

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email editorial.bmjopen@bmj.com

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:	<i>BMJ Open</i>
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

SCHOLARONE™
Manuscripts

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

4
5 **Authors:** Corresponding author: *George A. Kelley*, DA, FACSM, School of Public
6 Health, Department of Biostatistics, West Virginia University, Morgantown, WV, USA,
7 26506-9190, Office Phone: 304-293-6279, Fax: 304-293-5891, E-mail:
8 gkelley@hsc.wvu.edu

9
10 Co-author: *Kristi S. Kelley*, M.Ed., Research Instructor, School of Public Health,
11 Department of Biostatistics, Robert C. Byrd Health Sciences Center,
12 West Virginia University, PO Box 9190, Morgantown, WV, USA, 26506-9190, Office
13 Phone: 304-293-6280, Fax: 304-293-5891, E-mail: kskelley@hsc.wvu.edu

14
15 Co-author: *Leigh F. Callahan*, PhD, Mary Link Briggs Distinguished Professor of
16 Medicine, Professor, Departments of Social Medicine and Orthopaedics, Adjunct
17 Professor, Department of Epidemiology, 3300 Thurston Bldg, Campus Box 7280,
18 University of North Carolina, Chapel Hill, NC 27599-7280, Office Phone: 919-966-0564,
19 E-mail: leigh.callahan@med.unc.edu

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

21 **Abstract:** 300 words

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

23 ABSTRACT

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

27 **Methods:** Randomized controlled exercise intervention trials ≥ 4 weeks in adults ≥ 18
28 years of age with osteoarthritis, rheumatoid arthritis or fibromyalgia were included.
29 Studies were located by searching 8 electronic databases, cross-referencing and expert
30 review. Dual selection and data abstraction of studies were performed. Hedge's
31 standardized effect size (ES) was calculated for each result and pooled using the
32 recently developed inverse-heterogeneity (IVhet) model. Two-tailed z-alpha values \leq
33 0.05 and non-overlapping 95% confidence intervals (CI) were considered statistically
34 significant. Heterogeneity was estimated using Q and I^2 with alpha values ≤ 0.10 for Q
35 considered statistically significant. Small-study effects were examined using funnel
36 plots and Egger's regression test. In addition, the number-needed-to-treat (NNT),
37 percentile improvement and meta-regression were conducted. **Results:** Of the 639
38 citations screened, 14 studies representing 926 initially enrolled participants (539
39 exercise, 387 control) met the criteria for inclusion. Length of training averaged $15.8 \pm$
40 6.7 weeks, frequency 3.3 ± 1.3 times per week and duration 28.8 ± 14.3 minutes per
41 session. Overall, statistically significant exercise minus control reductions in anxiety
42 were found (ES = -0.40, 95% CI, -0.65, -0.15, $\tau^2 = 0.14$; Q = 40.3, p = 0.0004; $I^2 =$
43 62.8%). The NNT was 6 with a percentile improvement of 15.5% and an estimated 5.3
44 million inactive US adults with AORD improving their anxiety if they started exercising
45 regularly. Statistically significant small-study effects were observed (p < 0.0001).

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

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

For peer review only

1
2
3 **50 STRENGTHS AND LIMITATIONS OF THIS STUDY**
4

5
6 51 - To the best of the investigative team's knowledge, this is the first systematic review
7
8 52 with meta-analysis to examine the effects of exercise on anxiety as a primary outcome
9
10 53 in adults with AORD.

11
12 54 - The use of the recently developed IVhet model appears to provide more robust
13
14 55 estimates than those derived from other models.

15
16
17 56 - Common to all aggregate data meta-analyses, the possibility of ecological fallacy
18
19 57 exists and the meta-regression analyses conducted do not allow for causal inferences.

20
21 58 - Given that no adjustments for multiple testing were made because of concerns about
22
23 59 missing possibly important findings that could be tested in original trials, the possibility
24
25 60 of chance findings exist.
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

61 INTRODUCTION

62 Rationale

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

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

1
2
3 84 prevalence of anxiety and depression among US adults with doctor-diagnosed arthritis
4
5 85 was estimated to be almost twice as high for anxiety (30.5%) versus depression
6
7 86 (17.5%), with US population estimates of 11.5 million for anxiety and 6.6 million for
8
9 87 depression.⁸ Given the prevalence of anxiety, it was recommended that health care
10
11 88 providers screen people with arthritis for anxiety.⁸
12
13

14 89 Exercise is an intervention that is generally safe and appropriate for most persons with
15
16 90 various types of AORD.^{9 10} Recent meta-analytic work has shown that community-
17
18 91 deliverable exercise interventions reduce depressive symptoms in adults, with an
19
20 92 estimated 3.1 million inactive US adults with AORD improving their depressive
21
22 93 symptoms if they began and maintained a regular exercise program.¹¹ However, the
23
24 94 effects of community-deliverable exercise on anxiety as a primary outcome are not
25
26 95 known given a plethora of conflicting randomized controlled trials on this topic as well as
27
28 96 a lack of studies that assess both depression and anxiety within the same study (only
29
30 97 44.8% based on a previous meta-analysis).¹¹ Most importantly, a recent systematic
31
32 98 review of previous meta-analyses, not to be confused with an original systematic review
33
34 99 with meta-analyses, found that no meta-analysis of randomized controlled trials has
35
36 100 examined the effects of community-deliverable exercise on anxiety as a primary
37
38 101 outcome in adults with AORD.¹² Clearly, it is critically important to develop a better
39
40 102 understanding of the overall magnitude of effect, as well as factors associated with,
41
42 103 exercise for improving anxiety in adults with AORD.
43
44
45
46
47
48

104 **Objective**

105 The primary objective of this study was to conduct a systematic review with an
106 aggregate data meta-analysis of randomized controlled trials to determine the effects of
107
108
109
110
111
112

1
2
3 107 community-deliverable exercise interventions on anxiety in adults with AORD.
4

5 108 **METHODS**
6

7
8 109 **Overview**
9

10 110 This study followed the guidelines from the Preferred Reporting Items for Systematic
11
12 111 Reviews and Meta-Analysis (PRISMA) statement for meta-analyses of health care
13
14 112 interventions.¹³ The protocol for this study is registered in PROSPERO (trial registration
15
16 113 number CRD42016048728) and has been previously published in BMJ Open.¹⁴
17
18

19 114 **Eligibility criteria**
20

21 115 Studies that met the following criteria were included: (1) randomized controlled trials
22
23 116 with the unit of assignment at the participant level, (2) community-deliverable
24
25 117 exercise-only intervention group (aerobic, strength training, or both), (3) interventions
26
27 118 ≥ 4 weeks, (4) comparative control group (non-intervention, wait-list control, usual
28
29 119 care, attention control), (5) adults ≥ 18 years of age with doctor-diagnosed
30
31 120 osteoarthritis, rheumatoid arthritis or fibromyalgia, (6) studies (published and
32
33 121 unpublished in the form of Master's theses and dissertations) in any language,
34
35 122 assuming an English-language abstract was available, from January 1, 1981 forward,
36
37 123 and (7) data for anxiety, as defined by the authors of the original studies. Studies were
38
39 124 limited to those with osteoarthritis, rheumatoid arthritis or fibromyalgia based on
40
41 125 previous meta-analytic research showing a lack of exercise intervention studies for
42
43 126 other types of AORD.¹¹ Studies were limited to randomized trials because it is the
44
45 127 only way to control for confounders that are not known or measured as well as the
46
47 128 observation that nonrandomized controlled trials tend to overestimate the effects of
48
49 129 healthcare interventions.^{15 16} Aerobic and progressive resistance (strength training)
50
51
52
53
54
55
56
57
58
59
60

1
2
3 130 exercise were defined according to section C2 of the 2008 Physical Activity
4
5 131 Guidelines Advisory Committee Report.¹⁷ Specifically, aerobic exercise is defined as
6
7 132 any 'exercise that primarily uses the aerobic energy-producing systems, can improve
8
9 133 the capacity and efficiency of these systems, and is effective for improving
10
11 134 cardiorespiratory endurance,' while strength training is defined as 'exercise training
12
13 135 primarily designed to increase skeletal muscle strength, power, endurance, and
14
15 136 mass'.¹⁷

16
17
18
19 137 For this proposed project, community-deliverable exercise interventions were
20
21 138 considered to be those that could be performed, or have the potential to be adapted
22
23 139 and performed, by persons in a community setting (recreation or senior centers, in the
24
25 140 home or neighborhood, etc.) and meet the implementation guidelines for physical
26
27 141 activity interventions recently recommended by the Arthritis Program at the Centers
28
29 142 for Disease Control and Prevention: (1) no academic degree required for a
30
31 143 leader/implementer but leader training available, if needed, (2) no special facilities
32
33 144 beyond a community room (except a warm pool for aquatic exercise), (3) inexpensive
34
35 145 equipment, (4) cost to participants less than \$50.00, (5) implementation guide
36
37 146 available, (6) supporting structures judged to be adequate to support widespread
38
39 147 implementation.¹⁸ An exercise duration of at least 4 weeks was chosen based on
40
41 148 previous research in which statistically significant improvements in anxiety occurred
42
43 149 as a result of as little as 4 weeks of exercise training.¹⁹ There was no maximum limit
44
45 150 on the length of any interventions for the studies included in our proposed project. We
46
47 151 limited our studies to adults ages 18 and older because the inclusion of children and
48
49 152 adolescents pose additional confounding problems congruent with the many
50
51
52
53
54
55
56
57
58
59
60

1
2
3 153 developmental changes that occur during this period. In addition, the prevalence of
4
5 154 AORD is more common in adults than children and adolescents. We restricted our
6
7
8 155 studies to published articles, dissertations and master's theses and examined for
9
10 156 potential small-study effects such as publication bias when limited to published
11
12 157 articles in peer-reviewed journals. The year 1981 was chosen as the starting point for
13
14 158 eligibility based on a preliminary PubMed search in which it was found that this was
15
16
17 159 the first year that a randomized controlled trial on exercise and arthritis was
18
19 160 published.²⁰ Studies from both English and non-English-language sources were
20
21 161 included with the latter translated into English by the second author using the freely
22
23 162 available web-based Babelfish and Bing translators. Finally, while acknowledging that
24
25 163 the mechanisms for changes in anxiety may differ for different types of AORD, for
26
27 164 example fibromyalgia versus osteoarthritis and rheumatoid arthritis, the purpose of the
28
29 165 current systematic review with meta-analysis was to determine whether exercise
30
31 166 reduces anxiety in adults with AORD, not why it reduces anxiety.
32
33
34

35 167 **Information sources**

36
37 168 Eight electronic databases were searched for potentially eligible studies in any language
38
39 169 published from January 1, 1981 forward. The last searches were conducted on January
40
41 170 6, 2017. Databases searched included (1) PubMed, (2) SPORTDiscus, (3) Cochrane
42
43 171 Central Register of Controlled Clinical Trials (CENTRAL), (4) Cumulative Index to
44
45 172 Nursing and Allied Health Literature (CINAHL), (5) PsycINFO, (6) Web of Science, (7)
46
47 173 Scopus and (8) ProQuest (Master's theses and dissertations). In addition, cross-
48
49 174 referencing from retrieved studies was conducted. Furthermore, the third author, an
50
51 175 expert on physical activity and AORD, reviewed the reference list for completeness.
52
53
54
55
56
57
58
59
60

176 **Search strategy**

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

181 **Study records**

182 Study selection

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

1
2
3 199 identifying the final number of studies to be included, the overall precision of the
4
5 200 searches was calculated by dividing the number of studies included by the total number
6
7
8 201 of studies screened after removing duplicates.²² The number needed-to-read (NNR)
9
10 202 was then calculated as the inverse of the precision.²²

203 Data abstraction

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

218 Outcomes and prioritization

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

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

223 **Risk of bias assessment in individual studies**

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

240 **Data Synthesis**

241 **Calculation of effect sizes**

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

1
2
3 244 bias.²⁵ This was calculated by subtracting the change outcome difference in the
4
5 245 exercise group minus the change outcome difference in the control group, and then
6
7 246 dividing by the pooled standard deviation of the change outcome for the exercise and
8
9 247 control groups. If change score standard deviations were not available, they were
10
11 248 calculated from reported change outcomes, treatment effect 95% confidence intervals
12
13 249 (CI), or pre and post standard deviation values according to procedures developed by
14
15 249 Follmann et al.²⁶ Secondary outcomes (physical function, pain, quality of life,
16
17 250 depression, muscular strength) were calculated using the same procedures as for the
18
19 251 primary outcome while BMI and VO_{2max} were calculated using the original metric. For
20
21 252 studies in which outcomes were assessed at multiple time points, differences between
22
23 253 baseline values and the final time point closest to cessation of the exercise intervention
24
25 254 were used.

256 **Pooled estimates for changes in outcomes**

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

1
2
3 266 model, regardless of heterogeneity.²⁷ Two-tailed z-alpha values ≤ 0.05 and non-
4
5 267 overlapping 95% confidence intervals were considered statistically significant.

6
7 268 *Heterogeneity* and *inconsistency* for each pooled outcome were estimated using the
8
9 269 Q^{30} and I^2 statistic,³¹ respectively. An alpha level of ≤ 0.10 for Q was considered to
10
11 270 represent statistically significant heterogeneity while inconsistency was categorized as
12
13 271 very low (<25%), low (25% to <50%), moderate (50% to <75%) or large ($\geq 75\%$).³¹ To
14
15 272 improve practical relevance with respect to potential improvements in anxiety and all
16
17 273 secondary outcomes, percentile gain in the exercise groups was calculated using
18
19 274 Cohen's U_3 index³² In addition, the number-needed-to treat (NNT) was estimated using
20
21 275 the approach suggested by the Cochrane Collaboration²³ and a control group risk of
22
23 276 30% based on previous research on anxiolytics.³³ This was accomplished by converting
24
25 277 the standardized mean differences into a log odds ratio, odds ratio, assumed control
26
27 278 risk (30%) and then NNT. Extending the NNT, estimates of the number of US adults
28
29 279 with AORD who could improve their anxiety levels but were not currently meeting
30
31 280 physical activity recommendations were calculated. These were based on the reciprocal
32
33 281 of the NNT multiplied by the number of adults in the United States with doctor-
34
35 282 diagnosed arthritis who were not currently meeting exercise guidelines, currently
36
37 283 approximately 31.6 million.^{1 34} *Influence analysis* was conducted with each study
38
39 284 deleted from the model once while *cumulative meta-analysis*, ranked by year, was used
40
41 285 to examine the accumulation of results over time.

42
43 286 The primary pooling of results was based on group level findings. However, findings
44
45 287 were also examined by collapsing results so that only one ES represented each study.
46
47 288 In addition, for those outcomes that were assessed using multiple instruments, results
48
49
50
51
52
53
54
55
56
57
58
59

1
2
3 289 from these instruments were pooled into one ES. The rationale for this was based on
4
5 290 the lack of consensus regarding the most valid and reliable instrument for the outcome
6
7 291 and population of interest as well as the need to maintain as much independence as
8
9
10 292 possible. For those studies that reported both per protocol and intention-to-treat
11
12 293 analyses, results were also pooled into one ES.

14 294 Exploratory *meta-regression* based on the IVhet model was used to examine the
15
16
17 295 relationship between changes in our primary outcome (anxiety) and selected
18
19 296 covariates.²⁷ This was accomplished by (1) conducting simple meta-regression for
20
21 297 statistically significant associations between selected covariates and changes in
22
23 298 anxiety, (2) examining for multicollinearity between covariates ($r > 0.80$), and (3)
24
25 299 building a multiple meta-regression model. These models used a multiplicative versus
26
27
28 300 additive component for residual heterogeneity. To achieve matching error variances,
29
30
31 301 robust Huber-Ecker-White-sandwich error variances were used to account for the
32
33 302 underestimated dispersion. Such errors were expected to calculate the correct
34
35 303 standard errors for heterogeneous data that are traditionally heteroskedastic. Because
36
37
38 304 of the small sample size, a post hoc decision was made to include the three potential
39
40 305 predictors with the largest R^2 values as a result of simple regression analyses.
41
42 306 However, since the investigative team felt that total minutes of training per week was
43
44 307 more appropriate than total minutes of training over the entire duration of the study, the
45
46
47 308 former was included in the regression. Multiple imputation was used to impute missing
48
49 309 values for minutes of training per week so that the maximum sample size could be
50
51 310 achieved.

1
2
3 311 Based on the recommendations of Rothman,³⁵ no adjustments for multiple testing
4
5 312 were made because of concerns about missing possibly important findings that could be
6
7 313 pursued in future randomized controlled trials. While this could be viewed as a ‘fishing
8
9 314 expedition’, such analyses are important for providing investigators with potential
10
11 315 direction for future randomized controlled trials, one of the very reasons for conducting a
12
13 316 systematic review with meta-analysis.³⁶ This approach is especially appropriate for
14
15 317 meta-analysis since covariates are not randomly assigned in meta-analysis and thus,
16
17 318 such analyses are considered to be observational in nature.³⁷ As a result, causal
18
19 319 inferences cannot be derived from meta-regression. However, any observed
20
21 320 associations can provide direction for future research.
22
23
24
25

26 321 **Meta-biases**

27
28 322 *Small-study-effects* (publication bias, etc.) for primary and secondary outcomes were
29
30 323 assessed following current guidelines.³⁸ This included qualitative analysis using funnel
31
32 324 plots as well as quantitative analysis using Egger’s regression-intercept test for
33
34 325 continuous data.³⁸ An alpha level ≤ 0.05 and 95% CI that did not include zero (0) was
35
36 326 considered to represent statistically significant small-study effects.
37
38
39

40 327 **Confidence in cumulative evidence**

41
42 328 Strength of findings for our primary outcome (anxiety) was evaluated using the Grading
43
44 329 of Recommendations Assessment, Development and Evaluation (GRADE) for meta-
45
46 330 analysis.³⁹ The quality of evidence was assessed across the domains of risk of bias,
47
48 331 consistency, directness, precision and publication bias. Quality was judged as high
49
50 332 (further research is very unlikely to change our confidence in the estimate of effect),
51
52 333 moderate (further research is likely to have an important impact on our confidence in the
53
54
55
56
57
58
59
60

1
2
3 334 estimate of effect and may change the estimate), low (further research is very likely to
4
5 335 have an important impact on our confidence in the estimate of effect and is likely to
6
7 336 change the estimate), or very low (very uncertain about the estimate of effect).
8
9

10 337 **Software used for data synthesis**

11
12 338 All data was analyzed using Stata (V.14.1; Stata/SE for Windows (Version 14.1).
13
14 339 College Station, Texas: Stata Corporation LP, 2015), Microsoft Excel 2010 (Microsoft
15
16 340 Excel (Version 2010)), and three add-ins for Excel, Meta XL (V.5.3; Meta XL (Version
17
18 341 5.3). 2016), SSC-Stat (V.2.18; SSC-Stat (Version 2.18). University of Reading, UK:
19
20 342 Statistical Services Center, 2007), and EZ-Analyze (V.3.0; EZ Analyze (Version 3.0).
21
22 343 Boston, MA: Tim Poynton, 2007).
23
24
25

26 344 **RESULTS**

27 345 **Study Characteristics**

28
29
30 346 A flow diagram that depicts the search process for study selection is shown in Figure 1.
31
32 347 After initially identifying 639 citations and removing 240 duplicates both electronically
33
34 348 and manually, 399 citations were screened. Of these, 14 studies representing 30 groups
35
36 349 (16 exercise, 14 control) and 926 initially enrolled participants (539 exercise, 387
37
38 350 control) met the criteria for inclusion.⁴⁰⁻⁵³ Two studies included more than one
39
40 351 intervention group.^{48 51} One included a pool and walking group⁴⁸ while the other
41
42 352 included a long and short bout exercise group.⁵¹ The major reasons for exclusion were
43
44 353 (1) inappropriate intervention (47.8%), (2) inappropriate study design (32.2%), (3)
45
46 354 inappropriate population (11.9%), (4) inappropriate comparison group (4.7%), and (5)
47
48
49
50 355 inappropriate outcome (3.4%). The precision of the search, excluding duplicates, was
51
52
53
54
55
56
57
58
59
60

356 3.5% while the NNR was 29. A list of excluded studies, including the reasons for
357 exclusion, can be found in Supplementary File 2.

358 With respect to source, 1 study (7.1%) was published as a dissertation⁴¹ while the
359 remaining 13 (92.9%) were published in peer-reviewed journals.^{40 42-53} For the 12
360 studies (85.7%) in which data were available, the 5-year impact factor of the journals in
361 which studies were published ranged from 1.7 to 7.9 ($\bar{x} \pm SD$, 4.1 ± 2.4 , median = 2.9).
362 Five studies (35.7%) were published in the United States,^{41 42 46-48} 2 each in either
363 Canada,^{45 51} Portugal^{52 53} or Spain,^{49 50} and 1 each in either Australia,⁴³ Brazil,⁴⁰ or
364 Ireland.⁴⁴ Thirteen of the 14 studies (92.9%) were published in English-language
365 journals⁴⁰⁻⁵² while 1 (7.1%) was published in Spanish.⁵³ With respect to types of control
366 groups, 4 studies used either a wait-list control^{40 41 43 44} or what appeared to be some
367 type of attention control group,^{42 46 48 51} while three each used either a non-intervention⁴⁵
368 ^{47 52} or usual care group.^{49 50 53} Three studies (21.4%) reported using matching
369 procedures according to either sex,⁴⁵ age, sex and BMI,⁴⁶ or type of arthritis
370 (rheumatoid or osteoarthritis).⁴⁸ None of the studies reported using any type of
371 crossover design.⁴⁰⁻⁵³ For data analysis, 7 studies (50.0%) reported using the per-
372 protocol approach,^{41 46-48 50 52 53} 4 (28.6%) used intention-to-treat,^{40 42-44} while the
373 remaining 3 (21.4%) used both.^{45 49 51} Eight studies (57.1%) provided sample size
374 estimates.^{40 42-44 46 50 51 53} With respect to funding, 12 studies (85.7%), reported receiving
375 funding from government, university, or private sources for their work.^{40 42-52}

376 **Participant Characteristics**

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

1
2
3 379 and had low cardiorespiratory fitness. The majority of participants were women,
4
5 380 although 7 studies (50.0%) also included a small number of men.⁴²⁻⁴⁸ Nine studies
6
7 381 (64.3%) were limited to participants with fibromyalgia,^{40 41 45 46 49-53} 3 (21.4%) with
8
9 382 osteoarthritis,⁴²⁻⁴⁴ 1 with rheumatoid arthritis⁴⁷ and 1 with either rheumatoid arthritis or
10
11 383 osteoarthritis.⁴⁸ For those studies in which data were available, the number of years in
12
13 384 which rheumatic symptoms were present ranged from 3 to 24 ($\bar{x} \pm SD$, 13.1 ± 7.0 ,
14
15 385 median = 12.0),^{44-46 49 51-53} while years since diagnosis ranged from 3 to 7 ($\bar{x} \pm SD$, 4.1
16
17 386 ± 2.0 , median = 3).^{45 51-53} Nine of the 14 studies (64.3%) reported that one or more
18
19 387 participants were taking some type of medication for their condition.^{41 43-45 47-49 52 53}
20
21 388 These included, but were not necessarily limited to, non-steroidal anti-inflammatory
22
23 389 drugs (NSAIDs), analgesics, narcotics and non-narcotics for pain, muscle relaxants,
24
25 390 antidepressants, and anxiolytics. One study reported cigarette smoking in some of the
26
27 391 participants.⁵¹ Participant withdrawals or removal in the exercise groups ranged from
28
29 392 0% to 50% ($\bar{x} \pm SD$, 17.4 ± 13.4 , median = 17.0) while withdrawals or removal in the
30
31 393 control groups ranged from 0% to 41% ($\bar{x} \pm SD$, 11.5 ± 12.7 , median = 6.3). Reasons
32
33 394 for withdrawals or removal included such things as family issues, pain from exercising,
34
35 395 injuries, personal issues, time, unhappiness with group assignment, transportation
36
37 396 issues, moving, employment commitments, boredom with exercise routine, not enough
38
39 397 room or privacy to perform exercise, failure to complete lab assessments, not attending
40
41 398 a specific percentage of the exercise sessions, or changing medications that could
42
43 399 affect mood.
44
45
46
47
48
49
50

51 400 **Exercise Intervention Characteristics**

52
53
54
55
56
57
58
59
60

1
2
3 401 Exercise intervention characteristics for each group from each study are shown in
4
5 402 Tables 1 and 3. Intensity of training, categorized according to American College of
6
7 403 Sports Medicine⁵⁴ and limited to aerobic exercise only, included very light, light,
8
9 404 moderate and vigorous exercise for the 9 (64.3%) studies that reported such
10
11 405 information.^{41 45 46 48-53} For mode of training, 6 studies (42.9%) focused on aerobic types
12
13 406 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}
14
15 407 ⁵³ Specific types of aerobic activities included such things as aquatic exercise, walking,
16
17 408 jogging, exercising to music and cycling. For the few studies that provided detailed
18
19 409 information on resistance training, the number of sets ranged from 1 to 3,^{47 49} the
20
21 410 number of repetitions from 8 to 15,^{47 49} and the number of exercises from 2 to 10 or
22
23 411 more.^{46 47 49} One study reported a rest period for 30 seconds between sets.⁴⁷ For those
24
25 412 studies that reported data, the equipment used for resistance training included free
26
27 413 weights and elastic bands.^{42 46 47 52 53} Seven studies (50.0%) reported supervised
28
29 414 exercise,^{45 46 48-50 52 53} 5 (35.7%) reported both supervised and unsupervised exercise,⁴⁰⁻
30
31 415 ⁴⁴ while the remaining 2 (14.3%) reported unsupervised exercise.^{47 51} Three of the 14
32
33 416 studies (21.4%) reported some type of adverse event.^{41 42 51} Reasons included 1
34
35 417 participant dropping out due to pain after the first exercise session,⁴¹ 2 participants
36
37 418 because of a history of a herniated disk and low back and leg pain,⁴² and 1 participant
38
39 419 because of a metatarsal fracture.⁵¹ Another study reported that 1 participant withdrew
40
41 420 because of the exacerbation of back pain⁴³ while a final study reported the exclusion of
42
43 421 2 participants because of severe coronary artery disease.⁴⁷ None of the studies
44
45 422 provided data on the costs associated with conducting the intervention.⁴⁰⁻⁵³
46
47
48
49
50
51
52
53

423 Risk of Bias Assessment

1
2
3 424 Results for risk of bias assessment using the Cochrane Risk of Bias Assessment
4
5 425 Instrument are shown in Figure 2 and Supplementary file 3. As can be seen, greater
6
7 426 than 50% of the studies were at an unclear or high risk of bias with respect to (1)
8
9 427 incomplete outcome reporting (78.6%), (2) allocation concealment (78.6%), and (3)
10
11 428 blinding of outcome assessors (57.1%). Given the inability to truly blind participants in
12
13 429 exercise intervention trials, all studies (100%) were considered to be at a high risk of
14
15 430 bias for the category 'blinding of participants and personnel'.
16
17
18

19 431 **Data Synthesis**

20
21 432 **Overall results for primary outcome (anxiety).** Overall results for changes in anxiety
22
23 433 for the 14 included studies⁴⁰⁻⁵³ are shown in Table 4 and Figure 3. As can be seen,
24
25 434 statistically significant ($p = 0.002$) reductions in anxiety were observed. In addition,
26
27 435 statistically significant heterogeneity was observed while overall inconsistency was
28
29 436 categorized as moderate, (range = low to large). The NNT was 6 with a percentile
30
31 437 improvement of 15.5% and an estimated 5.3 million inactive US adults with AORD
32
33 438 improving their anxiety if they started exercising regularly. Statistically significant small-
34
35 439 study effects were observed ($p < 0.0001$) (Figure 4). With each result deleted from the
36
37 440 model once, results remained statistically significant across all deletions, ranging from -
38
39 441 0.44 (95% CI, -0.71 to -0.18) to -0.35 (-0.57 to -0.12). Cumulative meta-analysis, ranked
40
41 442 by year, demonstrated that results have been statistically significant since the first study
42
43 443 was conducted in 1989,⁴⁸ but with a trend towards smaller improvements in anxiety with
44
45 444 each accumulating year (Figure 5). Reductions in anxiety were similar to group-level
46
47 445 results when collapsed so that only one ES represented each study (ES, -0.40, 95% CI,
48
49 -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%,
50
51
52
53
54
55
56
57
58
59
60

1
2
3 447 $\tau^2 = 0.15$). With six outliers deleted from the model, overall reductions in anxiety were
4
5 448 similar but heterogeneity was no longer statistically significant and overall inconsistency
6
7 449 was reduced to a level categorized as small (ES, -0.40, 95% CI, -0.62 to -0.18, $p =$
8
9 450 0.0004; $Q = 11.8$, $p = 0.22$; $I^2 = 24.0\%$, 95% CI, 0% to 63.1%, $\tau^2 = 0.03$).

11
12 451 **Meta-regression results for anxiety.** Simple meta-regression results are shown in
13
14 452 Supplementary File 4. For study characteristics, greater reductions in anxiety were
15
16 453 associated with (1) earlier publication year, (2) studies at an unclear versus low risk of
17
18 454 bias, (3) studies in which sample size estimates were not provided, (4) trials in which a
19
20 455 larger percentage of participants initially agreed to participate in, and (5) studies that
21
22 456 were not funded versus funded. For participant characteristics, greater improvements
23
24 457 were associated with a larger percent dropout in the exercise groups as well as younger
25
26 458 age. For exercise intervention characteristics, greater reductions were associated with
27
28 459 (1) aerobic/strength training versus aerobic and strength training combined, (2) fewer
29
30 460 minutes of exercise per session, (3) minutes of exercise per week, and (4) total minutes
31
32 461 of exercise for the entire intervention period. Greater reductions were also associated
33
34 462 with (1) supervised and unsupervised exercise versus both, (2) facility and home-based
35
36 463 exercise versus both and (3) group and self-exercise versus both.

37
38 464 Results for the final multiple regression model are shown in Table 5. The overall model
39
40 465 was statistically significant ($F = 17.2$, $p = 0.0005$). Earlier year of publication and studies
41
42 466 at an unclear versus low risk of bias for incomplete outcome data were statistically
43
44 467 significant predictors for greater reductions in anxiety. However, minutes of exercise per
45
46 468 week was no longer statistically significant.

1
2
3 469 **GRADE findings for changes in anxiety.** An evidence profile for changes in anxiety is
4
5 470 shown in Supplementary file 5. As can be seen, the outcome (anxiety) was considered
6
7 471 critical and the overall strength of the finding was considered high, with future additional
8
9 472 studies unlikely to have an effect on the overall direction of findings.

10
11
12 473 **Results for secondary outcomes.** Overall results for changes in secondary outcomes
13
14 474 are shown in Table 4. *Physical function* was assessed in 10 studies^{40 42-45 47 48 51-53} using
15
16 475 the 10 meter walk test, 50 foot walk, 6 minute walk, Arthritis Impact and Measurement
17
18 476 Scale (AIMS), Fibromyalgia Impact Questionnaire (FIQ), Short Physical Performance
19
20 477 Battery, sit-to-stand test, stairclimbing test, up and go test, and the Western Ontario and
21
22 478 McMaster Osteoarthritis Index (WOMAC). As can be seen, statistically significant ($p <$
23
24 479 0.001) improvements in *physical function* were observed. Statistically significant
25
26 480 heterogeneity was observed while inconsistency was categorized as moderate, (range =
27
28 481 low to large). The NNT was 4 with a percentile improvement of 24.5% and an estimated
29
30 482 9 million inactive US adults with AORD improving their physical function if they started
31
32 483 exercising regularly. No statistically significant small-study effects were observed ($p =$
33
34 484 0.17). With each result deleted from the model once, results remained statistically
35
36 485 significant across all deletions, ranging from 0.54 (95% CI, 0.30 to 0.78) to 0.73 (95%
37
38 486 CI, 0.39 to 1.06). Cumulative meta-analysis, ranked by year, demonstrated that results
39
40 487 have been statistically significant since the first study was conducted in 1989,⁴⁸ but with
41
42 488 a trend towards smaller improvements in physical function with each accumulating year
43
44 489 (from 0.86 in 1989 to 0.66 in 2016). Improvements in physical function were similar to
45
46 490 group-level results when collapsed so that only one ES represented each study (ES,
47
48 491 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%

1
2
3 492 to 86.5%, $\tau^2 = 0.21$). With four outliers deleted from the model, overall improvements
4
5 493 in physical function were statistically significant but slightly smaller, heterogeneity was
6
7 494 no longer statistically significant, and overall inconsistency was reduced to a level
8
9
10 495 categorized as very low (ES, 0.57, 95% CI, 0.36 to 0.78, $p < 0.001$; $Q = 7.2$, $p = 0.41$; $I^2 =$
11
12 496 2.7%, 95% CI, 0% to 68.5%, $\tau^2 = 0.003$).

13
14 497 For *pain*, assessment was conducted in 13 studies^{40-44 46-53} using the AIMS, FIQ,
15
16 498 numerical rating scale, tender point count, visual analog scale and the WOMAC. As can
17
18 499 be seen in Table 4, statistically significant ($p = 0.017$) decreases in pain were found.
19
20 500 Statistically significant heterogeneity was observed while inconsistency was categorized
21
22 501 as large, including both CIs. The NNT was 6 with a percentile improvement of 23.1%
23
24 502 and an estimated 5.6 million inactive US adults with AORD decreasing their pain if they
25
26 503 started exercising regularly. No statistically significant small-study effects were
27
28 504 observed ($p = 0.34$). With each result deleted from the model once, results remained
29
30 505 statistically significant across all deletions, ranging from -0.70 (95% CI, -1.21 to -0.19) to
31
32 506 -0.47 (95% CI, -0.80 to -0.15). Cumulative meta-analysis, ranked by year, demonstrated
33
34 507 that results have been statistically significant, and remained statistically significant,
35
36 508 since only 2013. Decreases in pain were similar to group-level results when collapsed
37
38 509 so that only one ES represented each study (ES, -0.62, 95% CI, -1.16 to -0.07, $p = 0.03$;
39
40 510 = 123.7, $p < 0.001$; $I^2 = 90.3\%$, 95% CI, 85.3% to 93.6%, $\tau^2 = 0.75$). With ten outliers
41
42 511 deleted from the model, decreases in pain remained statistically significant but smaller,
43
44 512 heterogeneity was no longer statistically significant, and overall inconsistency was
45
46 513 reduced to a level categorized as very low (ES, -0.44, 95% CI, -0.70 to -0.18, $p = 0.001$;
47
48 514 $Q = 1.5$, $p = 0.68$; $I^2 = 0\%$, 95% CI, 0% to 69.5%, $\tau^2 = 0$).

1
2
3 515 *Depression* was assessed in 13 studies^{40-48 50-53} using the AIMS, Beck Depression
4
5 516 Inventory (BDI), Center for Epidemiologic Studies Depression Scale (CES-D),
6
7 517 Depression, Anxiety and Stress Scale (DASS21), FIQ, HADS, MHI, and VAS. As can
8
9
10 518 be seen in Table 4, statistically significant ($p = 0.009$) decreases in depression were
11
12 519 found. Statistically significant heterogeneity was observed while inconsistency was
13
14 520 categorized as moderate (95% CI = low to large). The NNT was 6 with a percentile
15
16 521 improvement of 15% and an estimated 5.1 million inactive US adults with AORD
17
18 522 reducing their depression if they started exercising regularly. Small-study effects were
19
20 523 not statistically significant ($p = 0.08$). With each result deleted from the model once,
21
22 524 results remained statistically significant across all deletions, ranging from -0.52 (95% CI,
23
24 525 -0.68 to -0.37) to -0.32 (95% CI, -0.61 to -0.03). Cumulative meta-analysis, ranked by
25
26 526 year, demonstrated that improvements have been statistically significant and remained
27
28 527 stable since 2013. Decreases in depression were similar to group-level results when
29
30 528 collapsed so that only one ES represented each study (ES, -0.38, 95% CI, -0.70 to -
31
32 529 0.07, $p = 0.02$; $Q = 45.6$, $p < 0.001$; $I^2 = 73.7\%$, 95% CI, 54.3% to 84.8%, $\tau^2 = 0.21$).
33
34 530 With three outliers deleted from the model, improvements in depression remained
35
36 531 statistically significant, slightly larger, but with non-significant heterogeneity and overall
37
38 532 inconsistency categorized as very low (ES, -0.43, 95% CI, -0.60 to -0.26, $p < 0.001$; $Q =$
39
40 533 5.7, $p = 0.89$; $I^2 = 0\%$, 95% CI, 0% to 19.3%, $\tau^2 = 0$).
41
42
43
44
45

46 534 *Quality-of-life* was assessed in 12 studies^{40-47 49 51-53} using the FIQ, Health Assessment
47
48 535 Questionnaire (HAQ), Quality of Life Scale (QOLS), SF-12, and SF-36. As shown in
49
50 536 Table 4, statistically significant ($p < 0.0001$) improvements in quality-of-life were found.
51
52
53 537 Statistically significant heterogeneity was observed while inconsistency was categorized
54
55
56
57
58
59
60

1
2
3 538 as large (95% CI = low to large). The NNT was 4 with a percentile improvement of
4
5 539 23.1% and an estimated 8.6 million inactive US adults with AORD improving their
6
7 540 quality-of-life if they started exercising regularly. Statistically significant small-study
8
9 541 effects were observed ($p < 0.001$). With each result deleted from the model once,
10
11 542 results remained statistically significant across all deletions, ranging from 0.58 (95% CI,
12
13 543 0.35 to 0.81) to 0.70 (95% CI, 0.41 to 0.99). Cumulative meta-analysis, ranked by year,
14
15 544 demonstrated that improvements have been statistically significant since 2001, but with
16
17 545 a trend towards a decrease in the magnitude of effect. Increases in quality-of-life were
18
19 546 similar to group-level results when collapsed so that only one ES represented each
20
21 547 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%
22
23 548 CI, 33.9% to 80.8%, $\tau^2 = 0.14$). With four outliers deleted from the model,
24
25 549 improvements in quality-of-life remained statistically significant, similar in magnitude, but
26
27 550 with non-significant heterogeneity and overall inconsistency categorized as low (ES,
28
29 551 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
30
31 552 67.5%, $\tau^2 = 0.04$).

32
33 553 *Maximum oxygen consumption* ($VO_{2\max}$ in $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) was assessed in 5 studies⁴⁶⁻⁴⁸
34
35 554 ^{51 52} using various maximal treadmill tests while one study used a submaximal step test
36
37 555 (Canadian Aerobic Fitness Test). As can be seen in Table 4, statistically significant ($p =$
38
39 556 0.001) improvements in $VO_{2\max}$ were observed. Statistically significant heterogeneity
40
41 557 was observed while inconsistency was categorized as moderate (95% CI = low to
42
43 558 large). The NNT was 3 with a percentile improvement of 25.7% and an estimated 9.5
44
45 559 million inactive US adults with AORD improving their relative $VO_{2\max}$ if they started
46
47 560 exercising regularly. No statistically significant small-study effects were observed ($p =$
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 561 0.18). With each result deleted from the model once, results remained statistically
4
5 562 significant across all deletions, ranging from 1.80 ml·kg⁻¹·min⁻¹ (95% CI, 0.58 to 3.01) to
6
7 563 2.47 ml·kg⁻¹·min⁻¹ (95% CI, 1.25 to 3.69). Cumulative meta-analysis, ranked by year,
8
9 564 demonstrated that improvements have been statistically significant since 2003, but with
10
11 565 a trend towards a decrease in the magnitude of effect over time. Increases in VO_{2max}
12
13 566 were similar to group-level results when collapsed so that only one ES represented
14
15 567 each study (ES, 2.01 ml·kg⁻¹·min⁻¹, 95% CI, 0.59 to 3.44, p = 0.01; Q = 19.4, p = 0.001;
16
17 568 I² = 79.4%, 95% CI, 51.2% to 91.3%, tau² = 1.7). With outliers deleted from the model,
18
19 569 improvements in VO_{2max} were smaller, with non-significant heterogeneity and overall
20
21 570 inconsistency categorized as low (ES, 1.93 ml·kg⁻¹·min⁻¹, 95% CI, 0.83 to 3.02, p =
22
23 571 0.001; Q = 0.03, p = 0.86; I² = 0%, 95% CI, 0% to 0%, tau² = 0).

24
25 572 Upper and lower body *muscular strength* was assessed in five studies^{45 47-49 52} using
26
27 573 free weights, grip strength, isokinetic strength and the sit-to-stand test with free weights.
28
29 574 As shown in Table 4, statistically significant (p < 0.001) improvements in strength were
30
31 575 observed. No statistically significant heterogeneity or mean inconsistency was observed
32
33 576 (95% CI = none to moderate). The NNT was 4 with a percentile improvement of 22.2%
34
35 577 and an estimated 8 million inactive US adults with AORD improving their strength if they
36
37 578 started exercising regularly. No statistically significant small-study effects were
38
39 579 observed (p = 0.65). With each result deleted from the model once, results remained
40
41 580 statistically significant across all deletions, ranging from 0.50 (95% CI, 0.21 to 0.79) to
42
43 581 0.68 (95% CI, 0.39 to 0.96). Cumulative meta-analysis, ranked by year, demonstrated
44
45 582 that improvements in strength have been statistically significant since the first included
46
47 583 study in 1989.⁴⁸ Changes in strength were similar to group-level results when collapsed

1
2
3 584 so that only one ES represented each study (ES, 0.59, 95% CI, 0.33 to 0.85, $p < 0.001$;
4
5 585 $Q = 3.5$, $p = 0.48$; $I^2 = 0\%$, 95% CI, 0% to 76.2%, $\tau^2 = 0$). There were no outliers.

7 586 Insufficient data were available to analyze *BMI*. The one study that did provide change
8
9
10 587 outcome results for BMI reported no statistically significant changes.⁴⁶

12 588 **DISCUSSION**

14 589 **Overall Findings**

16
17 590 The primary purpose of the current systematic review with meta-analysis was to
18
19 591 examine the effects of exercise (aerobic, strength training, or both) on anxiety in adults
20
21 592 with AORD. The overall findings, a primary purpose of meta-analysis,⁵⁵ suggest that
22
23 593 exercise results in both statistically significant and practically important reductions in
24
25 594 anxiety among adults with selected types of AORD. These findings are supported by (1)
26
27 595 a magnitude of effect comparable to or greater than anxiolytics,⁵⁶ (2) a large percentile
28
29 596 improvement (15.5), (3) low NNT (6), large number of physically inactive US adults with
30
31 597 AORD who could benefit from exercising regularly (5.3 million), (4) similar findings when
32
33 598 examined at the study versus group level, (5) continued existence of a statistically
34
35 599 significant effect when each result was deleted from the analysis once, (6) similar
36
37 600 findings when outliers were deleted and statistical heterogeneity was reduced to a non-
38
39 601 significant effect and overall inconsistency to zero, and (7) a consistent finding of
40
41 602 improvements in anxiety since the first included study was reported in 1989.⁴⁸ Based on
42
43 603 GRADE, it was concluded that anxiety was a critical outcome and that further research
44
45 604 would unlikely change the direction of effect.

47
48
49 605 While the current findings are encouraging, it is interesting to note that cumulative
50
51 606 meta-analysis revealed a distinct trend for a reduction in the pooled ES over time (from -
52
53
54
55
56
57
58
59
60

1
2
3 607 1.47 in 1989 to -0.40 in 2016) and based on meta-regression, a statistically significant
4
5 608 association between greater reductions in anxiety with older versus more recent
6
7 609 studies. While the specific reasons for this could not be determined, it may be that the
8
9 610 experimental design and conduct of studies have improved over time. However, from
10
11 611 the investigative team's perspective, it is highly unlikely that the results will become non-
12
13 612 significant in future years. The former notwithstanding, the general conclusion that
14
15 613 exercise reduces anxiety in adults with selected types of AORD may need to be viewed
16
17 614 with some caution given that the majority of included studies consisted of participants
18
19 615 with fibromyalgia^{40 41 45 46 49-53} while the remaining studies included those with
20
21 616 osteoarthritis and/or rheumatoid arthritis.^{42-44 47 48} While meta-regression revealed no
22
23 617 statistically significant association between type of AORD and changes in anxiety, such
24
25 618 analyses may have been underpowered to detect such an association. In addition, since
26
27 619 other types of AORD such as systemic lupus erythematosus were not included,
28
29 620 generalizing to populations with other types of AORD may not be appropriate.

30
31 621 The final meta-regression model resulted in two statistically significant variables being
32
33 622 included with earlier year of publication and studies at an unclear versus low risk of bias
34
35 623 for incomplete outcome data associated with greater reductions in anxiety. These
36
37 624 findings further reinforce the influence of year of publication on changes in anxiety in the
38
39 625 current systematic review with meta-analysis, a potential reason for such having been
40
41 626 previously mentioned. The greater reductions observed for studies at an unclear versus
42
43 627 low risk of bias suggests that more poorly reported, and possibly conducted, studies
44
45 628 may have led to inflated findings.

1
2
3 629 In addition to statistically significant and practically important improvements in anxiety,
4
5 630 similar improvements were also observed for all secondary outcomes assessed
6
7 631 (physical function, pain, depression, quality of life, VO_{2max} in $ml \cdot kg^{-1} \cdot min^{-1}$, muscular
8
9 632 strength). These findings are important because unlike pharmacologic interventions that
10
11 633 are usually targeted to address one condition, exercise has the potential to improve
12
13 634 multiple physiological and psychological outcomes. Given the former, it would seem
14
15 635 plausible to suggest that continued efforts be made to increase the exercise and
16
17 636 physical activity levels of adults with AORD.
18
19
20
21

22 637 **Implications for Research**

23
24 638 There are at least four implications for the conduct and reporting of future research on
25
26 639 exercise and anxiety in adults with AORD. First, since only five of the studies included
27
28 640 participants with osteoarthritis and/or rheumatoid arthritis, future randomized controlled
29
30 641 trials on exercise and anxiety in these populations appear warranted. Second, exercise
31
32 642 was performed indoors in the majority of included studies. Given that previous research
33
34 643 has suggested the exercise performed outdoors may have better mood-enhancing
35
36 644 effects than indoor exercise,^{57 58} future research examining this phenomenon with
37
38 645 respect to anxiety as well as other outcomes in adults with AORD seems appropriate.
39
40
41 646 Third, future studies should focus on examining the dose-response effects of exercise
42
43 647 on anxiety in adults with AORD and report complete information on the characteristics
44
45 648 of the intervention, including intervention fidelity.⁵⁹ Such information is critical for the
46
47 649 development of evidence-based recommendations aimed at practitioners. Fourth, since
48
49 650 more than half of the studies were considered to be at high or unclear risk of bias with
50
51 651 respect to allocation concealment, blinding of outcome assessors, and incomplete
52
53
54
55
56
57
58
59
60

1
2
3 652 outcome reporting, future studies should address these issues in their experimental
4
5 653 design and report such information. Notably, while all included studies were considered
6
7 654 to be at a high risk of bias with respect to blinding of participants, this is difficult for
8
9 655 researchers to address since unlike pharmacologic studies, it is almost impossible to
10
11 656 blind intervention participants to group assignment in exercise intervention studies.
12
13

14 657 **Implications for Practice**

15
16
17 658 The results of this study appear to have important implications for practice. First, since
18
19 659 changes in both anxiety and secondary outcomes resulted in statistically significant and
20
21 660 practically important improvements, exercise may be more vital than any other
22
23 661 intervention given the apparent multiple benefits of such. While the current systematic
24
25 662 review with meta-analysis was unable to establish with any degree of certainty the
26
27 663 dose-response effects of exercise on anxiety in adults with AORD, it would appear
28
29 664 prudent to adhere to the Active Adult or Active Older Adult Guidelines from the Physical
30
31 665 Activity Guidelines for Americans Physical Activity Guidelines¹⁷ as recommended by the
32
33 666 Centers for Disease Control and Prevention.⁶⁰ Broadly, this includes aerobic activities
34
35 667 on most, if not all, days of the week, muscle strengthening activities at least 2 days per
36
37 668 week, balance exercises at least 3 days per week, and flexibility exercises on a daily
38
39 669 basis.
40
41
42
43

44 670 **Strengths and Limitations**

45
46
47 671 There are at least four apparent *strengths* of the current study. First, to the best of our
48
49 672 knowledge, this is the first systematic review with meta-analysis to examine, as a
50
51 673 primary outcome, the effects of exercise on anxiety in adults with AORD. This is
52
53 674 important given (1) the prevalence of AORD,¹ (2) the expected future increase in the
54
55
56
57
58
59
60

1
2
3 675 prevalence of AORD,² (3) the financial costs associated with AORD,³ and (4) the
4
5 676 previously reported finding that the prevalence of anxiety is almost twice that of
6
7 677 depression.⁸ Second, a novel and recently developed approach, the IVhet model, was
8
9 678 used to pool findings.²⁷ This resulted in more robust estimates than those derived from
10
11 679 the traditional random-effects model.²⁸ This is noteworthy given the need to provide the
12
13 680 most accurate results possible when examining the effects of an intervention on
14
15 681 selected outcome(s). Third, the statistically significant and practically relevant
16
17 682 improvements in anxiety as well as selected secondary outcomes observed in the
18
19 683 current systematic review with meta-analysis should be useful to practitioners and
20
21 684 policy-makers for making informed decisions about the role of exercise in the treatment
22
23 685 of anxiety among adults with selected types of AORD. Fourth, the current findings as
24
25 686 well as gaps in the reviewed literature provide researchers with direction for the conduct
26
27 687 and reporting of future research on this topic.

28
29 688 While there are several strengths to this study, there are also at least four potential
30
31 689 *limitations*. First, similar to any aggregate data meta-analysis, the potential for
32
33 690 ecological fallacy exists. Thus, it may be that the observed findings in the current study
34
35 691 would not apply at the individual participant level. Second, and also common to any type
36
37 692 of aggregate data meta-analysis, meta-regression results do not support causal
38
39 693 inferences because the included studies are not randomly assigned to covariates.³⁷
40
41 694 Therefore, the associations observed in the current investigation would need to be
42
43 695 assessed in appropriately powered randomized trials. Third, while a large number of
44
45 696 statistical tests were conducted, no adjustments were made for such. Thus, some
46
47 697 findings could have been nothing more than the play of chance. However, common to
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 698 most aggregate data meta-analyses, no adjustments for multiple testing were made
4
5 699 because of concerns about missing possibly important findings that could be tested in
6
7 700 original trials.³⁵ Fourth, since anxiety was assessed using self-report instruments,⁴⁰⁻⁵³
8
9
10 701 the possibility of reporting bias in the original studies existed.

11 12 702 **CONCLUSIONS**

13
14 703 Exercise is associated with reductions in anxiety among adults with selected types of
15
16 704 AORD. However, a need exists for additional, well-designed, randomized controlled
17
18 705 trials on this topic.

19 20 706 **CONTRIBUTORS**

21
22 707 GAK was responsible for the conception and design, acquisition of data, analysis and
23
24 708 interpretation of data, drafting the initial manuscript and revising it critically for important
25
26 709 intellectual content. KSK was responsible for the conception and design, acquisition of
27
28 710 data, drafting the initial manuscript, and revising all drafts critically for important
29
30 711 intellectual content. LFC was responsible for the conception and design, acquisition of
31
32 712 data, drafting the initial manuscript, and revising all drafts critically for important
33
34 713 intellectual content. All authors read and approved the final manuscript.

35 36 714 **REGISTRATION**

37
38 715 In accordance with Primary Reporting Items for Systematics Reviews and Meta-
39
40 716 Analyses, our systematic review with network meta-analysis was registered with the
41
42 717 International Prospective Register of Systematic Reviews (PROSPERO) on October 4,
43
44 718 2016 (registration number CRD42016048728).

45 46 719 **COMPETING INTERESTS**

47
48 720 None.

1
2
3 721 **FUNDING**
4

5 722 This meta-analysis was funded by the National Institutes of Health, National Institute for
6
7 723 Arthritis, Musculoskeletal and Skin Diseases, grant number R01AR061346 (GAK,
8
9
10 724 Principal Investigator).

11
12 725 **DATA SHARING STATEMENT**
13

14
15 726 All data are available upon request from the corresponding author.
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

727 **REFERENCES**

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

- 1
2
3 749 9. Busch AJ, Schachter CL, Overend TJ, *et al.* Exercise for fibromyalgia: a systematic
4
5 750 review. *J Rheumatol* 2008;35(6):1130-44.
6
7
8 751 10. Hurkmans E, van der Giesen FJ, Vliet Vlieland TP, *et al.* Dynamic exercise
9
10 752 programs (aerobic capacity and/or muscle strength training) in patients with
11
12 753 rheumatoid arthritis. *Cochrane Database Syst Rev* 2009(4):CD006853.
13
14 754 11. Kelley GA, Kelley KS, Hootman JM. Effects of exercise on depression in adults with
15
16 755 arthritis: a systematic review with meta-analysis of randomized controlled trials.
17
18 756 *Arthritis Res Ther* 2015;17:21.
19
20
21 757 12. Kelley GA, Kelley KS. Effects of exercise on anxiety in adults with arthritis and other
22
23 758 rheumatic disease: A systematic review of meta-analyses. *J Nov Physiother*
24
25 759 2014;4(4):1-5.
26
27
28 760 13. Liberati A, Altman DG, Tetzlaff J, *et al.* The PRISMA statement for reporting
29
30 761 systematic reviews and meta-analyses of studies that evaluate health care
31
32 762 interventions: explanation and elaboration. *Ann Intern Med* 2009;151(4):W65-W94.
33
34
35 763 14. Kelley GA, Kelley KS, Callahan LF. Community-deliverable exercise and anxiety in
36
37 764 adults with arthritis and other rheumatic diseases: a protocol for a systematic review
38
39 765 and meta-analysis of randomised controlled trials. *BMJ Open* 2017;7(3):e014957.
40
41
42 766 15. Sacks HS, Chalmers TC, Smith H. Randomized versus historical controls for clinical
43
44 767 trials. *Am J Med* 1982;72:233-40.
45
46
47 768 16. Schulz KF, Chalmers I, Hayes R, *et al.* Empirical evidence of bias: Dimensions of
48
49 769 methodological quality associated with estimates of treatment effects in controlled
50
51 770 trials. *J Am Med Assoc* 1995;273:408-12.
52
53
54
55
56
57
58
59
60

- 1
2
3 771 17. Physical Activity Guidelines Advisory Committee. *Physical Activity Guidelines*
4
5 772 *Advisory Report*. Washington, DC: U.S. Department of Health and Human Services,
6
7 773 2008
8
9
10 774 18. Brady TJ, Jernick SL, Hootman JM, *et al*. Public health interventions for arthritis:
11
12 775 expanding the toolbox of evidence-based interventions. *J Womens Health (Larchmt)*
13
14 776 2009;18(12):1905-17.
15
16
17 777 19. Ide MR, Laurindo IMM, Rodrigues AL, *et al*. Effect of aquatic respiratory exercise-
18
19 778 based program in patients with fibromyalgia. *Int J Rheum Dis* 2008;11(2):131-40.
20
21 779 20. Waggoner CD, LeLievre RB. A method to increase compliance to exercise
22
23 780 regimens in rheumatoid arthritis patients. *J Behav Med* 1981;4(2):191-201.
24
25
26 781 21. Cohen J. Weighted kappa: nominal scale agreement with provision for scaled
27
28 782 disagreement or partial credit. *Psychol Bull* 1968;70:213-20.
29
30
31 783 22. Lee E, Dobbins M, DeCorby K, *et al*. An optimal search filter for retrieving
32
33 784 systematic reviews and meta-analyses. *BMC Med Res Methodol* 2012;12:51.
34
35 785 23. Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of*
36
37 786 *Interventions Version 5.1.0 [updated March 2011]*: The Cochrane Collaboration,
38
39 787 2011.
40
41
42 788 24. Ahn S, Becker BJ. Incorporating quality scores in meta-analysis. *J Educ Behav Stat*
43
44 789 2011;36(5):555-85.
45
46
47 790 25. Hedges LV, Olkin I. *Statistical methods for meta-analysis*. San Diego, CA: Academic
48
49 791 Press, 1985.
50
51 792 26. Follmann D, Elliot P, Suh I, *et al*. Variance imputation for overviews of clinical trials
52
53 793 with continuous response. *J Clin Epidemiol* 1992;45:769-73.
54
55
56
57
58
59

- 1
2
3 794 27. Doi SA, Barendregt JJ, Khan S, *et al.* Advances in the meta-analysis of
4
5 795 heterogeneous clinical trials I: The inverse variance heterogeneity model. *Contemp*
6
7 796 *Clin Trials* 2015;45(Pt A):130-38.
8
9
10 797 28. Dersimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*
11
12 798 1986;7:177-88.
13
14 799 29. Dersimonian R, Laird N. Meta-analysis in clinical trials revisited. *Contemp Clin Trials*
15
16 800 2015;45(Pt A):139-45.
17
18 801 30. Cochran WG. The combination of estimates from different experiments. *Biometrics*
19
20 802 1954;10:101-29.
21
22 803 31. Higgins JPT, Thompson SG, Deeks JJ, *et al.* Measuring inconsistency in meta-
23
24 804 analyses. *Br Med J* 2003;327(7414):557-60.
25
26 805 32. Cohen J. *Statistical power analysis for the behavioral sciences*. New York:
27
28 806 Academic Press, 1988.
29
30 807 33. Khan A, Khan S, Brown WA. Are placebo controls necessary to test new
31
32 808 antidepressants and anxiolytics? *Int J Neuropsychopharmacol* 2002;5(3):193-7.
33
34 809 34. Murphy LB, Hootman JM, Boring MA, *et al.* Leisure time physical activity among
35
36 810 U.S. adults with arthritis, 2008-2015. *Am J Prev Med* 2017
37
38 811 35. Rothman KJ. No adjustments are needed for multiple comparisons. *Epidemiology*
39
40 812 1990;1:43-46.
41
42 813 36. Sacks HS, Berrier J, Reitman D, *et al.* Meta-analysis of randomized controlled trials.
43
44 814 *N Engl J Med* 1987;316:450-55.
45
46 815 37. Littell JH, Corcoran J, Pillai V. *Systematic reviews and meta-analysis*. New York:
47
48 816 Oxford University Press, 2008:1-202.
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 817 38. Sterne JA, Sutton AJ, Ioannidis JP, *et al.* Recommendations for examining and
4
5 818 interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials.
6
7 819 *Br Med J* 2011;343:d4002.
8
9
10 820 39. Guyatt G, Oxman AD, Akl EA, *et al.* GRADE guidelines: 1. Introduction-GRADE
11
12 821 evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;64(4):383-
13
14 822 94.
15
16
17 823 40. Baptista AS, Villela AL, Jones A, *et al.* Effectiveness of dance in patients with
18
19 824 fibromyalgia: a randomized, single-blind, controlled study. *Clin Exp Rheumatol*
20
21 825 2012;30(6 Suppl 74):18-23.
22
23
24 826 41. Beltran R. The effects of a supervised group aerobic exercise program and a
25
26 827 chronobiologicary oriented treatment protocol on symptomotatogy and mood in
27
28 828 women with fibromyalgia [Dissertation]. Alliant University, 2003.
29
30
31 829 42. Cheung C, Wyman JF, Bronas U, *et al.* Managing knee osteoarthritis with yoga or
32
33 830 aerobic/strengthening exercise programs in older adults: a pilot randomized
34
35 831 controlled trial. *Rheumatol Int* 2017;37(3):389-98.
36
37
38 832 43. Fransen M, Nairn L, Winstanley J, *et al.* Physical activity for osteoarthritis
39
40 833 management: a randomized controlled clinical trial evaluating hydrotherapy or Tai
41
42 834 Chi classes. *Arthritis Rheum* 2007;57(3):407-14.
43
44
45 835 44. French HP, Cusack T, Brennan A, *et al.* Exercise and manual physiotherapy arthritis
46
47 836 research trial (EMPART) for osteoarthritis of the hip: a multicenter randomized
48
49 837 controlled trial. *Arch Phys Med Rehabil* 2013;94(2):302-14.
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 838 45. Gowans SE, deHueck A, Voss S, *et al.* Effect of a randomized, controlled trial of
4
5 839 exercise on mood and physical function in individuals with fibromyalgia. *Arthritis*
6
7 840 *Rheum* 2001;45(6):519-29.
8
9
10 841 46. Jones KD, Burckhardt CS, Deodhar AA, *et al.* A six-month randomized controlled
11
12 842 trial of exercise and pyridostigmine in the treatment of fibromyalgia. *Arthritis Rheum*
13
14 843 2008;58(2):612-22.
15
16
17 844 47. Komatireddy GR, Leitch RW, Cella K, *et al.* Efficacy of low load resistive muscle
18
19 845 training in patients with rheumatoid arthritis functional class II and III. *J Rheumatol*
20
21 846 1997;24(8):1531-39.
22
23
24 847 48. Minor MA, Hewett JE, Webel RR, *et al.* Efficacy of physical conditioning exercise in
25
26 848 patients with rheumatoid arthritis and osteoarthritis. *Arthritis Rheum*
27
28 849 1989;32(11):1396-405.
29
30
31 850 49. Munguia-Izquierdo D, Legaz-Arrese A. Assessment of the effects of aquatic therapy
32
33 851 on global symptomatology in patients with fibromyalgia syndrome: a randomized
34
35 852 controlled trial. *Arch Phys Med Rehabil* 2008;89(12):2250-7.
36
37
38 853 50. Sanudo B, Carrasco L, de Hoyo M, *et al.* Vagal modulation and symptomatology
39
40 854 following a 6-month aerobic exercise program for women with fibromyalgia. *Clin Exp*
41
42 855 *Rheumatol* 2015;33(1 Suppl 88):S41-5.
43
44
45 856 51. Schachter CL, Busch AJ, Peloso PM, *et al.* Effects of short versus long bouts of
46
47 857 aerobic exercise in sedentary women with fibromyalgia: a randomized controlled
48
49 858 trial. *Phys Ther* 2003;83(4):340-58.
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 859 52. Tomas-Carus P, Gusi N, Hakkinen A, *et al.* Eight months of physical training in
4
5 860 warm water improves physical and mental health in women with fibromyalgia: a
6
7 861 randomized controlled trial. *J Rehabil Med* 2008;40(4):248-52.
8
9
10 862 53. Tomas-Carus P, Gusi N, Leal A, *et al.* [The fibromyalgia treatment with physical
11
12 863 exercise in warm water reduces the impact of the disease on female patients'
13
14 864 physical and mental health]. *Rheumatol Clin* 2007;3(1):33-37.
15
16
17 865 54. Garber CE, Blissmer B, Deschenes MR, *et al.* Quantity and quality of exercise for
18
19 866 developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor
20
21 867 fitness in apparently healthy adults: Guidance for prescribing exercise. *Med Sci*
22
23 868 *Sports Exerc* 2011;43(7):1334-59.
24
25
26 869 55. Glass GV, McGaw B, Smith ML. *Meta-analysis in social research*. Newbury Park,
27
28 870 California: Sage, 1981.
29
30
31 871 56. Hidalgo RB, Tupler LA, Davidson JR. An effect-size analysis of pharmacologic
32
33 872 treatments for generalized anxiety disorder. *J Psychopharmacol* 2007;21(8):864-72.
34
35
36 873 57. Rogerson M, Gladwell VF, Gallagher DJ, *et al.* Influences of green outdoors versus
37
38 874 indoors environmental settings on psychological and social outcomes of controlled
39
40 875 exercise. *Int J Environ Res Public Health* 2016;13(4):363.
41
42
43 876 58. Pasanen TP, Tyrvaainen L, Korpela KM. The relationship between perceived health
44
45 877 and physical activity indoors, outdoors in built environments, and outdoors in nature.
46
47 878 *Appl Psychol Health Well Being* 2014;6(3):324-46.
48
49 879 59. Resnick B, Inguito P, Orwig D, *et al.* Treatment fidelity in behavior change research
50
51 880 - A case example. *Nurs Res* 2005;54(2):139-43.
52
53
54
55
56
57
58
59
60

- 1
2
3 881 60. CDC. Physical activity for arthritis Atlanta, Georgia: Centers for Disease Control and
4
5 882 Prevention; 2017 [updated April 18, 2017. Available from:
6
7 883 <https://www.cdc.gov/arthritis/basics/physical-activity-overview.html> accessed July 5
8
9 884 2017.
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

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 to exercise (n = 11, age, \bar{x} \pm SD = 50.1 \pm 12.6 yrs) or control (n = 10, age, \bar{x} \pm SD = 53.7 \pm 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) \geq 65 yrs of age with knee OA assigned to exercise (n = 28, age, \bar{x} \pm SD = 74.4 \pm 7.5 yrs), or control (n = 23, age, \bar{x} \pm SD = 71.8 \pm 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} \pm SD = 70 \pm 6.3 yrs), or wait-list control (n = 41, age, \bar{x} \pm SD = 69.6 \pm 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} \pm 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, $\bar{x} \pm SD =$	exercises	
			60.8 ± 9.7 yrs) group		
Gowans et al., 2001 ⁴⁵	Canada	Men and women (N = 57) with FM assigned to an	exercise (n = 30, age, $\bar{x} \pm SD = 44.6 \pm 8.7$ yrs), or	Aerobic exercise (2 walking/jogging	MHI, STAI
		control (n = 27, age, $\bar{x} \pm SD = 49.8 \pm 7.3$ yrs) group		classes in a gym, 1 pool class), 3 x/wk,	
				30 min/session, 60-75% MHR, for 23 wks	
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, $\bar{x} \pm SD =$	Aerobic exercise 3 x/wk, 30 min/session,	FIQ (Anxiety)
			49.6 ± 7.7 yrs), or control (n = 54, age, $\bar{x} \pm SD =$	40-50% MHR & strength exercise, 3	
			49.8 ± 7.9 yrs) group	x/wk, 10 min/session, for 24 wks	
Komatireddy et al. ⁴⁷	United States	Men and women (n = 49), 35-76 yrs of age with RA	assigned to exercise (n = 25, $\bar{x} \pm SD = 57.7 \pm 9.8$	Circuit weight training with light loads and	AIMS
			yrs of age, range 40-72 yrs) or control (n = 24, $\bar{x} \pm$	high repetitions, 7 exercises, 2-3	
			SD = 60.5 ± 11 yrs of age, range 35-76 yrs) group	circuits/session, 12-15 reps, 30-second	
				rest between sets, 20-27 min/session,	
				≥ 3 x/wk, RPE of 3-4, for 12 wks	
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 =	Aerobic aquatics or walking group, 3	AIMS
			36) or control group (n = 32)	x/wk, 60 min/session (30 min of this was	
				aerobic), 60-80% MHR, for 12 wks	
Munguia- Izquierdo & Legaz-Arrese,	Spain	Men and women (N = 60) 18-60 yrs of age with FM	assigned to exercise (n = 35, $\bar{x} \pm SD = 50.0 \pm 7.0$	Aerobic aquatic exercise, 3 x/wk, 20-30	STAI
			yrs) or control (n = 25 $\bar{x} \pm SD = 46.0 \pm 8.0$ yrs)	min/session, 50-80% MHR, & strength	
				exercise 3 x/wk, 8-20 min/session, 1-3	

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

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, $\bar{x} \pm SD = 55.0 \pm 8.0$ yrs of age), or control (n = 16, $\bar{x} \pm SD = 58.0 \pm 6.9$ 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, $\bar{x} \pm SD = 41.9 \pm 8.6$ yrs of age), long bout (n = 51, $\bar{x} \pm SD = 41.3 \pm 8.7$ yrs of age), or control group (n = 36, $\bar{x} \pm SD = 42.5 \pm 6.7$ 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, $\bar{x} \pm SD = 50.7 \pm 10.6$ yrs of age) or control group (n = 16, $\bar{x} \pm SD = 50.9 \pm 6.7$ 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, $\bar{x} \pm SD = 51 \pm 10.0$ yrs of age) or control group (n = 17, $\bar{x} \pm SD = 51 \pm 9.0$ 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; $\bar{x} \pm SD$, mean \pm 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,

1
2
3 State-Trait Anxiety Inventory; MHR, maximum heart rate; OA, osteoarthritis; RA, rheumatoid arthritis; reps, repetitions; RPE, rating of perceived
4 exertion; VAS, Visual Analog Scale; wk(s), week(s); yrs, years;
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

For peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Table 2. Baseline characteristics of participants.

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

Notes: Groups represents number of exercise and control groups reporting data; \bar{x} + SD, mean \pm 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 \pm 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 kg ⁻¹ 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 \pm SE	t (p)	95% CI
Year of publication	0.031 \pm 0.009	3.58 (0.01)	0.010 to 0.051
Incomplete data	-0.448 \pm 0.139	-3.23 (0.01)	-0.763 to -0.134
Minutes of training per week	0.007 \pm 0.004	1.71 (0.13)	-0.002 to 0.016
Intercept	-61.940 \pm 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.

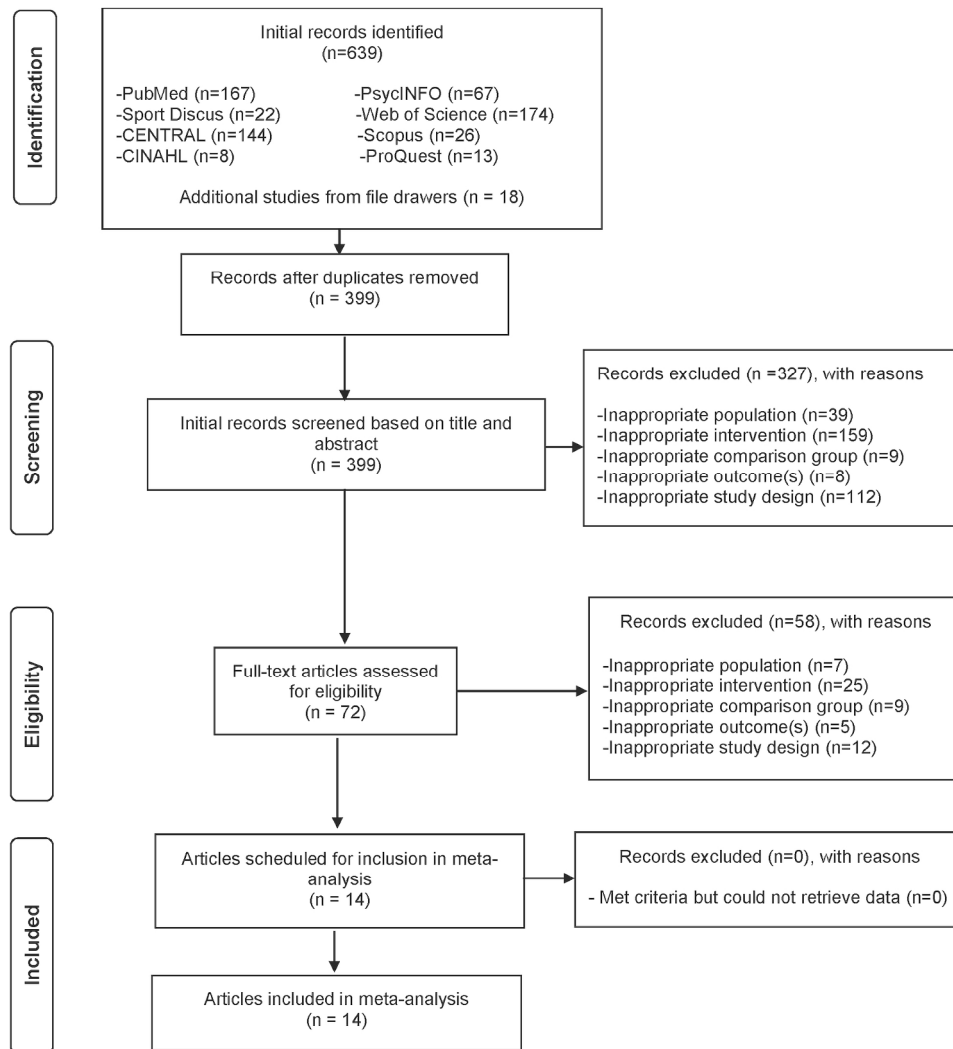


Figure 1. Flow diagram depicting the search process.

173x192mm (300 x 300 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

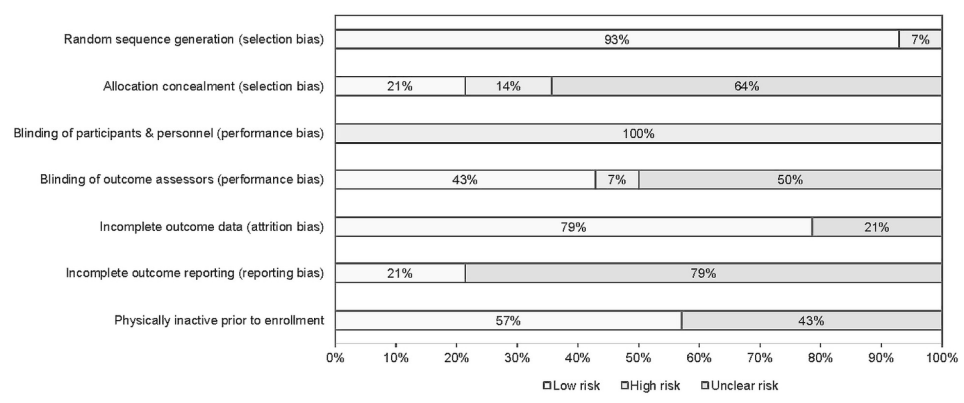


Figure 2. Risk of bias results using the Cochrane Risk of Bias Assessment Instrument.

173x77mm (300 x 300 DPI)

Peer review only

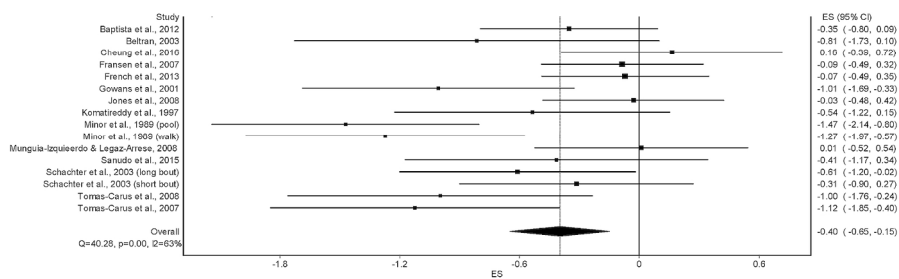


Figure 3. Forest plot for changes in anxiety.

173x57mm (300 x 300 DPI)

peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

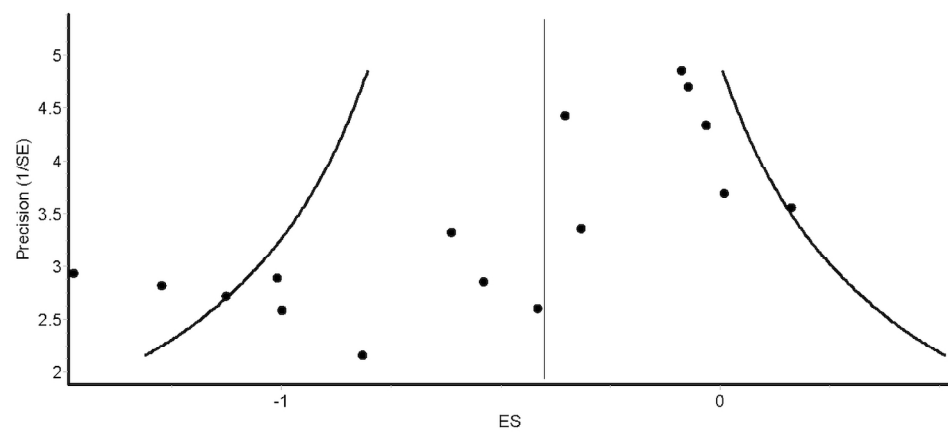


Figure 4. Funnel plot for changes in anxiety.

165x74mm (300 x 300 DPI)

er review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

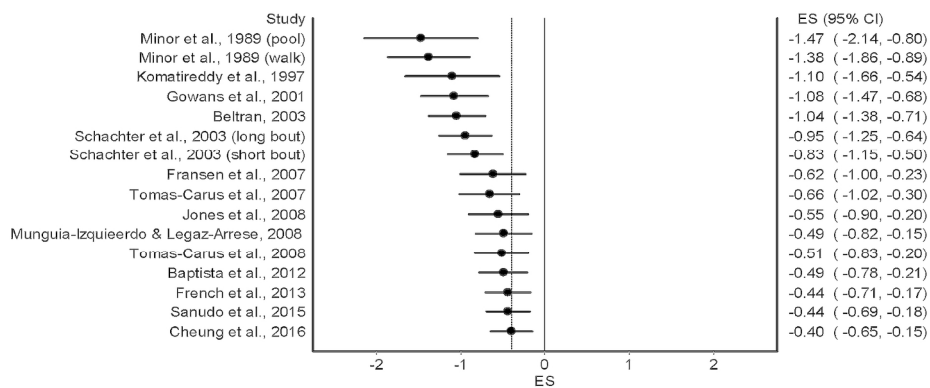


Figure 5. Cumulative meta-analysis for changes in anxiety.

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. *Prescribe 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*

- 1
 - 2
 - 3
 - 4
 - 5
 - 6
 - 7
 - 8
 - 9
 - 10
 - 11
 - 12
 - 13
 - 14
 - 15
 - 16
 - 17
 - 18
 - 19
 - 20
 - 21
 - 22
 - 23
 - 24
 - 25
 - 26
 - 27
 - 28
 - 29
 - 30
 - 31
 - 32
 - 33
 - 34
 - 35
 - 36
 - 37
 - 38
 - 39
 - 40
 - 41
 - 42
 - 43
 - 44
 - 45
 - 46
 - 47
 - 48
 - 49
 - 50
 - 51
 - 52
 - 53
 - 54
 - 55
 - 56
 - 57
 - 58
 - 59
 - 60
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. Ayrál 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*

- 1
2
3 35. Bae S, Gun S, Mok C, et al. Improved health outcomes with etanercept versus
4 usual DMARD therapy in an Asian population with established rheumatoid
5 arthritis. *BMC musculoskeletal disorders* 2013; 14.
6 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/280/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/280/CN-00864280/frame.html)
7 [00864280/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/280/CN-00864280/frame.html). *inappropriate intervention*
8
9 36. Bagdath AO, Donmez A, Eroksuz R, et al. Does addition of 'mud-pack and hot
10 pool treatment' to patient education make a difference in fibromyalgia patients? A
11 randomized controlled single blind study. *International journal of biometeorology*
12 2015;59(12):1905-11. doi: 10.1007/s00484-015-0997-7 *inappropriate intervention*
13
14 37. Barlow J, Turner A, Wright C. A randomized controlled study of the Arthritis Self-
15 Management Programme in the UK. *Health education research* 2000; 15(6).
16 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/444/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/444/CN-00330444/frame.html)
17 [00330444/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/444/CN-00330444/frame.html). *inappropriate intervention*
18
19 38. Barlow JH, Powell LA, Gilchrist M, et al. The effectiveness of the Training and
20 Support Program for parents of children with disabilities: a randomized controlled
21 trial. *Journal of psychosomatic research* 2008;64(1):55-62. doi:
22 10.1016/j.jpsychores.2007.06.006 [published Online First: 2007/12/26]
23 *inappropriate intervention*
24
25 39. Barsky AJ, Ahern DK, Orav EJ, et al. A Randomized Trial of Three Psychosocial
26 Treatments for the Symptoms of Rheumatoid Arthritis. *Seminars in arthritis and*
27 *rheumatism* 2010;40(3):222-32. doi: 10.1016/j.semarthrit.2010.04.001
28 *inappropriate intervention*
29
30 40. Basler HD. Group treatment for pain and discomfort. *Patient education and*
31 *counseling* 1993;20(2-3):167-75. [published Online First: 1993/05/01]
32 *inappropriate intervention*
33
34 41. Bassej EJ. Longitudinal changes in selected physical capabilities: muscle
35 strength, flexibility and body size. *Age and Ageing* 1998;27:12-16. *inappropriate*
36 *study design*
37
38 42. Bateman L, Sarzi-Puttini P, Burbridge CL, et al. Burden of illness in fibromyalgia
39 patients with comorbid depression. *Clinical and experimental rheumatology*
40 2016;34(2 Suppl 96):S106-13. [published Online First: 2016/04/09] *inappropriate*
41 *study design*
42
43 43. Baudic S, Attal N, Mhalla A, et al. Unilateral repetitive transcranial magnetic
44 stimulation of the motor cortex does not affect cognition in patients with
45 fibromyalgia. *Journal of Psychiatric Research* 2013;47(1):72-77. doi:
46 10.1016/j.jpsychires.2012.09.003 *inappropriate intervention*
47
48 44. Bearne L, Walsh N, Jessep S, et al. Feasibility of an exercise-based rehabilitation
49 programme for chronic hip pain. *Musculoskeletal care* 2011; 9(3).
50 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/898/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/898/CN-01124898/frame.html)
51 [01124898/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/898/CN-01124898/frame.html). *inappropriate intervention*
52
53 45. Bement MKH, Weyer A, Hartley S, et al. Pain Perception After Isometric Exercise
54 in Women With Fibromyalgia. *Archives of physical medicine and rehabilitation*
55 2011;92(1):89-95. doi: 10.1016/j.apmr.2010.10.006 *inappropriate study design*
56
57 46. Bennell K, Ahamed Y, Jull G, et al. Physical Therapist-Delivered Pain Coping
58 Skills Training and Exercise for Knee Osteoarthritis: Randomized Controlled Trial.
59 *Arthritis care & research* 2016; 68(5).
60

- <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*

- 1
2
3 57. Bojner-Horwitz E, Theorell T, Maria Anderberg U. Dance/movement therapy and
4 changes in stress-related hormones: a study of fibromyalgia patients with video-
5 interpretation. *The Arts in Psychotherapy* 2003;30(5):255-64. doi:
6 <http://dx.doi.org/10.1016/j.aip.2003.07.001> *inappropriate intervention*
7
8 58. Bongi SM, Del Rosso A, Di Felice C, et al. Ressequier method and Qi Gong
9 sequentially integrated in patients with fibromyalgia syndrome. *Clinical and*
10 *experimental rheumatology* 2012;30(6):S51-S58. *inappropriate comparison group*
11
12 59. Bongi SM, Paoletti G, Cala M, et al. Efficacy of rehabilitation with Tai Ji Quan in an
13 Italian cohort of patients with Fibromyalgia Syndrome. *Complementary therapies*
14 *in clinical practice* 2016;24:109-15. doi: 10.1016/j.ctcp.2016.05.010 *inappropriate*
15 *intervention*
16
17 60. Booth FW, Roberts CK, Laye MJ. Lack of Exercise Is a Major Cause of Chronic
18 Diseases. *Comprehensive Physiology* 2012;2(2):1143-211. doi:
19 10.1002/cphy.c110025 *inappropriate study design*
20
21 61. Boschen KA, Robinson E, Campbell KA, et al. Results from 10 Years of a CBT
22 Pain Self-Management Outpatient Program for Complex Chronic Conditions. *Pain*
23 *Research & Management* 2016 doi: 10.1155/2016/4678083 *inappropriate study*
24 *design*
25
26 62. Bossen D, Buskermolen M, Veenhof C, et al. Adherence to a web-based physical
27 activity intervention for patients with knee and/or hip Osteoarthritis: A mixed
28 method study. *Journal of medical Internet research* 2013;15(10):55-66. doi:
29 10.2196/jmir.2742 *inappropriate comparison group*
30
31 63. Bossen D, Veenhof C, Kloek C, et al. The association between psychological
32 factors and physical activity levels in patients with knee and hip osteoarthritis.
33 *Physiotherapy (United Kingdom)* 2015; 101.
34 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/535/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/535/CN-01126535/frame.html)
35 [01126535/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/535/CN-01126535/frame.html). *inappropriate study design*
36
37 64. Bossen D, Veenhof C, Van Beek KEC, et al. Effectiveness of a Web-Based
38 Physical Activity Intervention in Patients With Knee and/or Hip Osteoarthritis:
39 Randomized Controlled Trial. *Journal of medical Internet research* 2013;15(11)
40 doi: 10.2196/jmir.2662 *inappropriate intervention*
41
42 65. Boyer L, Dousset A, Roussel P, et al. rTMS in fibromyalgia: a randomized trial
43 evaluating QoL and its brain metabolic substrate. *Neurology* 2014;82(14):1231-8.
44 doi: 10.1212/wnl.0000000000000280 [published Online First: 2014/03/29]
45 *inappropriate intervention*
46
47 66. Bradt J, Norris M, Shim M, et al. Vocal Music Therapy for Chronic Pain
48 Management in Inner-City African Americans: A Mixed Methods Feasibility Study.
49 *Journal of Music Therapy* 2016;53(2):178-206. doi: 10.1093/jmt/thw004
50 *inappropriate intervention*
51
52 67. Braz AS, Morais LCS, Paula AP, et al. Effects of Panax ginseng extract in patients
53 with fibromyalgia: A 12-week, randomized, double-blind, placebo-controlled trial.
54 *Revista Brasileira de Psiquiatria* 2013;35(1):21-28. doi: 10.1016/j.rbp.2013.01.004
55 *inappropriate intervention*
56
57 68. Broderick J, Junghaenel D, Schwartz J. Written emotional expression produces
58 health benefits in fibromyalgia patients. *Psychosomatic medicine* 2005; 67(2).
59
60

- <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. Buttawat 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*

- 1
2
3 79. Carbonell-Baeza A, Aparicio VA, Chillon P, et al. Effectiveness of multidisciplinary
4 therapy on symptomatology and quality of life in women with fibromyalgia. *Clinical*
5 *and experimental rheumatology* 2011;29(6):S97-S103. *inappropriate study design*
6
7 80. Carbonell-Baeza A, Aparicio VA, Martins-Pereira CM, et al. Efficacy of Biodanza
8 for Treating Women with Fibromyalgia. *Journal of Alternative and Complementary*
9 *Medicine* 2010;16(11):1191-200. doi: 10.1089/acm.2010-0039 *inappropriate study*
10 *design*
11 81. Carbonell-Baeza A, Romero A, Aparicio VA, et al. Preliminary Findings of a 4-
12 Month Tai Chi Intervention on Tenderness, Functional Capacity, Symptomatology,
13 and Quality of Life in Men With Fibromyalgia. *American Journal of Mens Health*
14 2011;5(5):421-29. doi: 10.1177/1557988311400063 *inappropriate intervention*
15
16 82. Carbonell-Baeza A, Ruizz JR, Aparicio VA, et al. Multidisciplinary and biodanza
17 intervention for the management of fibromyalgia. *Acta Reumatologica Portuguesa*
18 2012;37(3):240-50. *inappropriate comparison group*
19
20 83. Carleton RN, Richter AA, Asmundson GJG. Attention modification in persons with
21 fibromyalgia: A double blind, randomized clinical trial. *Cognitive Behaviour*
22 *Therapy* 2011;40(4):279-90. doi: 10.1080/16506073.2011.616218 *inappropriate*
23 *intervention*
24 84. Carmichael NME, Katz J, Clarke H, et al. An intensive perioperative regimen of
25 pregabalin and celecoxib reduces pain and improves physical function scores six
26 weeks after total hip arthroplasty: A prospective randomized controlled trial. *Pain*
27 *Research & Management* 2013;18(3):127-32. doi: 10.1155/2013/258714
28 *inappropriate intervention*
29
30 85. Carson JW, Carson KM, Jones KD, et al. A pilot randomized controlled trial of the
31 Yoga of Awareness program in the management of fibromyalgia. *Pain*
32 2010;151(2):530-9. doi: 10.1016/j.pain.2010.08.020 [published Online First:
33 2010/10/16] *inappropriate intervention*
34
35 86. Carson JW, Carson KM, Jones KD, et al. Follow-up of yoga of awareness for
36 fibromyalgia: results at 3 months and replication in the wait-list group. *The Clinical*
37 *journal of pain* 2012;28(9):804-13. doi: 10.1097/AJP.0b013e31824549b5
38 [published Online First: 2012/07/04] *inappropriate study design*
39
40 87. Carta MG, Cardia C, Mannu F, et al. The high frequency of manic symptoms in
41 fibromyalgia does influence the choice of treatment? *Clinical Practice and*
42 *Epidemiology in Mental Health* 2006;2 *inappropriate study design*
43
44 88. Casanueva-Fernandez B, Llorca J, Rubio JBI, et al. Efficacy of a multidisciplinary
45 treatment program in patients with severe fibromyalgia. *Rheumatology*
46 *international* 2012;32(8):2497-502. doi: 10.1007/s00296-011-2045-1 *inappropriate*
47 *intervention*
48
49 89. Castel A, Castro S, Fontova R, et al. Body mass index and response to a
50 multidisciplinary treatment of fibromyalgia. *Rheumatology international*
51 2015;35(2):303-14. doi: 10.1007/s00296-014-3096-x [published Online First:
52 2014/08/02] *inappropriate intervention*
53
54 90. Castel A, Fontova R, Montull S, et al. Efficacy of a Multidisciplinary Fibromyalgia
55 Treatment Adapted for Women With Low Educational Levels: A Randomized
56 Controlled Trial. *Arthritis care & research* 2013;65(3):421-31. doi:
57 10.1002/acr.21818 *inappropriate intervention*
58
59
60

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
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).

- 1
2
3
4 <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/664/CN-01075664/frame.html>. *inappropriate outcomes*
- 5
6 101. Christensen SS, Frostholt 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*
- 7
8
9
10 102. 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*
- 11
12
13
14 103. 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*
- 15
16
17
18 104. Clarke-Jenssen A-C, Mengshoel AM, Staalesen Strumse Y, et al. EFFECT OF A FIBROMYALGIA 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*
- 19
20
21
22 105. 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*
- 23
24
25
26 106. 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*
- 27
28
29
30 107. 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*
- 31
32
33
34 108. 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*
- 35
36
37
38 109. 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*
- 39
40
41
42 110. 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*
- 43
44
45
46 111. 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*
- 47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 Conference Start: 20100420 Conference End: 20100423 Conference Publication:
4 (varpagings) 2010; 49.

5 <http://onlinelibrary.wiley.com/doi/10.1002/art.1790110607>
6 <http://onlinelibrary.wiley.com/doi/10.1002/art.1790110607>
7 <http://onlinelibrary.wiley.com/doi/10.1002/art.1790110607> *inappropriate study design*

- 8 112. Dailey DL, Frey Law LA, Vance CG, et al. Perceived function and physical
9 performance are associated with pain and fatigue in women with fibromyalgia.
10 *Arthritis research & therapy* 2016;18:68. doi: 10.1186/s13075-016-0954-9
11 [published Online First: 2015/01/01] *inappropriate study design*
- 12 113. Daltroy LH, Morlino CI, Eaton HM, et al. Preoperative education for total hip and
13 knee replacement patients. *Arthritis care & research* 1998;11(6):469-78. doi:
14 10.1002/art.1790110607 *inappropriate intervention*
- 15 114. das Nair R, Anderson P, Clarke S, et al. Home-administered pre-surgical
16 psychological intervention for knee osteoarthritis (HAPPiKNEES): study protocol
17 for a randomised controlled trial. *Trials* 2016;17:54. doi: 10.1186/s13063-016-
18 1165-z [published Online First: 2016/01/29] *inappropriate intervention*
- 19 115. Davis MC, Zautra AJ, Wolf LD, et al. Mindfulness and cognitive-behavioral
20 interventions for chronic pain: Differential effects on daily pain reactivity and
21 stress reactivity. *Journal of Consulting and Clinical Psychology* 2015;83(1):24-35.
22 doi: 10.1037/a0038200 *inappropriate intervention*
- 23 116. de Brouwer SJM, Kraaimaat FW, Sweep F, et al. Psychophysiological
24 Responses to Stress after Stress Management Training in Patients with
25 Rheumatoid Arthritis. *PloS one* 2011;6(12) doi: 10.1371/journal.pone.0027432
26 *inappropriate intervention*
- 27 117. D'Eon MS. Feasibility and Acceptability of Graded In-Vivo Exposure Therapy for
28 Fibromyalgia Patients [Ph.D.]. University of California, San Diego, 2016.
29 *inappropriate intervention*
- 30 118. Donmez A, Karagulle MZ, Tercan N, et al. SPA therapy in fibromyalgia: a
31 randomised controlled clinic study. *Rheumatology international* 2005;26(2):168-
32 72. doi: 10.1007/s00296-005-0623-9 [published Online First: 2005/06/21]
33 *inappropriate intervention*
- 34 119. Dougados M, Tsai WC, Saaibi DL, et al. Evaluation of Health Outcomes with
35 Etanercept Treatment in Patients with Early Nonradiographic Axial
36 Spondyloarthritis. *The Journal of rheumatology* 2015;42(10):1835-41. doi:
37 10.3899/jrheum.141313 [published Online First: 2015/08/16] *inappropriate*
38 *intervention*
- 39 120. Driban JB, Morgan N, Price LL, et al. Patient-Reported Outcomes Measurement
40 Information System (PROMIS) instruments among individuals with symptomatic
41 knee osteoarthritis: a cross-sectional study of floor/ceiling effects and construct
42 validity. *BMC musculoskeletal disorders* 2015;16 doi: 10.1186/s12891-015-0715-
43 y *inappropriate study design*
- 44 121. Dunn-Lewis C, Kraemer WJ, Kupchak BR, et al. A multi-nutrient supplement
45 reduced markers of inflammation and improved physical performance in active
46 individuals of middle to older age: a randomized, double-blind, placebo-controlled
47 study. *Nutrition Journal* 2011;10 doi: 10.1186/1475-2891-10-90 *inappropriate*
48 *intervention*
- 49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 122. Ekici G, Bakar Y, Akbayrak T, et al. Comparison of manual lymph drainage
4 therapy and connective tissue massage in women with fibromyalgia: a
5 randomized controlled trial. *Journal of manipulative and physiological*
6 *therapeutics* 2009;32(2):127-33. doi: 10.1016/j.jmpt.2008.12.001 [published
7 Online First: 2009/02/27] *inappropriate intervention*
- 8
9 123. Ekici G, Unal E, Akbayrak T, et al. Effects of active/passive interventions on pain,
10 anxiety, and quality of life in women with fibromyalgia: Randomized controlled
11 pilot trial. *Women & health* 2017;57(1):88-107. doi:
12 10.1080/03630242.2016.1153017 [published Online First: 2016/02/18]
13 *inappropriate comparison group*
- 14
15 124. Ekici G, Unal E, Akbayrak T, et al. Active versus passive therapy in females with
16 fibromyalgia; "pilates exercises and connective tissue massage": A randomized
17 controlled pilot trial, Fibromiyalji kadinlarda pasif tedaviye karsi aktif tedavi:
18 "pilates egzersizleri ve konnektif doku masajı": Randomize kontrollu pilot calisma.
19 [Turkish, English]. *Fizyoterapi Rehabilitasyon* 2014; 25(1 suppl. 1).
20 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/055/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/055/CN-01010055/frame.html)
21 [01010055/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/055/CN-01010055/frame.html). *inappropriate comparison group*
- 22
23 125. Elias A, Yaacob LH, Kadir AA, et al. Guided Imagery Relaxation Therapy in
24 Malaysian Patients with Knee Osteoarthritis: A Randomized Controlled Trial.
25 *International Journal of Collaborative Research on Internal Medicine & Public*
26 *Health* 2015;7(5):92-103. *inappropriate intervention*
- 27
28 126. Elliot DL, Kuehl KS, Jones KD, et al. Using an eccentric exercise-testing protocol
29 to assess the beneficial effects of tart cherry juice in fibromyalgia patients.
30 *Integrative Medicine: A Clinician's Journal* 2010;9(6):24-29. *inappropriate*
31 *intervention*
- 32
33 127. Emery P, Bingham C, Burmester G, et al. Improvements in patient-reported
34 outcomes following 52 weeks of treatment with certolizumab pegol in
35 combination with methotrexate in DMARD-naive patients with severe, active and
36 progressive rheumatoid arthritis: Results from the C-early randomized, double-
37 blind, controlled phase 3 study. *Value in health* 2015; 18(7).
38 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/114/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/114/CN-01164114/frame.html)
39 [01164114/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/114/CN-01164114/frame.html). *inappropriate intervention*
- 40
41 128. Engel C. Tailored cognitive-behavioral therapy plus exercise training improved
42 clinical and functional outcomes in fibromyalgia. *Annals of internal medicine*
43 2011; 154(8). [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/037/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/037/CN-00895037/frame.html)
44 [00895037/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/037/CN-00895037/frame.html). *inappropriate intervention*
- 45
46 129. Ericsson A, Bremell T, Cider A, et al. Effects of exercise on fatigue and physical
47 capacity in men with chronic widespread pain - a pilot study. *Bmc Sports Science*
48 *Medicine and Rehabilitation* 2016;8 doi: 10.1186/s13102-016-0054-9
49 *inappropriate population*
- 50
51 130. Ericsson A, Palstam A, Larsson A, et al. Resistance exercise improves physical
52 fatigue in women with fibromyalgia: a randomized controlled trial. *Arthritis*
53 *research & therapy* 2016;18 doi: 10.1186/s13075-016-1073-3 *inappropriate*
54 *comparison group*
- 55
56
57
58
59
60

- 1
2
3 131. Falcão DM, Sales L, Leite JR, et al. Cognitive behavioral therapy for the
4 treatment of fibromyalgia syndrome: a randomized controlled trial. *Journal of*
5 *Musculoskeletal Pain* 2008;16(3):133-40. *inappropriate intervention*
6
7 132. Fark AR. A pilot study of white-coat and labile hypertension: Associations with
8 diagnoses of psychosocial dysfunction. *Family Practice Research Journal*
9 1993;13(1):71-80. *inappropriate outcomes*
10
11 133. Feldthusen C, Dean E, Forsblad-d'Elia H, et al. Effects of Person-Centered
12 Physical Therapy on Fatigue-Related Variables in Persons With Rheumatoid
13 Arthritis: A Randomized Controlled Trial. *Archives of Physical Medicine &*
14 *Rehabilitation* 2016;97(1):26-36. *inappropriate intervention*
15
16 134. Fenton G, Morley S. A tale of two RCTs: Using randomized controlled trials to
17 benchmark routine clinical (psychological) treatments for chronic pain. *Pain*
18 2013;154(10):2108-19. doi: 10.1016/j.pain.2013.06.033 *inappropriate study*
19 *design*
20
21 135. Field T. Yoga research review. *Complementary therapies in clinical practice*
22 2016;24:145-61. doi: 10.1016/j.ctcp.2016.06.005 [published Online First:
23 2016/08/10] *inappropriate intervention*
24
25 136. Field T, Diego M, Cullen C, et al. Fibromyalgia pain and substance P decrease
26 and sleep improves after massage therapy. *Jcr-Journal of Clinical Rheumatology*
27 2002;8(2):72-76. doi: 10.1097/00124743-200204000-00002 *inappropriate*
28 *intervention*
29
30 137. Field T, Diego M, Delgado J, et al. Rheumatoid arthritis in upper limbs benefits
31 from moderate pressure massage therapy. *Complementary therapies in clinical*
32 *practice* 2013;19(2):101-3. doi: 10.1016/j.ctcp.2012.12.001 [published Online
33 First: 2013/04/09] *inappropriate intervention*
34
35 138. Field T, Hernandez-Reif M, Seligman S, et al. Juvenile rheumatoid arthritis:
36 benefits from massage therapy. *Journal of pediatric psychology* 1997;22(5):607-
37 17. [published Online First: 1998/02/12] *inappropriate population*
38
39 139. Fitzgerald GK, White DK, Piva SR. Associations for change in physical and
40 psychological factors and treatment response following exercise in knee
41 osteoarthritis: an exploratory study. *Arthritis care & research* 2012;64(11):1673-
42 80. doi: 10.1002/acr.21751 [published Online First: 2012/06/08] *inappropriate*
43 *outcomes*
44
45 140. Fjorback L, Schroder A, Ornbol E, et al. Mindfulness therapy for bodily distress
46 syndrome - A randomized controlled trial. *Journal of psychosomatic research*
47 2011; 70(6). [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/011/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/011/CN-01006011/frame.html)
48 [01006011/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/011/CN-01006011/frame.html). *inappropriate intervention*
49
50 141. Fjorback LO, Arendt M, Ørnbøl E, et al. Mindfulness therapy for somatization
51 disorder and functional somatic syndromes — randomized trial with one-year
52 follow-up. *Journal of psychosomatic research* 2013;74(1):31-40. doi:
53 10.1016/j.jpsychores.2012.09.006 *inappropriate intervention*
54
55 142. Fors EA, Göttestam KG. Patient education, guided imagery and pain related talk
56 in fibromyalgia coping. *The European Journal of Psychiatry* 2000;14(4):233-40.
57 *inappropriate intervention*
58
59 143. Fregni F, Gimenes R, Valle AC, et al. A randomized, sham-controlled, proof of
60 principle study of transcranial direct current stimulation for the treatment of pain

- 1
2
3 in fibromyalgia. *Arthritis and rheumatism* 2006;54(12):3988-98. doi:
4 10.1002/art.22195 [published Online First: 2006/11/30] *inappropriate*
5 *intervention*
6
7 144. French H, Cusack T, Brennan A, et al. The effectiveness of exercise with and
8 without manual therapy for hip osteoarthritis: A multi-centre randomised
9 controlled trial. *Arthritis and rheumatism* 2011; 63(10 suppl. 1).
10 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/130/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/130/CN-01005130/frame.html)
11 [01005130/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/130/CN-01005130/frame.html). *inappropriate study design*
12
13 145. French H, Cusack T, Brennan A, et al. The effectiveness of exercise therapy with
14 and without manual therapy for hip osteoarthritis: A multicentre randomised
15 controlled trial. *Rheumatology* 2011; 50.
16 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/722/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/722/CN-01003722/frame.html)
17 [01003722/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/722/CN-01003722/frame.html). *inappropriate study design*
18
19 146. French HP, Cusack T, Brennan A, et al. Exercise and manual physiotherapy
20 arthritis research trial (EMPART): a multicentre randomised controlled trial. *BMC*
21 *musculoskeletal disorders* 2009;10:9. doi: 10.1186/1471-2474-10-9 [published
22 Online First: 2009/01/21] *inappropriate study design*
23
24 147. French HP, Galvin R, Cusack T, et al. Predictors of short-term outcome to
25 exercise and manual therapy for people with hip osteoarthritis. *Physical therapy*
26 2014;94(1):31-9. doi: 10.2522/ptj.20130173 [published Online First: 2013/08/10]
27 *inappropriate study design*
28
29 148. Friedrich M, Hahne J, Wepner F. A controlled examination of medical and
30 psychosocial factors associated with low back pain in combination with
31 widespread musculoskeletal pain. *Physical therapy* 2009;89(8):786-803. doi:
32 10.2522/ptj.20080100 [published Online First: 2009/06/23] *inappropriate*
33 *population*
34
35 149. Fulton AS, Hill AM, Williams MT, et al. Feasibility of omega-3 fatty acid
36 supplementation as an adjunct therapy for people with chronic obstructive
37 pulmonary disease: study protocol for a randomized controlled trial. *Trials*
38 2013;14 doi: 10.1186/1468-6708-14-107 *inappropriate intervention*
39
40 150. Garcia-Campayo J, Pascual A, Alda M, et al. Coping with fibromyalgia:
41 Usefulness of the Chronic Pain Coping Inventory-42. *Pain* 2007;132(Suppl
42 1):S68-S76. doi: 10.1016/j.pain.2007.02.013 *inappropriate intervention*
43
44 151. Garcia-Palacios A, Herrero R, Vizcaino Y, et al. Integrating Virtual Reality With
45 Activity Management for the Treatment of Fibromyalgia Acceptability and
46 Preliminary Efficacy. *Clinical Journal of Pain* 2015;31(6):564-72. doi:
47 10.1097/ajp.000000000000196 *inappropriate intervention*
48
49 152. Garvey WT, Mechanick JI, Brett EM, et al. AMERICAN ASSOCIATION OF
50 CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF
51 ENDOCRINOLOGY COMPREHENSIVE CLINICAL PRACTICE GUIDELINES
52 FOR MEDICAL CARE OF PATIENTS WITH OBESITY. *Endocrine practice* :
53 *official journal of the American College of Endocrinology and the American*
54 *Association of Clinical Endocrinologists* 2016;22 Suppl 3:1-203. doi:
55 10.4158/ep161365.gl [published Online First: 2016/05/25] *inappropriate study*
56 *design*
57
58
59

- 1
2
3 153. Gavi M, Vassalo DV, Amaral FT, et al. Strengthening Exercises Improve
4 Symptoms and Quality of Life but Do Not Change Autonomic Modulation in
5 Fibromyalgia: A Randomized Clinical Trial. *PloS one* 2014;9(3) doi:
6 10.1371/journal.pone.0090767 *inappropriate comparison group*
7
8 154. Genc A, Tur BS, Aytur YK, et al. Does aerobic exercise affect the
9 hypothalamicpituitary- adrenal hormonal response in patients with fibromyalgia
10 syndrome? *Journal of Physical Therapy Science* 2015;27(7):2225-31.
11 *inappropriate outcomes*
12
13 155. Gerskowitch C, Norman I, Rimes KA. Patients with medically unexplained
14 physical symptoms experience of receiving treatment in a primary-care
15 psychological therapies service: a qualitative study. *Cognitive Behaviour*
16 *Therapist* 2015;8 doi: 10.1017/s1352465815000235 *inappropriate intervention*
17
18 156. Gniadecki R, Robertson D, Molta CT, et al. Self-reported health outcomes in
19 patients with psoriasis and psoriatic arthritis randomized to two etanercept
20 regimens. *Journal of the European Academy of Dermatology and Venereology* :
21 *JEADV* 2012;26(11):1436-43. doi: 10.1111/j.1468-3083.2011.04308.x
22 <http://dx.doi.org/10.1111/j.1468-3083.2011.04308.x> [published Online First:
23 2011/11/01] *inappropriate intervention*
24
25 157. Goodwin P, Al QK, Gregory W, et al. The effectiveness of aquatic physiotherapy
26 in patients with rheumatoid arthritis: A randomised controlled trial. *Physiotherapy*
27 *(United Kingdom)* 2015; 101.
28 <http://onlinelibrary.wiley.com/doi/10.1111/j.1468-3083.2011.04308.x>
29 *inappropriate comparison group*
30
31 158. Gowans SE, DeHueck A, Abbey SE. Measuring exercise-induced mood changes
32 in fibromyalgia: a comparison of several measures. *Arthritis and rheumatism*
33 2002;47(6):603-9. doi: 10.1002/art.10789 [published Online First: 2003/01/11]
34 *inappropriate population*
35
36 159. Gowans SE, Dehueck A, Voss S, et al. Six-month and one-year followup of 23
37 weeks of aerobic exercise for individuals with fibromyalgia. *Arthritis and*
38 *rheumatism* 2004;51(6):890-8. doi: 10.1002/art.20828 [published Online First:
39 2004/12/14] *inappropriate population*
40
41 160. Grace SL, Krepostman S, Brooks D, et al. Illness perceptions among cardiac
42 patients: Relation to depressive symptomatology and sex. *Journal of*
43 *psychosomatic research* 2005;59(3):153-60. doi:
44 10.1016/j.jpsychores.2005.05.005 *inappropriate study design*
45
46 161. Gremeaux V, Durand S, Benaim C, et al. Evaluation of various ways to deliver
47 information concerning non-steroidal anti-inflammatory drugs to osteoarthritis
48 patients. *Annals of physical and rehabilitation medicine* 2013;56(1):14-29. doi:
49 10.1016/j.rehab.2012.12.004 [published Online First: 2013/02/02] *inappropriate*
50 *study design*
51
52 162. Gronning K, Bratas O, Steinsbekk A. Which Factors Influence Self-Efficacy in
53 Patients with Chronic Inflammatory Polyarthritis? *Musculoskeletal care*
54 2016;14(2):77-86. doi: 10.1002/msc.1114 *inappropriate study design*
55
56 163. Gronning K, Rannestad T, Skomsvoll JF, et al. Long-term effects of a nurse-led
57 group and individual patient education programme for patients with chronic
58 inflammatory polyarthritis - a randomised controlled trial. *Journal of clinical*
59

- 1
2
3 *nursing* 2014;23(7-8):1005-17. doi: 10.1111/jocn.12353 [published Online First:
4 2013/07/24] *inappropriate intervention*
5
6 164. Gronning K, Skomsvoll JF, Rannestad T, et al. The effect of an educational
7 programme consisting of group and individual arthritis education for patients with
8 polyarthritis-A randomised controlled trial. *Patient education and counseling*
9 2012;88(1):113-20. doi: 10.1016/j.pec.2011.12.011 *inappropriate intervention*
10
11 165. Gulec H, Capkin E, Sayar K, et al. The evaluation of the effectiveness of
12 amitriptyline versus venlafaxine in female patients diagnosed with fibromyalgia
13 syndrome. [Turkish]. *Klinik Psikofarmakoloji Bulteni* 2007; 17(2).
14 <http://onlinelibrary.wiley.com/doi/10.1016/j.pec.2011.12.011>
15 *inappropriate intervention*
16 166. Gusi N, Tomas-Carus P, Hakkinen A, et al. Exercise in waist-high warm water
17 decreases pain and improves health-related quality of life and strength in the
18 lower extremities in women with fibromyalgia. *Arthritis and rheumatism*
19 2006;55(1):66-73. doi: 10.1002/art.21718 *inappropriate population*
20
21 167. Haak T, Scott B. The effect of Qigong on fibromyalgia (FMS): a controlled
22 randomized study. *DisabilRehabil* 2008;30(8):625-33. *inappropriate intervention*
23
24 168. Haugstad GK, Haugstad TS, Kirste UM, et al. Continuing improvement of chronic
25 pelvic pain in women after short-term Mensendieck somatocognitive therapy:
26 results of a 1-year follow-up study. *American Journal of Obstetrics and*
27 *Gynecology* 2008;199(6) doi: 10.1016/j.ajog.2008.06.019 *inappropriate*
28 *population*
29
30 169. Haun JN, Graham-Pole J, Shortley B. Children with cancer and blood diseases
31 experience positive physical and psychological effects from massage therapy.
32 *International journal of therapeutic massage & bodywork* 2009;2(2):7-14.
33 [published Online First: 2009/01/01] *inappropriate population*
34
35 170. Haupt M, Millen S, Janner M, et al. Improvement of coping abilities in patients
36 with systemic lupus erythematosus: a prospective study. *Annals of the rheumatic*
37 *diseases* 2005;64(11):1618-23. doi: 10.1136/ard.2004.029926 *inappropriate*
38 *population*
39
40 171. Hauser W. The german fibromyalgia consumer reports-a cross-sectional survey.
41 *Annals of the Rheumatic Disease* 2013; 71.
42 <http://onlinelibrary.wiley.com/doi/10.1136/ard.2004.029926>
43 *inappropriate study design*
44
45 172. Hecker CD, Melo C, Tomazoni SdS, et al. Analysis of effects of kinesiotherapy
46 and hydrokinesiotherapy on the quality of patients with fibromyalgia -- a
47 randomized clinical trial. *Fisioterapia em Movimento* 2011;24(1):57-64. doi:
48 10.1590/S0103-51502011000100007 *inappropriate comparison group*
49
50 173. Heffez DS, Ross RE, Shade-Zeldow Y, et al. Treatment of cervical myelopathy in
51 patients with the fibromyalgia syndrome: outcomes and implications. *European*
52 *spine journal : official publication of the European Spine Society, the European*
53 *Spinal Deformity Society, and the European Section of the Cervical Spine*
54 *Research Society* 2007;16(9):1423-33. doi: 10.1007/s00586-007-0366-2
55 [published Online First: 2007/04/12] *inappropriate study design*
56
57
58
59
60

- 1
2
3 174. Henkel K, Reimers CD, Knapp G, et al. Physical training for neurological and
4 mental diseases. *Der Nervenarzt* 2014;85(12):1521-+. doi: 10.1007/s00115-013-
5 3978-2 *inappropriate study design*
- 6
7 175. Hoeger Bement MK, Weyer A, Hartley S, et al. Pain Perception After Isometric
8 Exercise in Women With Fibromyalgia. *Archives of Physical Medicine &*
9 *Rehabilitation* 2011;92(1):89-95. *inappropriate study design*
- 10
11 176. Hsieh RL, Lee WC. Clinical effects of lateral wedge arch support insoles in knee
12 osteoarthritis: A prospective double-blind randomized study. *Medicine*
13 2016;95(27):e3952. doi: 10.1097/md.0000000000003952 [published Online First:
14 2016/07/12] *inappropriate intervention*
- 15
16 177. Hsieh RL, Lo MT, Lee WC, et al. Therapeutic effects of short-term
17 monochromatic infrared energy therapy on patients with knee osteoarthritis: a
18 double-blind, randomized, placebo-controlled study. *The Journal of orthopaedic*
19 *and sports physical therapy* 2012;42(11):947-56. doi: 10.2519/jospt.2012.3881
20 [published Online First: 2012/09/11] *inappropriate intervention*
- 21
22 178. Huber E, Roos E, Meichtry A, et al. Effect of preoperative neuromuscular training
23 (NEMEX-TJR) on functional outcome after total knee replacement: An assessor-
24 blinded randomized controlled trial. *BMC musculoskeletal disorders* 2015; 16(1).
25 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/584/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/584/CN-01088584/frame.html)
26 [01088584/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/584/CN-01088584/frame.html). *inappropriate intervention*
- 27
28 179. Hudson JI, Arnold LM, Bradley LA, et al. What makes patients with fibromyalgia
29 feel better? Correlations between Patient Global Impression of Improvement and
30 changes in clinical symptoms and function: a pooled analysis of 4 randomized
31 placebo-controlled trials of duloxetine. *The Journal of rheumatology*
32 2009;36(11):2517-22. doi: 10.3899/jrheum.090139 [published Online First:
33 2009/10/17] *inappropriate study design*
- 34
35 180. Hughes S, Seymour R, Campbell R, et al. Fit and Strong!: bolstering
36 maintenance of physical activity among older adults with lower-extremity
37 osteoarthritis. *American journal of health behavior* 2010; 34(6).
38 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/647/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/647/CN-00761647/frame.html)
39 [00761647/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/647/CN-00761647/frame.html). *inappropriate intervention*
- 40
41 181. Hurley M, Walsh N, Jessep S. Clinical effectiveness and costs of an integrated
42 rehabilitation programme compared with outpatient physiotherapy for chronic
43 knee pain. *Arthritis and rheumatism* 2012; 64.
44 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/235/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/235/CN-01008235/frame.html)
45 [01008235/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/235/CN-01008235/frame.html). *inappropriate study design*
- 46
47 182. Hurst NP, Lambert CM, Forbes J, et al. Does waiting matter? A randomized
48 controlled trial of new non-urgent rheumatology out-patient referrals.
49 *Rheumatology (Oxford, England)* 2000;39(4):369-76. [published Online First:
50 2000/05/19] *inappropriate intervention*
- 51
52 183. Ide MR, Laurindo IMM, Rodrigues AL, et al. Effect of aquatic respiratory exercise-
53 based program in patients with fibromyalgia. *International journal of rheumatic*
54 *diseases* 2008;11(2):131-40. doi: 10.1111/j.1756-185X.2008.00348.x
55 *inappropriate comparison group*
- 56
57 184. Jackel WH, Gerdes N, Cziske R, et al. RHEUMATIC COMPLAINTS IN THE
58 GENERAL-POPULATION OF GERMANY - PREVALENCE, PHYSICAL AND
59
60

- 1
2
3 PSYCHOSOCIAL IMPACT. *Zeitschrift fur Rheumatologie* 1993;52(5):281-88.
4 *inappropriate study design*
- 5 185. Jenkinson CM, Doherty M, Avery AJ, et al. Effects of dietary intervention and
6 quadriceps strengthening exercises on pain and function in overweight people
7 with knee pain: randomised controlled trial. *BMJ (Clinical research ed)*
8 2009;339:b3170. doi: 10.1136/bmj.b3170 [published Online First: 2009/08/20]
9 *inappropriate population*
- 10 186. Jensen KB, Kosek E, Wicksell R, et al. Cognitive Behavioral Therapy increases
11 pain-evoked activation of the prefrontal cortex in patients with fibromyalgia. *Pain*
12 2012;153(7):1495-503. doi: 10.1016/j.pain.2012.04.010 *inappropriate*
13 *intervention*
- 14 187. Jensen OK, Nielsen CV, Stengaard-Pedersen K. One-year prognosis in sick-
15 listed low back pain patients with and without radiculopathy. Prognostic factors
16 influencing pain and disability. *Spine Journal* 2010;10(8):659-75. doi:
17 10.1016/j.spinee.2010.03.026 *inappropriate population*
- 18 188. Jessep SA, Walsh NE, Ratcliffe J, et al. Long-term clinical benefits and costs of
19 an integrated rehabilitation programme compared with outpatient physiotherapy
20 for chronic knee pain. *Physiotherapy* 2009;95(2):94-102. doi:
21 10.1016/j.physio.2009.01.005 [published Online First: 2009/07/25] *inappropriate*
22 *population*
- 23 189. Johannesson E, Simren M, Strid H, et al. Physical activity improves symptoms in
24 irritable bowel syndrome: a randomized controlled trial. *The American journal of*
25 *gastroenterology* 2011;106(5):915-22. doi: 10.1038/ajg.2010.480 [published
26 Online First: 2011/01/06] *inappropriate population*
- 27 190. Jones KD. A randomized controlled trial of muscle strengthening versus flexibility
28 training in fibromyalgia. Microform Publications, University of Oregon, 2000.
29 *inappropriate comparison group*
- 30 191. Kamanli A, Kaya A, Ardicoglu O, et al. Comparison of lidocaine injection,
31 botulinum toxin injection, and dry needling to trigger points in myofascial pain
32 syndrome. *Rheumatology international* 2005;25(8):604-11. doi: 10.1007/s00296-
33 004-0485-6 *inappropriate intervention*
- 34 192. Kang J, Li N, Wu B. Therapeutic methods for knee osteoarthritis: Randomized
35 controlled trial and systemic evaluation. [Chinese]. *Zhongguo Linchuang Kangfu*
36 2005; 9(30). [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/890/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/890/CN-00643890/frame.html)
37 [00643890/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/890/CN-00643890/frame.html). *inappropriate study design*
- 38 193. Kapfhammer HP. [Psychopharmacological treatment in patients with somatoform
39 disorders and functional body syndromes]. *Der Nervenarzt* 2012;83(9):1128-41.
40 doi: 10.1007/s00115-011-3446-9 [published Online First: 2012/08/17]
41 *inappropriate study design*
- 42 194. Karp J, Dew M, Wahed A, et al. Challenges and Solutions for Depression
43 Prevention Research: Methodology for a Depression Prevention Trial for Older
44 Adults with Knee Arthritis and Emotional Distress. *American journal of geriatric*
45 *psychiatry* 2016; 24(6).
46 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/456/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/456/CN-01158456/frame.html)
47 [01158456/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/456/CN-01158456/frame.html). *inappropriate outcomes*
- 48
49
50
51
52
53
54
55
56
57
58
59

- 1
2
3 195. Katic B, Heywood J, Turek F, et al. New approach for analyzing self-reporting of
4 insomnia symptoms reveals a high rate of comorbid insomnia across a wide
5 spectrum of chronic diseases. *Sleep Medicine* 2015;16(11):1332-41. doi:
6 10.1016/j.sleep.2015.07.024 *inappropriate outcomes*
7
8 196. Kaya A, Kamanli A, Ardicoglu O, et al. Direct current therapy with/without
9 fidocaine iontophoresis in myofascial pain syndrome. *Bratislava Medical Journal-*
10 *Bratislavske Lekarske Listy* 2009;110(3):185-91. *inappropriate intervention*
11
12 197. Kayiran S, Dursun E, Dursun N, et al. Neurofeedback intervention in fibromyalgia
13 syndrome; a randomized, controlled, rater blind clinical trial. *Applied*
14 *psychophysiology and biofeedback* 2010;35(4):293-302. doi: 10.1007/s10484-
15 010-9135-9 [published Online First: 2010/07/09] *inappropriate intervention*
16
17 198. Keefe FJ, Shelby RA, Somers TJ, et al. Effects of coping skills training and
18 sertraline in patients with non-cardiac chest pain: A randomized controlled study.
19 *Pain* 2011;152(4):730-41. doi: 10.1016/j.pain.2010.08.040 *inappropriate*
20 *intervention*
21
22 199. Keeley T, Al-Janabi H, Nicholls E, et al. A longitudinal assessment of the
23 responsiveness of the ICECAP-A in a randomised controlled trial of a knee pain
24 intervention. *Quality of life research : an international journal of quality of life*
25 *aspects of treatment, care and rehabilitation* 2015;24(10):2319-31. doi:
26 10.1007/s11136-015-0980-0 [published Online First: 2015/04/22] *inappropriate*
27 *study design*
28
29 200. Kekow J, Moots R, Khandker R, et al. Improvements in patient-reported
30 outcomes, symptoms of depression and anxiety, and their association with
31 clinical remission among patients with moderate-to-severe active early
32 rheumatoid arthritis. *Rheumatology (Oxford, England)* 2011;50(2):401-9. doi:
33 10.1093/rheumatology/keq327 [published Online First: 2010/11/10] *inappropriate*
34 *study design*
35
36 201. Kekow J, Moots RJ, Emery P, et al. Patient-reported outcomes improve with
37 etanercept plus methotrexate in active early rheumatoid arthritis and the
38 improvement is strongly associated with remission: the COMET trial. *Annals of*
39 *the rheumatic diseases* 2010;69(1):222-5. doi: 10.1136/ard.2008.102509
40 [published Online First: 2009/03/19] *inappropriate intervention*
41
42 202. Kempke S, Goossens L, Luyten P, et al. Predictors of outcome in a multi-
43 component treatment program for chronic fatigue syndrome. *Journal of Affective*
44 *Disorders* 2010;126(1-2):174-79. doi: 10.1016/j.jad.2010.01.073 *inappropriate*
45 *intervention*
46
47 203. Knittle K, Maes S, de Gucht V. Psychological interventions for rheumatoid
48 arthritis: examining the role of self-regulation with a systematic review and meta-
49 analysis of randomized controlled trials. *Arthritis care & research*
50 2010;62(10):1460-72. doi: 10.1002/acr.20251
51 <http://dx.doi.org/10.1002/acr.20251> [published Online First: 2010/05/28] *inappropriate*
52 *study design*
53
54 204. Kolahi S, Pourghassem Gargari B, Mesgari Abbasi M, et al. Effects of
55 phylloquinone supplementation on lipid profile in women with rheumatoid arthritis:
56 a double blind placebo controlled study. *Nutrition research and practice*
57
58
59
60

- 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 amitryptiline 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. Lakhani 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*

- 1
2
3 *Movimiento Humano Y La Salud* 2015;11(2):1-19. doi: 10.15359/mhs.11-2.1
4 *inappropriate study design*
- 5 215. Li K, Hu XQ, Qiu WH, et al. Effects of physiotherapy versus combination of
6 physiotherapy and preventive education on quality of life in patients with
7 degenerative gonarthrosis. *Chinese Journal of Clinical Rehabilitation*
8 2006;10(4):32-33. *inappropriate intervention*
- 9 216. Li YH, Wang FY, Feng CQ, et al. Massage therapy for fibromyalgia: a systematic
10 review and meta-analysis of randomized controlled trials. *PloS one*
11 2014;9(2):e89304. doi: 10.1371/journal.pone.0089304 [published Online First:
12 2014/03/04] *inappropriate study design*
- 13 217. Ljótsson B, Atterlöf E, Lagerlöf M, et al. Internet-delivered acceptance and
14 values-based exposure treatment for fibromyalgia: A pilot study. *Cognitive*
15 *Behaviour Therapy* 2014;43(2):93-104. doi: 10.1080/16506073.2013.846401
16 *inappropriate intervention*
- 17 218. Lopez-Pousa S, Bassets Pages G, Monserrat-Vila S, et al. Sense of Well-Being
18 in Patients with Fibromyalgia: Aerobic Exercise Program in a Mature Forest-A
19 Pilot Study. *Evidence-based complementary and alternative medicine : eCAM*
20 2015;2015:614783. doi: 10.1155/2015/614783 [published Online First:
21 2015/11/12] *inappropriate comparison group*
- 22 219. Lopez-Rodriguez MD, Castro-Sanchez AM, Fernandez-Martinez M, et al.
23 Comparison between aquatic-biodanza and stretching for improving quality of life
24 and pain in patients with fibromyalgia. *Atencion Primaria* 2012;44(11):641-49. doi:
25 10.1016/j.aprim.2012.03.002 *inappropriate intervention*
- 26 220. Lopez-Rodriguez MM, Fernandez-Martinez M, Mataran-Penarrocha GA, et al.
27 [Effectiveness of aquatic biodance on sleep quality, anxiety and other symptoms
28 in patients with fibromyalgia]. *Medicina clinica* 2013;141(11):471-8. doi:
29 10.1016/j.medcli.2012.09.036 [published Online First: 2012/12/19] *inappropriate*
30 *intervention*
- 31 221. Luciano JV, Martinez N, Penarrubia-Maria MT, et al. Effectiveness of a
32 psychoeducational treatment program implemented in general practice for
33 fibromyalgia patients: a randomized controlled trial. *The Clinical journal of pain*
34 2011;27(5):383-91. doi: 10.1097/AJP.0b013e31820b131c [published Online
35 First: 2011/02/15] *inappropriate intervention*
- 36 222. Luedtke K, Rushton A, Wright C, et al. Effectiveness of anodal transcranial direct
37 current stimulation in patients with chronic low back pain: design, method and
38 protocol for a randomised controlled trial. *BMC musculoskeletal disorders*
39 2011;12:290. doi: 10.1186/1471-2474-12-290 [published Online First:
40 2011/12/30] *inappropriate intervention*
- 41 223. Lumley M, Schubiner H, Clauw D, et al. The PAST-FM (Pain and Stress
42 Treatment for Fibromyalgia) randomized, controlled trial: Main effects of
43 emotional awareness and expression and cognitive-behavioral therapies. *Journal*
44 *of pain* 2016; 17(4 suppl. 1).
45 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/566/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/566/CN-01142566/frame.html)
46 [01142566/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/566/CN-01142566/frame.html). *inappropriate intervention*
- 47 224. Lumley MA, Keefe FJ, Mosley-Williams A, et al. The effects of written emotional
48 disclosure and coping skills training in rheumatoid arthritis: A randomized clinical
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 trial. *Journal of Consulting and Clinical Psychology* 2014;82(4):644-58. doi:
4 10.1037/a0036958 *inappropriate intervention*
5
6 225. Lund I, Lundeberg T, Carleson J, et al. Corticotropin releasing factor in urine--a
7 possible biochemical marker of fibromyalgia. Responses to massage and guided
8 relaxation. *Neuroscience letters* 2006;403(1-2):166-71. doi:
9 10.1016/j.neulet.2006.04.038 [published Online First: 2006/05/24] *inappropriate*
10 *study design*
11 226. Mackintosh S. Hydrotherapy and Tai Chi each provide clinical improvements for
12 older people with osteoarthritis. *Australian Journal of Physiotherapy*
13 2008;54(2):143-43. *inappropriate study design*
14 227. Maddali Bongi S, Del Rosso A, Di Felice C, et al. Resseguier method and Qi
15 Gong sequentially integrated in patients with fibromyalgia syndrome. *Clinical and*
16 *experimental rheumatology* 2012;30(6 Suppl 74):51-8. [published Online First:
17 2012/11/01] *inappropriate intervention*
18 228. Mahagna H, Amital D, Amital H. A randomised, double-blinded study comparing
19 giving etoricoxib vs. placebo to female patients with fibromyalgia. *International*
20 *journal of clinical practice* 2016; 70(2 // (MSD) *Meso Scale Diagnostics*).
21 <http://onlinelibrary.wiley.com/doi/10.1111/ijcp.12727>.
22 <http://onlinelibrary.wiley.com/doi/10.1111/ijcp.12727>. *inappropriate intervention*
23 229. Mannerkorpi K, Nyberg B, Ahlmen M, et al. Pool exercise combined with an
24 education program for patients with fibromyalgia syndrome. A prospective,
25 randomized study. *J Rheumatol* 2000;27(10):2473-81. *inappropriate intervention*
26 230. Mao JJ, Bruner DW, Stricker C, et al. Feasibility trial of electroacupuncture for
27 aromatase inhibitor--related arthralgia in breast cancer survivors. *Integrative*
28 *cancer therapies* 2009;8(2):123-9. doi: 10.1177/1534735409332903 [published
29 Online First: 2009/08/15] *inappropriate population*
30 231. Marszalek J, Price LL, Harvey WF, et al. Outcome Expectations and
31 Osteoarthritis: Perceived Benefits of Exercise Are Associated with Self-Efficacy
32 and Depression. *Arthritis care & research* 2016 doi: 10.1002/acr.22969
33 [published Online First: 2016/07/09] *inappropriate study design*
34 232. Martin DP, Williams BA, Berger IH. Improvement in fibromyalgia symptoms with
35 acupuncture: Results of a randomized controlled trial. *Mayo Clinic proceedings*
36 2006;81(6):749-57. *inappropriate intervention*
37 233. Martín J, Torre F, Aguirre U, et al. Evaluation of the interdisciplinary PSYMEPHY
38 treatment on patients with fibromyalgia: A randomized control trial. *Pain Medicine*
39 2014;15(4):682-91. doi: 10.1111/pme.12375 *inappropriate intervention*
40 234. Martín J, Torre F, Padierna A, et al. Six-and 12-month follow-up of an
41 interdisciplinary fibromyalgia treatment programme: results of a randomised trial.
42 *Clinical and experimental rheumatology* 2012;30(6 Suppl 74):103-11. [published
43 Online First: 2013/02/27] *inappropriate intervention*
44 235. Martín J, Torre F, Padierna A, et al. Interdisciplinary treatment of patients with
45 fibromyalgia: improvement of their health-related quality of life. *Pain practice : the*
46 *official journal of World Institute of Pain* 2014; 14(8).
47 <http://onlinelibrary.wiley.com/doi/10.1111/ppm.12375>.
48 <http://onlinelibrary.wiley.com/doi/10.1111/ppm.12375>. *inappropriate intervention*
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 236. Martin J, Torre F, Padierna A, et al. Impact of interdisciplinary treatment on
4 physical and psychosocial parameters in patients with fibromyalgia: results of a
5 randomised trial. *International journal of clinical practice* 2014;68(5):618-27.
6 [published Online First: 2014/05/29] *inappropriate intervention*
7
8 237. Martín-Nogueras AM, Calvo-Arenillas JI. Efficacy of physiotherapy treatment on
9 pain and quality of life in patients with fibromyalgia. *Rehabilitacion*
10 2012;46(3):199-206. *inappropriate intervention*
11
12 238. Martins MRI, Gritti CC, dos Santos R, et al. Randomized controlled trial of a
13 therapeutic intervention group in patients with fibromyalgia syndrome. *Revista*
14 *Brasileira De Reumatologia* 2014;54(3):179-84. doi: 10.1016/j.rbre.2013.10.002
15 *inappropriate intervention*
16
17 239. Mata J, Cabrera S, Sanchis P, et al. Electro-acupuncture for treatment of knee
18 pain from osteoarthritis and the possible endocrinology changes: a study protocol
19 for a randomized controlled trial. *Trials* 2015;16:248. doi: 10.1186/s13063-015-
20 0766-2 [published Online First: 2015/06/04] *inappropriate study design*
21
22 240. Mataran-Penarrocha GA, Castro-Sanchez AM, Garcia GC, et al. Influence of
23 Craniosacral Therapy on Anxiety, Depression and Quality of Life in Patients with
24 Fibromyalgia. *Evidence-Based Complementary and Alternative Medicine* 2011:1-
25 9. doi: 10.1093/ecam/nep125 *inappropriate intervention*
26
27 241. Matcham F, Norton S, Scott D, et al. The impact of depression on long-term
28 physical health outcomes in rheumatoid arthritis. *Rheumatology (United*
29 *Kingdom)* 2014; 53.
30 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/273/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/273/CN-01057273/frame.html)
31 [01057273/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/273/CN-01057273/frame.html). *inappropriate study design*
32
33 242. Matcham F, Norton S, Scott DL, et al. Symptoms of depression and anxiety
34 predict treatment response and long-term physical health outcomes in
35 rheumatoid arthritis: secondary analysis of a randomized controlled trial.
36 *Rheumatology (Oxford, England)* 2016;55(2):268-78. doi:
37 10.1093/rheumatology/kev306 [published Online First: 2015/09/10] *inappropriate*
38 *study design*
39
40 243. McBain H, Shipley M, Olaleye A, et al. A patient-initiated DMARD self-monitoring
41 service for people with rheumatoid or psoriatic arthritis on methotrexate: A
42 randomised controlled trial. *Annals of the rheumatic diseases* 2016; 75(7).
43 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/299/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/299/CN-01178299/frame.html)
44 [01178299/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/299/CN-01178299/frame.html). *inappropriate intervention*
45
46 244. McVeigh JG, Hurley DA, Basford JR, et al. Effectiveness of a combined pool-
47 based exercise and education programme compared to usual medical care in
48 fibromyalgia syndrome: a randomised, controlled trial. *Physical Therapy Reviews*
49 2006;11(3):217-17. *inappropriate study design*
50
51 245. Mendonca ME, Simis M, Grecco LC, et al. Transcranial Direct Current
52 Stimulation Combined with Aerobic Exercise to Optimize Analgesic Responses in
53 Fibromyalgia: A Randomized Placebo-Controlled Clinical Trial. *Frontiers in*
54 *human neuroscience* 2016;10:68. doi: 10.3389/fnhum.2016.00068 [published
55 Online First: 2016/03/26] *inappropriate intervention*
56
57 246. Menkes CJ, Godeau P. Fibromyalgia. *Bulletin De L Academie Nationale De*
58 *Medecine* 2007;191(1):143-48. *inappropriate study design*
59
60

- 1
2
3 247. Mercadie L, Mick G, Guetin S, et al. Effects of Listening to Music versus
4 Environmental Sounds in Passive and Active Situations on Levels of Pain and
5 Fatigue in Fibromyalgia. *Pain Management Nursing* 2015;16(5):664-71. doi:
6 10.1016/j.pmn.2015.01.005 *inappropriate intervention*
7
8 248. Meyer BB, Lemley KJ. Utilizing exercise to affect the symptomology of
9 fibromyalgia: a pilot study. *Medicine and science in sports and exercise*
10 2000;32(10):1691-7. [published Online First: 2000/10/20] *inappropriate study*
11 *design*
12
13 249. Mibielli M, Nunes C, Cezar P, et al. Osteoarthritis: Clinical evaluation of
14 diclofenac combined with the B complex vitamins. *Revista brasileira de medicina*
15 2009; 66(7). [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/674/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/674/CN-00753674/frame.html)
16 [00753674/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/674/CN-00753674/frame.html). *inappropriate intervention*
17
18 250. Middleton KR, Ward MM, Haaz S, et al. A pilot study of yoga as self-care for
19 arthritis in minority communities. *Health and quality of life outcomes* 2013;11:55.
20 doi: 10.1186/1477-7525-11-55 [published Online First: 2013/04/04] *inappropriate*
21 *intervention*
22
23 251. Miles ALS. The effects of gentle yoga vs. cognitive behavioral therapy on
24 physical and psychological symptoms; neurocognitive functioning; and
25 physiology in women with Fibromyalgia. ProQuest Information & Learning, 2014.
26 *inappropriate intervention*
27
28 252. Minor MA. Exercise maintenance behavior of subjects with arthritis following
29 participation in a supervised exercise program [Ph.D.]. University of Missouri -
30 Columbia, 1989. *inappropriate study design*
31
32 253. Minor MA, Brown JD. Exercise maintenance of persons with arthritis after
33 participation in a class experience. *Health education quarterly* 1993;20(1):83-95.
34 [published Online First: 1993/01/01] *inappropriate study design*
35
36 254. Mirtaheri E, Gargari BP, Kolahi S, et al. Effects of Alpha-Lipoic Acid
37 Supplementation on Inflammatory Biomarkers and Matrix Metalloproteinase-3 in
38 Rheumatoid Arthritis Patients. *Journal of the American College of Nutrition*
39 2015;34(4):310-17. doi: 10.1080/07315724.2014.910740 *inappropriate*
40 *intervention*
41
42 255. Mishra P, Trivedi V. Acupuncture in the treatment of rheumatoid arthritis: Results
43 of a randomized controlled trial. *Annals of the rheumatic diseases* 2014; 73.
44 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/582/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/582/CN-01009582/frame.html)
45 [01009582/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/582/CN-01009582/frame.html). *inappropriate intervention*
46
47 256. Moore RA, Straube S, Paine J, et al. Fibromyalgia: Moderate and substantial
48 pain intensity reduction predicts improvement in other outcomes and substantial
49 quality of life gain. *Pain* 2010;149(2):360-64. doi: 10.1016/j.pain.2010.02.039
50 *inappropriate study design*
51
52 257. Morgan N, Driban J, Ransford G, et al. Construct validity of promis instruments
53 among patients with symptomatic knee osteoarthritis. *Osteoarthritis and cartilage*
54 2013; 21. [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/483/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/483/CN-01010483/frame.html)
55 [01010483/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/483/CN-01010483/frame.html). *inappropriate study design*
56
57 258. Morgan N, Ransford G, Morgan L, et al. Mindfulness is associated with
58 psychological symptoms, self-efficacy, and quality of life among patients with
59 symptomatic knee osteoarthritis. *Osteoarthritis and cartilage* 2013; 21.
60

- 1
2
3 <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/479/CN-01010479/frame.html>. *inappropriate study design*
- 4
5 259. Morone N, Karp J, Lynch C, et al. Impact of chronic musculoskeletal pathology
6 on older adults: a study of differences between knee OA and low back pain. *Pain*
7 *medicine (Malden, Mass)* 2009; 10(4).
8 <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/087/CN-00721087/frame.html>. *inappropriate study design*
- 9
10 260. Moroshko I, Brennan L, O'Brien P. Predictors of dropout in weight loss
11 interventions: A systematic review of the literature. *Obesity Reviews*
12 2011;12(11):912-34. doi: 10.1111/j.1467-789X.2011.00915.x *inappropriate study*
13 *design*
- 14
15 261. Morris LD, Grimmer-Somers KA, Spottiswoode B, et al. Virtual reality exposure
16 therapy as treatment for pain catastrophizing in fibromyalgia patients: proof-of-
17 concept study (Study Protocol). *BMC musculoskeletal disorders* 2011;12(1):85.
18 doi: 10.1186/1471-2474-12-85 [published Online First: 2011/05/03] *inappropriate*
19 *study design*
- 20
21 262. Moustafa IM, Diab AA. The addition of upper cervical manipulative therapy in the
22 treatment of patients with fibromyalgia: a randomized controlled trial.
23 *Rheumatology international* 2015;35(7):1163-74. doi: 10.1007/s00296-015-3248-
24 7 [published Online First: 2015/03/19] *inappropriate intervention*
- 25
26 263. Mu PF, Chen YC, Cheng SC. The effectiveness of non-pharmacological pain
27 management in relieving chronic pain for children and adolescents. *JBI library of*
28 *systematic reviews* 2009;7(34):1489-543. [published Online First: 2009/01/01]
29 *inappropriate population*
- 30
31 264. Munguia-Izquierdo D, Legaz-Arrese A. Determinants of sleep quality in middle-
32 aged women with fibromyalgia syndrome. *Journal of Sleep Research*
33 2012;21(1):73-79. doi: 10.1111/j.1365-2869.2011.00929.x *inappropriate*
34 *outcomes*
- 35
36 265. Murphy LB, Sacks JJ, Brady TJ, et al. Anxiety and depression among US adults
37 with arthritis: Prevalence and correlates. *Arthritis care & research*
38 2012;64(7):968-76. doi: 10.1002/acr.21685 *inappropriate study design*
- 39
40 266. Murphy SL, Lyden AK, Kratz AL, et al. Characterizing Pain Flares From the
41 Perspective of Individuals With Symptomatic Knee Osteoarthritis. *Arthritis care &*
42 *research* 2015;67(8):1103-11. doi: 10.1002/acr.22545 *inappropriate study design*
- 43
44 267. Nalamachu S, Rauck R, Hale M, et al. A long-term, open-label safety study of
45 single-entity hydrocodone bitartrate extended release for the treatment of
46 moderate to severe chronic pain. *Journal of pain research* 2014; 7.
47 <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/077/CN-01036077/frame.html>. *inappropriate intervention*
- 48
49 268. Navarrete-Navarrete N, Peralta-Ramirez MI, Sabio-Sanchez JM, et al. Efficacy of
50 Cognitive Behavioural Therapy for the Treatment of Chronic Stress in Patients
51 with Lupus Erythematosus: A Randomized Controlled Trial. *Psychotherapy and*
52 *Psychosomatics* 2010;79(2):107-15. doi: 10.1159/000276370 *inappropriate*
53 *population*
- 54
55 269. Nazareth I, Landau S, Yardley L, et al. Patterns of presentations of dizziness in
56 primary care - a cross-sectional cluster analysis study. *Journal of psychosomatic*
57
58
59

- 1
2
3 *research* 2006;60(4):395-401. doi: 10.1016/j.jpsychores.2005.07.011
4 *inappropriate study design*
- 5 270. Niedermann K, de Bie RA, Kubli R, et al. Effectiveness of individual resource-
6 oriented joint protection education in people with rheumatoid arthritis. A
7 randomized controlled trial. *Patient education and counseling* 2011;82(1):42-48.
8 doi: 10.1016/j.pec.2010.02.014 *inappropriate intervention*
- 9 271. Noiseux NO, Callaghan JJ, Clark CR, et al. Preoperative predictors of pain
10 following total knee arthroplasty. *The Journal of arthroplasty* 2014;29(7):1383-7.
11 doi: 10.1016/j.arth.2014.01.034 [published Online First: 2014/03/19]
12 *inappropriate study design*
- 13 272. Noppers I, Niesters M, Swartjes M, et al. Absence of long-term analgesic effect
14 from a short-term S-ketamine infusion on fibromyalgia pain: A randomized,
15 prospective, double blind, active placebo-controlled trial. *European Journal of*
16 *Pain* 2011;15(9):942-49. doi: 10.1016/j.ejpain.2011.03.008 *inappropriate*
17 *intervention*
- 18 273. Nordeman L, Gunnarsson R, Mannerkorpi K. Prevalence and Characteristics of
19 Widespread Pain in Female Primary Health Care Patients With Chronic Low
20 Back Pain. *Clinical Journal of Pain* 2012;28(1):65-72. doi:
21 10.1097/AJP.0b013e318223622c *inappropriate population*
- 22 274. Nugraha B, Korallus C, Dorffer D, et al. Aerobic exercise cognitive behavioural
23 therapy and combination of treatment in fibromyalgia syndrome patients: A
24 randomized control trial (effect on mood related disorder-a preliminary result).
25 *PM and R* 2014; 6(8 suppl. 2).
26 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/639/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/639/CN-01086639/frame.html)
27 [01086639/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/639/CN-01086639/frame.html). *inappropriate study design*
- 28 275. Nyssen OP, Taylor SJC, Wong G, et al. Does therapeutic writing help people with
29 long-term conditions? Systematic review, realist synthesis and economic
30 considerations. *Health Technology Assessment* 2016;20(27):1-367. doi:
31 10.3310/hta20270 *inappropriate study design*
- 32 276. Ohta H, Oka H, Usui C, et al. A randomized, double-blind, multicenter, placebo-
33 controlled phase III trial to evaluate the efficacy and safety of pregabalin in
34 Japanese patients with fibromyalgia. *Arthritis research & therapy* 2012; 14(5).
35 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/489/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/489/CN-00913489/frame.html)
36 [00913489/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/489/CN-00913489/frame.html). *inappropriate intervention*
- 37 277. Oktayoglu P, Gur A, Yardimeden I, et al. Comparison of the efficacy of
38 phonophoresis and conventional ultrasound therapy in patients with primary knee
39 osteoarthritis. *Erciyes Tip Dergisi* 2014; 36(1).
40 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/055/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/055/CN-00988055/frame.html)
41 [00988055/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/055/CN-00988055/frame.html). *inappropriate intervention*
- 42 278. Olin R, Klein R, Berg PA. A randomised double-blind 16-week study of ritanserin
43 in fibromyalgia syndrome: clinical outcome and analysis of autoantibodies to
44 serotonin, gangliosides and phospholipids. *Clinical rheumatology* 1998;17(2):89-
45 94. [published Online First: 1998/06/26] *inappropriate intervention*
- 46 279. Olivan-Blázquez B, Herrera-Mercadal P, Puebla-Guedea M, et al. Efficacy of
47 memantine in the treatment of fibromyalgia: A double-blind, randomised,
48
49
50
51
52
53
54
55
56
57
58
59

- 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/doi/10.1111/j.1469-7580.2011.01102.x> *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 &*

- 1
2
3 *Science in Sports* 2015;25:1-72. doi: 10.1111/sms.12581 *inappropriate study*
4 *design*
5 291. Peres M. Fibromyalgia and headache disorders. *Current pain and headache*
6 *reports* 2009; 13(5).
7 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/879/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/879/CN-00958879/frame.html)
8 [00958879/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/879/CN-00958879/frame.html). *inappropriate study design*
9
10 292. Perrot S, Russell IJ. More ubiquitous effects from non-pharmacologic than from
11 pharmacologic treatments for fibromyalgia syndrome: a meta-analysis examining
12 six core symptoms. *European journal of pain (London, England)*
13 2014;18(8):1067-80. doi: 10.1002/ejp.564 [published Online First: 2014/08/21]
14 *inappropriate study design*
15
16 293. Peters S, Stanley I, Rose M, et al. A randomized controlled trial of group aerobic
17 exercise in primary care patients with persistent, unexplained physical
18 symptoms. *Family Practice* 2002;19(6):665-74. doi: 10.1093/fampra/19.6.665
19 *inappropriate population*
20
21 294. Potvin S, Morin M, Cloutier C, et al. Add-on treatment of quetiapine for
22 fibromyalgia: A pilot, randomized, double-blind, placebo-controlled 12-week trial.
23 *Journal of Clinical Psychopharmacology* 2012;32(5):684-87. doi:
24 10.1097/JCP.0b013e318267b8ca *inappropriate intervention*
25
26 295. Preece JC. The relationship between family resilience and the successful
27 management of fibromyalgia [Ph.D.]. Syracuse University, 2001. *inappropriate*
28 *study design*
29
30 296. Rakel B, Zimmerman M, Geasland K, et al. Transcutaneous electrical nerve
31 stimulation for the control of pain during rehabilitation after total knee
32 arthroplasty: A randomized, blinded, placebo-controlled trial. *Pain* 2014; 155(12).
33 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/744/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/744/CN-01052744/frame.html)
34 [01052744/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/744/CN-01052744/frame.html). *inappropriate intervention*
35
36 297. Redondo JR, Justo CM, Moraleda FV, et al. Long-term efficacy of therapy in
37 patients with fibromyalgia: a physical exercise-based program and a cognitive-
38 behavioral approach. *Arthritis and rheumatism* 2004;51(2):184-92. doi:
39 10.1002/art.20252 [published Online First: 2004/04/13] *inappropriate*
40 *comparison group*
41
42 298. Richards DA, Hill JJ, Gask L, et al. Clinical effectiveness of collaborative care for
43 depression in UK primary care (CADET): Cluster randomised controlled trial.
44 *BMJ: British Medical Journal* 2013;347 *inappropriate population*
45
46 299. Rini C, Porter LS, Somers TJ, et al. Automated Internet-based pain coping skills
47 training to manage osteoarthritis pain: a randomized controlled trial. *Pain*
48 2015;156(5):837-48. doi: 10.1097/j.pain.000000000000121 [published Online
49 First: 2015/03/04] *inappropriate intervention*
50
51 300. Rodriguez Huerta MD, Trujillo-Martin MM, Rua-Figueroa I, et al. Healthy lifestyle
52 habits for patients with systemic lupus erythematosus: A systemic review.
53 *Seminars in arthritis and rheumatism* 2016;45(4):463-70. doi:
54 10.1016/j.semarthrit.2015.09.003 [published Online First: 2015/11/03]
55 *inappropriate population*
56
57 301. Rodriguez Torres J, Cabrera Martos I, Torres Sanchez I, et al. Results of an
58 Active Neurodynamic Mobilization Program in Patients With Fibromyalgia
59
60

- 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/doi/10.1136/annrheumdis-2012-021625>. *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

- 1
2
3 Trial. *Journal of Bone and Joint Surgery-American Volume* 2014;96A(11):944-50.
4 doi: 10.2106/jbjs.I.01696 *inappropriate population*
5
6 312. Schmidt S, Grossman P, Schwarzer B, et al. Treating fibromyalgia with
7 mindfulness-based stress reduction: results from a 3-armed randomized
8 controlled trial. *Pain* 2011;152(2):361-9. doi: 10.1016/j.pain.2010.10.043
9 [published Online First: 2010/12/15] *inappropriate intervention*
10
11 313. Scopaz KA, Piva SR, Wisniewski S, et al. Relationships of Fear, Anxiety, and
12 Depression With Physical Function in Patients With Knee Osteoarthritis. *Archives*
13 *of physical medicine and rehabilitation* 2009;90(11):1866-73. doi:
14 10.1016/j.apmr.2009.06.012 *inappropriate study design*
15
16 314. Selfridge N. Meditation for Fibromyalgia: Yea or Nay? *Alternative Medicine Alert*
17 2011;14(3):34-36. *inappropriate intervention*
18
19 315. Shadick NA, Sowell NF, Frits ML, et al. A randomized controlled trial of an
20 internal family systems-based psychotherapeutic intervention on outcomes in
21 rheumatoid arthritis: a proof-of-concept study. *The Journal of rheumatology*
22 2013;40(11):1831-41. doi: 10.3899/jrheum.121465 [published Online First:
23 2013/08/21] *inappropriate intervention*
24
25 316. Shahabi L, Naliboff BD, Shapiro D. Self-regulation evaluation of therapeutic yoga
26 and walking for patients with irritable bowel syndrome: a pilot study. *Psychology*
27 *Health & Medicine* 2016;21(2):176-88. doi: 10.1080/13548506.2015.1051557
28 *inappropriate population*
29
30 317. Shahrbanian S, Duquette P, Kuspinar A, et al. Contribution of symptom clusters
31 to multiple sclerosis consequences. *Quality of Life Research* 2015;24(3):617-29.
32 doi: 10.1007/s11136-014-0804-7 *inappropriate population*
33
34 318. Sharpe L, Gittins CB, Correia HM, et al. Problem-solving versus cognitive
35 restructuring of medically ill seniors with depression (PROMISE-D trial): study
36 protocol and design. *Bmc Psychiatry* 2012;12 doi: 10.1186/1471-244x-12-207
37 *inappropriate study design*
38
39 319. Sharpe L, Sensky T, Allard S. The course of depression in recent onset
40 rheumatoid arthritis: the predictive role of disability, illness perceptions, pain and
41 coping. *Journal of psychosomatic research* 2001;51(6):713-9. [published Online
42 First: 2001/12/26] *inappropriate study design*
43
44 320. Sharpe L, Sensky T, Timberlake N, et al. Long-term efficacy of a cognitive
45 behavioural treatment from a randomized controlled trial for patients recently
46 diagnosed with rheumatoid arthritis. *Rheumatology (Oxford, England)* 2003;
47 42(3). [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/463/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/463/CN-00431463/frame.html)
48 [00431463/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/463/CN-00431463/frame.html). *inappropriate intervention*
49
50 321. Sharpe L, Sensky T, Timberlake N, et al. A blind, randomized, controlled trial of
51 cognitive-behavioural intervention for patients with recent onset rheumatoid
52 arthritis: preventing psychological and physical morbidity. *Pain* 2001; 89(2-3).
53 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/279/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/279/CN-00327279/frame.html)
54 [00327279/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/279/CN-00327279/frame.html). *inappropriate intervention*
55
56 322. Shih M, Hootman JM, Kruger J, et al. Physical activity in men and women with
57 arthritis - National Health Interview Survey, 2002. *American Journal of Preventive*
58 *Medicine* 2006;30(5):385-93. doi: 10.1016/j.amepre.2005.12.005 *inappropriate*
59 *intervention*
60

- 1
2
3 323. Shupak NM, McKay JC, Nielson WR, et al. Exposure to a specific pulsed low-
4 frequency magnetic field: A double-blind placebo-controlled study of effects on
5 pain ratings in rheumatoid arthritis and fibromyalgia patients. *Pain Research &*
6 *Management* 2006;11(2):85-90. doi: 10.1155/2006/842162 *inappropriate*
7 *intervention*
8
9 324. Siegel KM. The effects of emotional disclosure on physical symptoms, healthcare
10 utilization, and psychosocial adjustment in patients with irritable bowel syndrome
11 [Ph.D.]. Alliant International University, San Diego, 2003. *inappropriate*
12 *population*
13
14 325. Skrabek RQ, Galimova L, Ethans K, et al. Nabilone for the treatment of pain in
15 fibromyalgia. *The journal of pain : official journal of the American Pain Society*
16 2008;9(2):164-73. doi: 10.1016/j.jpain.2007.09.002 [published Online First:
17 2007/11/03] *inappropriate intervention*
18
19 326. Slavich GM, Irwin MR. From Stress to Inflammation and Major Depressive
20 Disorder: A Social Signal Transduction Theory of Depression. *Psychological*
21 *Bulletin* 2014;140(3):774-815. doi: 10.1037/a0035302 *inappropriate study design*
22
23 327. Smeets RJ, Maher CG, Nicholas MK, et al. Do psychological characteristics
24 predict response to exercise and advice for subacute low back pain? *Arthritis and*
25 *rheumatism* 2009;61(9):1202-9. doi: 10.1002/art.24731 [published Online First:
26 2009/08/29] *inappropriate study design*
27
28 328. Smith-Ray R, Fitzgibbon M, Tussing-Humphreys L, et al. Fit and Strong! Plus:
29 Design of a comparative effectiveness evaluation of a weight management
30 program for older adults with osteoarthritis. *Contemporary clinical trials* 2014;
31 37(2). [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/212/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/212/CN-00959212/frame.html)
32 [00959212/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/212/CN-00959212/frame.html). *inappropriate study design*
33
34 329. Sørensen J, Bengtsson A, Ahlner J, et al. Fibromyalgia--are there different
35 mechanisms in the processing of pain? A double blind crossover comparison of
36 analgesic drugs. *The Journal of rheumatology* 1997; 24(8).
37 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/709/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/709/CN-00142709/frame.html)
38 [00142709/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/709/CN-00142709/frame.html). *inappropriate intervention*
39
40 330. Stehlik R, Ulfberg J, Hedner J, et al. High prevalence of restless legs syndrome
41 among women with multi-site pain: A population-based study in Dalarna,
42 Sweden. *European Journal of Pain* 2014;18(10):1402-09. doi: 10.1002/ejp.504
43 *inappropriate outcomes*
44
45 331. Stiller C. The effect of therapeutic touch on fibromyalgia pain and anxiety [Ph.D.].
46 Case Western Reserve University (Health Sciences), 2006. *inappropriate*
47 *intervention*
48
49 332. Stratz T, Mennet P, Benn H, et al. [Blocking of S2 receptors--a new treatment
50 principle in generalized tendomyopathy (fibromyalgia)?]. *Zeitschrift fur*
51 *Rheumatologie* 1991; 50(1).
52 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/788/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/788/CN-00353788/frame.html)
53 [00353788/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/788/CN-00353788/frame.html). *inappropriate intervention*
54
55 333. Sulenes K, Freitas J, Justice L, et al. Underuse of Yoga as a Referral Resource
56 by Health Professions Students. *Journal of Alternative and Complementary*
57 *Medicine* 2015;21(1):53-59. doi: 10.1089/acm.2014.0217 *inappropriate*
58 *intervention*
59
60

- 1
2
3 334. Sutbeyaz S, Sezer N, Koseoglu F, et al. Low-frequency pulsed electromagnetic
4 field therapy in fibromyalgia: a randomized, double-blind, sham-controlled clinical
5 study. *The Clinical journal of pain* 2009; 25(8).
6 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/605/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/605/CN-00728605/frame.html)
7 [00728605/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/605/CN-00728605/frame.html). *inappropriate intervention*
- 8
9 335. Sverdrup B. Use less cosmetics--suffer less from fibromyalgia? *Journal of*
10 *women's health (2002)* 2004; 13(2).
11 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/706/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/706/CN-00468706/frame.html)
12 [00468706/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/706/CN-00468706/frame.html). *inappropriate intervention*
- 13
14 336. Tang NK, Lereya ST, Boulton H, et al. Nonpharmacological Treatments of
15 Insomnia for Long-Term Painful Conditions: A Systematic Review and Meta-
16 analysis of Patient-Reported Outcomes in Randomized Controlled Trials. *Sleep*
17 2015;38(11):1751-64. doi: 10.5665/sleep.5158 [published Online First:
18 2015/04/24] *inappropriate study design*
- 19
20 337. Tang NKY, Goodchild CE, Salkovskis PM. Hybrid cognitive-behaviour therapy for
21 individuals with insomnia and chronic pain: A pilot randomised controlled trial.
22 *Behaviour Research and Therapy* 2012;50(12):814-21. doi:
23 10.1016/j.brat.2012.08.006 *inappropriate population*
- 24
25 338. Tarakci E, Yeldan I, Kaya Mutlu E, et al. The relationship between physical
26 activity level, anxiety, depression, and functional ability in children and
27 adolescents with juvenile idiopathic arthritis. *Clinical rheumatology*
28 2011;30(11):1415-20. doi: 10.1007/s10067-011-1832-0 [published Online First:
29 2011/09/03] *inappropriate population*
- 30
31 339. Teunis T, Thornton ER, Guitton TG, et al. Coaching of patients with an isolated
32 minimally displaced fracture of the radial head immediately increases range of
33 motion. *Journal of Hand Therapy* 2016;29(3):314-19. doi:
34 10.1016/j.jht.2016.02.003 *inappropriate population*
- 35
36 340. Thomas K, Muir K, Doherty M, et al. Home based exercise programme for knee
37 pain and knee osteoarthritis: randomised controlled trial. *BMJ (Clinical research*
38 *ed)* 2002; 325(7367).
39 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/283/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/283/CN-00398283/frame.html)
40 [00398283/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/283/CN-00398283/frame.html). *inappropriate population*
- 41
42 341. Tonkins WP, Jr. Effect of Hatha yoga on selected parameters of cardiac fitness in
43 African-American college students [Dr.P.H.]. Morgan State University, 2004.
44 *inappropriate intervention*
- 45
46 342. Torres JR, Martos IC, Sanchez IT, et al. Results of an Active Neurodynamic
47 Mobilization Program in Patients With Fibromyalgia Syndrome: A Randomized
48 Controlled Trial. *Archives of physical medicine and rehabilitation*
49 2015;96(10):1771-8. doi: 10.1016/j.apmr.2015.06.008 [published Online First:
50 2015/07/06] *inappropriate intervention*
- 51
52 343. Torres X, Herrero MJ, Marti M, et al. Why people with fibromyalgia persist in
53 activity despite the increasing pain? A Delphi Study of the content of the Clinic
54 Scale of Persistence in Activity in Fibromyalgia. *Revista De Psiquiatria Y Salud*
55 *Mental* 2013;6(1):33-44. doi: 10.1016/j.rpsm.2012.03.001 *inappropriate study*
56 *design*

- 1
2
3 344. Toth C, Brady S, Gagnon F, et al. A Randomized, Single-Blind, Controlled,
4 Parallel Assignment Study of Exercise Versus Education as Adjuvant in the
5 Treatment of Peripheral Neuropathic Pain. *Clinical Journal of Pain*
6 2014;30(2):111-18. doi: 10.1097/AJP.0b013e31828ccd0f *inappropriate*
7 *population*
8
9 345. Tousignant-Laflamme Y, Bourgault P, Masetto A, et al. Short term impact of brief
10 education for symptom management in fibromyalgia-the PEGASO study. *Journal*
11 *of pain* 2014; 15(4 suppl. 1).
12 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/679/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/679/CN-01058679/frame.html)
13 [01058679/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/679/CN-01058679/frame.html). *inappropriate intervention*
14
15 346. Trudeau KJ, Pujol LA, DasMahapatra P, et al. A randomized controlled trial of an
16 online self-management program for adults with arthritis pain. *Journal of*
17 *Behavioral Medicine* 2015;38(3):483-96. doi: 10.1007/s10865-015-9622-9
18 *inappropriate intervention*
19
20 347. Uceyler N, Hauser W, Sommer C. A systematic review on the effectiveness of
21 treatment with antidepressants in fibromyalgia syndrome. *Arthritis Care and*
22 *Research* 2008; 59(9).
23 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/590/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/590/CN-00898590/frame.html)
24 [00898590/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/590/CN-00898590/frame.html). *inappropriate study design*
25
26 348. Ulus Y, Tander B, Akyol Y, et al. Therapeutic ultrasound versus sham ultrasound
27 for the management of patients with knee osteoarthritis: a randomized double-
28 blind controlled clinical study. *International journal of rheumatic diseases* 2012;
29 15(2). [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/676/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/676/CN-00896676/frame.html)
30 [00896676/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/676/CN-00896676/frame.html). *inappropriate intervention*
31
32 349. Vaghef-Mehrabany E, Alipour B, Homayouni-Rad A, et al. Probiotic
33 supplementation improves inflammatory status in patients with rheumatoid
34 arthritis. *Nutrition* 2014;30(4):430-35. doi: 10.1016/j.nut.2013.09.007
35 *inappropriate intervention*
36
37 350. Vaghef-Mehrabany E, Homayouni-Rad A, Alipour B, et al. Effects of Probiotic
38 Supplementation on Oxidative Stress Indices in Women with Rheumatoid
39 Arthritis: A Randomized Double-Blind Clinical Trial. *Journal of the American*
40 *College of Nutrition* 2016;35(4):291-99. *inappropriate intervention*
41
42 351. Valencia M, Alonso B, Alvarez M, et al. Effects of 2 physiotherapy programs on
43 pain perception, muscular flexibility, and illness impact in women with
44 fibromyalgia: a pilot study. *Journal of manipulative and physiological therapeutics*
45 2009; 32(1). [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/935/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/935/CN-00680935/frame.html)
46 [00680935/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/935/CN-00680935/frame.html). *inappropriate comparison group*
47
48 352. Valim V, Oliveira L, Suda A, et al. Aerobic fitness effects in fibromyalgia. *The*
49 *Journal of rheumatology* 2003;30(5):1060-9. [published Online First: 2003/05/08]
50 *inappropriate intervention*
51
52 353. Vallejo MA, Ortega J, Rivera J, et al. Internet versus face-to-face group cognitive-
53 behavioral therapy for fibromyalgia: A randomized control trial. *Journal of*
54 *Psychiatric Research* 2015;68:106-13. doi: 10.1016/j.jpsychires.2015.06.006
55 *inappropriate intervention*
56
57 354. van Koullil S, Kraaimaat FW, van Lankveld W, et al. A patient's perspective on
58 multidisciplinary treatment gain for fibromyalgia: an indicator for pre-post
59

- 1
2
3 treatment effects? *Arthritis and rheumatism* 2009;61(12):1626-32. doi:
4 10.1002/art.24792 [published Online First: 2009/12/02] *inappropriate study*
5 *design*
6
7 355. van Koulil S, van Lankveld W, Kraaimaat FW, et al. Tailored cognitive-behavioral
8 therapy and exercise training for high-risk patients with fibromyalgia. *Arthritis*
9 *care & research* 2010;62(10):1377-85. doi: 10.1002/acr.20268 [published Online
10 First: 2010/06/04] *inappropriate intervention*
11
12 356. Van Puymbroeck M, Payne LL, Hsieh PC. A phase I feasibility study of yoga on
13 the physical health and coping of informal caregivers. *Evidence-Based*
14 *Complementary and Alternative Medicine* 2007;4(4):519-29. doi:
15 10.1093/ecam/nem075 *inappropriate population*
16
17 357. van Wilgen CP, Dijkstra PU, Versteegen GJ, et al. CHRONIC PAIN AND
18 SEVERE DISUSE SYNDROME: LONG-TERM OUTCOME OF AN INPATIENT
19 MULTIDISCIPLINARY COGNITIVE BEHAVIOURAL PROGRAMME. *Journal of*
20 *rehabilitation medicine* 2009;41(3):122-28. doi: 10.2340/16501977-0292
21 *inappropriate intervention*
22
23 358. Vayvay ES, Tok D, Turgut E, et al. The effect of Laser and taping on pain,
24 functional status and quality of life in patients with fibromyalgia syndrome: A
25 placebo- randomized controlled clinical trial. *Journal of back and musculoskeletal*
26 *rehabilitation* 2016;29(1):77-83. doi: 10.3233/bmr-150600 [published Online First:
27 2015/09/26] *inappropriate intervention*
28
29 359. Vendrig AA, Lousberg R. Within-person relationships among pain intensity, mood
30 and physical activity in chronic pain: a naturalistic approach. *Pain* 1997;73(1):71-
31 76. doi: 10.1016/s0304-3959(97)00075-4 *inappropriate intervention*
32
33 360. Vergne-Salle P, Dufauet-Lombard C, Bonnet C, et al. A randomised, double-
34 blind, placebo-controlled trial of dolasetron, a 5-hydroxytryptamine 3 receptor
35 antagonist, in patients with fibromyalgia. *European Journal of Pain*
36 2011;15(5):509-14. doi: 10.1016/j.ejpain.2010.09.013 *inappropriate intervention*
37
38 361. Verra ML, Angst F, Beck T, et al. Horticultural therapy for patients with chronic
39 musculoskeletal pain: results of a pilot study. *Alternative therapies in health and*
40 *medicine* 2012;18(2):44-50. [published Online First: 2012/04/21] *inappropriate*
41 *study design*
42
43 362. Verra ML, Angst F, Brioschi R, et al. Does classification of persons with
44 fibromyalgia into Multidimensional Pain Inventory subgroups detect differences in
45 outcome after a standard chronic pain management program? *Pain Research &*
46 *Management* 2009;14(6):445-53. *inappropriate study design*
47
48 363. Verra ML, Angst F, Staal JB, et al. Differences in pain, function and coping in
49 Multidimensional Pain Inventory subgroups of chronic back pain: a one-group
50 pretest-posttest study. *BMC musculoskeletal disorders* 2011;12 doi:
51 10.1186/1471-2474-12-145 *inappropriate study design*
52
53 364. VillafaÑe JH, Cleland JA, FernÁndez-De-Las-PeÑAs C. The Effectiveness of a
54 Manual Therapy and Exercise Protocol in Patients With Thumb Carpometacarpal
55 Osteoarthritis: A Randomized Controlled Trial. *Journal of Orthopaedic & Sports*
56 *Physical Therapy* 2013;43(4):204-13. *inappropriate intervention*
57
58 365. VillafaÑe JH, Silva GB, Bishop MD, et al. Radial Nerve Mobilization Decreases
59 Pain Sensitivity and Improves Motor Performance in Patients With Thumb
60

- 1
2
3 Carpometaacarpal Osteoarthritis: A Randomized Controlled Trial. *Archives of*
4 *Physical Medicine & Rehabilitation* 2012;93(3):396-403. *inappropriate*
5 *intervention*
6
7 366. Villanueva-Torrecillas I. Affectivity, quality of life and health resources utilization
8 in arthritis [Ph.D.]. The University of Arizona, 2003. *inappropriate outcomes*
9
10 367. Vincent KR, Vincent HK. Resistance exercise for knee osteoarthritis. *PM & R :*
11 *the journal of injury, function, and rehabilitation* 2012;4(5 Suppl):S45-52. doi:
12 10.1016/j.pmrj.2012.01.019 [published Online First: 2012/06/01] *inappropriate*
13 *study design*
14 368. Vriezokolk JE, Eijsbouts AMM, van Lankveld WGJM, et al. An acceptance-
15 oriented cognitive-behavioral therapy in multimodal rehabilitation: A pre-post test
16 evaluation in highly distressed patients with rheumatic diseases. *Patient*
17 *education and counseling* 2013;91(3):357-63. doi: 10.1016/j.pec.2013.01.018
18 *inappropriate study design*
19 369. Wang C, Schmid CH, Hibberd PL, et al. Tai Chi for treating knee osteoarthritis:
20 designing a long-term follow up randomized controlled trial. *BMC*
21 *musculoskeletal disorders* 2008;9:108. doi: 10.1186/1471-2474-9-108 [published
22 Online First: 2008/07/31] *inappropriate intervention*
23
24 370. Wang CC. Tai Chi and Rheumatic Diseases. *Rheumatic Disease Clinics of North*
25 *America* 2011;37(1):19-+. doi: 10.1016/j.rdc.2010.11.002 *inappropriate study*
26 *design*
27 371. Wang CC. Role of Tai Chi in the Treatment of Rheumatologic Diseases. *Current*
28 *Rheumatology Reports* 2012;14(6):598-603. doi: 10.1007/s11926-012-0294-y
29 *inappropriate study design*
30
31 372. Wang WR, Lopez V, Chow A, et al. A randomized controlled trial of the
32 effectiveness of a self-help psychoeducation programme on outcomes of
33 outpatients with coronary heart disease: study protocol. *Journal of Advanced*
34 *Nursing* 2014;70(12):2932-41. doi: 10.1111/jan.12397 *inappropriate population*
35
36 373. Wepner F, Scheuer R, Schuetz-Wieser B, et al. Effects of vitamin D on patients
37 with fibromyalgia syndrome: a randomized placebo-controlled trial. *Pain*
38 2014;155(2):261-8. doi: 10.1016/j.pain.2013.10.002 [published Online First:
39 2014/01/21] *inappropriate intervention*
40
41 374. Weze C, Leathard HL, Stevens G. Evaluation of Healing by Gentle Touch for the
42 Treatment of Musculoskeletal Disorders. *American Journal of Public Health*
43 2004;94(1):50-52. doi: 10.2105/AJPH.94.1.50 *inappropriate intervention*
44
45 375. Wicksell RK, Kemani M, Jensen K, et al. Acceptance and commitment therapy
46 for fibromyalgia: A randomized controlled trial. *European Journal of Pain*
47 2013;17(4):599-611. doi: 10.1002/j.1532-2149.2012.00224.x *inappropriate*
48 *intervention*
49
50 376. Williams DA, Kuper D, Segar M, et al. Internet-enhanced management of
51 fibromyalgia: a randomized controlled trial. *Pain* 2010;151(3):694-702. doi:
52 10.1016/j.pain.2010.08.034 [published Online First: 2010/09/22] *inappropriate*
53 *intervention*
54
55 377. Witjes S, Hoorntje A, Kuijer P, et al. Does Goal Attainment Scaling improve
56 satisfaction regarding performance of activities of younger knee arthroplasty
57 patients? Study protocol of the randomized controlled ACTION trial. *BMC*
58
59
60

- 1
2
3 *musculoskeletal disorders* 2016;17 doi: 10.1186/s12891-016-0965-3
4 *inappropriate study design*
5 378. Wyld V, Artz N, Marques E, et al. Effectiveness and cost-effectiveness of
6 outpatient physiotherapy after knee replacement for osteoarthritis: study protocol
7 for a randomised controlled trial. *Trials* 2016;17(1):289. doi: 10.1186/s13063-
8 016-1418-x [published Online First: 2016/06/15] *inappropriate study design*
9 379. Yang T, Wang H, Chen Y, et al. Effect of continuous administration of conjugated
10 estrogen plus medroxyprogesterone acetate (Premelle) in postmenopausal
11 women in Taiwan. *Journal of the Chinese Medical Association : JCMA* 2004;
12 67(7). <http://onlinelibrary.wiley.com/doi/10.1111/j.1526-4637.2006.00087.x>
13 67(7). <http://onlinelibrary.wiley.com/doi/10.1111/j.1526-4637.2006.00087.x>
14 00505366/frame.html. *inappropriate intervention*
15 380. Yelland MJ, Schluter PJ. Defining Worthwhile and Desired Responses to
16 Treatment of Chronic Low Back Pain. *Pain Medicine* 2006;7(1):38-45. doi:
17 10.1111/j.1526-4637.2006.00087.x *inappropriate population*
18 381. Young JL. Use of lisdexamfetamine dimesylate in treatment of executive
19 functioning deficits and chronic fatigue syndrome: A double blind, placebo-
20 controlled study. *Psychiatry Research* 2013;207(1-2):127-33. doi:
21 10.1016/j.psychres.2012.09.007 *inappropriate intervention*
22 382. Yuan SLK, Matsutani LA, Marques AP. Effectiveness of different styles of
23 massage therapy in fibromyalgia: A systematic review and meta-analysis.
24 *Manual therapy* 2015;20(2):257-64. *inappropriate study design*
25 383. Yuen AWC, Sander JW. Can slow breathing exercises improve seizure control in
26 people with refractory epilepsy? A hypothesis. *Epilepsy & Behavior*
27 2010;18(4):331-34. doi: 10.1016/j.yebeh.2010.05.019 *inappropriate population*
28 384. Zick SM, Wyatt GK, Murphy SL, et al. Acupressure for persistent cancer-related
29 fatigue in breast cancer survivors (AcuCrft): a study protocol for a randomized
30 controlled trial. *BMC Complementary and Alternative Medicine* 2012;12 doi:
31 10.1186/1472-6882-12-132 *inappropriate population*
32 385. Zietek P, Zietek J, Szczypior K, et al. Effect of adding one 15-minute-walk on the
33 day of surgery to fast-track rehabilitation after total knee arthroplasty: a
34 randomized, single-blind study. *European journal of physical and rehabilitation*
35 *medicine* 2015;51(3):245-52. [published Online First: 2014/09/19] *inappropriate*
36 *intervention*
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

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-Izquierdo & 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)
<i>Study Characteristics</i>				
- 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)
<i>Participant Characteristics</i>				
- 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							N ^o of patients		Effect		Quality	Importance
N ^o 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*	514	369	not estimable -	SMD 0.4 SD lower (0.65 lower to 0.15 lower)	⊕⊕⊕⊕ HGH	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

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

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

Page 1 of 2

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

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

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

Page 2 of 2

For peer review only

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:	<i>BMJ Open</i>
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

SCHOLARONE™
Manuscripts

1
2
3 1 Community-Deliverable Exercise and Anxiety in Adults with Arthritis and other
4
5 2 Rheumatic Diseases: A Systematic Review with Meta-Analysis of Randomized
6
7 3 Controlled Trials
8
9
10 4

11
12 5 **Authors:** Corresponding author: *George A. Kelley*, DA, FACSM, School of Public
13
14 6 Health, Department of Biostatistics, West Virginia University, Morgantown, WV, USA,
15
16 7 26506-9190, Office Phone: 304-293-6279, Fax: 304-293-5891, E-mail:
17
18 8 gkelley@hsc.wvu.edu
19
20
21 9

22
23
24 10 Co-author: *Kristi S. Kelley*, M.Ed., Research Instructor, School of Public Health,
25
26 11 Department of Biostatistics, Robert C. Byrd Health Sciences Center,
27
28 12 West Virginia University, PO Box 9190, Morgantown, WV, USA, 26506-9190, Office
29
30 13 Phone: 304-293-6280, Fax: 304-293-5891, E-mail: kskelley@hsc.wvu.edu
31
32
33 14

34
35 15 Co-author: *Leigh F. Callahan*, PhD, Mary Link Briggs Distinguished Professor of
36
37 16 Medicine, Professor, Departments of Social Medicine and Orthopaedics, Adjunct
38
39 17 Professor, Department of Epidemiology, 3300 Thurston Bldg, Campus Box 7280,
40
41 18 University of North Carolina, Chapel Hill, NC 27599-7280, Office Phone: 919-966-0564,
42
43 19 E-mail: leigh.callahan@med.unc.edu
44
45
46

47 20 **Keywords:** exercise, anxiety, arthritis, systematic review, meta-analysis.
48

49 21 **Abstract:** 300 words
50

51 22 **Introduction, Methods, Results, Conclusions:** 8,632 words
52
53
54
55
56
57
58
59
60

23 ABSTRACT

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

27 **Methods:** Randomized controlled exercise intervention trials ≥ 4 weeks in adults ≥ 18
28 years of age with osteoarthritis, rheumatoid arthritis or fibromyalgia were included.
29 Studies were located by searching 8 electronic databases, cross-referencing and expert
30 review. Dual selection and data abstraction of studies were performed. Hedge's
31 standardized effect size (ES) was calculated for each result and pooled using the
32 recently developed inverse-heterogeneity (IVhet) model. Two-tailed z-alpha values \leq
33 0.05 and non-overlapping 95% confidence intervals (CI) were considered statistically
34 significant. Heterogeneity was estimated using Q and I^2 with alpha values ≤ 0.10 for Q
35 considered statistically significant. Small-study effects were examined using funnel
36 plots and Egger's regression test. In addition, the number-needed-to-treat (NNT),
37 percentile improvement and meta-regression were conducted. **Results:** Of the 639
38 citations screened, 14 studies representing 926 initially enrolled participants (539
39 exercise, 387 control) met the criteria for inclusion. Length of training averaged $15.8 \pm$
40 6.7 weeks, frequency 3.3 ± 1.3 times per week and duration 28.8 ± 14.3 minutes per
41 session. Overall, statistically significant in reductions in anxiety were found (exercise
42 minus control changes ES = -0.40, 95% CI, -0.65, -0.15, $\tau^2 = 0.14$; Q = 40.3, p =
43 0.0004; $I^2 = 62.8\%$). The NNT was 6 with a percentile improvement of 15.5% and an
44 estimated 5.3 million inactive US adults with AORD improving their anxiety if they
45 started exercising regularly. Statistically significant small-study effects were observed (p

1
2
3 46 < 0.0001). **Conclusions:** Exercise is associated with reductions in anxiety among
4
5 47 adults with selected types of AORD. However, a need exists for additional, well-
6
7 48 designed, randomized controlled trials on this topic. **Trial registration number:**
9
10 49 PROSPERO (CRD42016048728)
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 50 **STRENGTHS AND LIMITATIONS OF THIS STUDY**
4

5 51 - To the best of the investigative team's knowledge, this is the first systematic review
6
7 52 with meta-analysis to examine the effects of exercise on anxiety as a primary outcome
8
9 53 in adults with AORD.

10
11
12 54 - The use of the recently developed IVhet model appears to provide more robust
13
14 55 estimates than those derived from other models.

15
16
17 56 - Common to all aggregate data meta-analyses, the possibility of ecological fallacy
18
19 57 exists and the meta-regression analyses conducted do not allow for causal inferences.

20
21 58 - Given that no adjustments for multiple testing were made because of concerns about
22
23 59 missing possibly important findings that could be tested in original trials, the possibility
24
25 60 of chance findings exist.
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

61 INTRODUCTION

62 Rationale

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

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

1
2
3 84 prevalence of anxiety and depression among US adults with doctor-diagnosed arthritis
4
5 85 was estimated to be almost twice as high for anxiety (30.5%) versus depression
6
7 86 (17.5%), with US population estimates of 11.5 million for anxiety and 6.6 million for
8
9 87 depression.⁸ In addition, an 18-country study found the prevalence of anxiety to be
10
11 88 greater in adults with AORD versus those without AORD.⁹ This included, separately,
12
13 89 generalized anxiety disorder, social phobia, agoraphobia/panic disorder, and post-
14
15 90 traumatic stress disorder.⁹ Given the prevalence of anxiety, it has been recommended
16
17 91 that health care providers screen people with AORD for anxiety.⁸
18
19
20

21 92 Exercise is an intervention that is generally safe and appropriate for most persons with
22
23 93 various types of AORD.^{10 11} While there is no firm consensus regarding the
24
25 94 mechanisms associated with the anxiolytic effects of exercise in adults with AORD as
26
27 95 well as other chronic diseases, a recent review on this topic has reported several
28
29 96 potential mechanisms, exclusive of specific chronic disease status, that may be
30
31 97 responsible for such.¹² These include physiological (decrease in sympathetic nervous
32
33 98 system and hypothalamic-pituitary-adrenal axis reactivity) as well as psychological
34
35 99 (improvements in anxiety sensitivity, self-efficacy, and distraction) processes.¹²
36
37
38
39

40 100 Recent meta-analytic work has shown that community-deliverable exercise
41
42 101 interventions reduce depressive symptoms in adults, with an estimated 3.1 million
43
44 102 inactive US adults with AORD improving their depressive symptoms if they began and
45
46 103 maintained a regular exercise program.¹³ However, the effects of community-
47
48 104 deliverable exercise on anxiety as a primary outcome are not known given a plethora of
49
50 105 conflicting randomized controlled trials on this topic as well as a lack of studies that
51
52 106 assess both depression and anxiety within the same study (only 44.8% based on a
53
54
55
56
57
58
59
60

1
2
3 107 previous meta-analysis).¹³ Most importantly, a recent systematic review of previous
4
5 108 meta-analyses, not to be confused with an original systematic review with meta-
6
7 109 analyses, found that no meta-analysis of randomized controlled trials has examined the
8
9 110 effects of community-deliverable exercise on anxiety as a primary outcome in adults
10
11 111 with AORD.¹⁴ Community-deliverable exercise may be especially important given its
12
13 112 potential convenience, ability to reach a large amount of people, and cost.¹⁵⁻¹⁸ In
14
15 113 addition, a systematic review found that greater levels of anxiety were a barrier to
16
17 114 exercise adherence in those with AORD.¹⁹ Thus, reductions in anxiety may increase
18
19 115 adherence to exercise in adults with AORD, a population in which meeting current
20
21 116 exercise guidelines is significantly lower than in those without AORD, approximately
22
23 117 40% versus 50%.²⁰ Clearly, it is critically important to develop a better understanding of
24
25 118 the overall magnitude of effect, as well as factors associated with, exercise for
26
27 119 improving anxiety in adults with AORD.
28
29
30
31

32 120 **Objective**

33 121 The primary objective of this study was to conduct a systematic review with an
34
35 122 aggregate data meta-analysis of randomized controlled trials to determine the effects of
36
37 123 community-deliverable exercise interventions on anxiety in adults with AORD.
38
39
40
41

42 124 **METHODS**

43 125 **Overview**

44
45 126 This study followed the guidelines from the Preferred Reporting Items for Systematic
46
47 127 Reviews and Meta-Analysis (PRISMA) statement for meta-analyses of health care
48
49 128 interventions.²¹ The protocol for this study is registered in PROSPERO (trial registration
50
51 129 number CRD42016048728) and has been previously published in BMJ Open.²²
52
53
54
55
56
57
58
59
60

130 **Eligibility criteria**

131 Studies that met the following criteria were included: (1) randomized controlled trials
132 with the unit of assignment at the participant level, (2) community-deliverable
133 exercise-only intervention group (aerobic, strength training, or both), (3) interventions
134 ≥ 4 weeks, (4) comparative control group (non-intervention, wait-list control, usual
135 care, attention control), (5) adults ≥ 18 years of age with doctor-diagnosed
136 osteoarthritis, rheumatoid arthritis or fibromyalgia, (6) studies (published and
137 unpublished in the form of Master's theses and dissertations) in any language,
138 assuming an English-language abstract was available, from January 1, 1981 forward,
139 and (7) data for anxiety, as defined by the authors of the original studies. Studies were
140 limited to those with osteoarthritis, rheumatoid arthritis or fibromyalgia based on
141 previous meta-analytic research showing a lack of exercise intervention studies for
142 other types of AORD.¹³ Studies were limited to randomized trials because it is the
143 only way to control for confounders that are not known or measured as well as the
144 observation that nonrandomized controlled trials tend to overestimate the effects of
145 healthcare interventions.^{23 24} Aerobic and progressive resistance (strength training)
146 exercise were defined according to section C2 of the 2008 Physical Activity
147 Guidelines Advisory Committee Report.²⁵ Specifically, aerobic exercise is defined as
148 any 'exercise that primarily uses the aerobic energy-producing systems, can improve
149 the capacity and efficiency of these systems, and is effective for improving
150 cardiorespiratory endurance,' while strength training is defined as 'exercise training
151 primarily designed to increase skeletal muscle strength, power, endurance, and
152 mass'.²⁵

1
2
3 153 For this proposed project, community-deliverable exercise interventions were
4
5 154 considered to be those that could be performed, or have the potential to be adapted
6
7 155 and performed, by persons in a community setting (recreation or senior centers, in the
8
9
10 156 home or neighborhood, etc.) and meet the implementation guidelines for physical
11
12 157 activity interventions recently recommended by the Arthritis Program at the Centers
13
14 158 for Disease Control and Prevention: (1) no academic degree required for a
15
16 159 leader/implementer but leader training available, if needed, (2) no special facilities
17
18 160 beyond a community room (except a warm pool for aquatic exercise), (3) inexpensive
19
20 161 equipment, (4) cost to participants less than \$50.00, (5) implementation guide
21
22 162 available, (6) supporting structures judged to be adequate to support widespread
23
24 163 implementation.²⁶ An exercise duration of at least 4 weeks was chosen based on
25
26 164 previous research in which statistically significant improvements in anxiety occurred
27
28 165 as a result of as little as 4 weeks of exercise training.²⁷ There was no maximum limit
29
30 166 on the length of any interventions for the studies included in our proposed project. We
31
32 167 limited our studies to adults ages 18 and older because the inclusion of children and
33
34 168 adolescents pose additional confounding problems congruent with the many
35
36 169 developmental changes that occur during this period. In addition, the prevalence of
37
38 170 AORD is more common in adults than children and adolescents. We restricted our
39
40 171 studies to published articles, dissertations and master's theses and examined for
41
42 172 potential small-study effects such as publication bias when limited to published
43
44 173 articles in peer-reviewed journals. The year 1981 was chosen as the starting point for
45
46 174 eligibility based on a preliminary PubMed search in which it was found that this was
47
48 175 the first year that a randomized controlled trial on exercise and arthritis was
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 176 published.²⁸ Studies from both English and non-English-language sources were
4
5 177 included with the latter translated into English by the second author using the freely
6
7 178 available web-based Babelfish and Bing translators. Finally, while acknowledging that
8
9 179 the mechanisms for changes in anxiety may differ for different types of AORD, for
10
11 180 example fibromyalgia versus osteoarthritis and rheumatoid arthritis, all three were
12
13 181 included in the current systematic review with meta-analysis because the focus was
14
15 182 on determining whether exercise reduces anxiety in adults with AORD, not why it
16
17 183 reduces anxiety. In addition, community-deliverable exercise programs, and exercise
18
19 184 programs in general, are not traditionally focused on one type of AORD, but rather,
20
21 185 across all types of AORD.¹⁷ Furthermore, meta-regression (see Data Synthesis) was
22
23 186 conducted to examine for any potential associations between type of AORD and
24
25 187 changes in anxiety. Finally, there has been recent criticism by others regarding the
26
27 188 publication of systematic reviews with meta-analysis using the “least publishable unit”
28
29 189 approach.²⁹

190 **Information sources**

191 Eight electronic databases were searched for potentially eligible studies in any language
192 published from January 1, 1981 forward. The last searches were conducted on January
193 6, 2017. Databases searched included (1) PubMed, (2) SPORTDiscus, (3) Cochrane
194 Central Register of Controlled Clinical Trials (CENTRAL), (4) Cumulative Index to
195 Nursing and Allied Health Literature (CINAHL), (5) PsycINFO, (6) Web of Science, (7)
196 Scopus and (8) ProQuest (Master’s theses and dissertations). In addition, cross-
197 referencing from retrieved studies was conducted. Furthermore, the third author, an
198 expert on physical activity and AORD, reviewed the reference list for completeness.

1
2
3 199 **Search strategy**
4

5 200 Search strategies were developed using text words as well as medical subject headings
6
7 201 (MeSH) associated with the effects of exercise on anxiety in adults with AORD. The
8
9 202 second author conducted all electronic database searches. A copy of the search
10
11 203 strategy for one of the databases searched (PubMed) is shown in Supplementary file 1.
12
13

14 204 **Study records**

15 205 Study selection

16
17 206 All studies to potentially be screened were imported into EndNote (EndNote, Version
18
19 207 X8. New York, NY: Thomson Reuters, 2016). Duplicates were then removed both
20
21 208 electronically and manually by the second author. A copy of the database was then
22
23 209 provided to the first author for duplicate screening. The first two authors selected all
24
25 210 studies, independent of each other. The full report for each article was obtained for all
26
27 211 titles and abstracts that appeared to meet the inclusion criteria or where there was any
28
29 212 uncertainty. Multiple reports of the same study were handled by including the most
30
31 213 recently published article as well as drawing from previous reports, assuming similar
32
33 214 methods and sample sizes. Neither of the screeners were blinded to the journal titles or
34
35 215 to the study authors or institutions. Reasons for exclusion were coded as one or more of
36
37 216 the following: (1) inappropriate population, (2) inappropriate intervention, (3)
38
39 217 inappropriate comparison(s), (4) inappropriate outcome(s), (5) inappropriate study
40
41 218 design, (6) other. Upon completion, the first two authors met and reviewed their
42
43 219 selections. Discrepancies were resolved by consensus. If consensus could not be
44
45 220 reached, the third author provided a recommendation. Using Cohen's kappa statistic
46
47 221 (κ),³⁰ the overall agreement rate prior to correcting disagreements was 0.90. After
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 222 identifying the final number of studies to be included, the overall precision of the
4
5 223 searches was calculated by dividing the number of studies included by the total number
6
7 224 of studies screened after removing duplicates.³¹ The number needed-to-read (NNR)
8
9 225 was then calculated as the inverse of the precision.³¹
10
11

12 226 Data abstraction

13
14 227 Prior to the abstraction of data, a codebook that could hold more than 200 items per
15
16 228 study was developed using Microsoft Excel (Microsoft Excel, Version 2010, Redmond,
17
18 229 WA). The codebook was developed by the first two authors with input from the third
19
20 230 author. The major categories of variables coded included (1) study characteristics
21
22 231 (author, journal, year, etc.), (2) participant characteristics (age, height, body weight,
23
24 232 etc.), (3) intervention characteristics (type, length, frequency, intensity, duration,
25
26 233 compliance, etc.), and (4) outcome characteristics for anxiety (sample sizes, baseline
27
28 234 and post-exercise means and standard deviations, etc.). The first two authors
29
30 235 abstracted data from all studies, independent of each other, using separate codebooks
31
32 236 in Microsoft Excel. Upon completion of coding, the codebooks were merged into one
33
34 237 primary codebook for review. Both authors then met and reviewed every item for
35
36 238 agreement. Discrepancies were resolved by consensus. If consensus could not be
37
38 239 reached, the third author provided a recommendation. Using Cohen's kappa statistic
39
40 240 (κ),³⁰ the overall agreement rate prior to correcting disagreements was 0.95.
41
42
43
44
45
46

47 241 **Outcomes and prioritization**

48
49 242 The primary outcome in this study was changes in anxiety. Secondary outcomes
50
51 243 included changes in physical function, pain, depression, quality of life, body mass index
52
53
54
55
56
57
58
59
60

1
2
3 244 (BMI in $\text{kg}\cdot\text{m}^{-2}$), maximum oxygen consumption ($\text{VO}_{2\text{max}}$ in $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$), and muscular
4
5 245 strength.

8 246 **Risk of bias assessment in individual studies**

9
10 247 Risk of bias was assessed at the study level using the Cochrane Risk of Bias
11
12 248 instrument,³² with a focus on the primary outcome of interest, changes in anxiety. Bias
13
14 249 was evaluated across six domains: (1) random sequence generation, (2) allocation
15
16
17 250 concealment, (3) blinding of participants and personnel, (4) blinding of outcome
18
19 251 assessment, (5) incomplete outcome data, (6) selective reporting and (7) whether
20
21 252 participants were exercising regularly, as defined by the original study authors, prior to
22
23
24 253 taking part in the study. Each item was classified as having either a high, low, or unclear
25
26 254 risk of bias. Because it's virtually impossible to blind participants to group assignment in
27
28 255 exercise intervention protocols, all studies were classified as high risk with respect to
29
30
31 256 the category "blinding of participants and personnel". Based on previous research, no
32
33 257 study was excluded based on the results of the risk of bias assessment.³³ The first two
34
35 258 authors conducted all assessments, independent of each other. Both authors then met
36
37
38 259 and reviewed all selections for agreement. Discrepancies were resolved by consensus,
39
40 260 and if necessary, consultation with the third author. Using Cohen's kappa statistic (κ),³⁰
41
42 261 the overall agreement rate for risk of bias assessment prior to correcting disagreements
43
44 262 was 0.71.

46 263 **Data Synthesis**

48 264 **Calculation of effect sizes**

49
50
51 265 The primary outcome for this proposed project was changes in anxiety, calculated as
52
53
54 266 Hedge's standardized mean difference effect size (ES), adjusted for small-sample
55
56
57
58
59
60

1
2
3 267 bias.³⁴ This was calculated by subtracting the change outcome difference in the
4
5 268 exercise group minus the change outcome difference in the control group, and then
6
7 269 dividing by the pooled standard deviation of the change outcome for the exercise and
8
9 270 control groups. If change score standard deviations were not available, they were
10
11 271 calculated from reported change outcomes, treatment effect 95% confidence intervals
12
13 272 (CI), or pre and post standard deviation values according to procedures developed by
14
15 273 Follmann et al.³⁵ Secondary outcomes (physical function, pain, quality of life,
16
17 274 depression, muscular strength) were calculated using the same procedures as for the
18
19 275 primary outcome while BMI and VO_{2max} were calculated using the original metric. For
20
21 276 studies in which outcomes were assessed at multiple time points, differences between
22
23 277 baseline values and the final time point closest to cessation of the exercise intervention
24
25 278 were used.

29 30 31 **Pooled estimates for changes in outcomes**

32
33 280 Effect size changes in anxiety and all secondary outcomes were pooled using the
34
35 281 recently developed inverse heterogeneity (IVhet) model.³⁶ The IVhet model is a quasi-
36
37 282 likelihood model that is computed by (1) calculating weights that sum to 1 from each
38
39 283 study, (2) pooling effects from all the studies, and (3) calculating the variance of the
40
41 284 pooled ES. The IVhet model has been shown to be superior to the original random-
42
43 285 effects, method-of-moments model of Dersimonian and Laird,³⁷ the most common
44
45 286 random-effects model used to pool aggregate data meta-analytic results.³⁸
46
47 287 Specifically, simulation studies have shown that the IVhet model retains correct
48
49 288 coverage probabilities as well as a lower observed variance than the random-effects
50
51
52
53
54
55
56
57
58
59
60

1
2
3 289 model, regardless of heterogeneity.³⁶ Two-tailed z-alpha values ≤ 0.05 and non-
4
5 290 overlapping 95% confidence intervals were considered statistically significant.

6
7 291 *Heterogeneity* and *inconsistency* for each pooled outcome were estimated using the
8
9 292 Q^{39} and I^2 statistic,⁴⁰ respectively. An alpha level of ≤ 0.10 for Q was considered to
10
11 293 represent statistically significant heterogeneity while inconsistency was categorized as
12
13 294 very low (<25%), low (25% to <50%), moderate (50% to <75%) or large ($\geq 75\%$).⁴⁰ To
14
15 295 improve practical relevance with respect to potential improvements in anxiety and all
16
17 296 secondary outcomes, percentile gain in the exercise groups was calculated using
18
19 297 Cohen's U_3 index⁴¹ In addition, the number-needed-to treat (NNT) was estimated using
20
21 298 the approach suggested by the Cochrane Collaboration³² and a control group risk of
22
23 299 30% based on previous research on anxiolytics.⁴² This was accomplished by converting
24
25 300 the standardized mean differences into a log odds ratio, odds ratio, assumed control
26
27 301 risk (30%) and then NNT. Extending the NNT, estimates of the number of US adults
28
29 302 with AORD who could improve their anxiety levels but were not currently meeting
30
31 303 physical activity recommendations were calculated. These were based on the reciprocal
32
33 304 of the NNT multiplied by the number of adults in the United States with doctor-
34
35 305 diagnosed arthritis who were not currently meeting exercise guidelines, currently
36
37 306 approximately 31.6 million.^{1 43} *Influence analysis* was conducted with each study
38
39 307 deleted from the model once while *cumulative meta-analysis*, ranked by year, was used
40
41 308 to examine the accumulation of results over time.

42
43 309 The primary pooling of results was based on group level findings. However, findings
44
45 310 were also examined by collapsing results so that only one ES represented each study.
46
47 311 In addition, for those outcomes that were assessed using multiple instruments, results
48
49
50
51
52
53
54
55
56
57
58
59

1
2
3 312 from these instruments were pooled into one ES. The rationale for this was based on
4
5 313 the lack of consensus regarding the most valid and reliable instrument for the outcome
6
7 314 and population of interest as well as the need to maintain as much independence as
8
9 315 possible. For those studies that reported both per protocol and intention-to-treat
10
11 316 analyses, results were also pooled into one ES.
12
13

14 317 Exploratory *meta-regression* based on the IVhet model was used to examine the
15
16 318 relationship between changes in our primary outcome (anxiety) and selected
17
18 319 covariates.³⁶ This was accomplished by (1) conducting simple meta-regression for
19
20 320 statistically significant associations between selected covariates and changes in
21
22 321 anxiety, (2) examining for multicollinearity between covariates ($r > 0.80$), and (3)
23
24 322 building a multiple meta-regression model. These models used a multiplicative versus
25
26 323 additive component for residual heterogeneity. To achieve matching error variances,
27
28 324 robust Huber-Ecker-White-sandwich error variances were used to account for the
29
30 325 underestimated dispersion. Such errors were expected to calculate the correct
31
32 326 standard errors for heterogeneous data that are traditionally heteroskedastic. Because
33
34 327 of the small sample size, a post hoc decision was made to include no more than three
35
36 328 potential predictors based on simple regression analyses. Multivariate imputation using
37
38 329 chained equations (MICE)⁴⁴ was used to impute missing values for minutes of training
39
40 330 per week (5 imputations) and changes in depression (1 imputation) so that the
41
42 331 maximum sample size could be achieved. Because of the small sample size, a post
43
44 332 hoc decision was made to conduct meta-regression with results for osteoarthritis and
45
46 333 rheumatoid arthritis combined.
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 334 Based on the recommendations of Rothman,⁴⁵ no adjustments for multiple testing
4
5 335 were made because of concerns about missing possibly important findings that could be
6
7 336 pursued in future randomized controlled trials. While this could be viewed as a 'fishing
8
9
10 337 expedition', such analyses are important for providing investigators with potential
11
12 338 direction for future randomized controlled trials, one of the very reasons for conducting a
13
14 339 systematic review with meta-analysis.⁴⁶ This approach is especially appropriate for
15
16 340 meta-analysis since covariates are not randomly assigned in meta-analysis and thus,
17
18 341 such analyses are considered to be observational in nature.⁴⁷ As a result, causal
19
20 342 inferences cannot be derived from meta-regression. However, any observed
21
22 343 associations can provide direction for future research.

23 24 25 26 344 **Meta-biases**

27
28 345 *Small-study-effects* (publication bias, etc.) for primary and secondary outcomes were
29
30 346 assessed following current guidelines.⁴⁸ This included qualitative analysis using funnel
31
32 347 plots as well as quantitative analysis using Egger's regression-intercept test for
33
34 348 continuous data.⁴⁸ An alpha level ≤ 0.05 and 95% CI that did not include zero (0) was
35
36 349 considered to represent statistically significant small-study effects.

37 38 39 40 350 **Confidence in cumulative evidence**

41
42 351 Strength of findings for our primary outcome (anxiety) was evaluated using the Grading
43
44 352 of Recommendations Assessment, Development and Evaluation (GRADE) for meta-
45
46 353 analysis.⁴⁹ The quality of evidence was assessed across the domains of risk of bias,
47
48 354 consistency, directness, precision and publication bias. Quality was judged as high
49
50 355 (further research is very unlikely to change our confidence in the estimate of effect),
51
52
53 356 moderate (further research is likely to have an important impact on our confidence in the

1
2
3 357 estimate of effect and may change the estimate), low (further research is very likely to
4
5 358 have an important impact on our confidence in the estimate of effect and is likely to
6
7 359 change the estimate), or very low (very uncertain about the estimate of effect).
8
9

10 360 **Software used for data synthesis**

11
12 361 All data were analyzed using Stata (V.14.1; Stata/SE for Windows (Version 14.1).
13
14 362 College Station, Texas: Stata Corporation LP, 2015), Microsoft Excel 2010 (Microsoft
15 363 Excel (Version 2010)), and three add-ins for Excel, Meta XL (V.5.3; Meta XL (Version
16
17 364 5.3). 2016), SSC-Stat (V.2.18; SSC-Stat (Version 2.18). University of Reading, UK:
18
19 365 Statistical Services Center, 2007), and EZ-Analyze (V.3.0; EZ Analyze (Version 3.0).
20
21 366 Boston, MA: Tim Poynton, 2007).
22
23
24
25

26 367 **RESULTS**

27 368 **Study Characteristics**

28
29 369 A flow diagram that depicts the search process for study selection is shown in Figure 1.
30
31 370 After initially identifying 639 citations and removing 240 duplicates both electronically
32
33 371 and manually, 399 citations were screened. Of these, 14 studies representing 30 groups
34
35 372 (16 exercise, 14 control) and 926 initially enrolled participants (539 exercise, 387
36
37 373 control) met the criteria for inclusion.⁵⁰⁻⁶³ Two studies included more than one
38
39 374 intervention group.^{58 61} One included a pool and walking group⁵⁸ while the other
40
41 375 included a long and short bout exercise group.⁶¹ The major reasons for exclusion were
42
43 376 (1) inappropriate intervention (47.8%), (2) inappropriate study design (32.2%), (3)
44
45 377 inappropriate population (11.9%), (4) inappropriate comparison group (4.7%), and (5)
46
47 378 inappropriate outcome (3.4%). The precision of the search, excluding duplicates, was
48
49
50
51
52
53
54
55
56
57
58
59
60

379 3.5% while the NNR was 29. A list of excluded studies, including the reasons for
380 exclusion, can be found in Supplementary File 2.

381 With respect to source, 1 study (7.1%) was published as a dissertation⁵¹ while the
382 remaining 13 (92.9%) were published in peer-reviewed journals.^{50 52-63} For the 12
383 studies (85.7%) in which data were available, the 5-year impact factor of the journals in
384 which studies were published ranged from 1.7 to 7.9 ($\bar{x} \pm SD$, 4.1 ± 2.4 , median = 2.9).
385 Five studies (35.7%) were published in the United States,^{51 52 56-58} 2 each in either
386 Canada,^{55 61} Portugal^{62 63} or Spain,^{59 60} and 1 each in either Australia,⁵³ Brazil,⁵⁰ or
387 Ireland.⁵⁴ Thirteen of the 14 studies (92.9%) were published in English-language
388 journals⁵⁰⁻⁶² while 1 (7.1%) was published in Spanish.⁶³ With respect to types of control
389 groups, 4 studies used either a wait-list control^{50 51 53 54} or what appeared to be some
390 type of attention control group,^{52 56 58 61} while three each used either a non-intervention⁵⁵
391 ^{57 62} or usual care group.^{59 60 63} Three studies (21.4%) reported using matching
392 procedures according to either sex,⁵⁵ age, sex and BMI,⁵⁶ or type of arthritis
393 (rheumatoid or osteoarthritis).⁵⁸ None of the studies reported using any type of
394 crossover design.⁵⁰⁻⁶³ For data analysis, 7 studies (50.0%) reported using the per-
395 protocol approach,^{51 56-58 60 62 63} 4 (28.6%) used intention-to-treat,^{50 52-54} while the
396 remaining 3 (21.4%) used both.^{55 59 61} Eight studies (57.1%) provided sample size
397 estimates.^{50 52-54 56 60 61 63} With respect to funding, 12 studies (85.7%), reported receiving
398 funding from government, university, or private sources for their work.^{50 52-62}

399 **Participant Characteristics**

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

1
2
3 402 and had low cardiorespiratory fitness. The majority of participants were women,
4
5 403 although 7 studies (50.0%) also included a small number of men.⁵²⁻⁵⁸ Nine studies
6
7 404 (64.3%) were limited to participants with fibromyalgia,^{50 51 55 56 59-63} 3 (21.4%) with
8
9 405 osteoarthritis,⁵²⁻⁵⁴ 1 with rheumatoid arthritis⁵⁷ and 1 with either rheumatoid arthritis or
10
11 406 osteoarthritis.⁵⁸ For those studies in which data were available, the number of years in
12
13 407 which rheumatic symptoms were present ranged from 3 to 24 ($\bar{x} \pm$ SD, 13.1 ± 7.0 ,
14
15 408 median = 12.0),^{54-56 59 61-63} while years since diagnosis ranged from 3 to 7 ($\bar{x} \pm$ SD, 4.1
16
17 409 ± 2.0 , median = 3).^{55 61-63} Nine of the 14 studies (64.3%) reported that one or more
18
19 410 participants were taking some type of medication for their condition.^{51 53-55 57-59 62 63}
20
21 411 These included, but were not necessarily limited to, non-steroidal anti-inflammatory
22
23 412 drugs (NSAIDs), analgesics, narcotics and non-narcotics for pain, muscle relaxants,
24
25 413 antidepressants, and anxiolytics. However, a lack of specific data was available on
26
27 414 exposure to medications both before and during the study, including any changes
28
29 415 during the intervention period. In addition, a lack of data was available on
30
31 416 pharmacologic equivalence between study arms both before and during the study. For
32
33 417 cigarette smoking, one study reported cigarette smoking in some of the participants.⁶¹
34
35 418 Participant withdrawals or removal in the exercise groups ranged from 0% to 50% ($\bar{x} \pm$
36
37 419 SD, 17.4 ± 13.4 , median = 17.0) while withdrawals or removal in the control groups
38
39 420 ranged from 0% to 41% ($\bar{x} \pm$ SD, 11.5 ± 12.7 , median = 6.3). Reasons for withdrawals
40
41 421 or removal included such things as family issues, pain from exercising, injuries,
42
43 422 personal issues, time, unhappiness with group assignment, transportation issues,
44
45 423 moving, employment commitments, boredom with exercise routine, not enough room or
46
47 424 privacy to perform exercise, failure to complete lab assessments, not attending a
48
49
50
51
52
53
54
55
56
57
58
59

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

427 **Exercise Intervention Characteristics**

428 Exercise intervention characteristics for each group from each study are shown in
429 Tables 1 and 3. Intensity of training, categorized according to American College of
430 Sports Medicine⁶⁴ and limited to aerobic exercise only, included very light, light,
431 moderate and vigorous exercise for the 9 (64.3%) studies that reported such
432 information.^{51 55 56 58-63} For mode of training, 6 studies (42.9%) focused on aerobic types
433 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}
434 ⁶³ Specific types of aerobic activities included such things as aquatic exercise, walking,
435 jogging, exercising to music and cycling. For the few studies that provided detailed
436 information on resistance training, the number of sets ranged from 1 to 3,^{57 59} the
437 number of repetitions from 8 to 15,^{57 59} and the number of exercises from 2 to 10 or
438 more.^{56 57 59} One study reported a rest period for 30 seconds between sets.⁵⁷ For those
439 studies that reported data, the equipment used for resistance training included free
440 weights and elastic bands.^{52 56 57 62 63} Seven studies (50.0%) reported supervised
441 exercise,^{55 56 58-60 62 63} 5 (35.7%) reported both supervised and unsupervised exercise,⁵⁰⁻
442 ⁵⁴ while the remaining 2 (14.3%) reported unsupervised exercise.^{57 61} Three of the 14
443 studies (21.4%) reported some type of adverse event.^{51 52 61} Reasons included 1
444 participant dropping out due to pain after the first exercise session,⁵¹ 2 participants
445 because of a history of a herniated disk and low back and leg pain,⁵² and 1 participant
446 because of a metatarsal fracture.⁶¹ Another study reported that 1 participant withdrew
447 because of the exacerbation of back pain⁵³ while a final study reported the exclusion of

1
2
3 448 2 participants because of severe coronary artery disease.⁵⁷ None of the studies
4
5 449 provided data on the costs associated with conducting the intervention.⁵⁰⁻⁶³
6
7

8 450 **Risk of Bias Assessment**

9
10 451 Results for risk of bias assessment using the Cochrane Risk of Bias Assessment
11
12 452 Instrument are shown in Figure 2 and Supplementary file 3. As can be seen, greater
13
14 453 than 50% of the studies were at an unclear or high risk of bias with respect to (1)
15
16 454 incomplete outcome reporting (78.6%), (2) allocation concealment (78.6%), and (3)
17
18 455 blinding of outcome assessors (57.1%). Given the inability to truly blind participants in
19
20 456 exercise intervention trials, all studies (100%) were considered to be at a high risk of
21
22 457 bias for the category 'blinding of participants and personnel'.
23
24

25 458 **Data Synthesis**

26
27
28 459 **Overall results for primary outcome (anxiety).** Overall results for changes in anxiety
29
30 460 for the 14 included studies⁵⁰⁻⁶³ are shown in Table 4 and Figure 3. As can be seen,
31
32 461 statistically significant ($p = 0.002$) reductions in anxiety were observed. In addition,
33
34 462 statistically significant heterogeneity was observed while overall inconsistency was
35
36 463 categorized as moderate, (range = low to large). The NNT was 6 with a percentile
37
38 464 improvement of 15.5% and an estimated 5.3 million inactive US adults with AORD
39
40 465 improving their anxiety if they started exercising regularly. Statistically significant small-
41
42 466 study effects were observed ($p < 0.0001$) (Figure 4). With each result deleted from the
43
44 467 model once, results remained statistically significant across all deletions, ranging from -
45
46 468 0.44 (95% CI, -0.71 to -0.18) to -0.35 (-0.57 to -0.12). Cumulative meta-analysis, ranked
47
48 469 by year, demonstrated that results have been statistically significant since the first study
49
50 470 was conducted in 1989,⁵⁸ but with a trend towards smaller improvements in anxiety with
51
52
53
54
55
56
57
58
59
60

1
2
3 471 each accumulating year (Figure 5). Reductions in anxiety were similar to group-level
4
5 472 results when collapsed so that only one ES represented each study (ES, -0.40, 95% CI,
6
7 473 -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%,
8
9 474 $\tau^2 = 0.15$). With six outliers deleted from the model, overall reductions in anxiety were
10
11 475 similar but heterogeneity was no longer statistically significant and overall inconsistency
12
13 476 was reduced to a level categorized as small (ES, -0.40, 95% CI, -0.62 to -0.18, $p =$
14
15 477 0.0004 ; $Q = 11.8$, $p = 0.22$; $I^2 = 24.0\%$, 95% CI, 0% to 63.1%, $\tau^2 = 0.03$).

16
17
18
19 478 **Meta-regression results for anxiety.** Simple meta-regression results are shown in
20
21 479 Supplementary File 4. For study characteristics, greater reductions in anxiety were
22
23 480 associated with (1) earlier publication year, (2) studies at an unclear versus low risk of
24
25 481 bias, (3) studies in which sample size estimates were not provided, (4) trials in which a
26
27 482 larger percentage of participants initially agreed to participate in, and (5) studies that
28
29 483 were not funded versus funded. For participant characteristics, greater improvements
30
31 484 were associated with a larger percent dropout in the exercise groups as well as younger
32
33 485 age. For exercise intervention characteristics, greater reductions were associated with
34
35 486 (1) aerobic/strength training versus aerobic and strength training combined, (2) fewer
36
37 487 minutes of exercise per session, (3) minutes of exercise per week, and (4) total minutes
38
39 488 of exercise for the entire intervention period. Greater reductions were also associated
40
41 489 with (1) supervised and unsupervised exercise versus both, (2) facility and home-based
42
43 490 exercise versus both and (3) group and self-exercise versus both. No statistically
44
45 491 significant association ($p = 0.71$) was observed between rheumatoid/osteoarthritis (ES =
46
47 492 -0.35) and fibromyalgia (ES = -0.44) while the overall ES for those studies in which the
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 493 participants had rheumatoid arthritis was -0.54 and the overall ES for those in which the
4
5 494 majority had osteoarthritis was -0.32.

6
7 495 Results for the final multiple regression model are shown in Table 5. The overall model
8
9 496 was statistically significant ($F = 13.4$, $p = 0.004$). Earlier year of publication and
10
11 497 decreases in depression were statistically significant predictors for greater reductions in
12
13 498 anxiety. However, minutes of exercise per week was no longer statistically significant.

14
15 499 **GRADE findings for changes in anxiety.** An evidence profile for changes in anxiety is
16
17 500 shown in Supplementary file 5. As can be seen, the outcome (anxiety) was considered
18
19 501 critical and the overall strength of the finding was considered high, with future additional
20
21 502 studies unlikely to have an effect on the overall direction of findings.

22
23 503 **Results for secondary outcomes.** Overall results for changes in secondary outcomes
24
25 504 are shown in Table 4. *Physical function* was assessed in 10 studies^{50 52-55 57 58 61-63} using
26
27 505 the 10 meter walk test, 50 foot walk, 6 minute walk, Arthritis Impact and Measurement
28
29 506 Scale (AIMS), Fibromyalgia Impact Questionnaire (FIQ), Short Physical Performance
30
31 507 Battery, sit-to-stand test, stairclimbing test, up and go test, and the Western Ontario and
32
33 508 McMaster Osteoarthritis Index (WOMAC). As can be seen, statistically significant ($p <$
34
35 509 0.001) improvements in *physical function* were observed. Statistically significant
36
37 510 heterogeneity was observed while inconsistency was categorized as moderate, (range =
38
39 511 low to large). The NNT was 4 with a percentile improvement of 24.5% and an estimated
40
41 512 9 million inactive US adults with AORD improving their physical function if they started
42
43 513 exercising regularly. No statistically significant small-study effects were observed ($p =$
44
45 514 0.17). With each result deleted from the model once, results remained statistically
46
47 515 significant across all deletions, ranging from 0.54 (95% CI, 0.30 to 0.78) to 0.73 (95%

1
2
3 516 CI, 0.39 to 1.06). Cumulative meta-analysis, ranked by year, demonstrated that results
4
5 517 have been statistically significant since the first study was conducted in 1989,⁵⁸ but with
6
7 518 a trend towards smaller improvements in physical function with each accumulating year
8
9 519 (from 0.86 in 1989 to 0.66 in 2016). Improvements in physical function were similar to
10
11 520 group-level results when collapsed so that only one ES represented each study (ES,
12
13 521 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%
14
15 522 to 86.5%, $\tau^2 = 0.21$). With four outliers deleted from the model, overall improvements
16
17 523 in physical function were statistically significant but slightly smaller, heterogeneity was
18
19 524 no longer statistically significant, and overall inconsistency was reduced to a level
20
21 525 categorized as very low (ES, 0.57, 95% CI, 0.36 to 0.78, $p < 0.001$; $Q = 7.2$, $p = 0.41$; $I^2 =$
22
23 526 2.7%, 95% CI, 0% to 68.5%, $\tau^2 = 0.003$).

24
25
26
27
28 527 For *pain*, assessment was conducted in 13 studies^{50-54 56-63} using the AIMS, FIQ,
29
30 528 numerical rating scale, tender point count, visual analog scale and the WOMAC. As can
31
32 529 be seen in Table 4, statistically significant ($p = 0.017$) decreases in pain were found.
33
34 530 Statistically significant heterogeneity was observed while inconsistency was categorized
35
36 531 as large, including both CIs. The NNT was 6 with a percentile improvement of 23.1%
37
38 532 and an estimated 5.6 million inactive US adults with AORD decreasing their pain if they
39
40 533 started exercising regularly. No statistically significant small-study effects were
41
42 534 observed ($p = 0.34$). With each result deleted from the model once, results remained
43
44 535 statistically significant across all deletions, ranging from -0.70 (95% CI, -1.21 to -0.19) to
45
46 536 -0.47 (95% CI, -0.80 to -0.15). Cumulative meta-analysis, ranked by year, demonstrated
47
48 537 that results have been statistically significant, and remained statistically significant,
49
50 538 since only 2013. Decreases in pain were similar to group-level results when collapsed
51
52
53
54
55
56
57
58
59
60

1
2
3 539 so that only one ES represented each study (ES, -0.62, 95% CI, -1.16 to -0.07, $p = 0.03$;
4
5 540 = 123.7, $p < 0.001$; $I^2 = 90.3\%$, 95% CI, 85.3% to 93.6%, $\tau^2 = 0.75$). With ten outliers
6
7 541 deleted from the model, decreases in pain remained statistically significant but smaller,
8
9 542 heterogeneity was no longer statistically significant, and overall inconsistency was
10
11 543 reduced to a level categorized as very low (ES, -0.44, 95% CI, -0.70 to -0.18, $p = 0.001$;
12
13 544 $Q = 1.5$, $p = 0.68$; $I^2 = 0\%$, 95% CI, 0% to 69.5%, $\tau^2 = 0$).

14
15
16
17 545 *Depression* was assessed in 13 studies^{50-58 60-63} using the AIMS, Beck Depression
18
19 546 Inventory (BDI), Center for Epidemiologic Studies Depression Scale (CES-D),
20
21 547 Depression, Anxiety and Stress Scale (DASS21), FIQ, HADS, MHI, and VAS. As can
22
23 548 be seen in Table 4, statistically significant ($p = 0.009$) decreases in depression were
24
25 549 found. Statistically significant heterogeneity was observed while inconsistency was
26
27 550 categorized as moderate (95% CI = low to large). The NNT was 6 with a percentile
28
29 551 improvement of 15% and an estimated 5.1 million inactive US adults with AORD
30
31 552 reducing their depression if they started exercising regularly. Small-study effects were
32
33 553 not statistically significant ($p = 0.08$). With each result deleted from the model once,
34
35 554 results remained statistically significant across all deletions, ranging from -0.52 (95% CI,
36
37 555 -0.68 to -0.37) to -0.32 (95% CI, -0.61 to -0.03). Cumulative meta-analysis, ranked by
38
39 556 year, demonstrated that improvements have been statistically significant and remained
40
41 557 stable since 2013. Decreases in depression were similar to group-level results when
42
43 558 collapsed so that only one ES represented each study (ES, -0.38, 95% CI, -0.70 to -
44
45 559 0.07, $p = 0.02$; $Q = 45.6$, $p < 0.001$; $I^2 = 73.7\%$, 95% CI, 54.3% to 84.8%, $\tau^2 = 0.21$).
46
47 560 With three outliers deleted from the model, improvements in depression remained
48
49 561 statistically significant, slightly larger, but with non-significant heterogeneity and overall
50
51
52
53
54
55
56
57
58
59
60

1
2
3 562 inconsistency categorized as very low (ES, -0.43, 95% CI, -0.60 to -0.26, $p < 0.001$; $Q =$
4
5 563 5.7, $p = 0.89$; $I^2 = 0\%$, 95% CI, 0% to 19.3%, $\tau^2 = 0$).

6
7 564 *Quality-of-life* was assessed in 12 studies^{50-57 59 61-63} using the FIQ, Health Assessment
8
9
10 565 Questionnaire (HAQ), Quality of Life Scale (QOLS), SF-12, and SF-36. As shown in
11
12 566 Table 4, statistically significant ($p < 0.0001$) improvements in quality-of-life were found.
13
14 567 Statistically significant heterogeneity was observed while inconsistency was categorized
15
16 568 as large (95% CI = low to large). The NNT was 4 with a percentile improvement of
17
18 569 23.1% and an estimated 8.6 million inactive US adults with AORD improving their
19
20 570 quality-of-life if they started exercising regularly. Statistically significant small-study
21
22 571 effects were observed ($p < 0.001$). With each result deleted from the model once,
23
24 572 results remained statistically significant across all deletions, ranging from 0.58 (95% CI,
25
26 573 0.35 to 0.81) to 0.70 (95% CI, 0.41 to 0.99). Cumulative meta-analysis, ranked by year,
27
28 574 demonstrated that improvements have been statistically significant since 2001, but with
29
30 575 a trend towards a decrease in the magnitude of effect. Increases in quality-of-life were
31
32 576 similar to group-level results when collapsed so that only one ES represented each
33
34 577 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%
35
36 578 CI, 33.9% to 80.8%, $\tau^2 = 0.14$). With four outliers deleted from the model,
37
38 579 improvements in quality-of-life remained statistically significant, similar in magnitude, but
39
40 580 with non-significant heterogeneity and overall inconsistency categorized as low (ES,
41
42 581 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
43
44 582 67.5%, $\tau^2 = 0.04$).

45
46 583 *Maximum oxygen consumption* ($VO_{2\max}$ in $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) was assessed in 5 studies⁵⁶⁻⁵⁸
47
48 584^{61 62} using various maximal treadmill tests while one study used a submaximal step test
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 585 (Canadian Aerobic Fitness Test). As can be seen in Table 4, statistically significant ($p =$
4
5 586 0.001) improvements in $VO_{2\max}$ were observed. Statistically significant heterogeneity
6
7 587 was observed while inconsistency was categorized as moderate (95% CI = low to
8
9 588 large). The NNT was 3 with a percentile improvement of 25.7% and an estimated 9.5
10
11 589 million inactive US adults with AORD improving their relative $VO_{2\max}$ if they started
12
13 590 exercising regularly. No statistically significant small-study effects were observed ($p =$
14
15 591 0.18). With each result deleted from the model once, results remained statistically
16
17 592 significant across all deletions, ranging from $1.80 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ (95% CI, 0.58 to 3.01) to
18
19 593 $2.47 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ (95% CI, 1.25 to 3.69). Cumulative meta-analysis, ranked by year,
20
21 594 demonstrated that improvements have been statistically significant since 2003, but with
22
23 595 a trend towards a decrease in the magnitude of effect over time. Increases in $VO_{2\max}$
24
25 596 were similar to group-level results when collapsed so that only one ES represented
26
27 597 each study (ES, $2.01 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, 95% CI, 0.59 to 3.44, $p = 0.01$; $Q = 19.4$, $p = 0.001$;
28
29 598 $I^2 = 79.4\%$, 95% CI, 51.2% to 91.3%, $\tau^2 = 1.7$). With outliers deleted from the model,
30
31 599 improvements in $VO_{2\max}$ were smaller, with non-significant heterogeneity and overall
32
33 600 inconsistency categorized as low (ES, $1.93 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, 95% CI, 0.83 to 3.02, $p =$
34
35 601 0.001 ; $Q = 0.03$, $p = 0.86$; $I^2 = 0\%$, 95% CI, 0% to 0%, $\tau^2 = 0$).

36
37 602 Upper and lower body *muscular strength* was assessed in five studies^{55 57-59 62} using
38
39 603 free weights, grip strength, isokinetic strength and the sit-to-stand test with free weights.
40
41 604 As shown in Table 4, statistically significant ($p < 0.001$) improvements in strength were
42
43 605 observed. No statistically significant heterogeneity or mean inconsistency was observed
44
45 606 (95% CI = none to moderate). The NNT was 4 with a percentile improvement of 22.2%
46
47 607 and an estimated 8 million inactive US adults with AORD improving their strength if they
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 608 started exercising regularly. No statistically significant small-study effects were
4
5 609 observed ($p = 0.65$). With each result deleted from the model once, results remained
6
7 610 statistically significant across all deletions, ranging from 0.50 (95% CI, 0.21 to 0.79) to
8
9 611 0.68 (95% CI, 0.39 to 0.96). Cumulative meta-analysis, ranked by year, demonstrated
10
11 612 that improvements in strength have been statistically significant since the first included
12
13 613 study in 1989.⁵⁸ Changes in strength were similar to group-level results when collapsed
14
15 614 so that only one ES represented each study (ES, 0.59, 95% CI, 0.33 to 0.85, $p < 0.001$;
16
17 615 $Q = 3.5$, $p = 0.48$; $I^2 = 0\%$, 95% CI, 0% to 76.2%, $\tau^2 = 0$). There were no outliers.

18
19 616 Insufficient data were available to analyze *BMI*. The one study that did provide change
20
21 617 outcome results for BMI reported no statistically significant changes.⁵⁶

22 618 **DISCUSSION**

23 619 **Overall Findings**

24
25 620 The primary purpose of the current systematic review with meta-analysis was to
26
27 621 examine the effects of exercise (aerobic, strength training, or both) on anxiety in adults
28
29 622 with AORD. The overall findings, a primary purpose of meta-analysis,⁶⁵ suggest that
30
31 623 exercise is associated with both statistically significant and practically important
32
33 624 reductions in anxiety among adults with selected types of AORD. These findings are
34
35 625 supported by (1) a magnitude of effect comparable to or greater than anxiolytics,⁶⁶ (2) a
36
37 626 large percentile improvement of 15.5, (3) a NNT of only 6, (4) a large number of
38
39 627 physically inactive US adults with AORD who could benefit from exercising regularly
40
41 628 (5.3 million), (5) similar findings when examined at the study versus group level, (6)
42
43 629 continued existence of a statistically significant effect when each result was deleted
44
45 630 from the analysis once, (7) similar findings when outliers were deleted and statistical

1
2
3 631 heterogeneity was reduced to a non-significant effect and overall inconsistency to zero,
4
5 632 and (8) a consistent finding of improvements in anxiety since the first included study
6
7 633 was reported in 1989.⁵⁸ Based on GRADE, it was concluded that anxiety was a critical
8
9 634 outcome and that further research would unlikely change the direction of effect.
10
11

12 635 While the current findings are encouraging, it is interesting to note that cumulative
13
14 636 meta-analysis revealed a distinct trend for a reduction in the pooled ES over time (from -
15
16 637 1.47 in 1989 to -0.40 in 2016) and based on meta-regression, a statistically significant
17
18 638 association between greater reductions in anxiety with older versus more recent
19
20 639 studies. While the specific reasons for this could not be determined, it may be that the
21
22 640 experimental design and conduct of studies have improved over time. However, from
23
24 641 the investigative team's perspective, it is highly unlikely that the results will become non-
25
26 642 significant in future years. The former notwithstanding, the general conclusion that
27
28 643 exercise is associated with reductions in anxiety among adults with selected types of
29
30 644 AORD may need to be viewed with some caution given that the majority of included
31
32 645 studies consisted of participants with fibromyalgia^{50 51 55 56 59-63} while the remaining
33
34 646 studies included those with osteoarthritis and/or rheumatoid arthritis.^{52-54 57 58} However,
35
36 647 meta-regression revealed no statistically significant association between type of AORD
37
38 648 and changes in anxiety, thus allowing for the pooling of findings and a resultant increase
39
40 649 in statistical power.
41
42
43
44
45

46
47 650 The final meta-regression model resulted in two statistically significant variables being
48
49 651 included with earlier year of publication and changes in depression associated with
50
51 652 greater reductions in anxiety. These findings further reinforce the influence of year of
52
53 653 publication on changes in anxiety in the current systematic review with meta-analysis, a
54
55
56
57
58
59
60

1
2
3 654 potential reason for such having been previously mentioned. The greater reductions in
4
5 655 anxiety associated with reductions in depression and quality-of-life based on simple
6
7 656 meta-regression as well as depression in the multiple regression model illustrates the
8
9
10 657 potential interaction between these factors and the difficulty in identifying such,
11
12 658 especially in a systematic review with meta-analysis. Finally, for those studies in which
13
14 659 data were available,⁵⁰⁻⁶³ it is worthy to note that while the focus was on community
15
16 660 deliverable exercise or exercise delivered in other settings in which the exercise
17
18
19 661 intervention could be adapted for delivery in the community, two were delivered in either
20
21 662 a university^{50 56} or hospital^{54 55} and one each in either a hospital and home,⁵³ university
22
23 663 and home,⁵⁷ YMCA,⁵¹ or home only.⁶¹

24
25
26 664 In addition to statistically significant and practically important improvements in anxiety,
27
28 665 similar improvements were also observed for all secondary outcomes assessed
29
30 666 (physical function, pain, depression, quality of life, VO_{2max} in $ml \cdot kg^{-1} \cdot min^{-1}$, muscular
31
32 667 strength). These findings are important because unlike pharmacologic interventions that
33
34
35 668 are usually targeted to address one condition, exercise has the potential to improve
36
37 669 multiple physiological and psychological outcomes. Given the former, it would seem
38
39 670 plausible to suggest that continued efforts be made to increase the exercise and
40
41 671 physical activity levels of adults with AORD.

42 672 **Implications for Research**

43
44
45 673 There are at least eight implications for the conduct and reporting of future research on
46
47 674 exercise and anxiety in adults with AORD. First, since only five of the studies included
48
49 675 participants with osteoarthritis and/or rheumatoid arthritis, future randomized controlled
50
51 676 trials on exercise and anxiety in these populations appear warranted. Second, exercise
52
53
54
55
56
57
58
59
60

1
2
3 677 was performed indoors in the majority of included studies. Given that previous research
4
5 678 has suggested the exercise performed outdoors may have better mood-enhancing
6
7 679 effects than indoor exercise,^{67 68} future research examining this phenomenon with
8
9 680 respect to anxiety as well as other outcomes in adults with AORD seems appropriate.
10
11 681 Third, future studies should focus on examining the dose-response effects of exercise
12
13 682 on anxiety in adults with AORD and report complete information on the characteristics
14
15 683 of the intervention, including intervention fidelity.⁶⁹ Such information is critical for the
16
17 684 development of evidence-based recommendations aimed at practitioners. Fourth, since
18
19 685 more than half of the studies were considered to be at high or unclear risk of bias with
20
21 686 respect to allocation concealment, blinding of outcome assessors, and incomplete
22
23 687 outcome reporting, future studies should address these issues in their experimental
24
25 688 design and report such information. Notably, while all included studies were considered
26
27 689 to be at a high risk of bias with respect to blinding of participants, this is difficult for
28
29 690 researchers to address since unlike pharmacologic studies, it is almost impossible to
30
31 691 blind intervention participants to group assignment in exercise intervention studies.
32
33 692 Fifth, given the lack of data on exposure to psychotropic and analgesic medications
34
35 693 before and during the studies, including any changes in medication during the study, it
36
37 694 is suggested that future trials track and report this information, including pharmacologic
38
39 695 equivalence between the intervention and control groups. Sixth, while a lack of data was
40
41 696 reported on how and what level anxiety was assessed, all the studies used instruments
42
43 697 apparently focused on generalized anxiety. However, anxiety is a heterogeneous
44
45 698 construct that includes generalized anxiety disorder, separation anxiety disorder,
46
47 699 selective mutism, specific phobia, social phobia, panic disorder and agoraphobia.⁷⁰
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 700 Given the former, it is suggested that future studies report detailed information on the
4
5 701 specific types of anxiety they are assessing so as to better identify what exact type(s)
6
7 702 might be affected. Seventh, given previous meta-analytic research by others,⁷¹ a focus
8
9 703 on group versus individualized exercise may be preferable because of increased
10
11 704 contact and social support. This may be especially true for ethnic and racial minorities.⁷²
12
13
14 705 Finally, and collectively, a study in which one might have clinical confidence in the
15
16 706 results of might consist of a randomized controlled trial that (1) uses random sequence
17
18 707 generation, for example, computer random generator, to assign to participants to an
19
20 708 exercise intervention and attention-control group, (2) conceals allocation to group
21
22 709 assignment using an approach such as sequentially numbered, sealed, opaque
23
24 710 envelopes, (3) blinds personnel and outcome assessors to group assignment while
25
26 711 noting the inherent risk that all exercise studies are traditionally unable to blind
27
28 712 participants to group assignment, (4) accounts for incomplete data (dropouts, etc.) by
29
30 713 conducting intention-to-treat analyses, (5) avoids selective reporting of data by providing
31
32 714 results for both statistically significant and non-significant results, (6) includes sedentary
33
34 715 participants with a selected type or types of arthritis and elevated baseline levels of
35
36 716 anxiety, (7) includes valid and reliable instruments for the assessment of the different
37
38 717 types of anxiety based on the most recent version of the Diagnostic and Statistical
39
40 718 Manual of Mental Disorders,⁷⁰ (8) accounts for potential confounders (age, gender,
41
42 719 race, ethnicity, education, income, pain, physical function, depression, co-morbidities,
43
44 720 baseline levels of anxiety, sleep, medication use before and during the study, other non-
45
46 721 exercise and non-medication uptake before and during the study), (9) based on a
47
48 722 theoretical model, conducts group exercise intervention sessions (aerobic, strength
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 723 training, or both), based on the recent Consensus on Exercise Reporting Template,⁷³
4
5 724 (10) examines the mechanisms for changes in anxiety, and (11) conducts cost-
6
7 725 effectiveness analysis of the intervention. While these recommendations are focused on
8
9 726 exercise, alternative treatments exist. Thus, the most clinically useful study might
10
11 727 consist of a mega-randomized controlled trial that addresses all currently available
12
13 728 treatments. However, this is probably not realistic. Therefore, an alternative approach
14
15 729 might be to conduct a network meta-analysis that includes both direct and indirect
16
17 730 evidence from randomized trials of all available interventions (exercise, pharmacologic,
18
19 731 etc.).⁷⁴ To the best of the authors' knowledge, no such study currently exists.

732 **Implications for Practice**

733 The results of this study appear to have important implications for practice. First, since
734 changes in both anxiety and secondary outcomes resulted in statistically significant and
735 practically important improvements, exercise may be more vital than any other
736 intervention given the apparent multiple benefits of such. In addition, the magnitude of
737 effect (-0.40), NNT (6) and percentile improvement (15.5) observed in the current study
738 were equivalent to a previous meta-analysis on the pharmacological treatment of
739 generalized anxiety disorder in which the overall SMD effect size was -0.39, the
740 calculated NNT was 6, and the percentile improvement was 15.2.⁶⁶ While the current
741 systematic review with meta-analysis was unable to establish with any degree of
742 certainty the dose-response effects of exercise on anxiety in adults with AORD, it would
743 appear plausible, given the numerous other benefits that can be derived as well as the
744 minimal adverse events associated with exercise, to adhere to the Active Adult or Active
745 Older Adult Guidelines from the Physical Activity Guidelines for Americans Physical

1
2
3 746 Activity Guidelines²⁵ as recommended by the Centers for Disease Control and
4
5 747 Prevention.⁷⁵ Broadly, this includes aerobic activities on most, if not all, days of the
6
7 748 week, muscle strengthening activities at least 2 days per week, balance exercises at
8
9 749 least 3 days per week, and flexibility exercises on a daily basis. However, these
10
11 750 recommendations as applied to exercise and anxiety should be considered with respect
12
13 751 to factors such as the lack of transparency with respect to risk of bias in the included
14
15 752 studies.
16
17
18

19 753 **Strengths and Limitations**

20
21 754 There are at least three apparent *strengths* of the current study. First, to the best of our
22
23 755 knowledge, this is the first systematic review with meta-analysis to examine, as a
24
25 756 primary outcome, the effects of exercise on anxiety in adults with AORD. This is
26
27 757 important given (1) the prevalence of AORD,¹ (2) the expected future increase in the
28
29 758 prevalence of AORD,² (3) the financial costs associated with AORD,³ and (4) the
30
31 759 previously reported finding that the prevalence of anxiety is almost twice that of
32
33 760 depression.⁸ Second, a novel and recently developed approach, the IVhet model, was
34
35 761 used to pool findings.³⁶ This resulted in more robust estimates than those derived from
36
37 762 the traditional random-effects model.³⁷ This is noteworthy given the need to provide the
38
39 763 most accurate results possible when examining the effects of an intervention on
40
41 764 selected outcome(s).
42
43
44
45
46

47 765 While there are several strengths to this study, there are also at least four potential
48
49 766 *limitations*. First, similar to any aggregate data meta-analysis, the potential for
50
51 767 ecological fallacy exists. Thus, it may be that the observed findings in the current study
52
53 768 would not apply at the individual participant level. Second, and also common to any type
54
55
56
57
58
59
60

1
2
3 769 of aggregate data meta-analysis, meta-regression results do not support causal
4
5 770 inferences because the included studies are not randomly assigned to covariates.⁴⁷
6
7
8 771 Therefore, the associations observed in the current investigation would need to be
9
10 772 assessed in appropriately powered randomized trials. Third, while a large number of
11
12 773 statistical tests were conducted, no adjustments were made for such. Thus, some
13
14 774 findings could have been nothing more than the play of chance. However, common to
15
16 775 most aggregate data meta-analyses, no adjustments for multiple testing were made
17
18 776 because of concerns about missing possibly important findings that could be tested in
19
20 777 original trials.⁴⁵ Fourth, since anxiety was assessed using self-report instruments,⁵⁰⁻⁶³
21
22 778 the possibility of reporting bias in the original studies existed.
23
24
25

26 779 **CONCLUSIONS**

27
28 780 Exercise is associated with reductions in anxiety among adults with selected types of
29
30 781 AORD. However, a need exists for additional, well-designed, randomized controlled
31
32 782 trials on this topic.
33
34

35 783 **CONTRIBUTORS**

36
37 784 GAK was responsible for the conception and design, acquisition of data, analysis and
38
39 785 interpretation of data, drafting the initial manuscript and revising it critically for important
40
41 786 intellectual content. KSK was responsible for the conception and design, acquisition of
42
43 787 data, drafting the initial manuscript, and revising all drafts critically for important
44
45 788 intellectual content. LFC was responsible for the conception and design, acquisition of
46
47 789 data, drafting the initial manuscript, and revising all drafts critically for important
48
49 790 intellectual content. All authors read and approved the final manuscript.
50
51
52

53 791 **REGISTRATION**

1
2
3 792 In accordance with Primary Reporting Items for Systematics Reviews and Meta-
4
5 793 Analyses, our systematic review with network meta-analysis was registered with the
6
7 794 International Prospective Register of Systematic Reviews (PROSPERO) on October 4,
8
9 795 2016 (registration number CRD42016048728).

10
11
12 796 **COMPETING INTERESTS**

13
14
15 797 None.

16
17 798 **FUNDING**

18
19 799 This meta-analysis was funded by the National Institutes of Health, National Institute for
20
21 800 Arthritis, Musculoskeletal and Skin Diseases, grant number R01AR061346 (GAK,
22
23 801 Principal Investigator).

24
25
26 802 **DATA SHARING STATEMENT**

27
28 803 All data are available upon request from the corresponding author.
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

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.

- 1
2
3 827 9. He Y, Zhang M, Lin EH, et al. Mental disorders among persons with arthritis: results
4
5 828 from the World Mental Health Surveys. *Psychol Med* 2008;38(11):1639-50.
6
7
8 829 10. Busch AJ, Schachter CL, Overend TJ, et al. Exercise for fibromyalgia: a systematic
9
10 830 review. *J Rheumatol* 2008;35(6):1130-44.
11
12 831 11. Hurkmans E, van der Giesen FJ, Vliet Vlieland TP, et al. Dynamic exercise
13
14 832 programs (aerobic capacity and/or muscle strength training) in patients with
15
16 833 rheumatoid arthritis. *Cochrane Database Syst Rev* 2009(4):CD006853.
17
18
19 834 12. Anderson E, Shivakumar G. Effects of exercise and physical activity on anxiety.
20
21 835 *Front Psychiatry* 2013;4:27.
22
23
24 836 13. Kelley GA, Kelley KS, Hootman JM. Effects of exercise on depression in adults with
25
26 837 arthritis: a systematic review with meta-analysis of randomized controlled trials.
27
28 838 *Arthritis Res Ther* 2015;17:21.
29
30
31 839 14. Kelley GA, Kelley KS. Effects of exercise on anxiety in adults with arthritis and other
32
33 840 rheumatic disease: A systematic review of meta-analyses. *J Nov Physiother*
34
35 841 2014;4(4):1-5.
36
37
38 842 15. Bruno M, Cummins S, Gaudiano L, et al. Effectiveness of two Arthritis Foundation
39
40 843 programs: Walk With Ease, and YOU Can Break the Pain Cycle. *Clin Interv Aging*
41
42 844 2006;1(3):295-306.
43
44
45 845 16. Callahan LF, Ambrose KR. Physical activity and osteoarthritis - Considerations at
46
47 846 the population and clinical level. *Osteoarthritis Cartilage*;23(1):31-33.
48
49 847 17. Hootman JM, Helmick CG, Brady TJ. A public health approach to addressing
50
51 848 arthritis in older adults: the most common cause of disability. *Am J Public Health*
52
53 849 2012;102(3):426-33.
54
55
56
57
58
59
60

- 1
2
3 850 18. Zgibor JC, Ye L, Boudreau RM, et al. Community-based healthy aging interventions
4
5 851 for older adults with arthritis and multimorbidity. *J Community Health*
6
7 852 2017;42(2):390-99.
8
9
10 853 19. Jack K, McLean SM, Moffett JK, et al. Barriers to treatment adherence in
11
12 854 physiotherapy outpatient clinics: a systematic review. *Man Ther* 2010;15(3):220-8.
13
14 855 20. Fontaine KR, Heo M, Bathon J. Are US adults with arthritis meeting public health
15
16 856 recommendations for physical activity? *Arthritis Rheum* 2004;50(2):624-8.
17
18 857 21. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting
19
20 858 systematic reviews and meta-analyses of studies that evaluate health care
21
22 859 interventions: explanation and elaboration. *Ann Intern Med* 2009;151(4):W65-W94.
23
24 860 22. Kelley GA, Kelley KS, Callahan LF. Community-deliverable exercise and anxiety in
25
26 861 adults with arthritis and other rheumatic diseases: a protocol for a systematic review
27
28 862 and meta-analysis of randomised controlled trials. *BMJ Open* 2017;7(3):e014957.
29
30
31 863 23. Sacks HS, Chalmers TC, Smith H. Randomized versus historical controls for clinical
32
33 864 trials. *Am J Med* 1982;72:233-40.
34
35
36 865 24. Schulz KF, Chalmers I, Hayes R, et al. Empirical evidence of bias: Dimensions of
37
38 866 methodological quality associated with estimates of treatment effects in controlled
39
40 867 trials. *J Am Med Assoc* 1995;273:408-12.
41
42
43 868 25. Physical Activity Guidelines Advisory Report. Physical Activity Guidelines Advisory
44
45 869 Committee. Washington, DC: U.S. Department of Health and Human Services: U.S.
46
47 870 Department of Health and Human Services, 2008.
48
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 871 26. Brady TJ, Jernick SL, Hootman JM, et al. Public health interventions for arthritis:
4
5 872 expanding the toolbox of evidence-based interventions. *J Womens Health (Larchmt)*
6
7 873 2009;18(12):1905-17.
8
9
10 874 27. Ide MR, Laurindo IMM, Rodrigues AL, et al. Effect of aquatic respiratory exercise-
11
12 875 based program in patients with fibromyalgia. *Int J Rheum Dis* 2008;11(2):131-40.
13
14 876 28. Waggoner CD, LeLievre RB. A method to increase compliance to exercise
15
16 877 regimens in rheumatoid arthritis patients. *J Behav Med* 1981;4(2):191-201.
17
18 878 29. Ioannidis JPA. The mass production of redundant, misleading, and conflicted
19
20 879 systematic reviews and meta-analyses. *Milbank Q* 2016;94(5):485-514.
21
22 880 30. Cohen J. Weighted kappa: nominal scale agreement with provision for scaled
23
24 881 disagreement or partial credit. *Psychol Bull* 1968;70:213-20.
25
26 882 31. Lee E, Dobbins M, DeCorby K, et al. An optimal search filter for retrieving
27
28 883 systematic reviews and meta-analyses. *BMC Med Res Methodol* 2012;12:51.
29
30 884 32. Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of*
31
32 885 *Interventions Version 5.1.0 [updated March 2011]*: The Cochrane Collaboration,
33
34 886 2011.
35
36 887 33. Ahn S, Becker BJ. Incorporating quality scores in meta-analysis. *J Educ Behav Stat*
37
38 888 2011;36(5):555-85.
39
40 889 34. Hedges LV, Olkin I. *Statistical methods for meta-analysis*. San Diego, CA: Academic
41
42 890 Press 1985.
43
44 891 35. Follmann D, Elliot P, Suh I, et al. Variance imputation for overviews of clinical trials
45
46 892 with continuous response. *J Clin Epidemiol* 1992;45:769-73.
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 893 36. Doi SA, Barendregt JJ, Khan S, et al. Advances in the meta-analysis of
4
5 894 heterogeneous clinical trials I: The inverse variance heterogeneity model. *Contemp*
6
7 895 *Clin Trials* 2015;45(Pt A):130-38.
8
9
10 896 37. Dersimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*
11
12 897 1986;7:177-88.
13
14 898 38. Dersimonian R, Laird N. Meta-analysis in clinical trials revisited. *Contemp Clin Trials*
15
16 899 2015;45(Pt A):139-45.
17
18 900 39. Cochran WG. The combination of estimates from different experiments. *Biometrics*
19
20 901 1954;10:101-29.
21
22 902 40. Higgins JPT, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-
23
24 903 analyses. *Br Med J* 2003;327(7414):557-60.
25
26 904 41. Cohen J. Statistical power analysis for the behavioral sciences. New York:
27
28 905 Academic Press 1988.
29
30 906 42. Khan A, Khan S, Brown WA. Are placebo controls necessary to test new
31
32 907 antidepressants and anxiolytics? *Int J Neuropsychopharmacol* 2002;5(3):193-7.
33
34 908 43. Murphy LB, Hootman JM, Boring MA, et al. Leisure time physical activity among
35
36 909 U.S. adults with arthritis, 2008-2015. *Am J Prev Med* 2017.
37
38 910 44. Lee KJ, Carlin JB. Multiple imputation for missing data: fully conditional specification
39
40 911 versus multivariate normal imputation. *Am J Epidemiol* 2010;171(5):624-32.
41
42 912 45. Rothman KJ. No adjustments are needed for multiple comparisons. *Epidemiology*
43
44 913 1990;1:43-46.
45
46 914 46. Sacks HS, Berrier J, Reitman D, et al. Meta-analysis of randomized controlled trials.
47
48
49
50
51
52
53
54 915 *N Engl J Med* 1987;316:450-55.
55
56
57
58
59
60

- 1
2
3 916 47. Littell JH, Corcoran J, Pillai V. Systematic reviews and meta-analysis. New York:
4
5 917 Oxford University Press 2008:1-202.
6
7
8 918 48. Sterne JA, Sutton AJ, Ioannidis JP, et al. Recommendations for examining and
9
10 919 interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials.
11
12 920 *Br Med J* 2011;343:d4002.
13
14
15 921 49. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE
16
17 922 evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;64(4):383-
18
19 923 94.
20
21
22 924 50. Baptista AS, Villela AL, Jones A, et al. Effectiveness of dance in patients with
23
24 925 fibromyalgia: a randomized, single-blind, controlled study. *Clin Exp Rheumatol*
25
26 926 2012;30(6 Suppl 74):18-23.
27
28
29 927 51. Beltran R. The effects of a supervised group aerobic exercise program and a
30
31 928 chronobiological oriented treatment protocol on symptomatology and mood in
32
33 929 women with fibromyalgia [Dissertation]. Alliant University, 2003.
34
35
36 930 52. Cheung C, Wyman JF, Bronas U, et al. Managing knee osteoarthritis with yoga or
37
38 931 aerobic/strengthening exercise programs in older adults: a pilot randomized
39
40 932 controlled trial. *Rheumatol Int* 2017;37(3):389-98.
41
42
43 933 53. Fransen M, Nairn L, Winstanley J, et al. Physical activity for osteoarthritis
44
45 934 management: a randomized controlled clinical trial evaluating hydrotherapy or Tai
46
47 935 Chi classes. *Arthritis Rheum* 2007;57(3):407-14.
48
49
50 936 54. French HP, Cusack T, Brennan A, et al. Exercise and manual physiotherapy arthritis
51
52 937 research trial (EMPART) for osteoarthritis of the hip: a multicenter randomized
53
54 938 controlled trial. *Arch Phys Med Rehabil* 2013;94(2):302-14.
55
56
57
58
59

- 1
2
3 939 55. Gowans SE, deHueck A, Voss S, et al. Effect of a randomized, controlled trial of
4
5 940 exercise on mood and physical function in individuals with fibromyalgia. *Arthritis*
6
7 941 *Rheum* 2001;45(6):519-29.
8
9
10 942 56. Jones KD, Burckhardt CS, Deodhar AA, et al. A six-month randomized controlled
11
12 943 trial of exercise and pyridostigmine in the treatment of fibromyalgia. *Arthritis Rheum*
13
14 944 2008;58(2):612-22.
15
16
17 945 57. Komatireddy GR, Leitch RW, Cella K, et al. Efficacy of low load resistive muscle
18
19 946 training in patients with rheumatoid arthritis functional class II and III. *J Rheumatol*
20
21 947 1997;24(8):1531-39.
22
23
24 948 58. Minor MA, Hewett JE, Webel RR, et al. Efficacy of physical conditioning exercise in
25
26 949 patients with rheumatoid arthritis and osteoarthritis. *Arthritis Rheum*
27
28 950 1989;32(11):1396-405.
29
30
31 951 59. Munguia-Izquierdo D, Legaz-Arrese A. Assessment of the effects of aquatic therapy
32
33 952 on global symptomatology in patients with fibromyalgia syndrome: a randomized
34
35 953 controlled trial. *Arch Phys Med Rehabil* 2008;89(12):2250-7.
36
37
38 954 60. Sanudo B, Carrasco L, de Hoyo M, et al. Vagal modulation and symptomatology
39
40 955 following a 6-month aerobic exercise program for women with fibromyalgia. *Clin Exp*
41
42 956 *Rheumatol* 2015;33(1 Suppl 88):S41-5.
43
44
45 957 61. Schachter CL, Busch AJ, Peloso PM, et al. Effects of short versus long bouts of
46
47 958 aerobic exercise in sedentary women with fibromyalgia: a randomized controlled
48
49 959 trial. *Phys Ther* 2003;83(4):340-58.
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 960 62. Tomas-Carus P, Gusi N, Hakkinen A, et al. Eight months of physical training in
4
5 961 warm water improves physical and mental health in women with fibromyalgia: a
6
7 962 randomized controlled trial. *J Rehabil Med* 2008;40(4):248-52.
8
9
10 963 63. Tomas-Carus P, Gusi N, Leal A, et al. [The fibromyalgia treatment with physical
11
12 964 exercise in warm water reduces the impact of the disease on female patients'
13
14 965 physical and mental health]. *Rheumatol Clin* 2007;3(1):33-37.
15
16
17 966 64. Garber CE, Blissmer B, Deschenes MR, et al. Quantity and quality of exercise for
18
19 967 developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor
20
21 968 fitness in apparently healthy adults: Guidance for prescribing exercise. *Med Sci*
22
23 969 *Sports Exerc* 2011;43(7):1334-59.
24
25
26 970 65. Glass GV, McGaw B, Smith ML. Meta-analysis in social research. Newbury Park,
27
28 971 California: Sage 1981.
29
30
31 972 66. Hidalgo RB, Tupler LA, Davidson JR. An effect-size analysis of pharmacologic
32
33 973 treatments for generalized anxiety disorder. *J Psychopharmacol* 2007;21(8):864-72.
34
35
36 974 67. Rogerson M, Gladwell VF, Gallagher DJ, et al. Influences of green outdoors versus
37
38 975 indoors environmental settings on psychological and social outcomes of controlled
39
40 976 exercise. *Int J Environ Res Public Health* 2016;13(4):363.
41
42
43 977 68. Pasanen TP, Tyrvaainen L, Korpela KM. The relationship between perceived health
44
45 978 and physical activity indoors, outdoors in built environments, and outdoors in nature.
46
47 979 *Appl Psychol Health Well Being* 2014;6(3):324-46.
48
49 980 69. Resnick B, Inguito P, Orwig D, et al. Treatment fidelity in behavior change research
50
51 981 - A case example. *Nurs Res* 2005;54(2):139-43.
52
53
54 982 70. Association AP. Diagnostic and statistical manual of mental disorders. 5th ed2013.
55
56
57
58
59

- 1
2
3 983 71. Burke SM, Carron AV, Eys MA, et al. Group versus individual approach? A meta-
4
5 984 analysis of the effectiveness of interventions to promote physical activity. *Sport*
6
7 985 *Exerc Psychol Rev* 2006;1:19-55.
- 8
9
10 986 72. Onge JMS, Krueger PM. Education and racial-ethnic differences in types of exercise
11
12 987 in the United States. *J Health Soc Behav* 2011;52(2):197-211.
- 13
14 988 73. Slade SC, Dionne CE, Underwood M, et al. Consensus on Exercise Reporting
15
16 989 Template (CERT): Modified Delphi Study. *Phys Ther* 2016;96(10):1514-24.
- 17
18 990 74. Rouse B, Chaimani A, Li TJ. Network meta-analysis: an introduction for clinicians.
19
20 991 *Intern Emerg Med* 2017;12(1):103-11.
- 21
22
23 992 75. CDC. Physical activity for arthritis Atlanta, Georgia: Centers for Disease Control and
24
25 993 Prevention; 2017 [updated April 18, 2017. Available from:
26
27 994 <https://www.cdc.gov/arthritis/basics/physical-activity-overview.html> accessed July 5
28
29 995 2017.
- 30
31
32
33
34 996

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 to exercise (n = 11, age, $\bar{x} \pm SD$ = 50.1 \pm 12.6 yrs) or control (n = 10, age, $\bar{x} \pm SD$ = 53.7 \pm 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) \geq 65 yrs of age with knee OA assigned to exercise (n = 28, age, $\bar{x} \pm SD$ = 74.4 \pm 7.5 yrs), or control (n = 23, age, $\bar{x} \pm SD$ = 71.8 \pm 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, $\bar{x} \pm SD$ = 70 \pm 6.3 yrs), or wait-list control (n = 41, age, $\bar{x} \pm SD$ = 69.6 \pm 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, $\bar{x} \pm SD$ =	Aerobic & strength training, 30 min/session, for 8 wks, up to 5 strength	HADS

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

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

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, $\bar{x} \pm SD = 55.0 \pm 8.0$ yrs of age), or control (n = 16, $\bar{x} \pm SD = 58.0 \pm 6.9$ 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, $\bar{x} \pm SD = 41.9 \pm 8.6$ yrs of age), long bout (n = 51, $\bar{x} \pm SD = 41.3 \pm 8.7$ yrs of age), or control group (n = 36, $\bar{x} \pm SD = 42.5 \pm 6.7$ 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, $\bar{x} \pm SD = 50.7 \pm 10.6$ yrs of age) or control group (n = 16, $\bar{x} \pm SD = 50.9 \pm 6.7$ 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, $\bar{x} \pm SD = 51 \pm 10.0$ yrs of age) or control group (n = 17, $\bar{x} \pm SD = 51 \pm 9.0$ 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; $\bar{x} \pm SD$, mean \pm 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,

1
2
3 State-Trait Anxiety Inventory; MHR, maximum heart rate; OA, osteoarthritis; RA, rheumatoid arthritis; reps, repetitions; RPE, rating of perceived
4 exertion; VAS, Visual Analog Scale; wk(s), week(s); yrs, years;
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

For peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Table 2. Baseline characteristics of participants.

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

Notes: Groups represents number of exercise and control groups reporting data; \bar{x} + SD, mean \pm 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 \pm 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 kg ⁻¹ 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 \pm SE	t (p)	95% CI
Year of publication	0.035 \pm 0.010	3.50 (0.006)*	0.012 to 0.057
Changes in depression	0.316 \pm 0.758	4.16 (0.01)	0.110 to 0.521
Minutes of training per week	0.007 \pm 0.003	2.40 (0.06)	-0.0002 to 0.016
Intercept	-70.718 \pm 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.

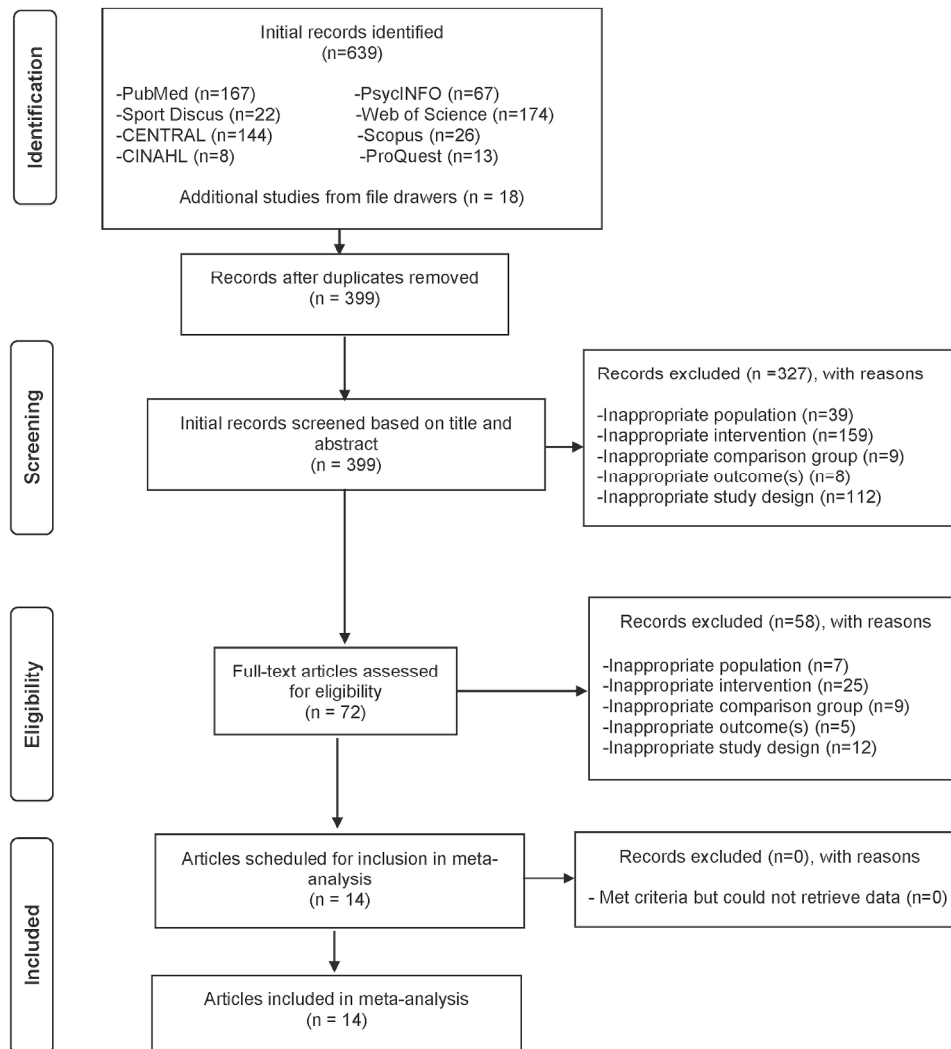


Figure 1. Flow diagram depicting the search process.

173x192mm (300 x 300 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

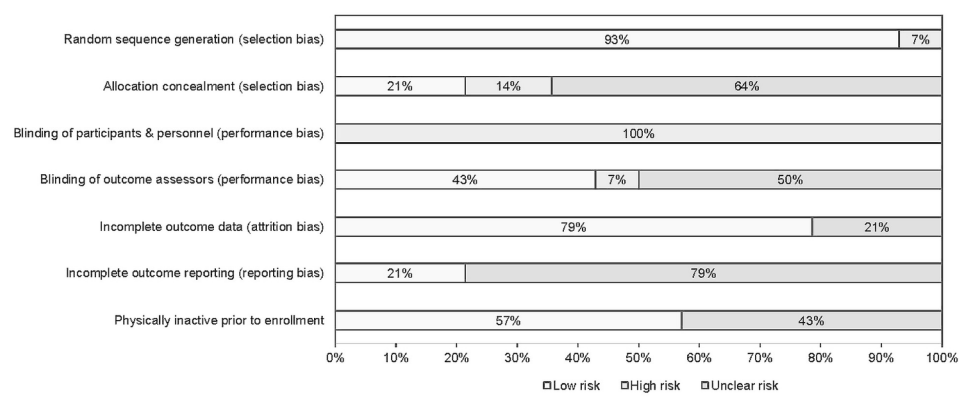


Figure 2. Risk of bias results using the Cochrane Risk of Bias Assessment Instrument.

173x77mm (300 x 300 DPI)

Peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

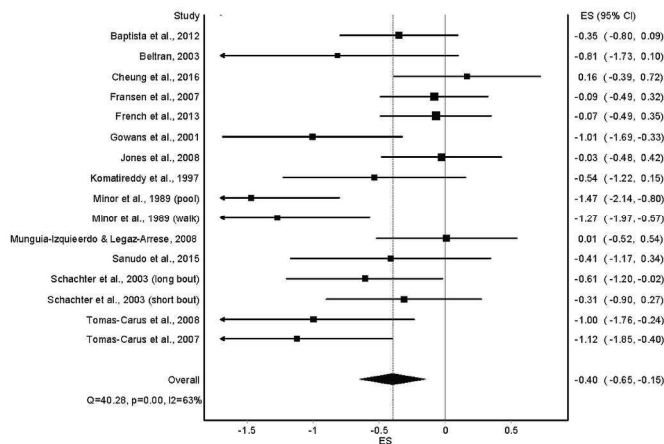


Figure 3. Forest plot for changes in anxiety.

173x224mm (300 x 300 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

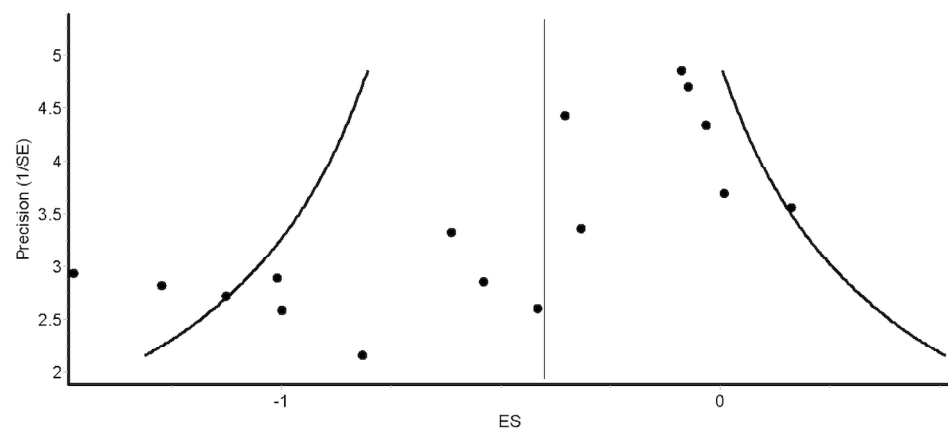


Figure 4. Funnel plot for changes in anxiety.

165x74mm (300 x 300 DPI)

er review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

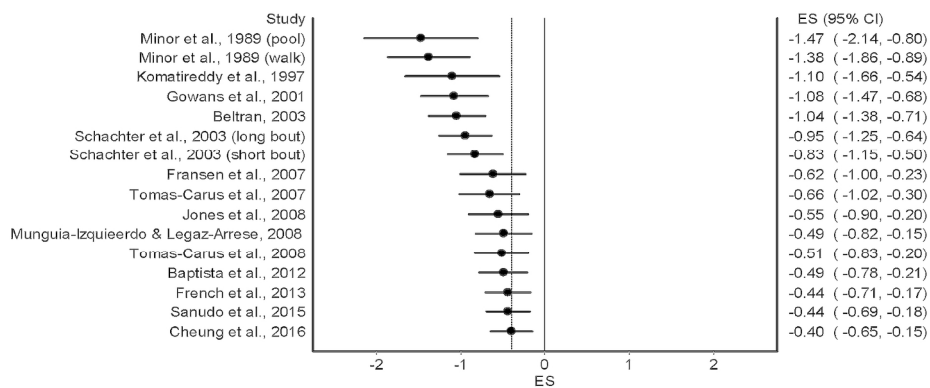


Figure 5. Cumulative meta-analysis for changes in anxiety.

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]

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. *Prescribe 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*

- 1
2
3 14. Ambrose KR, Golightly YM. Physical exercise as non-pharmacological treatment
4 of chronic pain: Why and when. *Best Practice & Research in Clinical*
5 *Rheumatology* 2015;29(1):120-30. doi: 10.1016/j.berh.2015.04.022 *inappropriate*
6 *study design*
- 7
8 15. Andrews NE, Strong J, Meredith PJ. Activity Pacing, Avoidance, Endurance, and
9 Associations With Patient Functioning in Chronic Pain: A Systematic Review and
10 Meta-Analysis. *Archives of physical medicine and rehabilitation* 2012;93(11):2109-
11 21. doi: 10.1016/j.apmr.2012.05.029 *inappropriate study design*
- 12
13 16. Ang D, Jensen M, Steiner J, et al. Combining cognitive-behavioral therapy and
14 milnacipran for fibromyalgia: a feasibility randomized-controlled trial. *The Clinical*
15 *journal of pain* 2013; 29(9).
16 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/880/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/880/CN-00918880/frame.html)
17 [00918880/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/880/CN-00918880/frame.html). *inappropriate study design*
- 18
19 17. Appelbaum KA, Blanchard EB, Hickling EJ, et al. Cognitive behavioral treatment of
20 a veteran population with moderate to severe rheumatoid arthritis. *Behavior*
21 *Therapy* 1988;19(4):489-502. doi: 10.1016/S0005-7894(88)80019-4 *inappropriate*
22 *intervention*
- 23
24 18. Archer T, Josefsson T, Lindwall M. Effects of Physical Exercise on Depressive
25 Symptoms and Biomarkers in Depression. *Cns & Neurological Disorders-Drug*
26 *Targets* 2014;13(10):1640-53. *inappropriate study design*
- 27
28 19. Arcos-Carmona IM, Castro-Sanchez AM, Mataran-Penarrocha GA, et al. [Effects
29 of aerobic exercise program and relaxation techniques on anxiety, quality of
30 sleep, depression, and quality of life in patients with fibromyalgia: a randomized
31 controlled trial]. *Medicina clinica* 2011;137(9):398-401. doi:
32 10.1016/j.medcli.2010.09.045 [published Online First: 2011/02/25] *inappropriate*
33 *intervention*
- 34
35 20. Arends RY, Bode C, Taal E, et al. A goal management intervention for polyarthritis
36 patients: rationale and design of a randomized controlled trial. *BMC*
37 *musculoskeletal disorders* 2013;14:239. doi: 10.1186/1471-2474-14-239
38 [published Online First: 2013/08/15] *inappropriate intervention*
- 39
40 21. Arne M, Janson C, Janson S, et al. Physical activity and quality of life in subjects
41 with chronic disease: chronic obstructive pulmonary disease compared with
42 rheumatoid arthritis and diabetes mellitus. *Scandinavian journal of primary health*
43 *care* 2009;27(3):141-7. doi: 10.1080/02813430902808643 [published Online First:
44 2009/03/24] *inappropriate study design*
- 45
46 22. Arnold L, Wang F, Ahl J, et al. Improvement in multiple dimensions of fatigue in
47 patients with fibromyalgia treated with duloxetine: secondary analysis of a
48 randomized, placebo-controlled trial. *Arthritis research & therapy* 2011; 13(3).
49 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/474/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/474/CN-00843474/frame.html)
50 [00843474/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/474/CN-00843474/frame.html). *inappropriate intervention*
- 51
52 23. Arnold L, Zlateva G, Sadosky A, et al. Correlations between Fibromyalgia
53 Symptom and Function Domains and Patient Global Impression of Change: A
54 Pooled Analysis of Three Randomized, Placebo-Controlled Trials of Pregabalin.
55 *Pain medicine (Malden, Mass)* 2011; 12(2).
56 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/608/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/608/CN-01016608/frame.html)
57 [01016608/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/608/CN-01016608/frame.html). *inappropriate study design*

- 1
 - 2
 - 3
 - 4
 - 5
 - 6
 - 7
 - 8
 - 9
 - 10
 - 11
 - 12
 - 13
 - 14
 - 15
 - 16
 - 17
 - 18
 - 19
 - 20
 - 21
 - 22
 - 23
 - 24
 - 25
 - 26
 - 27
 - 28
 - 29
 - 30
 - 31
 - 32
 - 33
 - 34
 - 35
 - 36
 - 37
 - 38
 - 39
 - 40
 - 41
 - 42
 - 43
 - 44
 - 45
 - 46
 - 47
 - 48
 - 49
 - 50
 - 51
 - 52
 - 53
 - 54
 - 55
 - 56
 - 57
 - 58
 - 59
 - 60
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*

- 1
2
3 35. Bae S, Gun S, Mok C, et al. Improved health outcomes with etanercept versus
4 usual DMARD therapy in an Asian population with established rheumatoid
5 arthritis. *BMC musculoskeletal disorders* 2013; 14.
6 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/280/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/280/CN-00864280/frame.html)
7 [00864280/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/280/CN-00864280/frame.html). *inappropriate intervention*
8
9 36. Bagdath AO, Donmez A, Eroksuz R, et al. Does addition of 'mud-pack and hot
10 pool treatment' to patient education make a difference in fibromyalgia patients? A
11 randomized controlled single blind study. *International journal of biometeorology*
12 2015;59(12):1905-11. doi: 10.1007/s00484-015-0997-7 *inappropriate intervention*
13
14 37. Barlow J, Turner A, Wright C. A randomized controlled study of the Arthritis Self-
15 Management Programme in the UK. *Health education research* 2000; 15(6).
16 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/444/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/444/CN-00330444/frame.html)
17 [00330444/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/444/CN-00330444/frame.html). *inappropriate intervention*
18
19 38. Barlow JH, Powell LA, Gilchrist M, et al. The effectiveness of the Training and
20 Support Program for parents of children with disabilities: a randomized controlled
21 trial. *Journal of psychosomatic research* 2008;64(1):55-62. doi:
22 10.1016/j.jpsychores.2007.06.006 [published Online First: 2007/12/26]
23 *inappropriate intervention*
24
25 39. Barsky AJ, Ahern DK, Orav EJ, et al. A Randomized Trial of Three Psychosocial
26 Treatments for the Symptoms of Rheumatoid Arthritis. *Seminars in arthritis and*
27 *rheumatism* 2010;40(3):222-32. doi: 10.1016/j.semarthrit.2010.04.001
28 *inappropriate intervention*
29
30 40. Basler HD. Group treatment for pain and discomfort. *Patient education and*
31 *counseling* 1993;20(2-3):167-75. [published Online First: 1993/05/01]
32 *inappropriate intervention*
33
34 41. Bassej EJ. Longitudinal changes in selected physical capabilities: muscle
35 strength, flexibility and body size. *Age and Ageing* 1998;27:12-16. *inappropriate*
36 *study design*
37
38 42. Bateman L, Sarzi-Puttini P, Burbridge CL, et al. Burden of illness in fibromyalgia
39 patients with comorbid depression. *Clinical and experimental rheumatology*
40 2016;34(2 Suppl 96):S106-13. [published Online First: 2016/04/09] *inappropriate*
41 *study design*
42
43 43. Baudic S, Attal N, Mhalla A, et al. Unilateral repetitive transcranial magnetic
44 stimulation of the motor cortex does not affect cognition in patients with
45 fibromyalgia. *Journal of Psychiatric Research* 2013;47(1):72-77. doi:
46 10.1016/j.jpsychires.2012.09.003 *inappropriate intervention*
47
48 44. Bearne L, Walsh N, Jessep S, et al. Feasibility of an exercise-based rehabilitation
49 programme for chronic hip pain. *Musculoskeletal care* 2011; 9(3).
50 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/898/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/898/CN-01124898/frame.html)
51 [01124898/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/898/CN-01124898/frame.html). *inappropriate intervention*
52
53 45. Bement MKH, Weyer A, Hartley S, et al. Pain Perception After Isometric Exercise
54 in Women With Fibromyalgia. *Archives of physical medicine and rehabilitation*
55 2011;92(1):89-95. doi: 10.1016/j.apmr.2010.10.006 *inappropriate study design*
56
57 46. Bennell K, Ahamed Y, Jull G, et al. Physical Therapist-Delivered Pain Coping
58 Skills Training and Exercise for Knee Osteoarthritis: Randomized Controlled Trial.
59 *Arthritis care & research* 2016; 68(5).
60

- <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*

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
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. Ressequier 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/doi/10.1111/j.1469-7610.2015.01653.x> *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. Buttawat 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, Aşti 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*

- 1
2
3 79. Carbonell-Baeza A, Aparicio VA, Chillon P, et al. Effectiveness of multidisciplinary
4 therapy on symptomatology and quality of life in women with fibromyalgia. *Clinical*
5 *and experimental rheumatology* 2011;29(6):S97-S103. *inappropriate study design*
6
7 80. Carbonell-Baeza A, Aparicio VA, Martins-Pereira CM, et al. Efficacy of Biodanza
8 for Treating Women with Fibromyalgia. *Journal of Alternative and Complementary*
9 *Medicine* 2010;16(11):1191-200. doi: 10.1089/acm.2010-0039 *inappropriate study*
10 *design*
11 81. Carbonell-Baeza A, Romero A, Aparicio VA, et al. Preliminary Findings of a 4-
12 Month Tai Chi Intervention on Tenderness, Functional Capacity, Symptomatology,
13 and Quality of Life in Men With Fibromyalgia. *American Journal of Mens Health*
14 2011;5(5):421-29. doi: 10.1177/1557988311400063 *inappropriate intervention*
15
16 82. Carbonell-Baeza A, Ruizz JR, Aparicio VA, et al. Multidisciplinary and biodanza
17 intervention for the management of fibromyalgia. *Acta Reumatologica Portuguesa*
18 2012;37(3):240-50. *inappropriate comparison group*
19
20 83. Carleton RN, Richter AA, Asmundson GJG. Attention modification in persons with
21 fibromyalgia: A double blind, randomized clinical trial. *Cognitive Behaviour*
22 *Therapy* 2011;40(4):279-90. doi: 10.1080/16506073.2011.616218 *inappropriate*
23 *intervention*
24 84. Carmichael NME, Katz J, Clarke H, et al. An intensive perioperative regimen of
25 pregabalin and celecoxib reduces pain and improves physical function scores six
26 weeks after total hip arthroplasty: A prospective randomized controlled trial. *Pain*
27 *Research & Management* 2013;18(3):127-32. doi: 10.1155/2013/258714
28 *inappropriate intervention*
29
30 85. Carson JW, Carson KM, Jones KD, et al. A pilot randomized controlled trial of the
31 Yoga of Awareness program in the management of fibromyalgia. *Pain*
32 2010;151(2):530-9. doi: 10.1016/j.pain.2010.08.020 [published Online First:
33 2010/10/16] *inappropriate intervention*
34
35 86. Carson JW, Carson KM, Jones KD, et al. Follow-up of yoga of awareness for
36 fibromyalgia: results at 3 months and replication in the wait-list group. *The Clinical*
37 *journal of pain* 2012;28(9):804-13. doi: 10.1097/AJP.0b013e31824549b5
38 [published Online First: 2012/07/04] *inappropriate study design*
39
40 87. Carta MG, Cardia C, Mannu F, et al. The high frequency of manic symptoms in
41 fibromyalgia does influence the choice of treatment? *Clinical Practice and*
42 *Epidemiology in Mental Health* 2006;2 *inappropriate study design*
43
44 88. Casanueva-Fernandez B, Llorca J, Rubio JBI, et al. Efficacy of a multidisciplinary
45 treatment program in patients with severe fibromyalgia. *Rheumatology*
46 *international* 2012;32(8):2497-502. doi: 10.1007/s00296-011-2045-1 *inappropriate*
47 *intervention*
48
49 89. Castel A, Castro S, Fontova R, et al. Body mass index and response to a
50 multidisciplinary treatment of fibromyalgia. *Rheumatology international*
51 2015;35(2):303-14. doi: 10.1007/s00296-014-3096-x [published Online First:
52 2014/08/02] *inappropriate intervention*
53
54 90. Castel A, Fontova R, Montull S, et al. Efficacy of a Multidisciplinary Fibromyalgia
55 Treatment Adapted for Women With Low Educational Levels: A Randomized
56 Controlled Trial. *Arthritis care & research* 2013;65(3):421-31. doi:
57 10.1002/acr.21818 *inappropriate intervention*
58
59
60

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
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/doi/10.1136/annrheumdis-2003-000471>. *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/doi/10.1016/j.joca.2016.07.009>. *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).

- 1
2
3
4 <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/664/CN-01075664/frame.html>. *inappropriate outcomes*
- 5
6 101. Christensen SS, Frosthalm 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*
- 7
8
9
10 102. 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*
- 11
12
13
14 103. 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*
- 15
16
17
18 104. Clarke-Jenssen A-C, Mengshoel AM, Staalesen Strumse Y, et al. EFFECT OF A FIBROMYALGIA 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*
- 19
20
21
22
23 105. 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*
- 24
25
26
27
28 106. 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*
- 29
30
31
32
33 107. 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*
- 34
35
36
37
38 108. 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*
- 39
40
41
42 109. 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*
- 43
44
45
46 110. 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*
- 47
48
49
50
51 111. 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*
- 52
53
54
55
56
57
58
59
60

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- Conference Start: 20100420 Conference End: 20100423 Conference Publication:
(varpagings) 2010; 49.
<http://onlinelibrary.wiley.com/doi/10.1002/art.1790110607> *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*

- 1
2
3 131. Falcão DM, Sales L, Leite JR, et al. Cognitive behavioral therapy for the
4 treatment of fibromyalgia syndrome: a randomized controlled trial. *Journal of*
5 *Musculoskeletal Pain* 2008;16(3):133-40. *inappropriate intervention*
6
7 132. Fark AR. A pilot study of white-coat and labile hypertension: Associations with
8 diagnoses of psychosocial dysfunction. *Family Practice Research Journal*
9 1993;13(1):71-80. *inappropriate outcomes*
10
11 133. Feldthusen C, Dean E, Forsblad-d'Elia H, et al. Effects of Person-Centered
12 Physical Therapy on Fatigue-Related Variables in Persons With Rheumatoid
13 Arthritis: A Randomized Controlled Trial. *Archives of Physical Medicine &*
14 *Rehabilitation* 2016;97(1):26-36. *inappropriate intervention*
15
16 134. Fenton G, Morley S. A tale of two RCTs: Using randomized controlled trials to
17 benchmark routine clinical (psychological) treatments for chronic pain. *Pain*
18 2013;154(10):2108-19. doi: 10.1016/j.pain.2013.06.033 *inappropriate study*
19 *design*
20
21 135. Field T. Yoga research review. *Complementary therapies in clinical practice*
22 2016;24:145-61. doi: 10.1016/j.ctcp.2016.06.005 [published Online First:
23 2016/08/10] *inappropriate intervention*
24
25 136. Field T, Diego M, Cullen C, et al. Fibromyalgia pain and substance P decrease
26 and sleep improves after massage therapy. *Jcr-Journal of Clinical Rheumatology*
27 2002;8(2):72-76. doi: 10.1097/00124743-200204000-00002 *inappropriate*
28 *intervention*
29
30 137. Field T, Diego M, Delgado J, et al. Rheumatoid arthritis in upper limbs benefits
31 from moderate pressure massage therapy. *Complementary therapies in clinical*
32 *practice* 2013;19(2):101-3. doi: 10.1016/j.ctcp.2012.12.001 [published Online
33 First: 2013/04/09] *inappropriate intervention*
34
35 138. Field T, Hernandez-Reif M, Seligman S, et al. Juvenile rheumatoid arthritis:
36 benefits from massage therapy. *Journal of pediatric psychology* 1997;22(5):607-
37 17. [published Online First: 1998/02/12] *inappropriate population*
38
39 139. Fitzgerald GK, White DK, Piva SR. Associations for change in physical and
40 psychological factors and treatment response following exercise in knee
41 osteoarthritis: an exploratory study. *Arthritis care & research* 2012;64(11):1673-
42 80. doi: 10.1002/acr.21751 [published Online First: 2012/06/08] *inappropriate*
43 *outcomes*
44
45 140. Fjorback L, Schroder A, Ornbol E, et al. Mindfulness therapy for bodily distress
46 syndrome - A randomized controlled trial. *Journal of psychosomatic research*
47 2011; 70(6). [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/011/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/011/CN-01006011/frame.html)
48 [01006011/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/011/CN-01006011/frame.html). *inappropriate intervention*
49
50 141. Fjorback LO, Arendt M, Ørnbøl E, et al. Mindfulness therapy for somatization
51 disorder and functional somatic syndromes — randomized trial with one-year
52 follow-up. *Journal of psychosomatic research* 2013;74(1):31-40. doi:
53 10.1016/j.jpsychores.2012.09.006 *inappropriate intervention*
54
55 142. Fors EA, Göttestam KG. Patient education, guided imagery and pain related talk
56 in fibromyalgia coping. *The European Journal of Psychiatry* 2000;14(4):233-40.
57 *inappropriate intervention*
58
59 143. Fregni F, Gimenes R, Valle AC, et al. A randomized, sham-controlled, proof of
60 principle study of transcranial direct current stimulation for the treatment of pain

- 1
2
3 in fibromyalgia. *Arthritis and rheumatism* 2006;54(12):3988-98. doi:
4 10.1002/art.22195 [published Online First: 2006/11/30] *inappropriate*
5 *intervention*
6
7 144. French H, Cusack T, Brennan A, et al. The effectiveness of exercise with and
8 without manual therapy for hip osteoarthritis: A multi-centre randomised
9 controlled trial. *Arthritis and rheumatism* 2011; 63(10 suppl. 1).
10 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/130/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/130/CN-01005130/frame.html)
11 [01005130/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/130/CN-01005130/frame.html). *inappropriate study design*
12
13 145. French H, Cusack T, Brennan A, et al. The effectiveness of exercise therapy with
14 and without manual therapy for hip osteoarthritis: A multicentre randomised
15 controlled trial. *Rheumatology* 2011; 50.
16 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/722/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/722/CN-01003722/frame.html)
17 [01003722/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/722/CN-01003722/frame.html). *inappropriate study design*
18
19 146. French HP, Cusack T, Brennan A, et al. Exercise and manual physiotherapy
20 arthritis research trial (EMPART): a multicentre randomised controlled trial. *BMC*
21 *musculoskeletal disorders* 2009;10:9. doi: 10.1186/1471-2474-10-9 [published
22 Online First: 2009/01/21] *inappropriate study design*
23
24 147. French HP, Galvin R, Cusack T, et al. Predictors of short-term outcome to
25 exercise and manual therapy for people with hip osteoarthritis. *Physical therapy*
26 2014;94(1):31-9. doi: 10.2522/ptj.20130173 [published Online First: 2013/08/10]
27 *inappropriate study design*
28
29 148. Friedrich M, Hahne J, Wepner F. A controlled examination of medical and
30 psychosocial factors associated with low back pain in combination with
31 widespread musculoskeletal pain. *Physical therapy* 2009;89(8):786-803. doi:
32 10.2522/ptj.20080100 [published Online First: 2009/06/23] *inappropriate*
33 *population*
34
35 149. Fulton AS, Hill AM, Williams MT, et al. Feasibility of omega-3 fatty acid
36 supplementation as an adjunct therapy for people with chronic obstructive
37 pulmonary disease: study protocol for a randomized controlled trial. *Trials*
38 2013;14 doi: 10.1186/1468-6708-14-107 *inappropriate intervention*
39
40 150. Garcia-Campayo J, Pascual A, Alda M, et al. Coping with fibromyalgia:
41 Usefulness of the Chronic Pain Coping Inventory-42. *Pain* 2007;132(Suppl
42 1):S68-S76. doi: 10.1016/j.pain.2007.02.013 *inappropriate intervention*
43
44 151. Garcia-Palacios A, Herrero R, Vizcaino Y, et al. Integrating Virtual Reality With
45 Activity Management for the Treatment of Fibromyalgia Acceptability and
46 Preliminary Efficacy. *Clinical Journal of Pain* 2015;31(6):564-72. doi:
47 10.1097/ajp.000000000000196 *inappropriate intervention*
48
49 152. Garvey WT, Mechanick JI, Brett EM, et al. AMERICAN ASSOCIATION OF
50 CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF
51 ENDOCRINOLOGY COMPREHENSIVE CLINICAL PRACTICE GUIDELINES
52 FOR MEDICAL CARE OF PATIENTS WITH OBESITY. *Endocrine practice* :
53 *official journal of the American College of Endocrinology and the American*
54 *Association of Clinical Endocrinologists* 2016;22 Suppl 3:1-203. doi:
55 10.4158/ep161365.gl [published Online First: 2016/05/25] *inappropriate study*
56 *design*
57
58
59

- 1
2
3 153. Gavi M, Vassalo DV, Amaral FT, et al. Strengthening Exercises Improve
4 Symptoms and Quality of Life but Do Not Change Autonomic Modulation in
5 Fibromyalgia: A Randomized Clinical Trial. *PloS one* 2014;9(3) doi:
6 10.1371/journal.pone.0090767 *inappropriate comparison group*
7
- 8 154. Genc A, Tur BS, Aytur YK, et al. Does aerobic exercise affect the
9 hypothalamicpituitary- adrenal hormonal response in patients with fibromyalgia
10 syndrome? *Journal of Physical Therapy Science* 2015;27(7):2225-31.
11 *inappropriate outcomes*
12
- 13 155. Gerskowitch C, Norman I, Rimes KA. Patients with medically unexplained
14 physical symptoms experience of receiving treatment in a primary-care
15 psychological therapies service: a qualitative study. *Cognitive Behaviour*
16 *Therapist* 2015;8 doi: 10.1017/s1352465815000235 *inappropriate intervention*
17
- 18 156. Gniadecki R, Robertson D, Molta CT, et al. Self-reported health outcomes in
19 patients with psoriasis and psoriatic arthritis randomized to two etanercept
20 regimens. *Journal of the European Academy of Dermatology and Venereology* :
21 *JEADV* 2012;26(11):1436-43. doi: 10.1111/j.1468-3083.2011.04308.x
22 <http://dx.doi.org/10.1111/j.1468-3083.2011.04308.x> [published Online First:
23 2011/11/01] *inappropriate intervention*
24
- 25 157. Goodwin P, Al QK, Gregory W, et al. The effectiveness of aquatic physiotherapy
26 in patients with rheumatoid arthritis: A randomised controlled trial. *Physiotherapy*
27 *(United Kingdom)* 2015; 101.
28 <http://onlinelibrary.wiley.com/doi/10.1111/j.1468-3083.2011.04308.x>
29 *inappropriate comparison group*
30
- 31 158. Gowans SE, DeHueck A, Abbey SE. Measuring exercise-induced mood changes
32 in fibromyalgia: a comparison of several measures. *Arthritis and rheumatism*
33 2002;47(6):603-9. doi: 10.1002/art.10789 [published Online First: 2003/01/11]
34 *inappropriate population*
35
- 36 159. Gowans SE, Dehueck A, Voss S, et al. Six-month and one-year followup of 23
37 weeks of aerobic exercise for individuals with fibromyalgia. *Arthritis and*
38 *rheumatism* 2004;51(6):890-8. doi: 10.1002/art.20828 [published Online First:
39 2004/12/14] *inappropriate population*
40
- 41 160. Grace SL, Krepostman S, Brooks D, et al. Illness perceptions among cardiac
42 patients: Relation to depressive symptomatology and sex. *Journal of*
43 *psychosomatic research* 2005;59(3):153-60. doi:
44 10.1016/j.jpsychores.2005.05.005 *inappropriate study design*
45
- 46 161. Gremeaux V, Durand S, Benaim C, et al. Evaluation of various ways to deliver
47 information concerning non-steroidal anti-inflammatory drugs to osteoarthritis
48 patients. *Annals of physical and rehabilitation medicine* 2013;56(1):14-29. doi:
49 10.1016/j.rehab.2012.12.004 [published Online First: 2013/02/02] *inappropriate*
50 *study design*
51
- 52 162. Gronning K, Bratas O, Steinsbekk A. Which Factors Influence Self-Efficacy in
53 Patients with Chronic Inflammatory Polyarthritis? *Musculoskeletal care*
54 2016;14(2):77-86. doi: 10.1002/msc.1114 *inappropriate study design*
55
- 56 163. Gronning K, Rannestad T, Skomsvoll JF, et al. Long-term effects of a nurse-led
57 group and individual patient education programme for patients with chronic
58 inflammatory polyarthritis - a randomised controlled trial. *Journal of clinical*
59

- 1
2
3 *nursing* 2014;23(7-8):1005-17. doi: 10.1111/jocn.12353 [published Online First:
4 2013/07/24] *inappropriate intervention*
5
6 164. Gronning K, Skomsvoll JF, Rannestad T, et al. The effect of an educational
7 programme consisting of group and individual arthritis education for patients with
8 polyarthritis-A randomised controlled trial. *Patient education and counseling*
9 2012;88(1):113-20. doi: 10.1016/j.pec.2011.12.011 *inappropriate intervention*
10
11 165. Gulec H, Capkin E, Sayar K, et al. The evaluation of the effectiveness of
12 amitriptyline versus venlafaxine in female patients diagnosed with fibromyalgia
13 syndrome. [Turkish]. *Klinik Psikofarmakoloji Bulteni* 2007; 17(2).
14 <http://onlinelibrary.wiley.com/doi/10.1002/art.21718> *inappropriate intervention*
15
16 166. Gusi N, Tomas-Carus P, Hakkinen A, et al. Exercise in waist-high warm water
17 decreases pain and improves health-related quality of life and strength in the
18 lower extremities in women with fibromyalgia. *Arthritis and rheumatism*
19 2006;55(1):66-73. doi: 10.1002/art.21718 *inappropriate population*
20
21 167. Haak T, Scott B. The effect of Qigong on fibromyalgia (FMS): a controlled
22 randomized study. *DisabilRehabil* 2008;30(8):625-33. *inappropriate intervention*
23
24 168. Haugstad GK, Haugstad TS, Kirste UM, et al. Continuing improvement of chronic
25 pelvic pain in women after short-term Mensendieck somatocognitive therapy:
26 results of a 1-year follow-up study. *American Journal of Obstetrics and*
27 *Gynecology* 2008;199(6) doi: 10.1016/j.ajog.2008.06.019 *inappropriate*
28 *population*
29
30 169. Haun JN, Graham-Pole J, Shortley B. Children with cancer and blood diseases
31 experience positive physical and psychological effects from massage therapy.
32 *International journal of therapeutic massage & bodywork* 2009;2(2):7-14.
33 [published Online First: 2009/01/01] *inappropriate population*
34
35 170. Haupt M, Millen S, Janner M, et al. Improvement of coping abilities in patients
36 with systemic lupus erythematosus: a prospective study. *Annals of the rheumatic*
37 *diseases* 2005;64(11):1618-23. doi: 10.1136/ard.2004.029926 *inappropriate*
38 *population*
39
40 171. Hauser W. The german fibromyalgia consumer reports-a cross-sectional survey.
41 *Annals of the Rheumatic Disease* 2013; 71.
42 <http://onlinelibrary.wiley.com/doi/10.1002/art.21718>
43 *inappropriate study design*
44
45 172. Hecker CD, Melo C, Tomazoni SdS, et al. Analysis of effects of kinesiotherapy
46 and hydrokinesiotherapy on the quality of patients with fibromyalgia -- a
47 randomized clinical trial. *Fisioterapia em Movimento* 2011;24(1):57-64. doi:
48 10.1590/S0103-51502011000100007 *inappropriate comparison group*
49
50 173. Heffez DS, Ross RE, Shade-Zeldow Y, et al. Treatment of cervical myelopathy in
51 patients with the fibromyalgia syndrome: outcomes and implications. *European*
52 *spine journal : official publication of the European Spine Society, the European*
53 *Spinal Deformity Society, and the European Section of the Cervical Spine*
54 *Research Society* 2007;16(9):1423-33. doi: 10.1007/s00586-007-0366-2
55 [published Online First: 2007/04/12] *inappropriate study design*
56
57
58
59
60

- 1
2
3 174. Henkel K, Reimers CD, Knapp G, et al. Physical training for neurological and
4 mental diseases. *Der Nervenarzt* 2014;85(12):1521-+. doi: 10.1007/s00115-013-
5 3978-2 *inappropriate study design*
- 6
7 175. Hoeger Bement MK, Weyer A, Hartley S, et al. Pain Perception After Isometric
8 Exercise in Women With Fibromyalgia. *Archives of Physical Medicine &*
9 *Rehabilitation* 2011;92(1):89-95. *inappropriate study design*
- 10
11 176. Hsieh RL, Lee WC. Clinical effects of lateral wedge arch support insoles in knee
12 osteoarthritis: A prospective double-blind randomized study. *Medicine*
13 2016;95(27):e3952. doi: 10.1097/md.0000000000003952 [published Online First:
14 2016/07/12] *inappropriate intervention*
- 15
16 177. Hsieh RL, Lo MT, Lee WC, et al. Therapeutic effects of short-term
17 monochromatic infrared energy therapy on patients with knee osteoarthritis: a
18 double-blind, randomized, placebo-controlled study. *The Journal of orthopaedic*
19 *and sports physical therapy* 2012;42(11):947-56. doi: 10.2519/jospt.2012.3881
20 [published Online First: 2012/09/11] *inappropriate intervention*
- 21
22 178. Huber E, Roos E, Meichtry A, et al. Effect of preoperative neuromuscular training
23 (NEMEX-TJR) on functional outcome after total knee replacement: An assessor-
24 blinded randomized controlled trial. *BMC musculoskeletal disorders* 2015; 16(1).
25 <http://onlinelibrary.wiley.com/doi/10.1186/s12913-015-01088-5>
26 *inappropriate intervention*
- 27
28 179. Hudson JI, Arnold LM, Bradley LA, et al. What makes patients with fibromyalgia
29 feel better? Correlations between Patient Global Impression of Improvement and
30 changes in clinical symptoms and function: a pooled analysis of 4 randomized
31 placebo-controlled trials of duloxetine. *The Journal of rheumatology*
32 2009;36(11):2517-22. doi: 10.3899/jrheum.090139 [published Online First:
33 2009/10/17] *inappropriate study design*
- 34
35 180. Hughes S, Seymour R, Campbell R, et al. Fit and Strong!: bolstering
36 maintenance of physical activity among older adults with lower-extremity
37 osteoarthritis. *American journal of health behavior* 2010; 34(6).
38 <http://onlinelibrary.wiley.com/doi/10.1186/1090-0008-34-6>
39 *inappropriate intervention*
- 40
41 181. Hurley M, Walsh N, Jessep S. Clinical effectiveness and costs of an integrated
42 rehabilitation programme compared with outpatient physiotherapy for chronic
43 knee pain. *Arthritis and rheumatism* 2012; 64.
44 <http://onlinelibrary.wiley.com/doi/10.1186/1090-0008-64-6>
45 *inappropriate study design*
- 46
47 182. Hurst NP, Lambert CM, Forbes J, et al. Does waiting matter? A randomized
48 controlled trial of new non-urgent rheumatology out-patient referrals.
49 *Rheumatology (Oxford, England)* 2000;39(4):369-76. [published Online First:
50 2000/05/19] *inappropriate intervention*
- 51
52 183. Ide MR, Laurindo IMM, Rodrigues AL, et al. Effect of aquatic respiratory exercise-
53 based program in patients with fibromyalgia. *International journal of rheumatic*
54 *diseases* 2008;11(2):131-40. doi: 10.1111/j.1756-185X.2008.00348.x
55 *inappropriate comparison group*
- 56
57 184. Jackel WH, Gerdes N, Cziske R, et al. RHEUMATIC COMPLAINTS IN THE
58 GENERAL-POPULATION OF GERMANY - PREVALENCE, PHYSICAL AND
59
60

- 1
2
3 PSYCHOSOCIAL IMPACT. *Zeitschrift fur Rheumatologie* 1993;52(5):281-88.
4 *inappropriate study design*
- 5 185. Jenkinson CM, Doherty M, Avery AJ, et al. Effects of dietary intervention and
6 quadriceps strengthening exercises on pain and function in overweight people
7 with knee pain: randomised controlled trial. *BMJ (Clinical research ed)*
8 2009;339:b3170. doi: 10.1136/bmj.b3170 [published Online First: 2009/08/20]
9 *inappropriate population*
- 10 186. Jensen KB, Kosek E, Wicksell R, et al. Cognitive Behavioral Therapy increases
11 pain-evoked activation of the prefrontal cortex in patients with fibromyalgia. *Pain*
12 2012;153(7):1495-503. doi: 10.1016/j.pain.2012.04.010 *inappropriate*
13 *intervention*
- 14 187. Jensen OK, Nielsen CV, Stengaard-Pedersen K. One-year prognosis in sick-
15 listed low back pain patients with and without radiculopathy. Prognostic factors
16 influencing pain and disability. *Spine Journal* 2010;10(8):659-75. doi:
17 10.1016/j.spinee.2010.03.026 *inappropriate population*
- 18 188. Jessep SA, Walsh NE, Ratcliffe J, et al. Long-term clinical benefits and costs of
19 an integrated rehabilitation programme compared with outpatient physiotherapy
20 for chronic knee pain. *Physiotherapy* 2009;95(2):94-102. doi:
21 10.1016/j.physio.2009.01.005 [published Online First: 2009/07/25] *inappropriate*
22 *population*
- 23 189. Johannesson E, Simren M, Strid H, et al. Physical activity improves symptoms in
24 irritable bowel syndrome: a randomized controlled trial. *The American journal of*
25 *gastroenterology* 2011;106(5):915-22. doi: 10.1038/ajg.2010.480 [published
26 Online First: 2011/01/06] *inappropriate population*
- 27 190. Jones KD. A randomized controlled trial of muscle strengthening versus flexibility
28 training in fibromyalgia. Microform Publications, University of Oregon, 2000.
29 *inappropriate comparison group*
- 30 191. Kamanli A, Kaya A, Ardicoglu O, et al. Comparison of lidocaine injection,
31 botulinum toxin injection, and dry needling to trigger points in myofascial pain
32 syndrome. *Rheumatology international* 2005;25(8):604-11. doi: 10.1007/s00296-
33 004-0485-6 *inappropriate intervention*
- 34 192. Kang J, Li N, Wu B. Therapeutic methods for knee osteoarthritis: Randomized
35 controlled trial and systemic evaluation. [Chinese]. *Zhongguo Linchuang Kangfu*
36 2005; 9(30). [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/890/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/890/CN-00643890/frame.html)
37 [00643890/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/890/CN-00643890/frame.html). *inappropriate study design*
- 38 193. Kapfhammer HP. [Psychopharmacological treatment in patients with somatoform
39 disorders and functional body syndromes]. *Der Nervenarzt* 2012;83(9):1128-41.
40 doi: 10.1007/s00115-011-3446-9 [published Online First: 2012/08/17]
41 *inappropriate study design*
- 42 194. Karp J, Dew M, Wahed A, et al. Challenges and Solutions for Depression
43 Prevention Research: Methodology for a Depression Prevention Trial for Older
44 Adults with Knee Arthritis and Emotional Distress. *American journal of geriatric*
45 *psychiatry* 2016; 24(6).
46 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/456/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/456/CN-01158456/frame.html)
47 [01158456/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/456/CN-01158456/frame.html). *inappropriate outcomes*
- 48
49
50
51
52
53
54
55
56
57
58
59

- 1
2
3 195. Katic B, Heywood J, Turek F, et al. New approach for analyzing self-reporting of
4 insomnia symptoms reveals a high rate of comorbid insomnia across a wide
5 spectrum of chronic diseases. *Sleep Medicine* 2015;16(11):1332-41. doi:
6 10.1016/j.sleep.2015.07.024 *inappropriate outcomes*
7
8 196. Kaya A, Kamanli A, Ardicoglu O, et al. Direct current therapy with/without
9 fidocaine iontophoresis in myofascial pain syndrome. *Bratislava Medical Journal-*
10 *Bratislavske Lekarske Listy* 2009;110(3):185-91. *inappropriate intervention*
11
12 197. Kayiran S, Dursun E, Dursun N, et al. Neurofeedback intervention in fibromyalgia
13 syndrome; a randomized, controlled, rater blind clinical trial. *Applied*
14 *psychophysiology and biofeedback* 2010;35(4):293-302. doi: 10.1007/s10484-
15 010-9135-9 [published Online First: 2010/07/09] *inappropriate intervention*
16
17 198. Keefe FJ, Shelby RA, Somers TJ, et al. Effects of coping skills training and
18 sertraline in patients with non-cardiac chest pain: A randomized controlled study.
19 *Pain* 2011;152(4):730-41. doi: 10.1016/j.pain.2010.08.040 *inappropriate*
20 *intervention*
21
22 199. Keeley T, Al-Janabi H, Nicholls E, et al. A longitudinal assessment of the
23 responsiveness of the ICECAP-A in a randomised controlled trial of a knee pain
24 intervention. *Quality of life research : an international journal of quality of life*
25 *aspects of treatment, care and rehabilitation* 2015;24(10):2319-31. doi:
26 10.1007/s11136-015-0980-0 [published Online First: 2015/04/22] *inappropriate*
27 *study design*
28
29 200. Kekow J, Moots R, Khandker R, et al. Improvements in patient-reported
30 outcomes, symptoms of depression and anxiety, and their association with
31 clinical remission among patients with moderate-to-severe active early
32 rheumatoid arthritis. *Rheumatology (Oxford, England)* 2011;50(2):401-9. doi:
33 10.1093/rheumatology/keq327 [published Online First: 2010/11/10] *inappropriate*
34 *study design*
35
36 201. Kekow J, Moots RJ, Emery P, et al. Patient-reported outcomes improve with
37 etanercept plus methotrexate in active early rheumatoid arthritis and the
38 improvement is strongly associated with remission: the COMET trial. *Annals of*
39 *the rheumatic diseases* 2010;69(1):222-5. doi: 10.1136/ard.2008.102509
40 [published Online First: 2009/03/19] *inappropriate intervention*
41
42 202. Kempke S, Goossens L, Luyten P, et al. Predictors of outcome in a multi-
43 component treatment program for chronic fatigue syndrome. *Journal of Affective*
44 *Disorders* 2010;126(1-2):174-79. doi: 10.1016/j.jad.2010.01.073 *inappropriate*
45 *intervention*
46
47 203. Knittle K, Maes S, de Gucht V. Psychological interventions for rheumatoid
48 arthritis: examining the role of self-regulation with a systematic review and meta-
49 analysis of randomized controlled trials. *Arthritis care & research*
50 2010;62(10):1460-72. doi: 10.1002/acr.20251
51 <http://dx.doi.org/10.1002/acr.20251> [published Online First: 2010/05/28] *inappropriate*
52 *study design*
53
54 204. Kolahi S, Pourghassem Gargari B, Mesgari Abbasi M, et al. Effects of
55 phylloquinone supplementation on lipid profile in women with rheumatoid arthritis:
56 a double blind placebo controlled study. *Nutrition research and practice*
57
58
59
60

- 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. Koullil 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. Lakhani 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*

- 1
2
3 *Movimiento Humano Y La Salud* 2015;11(2):1-19. doi: 10.15359/mhs.11-2.1
4 *inappropriate study design*
- 5 215. Li K, Hu XQ, Qiu WH, et al. Effects of physiotherapy versus combination of
6 physiotherapy and preventive education on quality of life in patients with
7 degenerative gonarthrosis. *Chinese Journal of Clinical Rehabilitation*
8 2006;10(4):32-33. *inappropriate intervention*
- 9 216. Li YH, Wang FY, Feng CQ, et al. Massage therapy for fibromyalgia: a systematic
10 review and meta-analysis of randomized controlled trials. *PloS one*
11 2014;9(2):e89304. doi: 10.1371/journal.pone.0089304 [published Online First:
12 2014/03/04] *inappropriate study design*
- 13 217. Ljótsson B, Atterlöf E, Lagerlöf M, et al. Internet-delivered acceptance and
14 values-based exposure treatment for fibromyalgia: A pilot study. *Cognitive*
15 *Behaviour Therapy* 2014;43(2):93-104. doi: 10.1080/16506073.2013.846401
16 *inappropriate intervention*
- 17 218. Lopez-Pousa S, Bassets Pages G, Monserrat-Vila S, et al. Sense of Well-Being
18 in Patients with Fibromyalgia: Aerobic Exercise Program in a Mature Forest-A
19 Pilot Study. *Evidence-based complementary and alternative medicine : eCAM*
20 2015;2015:614783. doi: 10.1155/2015/614783 [published Online First:
21 2015/11/12] *inappropriate comparison group*
- 22 219. Lopez-Rodriguez MD, Castro-Sanchez AM, Fernandez-Martinez M, et al.
23 Comparison between aquatic-biodanza and stretching for improving quality of life
24 and pain in patients with fibromyalgia. *Atencion Primaria* 2012;44(11):641-49. doi:
25 10.1016/j.aprim.2012.03.002 *inappropriate intervention*
- 26 220. Lopez-Rodriguez MM, Fernandez-Martinez M, Mataran-Penarrocha GA, et al.
27 [Effectiveness of aquatic biodance on sleep quality, anxiety and other symptoms
28 in patients with fibromyalgia]. *Medicina clinica* 2013;141(11):471-8. doi:
29 10.1016/j.medcli.2012.09.036 [published Online First: 2012/12/19] *inappropriate*
30 *intervention*
- 31 221. Luciano JV, Martinez N, Penarrubia-Maria MT, et al. Effectiveness of a
32 psychoeducational treatment program implemented in general practice for
33 fibromyalgia patients: a randomized controlled trial. *The Clinical journal of pain*
34 2011;27(5):383-91. doi: 10.1097/AJP.0b013e31820b131c [published Online
35 First: 2011/02/15] *inappropriate intervention*
- 36 222. Luedtke K, Rushton A, Wright C, et al. Effectiveness of anodal transcranial direct
37 current stimulation in patients with chronic low back pain: design, method and
38 protocol for a randomised controlled trial. *BMC musculoskeletal disorders*
39 2011;12:290. doi: 10.1186/1471-2474-12-290 [published Online First:
40 2011/12/30] *inappropriate intervention*
- 41 223. Lumley M, Schubiner H, Clauw D, et al. The PAST-FM (Pain and Stress
42 Treatment for Fibromyalgia) randomized, controlled trial: Main effects of
43 emotional awareness and expression and cognitive-behavioral therapies. *Journal*
44 *of pain* 2016; 17(4 suppl. 1).
45 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/566/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/566/CN-01142566/frame.html)
46 [01142566/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/566/CN-01142566/frame.html). *inappropriate intervention*
- 47 224. Lumley MA, Keefe FJ, Mosley-Williams A, et al. The effects of written emotional
48 disclosure and coping skills training in rheumatoid arthritis: A randomized clinical
49
50
51
52
53
54
55
56
57
58
59

- 1
2
3 trial. *Journal of Consulting and Clinical Psychology* 2014;82(4):644-58. doi:
4 10.1037/a0036958 *inappropriate intervention*
5
6 225. Lund I, Lundeberg T, Carleson J, et al. Corticotropin releasing factor in urine--a
7 possible biochemical marker of fibromyalgia. Responses to massage and guided
8 relaxation. *Neuroscience letters* 2006;403(1-2):166-71. doi:
9 10.1016/j.neulet.2006.04.038 [published Online First: 2006/05/24] *inappropriate*
10 *study design*
11 226. Mackintosh S. Hydrotherapy and Tai Chi each provide clinical improvements for
12 older people with osteoarthritis. *Australian Journal of Physiotherapy*
13 2008;54(2):143-43. *inappropriate study design*
14 227. Maddali Bongi S, Del Rosso A, Di Felice C, et al. Resseguier method and Qi
15 Gong sequentially integrated in patients with fibromyalgia syndrome. *Clinical and*
16 *experimental rheumatology* 2012;30(6 Suppl 74):51-8. [published Online First:
17 2012/11/01] *inappropriate intervention*
18 228. Mahagna H, Amital D, Amital H. A randomised, double-blinded study comparing
19 giving etoricoxib vs. placebo to female patients with fibromyalgia. *International*
20 *journal of clinical practice* 2016; 70(2 // (MSD) *Meso Scale Diagnostics*).
21 <http://onlinelibrary.wiley.com/doi/10.1111/ijcp.12727>.
22 <http://onlinelibrary.wiley.com/doi/10.1111/ijcp.12727>. *inappropriate intervention*
23 229. Mannerkorpi K, Nyberg B, Ahlmen M, et al. Pool exercise combined with an
24 education program for patients with fibromyalgia syndrome. A prospective,
25 randomized study. *J Rheumatol* 2000;27(10):2473-81. *inappropriate intervention*
26 230. Mao JJ, Bruner DW, Stricker C, et al. Feasibility trial of electroacupuncture for
27 aromatase inhibitor--related arthralgia in breast cancer survivors. *Integrative*
28 *cancer therapies* 2009;8(2):123-9. doi: 10.1177/1534735409332903 [published
29 Online First: 2009/08/15] *inappropriate population*
30 231. Marszalek J, Price LL, Harvey WF, et al. Outcome Expectations and
31 Osteoarthritis: Perceived Benefits of Exercise Are Associated with Self-Efficacy
32 and Depression. *Arthritis care & research* 2016 doi: 10.1002/acr.22969
33 [published Online First: 2016/07/09] *inappropriate study design*
34 232. Martin DP, Williams BA, Berger IH. Improvement in fibromyalgia symptoms with
35 acupuncture: Results of a randomized controlled trial. *Mayo Clinic proceedings*
36 2006;81(6):749-57. *inappropriate intervention*
37 233. Martín J, Torre F, Aguirre U, et al. Evaluation of the interdisciplinary PSYMEPHY
38 treatment on patients with fibromyalgia: A randomized control trial. *Pain Medicine*
39 2014;15(4):682-91. doi: 10.1111/pme.12375 *inappropriate intervention*
40 234. Martín J, Torre F, Padierna A, et al. Six-and 12-month follow-up of an
41 interdisciplinary fibromyalgia treatment programme: results of a randomised trial.
42 *Clinical and experimental rheumatology* 2012;30(6 Suppl 74):103-11. [published
43 Online First: 2013/02/27] *inappropriate intervention*
44 235. Martín J, Torre F, Padierna A, et al. Interdisciplinary treatment of patients with
45 fibromyalgia: improvement of their health-related quality of life. *Pain practice : the*
46 *official journal of World Institute of Pain* 2014; 14(8).
47 <http://onlinelibrary.wiley.com/doi/10.1111/ijcp.12727>.
48 <http://onlinelibrary.wiley.com/doi/10.1111/ijcp.12727>. *inappropriate intervention*
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 236. Martin J, Torre F, Padierna A, et al. Impact of interdisciplinary treatment on
4 physical and psychosocial parameters in patients with fibromyalgia: results of a
5 randomised trial. *International journal of clinical practice* 2014;68(5):618-27.
6 [published Online First: 2014/05/29] *inappropriate intervention*
7
8 237. Martín-Nogueras AM, Calvo-Arenillas JI. Efficacy of physiotherapy treatment on
9 pain and quality of life in patients with fibromyalgia. *Rehabilitacion*
10 2012;46(3):199-206. *inappropriate intervention*
11
12 238. Martins MRI, Gritti CC, dos Santos R, et al. Randomized controlled trial of a
13 therapeutic intervention group in patients with fibromyalgia syndrome. *Revista*
14 *Brasileira De Reumatologia* 2014;54(3):179-84. doi: 10.1016/j.rbre.2013.10.002
15 *inappropriate intervention*
16
17 239. Mata J, Cabrera S, Sanchis P, et al. Electro-acupuncture for treatment of knee
18 pain from osteoarthritis and the possible endocrinology changes: a study protocol
19 for a randomized controlled trial. *Trials* 2015;16:248. doi: 10.1186/s13063-015-
20 0766-2 [published Online First: 2015/06/04] *inappropriate study design*
21
22 240. Mataran-Penarrocha GA, Castro-Sanchez AM, Garcia GC, et al. Influence of
23 Craniosacral Therapy on Anxiety, Depression and Quality of Life in Patients with
24 Fibromyalgia. *Evidence-Based Complementary and Alternative Medicine* 2011:1-
25 9. doi: 10.1093/ecam/nep125 *inappropriate intervention*
26
27 241. Matcham F, Norton S, Scott D, et al. The impact of depression on long-term
28 physical health outcomes in rheumatoid arthritis. *Rheumatology (United*
29 *Kingdom)* 2014; 53.
30 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/273/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/273/CN-01057273/frame.html)
31 [01057273/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/273/CN-01057273/frame.html). *inappropriate study design*
32
33 242. Matcham F, Norton S, Scott DL, et al. Symptoms of depression and anxiety
34 predict treatment response and long-term physical health outcomes in
35 rheumatoid arthritis: secondary analysis of a randomized controlled trial.
36 *Rheumatology (Oxford, England)* 2016;55(2):268-78. doi:
37 10.1093/rheumatology/kev306 [published Online First: 2015/09/10] *inappropriate*
38 *study design*
39
40 243. McBain H, Shipley M, Olaleye A, et al. A patient-initiated DMARD self-monitoring
41 service for people with rheumatoid or psoriatic arthritis on methotrexate: A
42 randomised controlled trial. *Annals of the rheumatic diseases* 2016; 75(7).
43 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/299/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/299/CN-01178299/frame.html)
44 [01178299/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/299/CN-01178299/frame.html). *inappropriate intervention*
45
46 244. McVeigh JG, Hurley DA, Basford JR, et al. Effectiveness of a combined pool-
47 based exercise and education programme compared to usual medical care in
48 fibromyalgia syndrome: a randomised, controlled trial. *Physical Therapy Reviews*
49 2006;11(3):217-17. *inappropriate study design*
50
51 245. Mendonca ME, Simis M, Grecco LC, et al. Transcranial Direct Current
52 Stimulation Combined with Aerobic Exercise to Optimize Analgesic Responses in
53 Fibromyalgia: A Randomized Placebo-Controlled Clinical Trial. *Frontiers in*
54 *human neuroscience* 2016;10:68. doi: 10.3389/fnhum.2016.00068 [published
55 Online First: 2016/03/26] *inappropriate intervention*
56
57 246. Menkes CJ, Godeau P. Fibromyalgia. *Bulletin De L Academie Nationale De*
58 *Medecine* 2007;191(1):143-48. *inappropriate study design*
59
60

- 1
2
3 247. Mercadie L, Mick G, Guetin S, et al. Effects of Listening to Music versus
4 Environmental Sounds in Passive and Active Situations on Levels of Pain and
5 Fatigue in Fibromyalgia. *Pain Management Nursing* 2015;16(5):664-71. doi:
6 10.1016/j.pmn.2015.01.005 *inappropriate intervention*
7
8 248. Meyer BB, Lemley KJ. Utilizing exercise to affect the symptomology of
9 fibromyalgia: a pilot study. *Medicine and science in sports and exercise*
10 2000;32(10):1691-7. [published Online First: 2000/10/20] *inappropriate study*
11 *design*
12 249. Mibielli M, Nunes C, Cezar P, et al. Osteoarthritis: Clinical evaluation of
13 diclofenac combined with the B complex vitamins. *Revista brasileira de medicina*
14 2009; 66(7). [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/674/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/674/CN-00753674/frame.html)
15 [00753674/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/674/CN-00753674/frame.html). *inappropriate intervention*
16
17 250. Middleton KR, Ward MM, Haaz S, et al. A pilot study of yoga as self-care for
18 arthritis in minority communities. *Health and quality of life outcomes* 2013;11:55.
19 doi: 10.1186/1477-7525-11-55 [published Online First: 2013/04/04] *inappropriate*
20 *intervention*
21 251. Miles ALS. The effects of gentle yoga vs. cognitive behavioral therapy on
22 physical and psychological symptoms; neurocognitive functioning; and
23 physiology in women with Fibromyalgia. ProQuest Information & Learning, 2014.
24 *inappropriate intervention*
25
26 252. Minor MA. Exercise maintenance behavior of subjects with arthritis following
27 participation in a supervised exercise program [Ph.D.]. University of Missouri -
28 Columbia, 1989. *inappropriate study design*
29
30 253. Minor MA, Brown JD. Exercise maintenance of persons with arthritis after
31 participation in a class experience. *Health education quarterly* 1993;20(1):83-95.
32 [published Online First: 1993/01/01] *inappropriate study design*
33
34 254. Mirtaheri E, Gargari BP, Kolahi S, et al. Effects of Alpha-Lipoic Acid
35 Supplementation on Inflammatory Biomarkers and Matrix Metalloproteinase-3 in
36 Rheumatoid Arthritis Patients. *Journal of the American College of Nutrition*
37 2015;34(4):310-17. doi: 10.1080/07315724.2014.910740 *inappropriate*
38 *intervention*
39 255. Mishra P, Trivedi V. Acupuncture in the treatment of rheumatoid arthritis: Results
40 of a randomized controlled trial. *Annals of the rheumatic diseases* 2014; 73.
41 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/582/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/582/CN-01009582/frame.html)
42 [01009582/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/582/CN-01009582/frame.html). *inappropriate intervention*
43
44 256. Moore RA, Straube S, Paine J, et al. Fibromyalgia: Moderate and substantial
45 pain intensity reduction predicts improvement in other outcomes and substantial
46 quality of life gain. *Pain* 2010;149(2):360-64. doi: 10.1016/j.pain.2010.02.039
47 *inappropriate study design*
48
49 257. Morgan N, Driban J, Ransford G, et al. Construct validity of promis instruments
50 among patients with symptomatic knee osteoarthritis. *Osteoarthritis and cartilage*
51 2013; 21. [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/483/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/483/CN-01010483/frame.html)
52 [01010483/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/483/CN-01010483/frame.html). *inappropriate study design*
53
54 258. Morgan N, Ransford G, Morgan L, et al. Mindfulness is associated with
55 psychological symptoms, self-efficacy, and quality of life among patients with
56 symptomatic knee osteoarthritis. *Osteoarthritis and cartilage* 2013; 21.
57
58
59

- 1
2
3 <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/479/CN-01010479/frame.html>. *inappropriate study design*
- 4
5 259. Morone N, Karp J, Lynch C, et al. Impact of chronic musculoskeletal pathology
6 on older adults: a study of differences between knee OA and low back pain. *Pain*
7 *medicine (Malden, Mass)* 2009; 10(4).
8 <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/087/CN-00721087/frame.html>. *inappropriate study design*
- 9
10 260. Moroshko I, Brennan L, O'Brien P. Predictors of dropout in weight loss
11 interventions: A systematic review of the literature. *Obesity Reviews*
12 2011;12(11):912-34. doi: 10.1111/j.1467-789X.2011.00915.x *inappropriate study*
13 *design*
- 14
15 261. Morris LD, Grimmer-Somers KA, Spottiswoode B, et al. Virtual reality exposure
16 therapy as treatment for pain catastrophizing in fibromyalgia patients: proof-of-
17 concept study (Study Protocol). *BMC musculoskeletal disorders* 2011;12(1):85.
18 doi: 10.1186/1471-2474-12-85 [published Online First: 2011/05/03] *inappropriate*
19 *study design*
- 20
21 262. Moustafa IM, Diab AA. The addition of upper cervical manipulative therapy in the
22 treatment of patients with fibromyalgia: a randomized controlled trial.
23 *Rheumatology international* 2015;35(7):1163-74. doi: 10.1007/s00296-015-3248-
24 7 [published Online First: 2015/03/19] *inappropriate intervention*
- 25
26 263. Mu PF, Chen YC, Cheng SC. The effectiveness of non-pharmacological pain
27 management in relieving chronic pain for children and adolescents. *JBI library of*
28 *systematic reviews* 2009;7(34):1489-543. [published Online First: 2009/01/01]
29 *inappropriate population*
- 30
31 264. Munguia-Izquierdo D, Legaz-Arrese A. Determinants of sleep quality in middle-
32 aged women with fibromyalgia syndrome. *Journal of Sleep Research*
33 2012;21(1):73-79. doi: 10.1111/j.1365-2869.2011.00929.x *inappropriate*
34 *outcomes*
- 35
36 265. Murphy LB, Sacks JJ, Brady TJ, et al. Anxiety and depression among US adults
37 with arthritis: Prevalence and correlates. *Arthritis care & research*
38 2012;64(7):968-76. doi: 10.1002/acr.21685 *inappropriate study design*
- 39
40 266. Murphy SL, Lyden AK, Kratz AL, et al. Characterizing Pain Flares From the
41 Perspective of Individuals With Symptomatic Knee Osteoarthritis. *Arthritis care &*
42 *research* 2015;67(8):1103-11. doi: 10.1002/acr.22545 *inappropriate study design*
- 43
44 267. Nalamachu S, Rauck R, Hale M, et al. A long-term, open-label safety study of
45 single-entity hydrocodone bitartrate extended release for the treatment of
46 moderate to severe chronic pain. *Journal of pain research* 2014; 7.
47 <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/077/CN-01036077/frame.html>. *inappropriate intervention*
- 48
49 268. Navarrete-Navarrete N, Peralta-Ramirez MI, Sabio-Sanchez JM, et al. Efficacy of
50 Cognitive Behavioural Therapy for the Treatment of Chronic Stress in Patients
51 with Lupus Erythematosus: A Randomized Controlled Trial. *Psychotherapy and*
52 *Psychosomatics* 2010;79(2):107-15. doi: 10.1159/000276370 *inappropriate*
53 *population*
- 54
55 269. Nazareth I, Landau S, Yardley L, et al. Patterns of presentations of dizziness in
56 primary care - a cross-sectional cluster analysis study. *Journal of psychosomatic*
57
58
59
60

- 1
2
3 *research* 2006;60(4):395-401. doi: 10.1016/j.jpsychores.2005.07.011
4 *inappropriate study design*
- 5 270. Niedermann K, de Bie RA, Kubli R, et al. Effectiveness of individual resource-
6 oriented joint protection education in people with rheumatoid arthritis. A
7 randomized controlled trial. *Patient education and counseling* 2011;82(1):42-48.
8 doi: 10.1016/j.pec.2010.02.014 *inappropriate intervention*
- 9 271. Noiseux NO, Callaghan JJ, Clark CR, et al. Preoperative predictors of pain
10 following total knee arthroplasty. *The Journal of arthroplasty* 2014;29(7):1383-7.
11 doi: 10.1016/j.arth.2014.01.034 [published Online First: 2014/03/19]
12 *inappropriate study design*
- 13 272. Noppers I, Niesters M, Swartjes M, et al. Absence of long-term analgesic effect
14 from a short-term S-ketamine infusion on fibromyalgia pain: A randomized,
15 prospective, double blind, active placebo-controlled trial. *European Journal of*
16 *Pain* 2011;15(9):942-49. doi: 10.1016/j.ejpain.2011.03.008 *inappropriate*
17 *intervention*
- 18 273. Nordeman L, Gunnarsson R, Mannerkorpi K. Prevalence and Characteristics of
19 Widespread Pain in Female Primary Health Care Patients With Chronic Low
20 Back Pain. *Clinical Journal of Pain* 2012;28(1):65-72. doi:
21 10.1097/AJP.0b013e318223622c *inappropriate population*
- 22 274. Nugraha B, Korallus C, Dorffer D, et al. Aerobic exercise cognitive behavioural
23 therapy and combination of treatment in fibromyalgia syndrome patients: A
24 randomized control trial (effect on mood related disorder-a preliminary result).
25 *PM and R* 2014; 6(8 suppl. 2).
26 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/639/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/639/CN-01086639/frame.html)
27 [01086639/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/639/CN-01086639/frame.html). *inappropriate study design*
- 28 275. Nyssen OP, Taylor SJC, Wong G, et al. Does therapeutic writing help people with
29 long-term conditions? Systematic review, realist synthesis and economic
30 considerations. *Health Technology Assessment* 2016;20(27):1-367. doi:
31 10.3310/hta20270 *inappropriate study design*
- 32 276. Ohta H, Oka H, Usui C, et al. A randomized, double-blind, multicenter, placebo-
33 controlled phase III trial to evaluate the efficacy and safety of pregabalin in
34 Japanese patients with fibromyalgia. *Arthritis research & therapy* 2012; 14(5).
35 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/489/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/489/CN-00913489/frame.html)
36 [00913489/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/489/CN-00913489/frame.html). *inappropriate intervention*
- 37 277. Oktayoglu P, Gur A, Yardimeden I, et al. Comparison of the efficacy of
38 phonophoresis and conventional ultrasound therapy in patients with primary knee
39 osteoarthritis. *Erciyes Tip Dergisi* 2014; 36(1).
40 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/055/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/055/CN-00988055/frame.html)
41 [00988055/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/055/CN-00988055/frame.html). *inappropriate intervention*
- 42 278. Olin R, Klein R, Berg PA. A randomised double-blind 16-week study of ritanserin
43 in fibromyalgia syndrome: clinical outcome and analysis of autoantibodies to
44 serotonin, gangliosides and phospholipids. *Clinical rheumatology* 1998;17(2):89-
45 94. [published Online First: 1998/06/26] *inappropriate intervention*
- 46 279. Olivan-Blázquez B, Herrera-Mercadal P, Puebla-Guedea M, et al. Efficacy of
47 memantine in the treatment of fibromyalgia: A double-blind, randomised,
48
49
50
51
52
53
54
55
56
57
58
59

- 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/doi/10.1111/j.1469-7610.2011.02474.x> *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 &*

- 1
2
3 *Science in Sports* 2015;25:1-72. doi: 10.1111/sms.12581 *inappropriate study*
4 *design*
5 291. Peres M. Fibromyalgia and headache disorders. *Current pain and headache*
6 *reports* 2009; 13(5).
7 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/879/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/879/CN-00958879/frame.html)
8 [00958879/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/879/CN-00958879/frame.html). *inappropriate study design*
9
10 292. Perrot S, Russell IJ. More ubiquitous effects from non-pharmacologic than from
11 pharmacologic treatments for fibromyalgia syndrome: a meta-analysis examining
12 six core symptoms. *European journal of pain (London, England)*
13 2014;18(8):1067-80. doi: 10.1002/ejp.564 [published Online First: 2014/08/21]
14 *inappropriate study design*
15
16 293. Peters S, Stanley I, Rose M, et al. A randomized controlled trial of group aerobic
17 exercise in primary care patients with persistent, unexplained physical
18 symptoms. *Family Practice* 2002;19(6):665-74. doi: 10.1093/fampra/19.6.665
19 *inappropriate population*
20
21 294. Potvin S, Morin M, Cloutier C, et al. Add-on treatment of quetiapine for
22 fibromyalgia: A pilot, randomized, double-blind, placebo-controlled 12-week trial.
23 *Journal of Clinical Psychopharmacology* 2012;32(5):684-87. doi:
24 10.1097/JCP.0b013e318267b8ca *inappropriate intervention*
25
26 295. Preece JC. The relationship between family resilience and the successful
27 management of fibromyalgia [Ph.D.]. Syracuse University, 2001. *inappropriate*
28 *study design*
29
30 296. Rakel B, Zimmerman M, Geasland K, et al. Transcutaneous electrical nerve
31 stimulation for the control of pain during rehabilitation after total knee
32 arthroplasty: A randomized, blinded, placebo-controlled trial. *Pain* 2014; 155(12).
33 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/744/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/744/CN-01052744/frame.html)
34 [01052744/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/744/CN-01052744/frame.html). *inappropriate intervention*
35
36 297. Redondo JR, Justo CM, Moraleda FV, et al. Long-term efficacy of therapy in
37 patients with fibromyalgia: a physical exercise-based program and a cognitive-
38 behavioral approach. *Arthritis and rheumatism* 2004;51(2):184-92. doi:
39 10.1002/art.20252 [published Online First: 2004/04/13] *inappropriate*
40 *comparison group*
41
42 298. Richards DA, Hill JJ, Gask L, et al. Clinical effectiveness of collaborative care for
43 depression in UK primary care (CADET): Cluster randomised controlled trial.
44 *BMJ: British Medical Journal* 2013;347 *inappropriate population*
45
46 299. Rini C, Porter LS, Somers TJ, et al. Automated Internet-based pain coping skills
47 training to manage osteoarthritis pain: a randomized controlled trial. *Pain*
48 2015;156(5):837-48. doi: 10.1097/j.pain.000000000000121 [published Online
49 First: 2015/03/04] *inappropriate intervention*
50
51 300. Rodriguez Huerta MD, Trujillo-Martin MM, Rua-Figueroa I, et al. Healthy lifestyle
52 habits for patients with systemic lupus erythematosus: A systemic review.
53 *Seminars in arthritis and rheumatism* 2016;45(4):463-70. doi:
54 10.1016/j.semarthrit.2015.09.003 [published Online First: 2015/11/03]
55 *inappropriate population*
56
57 301. Rodriguez Torres J, Cabrera Martos I, Torres Sanchez I, et al. Results of an
58 Active Neurodynamic Mobilization Program in Patients With Fibromyalgia
59
60

- 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/doi/10.1136/annrheumdis-2012-021625>. *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

- 1
2
3 Trial. *Journal of Bone and Joint Surgery-American Volume* 2014;96A(11):944-50.
4 doi: 10.2106/jbjs.I.01696 *inappropriate population*
- 5 312. Schmidt S, Grossman P, Schwarzer B, et al. Treating fibromyalgia with
6 mindfulness-based stress reduction: results from a 3-armed randomized
7 controlled trial. *Pain* 2011;152(2):361-9. doi: 10.1016/j.pain.2010.10.043
8 [published Online First: 2010/12/15] *inappropriate intervention*
- 9 313. Scopaz KA, Piva SR, Wisniewski S, et al. Relationships of Fear, Anxiety, and
10 Depression With Physical Function in Patients With Knee Osteoarthritis. *Archives*
11 *of physical medicine and rehabilitation* 2009;90(11):1866-73. doi:
12 10.1016/j.apmr.2009.06.012 *inappropriate study design*
- 13 314. Selfridge N. Meditation for Fibromyalgia: Yea or Nay? *Alternative Medicine Alert*
14 2011;14(3):34-36. *inappropriate intervention*
- 15 315. Shadick NA, Sowell NF, Frits ML, et al. A randomized controlled trial of an
16 internal family systems-based psychotherapeutic intervention on outcomes in
17 rheumatoid arthritis: a proof-of-concept study. *The Journal of rheumatology*
18 2013;40(11):1831-41. doi: 10.3899/jrheum.121465 [published Online First:
19 2013/08/21] *inappropriate intervention*
- 20 316. Shahabi L, Naliboff BD, Shapiro D. Self-regulation evaluation of therapeutic yoga
21 and walking for patients with irritable bowel syndrome: a pilot study. *Psychology*
22 *Health & Medicine* 2016;21(2):176-88. doi: 10.1080/13548506.2015.1051557
23 *inappropriate population*
- 24 317. Shahrbanian S, Duquette P, Kuspinar A, et al. Contribution of symptom clusters
25 to multiple sclerosis consequences. *Quality of Life Research* 2015;24(3):617-29.
26 doi: 10.1007/s11136-014-0804-7 *inappropriate population*
- 27 318. Sharpe L, Gittins CB, Correia HM, et al. Problem-solving versus cognitive
28 restructuring of medically ill seniors with depression (PROMISE-D trial): study
29 protocol and design. *Bmc Psychiatry* 2012;12 doi: 10.1186/1471-244x-12-207
30 *inappropriate study design*
- 31 319. Sharpe L, Sensky T, Allard S. The course of depression in recent onset
32 rheumatoid arthritis: the predictive role of disability, illness perceptions, pain and
33 coping. *Journal of psychosomatic research* 2001;51(6):713-9. [published Online
34 First: 2001/12/26] *inappropriate study design*
- 35 320. Sharpe L, Sensky T, Timberlake N, et al. Long-term efficacy of a cognitive
36 behavioural treatment from a randomized controlled trial for patients recently
37 diagnosed with rheumatoid arthritis. *Rheumatology (Oxford, England)* 2003;
38 42(3). [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/463/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/463/CN-00431463/frame.html)
39 [00431463/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/463/CN-00431463/frame.html). *inappropriate intervention*
- 40 321. Sharpe L, Sensky T, Timberlake N, et al. A blind, randomized, controlled trial of
41 cognitive-behavioural intervention for patients with recent onset rheumatoid
42 arthritis: preventing psychological and physical morbidity. *Pain* 2001; 89(2-3).
43 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/279/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/279/CN-00327279/frame.html)
44 [00327279/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/279/CN-00327279/frame.html). *inappropriate intervention*
- 45 322. Shih M, Hootman JM, Kruger J, et al. Physical activity in men and women with
46 arthritis - National Health Interview Survey, 2002. *American Journal of Preventive*
47 *Medicine* 2006;30(5):385-93. doi: 10.1016/j.amepre.2005.12.005 *inappropriate*
48 *intervention*
- 49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 323. Shupak NM, McKay JC, Nielson WR, et al. Exposure to a specific pulsed low-
4 frequency magnetic field: A double-blind placebo-controlled study of effects on
5 pain ratings in rheumatoid arthritis and fibromyalgia patients. *Pain Research &*
6 *Management* 2006;11(2):85-90. doi: 10.1155/2006/842162 *inappropriate*
7 *intervention*
8
9 324. Siegel KM. The effects of emotional disclosure on physical symptoms, healthcare
10 utilization, and psychosocial adjustment in patients with irritable bowel syndrome
11 [Ph.D.]. Alliant International University, San Diego, 2003. *inappropriate*
12 *population*
13
14 325. Skrabek RQ, Galimova L, Ethans K, et al. Nabilone for the treatment of pain in
15 fibromyalgia. *The journal of pain : official journal of the American Pain Society*
16 2008;9(2):164-73. doi: 10.1016/j.jpain.2007.09.002 [published Online First:
17 2007/11/03] *inappropriate intervention*
18
19 326. Slavich GM, Irwin MR. From Stress to Inflammation and Major Depressive
20 Disorder: A Social Signal Transduction Theory of Depression. *Psychological*
21 *Bulletin* 2014;140(3):774-815. doi: 10.1037/a0035302 *inappropriate study design*
22
23 327. Smeets RJ, Maher CG, Nicholas MK, et al. Do psychological characteristics
24 predict response to exercise and advice for subacute low back pain? *Arthritis and*
25 *rheumatism* 2009;61(9):1202-9. doi: 10.1002/art.24731 [published Online First:
26 2009/08/29] *inappropriate study design*
27
28 328. Smith-Ray R, Fitzgibbon M, Tussing-Humphreys L, et al. Fit and Strong! Plus:
29 Design of a comparative effectiveness evaluation of a weight management
30 program for older adults with osteoarthritis. *Contemporary clinical trials* 2014;
31 37(2). [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/212/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/212/CN-00959212/frame.html)
32 [00959212/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/212/CN-00959212/frame.html). *inappropriate study design*
33
34 329. Sørensen J, Bengtsson A, Ahlner J, et al. Fibromyalgia--are there different
35 mechanisms in the processing of pain? A double blind crossover comparison of
36 analgesic drugs. *The Journal of rheumatology* 1997; 24(8).
37 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/709/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/709/CN-00142709/frame.html)
38 [00142709/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/709/CN-00142709/frame.html). *inappropriate intervention*
39
40 330. Stehlik R, Ulfberg J, Hedner J, et al. High prevalence of restless legs syndrome
41 among women with multi-site pain: A population-based study in Dalarna,
42 Sweden. *European Journal of Pain* 2014;18(10):1402-09. doi: 10.1002/ejp.504
43 *inappropriate outcomes*
44
45 331. Stiller C. The effect of therapeutic touch on fibromyalgia pain and anxiety [Ph.D.].
46 Case Western Reserve University (Health Sciences), 2006. *inappropriate*
47 *intervention*
48
49 332. Stratz T, Mennet P, Benn H, et al. [Blocking of S2 receptors--a new treatment
50 principle in generalized tendomyopathy (fibromyalgia)?]. *Zeitschrift fur*
51 *Rheumatologie* 1991; 50(1).
52 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/788/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/788/CN-00353788/frame.html)
53 [00353788/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/788/CN-00353788/frame.html). *inappropriate intervention*
54
55 333. Sulenes K, Freitas J, Justice L, et al. Underuse of Yoga as a Referral Resource
56 by Health Professions Students. *Journal of Alternative and Complementary*
57 *Medicine* 2015;21(1):53-59. doi: 10.1089/acm.2014.0217 *inappropriate*
58 *intervention*
59
60

- 1
2
3 334. Sutbeyaz S, Sezer N, Koseoglu F, et al. Low-frequency pulsed electromagnetic
4 field therapy in fibromyalgia: a randomized, double-blind, sham-controlled clinical
5 study. *The Clinical journal of pain* 2009; 25(8).
6 <http://onlinelibrary.wiley.com/doi/10.1002/9781118130171.ch60>. *inappropriate intervention*
- 7
8 335. Sverdrup B. Use less cosmetics--suffer less from fibromyalgia? *Journal of*
9 *women's health (2002)* 2004; 13(2).
10 <http://onlinelibrary.wiley.com/doi/10.1002/9781118130171.ch70>. *inappropriate intervention*
- 11
12 336. Tang NK, Lereya ST, Boulton H, et al. Nonpharmacological Treatments of
13 Insomnia for Long-Term Painful Conditions: A Systematic Review and Meta-
14 analysis of Patient-Reported Outcomes in Randomized Controlled Trials. *Sleep*
15 2015;38(11):1751-64. doi: 10.5665/sleep.5158 [published Online First:
16 2015/04/24] *inappropriate study design*
- 17
18 337. Tang NKY, Goodchild CE, Salkovskis PM. Hybrid cognitive-behaviour therapy for
19 individuals with insomnia and chronic pain: A pilot randomised controlled trial.
20 *Behaviour Research and Therapy* 2012;50(12):814-21. doi:
21 10.1016/j.brat.2012.08.006 *inappropriate population*
- 22
23 338. Tarakci E, Yeldan I, Kaya Mutlu E, et al. The relationship between physical
24 activity level, anxiety, depression, and functional ability in children and
25 adolescents with juvenile idiopathic arthritis. *Clinical rheumatology*
26 2011;30(11):1415-20. doi: 10.1007/s10067-011-1832-0 [published Online First:
27 2011/09/03] *inappropriate population*
- 28
29 339. Teunis T, Thornton ER, Guitton TG, et al. Coaching of patients with an isolated
30 minimally displaced fracture of the radial head immediately increases range of
31 motion. *Journal of Hand Therapy* 2016;29(3):314-19. doi:
32 10.1016/j.jht.2016.02.003 *inappropriate population*
- 33
34 340. Thomas K, Muir K, Doherty M, et al. Home based exercise programme for knee
35 pain and knee osteoarthritis: randomised controlled trial. *BMJ (Clinical research*
36 *ed)* 2002; 325(7367).
37 <http://onlinelibrary.wiley.com/doi/10.1136/bmj.325.7367>. *inappropriate population*
- 38
39 341. Tonkins WP, Jr. Effect of Hatha yoga on selected parameters of cardiac fitness in
40 African-American college students [Dr.P.H.]. Morgan State University, 2004.
41 *inappropriate intervention*
- 42
43 342. Torres JR, Martos IC, Sanchez IT, et al. Results of an Active Neurodynamic
44 Mobilization Program in Patients With Fibromyalgia Syndrome: A Randomized
45 Controlled Trial. *Archives of physical medicine and rehabilitation*
46 2015;96(10):1771-8. doi: 10.1016/j.apmr.2015.06.008 [published Online First:
47 2015/07/06] *inappropriate intervention*
- 48
49 343. Torres X, Herrero MJ, Marti M, et al. Why people with fibromyalgia persist in
50 activity despite the increasing pain? A Delphi Study of the content of the Clinic
51 Scale of Persistence in Activity in Fibromyalgia. *Revista De Psiquiatria Y Salud*
52 *Mental* 2013;6(1):33-44. doi: 10.1016/j.rpsm.2012.03.001 *inappropriate study*
53 *design*
- 54
55
56
57
58
59
60

- 1
2
3 344. Toth C, Brady S, Gagnon F, et al. A Randomized, Single-Blind, Controlled,
4 Parallel Assignment Study of Exercise Versus Education as Adjuvant in the
5 Treatment of Peripheral Neuropathic Pain. *Clinical Journal of Pain*
6 2014;30(2):111-18. doi: 10.1097/AJP.0b013e31828ccd0f *inappropriate*
7 *population*
8
9 345. Tousignant-Laflamme Y, Bourgault P, Masetto A, et al. Short term impact of brief
10 education for symptom management in fibromyalgia-the PEGASO study. *Journal*
11 *of pain* 2014; 15(4 suppl. 1).
12 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/679/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/679/CN-01058679/frame.html)
13 [01058679/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/679/CN-01058679/frame.html). *inappropriate intervention*
14
15 346. Trudeau KJ, Pujol LA, DasMahapatra P, et al. A randomized controlled trial of an
16 online self-management program for adults with arthritis pain. *Journal of*
17 *Behavioral Medicine* 2015;38(3):483-96. doi: 10.1007/s10865-015-9622-9
18 *inappropriate intervention*
19
20 347. Uceyler N, Hauser W, Sommer C. A systematic review on the effectiveness of
21 treatment with antidepressants in fibromyalgia syndrome. *Arthritis Care and*
22 *Research* 2008; 59(9).
23 [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/590/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/590/CN-00898590/frame.html)
24 [00898590/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/590/CN-00898590/frame.html). *inappropriate study design*
25
26 348. Ulus Y, Tander B, Akyol Y, et al. Therapeutic ultrasound versus sham ultrasound
27 for the management of patients with knee osteoarthritis: a randomized double-
28 blind controlled clinical study. *International journal of rheumatic diseases* 2012;
29 15(2). [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/676/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/676/CN-00896676/frame.html)
30 [00896676/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/676/CN-00896676/frame.html). *inappropriate intervention*
31
32 349. Vaghef-Mehrabany E, Alipour B, Homayouni-Rad A, et al. Probiotic
33 supplementation improves inflammatory status in patients with rheumatoid
34 arthritis. *Nutrition* 2014;30(4):430-35. doi: 10.1016/j.nut.2013.09.007
35 *inappropriate intervention*
36
37 350. Vaghef-Mehrabany E, Homayouni-Rad A, Alipour B, et al. Effects of Probiotic
38 Supplementation on Oxidative Stress Indices in Women with Rheumatoid
39 Arthritis: A Randomized Double-Blind Clinical Trial. *Journal of the American*
40 *College of Nutrition* 2016;35(4):291-99. *inappropriate intervention*
41
42 351. Valencia M, Alonso B, Alvarez M, et al. Effects of 2 physiotherapy programs on
43 pain perception, muscular flexibility, and illness impact in women with
44 fibromyalgia: a pilot study. *Journal of manipulative and physiological therapeutics*
45 2009; 32(1). [http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/935/CN-](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/935/CN-00680935/frame.html)
46 [00680935/frame.html](http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/935/CN-00680935/frame.html). *inappropriate comparison group*
47
48 352. Valim V, Oliveira L, Suda A, et al. Aerobic fitness effects in fibromyalgia. *The*
49 *Journal of rheumatology* 2003;30(5):1060-9. [published Online First: 2003/05/08]
50 *inappropriate intervention*
51
52 353. Vallejo MA, Ortega J, Rivera J, et al. Internet versus face-to-face group cognitive-
53 behavioral therapy for fibromyalgia: A randomized control trial. *Journal of*
54 *Psychiatric Research* 2015;68:106-13. doi: 10.1016/j.jpsychires.2015.06.006
55 *inappropriate intervention*
56
57 354. van Koullil S, Kraaimaat FW, van Lankveld W, et al. A patient's perspective on
58 multidisciplinary treatment gain for fibromyalgia: an indicator for pre-post
59

- 1
2
3 treatment effects? *Arthritis and rheumatism* 2009;61(12):1626-32. doi:
4 10.1002/art.24792 [published Online First: 2009/12/02] *inappropriate study*
5 *design*
6
7 355. van Koulil S, van Lankveld W, Kraaimaat FW, et al. Tailored cognitive-behavioral
8 therapy and exercise training for high-risk patients with fibromyalgia. *Arthritis*
9 *care & research* 2010;62(10):1377-85. doi: 10.1002/acr.20268 [published Online
10 First: 2010/06/04] *inappropriate intervention*
11
12 356. Van Puymbroeck M, Payne LL, Hsieh PC. A phase I feasibility study of yoga on
13 the physical health and coping of informal caregivers. *Evidence-Based*
14 *Complementary and Alternative Medicine* 2007;4(4):519-29. doi:
15 10.1093/ecam/nem075 *inappropriate population*
16
17 357. van Wilgen CP, Dijkstra PU, Versteegen GJ, et al. CHRONIC PAIN AND
18 SEVERE DISUSE SYNDROME: LONG-TERM OUTCOME OF AN INPATIENT
19 MULTIDISCIPLINARY COGNITIVE BEHAVIOURAL PROGRAMME. *Journal of*
20 *rehabilitation medicine* 2009;41(3):122-28. doi: 10.2340/16501977-0292
21 *inappropriate intervention*
22
23 358. Vayvay ES, Tok D, Turgut E, et al. The effect of Laser and taping on pain,
24 functional status and quality of life in patients with fibromyalgia syndrome: A
25 placebo- randomized controlled clinical trial. *Journal of back and musculoskeletal*
26 *rehabilitation* 2016;29(1):77-83. doi: 10.3233/bmr-150600 [published Online First:
27 2015/09/26] *inappropriate intervention*
28
29 359. Vendrig AA, Lousberg R. Within-person relationships among pain intensity, mood
30 and physical activity in chronic pain: a naturalistic approach. *Pain* 1997;73(1):71-
31 76. doi: 10.1016/s0304-3959(97)00075-4 *inappropriate intervention*
32
33 360. Vergne-Salle P, Dufauget-Lombard C, Bonnet C, et al. A randomised, double-
34 blind, placebo-controlled trial of dolasetron, a 5-hydroxytryptamine 3 receptor
35 antagonist, in patients with fibromyalgia. *European Journal of Pain*
36 2011;15(5):509-14. doi: 10.1016/j.ejpain.2010.09.013 *inappropriate intervention*
37
38 361. Verra ML, Angst F, Beck T, et al. Horticultural therapy for patients with chronic
39 musculoskeletal pain: results of a pilot study. *Alternative therapies in health and*
40 *medicine* 2012;18(2):44-50. [published Online First: 2012/04/21] *inappropriate*
41 *study design*
42
43 362. Verra ML, Angst F, Brioschi R, et al. Does classification of persons with
44 fibromyalgia into Multidimensional Pain Inventory subgroups detect differences in
45 outcome after a standard chronic pain management program? *Pain Research &*
46 *Management* 2009;14(6):445-53. *inappropriate study design*
47
48 363. Verra ML, Angst F, Staal JB, et al. Differences in pain, function and coping in
49 Multidimensional Pain Inventory subgroups of chronic back pain: a one-group
50 pretest-posttest study. *BMC musculoskeletal disorders* 2011;12 doi:
51 10.1186/1471-2474-12-145 *inappropriate study design*
52
53 364. VillafaÑE JH, Cleland JA, FernÁNdez-De-Las-PeÑAs C. The Effectiveness of a
54 Manual Therapy and Exercise Protocol in Patients With Thumb Carpometacarpal
55 Osteoarthritis: A Randomized Controlled Trial. *Journal of Orthopaedic & Sports*
56 *Physical Therapy* 2013;43(4):204-13. *inappropriate intervention*
57
58 365. VillafaÑe JH, Silva GB, Bishop MD, et al. Radial Nerve Mobilization Decreases
59 Pain Sensitivity and Improves Motor Performance in Patients With Thumb
60

- 1
2
3 Carpometaacarpal Osteoarthritis: A Randomized Controlled Trial. *Archives of*
4 *Physical Medicine & Rehabilitation* 2012;93(3):396-403. *inappropriate*
5 *intervention*
6
7 366. Villanueva-Torrecillas I. Affectivity, quality of life and health resources utilization
8 in arthritis [Ph.D.]. The University of Arizona, 2003. *inappropriate outcomes*
9
10 367. Vincent KR, Vincent HK. Resistance exercise for knee osteoarthritis. *PM & R :*
11 *the journal of injury, function, and rehabilitation* 2012;4(5 Suppl):S45-52. doi:
12 10.1016/j.pmrj.2012.01.019 [published Online First: 2012/06/01] *inappropriate*
13 *study design*
14 368. Vriezolk JE, Eijsbouts AMM, van Lankveld WGJM, et al. An acceptance-
15 oriented cognitive-behavioral therapy in multimodal rehabilitation: A pre-post test
16 evaluation in highly distressed patients with rheumatic diseases. *Patient*
17 *education and counseling* 2013;91(3):357-63. doi: 10.1016/j.pec.2013.01.018
18 *inappropriate study design*
19 369. Wang C, Schmid CH, Hibberd PL, et al. Tai Chi for treating knee osteoarthritis:
20 designing a long-term follow up randomized controlled trial. *BMC*
21 *musculoskeletal disorders* 2008;9:108. doi: 10.1186/1471-2474-9-108 [published
22 Online First: 2008/07/31] *inappropriate intervention*
23
24 370. Wang CC. Tai Chi and Rheumatic Diseases. *Rheumatic Disease Clinics of North*
25 *America* 2011;37(1):19-+. doi: 10.1016/j.rdc.2010.11.002 *inappropriate study*
26 *design*
27 371. Wang CC. Role of Tai Chi in the Treatment of Rheumatologic Diseases. *Current*
28 *Rheumatology Reports* 2012;14(6):598-603. doi: 10.1007/s11926-012-0294-y
29 *inappropriate study design*
30
31 372. Wang WR, Lopez V, Chow A, et al. A randomized controlled trial of the
32 effectiveness of a self-help psychoeducation programme on outcomes of
33 outpatients with coronary heart disease: study protocol. *Journal of Advanced*
34 *Nursing* 2014;70(12):2932-41. doi: 10.1111/jan.12397 *inappropriate population*
35
36 373. Wepner F, Scheuer R, Schuetz-Wieser B, et al. Effects of vitamin D on patients
37 with fibromyalgia syndrome: a randomized placebo-controlled trial. *Pain*
38 2014;155(2):261-8. doi: 10.1016/j.pain.2013.10.002 [published Online First:
39 2014/01/21] *inappropriate intervention*
40
41 374. Weze C, Leathard HL, Stevens G. Evaluation of Healing by Gentle Touch for the
42 Treatment of Musculoskeletal Disorders. *American Journal of Public Health*
43 2004;94(1):50-52. doi: 10.2105/AJPH.94.1.50 *inappropriate intervention*
44
45 375. Wicksell RK, Kemani M, Jensen K, et al. Acceptance and commitment therapy
46 for fibromyalgia: A randomized controlled trial. *European Journal of Pain*
47 2013;17(4):599-611. doi: 10.1002/j.1532-2149.2012.00224.x *inappropriate*
48 *intervention*
49
50 376. Williams DA, Kuper D, Segar M, et al. Internet-enhanced management of
51 fibromyalgia: a randomized controlled trial. *Pain* 2010;151(3):694-702. doi:
52 10.1016/j.pain.2010.08.034 [published Online First: 2010/09/22] *inappropriate*
53 *intervention*
54
55 377. Witjes S, Hoorntje A, Kuijer P, et al. Does Goal Attainment Scaling improve
56 satisfaction regarding performance of activities of younger knee arthroplasty
57 patients? Study protocol of the randomized controlled ACTION trial. *BMC*
58
59
60

- 1
2
3 *musculoskeletal disorders* 2016;17 doi: 10.1186/s12891-016-0965-3
4 *inappropriate study design*
5 378. Wylde V, Artz N, Marques E, et al. Effectiveness and cost-effectiveness of
6 outpatient physiotherapy after knee replacement for osteoarthritis: study protocol
7 for a randomised controlled trial. *Trials* 2016;17(1):289. doi: 10.1186/s13063-
8 016-1418-x [published Online First: 2016/06/15] *inappropriate study design*
9 379. Yang T, Wang H, Chen Y, et al. Effect of continuous administration of conjugated
10 estrogen plus medroxyprogesterone acetate (Premelle) in postmenopausal
11 women in Taiwan. *Journal of the Chinese Medical Association : JCMA* 2004;
12 67(7). <http://onlinelibrary.wiley.com/doi/10.1111/j.1526-4637.2006.00087.x> *inappropriate intervention*
13 380. Yelland MJ, Schluter PJ. Defining Worthwhile and Desired Responses to
14 Treatment of Chronic Low Back Pain. *Pain Medicine* 2006;7(1):38-45. doi:
15 10.1111/j.1526-4637.2006.00087.x *inappropriate population*
16 381. Young JL. Use of lisdexamfetamine dimesylate in treatment of executive
17 functioning deficits and chronic fatigue syndrome: A double blind, placebo-
18 controlled study. *Psychiatry Research* 2013;207(1-2):127-33. doi:
19 10.1016/j.psychres.2012.09.007 *inappropriate intervention*
20 382. Yuan SLK, Matsutani LA, Marques AP. Effectiveness of different styles of
21 massage therapy in fibromyalgia: A systematic review and meta-analysis.
22 *Manual therapy* 2015;20(2):257-64. *inappropriate study design*
23 383. Yuen AWC, Sander JW. Can slow breathing exercises improve seizure control in
24 people with refractory epilepsy? A hypothesis. *Epilepsy & Behavior*
25 2010;18(4):331-34. doi: 10.1016/j.yebeh.2010.05.019 *inappropriate population*
26 384. Zick SM, Wyatt GK, Murphy SL, et al. Acupressure for persistent cancer-related
27 fatigue in breast cancer survivors (AcuCrft): a study protocol for a randomized
28 controlled trial. *BMC Complementary and Alternative Medicine* 2012;12 doi:
29 10.1186/1472-6882-12-132 *inappropriate population*
30 385. Zietek P, Zietek J, Szczypior K, et al. Effect of adding one 15-minute-walk on the
31 day of surgery to fast-track rehabilitation after total knee arthroplasty: a
32 randomized, single-blind study. *European journal of physical and rehabilitation*
33 *medicine* 2015;51(3):245-52. [published Online First: 2014/09/19] *inappropriate*
34 *intervention*
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

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-Izquierdo & 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.

For peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

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

Comparison	ES (#)	R	R ²	F(p)
<i>Study Characteristics</i>				
- 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)
<i>Participant Characteristics</i>				
- 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)
<i>Changes in Secondary Outcomes</i>				
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·kg ⁻¹ ·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

1
2
3 and VAS; ^e. number of groups exceed 16 because three studies reported anxiety results using two different
4 instruments;
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

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

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

2 Setting: Home, Facility, Both

3

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise	control	Relative (95% CI)	Absolute (95% CI)		
Anxiety (follow up: mean 15.3 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

20 CI: Confidence interval; SMD: Standardized mean difference

21

22 Explanations

23

24 ^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.

26

27



PRISMA Checklist

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

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

Page 1 of 2

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

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

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

Page 2 of 2