10559 [published Online First: 2002/09/05] *inappropriate intervention*

35. Bae S, Gun S, Mok C, et al. Improved health outcomes with etanercept versus usual DMARD therapy in an Asian population with established rheumatoid arthritis. *BMC musculoskeletal disorders* 2013; 14. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/280/CN-00864280/frame.html. *inappropriate intervention*
36. Bagdath AO, Donmez A, Eroksuz R, et al. Does addition of 'mud-pack and hot pool treatment' to patient education make a difference in fibromyalgia patients? A randomized controlled single blind study. *International journal of biometeorology* 2015;59(12):1905-11. doi: 10.1007/s00484-015-0997-7 *inappropriate intervention*
37. Barlow J, Turner A, Wright C. A randomized controlled study of the Arthritis Self-Management Programme in the UK. *Health education research* 2000; 15(6). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/444/CN-00330444/frame.html. *inappropriate intervention*
38. Barlow JH, Powell LA, Gilchrist M, et al. The effectiveness of the Training and Support Program for parents of children with disabilities: a randomized controlled trial. *Journal of psychosomatic research* 2008;64(1):55-62. doi: 10.1016/j.jpsychores.2007.06.006 [published Online First: 2007/12/26] *inappropriate intervention*
39. Barsky AJ, Ahern DK, Orav EJ, et al. A Randomized Trial of Three Psychosocial Treatments for the Symptoms of Rheumatoid Arthritis. *Seminars in arthritis and rheumatism* 2010;40(3):222-32. doi: 10.1016/j.semarthrit.2010.04.001 *inappropriate intervention*
40. Basler HD. Group treatment for pain and discomfort. *Patient education and counseling* 1993;20(2-3):167-75. [published Online First: 1993/05/01] *inappropriate intervention*
41. Bassey EJ. Longitudinal changes in selected physical capabilities: muscle strength, flexibility and body size. *Age and Ageing* 1998;27:12-16. *inappropriate study design*
42. Bateman L, Sarzi-Puttini P, Burbridge CL, et al. Burden of illness in fibromyalgia patients with comorbid depression. *Clinical and experimental rheumatology* 2016;34(2 Suppl 96):S106-13. [published Online First: 2016/04/09] *inappropriate study design*
43. Baudic S, Attal N, Mhalla A, et al. Unilateral repetitive transcranial magnetic stimulation of the motor cortex does not affect cognition in patients with fibromyalgia. *Journal of Psychiatric Research* 2013;47(1):72-77. doi: 10.1016/j.jpsychires.2012.09.003 *inappropriate intervention*
44. Bearne L, Walsh N, Jessep S, et al. Feasibility of an exercise-based rehabilitation programme for chronic hip pain. *Musculoskeletal care* 2011; 9(3). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/898/CN-01124898/frame.html. *inappropriate intervention*
45. Bement MKH, Weyer A, Hartley S, et al. Pain Perception After Isometric Exercise in Women With Fibromyalgia. *Archives of physical medicine and rehabilitation* 2011;92(1):89-95. doi: 10.1016/j.apmr.2010.10.006 *inappropriate study design*
46. Bennell K, Ahamed Y, Jull G, et al. Physical Therapist-Delivered Pain Coping Skills Training and Exercise for Knee Osteoarthritis: Randomized Controlled Trial. *Arthritis care & research* 2016; 68(5).

http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/882/CN-01153882/frame.html. *inappropriate comparison group*

47. Bennell KL, Rini C, Keefe F, et al. Effects of Adding an Internet-Based Pain Coping Skills Training Protocol to a Standardized Education and Exercise Program for People With Persistent Hip Pain (HOPE Trial): Randomized Controlled Trial Protocol. *Physical therapy* 2015;95(10):1408-22. doi: 10.2522/ptj.20150119 [published Online First: 2015/05/30] *inappropriate study design*
48. Bennett R, Russell I, Choy E, et al. Evaluation of Patient-Rated Stiffness Associated With Fibromyalgia: A Post-Hoc Analysis of 4 Pooled, Randomized Clinical Trials of Duloxetine. *Clinical therapeutics* 2012; 34(4). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/551/CN-00896551/frame.html. *inappropriate intervention*
49. Bialosky JE, Bishop MD, Robinson ME, et al. Spinal Manipulative Therapy Has an Immediate Effect on Thermal Pain Sensitivity in People With Low Back Pain: A Randomized Controlled Trial. *Physical therapy* 2009;89(12):1292-303. doi: 10.2522/ptj.20090058 *inappropriate population*
50. Birbara C, Ruoff G, Sheldon E, et al. Efficacy and safety of rofecoxib 12.5 mg and celecoxib 200 mg in two similarly designed osteoarthritis studies. *Current medical research and opinion* 2006; 22(1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/019/CN-00554019/frame.html. *inappropriate intervention*
51. Bircan C, Karasel SA, Akgun B, et al. Effects of muscle strengthening versus aerobic exercise program in fibromyalgia. *Rheumatology international* 2008;28(6):527-32. doi: 10.1007/s00296-007-0484-5 [published Online First: 2007/11/06] *inappropriate comparison group*
52. Bishop MD, Beneciuk JM, George SZ. Immediate reduction in temporal sensory summation after thoracic spinal manipulation. *Spine Journal* 2011;11(5):440-46. doi: 10.1016/j.spinee.2011.03.001 *inappropriate intervention*
53. Blikman T, Rienstra W, van Raaij TM, et al. Duloxetine in OsteoArthritis (DOA) study: study protocol of a pragmatic open-label randomised controlled trial assessing the effect of preoperative pain treatment on postoperative outcome after total hip or knee arthroplasty. *BMJ open* 2016;6(3):e010343. doi: 10.1136/bmjopen-2015-010343 [published Online First: 2016/03/05] *inappropriate study design*
54. Blumenthal JA, Babyak MA, Moore KA, et al. Effects of exercise training on older patients with major depression. *Archives of Internal Medicine* 1999;159(19):2349-56. doi: 10.1001/archinte.159.19.2349 *inappropriate population*
55. Bojner Horwitz E, Kowalski J, Theorell T, et al. Dance/movement therapy in fibromyalgia patients: Changes in self-figure drawings and their relation to verbal self-rating scales. *The Arts in Psychotherapy* 2006;33(1):11-25. doi: http://dx.doi.org/10.1016/j.aip.2005.05.004 *inappropriate intervention*
56. Bojner-Horwitz E, Theorell T, Anderberg UM. Dance/movement therapy and changes in stress-related hormones: A study of fibromyalgia patients with video-interpretation. *The Arts in Psychotherapy* 2003;30(5):255-64. doi: 10.1016/j.aip.2003.07.001 *inappropriate outcomes*

57. Bojner-Horwitz E, Theorell T, Maria Anderberg U. Dance/movement therapy and changes in stress-related hormones: a study of fibromyalgia patients with video-interpretation. *The Arts in Psychotherapy* 2003;30(5):255-64. doi: http://dx.doi.org/10.1016/j.aip.2003.07.001 *inappropriate intervention*
58. Bongi SM, Del Rosso A, Di Felice C, et al. Resseguier method and Qi Gong sequentially integrated in patients with fibromyalgia syndrome. *Clinical and experimental rheumatology* 2012;30(6):S51-S58. *inappropriate comparison group*
59. Bongi SM, Paoletti G, Cala M, et al. Efficacy of rehabilitation with Tai Ji Quan in an Italian cohort of patients with Fibromyalgia Syndrome. *Complementary therapies in clinical practice* 2016;24:109-15. doi: 10.1016/j.ctcp.2016.05.010 *inappropriate intervention*
60. Booth FW, Roberts CK, Laye MJ. Lack of Exercise Is a Major Cause of Chronic Diseases. *Comprehensive Physiology* 2012;2(2):1143-211. doi: 10.1002/cphy.c110025 *inappropriate study design*
61. Boschen KA, Robinson E, Campbell KA, et al. Results from 10 Years of a CBT Pain Self-Management Outpatient Program for Complex Chronic Conditions. *Pain Research & Management* 2016 doi: 10.1155/2016/4678083 *inappropriate study design*
62. Bossen D, Buskermolen M, Veenhof C, et al. Adherence to a web-based physical activity intervention for patients with knee and/or hip Osteoarthritis: A mixed method study. *Journal of medical Internet research* 2013;15(10):55-66. doi: 10.2196/jmir.2742 *inappropriate comparison group*
63. Bossen D, Veenhof C, Kloek C, et al. The association between psychological factors and physical activity levels in patients with knee and hip osteoarthritis. *Physiotherapy (United Kingdom)* 2015; 101. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/535/CN-01126535/frame.html. *inappropriate study design*
64. Bossen D, Veenhof C, Van Beek KEC, et al. Effectiveness of a Web-Based Physical Activity Intervention in Patients With Knee and/or Hip Osteoarthritis: Randomized Controlled Trial. *Journal of medical Internet research* 2013;15(11) doi: 10.2196/jmir.2662 *inappropriate intervention*
65. Boyer L, Dousset A, Roussel P, et al. rTMS in fibromyalgia: a randomized trial evaluating QoL and its brain metabolic substrate. *Neurology* 2014;82(14):1231-8. doi: 10.1212/wnl.0000000000000280 [published Online First: 2014/03/29] *inappropriate intervention*
66. Bradt J, Norris M, Shim M, et al. Vocal Music Therapy for Chronic Pain Management in Inner-City African Americans: A Mixed Methods Feasibility Study. *Journal of Music Therapy* 2016;53(2):178-206. doi: 10.1093/jmt/thw004 *inappropriate intervention*
67. Braz AS, Morais LCS, Paula AP, et al. Effects of Panax ginseng extract in patients with fibromyalgia: A 12-week, randomized, double-blind, placebo-controlled trial. *Revista Brasileira de Psiquiatria* 2013;35(1):21-28. doi: 10.1016/j.rbp.2013.01.004 *inappropriate intervention*
68. Broderick J, Junghaenel D, Schwartz J. Written emotional expression produces health benefits in fibromyalgia patients. *Psychosomatic medicine* 2005; 67(2).

http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/627/CN-00560627/frame.html. *inappropriate intervention*

69. Brus H, Taal E, Laar M, et al. Patient education and disease activity: a study among rheumatoid arthritis patients. *Arthritis care and research : the official journal of the Arthritis Health Professions Association* 1997; 10(5). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/155/CN-00145155/frame.html. *inappropriate study design*
70. Busch A. Hydrotherapy improves pain, knee strength, and quality of life in women with fibromyalgia. *Australian Journal of Physiotherapy* 2007;53(1):64-64. *inappropriate study design*
71. Buskila D, Abu-Shakra M, Neumann L, et al. Balneotherapy for fibromyalgia at the Dead Sea. *Rheumatology international* 2001;20(3):105-8. doi: 10.1007/s002960000085 [published Online First: 2001/05/17] *inappropriate intervention*
72. Buszewicz M, Rait G, Griffin M, et al. Self management of arthritis in primary care: randomised controlled trial. *BMJ (Clinical research ed)* 2006;333(7574):879. doi: 10.1136/bmj.38965.375718.80 [published Online First: 2006/10/17] *inappropriate intervention*
73. Buttagat V, Eungpinichpong W, Kaber D, et al. Acute effects of traditional Thai massage on electroencephalogram in patients with scapulocostal syndrome. *Complementary Therapies in Medicine* 2012;20(4):167-74. doi: 10.1016/j.ctim.2012.02.002 *inappropriate intervention*
74. Büyükyılmaz F, Aştı T. The effect of relaxation techniques and back massage on pain and anxiety in Turkish total hip or knee arthroplasty patients. *Pain Management Nursing* 2013;14(3):143-54. doi: 10.1016/j.pmn.2010.11.001 *inappropriate intervention*
75. Calandre EP, Rico-Villademoros F. The role of antipsychotics in the management of fibromyalgia. *CNS drugs* 2012;26(2):135-53. doi: 10.2165/11597130-000000000-00000 [published Online First: 2012/02/03] *inappropriate study design*
76. Calandre EP, Rodriguez-Claro ML, Rico-Villademoros F, et al. Effects of pool-based exercise in fibromyalgia symptomatology and sleep quality: a prospective randomised comparison between stretching and Ai Chi. *Clinical and experimental rheumatology* 2009;27(5 Suppl 56):S21-8. [published Online First: 2010/03/12] *inappropriate intervention*
77. Campbell CM, McCauley L, Bounds SC, et al. Changes in pain catastrophizing predict later changes in fibromyalgia clinical and experimental pain report: cross-lagged panel analyses of dispositional and situational catastrophizing. *Arthritis research & therapy* 2012;14(5):R231. doi: 10.1186/ar4073 [published Online First: 2012/10/27] *inappropriate outcomes*
78. Cancelliere C. Are workplace health promotion/wellness programs effective at improving presenteeism (on-the-job productivity) in workers? A systematic review and best evidence synthesis of the literature [M.P.H.]. Lakehead University (Canada), 2011. *inappropriate study design*

79. Carbonell-Baeza A, Aparicio VA, Chillon P, et al. Effectiveness of multidisciplinary therapy on symptomatology and quality of life in women with fibromyalgia. *Clinical and experimental rheumatology* 2011;29(6):S97-S103. *inappropriate study design*
80. Carbonell-Baeza A, Aparicio VA, Martins-Pereira CM, et al. Efficacy of Biodanza for Treating Women with Fibromyalgia. *Journal of Alternative and Complementary Medicine* 2010;16(11):1191-200. doi: 10.1089/acm.2010-0039 *inappropriate study design*
81. Carbonell-Baeza A, Romero A, Aparicio VA, et al. Preliminary Findings of a 4-Month Tai Chi Intervention on Tenderness, Functional Capacity, Symptomatology, and Quality of Life in Men With Fibromyalgia. *American Journal of Mens Health* 2011;5(5):421-29. doi: 10.1177/1557988311400063 *inappropriate intervention*
82. Carbonell-Baeza A, Ruizz JR, Aparicio VA, et al. Multidisciplinary and biodanza intervention for the management of fibromyalgia. *Acta Reumatologica Portuguesa* 2012;37(3):240-50. *inappropriate comparison group*
83. Carleton RN, Richter AA, Asmundson GJG. Attention modification in persons with fibromyalgia: A double blind, randomized clinical trial. *Cognitive Behaviour Therapy* 2011;40(4):279-90. doi: 10.1080/16506073.2011.616218 *inappropriate intervention*
84. Carmichael NME, Katz J, Clarke H, et al. An intensive perioperative regimen of pregabalin and celecoxib reduces pain and improves physical function scores six weeks after total hip arthroplasty: A prospective randomized controlled trial. *Pain Research & Management* 2013;18(3):127-32. doi: 10.1155/2013/258714 *inappropriate intervention*
85. Carson JW, Carson KM, Jones KD, et al. A pilot randomized controlled trial of the Yoga of Awareness program in the management of fibromyalgia. *Pain* 2010;151(2):530-9. doi: 10.1016/j.pain.2010.08.020 [published Online First: 2010/10/16] *inappropriate intervention*
86. Carson JW, Carson KM, Jones KD, et al. Follow-up of yoga of awareness for fibromyalgia: results at 3 months and replication in the wait-list group. *The Clinical journal of pain* 2012;28(9):804-13. doi: 10.1097/AJP.0b013e31824549b5 [published Online First: 2012/07/04] *inappropriate study design*
87. Carta MG, Cardia C, Mannu F, et al. The high frequency of manic symptoms in fibromyalgia does influence the choice of treatment? *Clinical Practice and Epidemiology in Mental Health* 2006;2 *inappropriate study design*
88. Casanueva-Fernandez B, Llorca J, Rubio JBI, et al. Efficacy of a multidisciplinary treatment program in patients with severe fibromyalgia. *Rheumatology international* 2012;32(8):2497-502. doi: 10.1007/s00296-011-2045-1 *inappropriate intervention*
89. Castel A, Castro S, Fontova R, et al. Body mass index and response to a multidisciplinary treatment of fibromyalgia. *Rheumatology international* 2015;35(2):303-14. doi: 10.1007/s00296-014-3096-x [published Online First: 2014/08/02] *inappropriate intervention*
90. Castel A, Fontova R, Montull S, et al. Efficacy of a Multidisciplinary Fibromyalgia Treatment Adapted for Women With Low Educational Levels: A Randomized Controlled Trial. *Arthritis care & research* 2013;65(3):421-31. doi: 10.1002/acr.21818 *inappropriate intervention*

91. Castrejon I, Yazici Y, Samuels J, et al. Discordance of global estimates by patients and their physicians in usual care of many rheumatic diseases: association with 5 scores on a Multidimensional Health Assessment Questionnaire (MDHAQ) that are not found on the Health Assessment Questionnaire (HAQ). *Arthritis care & research* 2014;66(6):934-42. doi: 10.1002/acr.22237 [published Online First: 2013/12/05] *inappropriate study design*
92. Castro MMC, Daltro C, Kraychete DC, et al. The cognitive behavioral therapy causes an improvement in quality of life in patients with chronic musculoskeletal pain. *Arquivos De Neuro-Psiquiatria* 2012;70(11):864-68. *inappropriate population*
93. Castro-Sanchez AM, Mataran-Penarrocha GA, Granero-Molina J, et al. Benefits of massage-myofascial release therapy on pain, anxiety, quality of sleep, depression, and quality of life in patients with fibromyalgia. *Evidence-based complementary and alternative medicine : eCAM* 2011;2011:561753. doi: 10.1155/2011/561753 [published Online First: 2011/01/15] *inappropriate intervention*
94. Cedraschi C, Desmeules J, Rapiti E, et al. Fibromyalgia: a randomised, controlled trial of a treatment programme based on self management. *Annals of the rheumatic diseases* 2004; 63(3). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/285/CN-00471285/frame.html. *inappropriate intervention*
95. Celenay ST, Kaya DO, Akbayrak T. Cervical and scapulothoracic stabilization exercises with and without connective tissue massage for chronic mechanical neck pain: A prospective, randomised controlled trial. *Manual therapy* 2016;21:144-50. doi: 10.1016/j.math.2015.07.003 *inappropriate intervention*
96. Cella M, Sharpe M, Chalder T. Measuring disability in patients with chronic fatigue syndrome: reliability and validity of the Work and Social Adjustment Scale. *Journal of psychosomatic research* 2011;71(3):124-8. doi: 10.1016/j.jpsychores.2011.02.009 [published Online First: 2011/08/17] *inappropriate population*
97. Chatzitheodorou D, Mavromoustakos S, Milioti S. The effect of exercise on adrenocortical responsiveness of patients with chronic low back pain, controlled for psychological strain. *Clinical Rehabilitation* 2008;22(4):319-28. doi: 10.1177/0269215507079858 *inappropriate population*
98. Chen KW, Perlman A, Liao JG, et al. Effects of external qigong therapy on osteoarthritis of the knee. A randomized controlled trial. *Clinical rheumatology* 2008;27(12):1497-505. doi: 10.1007/s10067-008-0955-4 [published Online First: 2008/07/26] *inappropriate intervention*
99. Cheung C, Wyman J, Bronas U, et al. Is yoga better than aerobic/strengthening exercises for managing knee osteoarthritis in older adults? *Osteoarthritis and cartilage* 2016; 24. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/579/CN-01142579/frame.html. *inappropriate study design*
100. Christensen R, Henriksen M, Leeds A, et al. Effect of weight maintenance on symptoms of knee osteoarthritis in obese patients: a twelve-month randomized controlled trial. *Arthritis care & research* 2015; 67(5).

http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/664/CN-01075664/frame.html. *inappropriate outcomes*

101. Christensen SS, Frostholm L, Ørnbøl E, et al. Changes in illness perceptions mediated the effect of cognitive behavioural therapy in severe functional somatic syndromes. *Journal of psychosomatic research* 2015;78(4):363-70. doi: 10.1016/j.jpsychores.2014.12.005 *inappropriate study design*
102. Citrome L, Weiss-Citrome A. A systematic review of duloxetine for osteoarthritic pain: What is the number needed to treat, number needed to harm, and likelihood to be helped or harmed? *Postgraduate Medicine* 2012;124(1):83-93. doi: 10.3810/pgm.2012.01.2521 *inappropriate study design*
103. Clark DI, Downing N, Mitchell J, et al. Physiotherapy for anterior knee pain: a randomised controlled trial. *Annals of the rheumatic diseases* 2000;59(9):700-04. doi: 10.1136/ard.59.9.700 *inappropriate population*
104. Clarke-Jenssen A-C, Mengshoel AM, Staalesen Strumse Y, et al. EFFECT OF A FIBROMYAFGIA REHABILITATION PROGRAMME IN WARM VERSUS COLD CLIMATE: A RANDOMIZED CONTROLLED STUDY. *Journal of Rehabilitation Medicine (Stiftelsen Rehabiliteringsinformation)* 2014;46(7):676-83. doi: 10.2340/16501977-1819 *inappropriate intervention*
105. Cordoba-Torrecilla S, Aparicio VA, Soriano-Maldonado A, et al. Physical fitness is associated with anxiety levels in women with fibromyalgia: the al-Andalus project. *Quality of Life Research* 2016;25(4):1053-58. doi: 10.1007/s11136-015-1128-y *inappropriate study design*
106. Cöster L, Kendall S, Gerdle B, et al. Chronic widespread musculoskeletal pain--A comparison of those who meet criteria for fibromyalgia and those who do not. *European Journal of Pain* 2008;12(5):600-10. doi: 10.1016/j.ejpain.2007.10.001 *inappropriate study design*
107. Courtois I, Cools F, Calsius J. Effectiveness of body awareness interventions in fibromyalgia and chronic fatigue syndrome: a systematic review and meta-analysis. *Journal of bodywork and movement therapies* 2015;19(1):35-56. doi: 10.1016/j.jbmt.2014.04.003 [published Online First: 2015/01/22] *inappropriate study design*
108. Couto CI. Exercise training and pyridostigmine each have unique benefits for patients with fibromyalgia. *Australian Journal of Physiotherapy* 2008;54(3):219-19. *inappropriate study design*
109. Creavin ST, Dunn KM, Mallen CD, et al. Co-occurrence and associations of pain and fatigue in a community sample of Dutch adults. *European Journal of Pain* 2010;14(3):327-34. doi: 10.1016/j.ejpain.2009.05.010 *inappropriate study design*
110. Cuesta-Vargas A, Luciano JV, Peñarrubia-María MT, et al. Clinical dimensions of fibromyalgia symptoms and development of a combined index of severity: The CODI index. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care & Rehabilitation* 2013;22(1):153-60. doi: 10.1007/s11136-012-0134-6 *inappropriate study design*
111. Cuss A, Morris M, Ambler N, et al. Goal setting for managing rheumatoid arthritis fatigue: A qualitative exploration. *Rheumatology Conference: Rheumatology 2010 - British Society for Rheumatology, BSR and British Health Professionals in Rheumatology, BHPR Annual Meeting 2010 Birmingham United Kingdom*

Conference Start: 20100420 Conference End: 20100423 Conference Publication: (varpagings) 2010; 49. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/368/CN-00789368/frame.html. *inappropriate study design*

112. Dailey DL, Frey Law LA, Vance CG, et al. Perceived function and physical performance are associated with pain and fatigue in women with fibromyalgia. *Arthritis research & therapy* 2016;18:68. doi: 10.1186/s13075-016-0954-9 [published Online First: 2015/01/01] *inappropriate study design*
113. Daltroy LH, Morlino CI, Eaton HM, et al. Preoperative education for total hip and knee replacement patients. *Arthritis care & research* 1998;11(6):469-78. doi: 10.1002/art.1790110607 *inappropriate intervention*
114. das Nair R, Anderson P, Clarke S, et al. Home-administered pre-surgical psychological intervention for knee osteoarthritis (HAPPiKNEES): study protocol for a randomised controlled trial. *Trials* 2016;17:54. doi: 10.1186/s13063-016-1165-z [published Online First: 2016/01/29] *inappropriate intervention*
115. Davis MC, Zautra AJ, Wolf LD, et al. Mindfulness and cognitive-behavioral interventions for chronic pain: Differential effects on daily pain reactivity and stress reactivity. *Journal of Consulting and Clinical Psychology* 2015;83(1):24-35. doi: 10.1037/a0038200 *inappropriate intervention*
116. de Brouwer SJM, Kraaimaat FW, Sweep F, et al. Psychophysiological Responses to Stress after Stress Management Training in Patients with Rheumatoid Arthritis. *PloS one* 2011;6(12) doi: 10.1371/journal.pone.0027432 *inappropriate intervention*
117. D'Eon MS. Feasibility and Acceptability of Graded In-Vivo Exposure Therapy for Fibromyalgia Patients [Ph.D.]. University of California, San Diego, 2016. *inappropriate intervention*
118. Donmez A, Karagulle MZ, Tercan N, et al. SPA therapy in fibromyalgia: a randomised controlled clinic study. *Rheumatology international* 2005;26(2):168-72. doi: 10.1007/s00296-005-0623-9 [published Online First: 2005/06/21] *inappropriate intervention*
119. Dougados M, Tsai WC, Saaibi DL, et al. Evaluation of Health Outcomes with Etanercept Treatment in Patients with Early Nonradiographic Axial Spondyloarthritis. *The Journal of rheumatology* 2015;42(10):1835-41. doi: 10.3899/jrheum.141313 [published Online First: 2015/08/16] *inappropriate intervention*
120. Driban JB, Morgan N, Price LL, et al. Patient-Reported Outcomes Measurement Information System (PROMIS) instruments among individuals with symptomatic knee osteoarthritis: a cross-sectional study of floor/ceiling effects and construct validity. *BMC musculoskeletal disorders* 2015;16 doi: 10.1186/s12891-015-0715-y *inappropriate study design*
121. Dunn-Lewis C, Kraemer WJ, Kupchak BR, et al. A multi-nutrient supplement reduced markers of inflammation and improved physical performance in active individuals of middle to older age: a randomized, double-blind, placebo-controlled study. *Nutrition Journal* 2011;10 doi: 10.1186/1475-2891-10-90 *inappropriate intervention*

122. Ekici G, Bakar Y, Akbayrak T, et al. Comparison of manual lymph drainage therapy and connective tissue massage in women with fibromyalgia: a randomized controlled trial. *Journal of manipulative and physiological therapeutics* 2009;32(2):127-33. doi: 10.1016/j.jmpt.2008.12.001 [published Online First: 2009/02/27] *inappropriate intervention*
123. Ekici G, Unal E, Akbayrak T, et al. Effects of active/passive interventions on pain, anxiety, and quality of life in women with fibromyalgia: Randomized controlled pilot trial. *Women & health* 2017;57(1):88-107. doi: 10.1080/03630242.2016.1153017 [published Online First: 2016/02/18] *inappropriate comparison group*
124. Ekici G, Unal E, Akbayrak T, et al. Active versus passive therapy in females with fibromyalgia; "pilates exercises and connective tissue massage": A randomized controlled pilot trial, Fibromiyaljili kadinlarda pasif tedaviye karsi aktif tedavi: "pilates egzersizleri ve konnektif doku masaji": Randomize kontrollu pilot calisma. [Turkish, English]. *Fizyoterapi Rehabilitasyon* 2014; 25(1 suppl. 1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/055/CN-01010055/frame.html. *inappropriate comparison group*
125. Elias A, Yaacob LH, Kadir AA, et al. Guided Imagery Relaxation Therapy in Malaysian Patients with Knee Osteoarthritis: A Randomized Controlled Trial. *International Journal of Collaborative Research on Internal Medicine & Public Health* 2015;7(5):92-103. *inappropriate intervention*
126. Elliot DL, Kuehl KS, Jones KD, et al. Using an eccentric exercise-testing protocol to assess the beneficial effects of tart cherry juice in fibromyalgia patients. *Integrative Medicine: A Clinician's Journal* 2010;9(6):24-29. *inappropriate intervention*
127. Emery P, Bingham C, Burmester G, et al. Improvements in patient-reported outcomes following 52 weeks of treatment with certolizumab pegol in combination with methotrexate in DMARD-naive patients with severe, active and progressive rheumatoid arthritis: Results from the C-early randomized, double-blind, controlled phase 3 study. *Value in health* 2015; 18(7). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/114/CN-01164114/frame.html. *inappropriate intervention*
128. Engel C. Tailored cognitive-behavioral therapy plus exercise training improved clinical and functional outcomes in fibromyalgia. *Annals of internal medicine* 2011; 154(8). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/037/CN-00895037/frame.html. *inappropriate intervention*
129. Ericsson A, Bremell T, Cider A, et al. Effects of exercise on fatigue and physical capacity in men with chronic widespread pain - a pilot study. *Bmc Sports Science Medicine and Rehabilitation* 2016;8 doi: 10.1186/s13102-016-0054-9 *inappropriate population*
130. Ericsson A, Palstam A, Larsson A, et al. Resistance exercise improves physical fatigue in women with fibromyalgia: a randomized controlled trial. *Arthritis research & therapy* 2016;18 doi: 10.1186/s13075-016-1073-3 *inappropriate comparison group*

131. Falcão DM, Sales L, Leite JR, et al. Cognitive behavioral therapy for the treatment of fibromyalgia syndrome: a randomized controlled trial. *Journal of Musculoskeletal Pain* 2008;16(3):133-40. *inappropriate intervention*
132. Fark AR. A pilot study of white-coat and labile hypertension: Associations with diagnoses of psychosocial dysfunction. *Family Practice Research Journal* 1993;13(1):71-80. *inappropriate outcomes*
133. Feldthusen C, Dean E, Forsblad-d'Elia H, et al. Effects of Person-Centered Physical Therapy on Fatigue-Related Variables in Persons With Rheumatoid Arthritis: A Randomized Controlled Trial. *Archives of Physical Medicine & Rehabilitation* 2016;97(1):26-36. *inappropriate intervention*
134. Fenton G, Morley S. A tale of two RCTs: Using randomized controlled trials to benchmark routine clinical (psychological) treatments for chronic pain. *Pain* 2013;154(10):2108-19. doi: 10.1016/j.pain.2013.06.033 *inappropriate study design*
135. Field T. Yoga research review. *Complementary therapies in clinical practice* 2016;24:145-61. doi: 10.1016/j.ctcp.2016.06.005 [published Online First: 2016/08/10] *inappropriate intervention*
136. Field T, Diego M, Cullen C, et al. Fibromyalgia pain and substance P decrease and sleep improves after massage therapy. *Jcr-Journal of Clinical Rheumatology* 2002;8(2):72-76. doi: 10.1097/00124743-200204000-00002 *inappropriate intervention*
137. Field T, Diego M, Delgado J, et al. Rheumatoid arthritis in upper limbs benefits from moderate pressure massage therapy. *Complementary therapies in clinical practice* 2013;19(2):101-3. doi: 10.1016/j.ctcp.2012.12.001 [published Online First: 2013/04/09] *inappropriate intervention*
138. Field T, Hernandez-Reif M, Seligman S, et al. Juvenile rheumatoid arthritis: benefits from massage therapy. *Journal of pediatric psychology* 1997;22(5):607-17. [published Online First: 1998/02/12] *inappropriate population*
139. Fitzgerald GK, White DK, Piva SR. Associations for change in physical and psychological factors and treatment response following exercise in knee osteoarthritis: an exploratory study. *Arthritis care & research* 2012;64(11):1673-80. doi: 10.1002/acr.21751 [published Online First: 2012/06/08] *inappropriate outcomes*
140. Fjorback L, Schroder A, Ornbol E, et al. Mindfulness therapy for bodily distress syndrome - A randomized controlled trial. *Journal of psychosomatic research* 2011; 70(6). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/011/CN-01006011/frame.html. *inappropriate intervention*
141. Fjorback LO, Arendt M, Ørnbøl E, et al. Mindfulness therapy for somatization disorder and functional somatic syndromes — randomized trial with one-year follow-up. *Journal of psychosomatic research* 2013;74(1):31-40. doi: 10.1016/j.jpsychores.2012.09.006 *inappropriate intervention*
142. Fors EA, Götestam KG. Patient education, guided imagery and pain related talk in fibromyalgia coping. *The European Journal of Psychiatry* 2000;14(4):233-40. *inappropriate intervention*
143. Fregni F, Gimenes R, Valle AC, et al. A randomized, sham-controlled, proof of principle study of transcranial direct current stimulation for the treatment of pain

in fibromyalgia. *Arthritis and rheumatism* 2006;54(12):3988-98. doi: 10.1002/art.22195 [published Online First: 2006/11/30] *inappropriate intervention*

144. French H, Cusack T, Brennan A, et al. The effectiveness of exercise with and without manual therapy for hip osteoarthritis: A multi-centre randomised controlled trial. *Arthritis and rheumatism* 2011; 63(10 suppl. 1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/130/CN-01005130/frame.html. *inappropriate study design*
145. French H, Cusack T, Brennan A, et al. The effectiveness of exercise therapy with and without manual therapy for hip osteoarthritis: A multicentre randomised controlled trial. *Rheumatology* 2011; 50. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/722/CN-01003722/frame.html. *inappropriate study design*
146. French HP, Cusack T, Brennan A, et al. Exercise and manual physiotherapy arthritis research trial (EMPART): a multicentre randomised controlled trial. *BMC musculoskeletal disorders* 2009;10:9. doi: 10.1186/1471-2474-10-9 [published Online First: 2009/01/21] *inappropriate study design*
147. French HP, Galvin R, Cusack T, et al. Predictors of short-term outcome to exercise and manual therapy for people with hip osteoarthritis. *Physical therapy* 2014;94(1):31-9. doi: 10.2522/ptj.20130173 [published Online First: 2013/08/10] *inappropriate study design*
148. Friedrich M, Hahne J, Wepner F. A controlled examination of medical and psychosocial factors associated with low back pain in combination with widespread musculoskeletal pain. *Physical therapy* 2009;89(8):786-803. doi: 10.2522/ptj.20080100 [published Online First: 2009/06/23] *inappropriate population*
149. Fulton AS, Hill AM, Williams MT, et al. Feasibility of omega-3 fatty acid supplementation as an adjunct therapy for people with chronic obstructive pulmonary disease: study protocol for a randomized controlled trial. *Trials* 2013;14 doi: 10.1186/1468-6708-14-107 *inappropriate intervention*
150. Garcia-Campayo J, Pascual A, Alda M, et al. Coping with fibromialgia: Usefulness of the Chronic Pain Coping Inventory-42. *Pain* 2007;132(Suppl 1):S68-S76. doi: 10.1016/j.pain.2007.02.013 *inappropriate intervention*
151. Garcia-Palacios A, Herrero R, Vizcaino Y, et al. Integrating Virtual Reality With Activity Management for the Treatment of Fibromyalgia Acceptability and Preliminary Efficacy. *Clinical Journal of Pain* 2015;31(6):564-72. doi: 10.1097/ajp.0000000000000196 *inappropriate intervention*
152. Garvey WT, Mechanick JI, Brett EM, et al. AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY COMPREHENSIVE CLINICAL PRACTICE GUIDELINES FOR MEDICAL CARE OF PATIENTS WITH OBESITY. *Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists* 2016;22 Suppl 3:1-203. doi: 10.4158/ep161365.gl [published Online First: 2016/05/25] *inappropriate study design*

153. Gavi M, 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(3) doi: 10.1371/journal.pone.0090767 *inappropriate comparison group*
154. Genc A, Tur BS, Aytur YK, et al. Does aerobic exercise affect the hypothalamicpituitary- adrenal hormonal response in patients with fibromyalgia syndrome? *Journal of Physical Therapy Science* 2015;27(7):2225-31. *inappropriate outcomes*
155. Gerskowitch C, Norman I, Rimes KA. Patients with medically unexplained physical symptoms experience of receiving treatment in a primary-care psychological therapies service: a qualitative study. *Cognitive Behaviour Therapist* 2015;8 doi: 10.1017/s1352465815000235 *inappropriate intervention*
156. Gniadecki R, Robertson D, Molta CT, et al. Self-reported health outcomes in patients with psoriasis and psoriatic arthritis randomized to two etanercept regimens. *Journal of the European Academy of Dermatology and Venereology : JEADV* 2012;26(11):1436-43. doi: 10.1111/j.1468-3083.2011.04308.x http://dx.doi.org/10.1111/j.1468-3083.2011.04308.x [published Online First: 2011/11/01] *inappropriate intervention*
157. Goodwin P, Al QK, Gregory W, et al. The effectiveness of aquatic physiotherapy in patients with rheumatoid arthritis: A randomised controlled trial. *Physiotherapy (United Kingdom)* 2015; 101. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/496/CN-01126496/frame.html. *inappropriate comparison group*
158. Gowans SE, DeHueck A, Abbey SE. Measuring exercise-induced mood changes in fibromyalgia: a comparison of several measures. *Arthritis and rheumatism* 2002;47(6):603-9. doi: 10.1002/art.10789 [published Online First: 2003/01/11] *inappropriate population*
159. Gowans SE, Dehueck A, Voss S, et al. Six-month and one-year followup of 23 weeks of aerobic exercise for individuals with fibromyalgia. *Arthritis and rheumatism* 2004;51(6):890-8. doi: 10.1002/art.20828 [published Online First: 2004/12/14] *inappropriate population*
160. Grace SL, Krepostman S, Brooks D, et al. Illness perceptions among cardiac patients: Relation to depressive symptomatology and sex. *Journal of psychosomatic research* 2005;59(3):153-60. doi: 10.1016/j.jpsychores.2005.05.005 *inappropriate study design*
161. Gremeaux V, Durand S, Benaim C, et al. Evaluation of various ways to deliver information concerning non-steroidal anti-inflammatory drugs to osteoarthritis patients. *Annals of physical and rehabilitation medicine* 2013;56(1):14-29. doi: 10.1016/j.rehab.2012.12.004 [published Online First: 2013/02/02] *inappropriate study design*
162. Gronning K, Bratas O, Steinsbekk A. Which Factors Influence Self-Efficacy in Patients with Chronic Inflammatory Polyarthritis? *Musculoskeletal care* 2016;14(2):77-86. doi: 10.1002/msc.1114 *inappropriate study design*
163. Gronning K, Rannestad T, Skomsvoll JF, et al. Long-term effects of a nurse-led group and individual patient education programme for patients with chronic inflammatory polyarthritis - a randomised controlled trial. *Journal of clinical*

nursing 2014;23(7-8):1005-17. doi: 10.1111/jocn.12353 [published Online First: 2013/07/24] *inappropriate intervention*

164. Gronning K, Skomsvoll JF, Rannestad T, et al. The effect of an educational programme consisting of group and individual arthritis education for patients with polyarthritis-A randomised controlled trial. *Patient education and counseling* 2012;88(1):113-20. doi: 10.1016/j.pec.2011.12.011 *inappropriate intervention*
165. Gulec H, Capkin E, Sayar K, et al. The evaluation of the effectiveness of amitriptyline versus venlafaxine in female patients diagnosed with fibromyalgia syndrome. [Turkish]. *Klinik Psikofarmakoloji Bulteni* 2007; 17(2). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/184/CN-00642184/frame.html. *inappropriate intervention*
166. Gusi N, Tomas-Carus P, Hakkinen A, et al. Exercise in waist-high warm water decreases pain and improves health-related quality of life and strength in the lower extremities in women with fibromyalgia. *Arthritis and rheumatism* 2006;55(1):66-73. doi: 10.1002/art.21718 *inappropriate population*
167. Haak T, Scott B. The effect of Qigong on fibromyalgia (FMS): a controlled randomized study. *DisabilRehabil* 2008;30(8):625-33. *inappropriate intervention*
168. Haugstad GK, Haugstad TS, Kirste UM, et al. Continuing improvement of chronic pelvic pain in women after short-term Mensendieck somatocognitive therapy: results of a 1-year follow-up study. *American Journal of Obstetrics and Gynecology* 2008;199(6) doi: 10.1016/j.ajog.2008.06.019 *inappropriate population*
169. Haun JN, Graham-Pole J, Shortley B. Children with cancer and blood diseases experience positive physical and psychological effects from massage therapy. *International journal of therapeutic massage & bodywork* 2009;2(2):7-14. [published Online First: 2009/01/01] *inappropriate population*
170. Haupt M, Millen S, Janner M, et al. Improvement of coping abilities in patients with systemic lupus erythematosus: a prospective study. *Annals of the rheumatic diseases* 2005;64(11):1618-23. doi: 10.1136/ard.2004.029926 *inappropriate population*
171. Hauser W. The german fibromyalgia consumer reports-a cross-sectional survey. *Annals of the Rheumatic Disease* 2013; 71. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/601/CN-01011601/frame.html. *inappropriate study design*
172. Hecker CD, Melo C, Tomazoni SdS, et al. Analysis of effects of kinesiotherapy and hydrokinesiotherapy on the quality of patients with fibromyalgia -- a randomized clinical trial. *Fisioterapia em Movimento* 2011;24(1):57-64. doi: 10.1590/S0103-51502011000100007 *inappropriate comparison group*
173. Heffez DS, Ross RE, Shade-Zeldow Y, et al. Treatment of cervical myelopathy in patients with the fibromyalgia syndrome: outcomes and implications. *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society* 2007;16(9):1423-33. doi: 10.1007/s00586-007-0366-2 [published Online First: 2007/04/12] *inappropriate study design*

174. Henkel K, Reimers CD, Knapp G, et al. Physical training for neurological and mental diseases. *Der Nervenarzt* 2014;85(12):1521-+. doi: 10.1007/s00115-013-3978-2 *inappropriate study design*
175. Hoeger Bement MK, Weyer A, Hartley S, et al. Pain Perception After Isometric Exercise in Women With Fibromyalgia. *Archives of Physical Medicine & Rehabilitation* 2011;92(1):89-95. *inappropriate study design*
176. Hsieh RL, Lee WC. Clinical effects of lateral wedge arch support insoles in knee osteoarthritis: A prospective double-blind randomized study. *Medicine* 2016;95(27):e3952. doi: 10.1097/md.0000000000003952 [published Online First: 2016/07/12] *inappropriate intervention*
177. Hsieh RL, Lo MT, Lee WC, et al. Therapeutic effects of short-term monochromatic infrared energy therapy on patients with knee osteoarthritis: a double-blind, randomized, placebo-controlled study. *The Journal of orthopaedic and sports physical therapy* 2012;42(11):947-56. doi: 10.2519/jospt.2012.3881 [published Online First: 2012/09/11] *inappropriate intervention*
178. Huber E, Roos E, Meichtry A, et al. Effect of preoperative neuromuscular training (NEMEX-TJR) on functional outcome after total knee replacement: An assessor-blinded randomized controlled trial. *BMC musculoskeletal disorders* 2015; 16(1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/584/CN-01088584/frame.html. *inappropriate intervention*
179. Hudson JI, Arnold LM, Bradley LA, et al. What makes patients with fibromyalgia feel better? Correlations between Patient Global Impression of Improvement and changes in clinical symptoms and function: a pooled analysis of 4 randomized placebo-controlled trials of duloxetine. *The Journal of rheumatology* 2009;36(11):2517-22. doi: 10.3899/jrheum.090139 [published Online First: 2009/10/17] *inappropriate study design*
180. Hughes S, Seymour R, Campbell R, et al. Fit and Strong!: bolstering maintenance of physical activity among older adults with lower-extremity osteoarthritis. *American journal of health behavior* 2010; 34(6). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/647/CN-00761647/frame.html. *inappropriate intervention*
181. Hurley M, Walsh N, Jessep S. Clinical effectiveness and costs of an integrated rehabilitation programme compared with outpatient physiotherapy for chronic knee pain. *Arthritis and rheumatism* 2012; 64. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/235/CN-01008235/frame.html. *inappropriate study design*
182. Hurst NP, Lambert CM, Forbes J, et al. Does waiting matter? A randomized controlled trial of new non-urgent rheumatology out-patient referrals. *Rheumatology (Oxford, England)* 2000;39(4):369-76. [published Online First: 2000/05/19] *inappropriate intervention*
183. Ide MR, Laurindo IMM, Rodrigues AL, et al. Effect of aquatic respiratory exercise-based program in patients with fibromyalgia. *International journal of rheumatic diseases* 2008;11(2):131-40. doi: 10.1111/j.1756-185X.2008.00348.x *inappropriate comparison group*
184. Jackel WH, Gerdes N, Cziske R, et al. RHEUMATIC COMPLAINTS IN THE GENERAL-POPULATION OF GERMANY - PREVALENCE, PHYSICAL AND

PSYCHOSOCIAL IMPACT. *Zeitschrift fur Rheumatologie* 1993;52(5):281-88. *inappropriate study design*

185. Jenkinson CM, Doherty M, Avery AJ, et al. Effects of dietary intervention and quadriceps strengthening exercises on pain and function in overweight people with knee pain: randomised controlled trial. *BMJ (Clinical research ed)* 2009;339:b3170. doi: 10.1136/bmj.b3170 [published Online First: 2009/08/20] *inappropriate population*
186. Jensen KB, Kosek E, Wicksell R, et al. Cognitive Behavioral Therapy increases pain-evoked activation of the prefrontal cortex in patients with fibromyalgeia. *Pain* 2012;153(7):1495-503. doi: 10.1016/j.pain.2012.04.010 *inappropriate intervention*
187. Jensen OK, Nielsen CV, Stengaard-Pedersen K. One-year prognosis in sick-listed low back pain patients with and without radiculopathy. Prognostic factors influencing pain and disability. *Spine Journal* 2010;10(8):659-75. doi: 10.1016/j.spinee.2010.03.026 *inappropriate population*
188. Jessep SA, Walsh NE, Ratcliffe J, et al. Long-term clinical benefits and costs of an integrated rehabilitation programme compared with outpatient physiotherapy for chronic knee pain. *Physiotherapy* 2009;95(2):94-102. doi: 10.1016/j.physio.2009.01.005 [published Online First: 2009/07/25] *inappropriate population*
189. Johannesson E, Simren M, Strid H, et al. Physical activity improves symptoms in irritable bowel syndrome: a randomized controlled trial. *The American journal of gastroenterology* 2011;106(5):915-22. doi: 10.1038/ajg.2010.480 [published Online First: 2011/01/06] *inappropriate population*
190. Jones KD. A randomized controlled trial of muscle strengthening versus flexibility training in fibromyalgia. Microform Publications, University of Oregon, 2000. *inappropriate comparison group*
191. Kamanli A, Kaya A, Ardicoglu O, et al. Comparison of lidocaine injection, botulinum toxin injection, and dry needling to trigger points in myofascial pain syndrome. *Rheumatology international* 2005;25(8):604-11. doi: 10.1007/s00296-004-0485-6 *inappropriate intervention*
192. Kang J, Li N, Wu B. Therapeutic methods for knee osteoarthritis: Randomized controlled trial and systemic evaluation. [Chinese]. *Zhongguo Linchuang Kangfu* 2005; 9(30). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/890/CN-00643890/frame.html. *inappropriate study design*
193. Kapfhammer HP. [Psychopharmacological treatment in patients with somatoform disorders and functional body syndromes]. *Der Nervenarzt* 2012;83(9):1128-41. doi: 10.1007/s00115-011-3446-9 [published Online First: 2012/08/17] *inappropriate study design*
194. Karp J, Dew M, Wahed A, et al. Challenges and Solutions for Depression Prevention Research: Methodology for a Depression Prevention Trial for Older Adults with Knee Arthritis and Emotional Distress. *American journal of geriatric psychiatry* 2016; 24(6). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/456/CN-01158456/frame.html. *inappropriate outcomes*

195. Katic B, Heywood J, Turek F, et al. New approach for analyzing self-reporting of insomnia symptoms reveals a high rate of comorbid insomnia across a wide spectrum of chronic diseases. *Sleep Medicine* 2015;16(11):1332-41. doi: 10.1016/j.sleep.2015.07.024 *inappropriate outcomes*
196. Kaya A, Kamanli A, Ardicoglu O, et al. Direct current therapy with/without fidocaine iontophoresis in myofascial pain syndrome. *Bratislava Medical Journal-Bratislavske Lekarske Listy* 2009;110(3):185-91. *inappropriate intervention*
197. Kayiran S, Dursun E, Dursun N, et al. Neurofeedback intervention in fibromyalgia syndrome; a randomized, controlled, rater blind clinical trial. *Applied psychophysiology and biofeedback* 2010;35(4):293-302. doi: 10.1007/s10484-010-9135-9 [published Online First: 2010/07/09] *inappropriate intervention*
198. Keefe FJ, Shelby RA, Somers TJ, et al. Effects of coping skills training and sertraline in patients with non-cardiac chest pain: A randomized controlled study. *Pain* 2011;152(4):730-41. doi: 10.1016/j.pain.2010.08.040 *inappropriate intervention*
199. Keeley T, Al-Janabi H, Nicholls E, et al. A longitudinal assessment of the responsiveness of the ICECAP-A in a randomised controlled trial of a knee pain intervention. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation* 2015;24(10):2319-31. doi: 10.1007/s11136-015-0980-0 [published Online First: 2015/04/22] *inappropriate study design*
200. Kekow J, Moots R, Khandker R, et al. Improvements in patient-reported outcomes, symptoms of depression and anxiety, and their association with clinical remission among patients with moderate-to-severe active early rheumatoid arthritis. *Rheumatology (Oxford, England)* 2011;50(2):401-9. doi: 10.1093/rheumatology/keq327 [published Online First: 2010/11/10] *inappropriate study design*
201. Kekow J, Moots RJ, Emery P, et al. Patient-reported outcomes improve with etanercept plus methotrexate in active early rheumatoid arthritis and the improvement is strongly associated with remission: the COMET trial. *Annals of the rheumatic diseases* 2010;69(1):222-5. doi: 10.1136/ard.2008.102509 [published Online First: 2009/03/19] *inappropriate intervention*
202. Kempke S, Goossens L, Luyten P, et al. Predictors of outcome in a multi-component treatment program for chronic fatigue syndrome. *Journal of Affective Disorders* 2010;126(1-2):174-79. doi: 10.1016/j.jad.2010.01.073 *inappropriate intervention*
203. Knittle K, Maes S, de Gucht V. Psychological interventions for rheumatoid arthritis: examining the role of self-regulation with a systematic review and meta-analysis of randomized controlled trials. *Arthritis care & research* 2010;62(10):1460-72. doi: 10.1002/acr.20251
http://dx.doi.org/10.1002/acr.20251 [published Online First: 2010/05/28] *inappropriate study design*
204. Kolahi S, Pourghassem Gargari B, Mesgari Abbasi M, et al. Effects of phylloquinone supplementation on lipid profile in women with rheumatoid arthritis: a double blind placebo controlled study. *Nutrition research and practice*

2015;9(2):186-91. doi: 10.4162/nrp.2015.9.2.186 [published Online First: 2015/04/11] *inappropriate intervention*

205. Konuk N, Ortancil O, Bostanci B, et al. A comparison of reboxetine and amitryptilline in the treatment of fibromyalgia syndrome with co-morbid depressive symptoms: An open-label preliminary study. *Klinik Psikofarmakoloji Bülteni / Bulletin of Clinical Psychopharmacology* 2010;20(1):29-37. *inappropriate intervention*
206. Koulil S, Lankveld W, Kraaimaat F, et al. Tailored cognitive-behavioral therapy and exercise training for high-risk patients with fibromyalgia. *Arthritis care & research* 2010; 62(10). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/899/CN-00760899/frame.html. *inappropriate intervention*
207. Kravitz HM, Esty ML, Katz RS, et al. Treatment of fibromyalgia syndrome using low-intensity neurofeedback with the Flexyx Neurotherapy System: a randomized controlled clinical trial. *Journal of Neurotherapy* 2006;10(2/3):41-58. *inappropriate intervention*
208. Kwakkenbos L, Willems LM, van den Hoogen FHJ, et al. Cognitive-Behavioural Therapy Targeting Fear of Progression in an Interdisciplinary Care Program: A Case Study in Systemic Sclerosis. *Journal of Clinical Psychology in Medical Settings* 2014;21(4):297-312. doi: 10.1007/s10880-014-9414-3 *inappropriate study design*
209. Lakhan SE, Schofield KL. Mindfulness-based therapies in the treatment of somatization disorders: a systematic review and meta-analysis. *PloS one* 2013;8(8):e71834. doi: 10.1371/journal.pone.0071834 [published Online First: 2013/08/31] *inappropriate study design*
210. Lan CC, Tseng CH, Chen JH, et al. Increased risk of a suicide event in patients with primary fibromyalgia and in fibromyalgia patients with concomitant comorbidities A nationwide population-based cohort study. *Medicine* 2016;95(44) doi: 10.1097/md.0000000000005187 *inappropriate study design*
211. Lange M, Krohn-Grimberghe B, Petermann F. Medium-term effects of a multimodal therapy on patients with fibromyalgia. Results of a controlled efficacy study. *Schmerz* 2011;25(1):55-61. doi: 10.1007/s00482-010-1003-2 *inappropriate intervention*
212. Lelieveld O, Armbrust W, Geertzen J, et al. Promoting physical activity in children with juvenile idiopathic arthritis through an internet-based program: Results of a pilot randomised controlled trial. *Physiotherapy (United Kingdom)* 2011; 97. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/266/CN-01076266/frame.html. *inappropriate population*
213. Leombruni P, Miniotti M, Colonna F, et al. A randomised controlled trial comparing duloxetine and acetyl L-carnitine in fibromyalgic patients: preliminary data. *Clinical and experimental rheumatology* 2015;33(1 Suppl 88):S82-5. [published Online First: 2015/03/19] *inappropriate intervention*
214. Leon AAC, Morera M, Espinoza MB, et al. Case Study: Effect of a Physical Exercise and Nutritional Counseling Program on Physical and Psychological Variables in a Person with Fibromyalgia. *Mhsalud-Revista En Ciencias Del*

Movimiento Humano Y La Salud 2015;11(2):1-19. doi: 10.15359/mhs.11-2.1 *inappropriate study design*

215. Li K, Hu XQ, Qiu WH, et al. Effects of physiotherapy versus combination of physiotherapy and preventive education on quality of life in patients with degenerative gonarthritis. *Chinese Journal of Clinical Rehabilitation* 2006;10(4):32-33. *inappropriate intervention*
216. Li YH, Wang FY, Feng CQ, et al. Massage therapy for fibromyalgia: a systematic review and meta-analysis of randomized controlled trials. *PloS one* 2014;9(2):e89304. doi: 10.1371/journal.pone.0089304 [published Online First: 2014/03/04] *inappropriate study design*
217. Ljótsson B, Atterlöf E, Lagerlöf M, et al. Internet-delivered acceptance and values-based exposure treatment for fibromyalgia: A pilot study. *Cognitive Behaviour Therapy* 2014;43(2):93-104. doi: 10.1080/16506073.2013.846401 *inappropriate intervention*
218. Lopez-Pousa S, Bassets Pages G, Monserrat-Vila S, et al. Sense of Well-Being in Patients with Fibromyalgia: Aerobic Exercise Program in a Mature Forest-A Pilot Study. *Evidence-based complementary and alternative medicine : eCAM* 2015;2015:614783. doi: 10.1155/2015/614783 [published Online First: 2015/11/12] *inappropriate comparison group*
219. Lopez-Rodriguez MD, Castro-Sanchez AM, Fernandez-Martinez M, et al. Comparison between aquatic-biodanza and stretching for improving quality of life and pain in pations with fibromyalgia. *Atencion Primaria* 2012;44(11):641-49. doi: 10.1016/j.aprim.2012.03.002 *inappropriate intervention*
220. Lopez-Rodriguez MM, Fernandez-Martinez M, Mataran-Penarrocha GA, et al. [Effectiveness of aquatic biodance on sleep quality, anxiety and other symptoms in patients with fibromyalgia]. *Medicina clinica* 2013;141(11):471-8. doi: 10.1016/j.medcli.2012.09.036 [published Online First: 2012/12/19] *inappropriate intervention*
221. Luciano JV, Martinez N, Penarrubia-Maria MT, et al. Effectiveness of a psychoeducational treatment program implemented in general practice for fibromyalgia patients: a randomized controlled trial. *The Clinical journal of pain* 2011;27(5):383-91. doi: 10.1097/AJP.0b013e31820b131c [published Online First: 2011/02/15] *inappropriate intervention*
222. Luedtke K, Rushton A, Wright C, et al. Effectiveness of anodal transcranial direct current stimulation in patients with chronic low back pain: design, method and protocol for a randomised controlled trial. *BMC musculoskeletal disorders* 2011;12:290. doi: 10.1186/1471-2474-12-290 [published Online First: 2011/12/30] *inappropriate intervention*
223. Lumley M, Schubiner H, Clauw D, et al. The PAST-FM (Pain and Stress Treatment for Fibromyalgia) randomized, controlled trial: Main effects of emotional awareness and expression and cognitive-behavioral therapies. *Journal of pain* 2016; 17(4 suppl. 1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/566/CN-01142566/frame.html. *inappropriate intervention*
224. Lumley MA, Keefe FJ, Mosley-Williams A, et al. The effects of written emotional disclosure and coping skills training in rheumatoid arthritis: A randomized clinical

trial. *Journal of Consulting and Clinical Psychology* 2014;82(4):644-58. doi: 10.1037/a0036958 *inappropriate intervention*

225. Lund I, Lundeberg T, Carleson J, et al. Corticotropin releasing factor in urine--a possible biochemical marker of fibromyalgia. Responses to massage and guided relaxation. *Neuroscience letters* 2006;403(1-2):166-71. doi: 10.1016/j.neulet.2006.04.038 [published Online First: 2006/05/24] *inappropriate study design*
226. Mackintosh S. Hydrotherapy and Tai Chi each provide clinical improvements for older people with osteoarthritis. *Australian Journal of Physiotherapy* 2008;54(2):143-43. *inappropriate study design*
227. Maddali Bongi S, Del Rosso A, Di Felice C, et al. Resseguier method and Qi Gong sequentially integrated in patients with fibromyalgia syndrome. *Clinical and experimental rheumatology* 2012;30(6 Suppl 74):51-8. [published Online First: 2012/11/01] *inappropriate intervention*
228. Mahagna H, Amital D, Amital H. A randomised, double-blinded study comparing giving etoricoxib vs. placebo to female patients with fibromyalgia. *International journal of clinical practice* 2016; 70(2 // (MSD) *Meso Scale Diagnostics*). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/727/CN-01132727/frame.html. *inappropriate intervention*
229. Mannerkorpi K, Nyberg B, Ahlmen M, et al. Pool exercise combined with an education program for patients with fibromyalgia syndrome. A prospective, randomized study. *J Rheumatol* 2000;27(10):2473-81. *inappropriate intervention*
230. Mao JJ, Bruner DW, Stricker C, et al. Feasibility trial of electroacupuncture for aromatase inhibitor--related arthralgia in breast cancer survivors. *Integrative cancer therapies* 2009;8(2):123-9. doi: 10.1177/1534735409332903 [published Online First: 2009/08/15] *inappropriate population*
231. Marszalek J, Price LL, Harvey WF, et al. Outcome Expectations and Osteoarthritis: Perceived Benefits of Exercise Are Associated with Self-Efficacy and Depression. *Arthritis care & research* 2016 doi: 10.1002/acr.22969 [published Online First: 2016/07/09] *inappropriate study design*
232. Martin DP, Williams BA, Berger IH. Improvement in fibromyalgia symptoms with acupuncture: Results of a randomized controlled trial. *Mayo Clinic proceedings* 2006;81(6):749-57. *inappropriate intervention*
233. Martín J, Torre F, Aguirre U, et al. Evaluation of the interdisciplinary PSYMEPHY treatment on patients with fibromyalgia: A randomized control trial. *Pain Medicine* 2014;15(4):682-91. doi: 10.1111/pme.12375 *inappropriate intervention*
234. Martin J, Torre F, Padierna A, et al. Six-and 12-month follow-up of an interdisciplinary fibromyalgia treatment programme: results of a randomised trial. *Clinical and experimental rheumatology* 2012;30(6 Suppl 74):103-11. [published Online First: 2013/02/27] *inappropriate intervention*
235. Martín J, Torre F, Padierna A, et al. Interdisciplinary treatment of patients with fibromyalgia: improvement of their health-related quality of life. *Pain practice : the official journal of World Institute of Pain* 2014; 14(8). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/572/CN-01090572/frame.html. *inappropriate intervention*

236. Martin J, Torre F, Padierna A, et al. Impact of interdisciplinary treatment on physical and psychosocial parameters in patients with fibromyalgia: results of a randomised trial. *International journal of clinical practice* 2014;68(5):618-27. [published Online First: 2014/05/29] *inappropriate intervention*
237. Martín-Nogueras AM, Calvo-Arenillas JI. Efficacy of physiotherapy treatment on pain and quality of life in patients with fibromyalgia. *Rehabilitacion* 2012;46(3):199-206. *inappropriate intervention*
238. Martins MRI, Gritti CC, dos Santos R, et al. Randomized controlled trial of a therapeutic intervention group in patients with fibromyalgia syndrome. *Revista Brasileira De Reumatologia* 2014;54(3):179-84. doi: 10.1016/j.rbre.2013.10.002 *inappropriate intervention*
239. Mata J, Cabrera S, Sanchis P, et al. Electro-acupuncture for treatment of knee pain from osteoarthritis and the possible endocrinology changes: a study protocol for a randomized controlled trial. *Trials* 2015;16:248. doi: 10.1186/s13063-015-0766-2 [published Online First: 2015/06/04] *inappropriate study design*
240. Mataran-Penarrocha GA, Castro-Sanchez AM, Garcia GC, et al. Influence of Craniosacral Therapy on Anxiety, Depression and Quality of Life in Patients with Fibromyalgia. *Evidence-Based Complementary and Alternative Medicine* 2011:1-9. doi: 10.1093/ecam/nep125 *inappropriate intervention*
241. Matcham F, Norton S, Scott D, et al. The impact of depression on long-term physical health outcomes in rheumatoid arthritis. *Rheumatology (United Kingdom)* 2014; 53. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/273/CN-01057273/frame.html. *inappropriate study design*
242. Matcham F, Norton S, Scott DL, et al. Symptoms of depression and anxiety predict treatment response and long-term physical health outcomes in rheumatoid arthritis: secondary analysis of a randomized controlled trial. *Rheumatology (Oxford, England)* 2016;55(2):268-78. doi: 10.1093/rheumatology/kev306 [published Online First: 2015/09/10] *inappropriate study design*
243. McBain H, Shipley M, Olaleye A, et al. A patient-initiated DMARD self-monitoring service for people with rheumatoid or psoriatic arthritis on methotrexate: A randomised controlled trial. *Annals of the rheumatic diseases* 2016; 75(7). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/299/CN-01178299/frame.html. *inappropriate intervention*
244. McVeigh JG, Hurley DA, Basford JR, et al. Effectiveness of a combined pool-based exercise and education programme compared to usual medical care in fibromyalgia syndrome: a randomised, controlled trial. *Physical Therapy Reviews* 2006;11(3):217-17. *inappropriate study design*
245. Mendonca ME, Simis M, Grecco LC, et al. Transcranial Direct Current Stimulation Combined with Aerobic Exercise to Optimize Analgesic Responses in Fibromyalgia: A Randomized Placebo-Controlled Clinical Trial. *Frontiers in human neuroscience* 2016;10:68. doi: 10.3389/fnhum.2016.00068 [published Online First: 2016/03/26] *inappropriate intervention*
246. Menkes CJ, Godeau P. Fibromyalgia. *Bulletin De L Academie Nationale De Medecine* 2007;191(1):143-48. *inappropriate study design*

247. Mercadie L, Mick G, Guetin S, et al. Effects of Listening to Music versus Environmental Sounds in Passive and Active Situations on Levels of Pain and Fatigue in Fibromyalgia. *Pain Management Nursing* 2015;16(5):664-71. doi: 10.1016/j.pmn.2015.01.005 *inappropriate intervention*
248. Meyer BB, Lemley KJ. Utilizing exercise to affect the symptomology of fibromyalgia: a pilot study. *Medicine and science in sports and exercise* 2000;32(10):1691-7. [published Online First: 2000/10/20] *inappropriate study design*
249. Mibielli M, Nunes C, Cezar P, et al. Osteoarthritis: Clinical evaluation of diclofenac combined with the B complex vitamins. *Revista brasileira de medicina* 2009; 66(7). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/674/CN-00753674/frame.html. *inappropriate intervention*
250. Middleton KR, Ward MM, Haaz S, et al. A pilot study of yoga as self-care for arthritis in minority communities. *Health and quality of life outcomes* 2013;11:55. doi: 10.1186/1477-7525-11-55 [published Online First: 2013/04/04] *inappropriate intervention*
251. Miles ALS. The effects of gentle yoga vs. cognitive behavioral therapy on physical and psychological symptoms; neurocognitive functioning; and physiology in women with Fibromyalgia. ProQuest Information & Learning, 2014. *inappropriate intervention*
252. Minor MA. Exercise maintenance behavior of subjects with arthritis following participation in a supervised exercise program [Ph.D.]. University of Missouri - Columbia, 1989. *inappropriate study design*
253. Minor MA, Brown JD. Exercise maintenance of persons with arthritis after participation in a class experience. *Health education quarterly* 1993;20(1):83-95. [published Online First: 1993/01/01] *inappropriate study design*
254. Mirtaheri E, Gargari BP, Kolahi S, et al. Effects of Alpha-Lipoic Acid Supplementation on Inflammatory Biomarkers and Matrix Metalloproteinase-3 in Rheumatoid Arthritis Patients. *Journal of the American College of Nutrition* 2015;34(4):310-17. doi: 10.1080/07315724.2014.910740 *inappropriate intervention*
255. Mishra P, Trivedi V. Acupuncture in the treatment of rheumatoid arthritis: Results of a randomized controlled trial. *Annals of the rheumatic diseases* 2014; 73. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/582/CN-01009582/frame.html. *inappropriate intervention*
256. Moore RA, Straube S, Paine J, et al. Fibromyalgia: Moderate and substantial pain intensity reduction predicts improvement in other outcomes and substantial quality of life gain. *Pain* 2010;149(2):360-64. doi: 10.1016/j.pain.2010.02.039 *inappropriate study design*
257. Morgan N, Driban J, Ransford G, et al. Construct validity of promis instruments among patients with symptomatic knee osteoarthritis. *Osteoarthritis and cartilage* 2013; 21. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/483/CN-01010483/frame.html. *inappropriate study design*
258. Morgan N, Ransford G, Morgan L, et al. Mindfulness is associated with psychological symptoms, self-efficacy, and quality of life among patients with symptomatic knee osteoarthritis. *Osteoarthritis and cartilage* 2013; 21.

http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/479/CN-01010479/frame.html. *inappropriate study design*

259. Morone N, Karp J, Lynch C, et al. Impact of chronic musculoskeletal pathology on older adults: a study of differences between knee OA and low back pain. *Pain medicine (Malden, Mass)* 2009; 10(4). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/087/CN-00721087/frame.html. *inappropriate study design*
260. Moroshko I, Brennan L, O'Brien P. Predictors of dropout in weight loss interventions: A systematic review of the literature. *Obesity Reviews* 2011;12(11):912-34. doi: 10.1111/j.1467-789X.2011.00915.x *inappropriate study design*
261. Morris LD, Grimmer-Somers KA, Spottiswoode B, et al. Virtual reality exposure therapy as treatment for pain catastrophizing in fibromyalgia patients: proof-of-concept study (Study Protocol). *BMC musculoskeletal disorders* 2011;12(1):85. doi: 10.1186/1471-2474-12-85 [published Online First: 2011/05/03] *inappropriate study design*
262. Moustafa IM, Diab AA. The addition of upper cervical manipulative therapy in the treatment of patients with fibromyalgia: a randomized controlled trial. *Rheumatology international* 2015;35(7):1163-74. doi: 10.1007/s00296-015-3248-7 [published Online First: 2015/03/19] *inappropriate intervention*
263. Mu PF, Chen YC, Cheng SC. The effectiveness of non-pharmacological pain management in relieving chronic pain for children and adolescents. *JBI library of systematic reviews* 2009;7(34):1489-543. [published Online First: 2009/01/01] *inappropriate population*
264. Munguia-Izquierdo D, Legaz-Arrese A. Determinants of sleep quality in middle-aged women with fibromyalgia syndrome. *Journal of Sleep Research* 2012;21(1):73-79. doi: 10.1111/j.1365-2869.2011.00929.x *inappropriate outcomes*
265. Murphy LB, Sacks JJ, Brady TJ, et al. Anxiety and depression among US adults with arthritis: Prevalence and correlates. *Arthritis care & research* 2012;64(7):968-76. doi: 10.1002/acr.21685 *inappropriate study design*
266. Murphy SL, Lyden AK, Kratz AL, et al. Characterizing Pain Flares From the Perspective of Individuals With Symptomatic Knee Osteoarthritis. *Arthritis care & research* 2015;67(8):1103-11. doi: 10.1002/acr.22545 *inappropriate study design*
267. Nalamachu S, Rauck R, Hale M, et al. A long-term, open-label safety study of single-entity hydrocodone bitartrate extended release for the treatment of moderate to severe chronic pain. *Journal of pain research* 2014; 7. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/077/CN-01036077/frame.html. *inappropriate intervention*
268. Navarrete-Navarrete N, Peralta-Ramirez MI, Sabio-Sanchez JM, et al. Efficacy of Cognitive Behavioural Therapy for the Treatment of Chronic Stress in Patients with Lupus Erythematosus: A Randomized Controlled Trial. *Psychotherapy and Psychosomatics* 2010;79(2):107-15. doi: 10.1159/000276370 *inappropriate population*
269. Nazareth I, Landau S, Yardley L, et al. Patterns of presentations of dizziness in primary care - a cross-sectional cluster analysis study. *Journal of psychosomatic*

research 2006;60(4):395-401. doi: 10.1016/j.jpsychores.2005.07.011 *inappropriate study design*

270. Niedermann K, de Bie RA, Kubli R, et al. Effectiveness of individual resource-oriented joint protection education in people with rheumatoid arthritis. A randomized controlled trial. *Patient education and counseling* 2011;82(1):42-48. doi: 10.1016/j.pec.2010.02.014 *inappropriate intervention*
271. Noiseux NO, Callaghan JJ, Clark CR, et al. Preoperative predictors of pain following total knee arthroplasty. *The Journal of arthroplasty* 2014;29(7):1383-7. doi: 10.1016/j.arth.2014.01.034 [published Online First: 2014/03/19] *inappropriate study design*
272. Noppers I, Niesters M, Swartjes M, et al. Absence of long-term analgesic effect from a short-term S-ketamine infusion on fibromyalgia pain: A randomized, prospective, double blind, active placebo-controlled trial. *European Journal of Pain* 2011;15(9):942-49. doi: 10.1016/j.ejpain.2011.03.008 *inappropriate intervention*
273. Nordeman L, Gunnarsson R, Mannerkorpi K. Prevalence and Characteristics of Widespread Pain in Female Primary Health Care Patients With Chronic Low Back Pain. *Clinical Journal of Pain* 2012;28(1):65-72. doi: 10.1097/AJP.0b013e318223622c *inappropriate population*
274. Nugraha B, Korallus C, Dorffer D, et al. Aerobic exercise cognitive behavioural therapy and combination of treatment in fibromyalgia syndrome patients: A randomized control trial (effect on mood related disorder-a preliminary result). *PM and R* 2014; 6(8 suppl. 2). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/639/CN-01086639/frame.html. *inappropriate study design*
275. Nyssen OP, Taylor SJC, Wong G, et al. Does therapeutic writing help people with long-term conditions? Systematic review, realist synthesis and economic considerations. *Health Technology Assessment* 2016;20(27):1-367. doi: 10.3310/hta20270 *inappropriate study design*
276. Ohta H, Oka H, Usui C, et al. A randomized, double-blind, multicenter, placebo-controlled phase III trial to evaluate the efficacy and safety of pregabalin in Japanese patients with fibromyalgia. *Arthritis research & therapy* 2012; 14(5). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/489/CN-00913489/frame.html. *inappropriate intervention*
277. Oktayoglu P, Gur A, Yardimeden I, et al. Comparison of the efficacy of phonophoresis and conventional ultrasound therapy in patients with primary knee osteoarthritis. *Erciyes Tip Dergisi* 2014; 36(1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/055/CN-00988055/frame.html. *inappropriate intervention*
278. Olin R, Klein R, Berg PA. A randomised double-blind 16-week study of ritanserin in fibromyalgia syndrome: clinical outcome and analysis of autoantibodies to serotonin, gangliosides and phospholipids. *Clinical rheumatology* 1998;17(2):89-94. [published Online First: 1998/06/26] *inappropriate intervention*
279. Olivan-Blázquez B, Herrera-Mercadal P, Puebla-Guedea M, et al. Efficacy of memantine in the treatment of fibromyalgia: A double-blind, randomised,

controlled trial with 6-month follow-up. *Pain* 2014;155(12):2517-25. doi: 10.1016/j.pain.2014.09.004 *inappropriate intervention*
280. O'Mathúna DP. Exercise Programs Help Reduce Anxiety in Patients with Chronic Illnesses. *Alternative Medicine Alert* 2010;13(4):43-44. *inappropriate study design*
281. O'Reilly SC, Muir KR, Doherty M. Effectiveness of home exercise on pain and disability from osteoarthritis of the knee: a randomised controlled trial. *Annals of the rheumatic diseases* 1999;58(1):15-19. *inappropriate population*
282. Oren YK. Effectiveness of Mindfulness-Based Stress Reduction Bibliotherapy [Ph.D.]. University of Nevada, Reno, 2015. *inappropriate intervention*
283. Osteras H, Osteras B, Torstensen TA. Is postoperative exercise therapy necessary in patients with degenerative meniscus? A randomized controlled trial with one year follow-up. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA* 2014;22(1):200-6. doi: 10.1007/s00167-012-2354-2 [published Online First: 2012/12/25] *inappropriate population*
284. Osteras H, Torstensen T, Selven E, et al. High dosage medical exercise therapy or arthroscopic treatment for patients with degenerative meniscus injury: A pilot study. *Physiotherapy (United Kingdom)* 2011; 97. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/742/CN-01102742/frame.html. *inappropriate population*
285. Ottaviani S, Bernard JL, Bardin T, et al. Effect of music on anxiety and pain during joint lavage for knee osteoarthritis. *Clinical rheumatology* 2012;31(3):531-4. doi: 10.1007/s10067-011-1925-9 [published Online First: 2011/12/31] *inappropriate intervention*
286. Packham JC, Jordan KP, Haywood KL, et al. Evaluation of Ankylosing Spondylitis Quality of Life questionnaire: responsiveness of a new patient-reported outcome measure. *Rheumatology (Oxford, England)* 2012;51(4):707-14. doi: 10.1093/rheumatology/ker377 [published Online First: 2011/12/20] *inappropriate population*
287. Pae C-U, Masand PS, Marks DM, et al. History of depressive and/or anxiety disorders as a predictor of treatment response: A post hoc analysis of a 12-week, randomized, double-blind, placebo-controlled trial of paroxetine controlled release in patients with fibromyalgia. *Progress in Neuro-Psychopharmacology & Biological Psychiatry* 2009;33(6):996-1002. doi: 10.1016/j.pnpbp.2009.05.005 *inappropriate intervention*
288. Papadopoulou D, Fassoulaki A, Tsoulas C, et al. A meta-analysis to determine the effect of pharmacological and non-pharmacological treatments on fibromyalgia symptoms comprising OMERACT-10 response criteria. *Clinical rheumatology* 2016;35(3):573-86. doi: 10.1007/s10067-015-3144-2 [published Online First: 2015/12/18] *inappropriate study design*
289. Passard A, Attal N, Benadhira R, et al. Effects of unilateral repetitive transcranial magnetic stimulation of the motor cortex on chronic widespread pain in fibromyalgia. *Brain: A Journal of Neurology* 2007;130(10):2661-70. doi: 10.1093/brain/awm189 *inappropriate intervention*
290. Pedersen BK, Saltin B. Exercise as medicine - evidence for prescribing exercise as therapy in 26 different chronic diseases. *Scandinavian Journal of Medicine &*

Science in Sports 2015;25:1-72. doi: 10.1111/sms.12581 *inappropriate study design*

291. Peres M. Fibromyalgia and headache disorders. *Current pain and headache reports* 2009; 13(5). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/879/CN-00958879/frame.html. *inappropriate study design*
292. Perrot S, Russell IJ. More ubiquitous effects from non-pharmacologic than from pharmacologic treatments for fibromyalgia syndrome: a meta-analysis examining six core symptoms. *European journal of pain (London, England)* 2014;18(8):1067-80. doi: 10.1002/ejp.564 [published Online First: 2014/08/21] *inappropriate study design*
293. Peters S, Stanley I, Rose M, et al. A randomized controlled trial of group aerobic exercise in primary care patients with persistent, unexplained physical symptoms. *Family Practice* 2002;19(6):665-74. doi: 10.1093/fampra/19.6.665 *inappropriate population*
294. Potvin S, Morin M, Cloutier C, et al. Add-on treatment of quetiapine for fibromyalgia: A pilot, randomized, double-blind, placebo-controlled 12-week trial. *Journal of Clinical Psychopharmacology* 2012;32(5):684-87. doi: 10.1097/JCP.0b013e318267b8ca *inappropriate intervention*
295. Preece JC. The relationship between family resilience and the successful management of fibromyalgia [Ph.D.]. Syracuse University, 2001. *inappropriate study design*
296. Rakel B, Zimmerman M, Geasland K, et al. Transcutaneous electrical nerve stimulation for the control of pain during rehabilitation after total knee arthroplasty: A randomized, blinded, placebo-controlled trial. *Pain* 2014; 155(12). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/744/CN-01052744/frame.html. *inappropriate intervention*
297. Redondo JR, Justo CM, Moraleda FV, et al. Long-term efficacy of therapy in patients with fibromyalgia: a physical exercise-based program and a cognitive-behavioral approach. *Arthritis and rheumatism* 2004;51(2):184-92. doi: 10.1002/art.20252 [published Online First: 2004/04/13] *inappropriate comparison group*
298. Richards DA, Hill JJ, Gask L, et al. Clinical effectiveness of collaborative care for depression in UK primary care (CADET): Cluster randomised controlled trial. *BMJ: British Medical Journal* 2013;347 *inappropriate population*
299. Rini C, Porter LS, Somers TJ, et al. Automated Internet-based pain coping skills training to manage osteoarthritis pain: a randomized controlled trial. *Pain* 2015;156(5):837-48. doi: 10.1097/j.pain.0000000000000121 [published Online First: 2015/03/04] *inappropriate intervention*
300. Rodriguez Huerta MD, Trujillo-Martin MM, Rua-Figueroa I, et al. Healthy lifestyle habits for patients with systemic lupus erythematosus: A systemic review. *Seminars in arthritis and rheumatism* 2016;45(4):463-70. doi: 10.1016/j.semarthrit.2015.09.003 [published Online First: 2015/11/03] *inappropriate population*
301. Rodriguez Torres J, Cabrera Martos I, Torres Sanchez I, et al. Results of an Active Neurodynamic Mobilization Program in Patients With Fibromyalgia

Syndrome: A Randomized Controlled Trial. *Archives of Physical Medicine & Rehabilitation* 2015;96(10):1771-78. *inappropriate intervention*

302. Romero-Zurita A, Carbonell-Baeza A, Aparicio VA, et al. Effectiveness of a Tai-Chi Training and Detraining on Functional Capacity, Symptomatology and Psychological Outcomes in Women with Fibromyalgia. *Evidence-Based Complementary and Alternative Medicine* 2012 doi: 10.1155/2012/614196 *inappropriate intervention*
303. Rouse P, Duda J, Veldhuijzen VZJ, et al. Feelings of competence and relatedness during physical activity are related to well-being in rheumatoid arthritis patients: Preliminary findings from a randomized control trial. *Annals of the rheumatic diseases* 2013; 72. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/540/CN-01062540/frame.html. *inappropriate study design*
304. Rouse PC, Van Zanten J, Ntoumanis N, et al. Measuring the positive psychological wellbeing of people with rheumatoid arthritis: a cross-sectional validation of the subjective vitality scale. *Arthritis research & therapy* 2015;17 doi: 10.1186/s13075-015-0827-7 *inappropriate study design*
305. Russek LN, LaShomb EA, Ware AM, et al. United States Physical Therapists' Knowledge About Joint Hypermobility Syndrome Compared with Fibromyalgia and Rheumatoid Arthritis. *Physiotherapy research international : the journal for researchers and clinicians in physical therapy* 2016;21(1):22-35. doi: 10.1002/pri.1613 [published Online First: 2014/12/17] *inappropriate study design*
306. Russell IJ, Holman AJ, Swick TJ, et al. Sodium oxybate reduces pain, fatigue, and sleep disturbance and improves functionality in fibromyalgia: results from a 14-week, randomized, double-blind, placebo-controlled study. *Pain* 2011;152(5):1007-17. doi: 10.1016/j.pain.2010.12.022 [published Online First: 2011/03/15] *inappropriate intervention*
307. Rybarczyk B, DeMarco G, DelaCruz M, et al. Comparing mind-body wellness interventions for older adults with chronic illness: Classroom versus home instruction. *Behavioral Medicine* 1999;24(4):181-90. *inappropriate intervention*
308. Sancheti P, Hardikar M, Karne N, et al. A multicentric, randomized, comparative clinical trial to evaluate the efficacy and safety of S-etodolac in the treatment of osteoarthritis in Indian patients. *International journal of clinical pharmacology and therapeutics* 2010;48(7):429-34. [published Online First: 2010/06/19] *inappropriate intervention*
309. Schanberg LE, Anthony KK, Gil KM, et al. Daily pain and symptoms in children with polyarticular arthritis. *Arthritis and rheumatism* 2003;48(5):1390-7. doi: 10.1002/art.10986 [published Online First: 2003/05/15] *inappropriate population*
310. Scheidt CE, Waller E, Endorf K, et al. Is brief psychodynamic psychotherapy in primary fibromyalgia syndrome with concurrent depression an effective treatment? A randomized controlled trial. *General Hospital Psychiatry* 2013;35(2):160-67. doi: 10.1016/j.genhosppsych.2012.10.013 *inappropriate intervention*
311. Schmale GA, Mazor S, Mercer LD, et al. Lack of Benefit of Physical Therapy on Function Following Supracondylar Humeral Fracture A Randomized Controlled

Trial. *Journal of Bone and Joint Surgery-American Volume* 2014;96A(11):944-50. doi: 10.2106/jbjs.l.01696 *inappropriate population*

312. Schmidt S, Grossman P, Schwarzer B, et al. Treating fibromyalgia with mindfulness-based stress reduction: results from a 3-armed randomized controlled trial. *Pain* 2011;152(2):361-9. doi: 10.1016/j.pain.2010.10.043 [published Online First: 2010/12/15] *inappropriate intervention*
313. Scopaz KA, Piva SR, Wisniewski S, et al. Relationships of Fear, Anxiety, and Depression With Physical Function in Patients With Knee Osteoarthritis. *Archives of physical medicine and rehabilitation* 2009;90(11):1866-73. doi: 10.1016/j.apmr.2009.06.012 *inappropriate study design*
314. Selfridge N. Meditation for Fibromyalgia: Yea or Nay? *Alternative Medicine Alert* 2011;14(3):34-36. *inappropriate intervention*
315. Shadick NA, Sowell NF, Frits ML, et al. A randomized controlled trial of an internal family systems-based psychotherapeutic intervention on outcomes in rheumatoid arthritis: a proof-of-concept study. *The Journal of rheumatology* 2013;40(11):1831-41. doi: 10.3899/jrheum.121465 [published Online First: 2013/08/21] *inappropriate intervention*
316. Shahabi L, Naliboff BD, Shapiro D. Self-regulation evaluation of therapeutic yoga and walking for patients with irritable bowel syndrome: a pilot study. *Psychology Health & Medicine* 2016;21(2):176-88. doi: 10.1080/13548506.2015.1051557 *inappropriate population*
317. Shahrbanian S, Duquette P, Kuspinar A, et al. Contribution of symptom clusters to multiple sclerosis consequences. *Quality of Life Research* 2015;24(3):617-29. doi: 10.1007/s11136-014-0804-7 *inappropriate population*
318. Sharpe L, Gittins CB, Correia HM, et al. Problem-solving versus cognitive restructuring of medically ill seniors with depression (PROMISE-D trial): study protocol and design. *Bmc Psychiatry* 2012;12 doi: 10.1186/1471-244x-12-207 *inappropriate study design*
319. Sharpe L, Sensky T, Allard S. The course of depression in recent onset rheumatoid arthritis: the predictive role of disability, illness perceptions, pain and coping. *Journal of psychosomatic research* 2001;51(6):713-9. [published Online First: 2001/12/26] *inappropriate study design*
320. Sharpe L, Sensky T, Timberlake N, et al. Long-term efficacy of a cognitive behavioural treatment from a randomized controlled trial for patients recently diagnosed with rheumatoid arthritis. *Rheumatology (Oxford, England)* 2003; 42(3). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/463/CN-00431463/frame.html. *inappropriate intervention*
321. Sharpe L, Sensky T, Timberlake N, et al. A blind, randomized, controlled trial of cognitive-behavioural intervention for patients with recent onset rheumatoid arthritis: preventing psychological and physical morbidity. *Pain* 2001; 89(2-3). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/279/CN-00327279/frame.html. *inappropriate intervention*
322. Shih M, Hootman JM, Kruger J, et al. Physical activity in men and women with arthritis - National Health Interview Survey, 2002. *American Journal of Preventive Medicine* 2006;30(5):385-93. doi: 10.1016/j.amepre.2005.12.005 *inappropriate intervention*

323. Shupak NM, McKay JC, Nielson WR, et al. Exposure to a specific pulsed low-frequency magnetic field: A double-blind placebo-controlled study of effects on pain ratings in rheumatoid arthritis and fibromyalgia patients. *Pain Research & Management* 2006;11(2):85-90. doi: 10.1155/2006/842162 *inappropriate intervention*
324. Siegel KM. The effects of emotional disclosure on physical symptoms, healthcare utilization, and psychosocial adjustment in patients with irritable bowel syndrome [Ph.D.]. Alliant International University, San Diego, 2003. *inappropriate population*
325. Skrabek RQ, Galimova L, Ethans K, et al. Nabilone for the treatment of pain in fibromyalgia. *The journal of pain : official journal of the American Pain Society* 2008;9(2):164-73. doi: 10.1016/j.jpain.2007.09.002 [published Online First: 2007/11/03] *inappropriate intervention*
326. Slavich GM, Irwin MR. From Stress to Inflammation and Major Depressive Disorder: A Social Signal Transduction Theory of Depression. *Psychological Bulletin* 2014;140(3):774-815. doi: 10.1037/a0035302 *inappropriate study design*
327. Smeets RJ, Maher CG, Nicholas MK, et al. Do psychological characteristics predict response to exercise and advice for subacute low back pain? *Arthritis and rheumatism* 2009;61(9):1202-9. doi: 10.1002/art.24731 [published Online First: 2009/08/29] *inappropriate study design*
328. Smith-Ray R, Fitzgibbon M, Tussing-Humphreys L, et al. Fit and Strong! Plus: Design of a comparative effectiveness evaluation of a weight management program for older adults with osteoarthritis. *Contemporary clinical trials* 2014; 37(2). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/212/CN-00959212/frame.html. *inappropriate study design*
329. Sörensen J, Bengtsson A, Ahlner J, et al. Fibromyalgia--are there different mechanisms in the processing of pain? A double blind crossover comparison of analgesic drugs. *The Journal of rheumatology* 1997; 24(8). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/709/CN-00142709/frame.html. *inappropriate intervention*
330. Stehlik R, Ulfberg J, Hedner J, et al. High prevalence of restless legs syndrome among women with multi-site pain: A population-based study in Dalarna, Sweden. *European Journal of Pain* 2014;18(10):1402-09. doi: 10.1002/ejp.504 *inappropriate outcomes*
331. Stiller C. The effect of therapeutic touch on fibromyalgia pain and anxiety [Ph.D.]. Case Western Reserve University (Health Sciences), 2006. *inappropriate intervention*
332. Stratz T, Mennet P, Benn H, et al. [Blocking of S2 receptors--a new treatment principle in generalized tendomyopathy (fibromyalgia)?]. *Zeitschrift fur Rheumatologie* 1991; 50(1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/788/CN-00353788/frame.html. *inappropriate intervention*
333. Sulenes K, Freitas J, Justice L, et al. Underuse of Yoga as a Referral Resource by Health Professions Students. *Journal of Alternative and Complementary Medicine* 2015;21(1):53-59. doi: 10.1089/acm.2014.0217 *inappropriate intervention*

334. Sutbeyaz S, Sezer N, Koseoglu F, et al. Low-frequency pulsed electromagnetic field therapy in fibromyalgia: a randomized, double-blind, sham-controlled clinical study. *The Clinical journal of pain* 2009; 25(8). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/605/CN-00728605/frame.html. *inappropriate intervention*
335. Sverdrup B. Use less cosmetics--suffer less from fibromyalgia? *Journal of women's health (2002)* 2004; 13(2). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/706/CN-00468706/frame.html. *inappropriate intervention*
336. Tang NK, Lereya ST, Boulton H, et al. Nonpharmacological Treatments of Insomnia for Long-Term Painful Conditions: A Systematic Review and Meta-analysis of Patient-Reported Outcomes in Randomized Controlled Trials. *Sleep* 2015;38(11):1751-64. doi: 10.5665/sleep.5158 [published Online First: 2015/04/24] *inappropriate study design*
337. Tang NKY, Goodchild CE, Salkovskis PM. Hybrid cognitive-behaviour therapy for individuals with insomnia and chronic pain: A pilot randomised controlled trial. *Behaviour Research and Therapy* 2012;50(12):814-21. doi: 10.1016/j.brat.2012.08.006 *inappropriate population*
338. Tarakci E, Yeldan I, Kaya Mutlu E, et al. The relationship between physical activity level, anxiety, depression, and functional ability in children and adolescents with juvenile idiopathic arthritis. *Clinical rheumatology* 2011;30(11):1415-20. doi: 10.1007/s10067-011-1832-0 [published Online First: 2011/09/03] *inappropriate population*
339. Teunis T, Thornton ER, Guitton TG, et al. Coaching of patients with an isolated minimally displaced fracture of the radial head immediately increases range of motion. *Journal of Hand Therapy* 2016;29(3):314-19. doi: 10.1016/j.jht.2016.02.003 *inappropriate population*
340. Thomas K, Muir K, Doherty M, et al. Home based exercise programme for knee pain and knee osteoarthritis: randomised controlled trial. *BMJ (Clinical research ed)* 2002; 325(7367). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/283/CN-00398283/frame.html. *inappropriate population*
341. Tonkins WP, Jr. Effect of Hatha yoga on selected parameters of cardiac fitness in African-American college students [Dr.P.H.]. Morgan State University, 2004. *inappropriate intervention*
342. Torres JR, Martos IC, Sanchez IT, et al. Results of an Active Neurodynamic Mobilization Program in Patients With Fibromyalgia Syndrome: A Randomized Controlled Trial. *Archives of physical medicine and rehabilitation* 2015;96(10):1771-8. doi: 10.1016/j.apmr.2015.06.008 [published Online First: 2015/07/06] *inappropriate intervention*
343. Torres X, Herrero MJ, Marti M, et al. Why people with fibromyalgia persist in activity despite the increasing pain? A Delphi Study of the content of the Clinic Scale of Persistence in Activity in Fibromyalgia. *Revista De Psiquiatria Y Salud Mental* 2013;6(1):33-44. doi: 10.1016/j.rpsm.2012.03.001 *inappropriate study design*

344. Toth C, Brady S, Gagnon F, et al. A Randomized, Single-Blind, Controlled, Parallel Assignment Study of Exercise Versus Education as Adjuvant in the Treatment of Peripheral Neuropathic Pain. *Clinical Journal of Pain* 2014;30(2):111-18. doi: 10.1097/AJP.0b013e31828ccd0f *inappropriate population*
345. Tousignant-Laflamme Y, Bourgault P, Masetto A, et al. Short term impact of brief education for symptom management in fibromyalgia-the PEGASO study. *Journal of pain* 2014; 15(4 suppl. 1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/679/CN-01058679/frame.html. *inappropriate intervention*
346. Trudeau KJ, Pujol LA, DasMahapatra P, et al. A randomized controlled trial of an online self-management program for adults with arthritis pain. *Journal of Behavioral Medicine* 2015;38(3):483-96. doi: 10.1007/s10865-015-9622-9 *inappropriate intervention*
347. Uceyler N, Hauser W, Sommer C. A systematic review on the effectiveness of treatment with antidepressants in fibromyalgia syndrome. *Arthritis Care and Research* 2008; 59(9). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/590/CN-00898590/frame.html. *inappropriate study design*
348. Ulus Y, Tander B, Akyol Y, et al. Therapeutic ultrasound versus sham ultrasound for the management of patients with knee osteoarthritis: a randomized double-blind controlled clinical study. *International journal of rheumatic diseases* 2012; 15(2). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/676/CN-00896676/frame.html. *inappropriate intervention*
349. Vaghef-Mehrabany E, Alipour B, Homayouni-Rad A, et al. Probiotic supplementation improves inflammatory status in patients with rheumatoid arthritis. *Nutrition* 2014;30(4):430-35. doi: 10.1016/j.nut.2013.09.007 *inappropriate intervention*
350. Vaghef-Mehrabany E, Homayouni-Rad A, Alipour B, et al. Effects of Probiotic Supplementation on Oxidative Stress Indices in Women with Rheumatoid Arthritis: A Randomized Double-Blind Clinical Trial. *Journal of the American College of Nutrition* 2016;35(4):291-99. *inappropriate intervention*
351. Valencia M, Alonso B, Alvarez M, et al. Effects of 2 physiotherapy programs on pain perception, muscular flexibility, and illness impact in women with fibromyalgia: a pilot study. *Journal of manipulative and physiological therapeutics* 2009; 32(1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/935/CN-00680935/frame.html. *inappropriate comparison group*
352. Valim V, Oliveira L, Suda A, et al. Aerobic fitness effects in fibromyalgia. *The Journal of rheumatology* 2003;30(5):1060-9. [published Online First: 2003/05/08] *inappropriate intervention*
353. Vallejo MA, Ortega J, Rivera J, et al. Internet versus face-to-face group cognitive-behavioral therapy for fibromyalgia: A randomized control trial. *Journal of Psychiatric Research* 2015;68:106-13. doi: 10.1016/j.jpsychires.2015.06.006 *inappropriate intervention*
354. van Koulil S, Kraaimaat FW, van Lankveld W, et al. A patient's perspective on multidisciplinary treatment gain for fibromyalgia: an indicator for pre-post

treatment effects? *Arthritis and rheumatism* 2009;61(12):1626-32. doi: 10.1002/art.24792 [published Online First: 2009/12/02] *inappropriate study design*

355. van Koulil S, van Lankveld W, Kraaimaat FW, et al. Tailored cognitive-behavioral therapy and exercise training for high-risk patients with fibromyalgia. *Arthritis care & research* 2010;62(10):1377-85. doi: 10.1002/acr.20268 [published Online First: 2010/06/04] *inappropriate intervention*
356. Van Puymbroeck M, Payne LL, Hsieh PC. A phase I feasibility study of yoga on the physical health and coping of informal caregivers. *Evidence-Based Complementary and Alternative Medicine* 2007;4(4):519-29. doi: 10.1093/ecam/nem075 *inappropriate population*
357. van Wilgen CP, Dijkstra PU, Versteegen GJ, et al. CHRONIC PAIN AND SEVERE DISUSE SYNDROME: LONG-TERM OUTCOME OF AN INPATIENT MULTIDISCIPLINARY COGNITIVE BEHAVIOURAL PROGRAMME. *Journal of rehabilitation medicine* 2009;41(3):122-28. doi: 10.2340/16501977-0292 *inappropriate intervention*
358. Vayvay ES, Tok D, Turgut E, et al. The effect of Laser and taping on pain, functional status and quality of life in patients with fibromyalgia syndrome: A placebo- randomized controlled clinical trial. *Journal of back and musculoskeletal rehabilitation* 2016;29(1):77-83. doi: 10.3233/bmr-150600 [published Online First: 2015/09/26] *inappropriate intervention*
359. Vendrig AA, Lousberg R. Within-person relationships among pain intensity, mood and physical activity in chronic pain: a naturalistic approach. *Pain* 1997;73(1):71-76. doi: 10.1016/s0304-3959(97)00075-4 *inappropriate intervention*
360. Vergne-Salle P, Dufauret-Lombard C, Bonnet C, et al. A randomised, double-blind, placebo-controlled trial of dolasetron, a 5-hydroxytryptamine 3 receptor antagonist, in patients with fibromyalgia. *European Journal of Pain* 2011;15(5):509-14. doi: 10.1016/j.ejpain.2010.09.013 *inappropriate intervention*
361. Verra ML, Angst F, Beck T, et al. Horticultural therapy for patients with chronic musculoskeletal pain: results of a pilot study. *Alternative therapies in health and medicine* 2012;18(2):44-50. [published Online First: 2012/04/21] *inappropriate study design*
362. Verra ML, Angst F, Brioschi R, et al. Does classification of persons with fibromyalgia into Multidimensional Pain Inventory subgroups detect differences in outcome after a standard chronic pain management program? *Pain Research & Management* 2009;14(6):445-53. *inappropriate study design*
363. Verra ML, Angst F, Staal JB, et al. Differences in pain, function and coping in Multidimensional Pain Inventory subgroups of chronic back pain: a one-group pretest-posttest study. *BMC musculoskeletal disorders* 2011;12 doi: 10.1186/1471-2474-12-145 *inappropriate study design*
364. VillafaÑE JH, Cleland JA, FernÁNdez-De-Las-PeÑAs C. The Effectiveness of a Manual Therapy and Exercise Protocol in Patients With Thumb Carpometacarpal Osteoarthritis: A Randomized Controlled Trial. *Journal of Orthopaedic & Sports Physical Therapy* 2013;43(4):204-13. *inappropriate intervention*
365. Villafañe JH, Silva GB, Bishop MD, et al. Radial Nerve Mobilization Decreases Pain Sensitivity and Improves Motor Performance in Patients With Thumb

Carpometacarpal Osteoarthritis: A Randomized Controlled Trial. *Archives of Physical Medicine & Rehabilitation* 2012;93(3):396-403. *inappropriate intervention*

366. Villanueva-Torrecillas I. Affectivity, quality of life and health resources utilization in arthritis [Ph.D.]. The University of Arizona, 2003. *inappropriate outcomes*
367. Vincent KR, Vincent HK. Resistance exercise for knee osteoarthritis. *PM & R : the journal of injury, function, and rehabilitation* 2012;4(5 Suppl):S45-52. doi: 10.1016/j.pmrj.2012.01.019 [published Online First: 2012/06/01] *inappropriate study design*
368. Vriezekolk JE, Eijsbouts AMM, van Lankveld WGJM, et al. An acceptance-oriented cognitive-behavioral therapy in multimodal rehabilitation: A pre-post test evaluation in highly distressed patients with rheumatic diseases. *Patient education and counseling* 2013;91(3):357-63. doi: 10.1016/j.pec.2013.01.018 *inappropriate study design*
369. Wang C, Schmid CH, Hibberd PL, et al. Tai Chi for treating knee osteoarthritis: designing a long-term follow up randomized controlled trial. *BMC musculoskeletal disorders* 2008;9:108. doi: 10.1186/1471-2474-9-108 [published Online First: 2008/07/31] *inappropriate intervention*
370. Wang CC. Tai Chi and Rheumatic Diseases. *Rheumatic Disease Clinics of North America* 2011;37(1):19-+. doi: 10.1016/j.rdc.2010.11.002 *inappropriate study design*
371. Wang CC. Role of Tai Chi in the Treatment of Rheumatologic Diseases. *Current Rheumatology Reports* 2012;14(6):598-603. doi: 10.1007/s11926-012-0294-y *inappropriate study design*
372. Wang WR, Lopez V, Chow A, et al. A randomized controlled trial of the effectiveness of a self-help psychoeducation programme on outcomes of outpatients with coronary heart disease: study protocol. *Journal of Advanced Nursing* 2014;70(12):2932-41. doi: 10.1111/jan.12397 *inappropriate population*
373. Wepner F, Scheuer R, Schuetz-Wieser B, et al. Effects of vitamin D on patients with fibromyalgia syndrome: a randomized placebo-controlled trial. *Pain* 2014;155(2):261-8. doi: 10.1016/j.pain.2013.10.002 [published Online First: 2014/01/21] *inappropriate intervention*
374. Weze C, Leathard HL, Stevens G. Evaluation of Healing by Gentle Touch for the Treatment of Musculoskeletal Disorders. *American Journal of Public Health* 2004;94(1):50-52. doi: 10.2105/AJPH.94.1.50 *inappropriate intervention*
375. Wicksell RK, Kemani M, Jensen K, et al. Acceptance and commitment therapy for fibromyalgia: A randomized controlled trial. *European Journal of Pain* 2013;17(4):599-611. doi: 10.1002/j.1532-2149.2012.00224.x *inappropriate intervention*
376. Williams DA, Kuper D, Segar M, et al. Internet-enhanced management of fibromyalgia: a randomized controlled trial. *Pain* 2010;151(3):694-702. doi: 10.1016/j.pain.2010.08.034 [published Online First: 2010/09/22] *inappropriate intervention*
377. Witjes S, Hoorntje A, Kuijer P, et al. Does Goal Attainment Scaling improve satisfaction regarding performance of activities of younger knee arthroplasty patients? Study protocol of the randomized controlled ACTION trial. *BMC*

musculoskeletal disorders 2016;17 doi: 10.1186/s12891-016-0965-3 *inappropriate study design*

378. Wylde V, Artz N, Marques E, et al. Effectiveness and cost-effectiveness of outpatient physiotherapy after knee replacement for osteoarthritis: study protocol for a randomised controlled trial. *Trials* 2016;17(1):289. doi: 10.1186/s13063-016-1418-x [published Online First: 2016/06/15] *inappropriate study design*
379. Yang T, Wang H, Chen Y, et al. Effect of continuous administration of conjugated estrogen plus medroxyprogesterone acetate (Premelle) in postmenopausal women in Taiwan. *Journal of the Chinese Medical Association : JCMA* 2004; 67(7). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/366/CN-00505366/frame.html. *inappropriate intervention*
380. Yelland MJ, Schluter PJ. Defining Worthwhile and Desired Responses to Treatment of Chronic Low Back Pain. *Pain Medicine* 2006;7(1):38-45. doi: 10.1111/j.1526-4637.2006.00087.x *inappropriate population*
381. Young JL. Use of lisdexamfetamine dimesylate in treatment of executive functioning deficits and chronic fatigue syndrome: A double blind, placebo-controlled study. *Psychiatry Research* 2013;207(1-2):127-33. doi: 10.1016/j.psychres.2012.09.007 *inappropriate intervention*
382. Yuan SLK, Matsutani LA, Marques AP. Effectiveness of different styles of massage therapy in fibromyalgia: A systematic review and meta-analysis. *Manual therapy* 2015;20(2):257-64. *inappropriate study design*
383. Yuen AWC, Sander JW. Can slow breathing exercises improve seizure control in people with refractory epilepsy? A hypothesis. *Epilepsy & Behavior* 2010;18(4):331-34. doi: 10.1016/j.yebeh.2010.05.019 *inappropriate population*
384. Zick SM, Wyatt GK, Murphy SL, et al. Acupressure for persistent cancer-related fatigue in breast cancer survivors (AcuCrft): a study protocol for a randomized controlled trial. *BMC Complementary and Alternative Medicine* 2012;12 doi: 10.1186/1472-6882-12-132 *inappropriate population*
385. Zietek P, Zietek J, Szczypior K, et al. Effect of adding one 15-minute-walk on the day of surgery to fast-track rehabilitation after total knee arthroplasty: a randomized, single-blind study. *European journal of physical and rehabilitation medicine* 2015;51(3):245-52. [published Online First: 2014/09/19] *inappropriate intervention*

Supplementary File 3. Study-level risk of bias results using the Cochrane Collaboration Instrument.

Reference	Random Sequence	Allocation Concealment	Blinding (Participants & Personnel)	Blinding (Outcome Assessors)	Incomplete Outcome Data	Selective Reporting	Inactive
Baptista et al., 2012[40]	low	low	high	low	low	low	unclear
Beltran, 2003[41]	low	unclear	high	unclear	low	unclear	low
Cheung et al., 2017 [42]	low	high	high	unclear	low	low	unclear
Fransen et al., 2007[43]	low	unclear	high	low	low	low	low
French et al., 2013[44]	low	low	high	high	low	unclear	unclear
Gowans et al., 2001[45]	low	unclear	high	low	low	unclear	unclear
Jones et al., 2008[46]	low	unclear	high	unclear	low	unclear	low
Komatireddy et al.[47]	low	unclear	high	low	low	unclear	unclear
Minor et al., 1989[48]	low	unclear	high	unclear	unclear	unclear	low
Munguia-Izquieerdo & Legaz-Arrese, 2008[49]	low	unclear	high	low	low	unclear	low
Sanudo et al., 2015[50]	low	unclear	high	unclear	unclear	unclear	unclear
Schachter et al., 2003[51]	high	high	high	unclear	low	unclear	low
Tomas-Carus et al., 2008[52]	low	low	high	low	low	unclear	low
Tomas-Carus et al., 2007[53]	low	unclear	high	unclear	unclear	unclear	low

Notes: low, low risk of bias; high, high risk of bias; unclear, unclear risk of bias.

Supplementary file 4. Simple meta-regression results with changes in anxiety as the outcome.

Comparison	ES (#)	R	R^2	F(p)
Study Characteristics				
- Journal impact factor	16	.22	.05	0.4(0.52)
- Year of publication	**16**	**.75**	**.56**	**51.5(<0.001)***
- Country study conducted (USA vs. other)	16	.13	.02	0.2(0.69)
- Type of control (exposure vs. no exposure)[a]	16	.08	.02	0.01(0.76)
- Matching (yes vs. no)	16	.39	.15	1.2(0.29)
- Random sequencing (high/unclear vs. low)	16	.05	.0003	0.17(0.69)
- Allocation concealment (high/unclear vs. low)	16	.22	.05	0.87(0.37)
- Blinding of participants & personnel (high/unclear vs. low)[b]	NA	NA	NA	NA
- Blinding of outcome assessors (high/unclear vs low)	16	.08	.007	0.43(0.66)
- Incomplete outcome data (high/unclear vs low)	**16**	**.67**	**.45**	**14.4(0.002)***
- Selective reporting (Unclear vs low)	16	.39	.15	4.1(0.06)
- Participants physically inactive (high/unclear vs low)	16	.21	.04	0.75(0.40)
- Sample size estimates provided (no versus yes)	**16**	**.56**	**.32**	**4.6(0.05)***
- Agreed to participate in study (%)	**12**	**.47**	**.22**	**4.9(0.05)***
- Study funded (no versus yes)	**16**	**.34**	**.12**	**15.9(0.001)***
- Type of analysis (abp vs itt)[c]	19	.21	.05	0.89(0.36)
- Test used (STAI and FIQ vs. AIMS)[d,e]	19	.41	.17	2.3(0.14)
Participant Characteristics				
- Exercise dropouts (%)	**15**	**.34**	**.12**	**8.2(0.01)***
- Control dropouts (%)	13	.31	.10	1.3(0.27)
- Age (years)	**14**	**.53**	**.28**	**11.9(.005)***
- Gender (mixed vs. females)	16	.14	.02	.38(0.54)
- AORD (rheumatoid/osteoarthritis vs. fibromyalgia)	16	.10	.01	.15(0.71)
- Rheumatic symptoms (years)	8	.37	.14	1.45(0.27)
- Years since diagnosis	4	.23	.05	.33(0.62)

Exercise Intervention Characteristics				
Exercise modality (aerobic/weight training vs. both)	**16**	**.57**	**.32**	**8.19(0.01)***
Land vs. water-based exercise	16	.30	.09	1.03(0.33)
Length of training (weeks)	16	.16	.51	.44(0.52)
Frequency of training (times/week)	14	.02	.0004	.01(0.92)
Duration of training (min/session)	**12**	**.43**	**.18**	**7.7(0.02)***
Compliance (% of exercise sessions attended)	8	.04	.001	.02(0.90)
Minutes of training per week	**11**	**.61**	**.37**	**33.1(.0003)***
Minutes of training per week (adjusted for compliance)	7	.17	.03	.19(0.68)
Total minutes of training	**11**	**.63**	**.40**	**15.0(0.004)***
Total minutes of training (adjusted for compliance)	7	.22	0.05	0.32(0.60)
Supervision status (unsupervised or supervised vs. both)	**16**	**.49**	**0.24**	**4.20(0.04)***
Location of exercise (facility or home vs both)	**16**	**.49**	**0.24**	**4.20(0.04)***
Participation (group or self vs. both)	**16**	**.49**	**0.24**	**4.20(0.04)***
Adverse events (yes vs. no)	5	.23	.05	.17(0.71)

Notes: abp, analysis-by-protocol; itt, intention-to-treat; STAI, State-Trait Anxiety Inventory; FIQ, Fibromyalgia Impact Questionnaire; AIMS, Arthritis Impact Measurement Scale; [a,] Exposure, includes attention control, usual care and other types of exposure while no exposure, includes nonintervention and wait-list controls; [b], NA, not applicable because all studies considered at high risk of bias given the inability to blind participants to exercise interventions;[c,]number of groups exceed 16 because two studies reported results for both abp and itt analysis; [d,] insufficient number of outcomes to include the DASS, HADS, MHI and VAS; [e,] number of groups exceed 16 because three studies reported anxiety results using two different instruments.

Author(s): What are the effects of exercise (aerobic, strength training, or both) on anxiety in adults with arthritis and other rheumatic diseases?

Date: July 3, 2017

Question: Exercise compared to control for reducing anxiety in adults with arthritis and other rheumatic diseases

Setting: Home, Facility, Both

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise	control	Relative (95% CI)	Absolute (95% CI)		
Anxiety (follow up: mean 15.8 weeks; assessed with: Various self-report instruments)												
14	randomized trials	not serious	not serious	not serious	not serious	publication bias strongly suspected all plausible residual confounding would reduce the demonstrated effect [a]	514	369	not estimable -	SMD **0.4 SD lower** (0.65 lower to 0.15 lower)	⨁⨁⨁⨁ HIGH	CRITICAL

CI: Confidence interval; **SMD:** Standardized mean difference

Explanations

a. Statistically significant small-study effects, suggesting the possibility of publication bias; possible confounding by year of publication, with the magnitude of effect over time smaller with more recent studies.

176x131mm (300 x 300 DPI)

PRISMA Checklist

Section/topic	#	Checklist item	Reported on line #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1-3
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	23-49
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	62-103
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	104-107
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	48-49; 112-113; 714-718
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	114-166
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	167-175
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary file 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	182-202
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	203-217
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	204-211; 218-222
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	223-239
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	241-255

PRISMA Checklist

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	256-283

Section/topic	#	Checklist item	Reported on line #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	321-326
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	283-320; 327-336
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	346-357; Figure 1; Supplementary file 2
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	358-422; Tables 1-3
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Supplementary file 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figure 3
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Table 4; 432-450; 473-587
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	423-430; Figure 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	451-472
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	588-687
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	688-701
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	702-705

PRISMA Checklist

FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	721-724

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

BMJ Open

Community-Deliverable Exercise and Anxiety in Adults with Arthritis and other Rheumatic Diseases: A Systematic Review with Meta-Analysis of Randomized Controlled Trials

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-019138.R1
Article Type:	Research
Date Submitted by the Author:	03-Nov-2017
Complete List of Authors:	Kelley, George; West Virginia University, Biostatistics Kelley, Kristi; West Virginia University, Biostatistics Callahan, Leigh F; Thurston Arthritis Research Center, Department of Medicine
Primary Subject Heading:	Public health
Secondary Subject Heading:	Sports and exercise medicine, Evidence based practice
Keywords:	exercise, anxiety, arthritis, systematic review, meta-analysis

Community-Deliverable Exercise and Anxiety in Adults with Arthritis and other Rheumatic Diseases: A Systematic Review with Meta-Analysis of Randomized Controlled Trials

Authors: Corresponding author: *George A. Kelley*, DA, FACSM, School of Public Health, Department of Biostatistics, West Virginia University, Morgantown, WV, USA, 26506-9190, Office Phone: 304-293-6279, Fax: 304-293-5891,E-mail: gkelley@hsc.wvu.edu

Co-author: *Kristi S. Kelley*, M.Ed., Research Instructor, School of Public Health, Department of Biostatistics, Robert C. Byrd Health Sciences Center, West Virginia University, PO Box 9190, Morgantown, WV, USA, 26506-9190, Office Phone: 304-293-6280, Fax: 304-293-5891, E-mail: kskelley@hsc.wvu.edu

Co-author: *Leigh F. Callahan*, PhD, Mary Link Briggs Distinguished Professor of Medicine, Professor, Departments of Social Medicine and Orthopaedics, Adjunct Professor, Department of Epidemiology, 3300 Thurston Bldg, Campus Box 7280, University of North Carolina, Chapel Hill, NC 27599-7280, Office Phone: 919-966-0564, E-mail: leigh callahan@med.unc.edu

Keywords: exercise, anxiety, arthritis, systematic review, meta-analysis.

Abstract: 300 words

Introduction, Methods, Results, Conclusions: 8,632 words

ABSTRACT

Background/Purpose: Given conflicting findings, the purpose of this study was to use the meta-analytic approach to examine the effects of exercise (aerobic, strength training or both) on anxiety in adults with arthritis and other rheumatic diseases (AORD).

Methods: Randomized controlled exercise intervention trials ≥ 4 weeks in adults ≥ 18 years of age with osteoarthritis, rheumatoid arthritis or fibromyalgia were included. Studies were located by searching 8 electronic databases, cross-referencing and expert review. Dual selection and data abstraction of studies were performed. Hedge's standardized effect size (ES) was calculated for each result and pooled using the recently developed inverse-heterogeneity (IVhet) model. Two-tailed *z*-alpha values ≤ 0.05 and non-overlapping 95% confidence intervals (CI) were considered statistically significant. Heterogeneity was estimated using Q and I^2 with alpha values ≤ 0.10 for Q considered statistically significant. Small-study effects were examined using funnel plots and Egger's regression test. In addition, the number-needed-to-treat (NNT), percentile improvement and meta-regression were conducted. **Results:** Of the 639 citations screened, 14 studies representing 926 initially enrolled participants (539 exercise, 387 control) met the criteria for inclusion. Length of training averaged 15.8 ± 6.7 weeks, frequency 3.3 ± 1.3 times per week and duration 28.8 ± 14.3 minutes per session. Overall, statistically significant in reductions in anxiety were found (exercise minus control changes ES = -0.40, 95% CI, -0.65, -0.15, tau^2 = 0.14; Q = 40.3, p = 0.0004; I^2 = 62.8%). The NNT was 6 with a percentile improvement of 15.5% and an estimated 5.3 million inactive US adults with AORD improving their anxiety if they started exercising regularly. Statistically significant small-study effects were observed (p

< 0.0001). **Conclusions:** Exercise is associated with reductions in anxiety among adults with selected types of AORD. However, a need exists for additional, well-designed, randomized controlled trials on this topic. **Trial registration number:** PROSPERO (CRD42016048728)

STRENGTHS AND LIMITATIONS OF THIS STUDY

- To the best of the investigative team's knowledge, this is the first systematic review with meta-analysis to examine the effects of exercise on anxiety as a primary outcome in adults with AORD.
- The use of the recently developed IVhet model appears to provide more robust estimates than those derived from other models.
- Common to all aggregate data meta-analyses, the possibility of ecological fallacy exists and the meta-regression analyses conducted do not allow for causal inferences.
- Given that no adjustments for multiple testing were made because of concerns about missing possibly important findings that could be tested in original trials, the possibility of chance findings exist.

INTRODUCTION

Rationale

Arthritis and other rheumatic diseases (AORD) are major public health problems in the United States (US). Based on combined 2013-2015 data from the National Health Interview Survey, the annual prevalence of doctor-diagnosed arthritis in the civilian, non-institutionalized US population aged 18 years or older was 22.7% (54.4 million), with prevalence higher among women (23.5%) than men (18.1%).[1] By 2040, it is estimated that 78.4 million (25.9%) US adults 18 years of age and older will have doctor-diagnosed arthritis.[2] Compared to combined 2013-2015 data,[1] this represents an increase of approximately 24 million adults. Not surprisingly, the financial costs associated with AORD in the United States are high. In 2003, the total costs attributable to AORD were estimated to be approximately $128 billion, $80.8 billion in direct costs (medical expenditures) and $47 billion in indirect costs (lost earnings).[3] This represents an increase of 24% between 1997 and 2003 and was primarily the result of an increase in the number of people with AORD.[3]

Elevated and sustained levels of anxiety can result in a number of deleterious consequences. These include, but are not limited to, (1) an increased risk for coronary heart disease as a result of heightened arousal leading to an increased risk for hypertension and a pro-inflammatory state,[4-6] (2) an increased risk for cardiac death,[5] and (3) poorer health-related quality-of-life.[7] While it is well-recognized that depression is a common comorbidity among adults with AORD, recent research suggests that the prevalence of anxiety among US adults with arthritis is approximately twice as high as depression.[8] Using data from the Arthritis Conditions Health Effects Survey, the

prevalence of anxiety and depression among US adults with doctor-diagnosed arthritis was estimated to be almost twice as high for anxiety (30.5%) versus depression (17.5%), with US population estimates of 11.5 million for anxiety and 6.6 million for depression.[8] In addition, an 18-country study found the prevalence of anxiety to be greater in adults with AORD versus those without AORD.[9] This included, separately, generalized anxiety disorder, social phobia, agoraphobia/panic disorder, and post-traumatic stress disorder.[9] Given the prevalence of anxiety, it has been recommended that health care providers screen people with AORD for anxiety.[8]

Exercise is an intervention that is generally safe and appropriate for most persons with various types of AORD.[10 11] While there is no firm consensus regarding the mechanisms associated with the anxiolytic effects of exercise in adults with AORD as well as other chronic diseases, a recent review on this topic has reported several potential mechanisms, exclusive of specific chronic disease status, that may be responsible for such.[12] These include physiological (decrease in sympathetic nervous system and hypothalamic-pituitary-adrenal axis reactivity) as well as psychological (improvements in anxiety sensitivity, self-efficacy, and distraction) processes.[12]

Recent meta-analytic work has shown that community-deliverable exercise interventions reduce depressive symptoms in adults, with an estimated 3.1 million inactive US adults with AORD improving their depressive symptoms if they began and maintained a regular exercise program.[13] However, the effects of community-deliverable exercise on anxiety as a primary outcome are not known given a plethora of conflicting randomized controlled trials on this topic as well as a lack of studies that assess both depression and anxiety within the same study (only 44.8% based on a

previous meta-analysis).[13] Most importantly, a recent systematic review of previous meta-analyses, not to be confused with an original systematic review with meta-analyses, found that no meta-analysis of randomized controlled trials has examined the effects of community-deliverable exercise on anxiety as a primary outcome in adults with AORD.[14] Community-deliverable exercise may be especially important given its potential convenience, ability to reach a large amount of people, and cost.[15-18] In addition, a systematic review found that greater levels of anxiety were a barrier to exercise adherence in those with AORD.[19] Thus, reductions in anxiety may increase adherence to exercise in adults with AORD, a population in which meeting current exercise guidelines is significantly lower than in those without AORD, approximately 40% versus 50%.[20] Clearly, it is critically important to develop a better understanding of the overall magnitude of effect, as well as factors associated with, exercise for improving anxiety in adults with AORD.

Objective

The primary objective of this study was to conduct a systematic review with an aggregate data meta-analysis of randomized controlled trials to determine the effects of community-deliverable exercise interventions on anxiety in adults with AORD.

METHODS

Overview

This study followed the guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement for meta-analyses of health care interventions.[21] The protocol for this study is registered in PROSPERO (trial registration number CRD42016048728) and has been previously published in BMJ Open.[22]

Eligibility criteria

Studies that met the following criteria were included: (1) randomized controlled trials with the unit of assignment at the participant level, (2) community-deliverable exercise-only intervention group (aerobic, strength training, or both), (3) interventions ≥ 4 weeks, (4) comparative control group (non-intervention, wait-list control, usual care, attention control), (5) adults ≥ 18 years of age with doctor-diagnosed osteoarthritis, rheumatoid arthritis or fibromyalgia, (6) studies (published and unpublished in the form of Master's theses and dissertations) in any language, assuming an English-language abstract was available, from January 1, 1981 forward, and (7) data for anxiety, as defined by the authors of the original studies. Studies were limited to those with osteoarthritis, rheumatoid arthritis or fibromyalgia based on previous meta-analytic research showing a lack of exercise intervention studies for other types of AORD.[13] Studies were limited to randomized trials because it is the only way to control for confounders that are not known or measured as well as the observation that nonrandomized controlled trials tend to overestimate the effects of healthcare interventions.[23 24] Aerobic and progressive resistance (strength training) exercise were defined according to section C2 of the 2008 Physical Activity Guidelines Advisory Committee Report.[25] Specifically, aerobic exercise is defined as any 'exercise that primarily uses the aerobic energy-producing systems, can improve the capacity and efficiency of these systems, and is effective for improving cardiorespiratory endurance,' while strength training is defined as 'exercise training primarily designed to increase skeletal muscle strength, power, endurance, and mass'.[25]

For this proposed project, community-deliverable exercise interventions were considered to be those that could be performed, or have the potential to be adapted and performed, by persons in a community setting (recreation or senior centers, in the home or neighborhood, etc.) and meet the implementation guidelines for physical activity interventions recently recommended by the Arthritis Program at the Centers for Disease Control and Prevention: (1) no academic degree required for a leader/implementer but leader training available, if needed, (2) no special facilities beyond a community room (except a warm pool for aquatic exercise), (3) inexpensive equipment, (4) cost to participants less than $50.00, (5) implementation guide available, (6) supporting structures judged to be adequate to support widespread implementation.[26] An exercise duration of at least 4 weeks was chosen based on previous research in which statistically significant improvements in anxiety occurred as a result of as little as 4 weeks of exercise training.[27] There was no maximum limit on the length of any interventions for the studies included in our proposed project. We limited our studies to adults ages 18 and older because the inclusion of children and adolescents pose additional confounding problems congruent with the many developmental changes that occur during this period. In addition, the prevalence of AORD is more common in adults than children and adolescents. We restricted our studies to published articles, dissertations and master's theses and examined for potential small-study effects such as publication bias when limited to published articles in peer-reviewed journals. The year 1981 was chosen as the starting point for eligibility based on a preliminary PubMed search in which it was found that this was the first year that a randomized controlled trial on exercise and arthritis was

published.[28] Studies from both English and non-English-language sources were included with the latter translated into English by the second author using the freely available web-based Babelfish and Bing translators. Finally, while acknowledging that the mechanisms for changes in anxiety may differ for different types of AORD, for example fibromyalgia versus osteoarthritis and rheumatoid arthritis, all three were included in the current systematic review with meta-analysis because the focus was on determining whether exercise reduces anxiety in adults with AORD, not why it reduces anxiety. In addition, community-deliverable exercise programs, and exercise programs in general, are not traditionally focused on one type of AORD, but rather, across all types of AORD.[17] Furthermore, meta-regression (see Data Synthesis) was conducted to examine for any potential associations between type of AORD and changes in anxiety. Finally, there has been recent criticism by others regarding the publication of systematic reviews with meta-analysis using the "least publishable unit" approach.[29]

Information sources

Eight electronic databases were searched for potentially eligible studies in any language published from January 1, 1981 forward. The last searches were conducted on January 6, 2017. Databases searched included (1) PubMed, (2) SPORTDiscus, (3) Cochrane Central Register of Controlled Clinical Trials (CENTRAL), (4) Cumulative Index to Nursing and Allied Health Literature (CINAHL), (5) PsycINFO, (6) Web of Science, (7) Scopus and (8) ProQuest (Master's theses and dissertations). In addition, cross-referencing from retrieved studies was conducted. Furthermore, the third author, an expert on physical activity and AORD, reviewed the reference list for completeness.

Search strategy

Search strategies were developed using text words as well as medical subject headings (MeSH) associated with the effects of exercise on anxiety in adults with AORD. The second author conducted all electronic database searches. A copy of the search strategy for one of the databases searched (PubMed) is shown in Supplementary file 1.

Study records

Study selection

All studies to potentially be screened were imported into EndNote (EndNote, Version X8. New York, NY: Thomson Reuters, 2016). Duplicates were then removed both electronically and manually by the second author. A copy of the database was then provided to the first author for duplicate screening. The first two authors selected all studies, independent of each other. The full report for each article was obtained for all titles and abstracts that appeared to meet the inclusion criteria or where there was any uncertainty. Multiple reports of the same study were handled by including the most recently published article as well as drawing from previous reports, assuming similar methods and sample sizes. Neither of the screeners were blinded to the journal titles or to the study authors or institutions. Reasons for exclusion were coded as one or more of the following: (1) inappropriate population, (2) inappropriate intervention, (3) inappropriate comparison(s), (4) inappropriate outcome(s), (5) inappropriate study design, (6) other. Upon completion, the first two authors met and reviewed their selections. Discrepancies were resolved by consensus. If consensus could not be reached, the third author provided a recommendation. Using Cohen's kappa statistic (κ),[30] the overall agreement rate prior to correcting disagreements was 0.90. After

identifying the final number of studies to be included, the overall precision of the searches was calculated by dividing the number of studies included by the total number of studies screened after removing duplicates.[31] The number needed-to-read (NNR) was then calculated as the inverse of the precision.[31]

Data abstraction

Prior to the abstraction of data, a codebook that could hold more than 200 items per study was developed using Microsoft Excel (Microsoft Excel, Version 2010, Redmond, WA). The codebook was developed by the first two authors with input from the third author. The major categories of variables coded included (1) study characteristics (author, journal, year, etc.), (2) participant characteristics (age, height, body weight, etc.), (3) intervention characteristics (type, length, frequency, intensity, duration, compliance, etc.), and (4) outcome characteristics for anxiety (sample sizes, baseline and post-exercise means and standard deviations, etc.). The first two authors abstracted data from all studies, independent of each other, using separate codebooks in Microsoft Excel. Upon completion of coding, the codebooks were merged into one primary codebook for review. Both authors then met and reviewed every item for agreement. Discrepancies were resolved by consensus. If consensus could not be reached, the third author provided a recommendation. Using Cohen's kappa statistic (κ),[30] the overall agreement rate prior to correcting disagreements was 0.95.

Outcomes and prioritization

The primary outcome in this study was changes in anxiety. Secondary outcomes included changes in physical function, pain, depression, quality of life, body mass index

(BMI in $kg \cdot m^{-2}$), maximum oxygen consumption ($VO2_{max}$ in $ml \cdot kg^{-1} \cdot min^{-1}$), and muscular strength.

Risk of bias assessment in individual studies

Risk of bias was assessed at the study level using the Cochrane Risk of Bias instrument,[32] with a focus on the primary outcome of interest, changes in anxiety. Bias was evaluated across six domains: (1) random sequence generation, (2) allocation concealment, (3) blinding of participants and personnel, (4) blinding of outcome assessment, (5) incomplete outcome data, (6) selective reporting and (7) whether participants were exercising regularly, as defined by the original study authors, prior to taking part in the study. Each item was classified as having either a high, low, or unclear risk of bias. Because it's virtually impossible to blind participants to group assignment in exercise intervention protocols, all studies were classified as high risk with respect to the category "blinding of participants and personnel". Based on previous research, no study was excluded based on the results of the risk of bias assessment.[33] The first two authors conducted all assessments, independent of each other. Both authors then met and reviewed all selections for agreement. Discrepancies were resolved by consensus, and if necessary, consultation with the third author. Using Cohen's kappa statistic (κ),[30] the overall agreement rate for risk of bias assessment prior to correcting disagreements was 0.71.

Data Synthesis

Calculation of effect sizes

The primary outcome for this proposed project was changes in anxiety, calculated as Hedge's standardized mean difference effect size (ES), adjusted for small-sample

bias.[34] This was calculated by subtracting the change outcome difference in the exercise group minus the change outcome difference in the control group, and then dividing by the pooled standard deviation of the change outcome for the exercise and control groups. If change score standard deviations were not available, they were calculated from reported change outcomes, treatment effect 95% confidence intervals (CI), or pre and post standard deviation values according to procedures developed by Follmann et al.[35] Secondary outcomes (physical function, pain, quality of life, depression, muscular strength) were calculated using the same procedures as for the primary outcome while BMI and $VO2_{max}$ were calculated using the original metric. For studies in which outcomes were assessed at multiple time points, differences between baseline values and the final time point closest to cessation of the exercise intervention were used.

Pooled estimates for changes in outcomes

Effect size changes in anxiety and all secondary outcomes were pooled using the recently developed inverse heterogeneity (IVhet) model.[36] The IVhet model is a quasi-likelihood model that is computed by (1) calculating weights that sum to 1 from each study, (2) pooling effects from all the studies, and (3) calculating the variance of the pooled ES. The IVhet model has been shown to be superior to the original random-effects, method-of-moments model of Dersimonian and Laird,[37] the most common random-effects model used to pool aggregate data meta-analytic results.[38] Specifically, simulation studies have shown that the IVhet model retains correct coverage probabilities as well as a lower observed variance than the random-effects

model, regardless of heterogeneity.[36] Two-tailed z-alpha values ≤ 0.05 and non-overlapping 95% confidence intervals were considered statistically significant.

Heterogeneity and *inconsistency* for each pooled outcome were estimated using the Q[39] and I^2 statistic,[40] respectively. An alpha level of ≤ 0.10 for Q was considered to represent statistically significant heterogeneity while inconsistency was categorized as very low (<25%), low (25% to <50%), moderate (50% to <75%) or large (≥ 75%).[40] To improve practical relevance with respect to potential improvements in anxiety and all secondary outcomes, percentile gain in the exercise groups was calculated using Cohen's U_3 index[41] In addition, the number-needed-to treat (NNT) was estimated using the approach suggested by the Cochrane Collaboration[32] and a control group risk of 30% based on previous research on anxiolytics.[42] This was accomplished by converting the standardized mean differences into a log odds ratio, odds ratio, assumed control risk (30%) and then NNT. Extending the NNT, estimates of the number of US adults with AORD who could improve their anxiety levels but were not currently meeting physical activity recommendations were calculated. These were based on the reciprocal of the NNT multiplied by the number of adults in the United States with doctor-diagnosed arthritis who were not currently meeting exercise guidelines, currently approximately 31.6 million.[1 43] *Influence analysis* was conducted with each study deleted from the model once while *cumulative meta-analysis*, ranked by year, was used to examine the accumulation of results over time.

The primary pooling of results was based on group level findings. However, findings were also examined by collapsing results so that only one ES represented each study. In addition, for those outcomes that were assessed using multiple instruments, results

from these instruments were pooled into one ES. The rationale for this was based on the lack of consensus regarding the most valid and reliable instrument for the outcome and population of interest as well as the need to maintain as much independence as possible. For those studies that reported both per protocol and intention-to-treat analyses, results were also pooled into one ES.

Exploratory m*eta-regression* based on the IVhet model was used to examine the relationship between changes in our primary outcome (anxiety) and selected covariates.[36] This was accomplished by (1) conducting simple meta-regression for statistically significant associations between selected covariates and changes in anxiety, (2) examining for multicollinearity between covariates ($r > 0.80$), and (3) building a multiple meta-regression model. These models used a multiplicative versus additive component for residual heterogeneity. To achieve matching error variances, robust Huber-Ecker-White-sandwich error variances were used to account for the underestimated dispersion. Such errors were expected to calculate the correct standard errors for heterogeneous data that are traditionally heteroskedastic. Because of the small sample size, a post hoc decision was made to include no more than three potential predictors based on simple regression analyses. Multivariate imputation using chained equations (MICE)[44] was used to impute missing values for minutes of training per week (5 imputations) and changes in depression (1 imputation) so that the maximum sample size could be achieved. Because of the small sample size, a post hoc decision was made to conduct meta-regression with results for osteoarthritis and rheumatoid arthritis combined.

Based on the recommendations of Rothman,[45] no adjustments for multiple testing were made because of concerns about missing possibly important findings that could be pursued in future randomized controlled trials. While this could be viewed as a 'fishing expedition', such analyses are important for providing investigators with potential direction for future randomized controlled trials, one of the very reasons for conducting a systematic review with meta-analysis.[46] This approach is especially appropriate for meta-analysis since covariates are not randomly assigned in meta-analysis and thus, such analyses are considered to be observational in nature.[47] As a result, causal inferences cannot be derived from meta-regression. However, any observed associations can provide direction for future research.

Meta-biases

Small-study-effects (publication bias, etc.) for primary and secondary outcomes were assessed following current guidelines.[48] This included qualitative analysis using funnel plots as well as quantitative analysis using Egger's regression-intercept test for continuous data.[48] An alpha level $\leq$ 0.05 and 95% CI that did not include zero (0) was considered to represent statistically significant small-study effects.

Confidence in cumulative evidence

Strength of findings for our primary outcome (anxiety) was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) for meta-analysis.[49] The quality of evidence was assessed across the domains of risk of bias, consistency, directness, precision and publication bias. Quality was judged as high (further research is very unlikely to change our confidence in the estimate of effect), moderate (further research is likely to have an important impact on our confidence in the

estimate of effect and may change the estimate), low (further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate), or very low (very uncertain about the estimate of effect).

Software used for data synthesis

All data were analyzed using Stata (V.14.1; Stata/SE for Windows (Version 14.1). College Station, Texas: Stata Corporation LP, 2015), Microsoft Excel 2010 (Microsoft Excel (Version 2010)), and three add-ins for Excel, Meta XL (V.5.3; Meta XL (Version 5.3). 2016), SSC-Stat (V.2.18; SSC-Stat (Version 2.18). University of Reading, UK: Statistical Services Center, 2007), and EZ-Analyze (V.3.0; EZ Analyze (Version 3.0). Boston, MA: Tim Poynton, 2007).

RESULTS

Study Characteristics

A flow diagram that depicts the search process for study selection is shown in Figure 1. After initially identifying 639 citations and removing 240 duplicates both electronically and manually, 399 citations were screened. Of these, 14 studies representing 30 groups (16 exercise, 14 control) and 926 initially enrolled participants (539 exercise, 387 control) met the criteria for inclusion.[50-63] Two studies included more than one intervention group.[58 61] One included a pool and walking group[58] while the other included a long and short bout exercise group.[61] The major reasons for exclusion were (1) inappropriate intervention (47.8%), (2) inappropriate study design (32.2%), (3) inappropriate population (11.9%), (4) inappropriate comparison group (4.7%), and (5) inappropriate outcome (3.4%). The precision of the search, excluding duplicates, was

3.5% while the NNR was 29. A list of excluded studies, including the reasons for exclusion, can be found in Supplementary File 2.

With respect to source, 1 study (7.1%) was published as a dissertation[51] while the remaining 13 (92.9%) were published in peer-reviewed journals.[50 52-63] For the 12 studies (85.7%) in which data were available, the 5-year impact factor of the journals in which studies were published ranged from 1.7 to 7.9 ($\bar{x} \pm$ SD, 4.1 $\pm$ 2.4, median = 2.9). Five studies (35.7%) were published in the United States,[51 52 56-58] 2 each in either Canada,[55 61] Portugal[62 63] or Spain,[59 60] and 1 each in either Australia,[53] Brazil,[50] or Ireland.[54] Thirteen of the 14 studies (92.9%) were published in English-language journals[50-62] while 1 (7.1%) was published in Spanish.[63] With respect to types of control groups, 4 studies used either a wait-list control[50 51 53 54] or what appeared to be some type of attention control group,[52 56 58 61] while three each used either a non-intervention[55 57 62] or usual care group.[59 60 63] Three studies (21.4%) reported using matching procedures according to either sex,[55] age, sex and BMI,[56] or type of arthritis (rheumatoid or osteoarthritis).[58] None of the studies reported using any type of crossover design.[50-63] For data analysis, 7 studies (50.0%) reported using the per-protocol approach,[51 56-58 60 62 63] 4 (28.6%) used intention-to-treat,[50 52-54] while the remaining 3 (21.4%) used both.[55 59 61] Eight studies (57.1%) provided sample size estimates.[50 52-54 56 60 61 63] With respect to funding, 12 studies (85.7%), reported receiving funding from government, university, or private sources for their work.[50 52-62]

Participant Characteristics

A description of the physical characteristics of participants for those studies that reported data is shown in Tables 1 and 2. On average, participants were overweight

and had low cardiorespiratory fitness. The majority of participants were women, although 7 studies (50.0%) also included a small number of men.[52-58] Nine studies (64.3%) were limited to participants with fibromyalgia,[50 51 55 56 59-63] 3 (21.4%) with osteoarthritis,[52-54] 1 with rheumatoid arthritis[57] and 1 with either rheumatoid arthritis or osteoarthritis.[58] For those studies in which data were available, the number of years in which rheumatic symptoms were present ranged from 3 to 24 ($\bar{x} \pm$ SD, 13.1 $\pm$ 7.0, median = 12.0),[54-56 59 61-63] while years since diagnosis ranged from 3 to 7 ($\bar{x} \pm$ SD, 4.1 $\pm$ 2.0, median = 3).[55 61-63] Nine of the 14 studies (64.3%) reported that one or more participants were taking some type of medication for their condition.[51 53-55 57-59 62 63] These included, but were not necessarily limited to, non-steroidal anti-inflammatory drugs (NSAIDS), analgesics, narcotics and non-narcotics for pain, muscle relaxants, antidepressants, and anxiolytics. However, a lack of specific data was available on exposure to medications both before and during the study, including any changes during the intervention period. In addition, a lack of data was available on pharmacologic equivalence between study arms both before and during the study. For cigarette smoking, one study reported cigarette smoking in some of the participants.[61] Participant withdrawals or removal in the exercise groups ranged from 0% to 50% ($\bar{x} \pm$ SD, 17.4 $\pm$ 13.4, median = 17.0) while withdrawals or removal in the control groups ranged from 0% to 41% ($\bar{x} \pm$ SD, 11.5 $\pm$ 12.7, median = 6.3). Reasons for withdrawals or removal included such things as family issues, pain from exercising, injuries, personal issues, time, unhappiness with group assignment, transportation issues, moving, employment commitments, boredom with exercise routine, not enough room or privacy to perform exercise, failure to complete lab assessments, not attending a

specific percentage of the exercise sessions, or changing medications that could affect mood.

Exercise Intervention Characteristics

Exercise intervention characteristics for each group from each study are shown in Tables 1 and 3. Intensity of training, categorized according to American College of Sports Medicine[64] and limited to aerobic exercise only, included very light, light, moderate and vigorous exercise for the 9 (64.3%) studies that reported such information.[51 55 56 58-63] For mode of training, 6 studies (42.9%) focused on aerobic types of exercise,[50 51 55 58 60 61] 1 (7.1%) on weight training,[57] and 7 (50.0%) on both.[52-54 56 59 62 63] Specific types of aerobic activities included such things as aquatic exercise, walking, jogging, exercising to music and cycling. For the few studies that provided detailed information on resistance training, the number of sets ranged from 1 to 3,[57 59] the number of repetitions from 8 to 15,[57 59] and the number of exercises from 2 to 10 or more.[56 57 59] One study reported a rest period for 30 seconds between sets.[57] For those studies that reported data, the equipment used for resistance training included free weights and elastic bands.[52 56 57 62 63] Seven studies (50.0%) reported supervised exercise,[55 56 58-60 62 63] 5 (35.7%) reported both supervised and unsupervised exercise,[50-54] while the remaining 2 (14.3%) reported unsupervised exercise.[57 61] Three of the 14 studies (21.4%) reported some type of adverse event.[51 52 61] Reasons included 1 participant dropping out due to pain after the first exercise session,[51] 2 participants because of a history of a herniated disk and low back and leg pain,[52] and 1 participant because of a metatarsal fracture.[61] Another study reported that 1 participant withdrew because of the exacerbation of back pain[53] while a final study reported the exclusion of

2 participants because of severe coronary artery disease.[57] None of the studies provided data on the costs associated with conducting the intervention.[50-63]

Risk of Bias Assessment

Results for risk of bias assessment using the Cochrane Risk of Bias Assessment Instrument are shown in Figure 2 and Supplementary file 3. As can be seen, greater than 50% of the studies were at an unclear or high risk of bias with respect to (1) incomplete outcome reporting (78.6%), (2) allocation concealment (78.6%), and (3) blinding of outcome assessors (57.1%). Given the inability to truly blind participants in exercise intervention trials, all studies (100%) were considered to be at a high risk of bias for the category 'blinding of participants and personnel'.

Data Synthesis

Overall results for primary outcome (anxiety). Overall results for changes in anxiety for the 14 included studies[50-63] are shown in Table 4 and Figure 3. As can be seen, statistically significant ($p = 0.002$) reductions in anxiety were observed. In addition, statistically significant heterogeneity was observed while overall inconsistency was categorized as moderate, (range = low to large). The NNT was 6 with a percentile improvement of 15.5% and an estimated 5.3 million inactive US adults with AORD improving their anxiety if they started exercising regularly. Statistically significant small-study effects were observed ($p < 0.0001$) (Figure 4). With each result deleted from the model once, results remained statistically significant across all deletions, ranging from -0.44 (95% CI, -0.71 to -0.18) to -0.35 (-0.57 to -0.12). Cumulative meta-analysis, ranked by year, demonstrated that results have been statistically significant since the first study was conducted in 1989,[58] but with a trend towards smaller improvements in anxiety with

each accumulating year (Figure 5). Reductions in anxiety were similar to group-level results when collapsed so that only one ES represented each study (ES, -0.40, 95% CI, -0.67 to -0.13, p = 0.004; Q = 39.6, p = 0.0002; I^2 = 67.2%, 95% CI, 42.6% to 81.3%, tau^2 = 0.15). With six outliers deleted from the model, overall reductions in anxiety were similar but heterogeneity was no longer statistically significant and overall inconsistency was reduced to a level categorized as small (ES, -0.40, 95% CI, -0.62 to -0.18, p = 0.0004; Q = 11.8, p =0.22; I^2 = 24.0%, 95% CI, 0% to 63.1%, tau^2 = 0.03).

Meta-regression results for anxiety. Simple meta-regression results are shown in Supplementary File 4. For study characteristics, greater reductions in anxiety were associated with (1) earlier publication year, (2) studies at an unclear versus low risk of bias, (3) studies in which sample size estimates were not provided, (4) trials in which a larger percentage of participants initially agreed to participate in, and (5) studies that were not funded versus funded. For participant characteristics, greater improvements were associated with a larger percent dropout in the exercise groups as well as younger age. For exercise intervention characteristics, greater reductions were associated with (1) aerobic/strength training versus aerobic and strength training combined, (2) fewer minutes of exercise per session, (3) minutes of exercise per week, and (4) total minutes of exercise for the entire intervention period. Greater reductions were also associated with (1) supervised and unsupervised exercise versus both, (2) facility and home-based exercise versus both and (3) group and self-exercise versus both. No statistically significant association (p = 0.71) was observed between rheumatoid/osteoarthritis (ES = -0.35) and fibromyalgia (ES = -0.44) while the overall ES for those studies in which the

participants had rheumatoid arthritis was -0.54 and the overall ES for those in which the majority had osteoarthritis was -0.32.

Results for the final multiple regression model are shown in Table 5. The overall model was statistically significant (F = 13.4, p = 0.004). Earlier year of publication and decreases in depression were statistically significant predictors for greater reductions in anxiety. However, minutes of exercise per week was no longer statistically significant.

GRADE findings for changes in anxiety. An evidence profile for changes in anxiety is shown in Supplementary file 5. As can be seen, the outcome (anxiety) was considered critical and the overall strength of the finding was considered high, with future additional studies unlikely to have an effect on the overall direction of findings.

Results for secondary outcomes. Overall results for changes in secondary outcomes are shown in Table 4. *Physical function* was assessed in 10 studies[50 52-55 57 58 61-63] using the 10 meter walk test, 50 foot walk, 6 minute walk, Arthritis Impact and Measurement Scale (AIMS), Fibromyalgia Impact Questionnaire (FIQ), Short Physical Performance Battery, sit-to-stand test, stairclimbing test, up and go test, and the Western Ontario and McMaster Osteoarthritis Index (WOMAC). As can be seen, statistically significant ($p < 0.001$) improvements in *physical function* were observed. Statistically significant heterogeneity was observed while inconsistency was categorized as moderate, (range = low to large). The NNT was 4 with a percentile improvement of 24.5% and an estimated 9 million inactive US adults with AORD improving their physical function if they started exercising regularly. No statistically significant small-study effects were observed (p = 0.17). With each result deleted from the model once, results remained statistically significant across all deletions, ranging from 0.54 (95% CI, 0.30 to 0.78) to 0.73 (95%

CI, 0.39 to 1.06). Cumulative meta-analysis, ranked by year, demonstrated that results have been statistically significant since the first study was conducted in 1989,[58] but with a trend towards smaller improvements in physical function with each accumulating year (from 0.86 in 1989 to 0.66 in 2016). Improvements in physical function were similar to group-level results when collapsed so that only one ES represented each study (ES, 0.66, 95% CI, 0.31 to 1.01, p = 0.0002; Q = 35.6, p <0.001; I^2 = 74.7%, 95% CI, 52.8% to 86.5%, tau^2 = 0.21). With four outliers deleted from the model, overall improvements in physical function were statistically significant but slightly smaller, heterogeneity was no longer statistically significant, and overall inconsistency was reduced to a level categorized as very low (ES, 0.57, 95% CI, 0.36 to 0.78, p <0.001; Q = 7.2, p =0.41; I^2 = 2.7%, 95% CI, 0% to 68.5%, tau^2 = 0.003).

For *pain,* assessment was conducted in 13 studies[50-54 56-63] using the AIMS, FIQ, numerical rating scale, tender point count, visual analog scale and the WOMAC. As can be seen in Table 4, statistically significant (p = 0.017) decreases in pain were found. Statistically significant heterogeneity was observed while inconsistency was categorized as large, including both CIs. The NNT was 6 with a percentile improvement of 23.1% and an estimated 5.6 million inactive US adults with AORD decreasing their pain if they started exercising regularly. No statistically significant small-study effects were observed (p = 0.34). With each result deleted from the model once, results remained statistically significant across all deletions, ranging from -0.70 (95% CI, -1.21 to -0.19) to -0.47 (95% CI, -0.80 to -0.15). Cumulative meta-analysis, ranked by year, demonstrated that results have been statistically significant, and remained statistically significant, since only 2013. Decreases in pain were similar to group-level results when collapsed

so that only one ES represented each study (ES, -0.62, 95% CI, -1.16 to -0.07, p = 0.03; = 123.7, p <0.001; I^2 = 90.3%, 95% CI, 85.3% to 93.6%, tau^2 = 0.75). With ten outliers deleted from the model, decreases in pain remained statistically significant but smaller, heterogeneity was no longer statistically significant, and overall inconsistency was reduced to a level categorized as very low (ES, -0.44, 95% CI, -0.70 to -0.18, p = 0.001; Q = 1.5, p =0.68; I^2 = 0%, 95% CI, 0% to 69.5%, tau^2 = 0).

Depression was assessed in 13 studies[50-58 60-63] using the AIMS, Beck Depression Inventory (BDI), Center for Epidemiologic Studies Depression Scale (CES-D), Depression, Anxiety and Stress Scale (DASS21), FIQ, HADS, MHI, and VAS. As can be seen in Table 4, statistically significant (p = 0.009) decreases in depression were found. Statistically significant heterogeneity was observed while inconsistency was categorized as moderate (95% CI = low to large). The NNT was 6 with a percentile improvement of 15% and an estimated 5.1 million inactive US adults with AORD reducing their depression if they started exercising regularly. Small-study effects were not statistically significant (p = 0.08). With each result deleted from the model once, results remained statistically significant across all deletions, ranging from -0.52 (95% CI, -0.68 to -0.37) to -0.32 (95% CI, -0.61 to -0.0.3). Cumulative meta-analysis, ranked by year, demonstrated that improvements have been statistically significant and remained stable since 2013. Decreases in depression were similar to group-level results when collapsed so that only one ES represented each study (ES, -0.38, 95% CI, -0.70 to -0.07, p = 0.02; Q = 45.6, p < 0.001; I^2 = 73.7%, 95% CI, 54.3% to 84.8%, tau^2 = 0.21). With three outliers deleted from the model, improvements in depression remained statistically significant, slightly larger, but with non-significant heterogeneity and overall

inconsistency categorized as very low (ES, -0.43, 95% CI, -0.60 to -0.26, p < 0.001; Q = 5.7, p =0.89; I^2 = 0%, 95% CI, 0% to 19.3%, tau^2 = 0).

Quality-of-life was assessed in 12 studies[50-57 59 61-63] using the FIQ, Health Assessment Questionnaire (HAQ), Quality of Life Scale (QOLS), SF-12, and SF-36. As shown in Table 4, statistically significant (p < 0.0001) improvements in quality-of-life were found. Statistically significant heterogeneity was observed while inconsistency was categorized as large (95% CI = low to large). The NNT was 4 with a percentile improvement of 23.1% and an estimated 8.6 million inactive US adults with AORD improving their quality-of-life if they started exercising regularly. Statistically significant small-study effects were observed (p < 0.001). With each result deleted from the model once, results remained statistically significant across all deletions, ranging from 0.58 (95% CI, 0.35 to 0.81) to 0.70 (95% CI, 0.41 to 0.99). Cumulative meta-analysis, ranked by year, demonstrated that improvements have been statistically significant since 2001, but with a trend towards a decrease in the magnitude of effect. Increases in quality-of-life were similar to group-level results when collapsed so that only one ES represented each study (ES, 0.63, 95% CI, 0.34 to 0.92, p < 0.001; Q = 30.9, p = 0.001; I^2 = 64.3%, 95% CI, 33.9% to 80.8%, tau^2 = 0.14). With four outliers deleted from the model, improvements in quality-of-life remained statistically significant, similar in magnitude, but with non-significant heterogeneity and overall inconsistency categorized as low (ES, 0.64, 95% CI, 0.39 to 0.90, p < 0.001; Q = 11.4, p =0.18; I^2 = 29.8%, 95% CI, 0% to 67.5%, tau^2 = 0.04).

Maximum oxygen consumption ($VO2_{max}$ in $ml \cdot kg^{-1} \cdot min^{-1}$) was assessed in 5 studies[56-58 61 62] using various maximal treadmill tests while one study used a submaximal step test

(Canadian Aerobic Fitness Test). As can be seen in Table 4, statistically significant (p = 0.001) improvements in $VO2_{max}$ were observed. Statistically significant heterogeneity was observed while inconsistency was categorized as moderate (95% CI = low to large). The NNT was 3 with a percentile improvement of 25.7% and an estimated 9.5 million inactive US adults with AORD improving their relative $VO2_{max}$ if they started exercising regularly. No statistically significant small-study effects were observed (p = 0.18). With each result deleted from the model once, results remained statistically significant across all deletions, ranging from 1.80 $ml \cdot kg^{-1} \cdot min^{-1}$ (95% CI, 0.58 to 3.01) to 2.47 $ml \cdot kg^{-1} \cdot min^{-1}$ (95% CI, 1.25 to 3.69). Cumulative meta-analysis, ranked by year, demonstrated that improvements have been statistically significant since 2003, but with a trend towards a decrease in the magnitude of effect over time. Increases in $VO2_{max}$ were similar to group-level results when collapsed so that only one ES represented each study (ES, 2.01 $ml \cdot kg^{-1} \cdot min^{-1}$, 95% CI, 0.59 to 3.44, p = 0.01; Q = 19.4, p = 0.001; I^2 = 79.4%, 95% CI, 51.2% to 91.3%, tau^2 = 1.7). With outliers deleted from the model, improvements in $VO2_{max}$ were smaller, with non-significant heterogeneity and overall inconsistency categorized as low (ES, 1.93 $ml \cdot kg^{-1} \cdot min^{-1}$, 95% CI, 0.83 to 3.02, p = 0.001; Q = 0.03, p =0.86; I^2 = 0%, 95% CI, 0% to 0%, tau^2 = 0).

Upper and lower body *muscular strength* was assessed in five studies[55 57-59 62] using free weights, grip strength, isokinetic strength and the sit-to-stand test with free weights. As shown in Table 4, statistically significant (p < 0.001) improvements in strength were observed. No statistically significant heterogeneity or mean inconsistency was observed (95% CI = none to moderate). The NNT was 4 with a percentile improvement of 22.2% and an estimated 8 million inactive US adults with AORD improving their strength if they

started exercising regularly. No statistically significant small-study effects were observed (p = 0.65). With each result deleted from the model once, results remained statistically significant across all deletions, ranging from 0.50 (95% CI, 0.21 to 0.79) to 0.68 (95% CI, 0.39 to 0.96). Cumulative meta-analysis, ranked by year, demonstrated that improvements in strength have been statistically significant since the first included study in 1989.[58] Changes in strength were similar to group-level results when collapsed so that only one ES represented each study (ES, 0.59, 95% CI, 0.33 to 0.85, p < 0.001; Q = 3.5, p = 0.48; I^2 = 0%, 95% CI, 0% to 76.2%, tau^2 = 0). There were no outliers.

Insufficient data were available to analyze *BMI*. The one study that did provide change outcome results for BMI reported no statistically significant changes.[56]

DISCUSSION

Overall Findings

The primary purpose of the current systematic review with meta-analysis was to examine the effects of exercise (aerobic, strength training, or both) on anxiety in adults with AORD. The overall findings, a primary purpose of meta-analysis,[65] suggest that exercise is associated with both statistically significant and practically important reductions in anxiety among adults with selected types of AORD. These findings are supported by (1) a magnitude of effect comparable to or greater than anxiolytics,[66] (2) a large percentile improvement of 15.5, (3) a NNT of only 6, (4) a large number of physically inactive US adults with AORD who could benefit from exercising regularly (5.3 million), (5) similar findings when examined at the study versus group level, (6) continued existence of a statistically significant effect when each result was deleted from the analysis once, (7) similar findings when outliers were deleted and statistical

heterogeneity was reduced to a non-significant effect and overall inconsistency to zero, and (8) a consistent finding of improvements in anxiety since the first included study was reported in 1989.[58] Based on GRADE, it was concluded that anxiety was a critical outcome and that further research would unlikely change the direction of effect.

While the current findings are encouraging, it is interesting to note that cumulative meta-analysis revealed a distinct trend for a reduction in the pooled ES over time (from -1.47 in 1989 to -0.40 in 2016) and based on meta-regression, a statistically significant association between greater reductions in anxiety with older versus more recent studies. While the specific reasons for this could not be determined, it may be that the experimental design and conduct of studies have improved over time. However, from the investigative team's perspective, it is highly unlikely that the results will become non-significant in future years. The former notwithstanding, the general conclusion that exercise is associated with reductions in anxiety among adults with selected types of AORD may need to be viewed with some caution given that the majority of included studies consisted of participants with fibromyalgia[50 51 55 56 59-63] while the remaining studies included those with osteoarthritis and/or rheumatoid arthritis.[52-54 57 58] However, meta-regression revealed no statistically significant association between type of AORD and changes in anxiety, thus allowing for the pooling of findings and a resultant increase in statistical power.

The final meta-regression model resulted in two statistically significant variables being included with earlier year of publication and changes in depression associated with greater reductions in anxiety. These findings further reinforce the influence of year of publication on changes in anxiety in the current systematic review with meta-analysis, a

potential reason for such having been previously mentioned. The greater reductions in anxiety associated with reductions in depression and quality-of-life based on simple meta-regression as well as depression in the multiple regression model illustrates the potential interaction between these factors and the difficulty in identifying such, especially in a systematic review with meta-analysis. Finally, for those studies in which data were available, [50-63] it is worthy to note that while the focus was on community deliverable exercise or exercise delivered in other settings in which the exercise intervention could be adapted for delivery in the community, two were delivered in either a university[50 56] or hospital[54 55] and one each in either a hospital and home,[53] university and home,[57] YMCA,[51] or home only.[61]

In addition to statistically significant and practically important improvements in anxiety, similar improvements were also observed for all secondary outcomes assessed (physical function, pain, depression, quality of life, $VO2_{max}$ in $ml \cdot kg^{-1} \cdot min^{-1}$, muscular strength). These findings are important because unlike pharmacologic interventions that are usually targeted to address one condition, exercise has the potential to improve multiple physiological and psychological outcomes. Given the former, it would seem plausible to suggest that continued efforts be made to increase the exercise and physical activity levels of adults with AORD.

Implications for Research

There are at least eight implications for the conduct and reporting of future research on exercise and anxiety in adults with AORD. First, since only five of the studies included participants with osteoarthritis and/or rheumatoid arthritis, future randomized controlled trials on exercise and anxiety in these populations appear warranted. Second, exercise

was performed indoors in the majority of included studies. Given that previous research has suggested the exercise performed outdoors may have better mood-enhancing effects than indoor exercise,[67 68] future research examining this phenomenon with respect to anxiety as well as other outcomes in adults with AORD seems appropriate. Third, future studies should focus on examining the dose-response effects of exercise on anxiety in adults with AORD and report complete information on the characteristics of the intervention, including intervention fidelity.[69] Such information is critical for the development of evidence-based recommendations aimed at practitioners. Fourth, since more than half of the studies were considered to be at high or unclear risk of bias with respect to allocation concealment, blinding of outcome assessors, and incomplete outcome reporting, future studies should address these issues in their experimental design and report such information. Notably, while all included studies were considered to be at a high risk of bias with respect to blinding of participants, this is difficult for researchers to address since unlike pharmacologic studies, it is almost impossible to blind intervention participants to group assignment in exercise intervention studies. Fifth, given the lack of data on exposure to psychotropic and analgesic medications before and during the studies, including any changes in medication during the study, it is suggested that future trials track and report this information, including pharmacologic equivalence between the intervention and control groups. Sixth, while a lack of data was reported on how and what level anxiety was assessed, all the studies used instruments apparently focused on generalized anxiety. However, anxiety is a heterogeneous construct that includes generalized anxiety disorder, separation anxiety disorder, selective mutism, specific phobia, social phobia, panic disorder and agoraphobia.[70]

Given the former, it is suggested that future studies report detailed information on the specific types of anxiety they are assessing so as to better identify what exact type(s) might be affected. Seventh, given previous meta-analytic research by others,[71] a focus on group versus individualized exercise may be preferable because of increased contact and social support. This may be especially true for ethnic and racial minorities.[72] Finally, and collectively, a study in which one might have clinical confidence in the results of might consist of a randomized controlled trial that (1) uses random sequence generation, for example, computer random generator, to assign to participants to an exercise intervention and attention-control group, (2) conceals allocation to group assignment using an approach such as sequentially numbered, sealed, opaque envelopes, (3) blinds personnel and outcome assessors to group assignment while noting the inherent risk that all exercise studies are traditionally unable to blind participants to group assignment, (4) accounts for incomplete data (dropouts, etc.) by conducting intention-to-treat analyses, (5) avoids selective reporting of data by providing results for both statistically significant and non-significant results, (6) includes sedentary participants with a selected type or types of arthritis and elevated baseline levels of anxiety, (7) includes valid and reliable instruments for the assessment of the different types of anxiety based on the most recent version of the Diagnostic and Statistical Manual of Mental Disorders,[70] (8) accounts for potential confounders (age, gender, race, ethnicity, education, income, pain, physical function, depression, co-morbidities, baseline levels of anxiety, sleep, medication use before and during the study, other non-exercise and non-medication uptake before and during the study), (9) based on a theoretical model, conducts group exercise intervention sessions (aerobic, strength

training, or both), based on the recent Consensus on Exercise Reporting Template,[73] (10) examines the mechanisms for changes in anxiety, and (11) conducts cost-effectiveness analysis of the intervention. While these recommendations are focused on exercise, alternative treatments exist. Thus, the most clinically useful study might consist of a mega-randomized controlled trial that addresses all currently available treatments. However, this is probably not realistic. Therefore, an alternative approach might be to conduct a network meta-analysis that includes both direct and indirect evidence from randomized trials of all available interventions (exercise, pharmacologic, etc.).[74] To the best of the authors' knowledge, no such study currently exists.

Implications for Practice

The results of this study appear to have important implications for practice. First, since changes in both anxiety and secondary outcomes resulted in statistically significant and practically important improvements, exercise may be more vital than any other intervention given the apparent multiple benefits of such. In addition, the magnitude of effect (-0.40), NNT (6) and percentile improvement (15.5) observed in the current study were equivalent to a previous meta-analysis on the pharmacological treatment of generalized anxiety disorder in which the overall SMD effect size was -0.39, the calculated NNT was 6, and the percentile improvement was15.2.[66] While the current systematic review with meta-analysis was unable to establish with any degree of certainty the dose-response effects of exercise on anxiety in adults with AORD, it would appear plausible, given the numerous other benefits that can be derived as well as the minimal adverse events associated with exercise, to adhere to the Active Adult or Active Older Adult Guidelines from the Physical Activity Guidelines for Americans Physical

Activity Guidelines[25] as recommended by the Centers for Disease Control and Prevention.[75] Broadly, this includes aerobic activities on most, if not all, days of the week, muscle strengthening activities at least 2 days per week, balance exercises at least 3 days per week, and flexibility exercises on a daily basis. However, these recommendations as applied to exercise and anxiety should be considered with respect to factors such as the lack of transparency with respect to risk of bias in the included studies.

Strengths and Limitations

There are at least three apparent *strengths* of the current study. First, to the best of our knowledge, this is the first systematic review with meta-analysis to examine, as a primary outcome, the effects of exercise on anxiety in adults with AORD. This is important given (1) the prevalence of AORD,[1] (2) the expected future increase in the prevalence of AORD,[2] (3) the financial costs associated with AORD,[3] and (4) the previously reported finding that the prevalence of anxiety is almost twice that of depression.[8] Second, a novel and recently developed approach, the IVhet model, was used to pool findings.[36] This resulted in more robust estimates than those derived from the traditional random-effects model.[37] This is noteworthy given the need to provide the most accurate results possible when examining the effects of an intervention on selected outcome(s).

While there are several strengths to this study, there are also at least four potential *limitations*. First, similar to any aggregate data meta-analysis, the potential for ecological fallacy exists. Thus, it may be that the observed findings in the current study would not apply at the individual participant level. Second, and also common to any type

of aggregate data meta-analysis, meta-regression results do not support causal inferences because the included studies are not randomly assigned to covariates.[47] Therefore, the associations observed in the current investigation would need to be assessed in appropriately powered randomized trials. Third, while a large number of statistical tests were conducted, no adjustments were made for such. Thus, some findings could have been nothing more than the play of chance. However, common to most aggregate data meta-analyses, no adjustments for multiple testing were made because of concerns about missing possibly important findings that could be tested in original trials.[45] Fourth, since anxiety was assessed using self-report instruments,[50-63] the possibility of reporting bias in the original studies existed.

CONCLUSIONS

Exercise is associated with reductions in anxiety among adults with selected types of AORD. However, a need exists for additional, well-designed, randomized controlled trials on this topic.

CONTRIBUTORS

GAK was responsible for the conception and design, acquisition of data, analysis and interpretation of data, drafting the initial manuscript and revising it critically for important intellectual content. KSK was responsible for the conception and design, acquisition of data, drafting the initial manuscript, and revising all drafts critically for important intellectual content. LFC was responsible for the conception and design, acquisition of data, drafting the initial manuscript, and revising all drafts critically for important intellectual content. All authors read and approved the final manuscript.

REGISTRATION

In accordance with Primary Reporting Items for Systematics Reviews and Meta-Analyses, our systematic review with network meta-analysis was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on October 4, 2016 (registration number CRD42016048728).

COMPETING INTERESTS

None.

FUNDING

This meta-analysis was funded by the National Institutes of Health, National Institute for Arthritis, Musculoskeletal and Skin Diseases, grant number R01AR061346 (GAK, Principal Investigator).

DATA SHARING STATEMENT

All data are available upon request from the corresponding author.

REFERENCES

1. Barbour KE, Helmick CG, Boring M, et al. Vital signs: Prevalence of doctor-diagnosed arthritis and arthritis-attributable activity limitation — United States, 2013–2015. *Morb Mortal Wkly Rep* 2017;66(9):8.
2. Hootman JM, Helmick CG, Barbour KE, et al. Updated projected prevalence of self-reported doctor-diagnosed arthritis and arthritis-attributable activity limitation among us adults, 2015-2040. *Arthritis Rheumatol* 2016;68(7):1582-7.
3. Yelin E, Murphy L, Cisternas MG, et al. Medical care expenditures and earnings losses among persons with arthritis and other rheumatic conditions in 2003, and comparisons with 1997. *Arthritis Rheum* 2007;56(5):1397-407.
4. Player MS, Peterson LE. Anxiety disorders, hypertension, and cardiovascular risk: a review. *Int J Psychiatry Med* 2011;41(4):365-77.
5. Roest AM, Martens EJ, de JP, et al. Anxiety and risk of incident coronary heart disease: a meta-analysis. *J Am Coll Cardiol* 2010;56(1):38-46.
6. Janszky I, Ahnve S, Lundberg I, et al. Early-onset depression, anxiety, and risk of subsequent coronary heart disease: 37-year follow-up of 49,321 young Swedish men. *J Am Coll Cardiol* 2010;56(1):31-37.
7. Blakemore A, Dickens C, Guthrie E, et al. Depression and anxiety predict health-related quality of life in chronic obstructive pulmonary disease: systematic review and meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2014;9:501-12.
8. Murphy LB, Sacks JJ, Brady TJ, et al. Anxiety and depression among US adults with arthritis: Prevalence and correlates. *Arthritis Care Res* 2012;64(7):968-76.

9. He Y, Zhang M, Lin EH, et al. Mental disorders among persons with arthritis: results from the World Mental Health Surveys. *Psychol Med* 2008;38(11):1639-50.

10. Busch AJ, Schachter CL, Overend TJ, et al. Exercise for fibromyalgia: a systematic review. *J Rheumatol* 2008;35(6):1130-44.

11. Hurkmans E, van der Giesen FJ, Vliet Vlieland TP, et al. Dynamic exercise programs (aerobic capacity and/or muscle strength training) in patients with rheumatoid arthritis. *Cochrane Database Syst Rev* 2009(4):CD006853.

12. Anderson E, Shivakumar G. Effects of exercise and physical activity on anxiety. *Front Psychiatry* 2013;4:27.

13. Kelley GA, Kelley KS, Hootman JM. Effects of exercise on depression in adults with arthritis: a systematic review with meta-analysis of randomized controlled trials. *Arthritis Res Ther* 2015;17:21.

14. Kelley GA, Kelley KS. Effects of exercise on anxiety in adults with arthritis and other rheumatic disease: A systematic review of meta-analyses. *J Nov Physiother* 2014;4(4):1-5.

15. Bruno M, Cummins S, Gaudiano L, et al. Effectiveness of two Arthritis Foundation programs: Walk With Ease, and YOU Can Break the Pain Cycle. *Clin Interv Aging* 2006;1(3):295-306.

16. Callahan LF, Ambrose KR. Physical activity and osteoarthritis - Considerations at the population and clinical level. *Osteoarthritis Cartilage*;23(1):31-33.

17. Hootman JM, Helmick CG, Brady TJ. A public health approach to addressing arthritis in older adults: the most common cause of disability. *Am J Public Health* 2012;102(3):426-33.

18. Zgibor JC, Ye L, Boudreau RM, et al. Community-based healthy aging interventions for older adults with arthritis and multimorbidity. *J Community Health* 2017;42(2):390-99.

19. Jack K, McLean SM, Moffett JK, et al. Barriers to treatment adherence in physiotherapy outpatient clinics: a systematic review. *Man Ther* 2010;15(3):220-8.

20. Fontaine KR, Heo M, Bathon J. Are US adults with arthritis meeting public health recommendations for physical activity? *Arthritis Rheum* 2004;50(2):624-8.

21. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Ann Intern Med* 2009;151(4):W65-W94.

22. Kelley GA, Kelley KS, Callahan LF. Community-deliverable exercise and anxiety in adults with arthritis and other rheumatic diseases: a protocol for a systematic review and meta-analysis of randomised controlled trials. *BMJ Open* 2017;7(3):e014957.

23. Sacks HS, Chalmers TC, Smith H. Randomized versus historical controls for clinical trials. *Am J Med* 1982;72:233-40.

24. Schulz KF, Chalmers I, Hayes R, et al. Empirical evidence of bias: Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *J Am Med Assoc* 1995;273:408-12.

25. Physical Activity Guidelines Advisory Report. Physical Activity Guidelines Advisory Committee. Washington, DC: U.S. Department of Health and Human Services: U.S. Department of Health and Human Services, 2008.

26. Brady TJ, Jernick SL, Hootman JM, et al. Public health interventions for arthritis: expanding the toolbox of evidence-based interventions. *J Womens Health (Larchmt)* 2009;18(12):1905-17.

27. Ide MR, Laurindo IMM, Rodrigues AL, et al. Effect of aquatic respiratory exercise-based program in patients with fibromyalgia. *Int J Rheum Dis* 2008;11(2):131-40.

28. Waggoner CD, LeLieuvre RB. A method to increase compliance to exercise regimens in rheumatoid arthritis patients. *J Behav Med* 1981;4(2):191-201.

29. Ioannidis JPA. The mass production of redundant, misleading, and conflicted systematic reviews and meta-analyses. *Milbank Q* 2016;94(5):485-514.

30. Cohen J. Weighted kappa: nominal scale agreement with provision for scaled disagreement or partial credit. *Psychol Bull* 1968;70:213-20.

31. Lee E, Dobbins M, DeCorby K, et al. An optimal search filter for retrieving systematic reviews and meta-analyses. *BMC Med Res Methodol* 2012;12:51.

32. Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]*: The Cochrane Collaboration, 2011.

33. Ahn S, Becker BJ. Incorporating quality scores in meta-analysis. *J Educ Behav Stat* 2011;36(5):555-85.

34. Hedges LV, Olkin I. Statistical methods for meta-analysis. San Diego, CA: Academic Press 1985.

35. Follmann D, Elliot P, Suh I, et al. Variance imputation for overviews of clinical trials with continuous response. *J Clin Epidemiol* 1992;45:769-73.

36. Doi SA, Barendregt JJ, Khan S, et al. Advances in the meta-analysis of heterogeneous clinical trials I: The inverse variance heterogeneity model. *Contemp Clin Trials* 2015;45(Pt A):130-38.

37. Dersimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;7:177-88.

38. Dersimonian R, Laird N. Meta-analysis in clinical trials revisited. *Contemp Clin Trials* 2015;45(Pt A):139-45.

39. Cochran WG. The combination of estimates from different experiments. *Biometrics* 1954;10:101-29.

40. Higgins JPT, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. *Br Med J* 2003;327(7414):557-60.

41. Cohen J. Statistical power analysis for the behavioral sciences. New York: Academic Press 1988.

42. Khan A, Khan S, Brown WA. Are placebo controls necessary to test new antidepressants and anxiolytics? *Int J Neuropsychopharmacol* 2002;5(3):193-7.

43. Murphy LB, Hootman JM, Boring MA, et al. Leisure time physical activity among U.S. adults with arthritis, 2008-2015. *Am J Prev Med* 2017.

44. Lee KJ, Carlin JB. Multiple imputation for missing data: fully conditional specification versus multivariate normal imputation. *Am J Epidemiol* 2010;171(5):624-32.

45. Rothman KJ. No adjustments are needed for multiple comparisons. *Epidemiology* 1990;1:43-46.

46. Sacks HS, Berrier J, Reitman D, et al. Meta-analysis of randomized controlled trials. *N Engl J Med* 1987;316:450-55.

47. Littell JH, Corcoran J, Pillai V. Systematic reviews and meta-analysis. New York: Oxford University Press 2008:1-202.

48. Sterne JA, Sutton AJ, Ioannidis JP, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *Br Med J* 2011;343:d4002.

49. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;64(4):383-94.

50. Baptista AS, Villela AL, Jones A, et al. Effectiveness of dance in patients with fibromyalgia: a randomized, single-blind, controlled study. *Clin Exp Rheumatol* 2012;30(6 Suppl 74):18-23.

51. Beltran R. The effects of a supervised group aerobic exercise program and a chronobiologicary oriented treatment protocol on symptomotatogy and mood in women with fibromyalgia [Dissertation]. Alliant University, 2003.

52. Cheung C, Wyman JF, Bronas U, et al. Managing knee osteoarthritis with yoga or aerobic/strengthening exercise programs in older adults: a pilot randomized controlled trial. *Rheumatol Int* 2017;37(3):389-98.

53. Fransen M, Nairn L, Winstanley J, et al. Physical activity for osteoarthritis management: a randomized controlled clinical trial evaluating hydrotherapy or Tai Chi classes. *Arthritis Rheum* 2007;57(3):407-14.

54. French HP, Cusack T, Brennan A, et al. Exercise and manual physiotherapy arthritis research trial (EMPART) for osteoarthritis of the hip: a multicenter randomized controlled trial. *Arch Phys Med Rehabil* 2013;94(2):302-14.

55. Gowans SE, deHueck A, Voss S, et al. Effect of a randomized, controlled trial of exercise on mood and physical function in individuals with fibromyalgia. *Arthritis Rheum* 2001;45(6):519-29.

56. Jones KD, Burckhardt CS, Deodhar AA, et al. A six-month randomized controlled trial of exercise and pyridostigmine in the treatment of fibromyalgia. *Arthritis Rheum* 2008;58(2):612-22.

57. Komatireddy GR, Leitch RW, Cella K, et al. Efficacy of low load resistive muscle training in patients with rheumatoid arthritis functional class II and III. *J Rheumatol* 1997;24(8):1531-39.

58. Minor MA, Hewett JE, Webel RR, et al. Efficacy of physical conditioning exercise in patients with rheumatoid arthritis and osteoarthritis. *Arthritis Rheum* 1989;32(11):1396-405.

59. Munguia-Izquierdo D, Legaz-Arrese A. Assessment of the effects of aquatic therapy on global symptomatology in patients with fibromyalgia syndrome: a randomized controlled trial. *Arch Phys Med Rehabil* 2008;89(12):2250-7.

60. Sanudo B, Carrasco L, de Hoyo M, et al. Vagal modulation and symptomatology following a 6-month aerobic exercise program for women with fibromyalgia. *Clin Exp Rheumatol* 2015;33(1 Suppl 88):S41-5.

61. Schachter CL, Busch AJ, Peloso PM, et al. Effects of short versus long bouts of aerobic exercise in sedentary women with fibromyalgia: a randomized controlled trial. *Phys Ther* 2003;83(4):340-58.

62. Tomas-Carus P, Gusi N, Hakkinen A, et al. Eight months of physical training in warm water improves physical and mental health in women with fibromyalgia: a randomized controlled trial. *J Rehabil Med* 2008;40(4):248-52.

63. Tomas-Carus P, Gusi N, Leal A, et al. [The fibromyalgia treatment with physical exercise in warm water reduces the impact of the disease on female patients' physical and mental health]. *Rheumatol Clin* 2007;3(1):33-37.

64. Garber CE, Blissmer B, Deschenes MR, et al. 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(7):1334-59.

65. Glass GV, McGaw B, Smith ML. Meta-analysis in social research. Newbury Park, California: Sage 1981.

66. Hidalgo RB, Tupler LA, Davidson JR. An effect-size analysis of pharmacologic treatments for generalized anxiety disorder. *J Psychopharmacol* 2007;21(8):864-72.

67. Rogerson M, Gladwell VF, Gallagher DJ, et al. Influences of green outdoors versus indoors environmental settings on psychological and social outcomes of controlled exercise. *Int J Environ Res Public Health* 2016;13(4):363.

68. Pasanen TP, Tyrvainen L, Korpela KM. The relationship between perceived health and physical activity indoors, outdoors in built environments, and outdoors in nature. *Appl Psychol Health Well Being* 2014;6(3):324-46.

69. Resnick B, Inguito P, Orwig D, et al. Treatment fidelity in behavior change research - A case example. *Nurs Res* 2005;54(2):139-43.

70. Association AP. Diagnostic and statistical manual of mental disorders. 5th ed2013.

71. Burke SM, Carron AV, Eys MA, et al. Group versus individual approach? A meta-analysis of the effectiveness of interventions to promote physical activity. *Sport Exerc Psychol Rev* 2006;1:19-55.

72. Onge JMS, Krueger PM. Education and racial-ethnic differences in types of exercise in the United States. *J Health Soc Behav* 2011;52(2):197-211.

73. Slade SC, Dionne CE, Underwood M, et al. Consensus on Exercise Reporting Template (CERT): Modified Delphi Study. *Phys Ther* 2016;96(10):1514-24.

74. Rouse B, Chaimani A, Li TJ. Network meta-analysis: an introduction for clinicians. *Intern Emerg Med* 2017;12(1):103-11.

75. CDC. Physical activity for arthritis Atlanta, Georgia: Centers for Disease Control and Prevention; 2017 [updated April 18, 2017. Available from: https://www.cdc.gov/arthritis/basics/physical-activity-overview.html accessed July 5 2017.

Table 1. Study characteristics.

Study and Year	Country	Participants	Exercise Intervention	Anxiety Assessment
Baptista et al., 2012[50]	Brazil	Women (N = 80) 18-65 yrs of age with FM assigned to exercise (n = 40, age, $\bar{x}$ = 49.5 yrs) or control (n = 40, age, $\bar{x}$ = 49.1 yrs) group	Dance exercise 2 x/wk, 60 min/session, for 12 wks	STAI
Beltran, 2003[51]	United States	Women (N = 21) 22-65 yrs of age with FM assigned exercise (n = 11, age, $\bar{x}$ ± SD = 50.1 ± 12.6 yrs) or control (n = 10, age, $\bar{x}$ ± SD = 53.7 ± 6.9 yrs) group	Aerobic aquatic exercise, 3 x/wk, 25 min/session, 60-85% MHR, for 10 wks	AIMS
Cheung et al., 2017 [52]	United States	Men and women (N=51) ≥ 65 yrs of age with knee OA assigned to exercise (n = 28, age, $\bar{x}$ ± SD = 74.4 ± 7.5 yrs), or control (n = 23, age, $\bar{x}$ ± SD = 71.8 ± 8.0 yrs) group	Aerobic exercise, 5 x/wk, 20-30 min/session for 8 wks, and strength exercise 3 x/wk, 30 min/session for 8 wks (10+ exercises)	HADS
Fransen et al., 2007[53]	Australia	Men and women (N=96) 59-85 yrs of age with hip or knee OA assigned to hydrotherapy (n = 55, age, $\bar{x}$ ± SD = 70 ± 6.3 yrs), or wait-list control (n = 41, age, $\bar{x}$ ± SD = 69.6 ± 6.1 yrs) group	Hydrotherapy exercises in warm water, 2 x/wk, 60 min/session, for 12 wks	DASS21
French et al., 2013[54]	Ireland	Men and women (N = 88) 40-80 yrs of age with hip OA assigned to exercise (n = 45, age, $\bar{x}$ ± SD =	Aerobic & strength training, 30 min/session, for 8 wks, up to 5 strength	HADS

		61.8 ± 9.7 yrs), or control (n = 43, age, $\bar{x}$ ± SD = 60.8 ± 9.7 yrs) group	exercises	
Gowans et al., 2001[55]	Canada	Men and women (N = 57) with FM assigned to an exercise (n = 30, age, $\bar{x}$ ± SD = 44.6 ± 8.7 yrs), or control (n = 27, age, $\bar{x}$ ± SD = 49.8 ± 7.3 yrs) group	Aerobic exercise (2 walking/jogging classes in a gym, 1 pool class), 3 x/wk, 30 min/session, 60-75% MHR, for 23 wks	MHI, STAI
Jones et al., 2008[56]	United States	Men and women (N = 101) 18-65 yrs of age with FM assigned to an exercise (n = 47, age, $\bar{x}$ ± SD = 49.6 ± 7.7 yrs), or control (n = 54, age, $\bar{x}$ ± SD = 49.8 ± 7.9 yrs) group	Aerobic exercise 3 x/wk, 30 min/session, 40-50% MHR & strength exercise, 3 x/wk, 10 min/session, for 24 wks	FIQ (Anxiety)
Komatireddy et al.[57]	United States	Men and women (n = 49), 35-76 yrs of age with RA assigned to exercise (n = 25, $\bar{x}$ ± SD = 57.7 ± 9.8 yrs of age, range 40–72 yrs) or control (n = 24, $\bar{x}$ ± SD = 60.5 ± 11 yrs of age, range 35–76 yrs) group	Circuit weight training with light loads and high repetitions, 7 exercises, 2–3 circuits/session, 12–15 reps, 30-second rest between sets, 20–27 min/session, $\geq$ 3 x/wk, RPE of 3–4, for 12 wks	AIMS
Minor et al., 1989[58]	United States	Men and women (N = 115) 21–83 yrs of age with RA or OA assigned to a pool (n = 47), walking (n = 36) or control group (n = 32)	Aerobic aquatics or walking group, 3 x/wk, 60 min/session (30 min of this was aerobic), 60-80% MHR, for 12 wks	AIMS
Munguia-Izquieerdo & Legaz-Arrese,	Spain	Men and women (N = 60) 18-60 yrs of age with FM assigned to exercise (n = 35, $\bar{x}$ ± SD = 50.0 ± 7.0 yrs) or control (n = 25 $\bar{x}$ ± SD = 46.0 ± 8.0 yrs)	Aerobic aquatic exercise, 3 x/wk, 20-30 min/session, 50-80% MHR, & strength exercise 3 x/wk, 8-20 min/session, 1-3	STAI

2008[59]		group	sets, 8-15 reps, for 16 wks	
Sanudo et al., 2015[60]	Spain	Women (N = 32) with FM assigned to exercise (n = 16, $\bar{x}$ ± SD = 55.0 ± 8.0 yrs of age), or control (n = 16, $\bar{x}$ ± SD = 58.0 ± 6.9 yrs of age) group	Aerobic/interval training, 2 x/wk, 30-35 min/session, 60-80% MHR, for 24 weeks	VAS
Schachter et al., 2003[61]	Canada	Women (N = 143) 20–55 yrs of age with FM assigned to a short bout (n = 56, $\bar{x}$ ± SD = 41.9 ± 8.6 yrs of age), long bout (n = 51, $\bar{x}$ ± SD = 41.3 ± 8.7 yrs of age), or control group (n = 36, $\bar{x}$ ± SD = 42.5 ± 6.7 yrs of age)	Low impact, videotape-based, aerobic exercise to music. Short bout, 2 x/d, 7.1 x/wk, 12.3 min/session, 60% HRR; Long-bout group: 1 x/d, 3.6 x/wk, 24.5 min/session, 60% HRR, for 16 wks	FIQ (Anxiety)
Tomas-Carus et al., 2008[62]	Portugal	Women with FM (N = 33) assigned to aquatic exercise (n = 17, $\bar{x}$ ± SD = 50.7 ± 10.6 yrs of age) or control group (n = 16, $\bar{x}$ ± SD = 50.9 ± 6.7 yrs of age)	Pool exercises performed in warm water, 3 x/wk, 20 min, aerobic phase, 60-65% MHR, strength exercise, 20 min, 4 sets, 10 reps, for 32 wks	FIQ (Anxiety), STAI
Tomas-Carus et al., 2007[63]	Portugal	Women with FM (N = 34) assigned to aquatic exercise (n = 17, $\bar{x}$ ± SD = 51 ± 10.0 yrs of age) or control group (n = 17, $\bar{x}$ ± SD = 51 ± 9.0 yrs of age)	Pool exercises performed in warm water, 3 x/wk, 20 min, aerobic phase, 60-65% MHR, strength exercises, 20 min, 4 sets, 10 reps, for 12 wks	FIQ (Anxiety)

Notes: Description of groups from each study limited to those that met the criteria for inclusion; $\bar{x}$ ± SD, mean ± standard deviation; AIMS, Arthritis Measurement Impact Scale; DASS21, Depression, Anxiety and Stress Scale; FIQ, Fibromyalgia Impact Questionnaire; FM, fibromyalgia; HADS, Hospital Anxiety & Depression Scale; HRR, heart rate reserve; MHI, Mental Health Inventory; min, minutes; MHR, maximum heart rate; STAI,

State-Trait Anxiety Inventory; MHR, maximum heart rate; OA, osteoarthritis; RA, rheumatoid arthritis; reps, repetitions; RPE, rating of perceived exertion; VAS, Visual Analog Scale; wk(s), week(s); yrs, years;

Table 2. Baseline characteristics of participants.

	Exercise				Control			
Variable	Groups/Participants	$\bar{x} \pm$ SD	Median	Range	Groups/Participants	$\bar{x} \pm$ SD	Median	Range
Age (years)	14/458	53.4 ± 9.7	50	41 – 74	13/349	54.9 ± 8.8	50	43 - 72
BMI ($kg \cdot m^2$)	7/204	29.0 ± 1.5	29	27 - 31	7/170	28.4 ± 1.7	28	27 – 31
VO_{2max} ($ml \cdot kg^{-1} \cdot min^{-1}$)	7/245	21.3 ± 2.3	21	19 – 24	5/101	20.7 ± 2.7	21	17 – 24

Notes: Groups represents number of exercise and control groups reporting data; $\bar{x} + SD$, mean ± standard deviation; BMI, body mass index; $VO_{2max,}$ maximum oxygen consumption.

Table 3. Exercise program characteristics.

Variable	Groups/Participants	$\bar{x} \pm$ SD	Median	Range
Length (weeks)	16/514	16 ± 7	14	8 - 32
Frequency (times/week)	14/469	3.3 ± 1.3	3	2 – 7
Duration (min/session)	14/450	28.8 ± 14.3	30	10 – 60
Minutes per week	11/407	85.5 ± 21.2	88	60 – 120
Minutes per week (adj)	7/277	61.3 ± 22.7	58	33 – 99
Compliance (%)	8/312	74.3 ± 19	80	38 - 97

Notes: Groups represents number of exercise groups reporting data; $\bar{x} \pm$ SD, mean ± standard deviation; min, minutes; adj, adjusted for compliance.

Table 4. Results for primary and secondary outcomes (data reported as standardized effect size unless otherwise noted).

Variable	ES (#)	Participants (#)	$\bar{x}$ (95% CI)	Q (p)	I^2 (95% CI)	τ^2
Primary outcome						
- Anxiety	16	883	-0.40 (-0.65, -0.15)*	40.3 (<0.001)**	62.8 (36.2, 78.3	0.14
Secondary outcomes						
- Physical function	12	677	0.66 (0.34, 0.97)*	36.0 (0.0002)**	69.4 (44.5, 83.1)	0.19
- Pain	15	803	-0.62 (-1.12, -0.11)*	128.6 (<0.001)**	89.1 (83.7, 92.7)	0.75
- QOL	13	730	0.63 (0.35, 0.91)*	32.4 (0.001)**	63.0 (32.7, 79.7)	0.15
- Depression	15	813	-0.38 (-0.67, -0.10)*	46.3 (<0.001)**	69.7 (48.6, 82.2)	0.20
- VO2max ($ml \cdot kg^{-1} \cdot min^{-1}$)	7	346	2.01 (0.85, 3.2)*	20.2 (0.003)**	70.3 (35.0, 86.4)	1.40
- Muscular strength	6	261	0.59 (0.33, 0.85)*	3.9 (0.6)	0 (0, 67.1)	0

Notes: ES, effect size; #, number; $\bar{x}$ (95% CI), mean effect size and 95% confidence interval; Q (p), Cochran Q statistic and alpha value for Q; I^2 (95% CI), I-squared and 95% confidence interval; τ^2, tau-squared; *, statistically significant (two-tailed alpha value $\leq$ 0.05 and non-overlapping 95% confidence intervals); **, statistically significant (alpha value $\leq$ 0.10);

Table 5. Final multiple regression model for changes in anxiety (N = 16).

Variable	Coefficient ± SE	*t* (p)	95% CI
Year of publication	0.035 ± 0.010	3.50 (0.006)*	0.012 to 0.057
Changes in depression	0.316 ± 0.758	4.16 (0.01)	0.110 to 0.521
Minutes of training per week	0.007 ± 0.003	2.40 (0.06)	-0.0002 to 0.016
Intercept	-70.718 ± 19.74	-3.58 (0.006)*	-115.19 to -26.24

Notes: SE, standard error; *t*, t-value; p, alpha value for *t*; CI, confidence interval.

FIGURE LEGEND

Figure 1. Flow diagram depicting the search process.

Figure 2. Risk of bias results using the Cochrane Risk of Bias Assessment Instrument.

Figure 3. Forest plot for changes in anxiety.

Figure 4. Funnel plot for changes in anxiety.

Figure 5. Cumulative meta-analysis for changes in anxiety.

SUPPLEMENTARY FILES

Supplementary File 1. Search strategy for PubMed.

Supplementary file 2. List of excluded studies, including reasons for exclusion.

Supplementary file 3. Study-level risk of bias results using the Cochrane Risk of Bias Assessment Instrument.

Supplementary file 4. Simple meta-regression results with changes in anxiety as the outcome.

Supplementary file 5. Evidence profile for changes in anxiety based on GRADE.

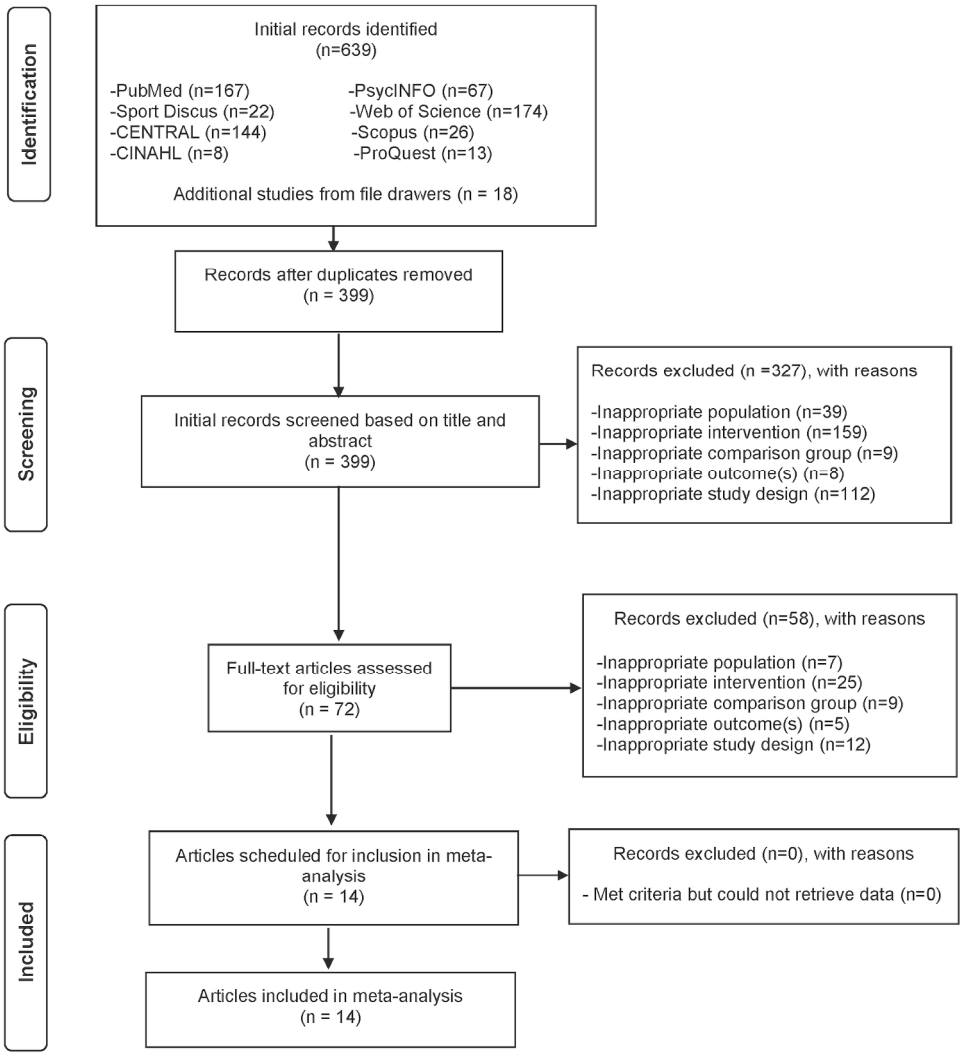


Figure 1. Flow diagram depicting the search process.

173x192mm (300 x 300 DPI)

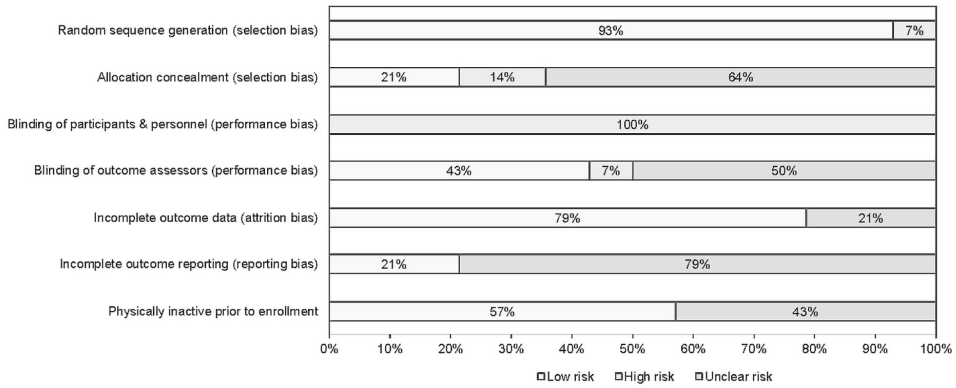


Figure 2. Risk of bias results using the Cochrane Risk of Bias Assessment Instrument.

173x77mm (300 x 300 DPI)

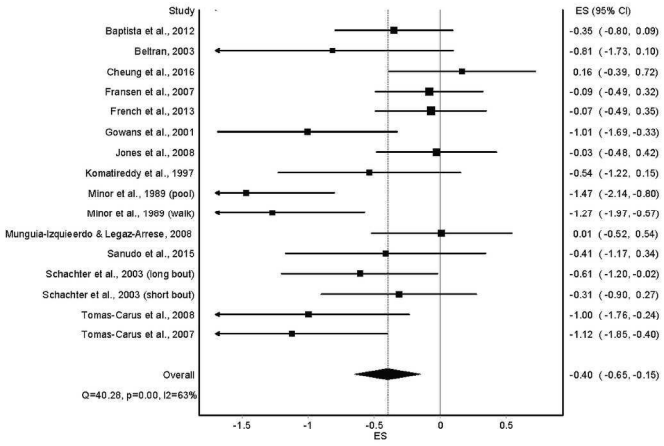


Figure 3. Forest plot for changes in anxiety.

173x224mm (300 x 300 DPI)

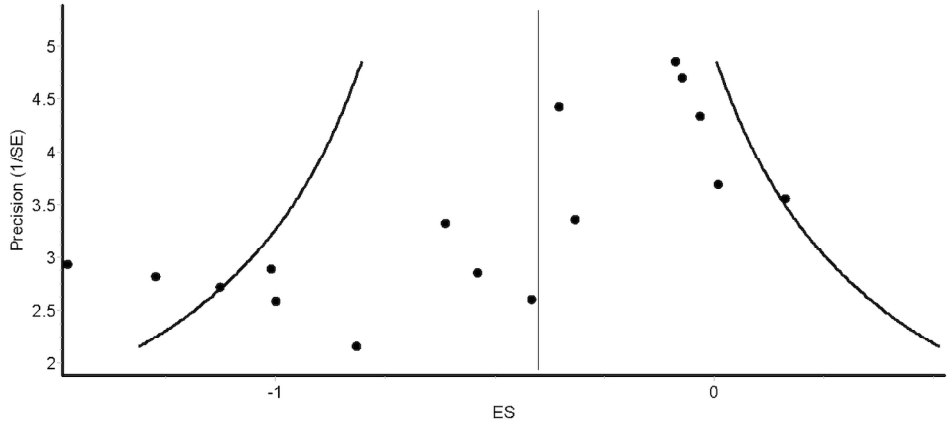


Figure 4. Funnel plot for changes in anxiety.

165x74mm (300 x 300 DPI)

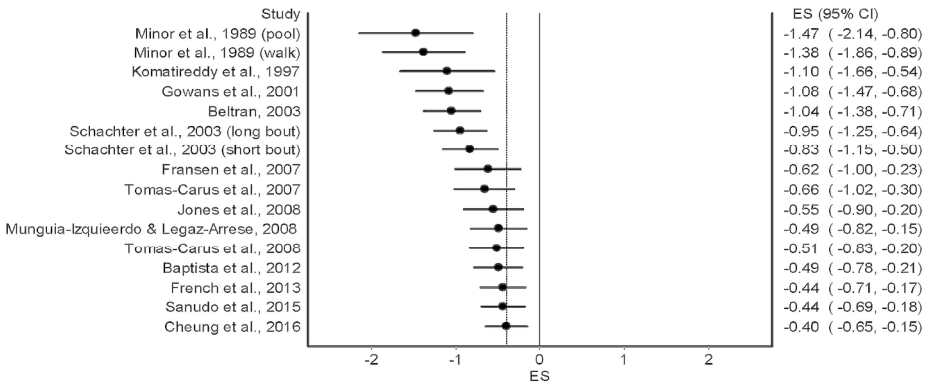


Figure 5. Cumulative meta-analysis for changes in anxiety.

173x87mm (300 x 300 DPI)

Supplementary file 1. PubMed search

Details - PubMed - NCBI

Search Details

Query Translation:

```
(("exercise"[MeSH Terms] OR "exercise"[All Fields]) OR
("exercise"[MeSH Terms] OR "exercise"[All Fields] OR
("physical"[All Fields] AND "activity"[All Fields])
OR "physical activity"[All Fields]) OR ("physical
fitness"[MeSH Terms] OR ("physical"[All Fields]
AND "fitness"[All Fields]) OR "physical fitness"[All
Fields]) OR ("physical therapy modalities"[MeSH Terms] OR
("physical"[All Fields] AND "therapy"[All Fields]
AND "modalities"[All Fields]) OR "physical therapy
modalities"[All Fields] OR ("physical"[All Fields]
```

Search | URL

Result:

167

Translations:

exercise	"exercise"[MeSH Terms] OR "exercise"[All Fields]
physical activity	"exercise"[MeSH Terms] OR "exercise"[All Fields] OR ("physical"[All Fields] AND "activity"[All Fields]) OR "physical activity"[All Fields]
physical fitness	"physical fitness"[MeSH Terms] OR ("physical"[All Fields] AND "fitness"[All Fields]) OR "physical fitness"[All Fields]
physical therapy	"physical therapy modalities"[MeSH Terms] OR ("physical"[All Fields] AND "therapy"[All Fields] AND "modalities"[All Fields]) OR "physical therapy modalities"[All Fields] OR ("physical"[All Fields] AND "therapy"[All Fields]) OR "physical therapy"[All Fields]
osteoarthritis	"osteoarthritis"[MeSH Terms] OR "osteoarthritis"[All Fields]
rheumatoid arthritis	"arthritis, rheumatoid"[MeSH Terms] OR ("arthritis"[All Fields] AND "rheumatoid"[All Fields]) OR "rheumatoid arthritis"[All Fields] OR ("rheumatoid"[All Fields] AND "arthritis"[All Fields])
arthritis	"arthritis"[MeSH Terms] OR "arthritis"[All Fields]
fibromyalgia	"fibromyalgia"[MeSH Terms] OR "fibromyalgia"[All Fields]
anxiety	"anxiety"[MeSH Terms] OR "anxiety"[All Fields]

Supplementary File 2. Excluded Studies, including reasons for exclusion.

1. 12th Commonwealth International Sport conference, 19-23 July 2002, Manchester, United Kingdom: abstract book. London;: Association of Commonwealth Universities 2002. *inappropriate study design*
2. ABSTRACTS. *Journal of Orthopaedic & Sports Physical Therapy* 2005;35(6):389-96. *inappropriate study design*
3. Fibromyalgia: poorly understood; treatments are disappointing. *Prescrire international* 2009;18(102):169-73. [published Online First: 2009/09/15] *inappropriate study design*
4. A Controlled Examination of Medical and Psychosocial Factors Associated With Low Back Pain in Combination With Widespread Musculoskeletal Pain. *Physical therapy* 2009;89(8):786-803. *inappropriate study design*
5. Acupuncture. *Focus on Alternative and Complementary Therapies* 2010;15(2):163-69. doi: 10.1211/fact.15.2.0065 *inappropriate intervention*
6. 2013 SYR Accepted Poster Abstracts. *International journal of yoga therapy* 2013;23 Suppl:32-53. [published Online First: 2013/01/01] *inappropriate study design*
7. Abbott R, Whear R, Nikolaou V, et al. Tumour necrosis factor-alpha inhibitor therapy in chronic physical illness: A systematic review and meta-analysis of the effect on depression and anxiety. *Journal of psychosomatic research* 2015;79(3):175-84. doi: 10.1016/j.jpsychores.2015.04.008 [published Online First: 2015/05/04] *inappropriate study design*
8. Adachi T, Nakae A, Maruo T, et al. Validation of the Japanese Version of the Pain Self-Efficacy Questionnaire in Japanese Patients with Chronic Pain. *Pain Medicine* 2014;15(8):1405-17. doi: 10.1111/pme.12446 *inappropriate study design*
9. Akhavan J. The effect of a dyadic intervention on self-efficacy, physical functioning, and anxiety/depression in older adults post joint replacement surgery [Ph.D.]. University of California, Los Angeles, 2008. *inappropriate study design*
10. Akman-Demir G, Saip S, Siva A. Behçet's disease. *Current Treatment Options in Neurology* 2011;13(3):290-310. doi: 10.1007/s11940-011-0120-2 *inappropriate study design*
11. Alamo MM, Moral RR, de Torres LAP. Evaluation of a patient-centred approach in generalized musculoskeletal chronic pain/fibromyalgia patients in primary care. *Patient education and counseling* 2002;48(1):23-31. doi: 10.1016/S0738-3991(02)00095-2 *inappropriate intervention*
12. Alayli G, Kuru O, Bilgici A. The effects of aerobic exercise and home exercise on pain and disability in patients with knee osteoarthritis. [Turkish]. *Journal of Rheumatology and Medical Rehabilitation* 2007; 18(2). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/761/CN-00707761/frame.html. *inappropriate comparison group*
13. Alipour B, Homayouni-Rad A, Vaghef-Mehrabany E, et al. Effects of Lactobacillus casei supplementation on disease activity and inflammatory cytokines in rheumatoid arthritis patients: a randomized double-blind clinical trial. *International journal of rheumatic diseases* 2014;17(5):519-27. doi: 10.1111/1756-185X.12333 *inappropriate intervention*

14. Ambrose KR, Golightly YM. Physical exercise as non-pharmacological treatment of chronic pain: Why and when. *Best Practice & Research in Clinical Rheumatology* 2015;29(1):120-30. doi: 10.1016/j.berh.2015.04.022 *inappropriate study design*
15. Andrews NE, Strong J, Meredith PJ. Activity Pacing, Avoidance, Endurance, and Associations With Patient Functioning in Chronic Pain: A Systematic Review and Meta-Analysis. *Archives of physical medicine and rehabilitation* 2012;93(11):2109-21. doi: 10.1016/j.apmr.2012.05.029 *inappropriate study design*
16. Ang D, Jensen M, Steiner J, et al. Combining cognitive-behavioral therapy and milnacipran for fibromyalgia: a feasibility randomized-controlled trial. *The Clinical journal of pain* 2013; 29(9). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/880/CN-00918880/frame.html. *inappropriate study design*
17. Appelbaum KA, Blanchard EB, Hickling EJ, et al. Cognitive behavioral treatment of a veteran population with moderate to severe rheumatoid arthritis. *Behavior Therapy* 1988;19(4):489-502. doi: 10.1016/S0005-7894(88)80019-4 *inappropriate intervention*
18. Archer T, Josefsson T, Lindwall M. Effects of Physical Exercise on Depressive Symptoms and Biomarkers in Depression. *Cns & Neurological Disorders-Drug Targets* 2014;13(10):1640-53. *inappropriate study design*
19. Arcos-Carmona IM, Castro-Sanchez AM, Mataran-Penarrocha GA, et al. [Effects of aerobic exercise program and relaxation techniques on anxiety, quality of sleep, depression, and quality of life in patients with fibromyalgia: a randomized controlled trial]. *Medicina clinica* 2011;137(9):398-401. doi: 10.1016/j.medcli.2010.09.045 [published Online First: 2011/02/25] *inappropriate intervention*
20. Arends RY, Bode C, Taal E, et al. A goal management intervention for polyarthritis patients: rationale and design of a randomized controlled trial. *BMC musculoskeletal disorders* 2013;14:239. doi: 10.1186/1471-2474-14-239 [published Online First: 2013/08/15] *inappropriate intervention*
21. Arne M, Janson C, Janson S, et al. Physical activity and quality of life in subjects with chronic disease: chronic obstructive pulmonary disease compared with rheumatoid arthritis and diabetes mellitus. *Scandinavian journal of primary health care* 2009;27(3):141-7. doi: 10.1080/02813430902808643 [published Online First: 2009/03/24] *inappropriate study design*
22. Arnold L, Wang F, Ahl J, et al. Improvement in multiple dimensions of fatigue in patients with fibromyalgia treated with duloxetine: secondary analysis of a randomized, placebo-controlled trial. *Arthritis research & therapy* 2011; 13(3). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/474/CN-00843474/frame.html. *inappropriate intervention*
23. Arnold L, Zlateva G, Sadosky A, et al. Correlations between Fibromyalgia Symptom and Function Domains and Patient Global Impression of Change: A Pooled Analysis of Three Randomized, Placebo-Controlled Trials of Pregabalin. *Pain medicine (Malden, Mass)* 2011; 12(2). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/608/CN-01016608/frame.html. *inappropriate study design*

24. Arnold LM. Strategies for managing fibromyalgia. *The American journal of medicine* 2009;122(12 Suppl):S31-43. doi: 10.1016/j.amjmed.2009.09.009 [published Online First: 2010/01/09] *inappropriate study design*
25. Arnold LM, Arsenault P, Huffman C, et al. Once daily controlled-release pregabalin in the treatment of patients with fibromyalgia: A phase III, double-blind, randomized withdrawal, placebo-controlled study. *Current Medical Research and Opinion* 2014;30(10):2069-83. doi: 10.1185/03007995.2014.928275 *inappropriate intervention*
26. Arnold LM, Clauw D, Wang F, et al. Flexible dosed duloxetine in the treatment of fibromyalgia: a randomized, double-blind, placebo-controlled trial. *The Journal of rheumatology* 2010;37(12):2578-86. doi: 10.3899/jrheum.100365 [published Online First: 2010/09/17] *inappropriate intervention*
27. Arnold LM, Crofford LJ, Martin SA, et al. The effect of anxiety and depression on improvements in pain in a randomized, controlled trial of pregabalin for treatment of fibromyalgia. *Pain Medicine* 2007;8(8):633-38. doi: 10.1111/j.1526-4637.2007.00332.x *inappropriate intervention*
28. Arnold LM, Russell IJ, Diri EW, et al. A 14-week, randomized, double-blinded, placebo-controlled monotherapy trial of pregabalin in patients with fibromyalgia. *The Journal of Pain* 2008;9(9):792-805. doi: 10.1016/j.jpain.2008.03.013 *inappropriate intervention*
29. Arnold LM, Wang F, Ahl J, et al. Improvement in multiple dimensions of fatigue in patients with fibromyalgia treated with duloxetine: secondary analysis of a randomized, placebo-controlled trial. *Arthritis research & therapy* 2011;13(3):R86. doi: 10.1186/ar3359 [published Online First: 2011/06/15] *inappropriate intervention*
30. Arnold LM, Williams DA, Hudson JI, et al. Development of responder definitions for fibromyalgia clinical trials. *Arthritis and rheumatism* 2012;64(3):885-94. doi: 10.1002/art.33360 [published Online First: 2011/09/29] *inappropriate outcomes*
31. Arnold LM, Zhang S, Pangallo BA. Efficacy and safety of duloxetine 30 mg/d in patients with fibromyalgia: A randomized, double-blind, placebo-controlled study. *The Clinical journal of pain* 2012;28(9):775-81. doi: 10.1097/AJP.0b013e3182510295 *inappropriate outcomes*
32. Arnold LM, Zlateva G, Sadosky A, et al. Correlations between fibromyalgia symptom and function domains and patient global impression of change: a pooled analysis of three randomized, placebo-controlled trials of pregabalin. *Pain medicine (Malden, Mass)* 2011;12(2):260-7. doi: 10.1111/j.1526-4637.2010.01047.x [published Online First: 2011/01/27] *inappropriate study design*
33. Assis MR, Silva LE, Alves AM, et al. A randomized controlled trial of deep water running: clinical effectiveness of aquatic exercise to treat fibromyalgia. *Arthritis and rheumatism* 2006;55(1):57-65. doi: 10.1002/art.21693 *inappropriate comparison group*
34. Ayral X, Gicquere C, Duhalde A, et al. Effects of video information on preoperative anxiety level and tolerability of joint lavage in knee osteoarthritis. *Arthritis and rheumatism* 2002;47(4):380-2. doi: 10.1002/art.10559 [published Online First: 2002/09/05] *inappropriate intervention*

35. Bae S, Gun S, Mok C, et al. Improved health outcomes with etanercept versus usual DMARD therapy in an Asian population with established rheumatoid arthritis. *BMC musculoskeletal disorders* 2013; 14. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/280/CN-00864280/frame.html. *inappropriate intervention*
36. Bagdath AO, Donmez A, Eroksuz R, et al. Does addition of 'mud-pack and hot pool treatment' to patient education make a difference in fibromyalgia patients? A randomized controlled single blind study. *International journal of biometeorology* 2015;59(12):1905-11. doi: 10.1007/s00484-015-0997-7 *inappropriate intervention*
37. Barlow J, Turner A, Wright C. A randomized controlled study of the Arthritis Self-Management Programme in the UK. *Health education research* 2000; 15(6). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/444/CN-00330444/frame.html. *inappropriate intervention*
38. Barlow JH, Powell LA, Gilchrist M, et al. The effectiveness of the Training and Support Program for parents of children with disabilities: a randomized controlled trial. *Journal of psychosomatic research* 2008;64(1):55-62. doi: 10.1016/j.jpsychores.2007.06.006 [published Online First: 2007/12/26] *inappropriate intervention*
39. Barsky AJ, Ahern DK, Orav EJ, et al. A Randomized Trial of Three Psychosocial Treatments for the Symptoms of Rheumatoid Arthritis. *Seminars in arthritis and rheumatism* 2010;40(3):222-32. doi: 10.1016/j.semarthrit.2010.04.001 *inappropriate intervention*
40. Basler HD. Group treatment for pain and discomfort. *Patient education and counseling* 1993;20(2-3):167-75. [published Online First: 1993/05/01] *inappropriate intervention*
41. Bassey EJ. Longitudinal changes in selected physical capabilities: muscle strength, flexibility and body size. *Age and Ageing* 1998;27:12-16. *inappropriate study design*
42. Bateman L, Sarzi-Puttini P, Burbridge CL, et al. Burden of illness in fibromyalgia patients with comorbid depression. *Clinical and experimental rheumatology* 2016;34(2 Suppl 96):S106-13. [published Online First: 2016/04/09] *inappropriate study design*
43. Baudic S, Attal N, Mhalla A, et al. Unilateral repetitive transcranial magnetic stimulation of the motor cortex does not affect cognition in patients with fibromyalgia. *Journal of Psychiatric Research* 2013;47(1):72-77. doi: 10.1016/j.jpsychires.2012.09.003 *inappropriate intervention*
44. Bearne L, Walsh N, Jessep S, et al. Feasibility of an exercise-based rehabilitation programme for chronic hip pain. *Musculoskeletal care* 2011; 9(3). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/898/CN-01124898/frame.html. *inappropriate intervention*
45. Bement MKH, Weyer A, Hartley S, et al. Pain Perception After Isometric Exercise in Women With Fibromyalgia. *Archives of physical medicine and rehabilitation* 2011;92(1):89-95. doi: 10.1016/j.apmr.2010.10.006 *inappropriate study design*
46. Bennell K, Ahamed Y, Jull G, et al. Physical Therapist-Delivered Pain Coping Skills Training and Exercise for Knee Osteoarthritis: Randomized Controlled Trial. *Arthritis care & research* 2016; 68(5).

http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/882/CN-01153882/frame.html. *inappropriate comparison group*

47. Bennell KL, Rini C, Keefe F, et al. Effects of Adding an Internet-Based Pain Coping Skills Training Protocol to a Standardized Education and Exercise Program for People With Persistent Hip Pain (HOPE Trial): Randomized Controlled Trial Protocol. *Physical therapy* 2015;95(10):1408-22. doi: 10.2522/ptj.20150119 [published Online First: 2015/05/30] *inappropriate study design*
48. Bennett R, Russell I, Choy E, et al. Evaluation of Patient-Rated Stiffness Associated With Fibromyalgia: A Post-Hoc Analysis of 4 Pooled, Randomized Clinical Trials of Duloxetine. *Clinical therapeutics* 2012; 34(4). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/551/CN-00896551/frame.html. *inappropriate intervention*
49. Bialosky JE, Bishop MD, Robinson ME, et al. Spinal Manipulative Therapy Has an Immediate Effect on Thermal Pain Sensitivity in People With Low Back Pain: A Randomized Controlled Trial. *Physical therapy* 2009;89(12):1292-303. doi: 10.2522/ptj.20090058 *inappropriate population*
50. Birbara C, Ruoff G, Sheldon E, et al. Efficacy and safety of rofecoxib 12.5 mg and celecoxib 200 mg in two similarly designed osteoarthritis studies. *Current medical research and opinion* 2006; 22(1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/019/CN-00554019/frame.html. *inappropriate intervention*
51. Bircan C, Karasel SA, Akgun B, et al. Effects of muscle strengthening versus aerobic exercise program in fibromyalgia. *Rheumatology international* 2008;28(6):527-32. doi: 10.1007/s00296-007-0484-5 [published Online First: 2007/11/06] *inappropriate comparison group*
52. Bishop MD, Beneciuk JM, George SZ. Immediate reduction in temporal sensory summation after thoracic spinal manipulation. *Spine Journal* 2011;11(5):440-46. doi: 10.1016/j.spinee.2011.03.001 *inappropriate intervention*
53. Blikman T, Rienstra W, van Raaij TM, et al. Duloxetine in OsteoArthritis (DOA) study: study protocol of a pragmatic open-label randomised controlled trial assessing the effect of preoperative pain treatment on postoperative outcome after total hip or knee arthroplasty. *BMJ open* 2016;6(3):e010343. doi: 10.1136/bmjopen-2015-010343 [published Online First: 2016/03/05] *inappropriate study design*
54. Blumenthal JA, Babyak MA, Moore KA, et al. Effects of exercise training on older patients with major depression. *Archives of Internal Medicine* 1999;159(19):2349-56. doi: 10.1001/archinte.159.19.2349 *inappropriate population*
55. Bojner Horwitz E, Kowalski J, Theorell T, et al. Dance/movement therapy in fibromyalgia patients: Changes in self-figure drawings and their relation to verbal self-rating scales. *The Arts in Psychotherapy* 2006;33(1):11-25. doi: http://dx.doi.org/10.1016/j.aip.2005.05.004 *inappropriate intervention*
56. Bojner-Horwitz E, Theorell T, Anderberg UM. Dance/movement therapy and changes in stress-related hormones: A study of fibromyalgia patients with video-interpretation. *The Arts in Psychotherapy* 2003;30(5):255-64. doi: 10.1016/j.aip.2003.07.001 *inappropriate outcomes*

57. Bojner-Horwitz E, Theorell T, Maria Anderberg U. Dance/movement therapy and changes in stress-related hormones: a study of fibromyalgia patients with video-interpretation. *The Arts in Psychotherapy* 2003;30(5):255-64. doi: http://dx.doi.org/10.1016/j.aip.2003.07.001 *inappropriate intervention*
58. Bongi SM, Del Rosso A, Di Felice C, et al. Resseguier method and Qi Gong sequentially integrated in patients with fibromyalgia syndrome. *Clinical and experimental rheumatology* 2012;30(6):S51-S58. *inappropriate comparison group*
59. Bongi SM, Paoletti G, Cala M, et al. Efficacy of rehabilitation with Tai Ji Quan in an Italian cohort of patients with Fibromyalgia Syndrome. *Complementary therapies in clinical practice* 2016;24:109-15. doi: 10.1016/j.ctcp.2016.05.010 *inappropriate intervention*
60. Booth FW, Roberts CK, Laye MJ. Lack of Exercise Is a Major Cause of Chronic Diseases. *Comprehensive Physiology* 2012;2(2):1143-211. doi: 10.1002/cphy.c110025 *inappropriate study design*
61. Boschen KA, Robinson E, Campbell KA, et al. Results from 10 Years of a CBT Pain Self-Management Outpatient Program for Complex Chronic Conditions. *Pain Research & Management* 2016 doi: 10.1155/2016/4678083 *inappropriate study design*
62. Bossen D, Buskermolen M, Veenhof C, et al. Adherence to a web-based physical activity intervention for patients with knee and/or hip Osteoarthritis: A mixed method study. *Journal of medical Internet research* 2013;15(10):55-66. doi: 10.2196/jmir.2742 *inappropriate comparison group*
63. Bossen D, Veenhof C, Kloek C, et al. The association between psychological factors and physical activity levels in patients with knee and hip osteoarthritis. *Physiotherapy (United Kingdom)* 2015; 101. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/535/CN-01126535/frame.html. *inappropriate study design*
64. Bossen D, Veenhof C, Van Beek KEC, et al. Effectiveness of a Web-Based Physical Activity Intervention in Patients With Knee and/or Hip Osteoarthritis: Randomized Controlled Trial. *Journal of medical Internet research* 2013;15(11) doi: 10.2196/jmir.2662 *inappropriate intervention*
65. Boyer L, Dousset A, Roussel P, et al. rTMS in fibromyalgia: a randomized trial evaluating QoL and its brain metabolic substrate. *Neurology* 2014;82(14):1231-8. doi: 10.1212/wnl.0000000000000280 [published Online First: 2014/03/29] *inappropriate intervention*
66. Bradt J, Norris M, Shim M, et al. Vocal Music Therapy for Chronic Pain Management in Inner-City African Americans: A Mixed Methods Feasibility Study. *Journal of Music Therapy* 2016;53(2):178-206. doi: 10.1093/jmt/thw004 *inappropriate intervention*
67. Braz AS, Morais LCS, Paula AP, et al. Effects of Panax ginseng extract in patients with fibromyalgia: A 12-week, randomized, double-blind, placebo-controlled trial. *Revista Brasileira de Psiquiatria* 2013;35(1):21-28. doi: 10.1016/j.rbp.2013.01.004 *inappropriate intervention*
68. Broderick J, Junghaenel D, Schwartz J. Written emotional expression produces health benefits in fibromyalgia patients. *Psychosomatic medicine* 2005; 67(2).

http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/627/CN-00560627/frame.html. *inappropriate intervention*

69. Brus H, Taal E, Laar M, et al. Patient education and disease activity: a study among rheumatoid arthritis patients. *Arthritis care and research : the official journal of the Arthritis Health Professions Association* 1997; 10(5). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/155/CN-00145155/frame.html. *inappropriate study design*
70. Busch A. Hydrotherapy improves pain, knee strength, and quality of life in women with fibromyalgia. *Australian Journal of Physiotherapy* 2007;53(1):64-64. *inappropriate study design*
71. Buskila D, Abu-Shakra M, Neumann L, et al. Balneotherapy for fibromyalgia at the Dead Sea. *Rheumatology international* 2001;20(3):105-8. doi: 10.1007/s002960000085 [published Online First: 2001/05/17] *inappropriate intervention*
72. Buszewicz M, Rait G, Griffin M, et al. Self management of arthritis in primary care: randomised controlled trial. *BMJ (Clinical research ed)* 2006;333(7574):879. doi: 10.1136/bmj.38965.375718.80 [published Online First: 2006/10/17] *inappropriate intervention*
73. Buttagat V, Eungpinichpong W, Kaber D, et al. Acute effects of traditional Thai massage on electroencephalogram in patients with scapulocostal syndrome. *Complementary Therapies in Medicine* 2012;20(4):167-74. doi: 10.1016/j.ctim.2012.02.002 *inappropriate intervention*
74. Büyükyılmaz F, Aştı T. The effect of relaxation techniques and back massage on pain and anxiety in Turkish total hip or knee arthroplasty patients. *Pain Management Nursing* 2013;14(3):143-54. doi: 10.1016/j.pmn.2010.11.001 *inappropriate intervention*
75. Calandre EP, Rico-Villademoros F. The role of antipsychotics in the management of fibromyalgia. *CNS drugs* 2012;26(2):135-53. doi: 10.2165/11597130-000000000-00000 [published Online First: 2012/02/03] *inappropriate study design*
76. Calandre EP, Rodriguez-Claro ML, Rico-Villademoros F, et al. Effects of pool-based exercise in fibromyalgia symptomatology and sleep quality: a prospective randomised comparison between stretching and Ai Chi. *Clinical and experimental rheumatology* 2009;27(5 Suppl 56):S21-8. [published Online First: 2010/03/12] *inappropriate intervention*
77. Campbell CM, McCauley L, Bounds SC, et al. Changes in pain catastrophizing predict later changes in fibromyalgia clinical and experimental pain report: cross-lagged panel analyses of dispositional and situational catastrophizing. *Arthritis research & therapy* 2012;14(5):R231. doi: 10.1186/ar4073 [published Online First: 2012/10/27] *inappropriate outcomes*
78. Cancelliere C. Are workplace health promotion/wellness programs effective at improving presenteeism (on-the-job productivity) in workers? A systematic review and best evidence synthesis of the literature [M.P.H.]. Lakehead University (Canada), 2011. *inappropriate study design*

79. Carbonell-Baeza A, Aparicio VA, Chillon P, et al. Effectiveness of multidisciplinary therapy on symptomatology and quality of life in women with fibromyalgia. *Clinical and experimental rheumatology* 2011;29(6):S97-S103. *inappropriate study design*
80. Carbonell-Baeza A, Aparicio VA, Martins-Pereira CM, et al. Efficacy of Biodanza for Treating Women with Fibromyalgia. *Journal of Alternative and Complementary Medicine* 2010;16(11):1191-200. doi: 10.1089/acm.2010-0039 *inappropriate study design*
81. Carbonell-Baeza A, Romero A, Aparicio VA, et al. Preliminary Findings of a 4-Month Tai Chi Intervention on Tenderness, Functional Capacity, Symptomatology, and Quality of Life in Men With Fibromyalgia. *American Journal of Mens Health* 2011;5(5):421-29. doi: 10.1177/1557988311400063 *inappropriate intervention*
82. Carbonell-Baeza A, Ruizz JR, Aparicio VA, et al. Multidisciplinary and biodanza intervention for the management of fibromyalgia. *Acta Reumatologica Portuguesa* 2012;37(3):240-50. *inappropriate comparison group*
83. Carleton RN, Richter AA, Asmundson GJG. Attention modification in persons with fibromyalgia: A double blind, randomized clinical trial. *Cognitive Behaviour Therapy* 2011;40(4):279-90. doi: 10.1080/16506073.2011.616218 *inappropriate intervention*
84. Carmichael NME, Katz J, Clarke H, et al. An intensive perioperative regimen of pregabalin and celecoxib reduces pain and improves physical function scores six weeks after total hip arthroplasty: A prospective randomized controlled trial. *Pain Research & Management* 2013;18(3):127-32. doi: 10.1155/2013/258714 *inappropriate intervention*
85. Carson JW, Carson KM, Jones KD, et al. A pilot randomized controlled trial of the Yoga of Awareness program in the management of fibromyalgia. *Pain* 2010;151(2):530-9. doi: 10.1016/j.pain.2010.08.020 [published Online First: 2010/10/16] *inappropriate intervention*
86. Carson JW, Carson KM, Jones KD, et al. Follow-up of yoga of awareness for fibromyalgia: results at 3 months and replication in the wait-list group. *The Clinical journal of pain* 2012;28(9):804-13. doi: 10.1097/AJP.0b013e31824549b5 [published Online First: 2012/07/04] *inappropriate study design*
87. Carta MG, Cardia C, Mannu F, et al. The high frequency of manic symptoms in fibromyalgia does influence the choice of treatment? *Clinical Practice and Epidemiology in Mental Health* 2006;2 *inappropriate study design*
88. Casanueva-Fernandez B, Llorca J, Rubio JBI, et al. Efficacy of a multidisciplinary treatment program in patients with severe fibromyalgia. *Rheumatology international* 2012;32(8):2497-502. doi: 10.1007/s00296-011-2045-1 *inappropriate intervention*
89. Castel A, Castro S, Fontova R, et al. Body mass index and response to a multidisciplinary treatment of fibromyalgia. *Rheumatology international* 2015;35(2):303-14. doi: 10.1007/s00296-014-3096-x [published Online First: 2014/08/02] *inappropriate intervention*
90. Castel A, Fontova R, Montull S, et al. Efficacy of a Multidisciplinary Fibromyalgia Treatment Adapted for Women With Low Educational Levels: A Randomized Controlled Trial. *Arthritis care & research* 2013;65(3):421-31. doi: 10.1002/acr.21818 *inappropriate intervention*

91. Castrejon I, Yazici Y, Samuels J, et al. Discordance of global estimates by patients and their physicians in usual care of many rheumatic diseases: association with 5 scores on a Multidimensional Health Assessment Questionnaire (MDHAQ) that are not found on the Health Assessment Questionnaire (HAQ). *Arthritis care & research* 2014;66(6):934-42. doi: 10.1002/acr.22237 [published Online First: 2013/12/05] *inappropriate study design*
92. Castro MMC, Daltro C, Kraychete DC, et al. The cognitive behavioral therapy causes an improvement in quality of life in patients with chronic musculoskeletal pain. *Arquivos De Neuro-Psiquiatria* 2012;70(11):864-68. *inappropriate population*
93. Castro-Sanchez AM, Mataran-Penarrocha GA, Granero-Molina J, et al. Benefits of massage-myofascial release therapy on pain, anxiety, quality of sleep, depression, and quality of life in patients with fibromyalgia. *Evidence-based complementary and alternative medicine : eCAM* 2011;2011:561753. doi: 10.1155/2011/561753 [published Online First: 2011/01/15] *inappropriate intervention*
94. Cedraschi C, Desmeules J, Rapiti E, et al. Fibromyalgia: a randomised, controlled trial of a treatment programme based on self management. *Annals of the rheumatic diseases* 2004; 63(3). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/285/CN-00471285/frame.html. *inappropriate intervention*
95. Celenay ST, Kaya DO, Akbayrak T. Cervical and scapulothoracic stabilization exercises with and without connective tissue massage for chronic mechanical neck pain: A prospective, randomised controlled trial. *Manual therapy* 2016;21:144-50. doi: 10.1016/j.math.2015.07.003 *inappropriate intervention*
96. Cella M, Sharpe M, Chalder T. Measuring disability in patients with chronic fatigue syndrome: reliability and validity of the Work and Social Adjustment Scale. *Journal of psychosomatic research* 2011;71(3):124-8. doi: 10.1016/j.jpsychores.2011.02.009 [published Online First: 2011/08/17] *inappropriate population*
97. Chatzitheodorou D, Mavromoustakos S, Milioti S. The effect of exercise on adrenocortical responsiveness of patients with chronic low back pain, controlled for psychological strain. *Clinical Rehabilitation* 2008;22(4):319-28. doi: 10.1177/0269215507079858 *inappropriate population*
98. Chen KW, Perlman A, Liao JG, et al. Effects of external qigong therapy on osteoarthritis of the knee. A randomized controlled trial. *Clinical rheumatology* 2008;27(12):1497-505. doi: 10.1007/s10067-008-0955-4 [published Online First: 2008/07/26] *inappropriate intervention*
99. Cheung C, Wyman J, Bronas U, et al. Is yoga better than aerobic/strengthening exercises for managing knee osteoarthritis in older adults? *Osteoarthritis and cartilage* 2016; 24. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/579/CN-01142579/frame.html. *inappropriate study design*
100. Christensen R, Henriksen M, Leeds A, et al. Effect of weight maintenance on symptoms of knee osteoarthritis in obese patients: a twelve-month randomized controlled trial. *Arthritis care & research* 2015; 67(5).

http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/664/CN-01075664/frame.html. *inappropriate outcomes*

101. Christensen SS, Frostholm L, Ørnbøl E, et al. Changes in illness perceptions mediated the effect of cognitive behavioural therapy in severe functional somatic syndromes. *Journal of psychosomatic research* 2015;78(4):363-70. doi: 10.1016/j.jpsychores.2014.12.005 *inappropriate study design*
102. Citrome L, Weiss-Citrome A. A systematic review of duloxetine for osteoarthritic pain: What is the number needed to treat, number needed to harm, and likelihood to be helped or harmed? *Postgraduate Medicine* 2012;124(1):83-93. doi: 10.3810/pgm.2012.01.2521 *inappropriate study design*
103. Clark DI, Downing N, Mitchell J, et al. Physiotherapy for anterior knee pain: a randomised controlled trial. *Annals of the rheumatic diseases* 2000;59(9):700-04. doi: 10.1136/ard.59.9.700 *inappropriate population*
104. Clarke-Jenssen A-C, Mengshoel AM, Staalesen Strumse Y, et al. EFFECT OF A FIBROMYAFGIA REHABILITATION PROGRAMME IN WARM VERSUS COLD CLIMATE: A RANDOMIZED CONTROLLED STUDY. *Journal of Rehabilitation Medicine (Stiftelsen Rehabiliteringsinformation)* 2014;46(7):676-83. doi: 10.2340/16501977-1819 *inappropriate intervention*
105. Cordoba-Torrecilla S, Aparicio VA, Soriano-Maldonado A, et al. Physical fitness is associated with anxiety levels in women with fibromyalgia: the al-Andalus project. *Quality of Life Research* 2016;25(4):1053-58. doi: 10.1007/s11136-015-1128-y *inappropriate study design*
106. Cöster L, Kendall S, Gerdle B, et al. Chronic widespread musculoskeletal pain--A comparison of those who meet criteria for fibromyalgia and those who do not. *European Journal of Pain* 2008;12(5):600-10. doi: 10.1016/j.ejpain.2007.10.001 *inappropriate study design*
107. Courtois I, Cools F, Calsius J. Effectiveness of body awareness interventions in fibromyalgia and chronic fatigue syndrome: a systematic review and meta-analysis. *Journal of bodywork and movement therapies* 2015;19(1):35-56. doi: 10.1016/j.jbmt.2014.04.003 [published Online First: 2015/01/22] *inappropriate study design*
108. Couto CI. Exercise training and pyridostigmine each have unique benefits for patients with fibromyalgia. *Australian Journal of Physiotherapy* 2008;54(3):219-19. *inappropriate study design*
109. Creavin ST, Dunn KM, Mallen CD, et al. Co-occurrence and associations of pain and fatigue in a community sample of Dutch adults. *European Journal of Pain* 2010;14(3):327-34. doi: 10.1016/j.ejpain.2009.05.010 *inappropriate study design*
110. Cuesta-Vargas A, Luciano JV, Peñarrubia-María MT, et al. Clinical dimensions of fibromyalgia symptoms and development of a combined index of severity: The CODI index. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care & Rehabilitation* 2013;22(1):153-60. doi: 10.1007/s11136-012-0134-6 *inappropriate study design*
111. Cuss A, Morris M, Ambler N, et al. Goal setting for managing rheumatoid arthritis fatigue: A qualitative exploration. *Rheumatology Conference: Rheumatology 2010 - British Society for Rheumatology, BSR and British Health Professionals in Rheumatology, BHPR Annual Meeting 2010 Birmingham United Kingdom*

Conference Start: 20100420 Conference End: 20100423 Conference Publication: (varpagings) 2010; 49. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/368/CN-00789368/frame.html. *inappropriate study design*

112. Dailey DL, Frey Law LA, Vance CG, et al. Perceived function and physical performance are associated with pain and fatigue in women with fibromyalgia. *Arthritis research & therapy* 2016;18:68. doi: 10.1186/s13075-016-0954-9 [published Online First: 2015/01/01] *inappropriate study design*
113. Daltroy LH, Morlino CI, Eaton HM, et al. Preoperative education for total hip and knee replacement patients. *Arthritis care & research* 1998;11(6):469-78. doi: 10.1002/art.1790110607 *inappropriate intervention*
114. das Nair R, Anderson P, Clarke S, et al. Home-administered pre-surgical psychological intervention for knee osteoarthritis (HAPPiKNEES): study protocol for a randomised controlled trial. *Trials* 2016;17:54. doi: 10.1186/s13063-016-1165-z [published Online First: 2016/01/29] *inappropriate intervention*
115. Davis MC, Zautra AJ, Wolf LD, et al. Mindfulness and cognitive-behavioral interventions for chronic pain: Differential effects on daily pain reactivity and stress reactivity. *Journal of Consulting and Clinical Psychology* 2015;83(1):24-35. doi: 10.1037/a0038200 *inappropriate intervention*
116. de Brouwer SJM, Kraaimaat FW, Sweep F, et al. Psychophysiological Responses to Stress after Stress Management Training in Patients with Rheumatoid Arthritis. *PloS one* 2011;6(12) doi: 10.1371/journal.pone.0027432 *inappropriate intervention*
117. D'Eon MS. Feasibility and Acceptability of Graded In-Vivo Exposure Therapy for Fibromyalgia Patients [Ph.D.]. University of California, San Diego, 2016. *inappropriate intervention*
118. Donmez A, Karagulle MZ, Tercan N, et al. SPA therapy in fibromyalgia: a randomised controlled clinic study. *Rheumatology international* 2005;26(2):168-72. doi: 10.1007/s00296-005-0623-9 [published Online First: 2005/06/21] *inappropriate intervention*
119. Dougados M, Tsai WC, Saaibi DL, et al. Evaluation of Health Outcomes with Etanercept Treatment in Patients with Early Nonradiographic Axial Spondyloarthritis. *The Journal of rheumatology* 2015;42(10):1835-41. doi: 10.3899/jrheum.141313 [published Online First: 2015/08/16] *inappropriate intervention*
120. Driban JB, Morgan N, Price LL, et al. Patient-Reported Outcomes Measurement Information System (PROMIS) instruments among individuals with symptomatic knee osteoarthritis: a cross-sectional study of floor/ceiling effects and construct validity. *BMC musculoskeletal disorders* 2015;16 doi: 10.1186/s12891-015-0715-y *inappropriate study design*
121. Dunn-Lewis C, Kraemer WJ, Kupchak BR, et al. A multi-nutrient supplement reduced markers of inflammation and improved physical performance in active individuals of middle to older age: a randomized, double-blind, placebo-controlled study. *Nutrition Journal* 2011;10 doi: 10.1186/1475-2891-10-90 *inappropriate intervention*

122. Ekici G, Bakar Y, Akbayrak T, et al. Comparison of manual lymph drainage therapy and connective tissue massage in women with fibromyalgia: a randomized controlled trial. *Journal of manipulative and physiological therapeutics* 2009;32(2):127-33. doi: 10.1016/j.jmpt.2008.12.001 [published Online First: 2009/02/27] *inappropriate intervention*
123. Ekici G, Unal E, Akbayrak T, et al. Effects of active/passive interventions on pain, anxiety, and quality of life in women with fibromyalgia: Randomized controlled pilot trial. *Women & health* 2017;57(1):88-107. doi: 10.1080/03630242.2016.1153017 [published Online First: 2016/02/18] *inappropriate comparison group*
124. Ekici G, Unal E, Akbayrak T, et al. Active versus passive therapy in females with fibromyalgia; "pilates exercises and connective tissue massage": A randomized controlled pilot trial, Fibromiyaljili kadinlarda pasif tedaviye karsi aktif tedavi: "pilates egzersizleri ve konnektif doku masaji": Randomize kontrollu pilot calisma. [Turkish, English]. *Fizyoterapi Rehabilitasyon* 2014; 25(1 suppl. 1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/055/CN-01010055/frame.html. *inappropriate comparison group*
125. Elias A, Yaacob LH, Kadir AA, et al. Guided Imagery Relaxation Therapy in Malaysian Patients with Knee Osteoarthritis: A Randomized Controlled Trial. *International Journal of Collaborative Research on Internal Medicine & Public Health* 2015;7(5):92-103. *inappropriate intervention*
126. Elliot DL, Kuehl KS, Jones KD, et al. Using an eccentric exercise-testing protocol to assess the beneficial effects of tart cherry juice in fibromyalgia patients. *Integrative Medicine: A Clinician's Journal* 2010;9(6):24-29. *inappropriate intervention*
127. Emery P, Bingham C, Burmester G, et al. Improvements in patient-reported outcomes following 52 weeks of treatment with certolizumab pegol in combination with methotrexate in DMARD-naive patients with severe, active and progressive rheumatoid arthritis: Results from the C-early randomized, double-blind, controlled phase 3 study. *Value in health* 2015; 18(7). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/114/CN-01164114/frame.html. *inappropriate intervention*
128. Engel C. Tailored cognitive-behavioral therapy plus exercise training improved clinical and functional outcomes in fibromyalgia. *Annals of internal medicine* 2011; 154(8). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/037/CN-00895037/frame.html. *inappropriate intervention*
129. Ericsson A, Bremell T, Cider A, et al. Effects of exercise on fatigue and physical capacity in men with chronic widespread pain - a pilot study. *Bmc Sports Science Medicine and Rehabilitation* 2016;8 doi: 10.1186/s13102-016-0054-9 *inappropriate population*
130. Ericsson A, Palstam A, Larsson A, et al. Resistance exercise improves physical fatigue in women with fibromyalgia: a randomized controlled trial. *Arthritis research & therapy* 2016;18 doi: 10.1186/s13075-016-1073-3 *inappropriate comparison group*

131. Falcão DM, Sales L, Leite JR, et al. Cognitive behavioral therapy for the treatment of fibromyalgia syndrome: a randomized controlled trial. *Journal of Musculoskeletal Pain* 2008;16(3):133-40. *inappropriate intervention*
132. Fark AR. A pilot study of white-coat and labile hypertension: Associations with diagnoses of psychosocial dysfunction. *Family Practice Research Journal* 1993;13(1):71-80. *inappropriate outcomes*
133. Feldthusen C, Dean E, Forsblad-d'Elia H, et al. Effects of Person-Centered Physical Therapy on Fatigue-Related Variables in Persons With Rheumatoid Arthritis: A Randomized Controlled Trial. *Archives of Physical Medicine & Rehabilitation* 2016;97(1):26-36. *inappropriate intervention*
134. Fenton G, Morley S. A tale of two RCTs: Using randomized controlled trials to benchmark routine clinical (psychological) treatments for chronic pain. *Pain* 2013;154(10):2108-19. doi: 10.1016/j.pain.2013.06.033 *inappropriate study design*
135. Field T. Yoga research review. *Complementary therapies in clinical practice* 2016;24:145-61. doi: 10.1016/j.ctcp.2016.06.005 [published Online First: 2016/08/10] *inappropriate intervention*
136. Field T, Diego M, Cullen C, et al. Fibromyalgia pain and substance P decrease and sleep improves after massage therapy. *Jcr-Journal of Clinical Rheumatology* 2002;8(2):72-76. doi: 10.1097/00124743-200204000-00002 *inappropriate intervention*
137. Field T, Diego M, Delgado J, et al. Rheumatoid arthritis in upper limbs benefits from moderate pressure massage therapy. *Complementary therapies in clinical practice* 2013;19(2):101-3. doi: 10.1016/j.ctcp.2012.12.001 [published Online First: 2013/04/09] *inappropriate intervention*
138. Field T, Hernandez-Reif M, Seligman S, et al. Juvenile rheumatoid arthritis: benefits from massage therapy. *Journal of pediatric psychology* 1997;22(5):607-17. [published Online First: 1998/02/12] *inappropriate population*
139. Fitzgerald GK, White DK, Piva SR. Associations for change in physical and psychological factors and treatment response following exercise in knee osteoarthritis: an exploratory study. *Arthritis care & research* 2012;64(11):1673-80. doi: 10.1002/acr.21751 [published Online First: 2012/06/08] *inappropriate outcomes*
140. Fjorback L, Schroder A, Ornbol E, et al. Mindfulness therapy for bodily distress syndrome - A randomized controlled trial. *Journal of psychosomatic research* 2011; 70(6). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/011/CN-01006011/frame.html. *inappropriate intervention*
141. Fjorback LO, Arendt M, Ørnbøl E, et al. Mindfulness therapy for somatization disorder and functional somatic syndromes — randomized trial with one-year follow-up. *Journal of psychosomatic research* 2013;74(1):31-40. doi: 10.1016/j.jpsychores.2012.09.006 *inappropriate intervention*
142. Fors EA, Götestam KG. Patient education, guided imagery and pain related talk in fibromyalgia coping. *The European Journal of Psychiatry* 2000;14(4):233-40. *inappropriate intervention*
143. Fregni F, Gimenes R, Valle AC, et al. A randomized, sham-controlled, proof of principle study of transcranial direct current stimulation for the treatment of pain

in fibromyalgia. *Arthritis and rheumatism* 2006;54(12):3988-98. doi: 10.1002/art.22195 [published Online First: 2006/11/30] *inappropriate intervention*

144. French H, Cusack T, Brennan A, et al. The effectiveness of exercise with and without manual therapy for hip osteoarthritis: A multi-centre randomised controlled trial. *Arthritis and rheumatism* 2011; 63(10 suppl. 1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/130/CN-01005130/frame.html. *inappropriate study design*
145. French H, Cusack T, Brennan A, et al. The effectiveness of exercise therapy with and without manual therapy for hip osteoarthritis: A multicentre randomised controlled trial. *Rheumatology* 2011; 50. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/722/CN-01003722/frame.html. *inappropriate study design*
146. French HP, Cusack T, Brennan A, et al. Exercise and manual physiotherapy arthritis research trial (EMPART): a multicentre randomised controlled trial. *BMC musculoskeletal disorders* 2009;10:9. doi: 10.1186/1471-2474-10-9 [published Online First: 2009/01/21] *inappropriate study design*
147. French HP, Galvin R, Cusack T, et al. Predictors of short-term outcome to exercise and manual therapy for people with hip osteoarthritis. *Physical therapy* 2014;94(1):31-9. doi: 10.2522/ptj.20130173 [published Online First: 2013/08/10] *inappropriate study design*
148. Friedrich M, Hahne J, Wepner F. A controlled examination of medical and psychosocial factors associated with low back pain in combination with widespread musculoskeletal pain. *Physical therapy* 2009;89(8):786-803. doi: 10.2522/ptj.20080100 [published Online First: 2009/06/23] *inappropriate population*
149. Fulton AS, Hill AM, Williams MT, et al. Feasibility of omega-3 fatty acid supplementation as an adjunct therapy for people with chronic obstructive pulmonary disease: study protocol for a randomized controlled trial. *Trials* 2013;14 doi: 10.1186/1468-6708-14-107 *inappropriate intervention*
150. Garcia-Campayo J, Pascual A, Alda M, et al. Coping with fibromialgia: Usefulness of the Chronic Pain Coping Inventory-42. *Pain* 2007;132(Suppl 1):S68-S76. doi: 10.1016/j.pain.2007.02.013 *inappropriate intervention*
151. Garcia-Palacios A, Herrero R, Vizcaino Y, et al. Integrating Virtual Reality With Activity Management for the Treatment of Fibromyalgia Acceptability and Preliminary Efficacy. *Clinical Journal of Pain* 2015;31(6):564-72. doi: 10.1097/ajp.0000000000000196 *inappropriate intervention*
152. Garvey WT, Mechanick JI, Brett EM, et al. AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY COMPREHENSIVE CLINICAL PRACTICE GUIDELINES FOR MEDICAL CARE OF PATIENTS WITH OBESITY. *Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists* 2016;22 Suppl 3:1-203. doi: 10.4158/ep161365.gl [published Online First: 2016/05/25] *inappropriate study design*

153. Gavi M, 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(3) doi: 10.1371/journal.pone.0090767 *inappropriate comparison group*
154. Genc A, Tur BS, Aytur YK, et al. Does aerobic exercise affect the hypothalamicpituitary- adrenal hormonal response in patients with fibromyalgia syndrome? *Journal of Physical Therapy Science* 2015;27(7):2225-31. *inappropriate outcomes*
155. Gerskowitch C, Norman I, Rimes KA. Patients with medically unexplained physical symptoms experience of receiving treatment in a primary-care psychological therapies service: a qualitative study. *Cognitive Behaviour Therapist* 2015;8 doi: 10.1017/s1352465815000235 *inappropriate intervention*
156. Gniadecki R, Robertson D, Molta CT, et al. Self-reported health outcomes in patients with psoriasis and psoriatic arthritis randomized to two etanercept regimens. *Journal of the European Academy of Dermatology and Venereology : JEADV* 2012;26(11):1436-43. doi: 10.1111/j.1468-3083.2011.04308.x http://dx.doi.org/10.1111/j.1468-3083.2011.04308.x [published Online First: 2011/11/01] *inappropriate intervention*
157. Goodwin P, Al QK, Gregory W, et al. The effectiveness of aquatic physiotherapy in patients with rheumatoid arthritis: A randomised controlled trial. *Physiotherapy (United Kingdom)* 2015; 101. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/496/CN-01126496/frame.html. *inappropriate comparison group*
158. Gowans SE, DeHueck A, Abbey SE. Measuring exercise-induced mood changes in fibromyalgia: a comparison of several measures. *Arthritis and rheumatism* 2002;47(6):603-9. doi: 10.1002/art.10789 [published Online First: 2003/01/11] *inappropriate population*
159. Gowans SE, Dehueck A, Voss S, et al. Six-month and one-year followup of 23 weeks of aerobic exercise for individuals with fibromyalgia. *Arthritis and rheumatism* 2004;51(6):890-8. doi: 10.1002/art.20828 [published Online First: 2004/12/14] *inappropriate population*
160. Grace SL, Krepostman S, Brooks D, et al. Illness perceptions among cardiac patients: Relation to depressive symptomatology and sex. *Journal of psychosomatic research* 2005;59(3):153-60. doi: 10.1016/j.jpsychores.2005.05.005 *inappropriate study design*
161. Gremeaux V, Durand S, Benaim C, et al. Evaluation of various ways to deliver information concerning non-steroidal anti-inflammatory drugs to osteoarthritis patients. *Annals of physical and rehabilitation medicine* 2013;56(1):14-29. doi: 10.1016/j.rehab.2012.12.004 [published Online First: 2013/02/02] *inappropriate study design*
162. Gronning K, Bratas O, Steinsbekk A. Which Factors Influence Self-Efficacy in Patients with Chronic Inflammatory Polyarthritis? *Musculoskeletal care* 2016;14(2):77-86. doi: 10.1002/msc.1114 *inappropriate study design*
163. Gronning K, Rannestad T, Skomsvoll JF, et al. Long-term effects of a nurse-led group and individual patient education programme for patients with chronic inflammatory polyarthritis - a randomised controlled trial. *Journal of clinical*

nursing 2014;23(7-8):1005-17. doi: 10.1111/jocn.12353 [published Online First: 2013/07/24] *inappropriate intervention*
164. Gronning K, Skomsvoll JF, Rannestad T, et al. The effect of an educational programme consisting of group and individual arthritis education for patients with polyarthritis-A randomised controlled trial. *Patient education and counseling* 2012;88(1):113-20. doi: 10.1016/j.pec.2011.12.011 *inappropriate intervention*
165. Gulec H, Capkin E, Sayar K, et al. The evaluation of the effectiveness of amitriptyline versus venlafaxine in female patients diagnosed with fibromyalgia syndrome. [Turkish]. *Klinik Psikofarmakoloji Bulteni* 2007; 17(2). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/184/CN-00642184/frame.html. *inappropriate intervention*
166. Gusi N, Tomas-Carus P, Hakkinen A, et al. Exercise in waist-high warm water decreases pain and improves health-related quality of life and strength in the lower extremities in women with fibromyalgia. *Arthritis and rheumatism* 2006;55(1):66-73. doi: 10.1002/art.21718 *inappropriate population*
167. Haak T, Scott B. The effect of Qigong on fibromyalgia (FMS): a controlled randomized study. *DisabilRehabil* 2008;30(8):625-33. *inappropriate intervention*
168. Haugstad GK, Haugstad TS, Kirste UM, et al. Continuing improvement of chronic pelvic pain in women after short-term Mensendieck somatocognitive therapy: results of a 1-year follow-up study. *American Journal of Obstetrics and Gynecology* 2008;199(6) doi: 10.1016/j.ajog.2008.06.019 *inappropriate population*
169. Haun JN, Graham-Pole J, Shortley B. Children with cancer and blood diseases experience positive physical and psychological effects from massage therapy. *International journal of therapeutic massage & bodywork* 2009;2(2):7-14. [published Online First: 2009/01/01] *inappropriate population*
170. Haupt M, Millen S, Janner M, et al. Improvement of coping abilities in patients with systemic lupus erythematosus: a prospective study. *Annals of the rheumatic diseases* 2005;64(11):1618-23. doi: 10.1136/ard.2004.029926 *inappropriate population*
171. Hauser W. The german fibromyalgia consumer reports-a cross-sectional survey. *Annals of the Rheumatic Disease* 2013; 71. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/601/CN-01011601/frame.html. *inappropriate study design*
172. Hecker CD, Melo C, Tomazoni SdS, et al. Analysis of effects of kinesiotherapy and hydrokinesiotherapy on the quality of patients with fibromyalgia -- a randomized clinical trial. *Fisioterapia em Movimento* 2011;24(1):57-64. doi: 10.1590/S0103-51502011000100007 *inappropriate comparison group*
173. Heffez DS, Ross RE, Shade-Zeldow Y, et al. Treatment of cervical myelopathy in patients with the fibromyalgia syndrome: outcomes and implications. *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society* 2007;16(9):1423-33. doi: 10.1007/s00586-007-0366-2 [published Online First: 2007/04/12] *inappropriate study design*

174. Henkel K, Reimers CD, Knapp G, et al. Physical training for neurological and mental diseases. *Der Nervenarzt* 2014;85(12):1521-+. doi: 10.1007/s00115-013-3978-2 *inappropriate study design*
175. Hoeger Bement MK, Weyer A, Hartley S, et al. Pain Perception After Isometric Exercise in Women With Fibromyalgia. *Archives of Physical Medicine & Rehabilitation* 2011;92(1):89-95. *inappropriate study design*
176. Hsieh RL, Lee WC. Clinical effects of lateral wedge arch support insoles in knee osteoarthritis: A prospective double-blind randomized study. *Medicine* 2016;95(27):e3952. doi: 10.1097/md.0000000000003952 [published Online First: 2016/07/12] *inappropriate intervention*
177. Hsieh RL, Lo MT, Lee WC, et al. Therapeutic effects of short-term monochromatic infrared energy therapy on patients with knee osteoarthritis: a double-blind, randomized, placebo-controlled study. *The Journal of orthopaedic and sports physical therapy* 2012;42(11):947-56. doi: 10.2519/jospt.2012.3881 [published Online First: 2012/09/11] *inappropriate intervention*
178. Huber E, Roos E, Meichtry A, et al. Effect of preoperative neuromuscular training (NEMEX-TJR) on functional outcome after total knee replacement: An assessor-blinded randomized controlled trial. *BMC musculoskeletal disorders* 2015; 16(1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/584/CN-01088584/frame.html. *inappropriate intervention*
179. Hudson JI, Arnold LM, Bradley LA, et al. What makes patients with fibromyalgia feel better? Correlations between Patient Global Impression of Improvement and changes in clinical symptoms and function: a pooled analysis of 4 randomized placebo-controlled trials of duloxetine. *The Journal of rheumatology* 2009;36(11):2517-22. doi: 10.3899/jrheum.090139 [published Online First: 2009/10/17] *inappropriate study design*
180. Hughes S, Seymour R, Campbell R, et al. Fit and Strong!: bolstering maintenance of physical activity among older adults with lower-extremity osteoarthritis. *American journal of health behavior* 2010; 34(6). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/647/CN-00761647/frame.html. *inappropriate intervention*
181. Hurley M, Walsh N, Jessep S. Clinical effectiveness and costs of an integrated rehabilitation programme compared with outpatient physiotherapy for chronic knee pain. *Arthritis and rheumatism* 2012; 64. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/235/CN-01008235/frame.html. *inappropriate study design*
182. Hurst NP, Lambert CM, Forbes J, et al. Does waiting matter? A randomized controlled trial of new non-urgent rheumatology out-patient referrals. *Rheumatology (Oxford, England)* 2000;39(4):369-76. [published Online First: 2000/05/19] *inappropriate intervention*
183. Ide MR, Laurindo IMM, Rodrigues AL, et al. Effect of aquatic respiratory exercise-based program in patients with fibromyalgia. *International journal of rheumatic diseases* 2008;11(2):131-40. doi: 10.1111/j.1756-185X.2008.00348.x *inappropriate comparison group*
184. Jackel WH, Gerdes N, Cziske R, et al. RHEUMATIC COMPLAINTS IN THE GENERAL-POPULATION OF GERMANY - PREVALENCE, PHYSICAL AND

PSYCHOSOCIAL IMPACT. *Zeitschrift fur Rheumatologie* 1993;52(5):281-88. *inappropriate study design*

185. Jenkinson CM, Doherty M, Avery AJ, et al. Effects of dietary intervention and quadriceps strengthening exercises on pain and function in overweight people with knee pain: randomised controlled trial. *BMJ (Clinical research ed)* 2009;339:b3170. doi: 10.1136/bmj.b3170 [published Online First: 2009/08/20] *inappropriate population*
186. Jensen KB, Kosek E, Wicksell R, et al. Cognitive Behavioral Therapy increases pain-evoked activation of the prefrontal cortex in patients with fibromyalgeia. *Pain* 2012;153(7):1495-503. doi: 10.1016/j.pain.2012.04.010 *inappropriate intervention*
187. Jensen OK, Nielsen CV, Stengaard-Pedersen K. One-year prognosis in sick-listed low back pain patients with and without radiculopathy. Prognostic factors influencing pain and disability. *Spine Journal* 2010;10(8):659-75. doi: 10.1016/j.spinee.2010.03.026 *inappropriate population*
188. Jessep SA, Walsh NE, Ratcliffe J, et al. Long-term clinical benefits and costs of an integrated rehabilitation programme compared with outpatient physiotherapy for chronic knee pain. *Physiotherapy* 2009;95(2):94-102. doi: 10.1016/j.physio.2009.01.005 [published Online First: 2009/07/25] *inappropriate population*
189. Johannesson E, Simren M, Strid H, et al. Physical activity improves symptoms in irritable bowel syndrome: a randomized controlled trial. *The American journal of gastroenterology* 2011;106(5):915-22. doi: 10.1038/ajg.2010.480 [published Online First: 2011/01/06] *inappropriate population*
190. Jones KD. A randomized controlled trial of muscle strengthening versus flexibility training in fibromyalgia. Microform Publications, University of Oregon, 2000. *inappropriate comparison group*
191. Kamanli A, Kaya A, Ardicoglu O, et al. Comparison of lidocaine injection, botulinum toxin injection, and dry needling to trigger points in myofascial pain syndrome. *Rheumatology international* 2005;25(8):604-11. doi: 10.1007/s00296-004-0485-6 *inappropriate intervention*
192. Kang J, Li N, Wu B. Therapeutic methods for knee osteoarthritis: Randomized controlled trial and systemic evaluation. [Chinese]. *Zhongguo Linchuang Kangfu* 2005; 9(30). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/890/CN-00643890/frame.html. *inappropriate study design*
193. Kapfhammer HP. [Psychopharmacological treatment in patients with somatoform disorders and functional body syndromes]. *Der Nervenarzt* 2012;83(9):1128-41. doi: 10.1007/s00115-011-3446-9 [published Online First: 2012/08/17] *inappropriate study design*
194. Karp J, Dew M, Wahed A, et al. Challenges and Solutions for Depression Prevention Research: Methodology for a Depression Prevention Trial for Older Adults with Knee Arthritis and Emotional Distress. *American journal of geriatric psychiatry* 2016; 24(6). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/456/CN-01158456/frame.html. *inappropriate outcomes*

195. Katic B, Heywood J, Turek F, et al. New approach for analyzing self-reporting of insomnia symptoms reveals a high rate of comorbid insomnia across a wide spectrum of chronic diseases. *Sleep Medicine* 2015;16(11):1332-41. doi: 10.1016/j.sleep.2015.07.024 *inappropriate outcomes*
196. Kaya A, Kamanli A, Ardicoglu O, et al. Direct current therapy with/without fidocaine iontophoresis in myofascial pain syndrome. *Bratislava Medical Journal-Bratislavske Lekarske Listy* 2009;110(3):185-91. *inappropriate intervention*
197. Kayiran S, Dursun E, Dursun N, et al. Neurofeedback intervention in fibromyalgia syndrome; a randomized, controlled, rater blind clinical trial. *Applied psychophysiology and biofeedback* 2010;35(4):293-302. doi: 10.1007/s10484-010-9135-9 [published Online First: 2010/07/09] *inappropriate intervention*
198. Keefe FJ, Shelby RA, Somers TJ, et al. Effects of coping skills training and sertraline in patients with non-cardiac chest pain: A randomized controlled study. *Pain* 2011;152(4):730-41. doi: 10.1016/j.pain.2010.08.040 *inappropriate intervention*
199. Keeley T, Al-Janabi H, Nicholls E, et al. A longitudinal assessment of the responsiveness of the ICECAP-A in a randomised controlled trial of a knee pain intervention. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation* 2015;24(10):2319-31. doi: 10.1007/s11136-015-0980-0 [published Online First: 2015/04/22] *inappropriate study design*
200. Kekow J, Moots R, Khandker R, et al. Improvements in patient-reported outcomes, symptoms of depression and anxiety, and their association with clinical remission among patients with moderate-to-severe active early rheumatoid arthritis. *Rheumatology (Oxford, England)* 2011;50(2):401-9. doi: 10.1093/rheumatology/keq327 [published Online First: 2010/11/10] *inappropriate study design*
201. Kekow J, Moots RJ, Emery P, et al. Patient-reported outcomes improve with etanercept plus methotrexate in active early rheumatoid arthritis and the improvement is strongly associated with remission: the COMET trial. *Annals of the rheumatic diseases* 2010;69(1):222-5. doi: 10.1136/ard.2008.102509 [published Online First: 2009/03/19] *inappropriate intervention*
202. Kempke S, Goossens L, Luyten P, et al. Predictors of outcome in a multi-component treatment program for chronic fatigue syndrome. *Journal of Affective Disorders* 2010;126(1-2):174-79. doi: 10.1016/j.jad.2010.01.073 *inappropriate intervention*
203. Knittle K, Maes S, de Gucht V. Psychological interventions for rheumatoid arthritis: examining the role of self-regulation with a systematic review and meta-analysis of randomized controlled trials. *Arthritis care & research* 2010;62(10):1460-72. doi: 10.1002/acr.20251
http://dx.doi.org/10.1002/acr.20251 [published Online First: 2010/05/28] *inappropriate study design*
204. Kolahi S, Pourghassem Gargari B, Mesgari Abbasi M, et al. Effects of phylloquinone supplementation on lipid profile in women with rheumatoid arthritis: a double blind placebo controlled study. *Nutrition research and practice*

2015;9(2):186-91. doi: 10.4162/nrp.2015.9.2.186 [published Online First: 2015/04/11] *inappropriate intervention*

205. Konuk N, Ortancil O, Bostanci B, et al. A comparison of reboxetine and amitryptilline in the treatment of fibromyalgia syndrome with co-morbid depressive symptoms: An open-label preliminary study. *Klinik Psikofarmakoloji Bülteni / Bulletin of Clinical Psychopharmacology* 2010;20(1):29-37. *inappropriate intervention*
206. Koulil S, Lankveld W, Kraaimaat F, et al. Tailored cognitive-behavioral therapy and exercise training for high-risk patients with fibromyalgia. *Arthritis care & research* 2010; 62(10). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/899/CN-00760899/frame.html. *inappropriate intervention*
207. Kravitz HM, Esty ML, Katz RS, et al. Treatment of fibromyalgia syndrome using low-intensity neurofeedback with the Flexyx Neurotherapy System: a randomized controlled clinical trial. *Journal of Neurotherapy* 2006;10(2/3):41-58. *inappropriate intervention*
208. Kwakkenbos L, Willems LM, van den Hoogen FHJ, et al. Cognitive-Behavioural Therapy Targeting Fear of Progression in an Interdisciplinary Care Program: A Case Study in Systemic Sclerosis. *Journal of Clinical Psychology in Medical Settings* 2014;21(4):297-312. doi: 10.1007/s10880-014-9414-3 *inappropriate study design*
209. Lakhan SE, Schofield KL. Mindfulness-based therapies in the treatment of somatization disorders: a systematic review and meta-analysis. *PloS one* 2013;8(8):e71834. doi: 10.1371/journal.pone.0071834 [published Online First: 2013/08/31] *inappropriate study design*
210. Lan CC, Tseng CH, Chen JH, et al. Increased risk of a suicide event in patients with primary fibromyalgia and in fibromyalgia patients with concomitant comorbidities A nationwide population-based cohort study. *Medicine* 2016;95(44) doi: 10.1097/md.0000000000005187 *inappropriate study design*
211. Lange M, Krohn-Grimberghe B, Petermann F. Medium-term effects of a multimodal therapy on patients with fibromyalgia. Results of a controlled efficacy study. *Schmerz* 2011;25(1):55-61. doi: 10.1007/s00482-010-1003-2 *inappropriate intervention*
212. Lelieveld O, Armbrust W, Geertzen J, et al. Promoting physical activity in children with juvenile idiopathic arthritis through an internet-based program: Results of a pilot randomised controlled trial. *Physiotherapy (United Kingdom)* 2011; 97. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/266/CN-01076266/frame.html. *inappropriate population*
213. Leombruni P, Miniotti M, Colonna F, et al. A randomised controlled trial comparing duloxetine and acetyl L-carnitine in fibromyalgic patients: preliminary data. *Clinical and experimental rheumatology* 2015;33(1 Suppl 88):S82-5. [published Online First: 2015/03/19] *inappropriate intervention*
214. Leon AAC, Morera M, Espinoza MB, et al. Case Study: Effect of a Physical Exercise and Nutritional Counseling Program on Physical and Psychological Variables in a Person with Fibromyalgia. *Mhsalud-Revista En Ciencias Del*

Movimiento Humano Y La Salud 2015;11(2):1-19. doi: 10.15359/mhs.11-2.1 *inappropriate study design*
215. Li K, Hu XQ, Qiu WH, et al. Effects of physiotherapy versus combination of physiotherapy and preventive education on quality of life in patients with degenerative gonarthritis. *Chinese Journal of Clinical Rehabilitation* 2006;10(4):32-33. *inappropriate intervention*
216. Li YH, Wang FY, Feng CQ, et al. Massage therapy for fibromyalgia: a systematic review and meta-analysis of randomized controlled trials. *PloS one* 2014;9(2):e89304. doi: 10.1371/journal.pone.0089304 [published Online First: 2014/03/04] *inappropriate study design*
217. Ljótsson B, Atterlöf E, Lagerlöf M, et al. Internet-delivered acceptance and values-based exposure treatment for fibromyalgia: A pilot study. *Cognitive Behaviour Therapy* 2014;43(2):93-104. doi: 10.1080/16506073.2013.846401 *inappropriate intervention*
218. Lopez-Pousa S, Bassets Pages G, Monserrat-Vila S, et al. Sense of Well-Being in Patients with Fibromyalgia: Aerobic Exercise Program in a Mature Forest-A Pilot Study. *Evidence-based complementary and alternative medicine : eCAM* 2015;2015:614783. doi: 10.1155/2015/614783 [published Online First: 2015/11/12] *inappropriate comparison group*
219. Lopez-Rodriguez MD, Castro-Sanchez AM, Fernandez-Martinez M, et al. Comparison between aquatic-biodanza and stretching for improving quality of life and pain in pations with fibromyalgia. *Atencion Primaria* 2012;44(11):641-49. doi: 10.1016/j.aprim.2012.03.002 *inappropriate intervention*
220. Lopez-Rodriguez MM, Fernandez-Martinez M, Mataran-Penarrocha GA, et al. [Effectiveness of aquatic biodance on sleep quality, anxiety and other symptoms in patients with fibromyalgia]. *Medicina clinica* 2013;141(11):471-8. doi: 10.1016/j.medcli.2012.09.036 [published Online First: 2012/12/19] *inappropriate intervention*
221. Luciano JV, Martinez N, Penarrubia-Maria MT, et al. Effectiveness of a psychoeducational treatment program implemented in general practice for fibromyalgia patients: a randomized controlled trial. *The Clinical journal of pain* 2011;27(5):383-91. doi: 10.1097/AJP.0b013e31820b131c [published Online First: 2011/02/15] *inappropriate intervention*
222. Luedtke K, Rushton A, Wright C, et al. Effectiveness of anodal transcranial direct current stimulation in patients with chronic low back pain: design, method and protocol for a randomised controlled trial. *BMC musculoskeletal disorders* 2011;12:290. doi: 10.1186/1471-2474-12-290 [published Online First: 2011/12/30] *inappropriate intervention*
223. Lumley M, Schubiner H, Clauw D, et al. The PAST-FM (Pain and Stress Treatment for Fibromyalgia) randomized, controlled trial: Main effects of emotional awareness and expression and cognitive-behavioral therapies. *Journal of pain* 2016; 17(4 suppl. 1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/566/CN-01142566/frame.html. *inappropriate intervention*
224. Lumley MA, Keefe FJ, Mosley-Williams A, et al. The effects of written emotional disclosure and coping skills training in rheumatoid arthritis: A randomized clinical

trial. *Journal of Consulting and Clinical Psychology* 2014;82(4):644-58. doi: 10.1037/a0036958 *inappropriate intervention*

225. Lund I, Lundeberg T, Carleson J, et al. Corticotropin releasing factor in urine--a possible biochemical marker of fibromyalgia. Responses to massage and guided relaxation. *Neuroscience letters* 2006;403(1-2):166-71. doi: 10.1016/j.neulet.2006.04.038 [published Online First: 2006/05/24] *inappropriate study design*
226. Mackintosh S. Hydrotherapy and Tai Chi each provide clinical improvements for older people with osteoarthritis. *Australian Journal of Physiotherapy* 2008;54(2):143-43. *inappropriate study design*
227. Maddali Bongi S, Del Rosso A, Di Felice C, et al. Resseguier method and Qi Gong sequentially integrated in patients with fibromyalgia syndrome. *Clinical and experimental rheumatology* 2012;30(6 Suppl 74):51-8. [published Online First: 2012/11/01] *inappropriate intervention*
228. Mahagna H, Amital D, Amital H. A randomised, double-blinded study comparing giving etoricoxib vs. placebo to female patients with fibromyalgia. *International journal of clinical practice* 2016; 70(2 // (MSD) *Meso Scale Diagnostics*). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/727/CN-01132727/frame.html. *inappropriate intervention*
229. Mannerkorpi K, Nyberg B, Ahlmen M, et al. Pool exercise combined with an education program for patients with fibromyalgia syndrome. A prospective, randomized study. *J Rheumatol* 2000;27(10):2473-81. *inappropriate intervention*
230. Mao JJ, Bruner DW, Stricker C, et al. Feasibility trial of electroacupuncture for aromatase inhibitor--related arthralgia in breast cancer survivors. *Integrative cancer therapies* 2009;8(2):123-9. doi: 10.1177/1534735409332903 [published Online First: 2009/08/15] *inappropriate population*
231. Marszalek J, Price LL, Harvey WF, et al. Outcome Expectations and Osteoarthritis: Perceived Benefits of Exercise Are Associated with Self-Efficacy and Depression. *Arthritis care & research* 2016 doi: 10.1002/acr.22969 [published Online First: 2016/07/09] *inappropriate study design*
232. Martin DP, Williams BA, Berger IH. Improvement in fibromyalgia symptoms with acupuncture: Results of a randomized controlled trial. *Mayo Clinic proceedings* 2006;81(6):749-57. *inappropriate intervention*
233. Martín J, Torre F, Aguirre U, et al. Evaluation of the interdisciplinary PSYMEPHY treatment on patients with fibromyalgia: A randomized control trial. *Pain Medicine* 2014;15(4):682-91. doi: 10.1111/pme.12375 *inappropriate intervention*
234. Martin J, Torre F, Padierna A, et al. Six-and 12-month follow-up of an interdisciplinary fibromyalgia treatment programme: results of a randomised trial. *Clinical and experimental rheumatology* 2012;30(6 Suppl 74):103-11. [published Online First: 2013/02/27] *inappropriate intervention*
235. Martín J, Torre F, Padierna A, et al. Interdisciplinary treatment of patients with fibromyalgia: improvement of their health-related quality of life. *Pain practice : the official journal of World Institute of Pain* 2014; 14(8). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/572/CN-01090572/frame.html. *inappropriate intervention*

236. Martin J, Torre F, Padierna A, et al. Impact of interdisciplinary treatment on physical and psychosocial parameters in patients with fibromyalgia: results of a randomised trial. *International journal of clinical practice* 2014;68(5):618-27. [published Online First: 2014/05/29] *inappropriate intervention*
237. Martín-Nogueras AM, Calvo-Arenillas JI. Efficacy of physiotherapy treatment on pain and quality of life in patients with fibromyalgia. *Rehabilitacion* 2012;46(3):199-206. *inappropriate intervention*
238. Martins MRI, Gritti CC, dos Santos R, et al. Randomized controlled trial of a therapeutic intervention group in patients with fibromyalgia syndrome. *Revista Brasileira De Reumatologia* 2014;54(3):179-84. doi: 10.1016/j.rbre.2013.10.002 *inappropriate intervention*
239. Mata J, Cabrera S, Sanchis P, et al. Electro-acupuncture for treatment of knee pain from osteoarthritis and the possible endocrinology changes: a study protocol for a randomized controlled trial. *Trials* 2015;16:248. doi: 10.1186/s13063-015-0766-2 [published Online First: 2015/06/04] *inappropriate study design*
240. Mataran-Penarrocha GA, Castro-Sanchez AM, Garcia GC, et al. Influence of Craniosacral Therapy on Anxiety, Depression and Quality of Life in Patients with Fibromyalgia. *Evidence-Based Complementary and Alternative Medicine* 2011:1-9. doi: 10.1093/ecam/nep125 *inappropriate intervention*
241. Matcham F, Norton S, Scott D, et al. The impact of depression on long-term physical health outcomes in rheumatoid arthritis. *Rheumatology (United Kingdom)* 2014; 53. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/273/CN-01057273/frame.html. *inappropriate study design*
242. Matcham F, Norton S, Scott DL, et al. Symptoms of depression and anxiety predict treatment response and long-term physical health outcomes in rheumatoid arthritis: secondary analysis of a randomized controlled trial. *Rheumatology (Oxford, England)* 2016;55(2):268-78. doi: 10.1093/rheumatology/kev306 [published Online First: 2015/09/10] *inappropriate study design*
243. McBain H, Shipley M, Olaleye A, et al. A patient-initiated DMARD self-monitoring service for people with rheumatoid or psoriatic arthritis on methotrexate: A randomised controlled trial. *Annals of the rheumatic diseases* 2016; 75(7). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/299/CN-01178299/frame.html. *inappropriate intervention*
244. McVeigh JG, Hurley DA, Basford JR, et al. Effectiveness of a combined pool-based exercise and education programme compared to usual medical care in fibromyalgia syndrome: a randomised, controlled trial. *Physical Therapy Reviews* 2006;11(3):217-17. *inappropriate study design*
245. Mendonca ME, Simis M, Grecco LC, et al. Transcranial Direct Current Stimulation Combined with Aerobic Exercise to Optimize Analgesic Responses in Fibromyalgia: A Randomized Placebo-Controlled Clinical Trial. *Frontiers in human neuroscience* 2016;10:68. doi: 10.3389/fnhum.2016.00068 [published Online First: 2016/03/26] *inappropriate intervention*
246. Menkes CJ, Godeau P. Fibromyalgia. *Bulletin De L Academie Nationale De Medecine* 2007;191(1):143-48. *inappropriate study design*

247. Mercadie L, Mick G, Guetin S, et al. Effects of Listening to Music versus Environmental Sounds in Passive and Active Situations on Levels of Pain and Fatigue in Fibromyalgia. *Pain Management Nursing* 2015;16(5):664-71. doi: 10.1016/j.pmn.2015.01.005 *inappropriate intervention*
248. Meyer BB, Lemley KJ. Utilizing exercise to affect the symptomology of fibromyalgia: a pilot study. *Medicine and science in sports and exercise* 2000;32(10):1691-7. [published Online First: 2000/10/20] *inappropriate study design*
249. Mibielli M, Nunes C, Cezar P, et al. Osteoarthritis: Clinical evaluation of diclofenac combined with the B complex vitamins. *Revista brasileira de medicina* 2009; 66(7). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/674/CN-00753674/frame.html. *inappropriate intervention*
250. Middleton KR, Ward MM, Haaz S, et al. A pilot study of yoga as self-care for arthritis in minority communities. *Health and quality of life outcomes* 2013;11:55. doi: 10.1186/1477-7525-11-55 [published Online First: 2013/04/04] *inappropriate intervention*
251. Miles ALS. The effects of gentle yoga vs. cognitive behavioral therapy on physical and psychological symptoms; neurocognitive functioning; and physiology in women with Fibromyalgia. ProQuest Information & Learning, 2014. *inappropriate intervention*
252. Minor MA. Exercise maintenance behavior of subjects with arthritis following participation in a supervised exercise program [Ph.D.]. University of Missouri - Columbia, 1989. *inappropriate study design*
253. Minor MA, Brown JD. Exercise maintenance of persons with arthritis after participation in a class experience. *Health education quarterly* 1993;20(1):83-95. [published Online First: 1993/01/01] *inappropriate study design*
254. Mirtaheri E, Gargari BP, Kolahi S, et al. Effects of Alpha-Lipoic Acid Supplementation on Inflammatory Biomarkers and Matrix Metalloproteinase-3 in Rheumatoid Arthritis Patients. *Journal of the American College of Nutrition* 2015;34(4):310-17. doi: 10.1080/07315724.2014.910740 *inappropriate intervention*
255. Mishra P, Trivedi V. Acupuncture in the treatment of rheumatoid arthritis: Results of a randomized controlled trial. *Annals of the rheumatic diseases* 2014; 73. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/582/CN-01009582/frame.html. *inappropriate intervention*
256. Moore RA, Straube S, Paine J, et al. Fibromyalgia: Moderate and substantial pain intensity reduction predicts improvement in other outcomes and substantial quality of life gain. *Pain* 2010;149(2):360-64. doi: 10.1016/j.pain.2010.02.039 *inappropriate study design*
257. Morgan N, Driban J, Ransford G, et al. Construct validity of promis instruments among patients with symptomatic knee osteoarthritis. *Osteoarthritis and cartilage* 2013; 21. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/483/CN-01010483/frame.html. *inappropriate study design*
258. Morgan N, Ransford G, Morgan L, et al. Mindfulness is associated with psychological symptoms, self-efficacy, and quality of life among patients with symptomatic knee osteoarthritis. *Osteoarthritis and cartilage* 2013; 21.

http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/479/CN-01010479/frame.html. *inappropriate study design*

259. Morone N, Karp J, Lynch C, et al. Impact of chronic musculoskeletal pathology on older adults: a study of differences between knee OA and low back pain. *Pain medicine (Malden, Mass)* 2009; 10(4). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/087/CN-00721087/frame.html. *inappropriate study design*
260. Moroshko I, Brennan L, O'Brien P. Predictors of dropout in weight loss interventions: A systematic review of the literature. *Obesity Reviews* 2011;12(11):912-34. doi: 10.1111/j.1467-789X.2011.00915.x *inappropriate study design*
261. Morris LD, Grimmer-Somers KA, Spottiswoode B, et al. Virtual reality exposure therapy as treatment for pain catastrophizing in fibromyalgia patients: proof-of-concept study (Study Protocol). *BMC musculoskeletal disorders* 2011;12(1):85. doi: 10.1186/1471-2474-12-85 [published Online First: 2011/05/03] *inappropriate study design*
262. Moustafa IM, Diab AA. The addition of upper cervical manipulative therapy in the treatment of patients with fibromyalgia: a randomized controlled trial. *Rheumatology international* 2015;35(7):1163-74. doi: 10.1007/s00296-015-3248-7 [published Online First: 2015/03/19] *inappropriate intervention*
263. Mu PF, Chen YC, Cheng SC. The effectiveness of non-pharmacological pain management in relieving chronic pain for children and adolescents. *JBI library of systematic reviews* 2009;7(34):1489-543. [published Online First: 2009/01/01] *inappropriate population*
264. Munguia-Izquierdo D, Legaz-Arrese A. Determinants of sleep quality in middle-aged women with fibromyalgia syndrome. *Journal of Sleep Research* 2012;21(1):73-79. doi: 10.1111/j.1365-2869.2011.00929.x *inappropriate outcomes*
265. Murphy LB, Sacks JJ, Brady TJ, et al. Anxiety and depression among US adults with arthritis: Prevalence and correlates. *Arthritis care & research* 2012;64(7):968-76. doi: 10.1002/acr.21685 *inappropriate study design*
266. Murphy SL, Lyden AK, Kratz AL, et al. Characterizing Pain Flares From the Perspective of Individuals With Symptomatic Knee Osteoarthritis. *Arthritis care & research* 2015;67(8):1103-11. doi: 10.1002/acr.22545 *inappropriate study design*
267. Nalamachu S, Rauck R, Hale M, et al. A long-term, open-label safety study of single-entity hydrocodone bitartrate extended release for the treatment of moderate to severe chronic pain. *Journal of pain research* 2014; 7. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/077/CN-01036077/frame.html. *inappropriate intervention*
268. Navarrete-Navarrete N, Peralta-Ramirez MI, Sabio-Sanchez JM, et al. Efficacy of Cognitive Behavioural Therapy for the Treatment of Chronic Stress in Patients with Lupus Erythematosus: A Randomized Controlled Trial. *Psychotherapy and Psychosomatics* 2010;79(2):107-15. doi: 10.1159/000276370 *inappropriate population*
269. Nazareth I, Landau S, Yardley L, et al. Patterns of presentations of dizziness in primary care - a cross-sectional cluster analysis study. *Journal of psychosomatic*

research 2006;60(4):395-401. doi: 10.1016/j.jpsychores.2005.07.011 *inappropriate study design*
270. Niedermann K, de Bie RA, Kubli R, et al. Effectiveness of individual resource-oriented joint protection education in people with rheumatoid arthritis. A randomized controlled trial. *Patient education and counseling* 2011;82(1):42-48. doi: 10.1016/j.pec.2010.02.014 *inappropriate intervention*
271. Noiseux NO, Callaghan JJ, Clark CR, et al. Preoperative predictors of pain following total knee arthroplasty. *The Journal of arthroplasty* 2014;29(7):1383-7. doi: 10.1016/j.arth.2014.01.034 [published Online First: 2014/03/19] *inappropriate study design*
272. Noppers I, Niesters M, Swartjes M, et al. Absence of long-term analgesic effect from a short-term S-ketamine infusion on fibromyalgia pain: A randomized, prospective, double blind, active placebo-controlled trial. *European Journal of Pain* 2011;15(9):942-49. doi: 10.1016/j.ejpain.2011.03.008 *inappropriate intervention*
273. Nordeman L, Gunnarsson R, Mannerkorpi K. Prevalence and Characteristics of Widespread Pain in Female Primary Health Care Patients With Chronic Low Back Pain. *Clinical Journal of Pain* 2012;28(1):65-72. doi: 10.1097/AJP.0b013e318223622c *inappropriate population*
274. Nugraha B, Korallus C, Dorffer D, et al. Aerobic exercise cognitive behavioural therapy and combination of treatment in fibromyalgia syndrome patients: A randomized control trial (effect on mood related disorder-a preliminary result). *PM and R* 2014; 6(8 suppl. 2). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/639/CN-01086639/frame.html. *inappropriate study design*
275. Nyssen OP, Taylor SJC, Wong G, et al. Does therapeutic writing help people with long-term conditions? Systematic review, realist synthesis and economic considerations. *Health Technology Assessment* 2016;20(27):1-367. doi: 10.3310/hta20270 *inappropriate study design*
276. Ohta H, Oka H, Usui C, et al. A randomized, double-blind, multicenter, placebo-controlled phase III trial to evaluate the efficacy and safety of pregabalin in Japanese patients with fibromyalgia. *Arthritis research & therapy* 2012; 14(5). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/489/CN-00913489/frame.html. *inappropriate intervention*
277. Oktayoglu P, Gur A, Yardimeden I, et al. Comparison of the efficacy of phonophoresis and conventional ultrasound therapy in patients with primary knee osteoarthritis. *Erciyes Tip Dergisi* 2014; 36(1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/055/CN-00988055/frame.html. *inappropriate intervention*
278. Olin R, Klein R, Berg PA. A randomised double-blind 16-week study of ritanserin in fibromyalgia syndrome: clinical outcome and analysis of autoantibodies to serotonin, gangliosides and phospholipids. *Clinical rheumatology* 1998;17(2):89-94. [published Online First: 1998/06/26] *inappropriate intervention*
279. Olivan-Blázquez B, Herrera-Mercadal P, Puebla-Guedea M, et al. Efficacy of memantine in the treatment of fibromyalgia: A double-blind, randomised,

controlled trial with 6-month follow-up. *Pain* 2014;155(12):2517-25. doi: 10.1016/j.pain.2014.09.004 *inappropriate intervention*
280. O'Mathúna DP. Exercise Programs Help Reduce Anxiety in Patients with Chronic Illnesses. *Alternative Medicine Alert* 2010;13(4):43-44. *inappropriate study design*
281. O'Reilly SC, Muir KR, Doherty M. Effectiveness of home exercise on pain and disability from osteoarthritis of the knee: a randomised controlled trial. *Annals of the rheumatic diseases* 1999;58(1):15-19. *inappropriate population*
282. Oren YK. Effectiveness of Mindfulness-Based Stress Reduction Bibliotherapy [Ph.D.]. University of Nevada, Reno, 2015. *inappropriate intervention*
283. Osteras H, Osteras B, Torstensen TA. Is postoperative exercise therapy necessary in patients with degenerative meniscus? A randomized controlled trial with one year follow-up. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA* 2014;22(1):200-6. doi: 10.1007/s00167-012-2354-2 [published Online First: 2012/12/25] *inappropriate population*
284. Osteras H, Torstensen T, Selven E, et al. High dosage medical exercise therapy or arthroscopic treatment for patients with degenerative meniscus injury: A pilot study. *Physiotherapy (United Kingdom)* 2011; 97. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/742/CN-01102742/frame.html. *inappropriate population*
285. Ottaviani S, Bernard JL, Bardin T, et al. Effect of music on anxiety and pain during joint lavage for knee osteoarthritis. *Clinical rheumatology* 2012;31(3):531-4. doi: 10.1007/s10067-011-1925-9 [published Online First: 2011/12/31] *inappropriate intervention*
286. Packham JC, Jordan KP, Haywood KL, et al. Evaluation of Ankylosing Spondylitis Quality of Life questionnaire: responsiveness of a new patient-reported outcome measure. *Rheumatology (Oxford, England)* 2012;51(4):707-14. doi: 10.1093/rheumatology/ker377 [published Online First: 2011/12/20] *inappropriate population*
287. Pae C-U, Masand PS, Marks DM, et al. History of depressive and/or anxiety disorders as a predictor of treatment response: A post hoc analysis of a 12-week, randomized, double-blind, placebo-controlled trial of paroxetine controlled release in patients with fibromyalgia. *Progress in Neuro-Psychopharmacology & Biological Psychiatry* 2009;33(6):996-1002. doi: 10.1016/j.pnpbp.2009.05.005 *inappropriate intervention*
288. Papadopoulou D, Fassoulaki A, Tsoulas C, et al. A meta-analysis to determine the effect of pharmacological and non-pharmacological treatments on fibromyalgia symptoms comprising OMERACT-10 response criteria. *Clinical rheumatology* 2016;35(3):573-86. doi: 10.1007/s10067-015-3144-2 [published Online First: 2015/12/18] *inappropriate study design*
289. Passard A, Attal N, Benadhira R, et al. Effects of unilateral repetitive transcranial magnetic stimulation of the motor cortex on chronic widespread pain in fibromyalgia. *Brain: A Journal of Neurology* 2007;130(10):2661-70. doi: 10.1093/brain/awm189 *inappropriate intervention*
290. Pedersen BK, Saltin B. Exercise as medicine - evidence for prescribing exercise as therapy in 26 different chronic diseases. *Scandinavian Journal of Medicine &*

Science in Sports 2015;25:1-72. doi: 10.1111/sms.12581 *inappropriate study design*

291. Peres M. Fibromyalgia and headache disorders. *Current pain and headache reports* 2009; 13(5). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/879/CN-00958879/frame.html. *inappropriate study design*
292. Perrot S, Russell IJ. More ubiquitous effects from non-pharmacologic than from pharmacologic treatments for fibromyalgia syndrome: a meta-analysis examining six core symptoms. *European journal of pain (London, England)* 2014;18(8):1067-80. doi: 10.1002/ejp.564 [published Online First: 2014/08/21] *inappropriate study design*
293. Peters S, Stanley I, Rose M, et al. A randomized controlled trial of group aerobic exercise in primary care patients with persistent, unexplained physical symptoms. *Family Practice* 2002;19(6):665-74. doi: 10.1093/fampra/19.6.665 *inappropriate population*
294. Potvin S, Morin M, Cloutier C, et al. Add-on treatment of quetiapine for fibromyalgia: A pilot, randomized, double-blind, placebo-controlled 12-week trial. *Journal of Clinical Psychopharmacology* 2012;32(5):684-87. doi: 10.1097/JCP.0b013e318267b8ca *inappropriate intervention*
295. Preece JC. The relationship between family resilience and the successful management of fibromyalgia [Ph.D.]. Syracuse University, 2001. *inappropriate study design*
296. Rakel B, Zimmerman M, Geasland K, et al. Transcutaneous electrical nerve stimulation for the control of pain during rehabilitation after total knee arthroplasty: A randomized, blinded, placebo-controlled trial. *Pain* 2014; 155(12). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/744/CN-01052744/frame.html. *inappropriate intervention*
297. Redondo JR, Justo CM, Moraleda FV, et al. Long-term efficacy of therapy in patients with fibromyalgia: a physical exercise-based program and a cognitive-behavioral approach. *Arthritis and rheumatism* 2004;51(2):184-92. doi: 10.1002/art.20252 [published Online First: 2004/04/13] *inappropriate comparison group*
298. Richards DA, Hill JJ, Gask L, et al. Clinical effectiveness of collaborative care for depression in UK primary care (CADET): Cluster randomised controlled trial. *BMJ: British Medical Journal* 2013;347 *inappropriate population*
299. Rini C, Porter LS, Somers TJ, et al. Automated Internet-based pain coping skills training to manage osteoarthritis pain: a randomized controlled trial. *Pain* 2015;156(5):837-48. doi: 10.1097/j.pain.0000000000000121 [published Online First: 2015/03/04] *inappropriate intervention*
300. Rodriguez Huerta MD, Trujillo-Martin MM, Rua-Figueroa I, et al. Healthy lifestyle habits for patients with systemic lupus erythematosus: A systemic review. *Seminars in arthritis and rheumatism* 2016;45(4):463-70. doi: 10.1016/j.semarthrit.2015.09.003 [published Online First: 2015/11/03] *inappropriate population*
301. Rodriguez Torres J, Cabrera Martos I, Torres Sanchez I, et al. Results of an Active Neurodynamic Mobilization Program in Patients With Fibromyalgia

Syndrome: A Randomized Controlled Trial. *Archives of Physical Medicine & Rehabilitation* 2015;96(10):1771-78. *inappropriate intervention*

302. Romero-Zurita A, Carbonell-Baeza A, Aparicio VA, et al. Effectiveness of a Tai-Chi Training and Detraining on Functional Capacity, Symptomatology and Psychological Outcomes in Women with Fibromyalgia. *Evidence-Based Complementary and Alternative Medicine* 2012 doi: 10.1155/2012/614196 *inappropriate intervention*
303. Rouse P, Duda J, Veldhuijzen VZJ, et al. Feelings of competence and relatedness during physical activity are related to well-being in rheumatoid arthritis patients: Preliminary findings from a randomized control trial. *Annals of the rheumatic diseases* 2013; 72. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/540/CN-01062540/frame.html. *inappropriate study design*
304. Rouse PC, Van Zanten J, Ntoumanis N, et al. Measuring the positive psychological wellbeing of people with rheumatoid arthritis: a cross-sectional validation of the subjective vitality scale. *Arthritis research & therapy* 2015;17 doi: 10.1186/s13075-015-0827-7 *inappropriate study design*
305. Russek LN, LaShomb EA, Ware AM, et al. United States Physical Therapists' Knowledge About Joint Hypermobility Syndrome Compared with Fibromyalgia and Rheumatoid Arthritis. *Physiotherapy research international : the journal for researchers and clinicians in physical therapy* 2016;21(1):22-35. doi: 10.1002/pri.1613 [published Online First: 2014/12/17] *inappropriate study design*
306. Russell IJ, Holman AJ, Swick TJ, et al. Sodium oxybate reduces pain, fatigue, and sleep disturbance and improves functionality in fibromyalgia: results from a 14-week, randomized, double-blind, placebo-controlled study. *Pain* 2011;152(5):1007-17. doi: 10.1016/j.pain.2010.12.022 [published Online First: 2011/03/15] *inappropriate intervention*
307. Rybarczyk B, DeMarco G, DelaCruz M, et al. Comparing mind-body wellness interventions for older adults with chronic illness: Classroom versus home instruction. *Behavioral Medicine* 1999;24(4):181-90. *inappropriate intervention*
308. Sancheti P, Hardikar M, Karne N, et al. A multicentric, randomized, comparative clinical trial to evaluate the efficacy and safety of S-etodolac in the treatment of osteoarthritis in Indian patients. *International journal of clinical pharmacology and therapeutics* 2010;48(7):429-34. [published Online First: 2010/06/19] *inappropriate intervention*
309. Schanberg LE, Anthony KK, Gil KM, et al. Daily pain and symptoms in children with polyarticular arthritis. *Arthritis and rheumatism* 2003;48(5):1390-7. doi: 10.1002/art.10986 [published Online First: 2003/05/15] *inappropriate population*
310. Scheidt CE, Waller E, Endorf K, et al. Is brief psychodynamic psychotherapy in primary fibromyalgia syndrome with concurrent depression an effective treatment? A randomized controlled trial. *General Hospital Psychiatry* 2013;35(2):160-67. doi: 10.1016/j.genhosppsych.2012.10.013 *inappropriate intervention*
311. Schmale GA, Mazor S, Mercer LD, et al. Lack of Benefit of Physical Therapy on Function Following Supracondylar Humeral Fracture A Randomized Controlled

Trial. *Journal of Bone and Joint Surgery-American Volume* 2014;96A(11):944-50. doi: 10.2106/jbjs.l.01696 *inappropriate population*

312. Schmidt S, Grossman P, Schwarzer B, et al. Treating fibromyalgia with mindfulness-based stress reduction: results from a 3-armed randomized controlled trial. *Pain* 2011;152(2):361-9. doi: 10.1016/j.pain.2010.10.043 [published Online First: 2010/12/15] *inappropriate intervention*
313. Scopaz KA, Piva SR, Wisniewski S, et al. Relationships of Fear, Anxiety, and Depression With Physical Function in Patients With Knee Osteoarthritis. *Archives of physical medicine and rehabilitation* 2009;90(11):1866-73. doi: 10.1016/j.apmr.2009.06.012 *inappropriate study design*
314. Selfridge N. Meditation for Fibromyalgia: Yea or Nay? *Alternative Medicine Alert* 2011;14(3):34-36. *inappropriate intervention*
315. Shadick NA, Sowell NF, Frits ML, et al. A randomized controlled trial of an internal family systems-based psychotherapeutic intervention on outcomes in rheumatoid arthritis: a proof-of-concept study. *The Journal of rheumatology* 2013;40(11):1831-41. doi: 10.3899/jrheum.121465 [published Online First: 2013/08/21] *inappropriate intervention*
316. Shahabi L, Naliboff BD, Shapiro D. Self-regulation evaluation of therapeutic yoga and walking for patients with irritable bowel syndrome: a pilot study. *Psychology Health & Medicine* 2016;21(2):176-88. doi: 10.1080/13548506.2015.1051557 *inappropriate population*
317. Shahrbanian S, Duquette P, Kuspinar A, et al. Contribution of symptom clusters to multiple sclerosis consequences. *Quality of Life Research* 2015;24(3):617-29. doi: 10.1007/s11136-014-0804-7 *inappropriate population*
318. Sharpe L, Gittins CB, Correia HM, et al. Problem-solving versus cognitive restructuring of medically ill seniors with depression (PROMISE-D trial): study protocol and design. *Bmc Psychiatry* 2012;12 doi: 10.1186/1471-244x-12-207 *inappropriate study design*
319. Sharpe L, Sensky T, Allard S. The course of depression in recent onset rheumatoid arthritis: the predictive role of disability, illness perceptions, pain and coping. *Journal of psychosomatic research* 2001;51(6):713-9. [published Online First: 2001/12/26] *inappropriate study design*
320. Sharpe L, Sensky T, Timberlake N, et al. Long-term efficacy of a cognitive behavioural treatment from a randomized controlled trial for patients recently diagnosed with rheumatoid arthritis. *Rheumatology (Oxford, England)* 2003; 42(3). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/463/CN-00431463/frame.html. *inappropriate intervention*
321. Sharpe L, Sensky T, Timberlake N, et al. A blind, randomized, controlled trial of cognitive-behavioural intervention for patients with recent onset rheumatoid arthritis: preventing psychological and physical morbidity. *Pain* 2001; 89(2-3). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/279/CN-00327279/frame.html. *inappropriate intervention*
322. Shih M, Hootman JM, Kruger J, et al. Physical activity in men and women with arthritis - National Health Interview Survey, 2002. *American Journal of Preventive Medicine* 2006;30(5):385-93. doi: 10.1016/j.amepre.2005.12.005 *inappropriate intervention*

323. Shupak NM, McKay JC, Nielson WR, et al. Exposure to a specific pulsed low-frequency magnetic field: A double-blind placebo-controlled study of effects on pain ratings in rheumatoid arthritis and fibromyalgia patients. *Pain Research & Management* 2006;11(2):85-90. doi: 10.1155/2006/842162 *inappropriate intervention*
324. Siegel KM. The effects of emotional disclosure on physical symptoms, healthcare utilization, and psychosocial adjustment in patients with irritable bowel syndrome [Ph.D.]. Alliant International University, San Diego, 2003. *inappropriate population*
325. Skrabek RQ, Galimova L, Ethans K, et al. Nabilone for the treatment of pain in fibromyalgia. *The journal of pain : official journal of the American Pain Society* 2008;9(2):164-73. doi: 10.1016/j.jpain.2007.09.002 [published Online First: 2007/11/03] *inappropriate intervention*
326. Slavich GM, Irwin MR. From Stress to Inflammation and Major Depressive Disorder: A Social Signal Transduction Theory of Depression. *Psychological Bulletin* 2014;140(3):774-815. doi: 10.1037/a0035302 *inappropriate study design*
327. Smeets RJ, Maher CG, Nicholas MK, et al. Do psychological characteristics predict response to exercise and advice for subacute low back pain? *Arthritis and rheumatism* 2009;61(9):1202-9. doi: 10.1002/art.24731 [published Online First: 2009/08/29] *inappropriate study design*
328. Smith-Ray R, Fitzgibbon M, Tussing-Humphreys L, et al. Fit and Strong! Plus: Design of a comparative effectiveness evaluation of a weight management program for older adults with osteoarthritis. *Contemporary clinical trials* 2014; 37(2). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/212/CN-00959212/frame.html. *inappropriate study design*
329. Sörensen J, Bengtsson A, Ahlner J, et al. Fibromyalgia--are there different mechanisms in the processing of pain? A double blind crossover comparison of analgesic drugs. *The Journal of rheumatology* 1997; 24(8). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/709/CN-00142709/frame.html. *inappropriate intervention*
330. Stehlik R, Ulfberg J, Hedner J, et al. High prevalence of restless legs syndrome among women with multi-site pain: A population-based study in Dalarna, Sweden. *European Journal of Pain* 2014;18(10):1402-09. doi: 10.1002/ejp.504 *inappropriate outcomes*
331. Stiller C. The effect of therapeutic touch on fibromyalgia pain and anxiety [Ph.D.]. Case Western Reserve University (Health Sciences), 2006. *inappropriate intervention*
332. Stratz T, Mennet P, Benn H, et al. [Blocking of S2 receptors--a new treatment principle in generalized tendomyopathy (fibromyalgia)?]. *Zeitschrift fur Rheumatologie* 1991; 50(1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/788/CN-00353788/frame.html. *inappropriate intervention*
333. Sulenes K, Freitas J, Justice L, et al. Underuse of Yoga as a Referral Resource by Health Professions Students. *Journal of Alternative and Complementary Medicine* 2015;21(1):53-59. doi: 10.1089/acm.2014.0217 *inappropriate intervention*

334. Sutbeyaz S, Sezer N, Koseoglu F, et al. Low-frequency pulsed electromagnetic field therapy in fibromyalgia: a randomized, double-blind, sham-controlled clinical study. *The Clinical journal of pain* 2009; 25(8). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/605/CN-00728605/frame.html. *inappropriate intervention*
335. Sverdrup B. Use less cosmetics--suffer less from fibromyalgia? *Journal of women's health (2002)* 2004; 13(2). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/706/CN-00468706/frame.html. *inappropriate intervention*
336. Tang NK, Lereya ST, Boulton H, et al. Nonpharmacological Treatments of Insomnia for Long-Term Painful Conditions: A Systematic Review and Meta-analysis of Patient-Reported Outcomes in Randomized Controlled Trials. *Sleep* 2015;38(11):1751-64. doi: 10.5665/sleep.5158 [published Online First: 2015/04/24] *inappropriate study design*
337. Tang NKY, Goodchild CE, Salkovskis PM. Hybrid cognitive-behaviour therapy for individuals with insomnia and chronic pain: A pilot randomised controlled trial. *Behaviour Research and Therapy* 2012;50(12):814-21. doi: 10.1016/j.brat.2012.08.006 *inappropriate population*
338. Tarakci E, Yeldan I, Kaya Mutlu E, et al. The relationship between physical activity level, anxiety, depression, and functional ability in children and adolescents with juvenile idiopathic arthritis. *Clinical rheumatology* 2011;30(11):1415-20. doi: 10.1007/s10067-011-1832-0 [published Online First: 2011/09/03] *inappropriate population*
339. Teunis T, Thornton ER, Guitton TG, et al. Coaching of patients with an isolated minimally displaced fracture of the radial head immediately increases range of motion. *Journal of Hand Therapy* 2016;29(3):314-19. doi: 10.1016/j.jht.2016.02.003 *inappropriate population*
340. Thomas K, Muir K, Doherty M, et al. Home based exercise programme for knee pain and knee osteoarthritis: randomised controlled trial. *BMJ (Clinical research ed)* 2002; 325(7367). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/283/CN-00398283/frame.html. *inappropriate population*
341. Tonkins WP, Jr. Effect of Hatha yoga on selected parameters of cardiac fitness in African-American college students [Dr.P.H.]. Morgan State University, 2004. *inappropriate intervention*
342. Torres JR, Martos IC, Sanchez IT, et al. Results of an Active Neurodynamic Mobilization Program in Patients With Fibromyalgia Syndrome: A Randomized Controlled Trial. *Archives of physical medicine and rehabilitation* 2015;96(10):1771-8. doi: 10.1016/j.apmr.2015.06.008 [published Online First: 2015/07/06] *inappropriate intervention*
343. Torres X, Herrero MJ, Marti M, et al. Why people with fibromyalgia persist in activity despite the increasing pain? A Delphi Study of the content of the Clinic Scale of Persistence in Activity in Fibromyalgia. *Revista De Psiquiatria Y Salud Mental* 2013;6(1):33-44. doi: 10.1016/j.rpsm.2012.03.001 *inappropriate study design*

344. Toth C, Brady S, Gagnon F, et al. A Randomized, Single-Blind, Controlled, Parallel Assignment Study of Exercise Versus Education as Adjuvant in the Treatment of Peripheral Neuropathic Pain. *Clinical Journal of Pain* 2014;30(2):111-18. doi: 10.1097/AJP.0b013e31828ccd0f *inappropriate population*
345. Tousignant-Laflamme Y, Bourgault P, Masetto A, et al. Short term impact of brief education for symptom management in fibromyalgia-the PEGASO study. *Journal of pain* 2014; 15(4 suppl. 1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/679/CN-01058679/frame.html. *inappropriate intervention*
346. Trudeau KJ, Pujol LA, DasMahapatra P, et al. A randomized controlled trial of an online self-management program for adults with arthritis pain. *Journal of Behavioral Medicine* 2015;38(3):483-96. doi: 10.1007/s10865-015-9622-9 *inappropriate intervention*
347. Uceyler N, Hauser W, Sommer C. A systematic review on the effectiveness of treatment with antidepressants in fibromyalgia syndrome. *Arthritis Care and Research* 2008; 59(9). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/590/CN-00898590/frame.html. *inappropriate study design*
348. Ulus Y, Tander B, Akyol Y, et al. Therapeutic ultrasound versus sham ultrasound for the management of patients with knee osteoarthritis: a randomized double-blind controlled clinical study. *International journal of rheumatic diseases* 2012; 15(2). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/676/CN-00896676/frame.html. *inappropriate intervention*
349. Vaghef-Mehrabany E, Alipour B, Homayouni-Rad A, et al. Probiotic supplementation improves inflammatory status in patients with rheumatoid arthritis. *Nutrition* 2014;30(4):430-35. doi: 10.1016/j.nut.2013.09.007 *inappropriate intervention*
350. Vaghef-Mehrabany E, Homayouni-Rad A, Alipour B, et al. Effects of Probiotic Supplementation on Oxidative Stress Indices in Women with Rheumatoid Arthritis: A Randomized Double-Blind Clinical Trial. *Journal of the American College of Nutrition* 2016;35(4):291-99. *inappropriate intervention*
351. Valencia M, Alonso B, Alvarez M, et al. Effects of 2 physiotherapy programs on pain perception, muscular flexibility, and illness impact in women with fibromyalgia: a pilot study. *Journal of manipulative and physiological therapeutics* 2009; 32(1). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/935/CN-00680935/frame.html. *inappropriate comparison group*
352. Valim V, Oliveira L, Suda A, et al. Aerobic fitness effects in fibromyalgia. *The Journal of rheumatology* 2003;30(5):1060-9. [published Online First: 2003/05/08] *inappropriate intervention*
353. Vallejo MA, Ortega J, Rivera J, et al. Internet versus face-to-face group cognitive-behavioral therapy for fibromyalgia: A randomized control trial. *Journal of Psychiatric Research* 2015;68:106-13. doi: 10.1016/j.jpsychires.2015.06.006 *inappropriate intervention*
354. van Koulil S, Kraaimaat FW, van Lankveld W, et al. A patient's perspective on multidisciplinary treatment gain for fibromyalgia: an indicator for pre-post

treatment effects? *Arthritis and rheumatism* 2009;61(12):1626-32. doi: 10.1002/art.24792 [published Online First: 2009/12/02] *inappropriate study design*

355. van Koulil S, van Lankveld W, Kraaimaat FW, et al. Tailored cognitive-behavioral therapy and exercise training for high-risk patients with fibromyalgia. *Arthritis care & research* 2010;62(10):1377-85. doi: 10.1002/acr.20268 [published Online First: 2010/06/04] *inappropriate intervention*
356. Van Puymbroeck M, Payne LL, Hsieh PC. A phase I feasibility study of yoga on the physical health and coping of informal caregivers. *Evidence-Based Complementary and Alternative Medicine* 2007;4(4):519-29. doi: 10.1093/ecam/nem075 *inappropriate population*
357. van Wilgen CP, Dijkstra PU, Versteegen GJ, et al. CHRONIC PAIN AND SEVERE DISUSE SYNDROME: LONG-TERM OUTCOME OF AN INPATIENT MULTIDISCIPLINARY COGNITIVE BEHAVIOURAL PROGRAMME. *Journal of rehabilitation medicine* 2009;41(3):122-28. doi: 10.2340/16501977-0292 *inappropriate intervention*
358. Vayvay ES, Tok D, Turgut E, et al. The effect of Laser and taping on pain, functional status and quality of life in patients with fibromyalgia syndrome: A placebo- randomized controlled clinical trial. *Journal of back and musculoskeletal rehabilitation* 2016;29(1):77-83. doi: 10.3233/bmr-150600 [published Online First: 2015/09/26] *inappropriate intervention*
359. Vendrig AA, Lousberg R. Within-person relationships among pain intensity, mood and physical activity in chronic pain: a naturalistic approach. *Pain* 1997;73(1):71-76. doi: 10.1016/s0304-3959(97)00075-4 *inappropriate intervention*
360. Vergne-Salle P, Dufauret-Lombard C, Bonnet C, et al. A randomised, double-blind, placebo-controlled trial of dolasetron, a 5-hydroxytryptamine 3 receptor antagonist, in patients with fibromyalgia. *European Journal of Pain* 2011;15(5):509-14. doi: 10.1016/j.ejpain.2010.09.013 *inappropriate intervention*
361. Verra ML, Angst F, Beck T, et al. Horticultural therapy for patients with chronic musculoskeletal pain: results of a pilot study. *Alternative therapies in health and medicine* 2012;18(2):44-50. [published Online First: 2012/04/21] *inappropriate study design*
362. Verra ML, Angst F, Brioschi R, et al. Does classification of persons with fibromyalgia into Multidimensional Pain Inventory subgroups detect differences in outcome after a standard chronic pain management program? *Pain Research & Management* 2009;14(6):445-53. *inappropriate study design*
363. Verra ML, Angst F, Staal JB, et al. Differences in pain, function and coping in Multidimensional Pain Inventory subgroups of chronic back pain: a one-group pretest-posttest study. *BMC musculoskeletal disorders* 2011;12 doi: 10.1186/1471-2474-12-145 *inappropriate study design*
364. VillafaÑE JH, Cleland JA, FernÁNdez-De-Las-PeÑAs C. The Effectiveness of a Manual Therapy and Exercise Protocol in Patients With Thumb Carpometacarpal Osteoarthritis: A Randomized Controlled Trial. *Journal of Orthopaedic & Sports Physical Therapy* 2013;43(4):204-13. *inappropriate intervention*
365. Villafañe JH, Silva GB, Bishop MD, et al. Radial Nerve Mobilization Decreases Pain Sensitivity and Improves Motor Performance in Patients With Thumb

Carpometacarpal Osteoarthritis: A Randomized Controlled Trial. *Archives of Physical Medicine & Rehabilitation* 2012;93(3):396-403. *inappropriate intervention*

366. Villanueva-Torrecillas I. Affectivity, quality of life and health resources utilization in arthritis [Ph.D.]. The University of Arizona, 2003. *inappropriate outcomes*
367. Vincent KR, Vincent HK. Resistance exercise for knee osteoarthritis. *PM & R : the journal of injury, function, and rehabilitation* 2012;4(5 Suppl):S45-52. doi: 10.1016/j.pmrj.2012.01.019 [published Online First: 2012/06/01] *inappropriate study design*
368. Vriezekolk JE, Eijsbouts AMM, van Lankveld WGJM, et al. An acceptance-oriented cognitive-behavioral therapy in multimodal rehabilitation: A pre-post test evaluation in highly distressed patients with rheumatic diseases. *Patient education and counseling* 2013;91(3):357-63. doi: 10.1016/j.pec.2013.01.018 *inappropriate study design*
369. Wang C, Schmid CH, Hibberd PL, et al. Tai Chi for treating knee osteoarthritis: designing a long-term follow up randomized controlled trial. *BMC musculoskeletal disorders* 2008;9:108. doi: 10.1186/1471-2474-9-108 [published Online First: 2008/07/31] *inappropriate intervention*
370. Wang CC. Tai Chi and Rheumatic Diseases. *Rheumatic Disease Clinics of North America* 2011;37(1):19-+. doi: 10.1016/j.rdc.2010.11.002 *inappropriate study design*
371. Wang CC. Role of Tai Chi in the Treatment of Rheumatologic Diseases. *Current Rheumatology Reports* 2012;14(6):598-603. doi: 10.1007/s11926-012-0294-y *inappropriate study design*
372. Wang WR, Lopez V, Chow A, et al. A randomized controlled trial of the effectiveness of a self-help psychoeducation programme on outcomes of outpatients with coronary heart disease: study protocol. *Journal of Advanced Nursing* 2014;70(12):2932-41. doi: 10.1111/jan.12397 *inappropriate population*
373. Wepner F, Scheuer R, Schuetz-Wieser B, et al. Effects of vitamin D on patients with fibromyalgia syndrome: a randomized placebo-controlled trial. *Pain* 2014;155(2):261-8. doi: 10.1016/j.pain.2013.10.002 [published Online First: 2014/01/21] *inappropriate intervention*
374. Weze C, Leathard HL, Stevens G. Evaluation of Healing by Gentle Touch for the Treatment of Musculoskeletal Disorders. *American Journal of Public Health* 2004;94(1):50-52. doi: 10.2105/AJPH.94.1.50 *inappropriate intervention*
375. Wicksell RK, Kemani M, Jensen K, et al. Acceptance and commitment therapy for fibromyalgia: A randomized controlled trial. *European Journal of Pain* 2013;17(4):599-611. doi: 10.1002/j.1532-2149.2012.00224.x *inappropriate intervention*
376. Williams DA, Kuper D, Segar M, et al. Internet-enhanced management of fibromyalgia: a randomized controlled trial. *Pain* 2010;151(3):694-702. doi: 10.1016/j.pain.2010.08.034 [published Online First: 2010/09/22] *inappropriate intervention*
377. Witjes S, Hoorntje A, Kuijer P, et al. Does Goal Attainment Scaling improve satisfaction regarding performance of activities of younger knee arthroplasty patients? Study protocol of the randomized controlled ACTION trial. *BMC*

musculoskeletal disorders 2016;17 doi: 10.1186/s12891-016-0965-3 *inappropriate study design*

378. Wylde V, Artz N, Marques E, et al. Effectiveness and cost-effectiveness of outpatient physiotherapy after knee replacement for osteoarthritis: study protocol for a randomised controlled trial. *Trials* 2016;17(1):289. doi: 10.1186/s13063-016-1418-x [published Online First: 2016/06/15] *inappropriate study design*
379. Yang T, Wang H, Chen Y, et al. Effect of continuous administration of conjugated estrogen plus medroxyprogesterone acetate (Premelle) in postmenopausal women in Taiwan. *Journal of the Chinese Medical Association : JCMA* 2004; 67(7). http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/366/CN-00505366/frame.html. *inappropriate intervention*
380. Yelland MJ, Schluter PJ. Defining Worthwhile and Desired Responses to Treatment of Chronic Low Back Pain. *Pain Medicine* 2006;7(1):38-45. doi: 10.1111/j.1526-4637.2006.00087.x *inappropriate population*
381. Young JL. Use of lisdexamfetamine dimesylate in treatment of executive functioning deficits and chronic fatigue syndrome: A double blind, placebo-controlled study. *Psychiatry Research* 2013;207(1-2):127-33. doi: 10.1016/j.psychres.2012.09.007 *inappropriate intervention*
382. Yuan SLK, Matsutani LA, Marques AP. Effectiveness of different styles of massage therapy in fibromyalgia: A systematic review and meta-analysis. *Manual therapy* 2015;20(2):257-64. *inappropriate study design*
383. Yuen AWC, Sander JW. Can slow breathing exercises improve seizure control in people with refractory epilepsy? A hypothesis. *Epilepsy & Behavior* 2010;18(4):331-34. doi: 10.1016/j.yebeh.2010.05.019 *inappropriate population*
384. Zick SM, Wyatt GK, Murphy SL, et al. Acupressure for persistent cancer-related fatigue in breast cancer survivors (AcuCrft): a study protocol for a randomized controlled trial. *BMC Complementary and Alternative Medicine* 2012;12 doi: 10.1186/1472-6882-12-132 *inappropriate population*
385. Zietek P, Zietek J, Szczypior K, et al. Effect of adding one 15-minute-walk on the day of surgery to fast-track rehabilitation after total knee arthroplasty: a randomized, single-blind study. *European journal of physical and rehabilitation medicine* 2015;51(3):245-52. [published Online First: 2014/09/19] *inappropriate intervention*

Supplementary File 3. Study-level risk of bias results using the Cochrane Collaboration Instrument.

Reference	Random Sequence	Allocation Concealment	Blinding (Participants & Personnel)	Blinding (Outcome Assessors)	Incomplete Outcome Data	Selective Reporting	Inactive
Baptista et al., 2012[40]	low	low	high	low	low	low	unclear
Beltran, 2003[41]	low	unclear	high	unclear	low	unclear	low
Cheung et al., 2017 [42]	low	high	high	unclear	low	low	unclear
Fransen et al., 2007[43]	low	unclear	high	low	low	low	low
French et al., 2013[44]	low	low	high	high	low	unclear	unclear
Gowans et al., 2001[45]	low	unclear	high	low	low	unclear	unclear
Jones et al., 2008[46]	low	unclear	high	unclear	low	unclear	low
Komatireddy et al.[47]	low	unclear	high	low	low	unclear	unclear
Minor et al., 1989[48]	low	unclear	high	unclear	unclear	unclear	low
Munguia-Izquieerdo & Legaz-Arrese, 2008[49]	low	unclear	high	low	low	unclear	low
Sanudo et al., 2015[50]	low	unclear	high	unclear	unclear	unclear	unclear
Schachter et al., 2003[51]	high	high	high	unclear	low	unclear	low
Tomas-Carus et al., 2008[52]	low	low	high	low	low	unclear	low
Tomas-Carus et al., 2007[53]	low	unclear	high	unclear	unclear	unclear	low

Notes: low, low risk of bias; high, high risk of bias; unclear, unclear risk of bias.

Supplementary file 4. Simple meta-regression results with changes in anxiety as the outcome.

Comparison	ES (#)	R	R^2	F(p)
Study Characteristics				
- Journal impact factor	16	.22	.05	0.4(0.52)
- Year of publication	**16**	**.75**	**.56**	**51.5(<0.001)***
- Country study conducted (USA vs. other)	16	.13	.02	0.2(0.69)
- Type of control (exposure vs. no exposure)[a]	16	.08	.02	0.01(0.76)
- Matching (yes vs. no)	16	.39	.15	1.2(0.29)
- Random sequencing (high/unclear vs. low)	16	.05	.0003	0.17(0.69)
- Allocation concealment (high/unclear vs. low)	16	.22	.05	0.87(0.37)
- Blinding of participants & personnel (high/unclear vs. low)[b]	NA	NA	NA	NA
- Blinding of outcome assessors (high/unclear vs low)	16	.08	.007	0.43(0.66)
- Incomplete outcome data (high/unclear vs low)	**16**	**.67**	**.45**	**14.4(0.002)***
- Selective reporting (Unclear vs low)	16	.39	.15	4.1(0.06)
- Participants physically inactive (hig4h/unclear vs low)	16	.21	.04	0.75(0.40)
- Sample size estimates provided (no versus yes)	**16**	**.56**	**.32**	**4.6(0.05)***
- Agreed to participate in study (%)	**12**	**.47**	**.22**	**4.9(0.05)***
- Study funded (no versus yes)	**16**	**.34**	**.12**	**15.9(0.001)***
- Type of analysis (abp vs itt)[c]	19	.21	.05	0.89(0.36)
- Test used (STAI and FIQ vs. AIMS)[d,e]	19	.41	.17	2.3(0.14)
Participant Characteristics				
- Exercise dropouts (%)	**15**	**.34**	**.12**	**8.2(0.01)***
- Control dropouts (%)	13	.31	.10	1.3(0.27)
- Age (years)	**14**	**.53**	**.28**	**11.9(.005)***
- Gender (mixed vs. females)	16	.14	.02	.38(0.54)
- AORD (rheumatoid/osteoarthritis vs. fibromyalgia)	16	.10	.01	.15(0.71)
- Rheumatic symptoms (years)	8	.37	.14	1.45(0.27)
- Years since diagnosis	4	.23	.05	.33(0.62)

Exercise Intervention Characteristics				
Exercise modality (aerobic/weight training vs. both)	**16**	**.57**	**.32**	**8.19(0.01)***
Land vs. water-based exercise	16	.30	.09	1.03(0.33)
Length of training (weeks)	16	.16	.51	.44(0.52)
Frequency of training (times/week)	14	.02	.0004	.01(0.92)
Duration of training (min/session)	**12**	**.43**	**.18**	**7.7(0.02)***
Compliance (% of exercise sessions attended)	8	.04	.001	.02(0.90)
Minutes of training per week	**11**	**.61**	**.37**	**33.1(.0003)***
Minutes of training per week (adjusted for compliance)	7	.17	.03	.19(0.68)
Total minutes of training	**11**	**.63**	**.40**	**15.0(0.004)***
Total minutes of training (adjusted for compliance)	7	.22	.05	0.32(0.60)
Supervision status (unsupervised or supervised vs. both)	**16**	**.49**	**.24**	**4.20(0.04)***
Location of exercise (facility or home vs both)	**16**	**.49**	**.24**	**4.20(0.04)***
Participation (group or self vs. both)	**16**	**.49**	**.24**	**4.20(0.04)***
Adverse events (yes vs. no)	5	.23	.05	.17(0.71)
Changes in Secondary Outcomes				
Physical function	12	.26	.07	0.87(0.37)
Pain	15	.09	.008	0.32(0.58)
Depression	**13**	**.35**	**.12**	**7.49(0.01)***
Quality of life	**13**	**.79**	**.63**	**45.8(<0.001)***
VO_{2max} ($ml \cdot kg^{-1} \cdot min^{-1}$)	7	.62	.38	2.27(0.19)
Muscular strength	6	0.30	.09	.30(0.61)

Notes: abp, analysis-by-protocol; itt, intention-to-treat; STAI, State-Trait Anxiety Inventory; FIQ, Fibromyalgia Impact Questionnaire; AIMS, Arthritis Impact Measurement Scale; [a,] Exposure, includes attention control, usual care and other types of exposure while no exposure, includes nonintervention and wait-list controls; [b], NA, not applicable because all studies considered at high risk of bias given the inability to blind participants to exercise interventions;[c,]number of groups exceed 16 because two studies reported results for both abp and itt analysis; [d,] insufficient number of outcomes to include the DASS, HADS, MHI

and VAS; [e,] number of groups exceed 16 because three studies reported anxiety results using two different instruments;

Supplementary file 5. GRADE results.

Author(s): What are the effects of exercise (aerobic, strength training, or both) on anxiety in adults with arthritis and other rheumatic diseases? **Date** July 3, 2017

Question: Exercise compared to control for reducing anxiety in adults with arthritis and other rheumatic diseases

Setting: Home, Facility, Both

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise	control	Relative (95% CI)	Absolute (95% CI)		
Anxiety (follow up: mean 15.8 weeks; assessed with: Various self-report instruments)												
14	randomized trials	not serious	not serious	not serious	not serious	publication bias strongly suspected all plausible residual confounding would reduce the demonstrated effect [a]	514	369	not estimable -	SMD **0.4 SD lower** (0.65 lower to 0.15 lower)	⨁⨁⨁⨁ HIGH	CRITICAL

CI: Confidence interval; **SMD**: Standardized mean difference

Explanations

a. Statistically significant small-study effects, suggesting the possibility of publication bias, possible confounding by year of publication, with the magnitude of effect over time smaller with more recent studies.

PRISMA Checklist

Section/topic	#	Checklist item	Reported on line #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1-3
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	23-49
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	62-119
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	120-123
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	48-49; 128-129; 792-795
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	130-189
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	190-198
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	199-203; Supplementary file 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	205-225
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	226-240
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	227-234; 241-245
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	246-262
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	264-278

PRISMA Checklist

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	279-316

Section/topic	#	Checklist item	Reported on line #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	334-349
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	317-343; 350-360
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	369-373; Figure 1; Supplementary file 2
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	371-449; Tables 1-3
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Supplementary file 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figure 3
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Table 4; 459-477; 503-617
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	450-457; Figure 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	478-502; Table 5, Figures 4 & 5; Supplementary files 4 & 5
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	619-764

PRISMA Checklist

Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	765-778
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	779-782
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	799-801

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097