

# UWL REPOSITORY repository.uwl.ac.uk

The evidence base for psychological interventions for rheumatoid arthritis: a systematic review of reviews

Prothero, Louise, Barley, Elizabeth ORCID logoORCID: https://orcid.org/0000-0001-9955-0384, Galloway, James, Georgopoulou, Sofia and Sturt, Jackie (2018) The evidence base for psychological interventions for rheumatoid arthritis: a systematic review of reviews. International Journal of Nursing Studies, 82. pp. 20-29. ISSN 0020-7489

http://dx.doi.org/10.1016/j.ijnurstu.2018.03.008

This is the Accepted Version of the final output.

**UWL repository link:** https://repository.uwl.ac.uk/id/eprint/4729/

**Alternative formats**: If you require this document in an alternative format, please contact: open.research@uwl.ac.uk

Copyright: Creative Commons: Attribution-Noncommercial-No Derivative Works 4.0

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

**Take down policy**: If you believe that this document breaches copyright, please contact us at <a href="mailto:open.research@uwl.ac.uk">open.research@uwl.ac.uk</a> providing details, and we will remove access to the work immediately and investigate your claim.

## Accepted Manuscript

Title: The Evidence Base for Psychological Interventions for Rheumatoid Arthritis: A Systematic Review of Reviews

Authors: Louise Prothero, Elizabeth Barley, James Galloway, Sofia Georgopoulou, Jackie Sturt

PII: S0020-7489(18)30059-2

DOI: https://doi.org/10.1016/j.ijnurstu.2018.03.008

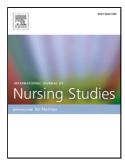
Reference: NS 3111

To appear in:

Received date: 8-8-2017 Revised date: 4-3-2018 Accepted date: 9-3-2018

Please cite this article as: Prothero, Louise, Barley, Elizabeth, Galloway, James, Georgopoulou, Sofia, Sturt, Jackie, The Evidence Base for Psychological Interventions for Rheumatoid Arthritis: A Systematic Review of Reviews.International Journal of Nursing Studies https://doi.org/10.1016/j.ijnurstu.2018.03.008

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



ACCEPTED MANUSCRIPT

The Evidence Base for Psychological Interventions for Rheumatoid Arthritis: A Systematic

**Review of Reviews** 

Louise Prothero <sup>a,b</sup>, Elizabeth Barley <sup>c</sup>, James Galloway <sup>a</sup>, Sofia Georgopoulou <sup>a,d</sup> and Jackie

Sturt b

<sup>a</sup> Department of Inflammation Biology, School of Immunology and Microbial Sciences,

Faculty of Life Sciences and Medicine, King's College London, 10 Cutcombe Road, Denmark

Hill, London, SE5 9RJ, UK.

<sup>b</sup> Florence Nightingale Faculty of Nursing, Midwifery and Palliative Care, King's College

London, 57 Waterloo Road, London, SE1 8WA, UK.

<sup>c</sup> College of Nursing, Midwifery and Healthcare, University of West London, Boston Manor

Road, Brentford, Middlesex, TW8 9GA, UK.

<sup>d</sup> School of Psychology, University of East London, Water Lane, London, E15 4LZ, UK.

Email addresses:

elizabeth.barley@uwl.ac.uk

james.galloway@kcl.ac.uk

jackie.sturt@kcl.ac.uk

s.georgopoulou@uel.ac.uk

\*Correspondence to: Louise Prothero, Department of Inflammation Biology, School of Immunology and Microbial Sciences, Faculty of Life Sciences and Medicine, King's College London, 10 Cutcombe Road, Denmark Hill, London, SE5 9RJ, UK.

Telephone: 0207 848 5939. Email: louise.prothero@kcl.ac.uk

#### **Abstract**

Background: Psychological interventions are an important but often overlooked adjunctive treatment option for patients with rheumatoid arthritis. Findings from systematic reviews of psychological interventions for this patient group are conflicting. A systematic review of reviews can explain inconsistencies between studies and provide a clearer understanding of the effects of interventions.

Objectives: To: 1) determine the effectiveness of psychological interventions in improving biopsychosocial outcomes for adults with rheumatoid arthritis, 2) determine the relationship between the intensity of the psychological interventions (number of sessions, duration of sessions, duration of intervention) on outcomes, and 3) assess the impact of comparator group (usual care, education only) on outcomes.

Design: We conducted a systematic review of reviews using the following inclusion criteria:

1) randomised controlled trials of psychological interventions (including cognitive behavioural therapy, supportive counselling, psychotherapy, self-regulatory techniques, mindfulness-based cognitive therapy and disclosure therapy) provided as an adjunct to medication, 2) included rheumatoid arthritis patients aged  $\geq$  18 years, 3) reported findings for at least 1 of the primary outcomes: pain, fatigue, psychological status, functional

disability and disease activity and 4) were published in English between January 2000 and March 2015 (updated January 2018).

Data sources: We searched in MEDLINE, EMBASE, CINAHL, PsycINFO, the Cochrane

Database of Systematic Reviews and the Database of Abstracts of Reviews of Effects.

Reference lists were searched for additional reviews.

Review methods: Study selection and 50% of the quality assessments were performed by two independent reviewers. Methodological quality was measured using the Assessment of Multiple Systematic Reviews checklist. Data extraction was conducted by one reviewer using a predesigned data extraction form.

Results: Eight systematic reviews met inclusion criteria (one review was excluded due to its low-quality score). Small post intervention improvements in patient global assessment, functional disability, pain, fatigue, anxiety and depression were observed. The effect on coping, self-efficacy and physical activity was greater. Improvements in depression, coping and physical activity were maintained (8.5-14 months). Interventions delivered over a longer period with a maintenance component appeared more effective. Attention, education, and placebo control groups produced some improvements but not as large as those produced by the psychological interventions.

Conclusions: Psychological interventions result in small to moderate improvements in biopsychosocial outcomes for patients with rheumatoid arthritis in addition to those achieved by standard care. Several priorities for future research were identified, including determining the cost effectiveness of non-psychologically trained health professionals delivering psychological interventions.

ACCEPTED MANUSCRIPT

List of abbreviations

AMSTAR: Assessment of Multiple Systematic Reviews, CBT: Cognitive Behavioural Therapy,

MI: Motivational Interviewing, OMERACT: Outcome Measures in Rheumatology, OT:

Occupational Therapy, RA: Rheumatoid Arthritis, RCT: Randomized Controlled Trial, TAU:

Treatment As Usual

Key words: Assessment of Multiple Systematic Reviews checklist; evidence-based practice;

mental health status; physical health status; psychological interventions; rheumatoid

arthritis; systematic review of reviews.

Background

Rheumatoid arthritis is a chronic autoimmune disease characterised by persistent joint pain

and swelling. Uncontrolled active rheumatoid arthritis leads to decreased quality of life,

disability, and comorbidity (e.g. heart disease and diabetes) (1). The global prevalence of

rheumatoid arthritis in 2010 was estimated to be 0.24%; and was approximately twice as

common in females (0.35%) than in males (0.13%) (2). Despite pharmacological

intervention, many patients with rheumatoid arthritis continue to experience symptoms

such as pain, fatigue, and psychological distress (3). Rheumatoid arthritis medications also

have side-effects especially when taken over long periods making psychological

interventions an important but often overlooked adjunctive treatment option.

theory, having the intention of improving functioning and delivered via a therapeutically

structured relationship (4). Findings from systematic reviews of psychological interventions

for patients with rheumatoid arthritis are conflicting (3). A systematic review of reviews can

explain inconsistencies between studies and provide a clearer understanding of the effects

of interventions (5,6).

This work systematically reviewed the available evidence from systematic reviews on the

effect of psychological interventions for adults with rheumatoid arthritis . The objectives

were to: 1) determine the effectiveness of psychological interventions in improving

outcomes for adults with rheumatoid arthritis, 2) determine the relationship between the

intensity of the psychological interventions (number of sessions, duration of sessions,

duration of intervention) on outcomes and 3) assess the impact of comparator groups (e.g.

usual care, education only) on outcomes.

Methods

Search methods and identification of reviews

The search strategy followed that of one included in a protocol for a systematic review of

self-management education programmes for rheumatoid arthritis (7). The search strategy,

originally for Ovid MEDLINE, was modified for this review (see Supplementary File 1) and

adapted for use with the other databases. All keywords in the search are based on Medical

Subject Headings. Electronic searches of the following 6 databases were performed in

March 2015 by the lead author to identify relevant articles: MEDLINE via Ovid , EMBASE via

Ovid, CINAHL via EBSCOhost, PsycINFO via Ovid, CDSR and DARE. The reference lists of

selected articles were also hand-searched. A further search of the same databases was conducted by the lead author in January 2018, to cover the three years since the previous search.

#### Eligibility criteria

The eligibility criteria were systematic reviews: 1) of randomized controlled trials , 2) which test the efficacy of ≥1 psychological component listed in Table 1 as an adjunct to medication, 3) with a population of adult participants ≥18 years, 4) with a diagnosis of rheumatoid arthritis (reviews of patients with other health conditions were included if data for rheumatoid arthritis patients were reported separately), 5) reporting findings for at least one of the following primary outcomes: pain, quality of life, functional disability, psychological status and disease activity (secondary outcomes included self-efficacy, coping and self-management behaviours), 5) published in the English language, 6) between January 2000 and March 2015 (updated to January 2018).

January 2000 was chosen as the earliest search date because psychological interventions have changed over time.

Table 1 lists the more prominent categories of psychological intervention and their techniques defined in the protocol. The interventions categories identified are commonly delivered by Clinical Psychologists, or, by people trained by Clinical Psychologists. Where systematic reviews included a sub-group analysis of psychological interventions, findings from the sub-group analysis were included. Where systematic reviews included a mixture of psychological interventions defined in the protocol (see Table 1) and other psychological

ACCEPTED MANUSCRIPT

interventions and/or educational interventions, they were included if at least 80% of studies

included psychological interventions defined in the protocol.

Selection of reviews

The lead author screened retrieved titles and abstracts to identify potentially relevant

reviews. The full texts of these reviews were assessed independently by the lead author and

a second reviewer for eligibility. Discussion was used to resolve differences in selection. This

was required for six of the full-texts

Quality assessment and data abstraction

The methodological quality of all reviews was measured using the validated Assessment of

Multiple Systematic Reviews (AMSTAR) (8) checklist. The methodological quality of a 50%

subsample of the reviews was assessed independently by the lead author and a second

reviewer. As good agreement was reached the remaining reviews were assessed by the lead

author only. We considered studies with a score between 0 and 4 to be low quality, studies

with a score between 5 and 8 to be of moderate quality, and studies with a score between 9

and 11 to be of high quality, consistent with previous studies (9,10). Discussion was used to

resolve small differences in scoring.

The following data were extracted by the lead author using a predesigned data extraction

form: 1) review details (e.g. author, year of publication); 2) aim, inclusion/exclusion criteria;

3) interventions (e.g. psychological content, comparator group); 4) results (e.g. number of

studies/ participants, findings relating to primary/secondary outcomes of this review) and 5)

discussion points (e.g. key findings, suggestions for future research).

#### **Results**

where available (see Table 4).

The electronic and reference list searches revealed 1,119 citations; 158 were removed using Endnote X6 via duplicate checking. Additionally, 924 articles were excluded following title and abstract filtering because they did not meet the eligibility criteria. This left 38 reviews which were potentially relevant and retrieved in full-text (3,11-47), 29 were excluded before data extraction (11-39) and 9 met the inclusion criteria (3,40-47). This process, and reasons for exclusion, is depicted in Figure 1.

#### Review characteristics

One of the reviews was excluded due to its low-quality score (45). The 8 selected reviews (3,40,41,42,43,44,46,47), which included 2 Cochrane reviews (42,47), were published between 2002 and 2016. For 5 reviews (40,41,42,46,47), only findings from sub-group analyses were included (see Table 2). For 3 of these (42,46,46) this was because a mixture of interventions were included e.g. psychoeducational and educational (46). For the fourth (40) and fifth review (41) this was because of a mixed patient group. Considering the complete and sub-group analyses, the number of randomized controlled trials included in the reviews ranged from 3 (41) to 34 (43) and the number of participants ranged from 194

ACCEPTED MANUSCRIPT

(41) to 2,021 (43) . A table of all unique primary studies identified and included (see

Supplementary File 2) which details all the interventions reviewed, was compiled. In total 66

primary studies published between 1981 and 2014 and representing 7,279 participants

were contained within this review of reviews.

Supplementary File 3 shows the overlap between interventions used in the individual

studies included in the 8 reviews. Cognitive behavioural therapy was the most common

intervention included in more than 3 reviews. There were no motivational interviewing

interventions included in any of the reviews.

Review quality

The low-quality review (45) was excluded, leaving 8 included reviews. Three reviews met the

predefined score for high quality (40,42,47) and 5 for moderate quality (3,41,43,44,46). Overall,

the methodological quality of included reviews (Table 3) was moderate (mean AMSTAR score = 8).

1. Effectiveness of psychological interventions on outcomes (see Table 4 Summary of Effect

Sizes)

Primary outcomes

Disease activity

Disease activity/severity

Nyssen et al. (2016) examined the effect of expressive writing on disease activity/severity

(n=3) studies (40). They found that expressive writing showed no significant effects post

intervention (d= -0.02; 95% CI: = -0.37, 0.32, P=0.89). Significant effects were, however, observed as follow-up averaged 10 weeks (d = -0.61; 95%CI: = -0.96, -0.26, P<0.001).

#### Patient global assessment

One review (n = 5 studies) examined Patient global assessment. Riesma et al. (47) found that a counselling intervention (1 study) showed no significant effects for scores on patient global assessment. Behaviour change interventions (4 studies) showed small significant effects for patient global assessment which were not maintained at follow-up (3-14 months).

#### Tender and/or swollen joints

Tender and/or swollen joints were examined in two reviews (n=9 studies). Astin et al. (3) found that psychological interventions had no effect on tender joints post-intervention (d = 0.15; 95% CI: = -0.09, -0.39); however, small significant effects were observed at follow-up averaged 8.5 months (d = 0.30; 95% CI: = 0.04, -0.56; P=0.005). The review by Cramp et al. (42) included 2 studies which reported on tender and swollen joint counts neither of which reported significant findings. One of these studies reported a statistically non-significant increase in scores on a measurement for joint tenderness (the Richie Articular Index) for patients in both the control and intervention arm.

#### Inflammation

One review (n=3 studies) examined the effects of expressive writing on Inflammation. Nyssen et al. (2016) found that expressive writing had no effect on inflammation post intervention.

#### Functional disability

Four reviews (n = 41 studies) examined functional disability. Astin et al. (3) and Knittle et al. (44) both found that psychological interventions had a small effect on disability post intervention. Astin et al. (3) tested this effect at follow-up (averaged 8.5 months) which was reduced to non-significance. Riesma et al. (47) found that counselling interventions did not significantly reduce disability whereas behaviour change interventions showed small reductions post intervention. At follow-up (3-14 months) these effects were no longer significant, however, a trend favouring behaviour change interventions was observed. Cramp et al. (42) reported that 5 out of 6 studies did not have significant effects on disability.

#### Pain

Five reviews (n = 49 studies) considered pain. Riesma et al. (47) found that counselling and behaviour change interventions did not significantly reduce pain, however, a trend favouring behaviour change interventions was observed. Using Cohen's classification of effect sizes (48), the reviews by Astin et al. (3) and Knittle et al. (44) reported that psychological interventions had small effects on pain reduction post intervention. Astin et al. (3) tested the effect of psychological interventions on pain at follow-up (averaged 8.5 months) which was reduced to non-significance. Cramp et al. (42) found that 4 out of 6 studies did not show significant effects for pain. Niedermann et al. (46) found that 2 out of 4 studies showed a positive change both in the short-term (averaged 12.5 weeks) and the long-term (averaged 10.5 months). One study, which examined the effectiveness of cognitive behavioral therapy, showed a progressive worsening of pain at follow-up (6

months) The final study's findings were non-significant post interventions and at 12-month follow-up.

#### **Fatigue**

One review (42) reported meta-analysis for fatigue based on findings from 13 studies. The authors found that psychosocial interventions reduced fatigue demonstrating a small effect.

The impact of the psychosocial interventions on fatigue at follow-up was not measured.

#### Depression

Five reviews (n = 28 studies) examined depression. Astin et al. (3) and Knittle et al. (44) found that psychological interventions resulted in small reductions in depression post intervention. Astin et al. (3) tested this effect at follow-up (averaged 8.5 months) which remained significant. Riesma et al. (47) found that behaviour change interventions led to small reductions in depression which were not maintained at follow-up (3-14 months), however, a trend favouring behaviour change interventions was observed. Beltman et al. (41) and Cramp et al. (42) found that patients in 2 out of the 3 randomized controlled trials included in their reviews (both testing cognitive behavioral therapy) showed a significant reduction in depressive symptoms post intervention. The third study in the review by Cramp et al. (42) tested the effectiveness of group education and had no significant effects in relation to depression. The third study in the review by Beltman et al. (41) (also testing cognitive behavioral therapy) reported an increase in depressive symptoms post intervention.

#### **Anxiety**

Anxiety was examined in 3 reviews (n = 14 studies). Knittle et al. (44) found psychological interventions resulted in small significant reductions in anxiety. Niedermann et al. (46) included one study which tested for anxiety. The cognitive behavioral therapy group showed significant positive change at both 15 weeks and 6 months. In comparison, the social group therapy arm showed significant positive change at 15 weeks, but this effect was not maintained at 6 months. The 4 studies included in the review by Cramp et al. (42) which tested for anxiety did not find significant changes.

Secondary outcomes

Self-efficacy

Two reviews (n = 8 studies) examined this outcome. Astin et al. (3) reported that psychological interventions had a moderate effect on self-efficacy post intervention which was reduced to non-significance at follow-up (average 8.5 months). Niedermann et al. (46) reported that only 1 of the 4 psychoeducational intervention studies included self-efficacy as an outcome measure. The study, which examined the effectiveness of a stress management program, found significant improvements post interventions and at 15-month follow-up.

Coping

Coping was examined in 2 reviews (n=12 studies). Astin et al. (3) reported that psychological interventions had a moderate effect on improvements in coping post intervention (d = 0.46; 95% CI: = 0.09, -0.83; P=0.007). At follow-up (average 8.5 months) the effect size remained significant and had increased slightly (d = 0.52; 95% CI: -0.07, -1.11; P=0.04). Strong evidence for psychoeducational programmes was found by Niedermann et al. (46) for

coping with pain. All 4 psychoeducational programs (3 of which were high quality studies) showed at least 1 pain-coping behavior that improved significantly after intervention. There was, however, limited evidence for long-term increase of coping behaviour (averaged 10 months) because of inconsistent results across studies.

#### Physical activity

Physical activity was examined by 1 review (n = 4 studies). Knittle et al. (44) reported that psychological interventions had a moderate effect on improvements in physical activity . Small significant improvements were observed at follow-up (10-14 month)..

#### 2. Impact of intervention intensity on outcomes

There were limited available data to examine this objective. Dissanayake and Bertouch (43) subdivided cognitive behavioural therapy interventions according to the duration of the treatment: 'short' less than 6 weeks (6 studies), 'long' more than 6 weeks (5 studies) and cognitive behavioural therapy with maintenance therapy throughout the follow-up period (5 studies). They found consistent supportive evidence for cognitive behavioural therapy of more than 6 weeks duration with maintenance therapy; however, they advised that findings should be interpreted with caution due to the small number of studies. They also found supportive evidence for improvement with cognitive behavioural therapy of greater than 6 weeks duration in the short-term but conflicting evidence for its long-term efficacy. There was conflicting evidence for the benefits of cognitive behavioural therapy of less than 6 weeks duration.

#### 3. Impact of the comparator group on outcomes

ACCEPTED MANUSCRIPT

Astin et al. (3) compared effect sizes in studies that used a wait list or treatment as usual

control condition with those that employed an attention, education, or placebo control. For

pain, disability, and psychological status the effects sizes were larger for studies that used a

wait list or treatment as usual control condition compared to those which used attention,

education, or placebo control. The effect sizes (with wait list or treatment as usual listed

first) were pain 0.21, 0.05; disability 0.29, 0.12 and psychological status 0.29, 0.08. For

tender joints, however, the reverse was found; -0.01, 0.31. Beltman et al. (41) found that for

patients with depressive symptoms cognitive behavioural therapy

was superior to treatment as usual, however, was no better when compared to another

psychological therapy.

Discussion

**Principal findings** 

Primary outcomes

This review found that psychological interventions result in small post intervention

improvements in patient global assessment, functional disability, pain, fatigue, anxiety, and

depression. These small improvements were maintained at follow-up for depression (8.5

months), but not for functional disability (averaged 11.25 months) or pain (8.5 months). The

effects of psychological interventions on fatigue and anxiety were not measured at follow-

up. Interestingly, psychological interventions did not improve disease activity/severity or

tender and swollen joints post intervention. At follow-up, however, small significant

improvements were found after 10 weeks and 8.5 months, respectively. This may have

occurred because post intervention improvements in mediating variables (e.g. depressions, coping) had time to produce long-term benefits in disease activity.

#### Secondary outcomes

The effect on secondary outcomes (e.g. coping, self-efficacy, physical activity) was greater, revealing moderate effect sizes post intervention. Moderate improvements were maintained at follow-up for coping (8.5 months) and small improvements for physical activity (10-14 months). No significant findings were found for self-efficacy (8.5 months). This finding is in line with evidence [2,36] that the effects of psychological interventions on outcomes are mediated by improvements in self-efficacy and coping.

None of the reviews included quality of life or medication adherence as outcome measures which is surprising as they are often selected as outcomes of randomized controlled trials and are associated with changes in disease activity.

Conclusions reached by systematic review authors indicate that cognitive behavioural therapy is no more effective than any other psychological therapies. Although the impact of cognitive behavioural therapy relative to other psychological therapies is not a stated aim of this research it is interesting to note this pattern across reviews. Beltman et al. (41) found that for patients with depressive symptoms cognitive behavioural therapy was superior to treatment as usual, however, it was no better when compared to another psychological therapy (mainly supportive-expressive therapies e.g. social support). This indicates a general therapeutic effect of psychological interventions which is not specific to cognitive behavioural therapy. This is supported by Astin et al. (3) and Knittle et al. (44) who compared the findings from cognitive behavioural therapy interventions to findings from other interventions and observed only minor differences on outcomes.

There were limited data examining the impact of intervention intensity and comparator group on outcomes. Dissanayake and Bertouch (43) found consistent supportive evidence for cognitive behavioural therapy of more than 6 weeks duration with maintenance therapy. However, they advised that findings should be interpreted with caution due to the small number of studies. Interventions delivered for longer with a maintenance component may therefore be more effective. Larger effect sizes were also observed in studies which used a wait list or treatment as usual control condition compared to those which employed an attention, education, or placebo control (3). This suggests that attention, education, or placebo control produce some improvements in outcomes, though not as large as those produced by psychological interventions.

#### Quality of the included reviews

The methodological quality of the selected systematic reviews is a strength. Apart from 1 review (45) which was excluded from further analysis, all were rated as either moderate or high quality. Apart from 1 (41), which categorised participants as either having depressive disorder or depressive symptoms, reviews did not identify the presence of any symptoms as specific inclusion criteria. It is, therefore, possible that these outcomes were not clinically significant problems for the participants thus resulting in a 'ceiling effect' and reducing the potential for improvement. It is also unclear whether the modest effects sizes found translate into clinically meaningful improvements.

#### Strengths and limitations of the study

This is the first systematic review of reviews of psychological interventions for adults with rheumatoid arthritis. The methodology of the review is a strength. Selection of reviews and

quality assessment were carried out by two independent reviewers with good inter-rater reliability. The quality assessment was conducted using the AMSTAR tool (8).

Limitations of this review include the quality of the included primary studies. Review authors described the quality as being 'highly variable' (41) and 'not very high' (47) which may have confounded the results. Review authors criticized the studies for using multiple health status measurements with no defined primary outcome. This means the interventions may have not been targeted. Overlap between the analyses from the studies is also a limitation as it will have inflated their results. This was dealt with by acknowledging the number of studies which overlap and their corresponding interventions.

A limitation of the methodology is that the review does not only include the psychological interventions defined in the protocol i.e. some education interventions were included. The Cochrane Musculoskeletal Review Group's Trials Search coordinator helped to develop each search equation for the original search strategy (7); however, our modified version was not peer reviewed which is a limitation. The electronic database searches failed to identify one article (see Figure 1). It is possible that the search strategy did not identify further reviews. Further to this, our search did not include grey literature or non-English language reviews, although no non-English reviews were found in either search.

Some of the psychological interventions were delivered in a group setting, whereas other were facilitated in a one-to-one environment. Analysis of the effect this difference has on outcomes would have been useful for the further interpretation of the results. This question is, however, beyond the scope of this review but is noted as a limitation.

Recommendations for future practice

The Outcome Measures in Rheumatology (OMERACT) group is an international organization which aims to develop optimal outcome measures for use in clinical trials (49). Recommendations for future practice identified by the review authors included randomized controlled trials using the core set of outcome measures agreed by the OMERACT group together with measures of psychological status. The reason for this recommendation is to aide comparisons of findings across studies. They also suggested researchers try to accurately report the techniques that have been used in psychological interventions and provide some form of fidelity assessment. This is so both the intervention content, and the level to which the techniques were successfully applied, is transparent. This transparency is helpful for other researchers who wish to comment on or synthesize the findings (49). Importantly, randomized controlled trials should have adequate statistical power and be high quality to not bias the review findings.

#### Gap in the evidence base

Gaps in the evidence base described in the reviews can be summarised across 5 themes: 1) 'Patient Characteristics', 2) 'Maintaining Improvements', 3) 'Longitudinal Research', 4) 'Mechanism of Action' and 5) 'Categories of Intervention'. There was consensus amongst review authors: themes numbered 1, 3 and 5 were cited in 4 reviews, and themes numbered 2 and 4 were cited in 3 reviews.

#### Patient Characteristics

Future studies should be disease specific and seek to identify characteristics (e.g. personality, illness perceptions) or coping styles that make patients responsive to psychological interventions. They should also examine how the permutations of the

rheumatoid arthritis itself (e.g. disease severity, disease duration) affect the efficacy of psychological interventions.

#### Maintaining Improvements

Small short-term symptoms improvements were generally observed in the reviews but there was limited evidence for any long-term changes. Strategies to increase and better maintain small symptom improvements and behavioural changes should be considered (e.g. by building booster or relapse prevention strategies into the trial design). Interventions should include two treatment groups, one with and one without maintenance, in addition to standard medical care or attention controls.

#### Longitudinal Research

Longitudinal research was considered necessary to examine whether improvements in psychological status produce carry-over effects on physical outcomes (e.g. pain, disability). There may be a need to look at strategies which enhance patients' long-term adherence to programs.

#### Mechanism of Action.

Exploring the mechanisms through which these interventions work was suggested as an area for future research (e.g. whether observed changes are mediated by certain personality characteristics or coping styles).

#### Categories of Intervention

As psychological interventions are heterogeneous, based on different theoretical frameworks and assumptions, researchers should try to determine which interventions (and

intervention components) are most effective. Authors suggested comparing different types of intervention to one another, planning meta-analysis in homogenous intervention subgroups and studying the value of the many other types of psychological interventions available.

Several additional gaps in the evidence base were identified in this review. Firstly, fatigue is an outcome which is important to patients but was only explored in one review (42). Similarly, none of the reviews examined medication adherence or quality of life. Future research into the effect of psychological interventions on rheumatoid arthritis should include fatigue, medication adherence and quality of life as outcome measures. Including quality of life measures will help to determine how valuable improvements resulting from psychological interventions are to patients.

Psychological interventions effect on disease specific outcomes are modest. However, with the advancement of rheumatoid arthritis treatment (e.g. biologics), many patients' disease activity is improved without psychological intervention. The psychological interventions included in this review, which were mainly cognitive behavioural therapy, improved depression. Future research should focus on finding psychological interventions that can improve other symptoms, such as pain and fatigue.

Psychological interventions improve depression, coping, self-efficacy, and physical activity for patients with rheumatoid arthritis. Their use should be more widespread; however, rheumatology departments do not always have the resources available to employ a psychologist. Future research could investigate the cost-effectiveness of other health professionals (e.g. nurses) delivering psychological interventions.

Psychological interventions treat low mood in rheumatoid arthritis. Their effect on disease specific outcomes are modest and not sustained over time. Secondary outcomes show greater improvement and there is evidence that these benefits are sustained.

Priorities for future research include 'Patient Characteristics', 'Maintaining Improvements', 'Longitudinal Research', 'Mechanism of Action' and 'Categories of Intervention'. Future research should also examine interventions that improve pain and fatigue, and the cost effectiveness of non-psychologically trained health professionals delivering psychological interventions.

#### Contribution of the paper

#### What is already known about the topic?

- Psychological interventions have small but measurable effects upon rheumatoid arthritis outcomes.
- •There is evidence that the effects of psychological interventions are mediated by improvements in self-efficacy and coping.

#### What this paper adds?

- Psychological interventions improve depression in patients with rheumatoid arthritis.
- •The effects of psychological interventions on disease specific outcomes are modest and not sustained.

•The effects of psychological interventions on secondary outcomes are significant and there is evidence that they are sustained.

#### **Declarations**

Ethics approval and consent to participate

Not applicable

**Consent for publication** 

Not applicable

#### **Competing interests**

The authors declare that they have no competing interests

#### Acknowledgements

This research has been funded by the National Institute for Health Research (NIHR) as one of its Programme Grants for Applied Research (Grant Reference Number: RP-PG-0610-10066; Programme title: Treatment Intensities and Targets in Rheumatoid Arthritis Therapy: Integrating Patients' And Clinicians' Views—The TITRATE Programme). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. This work was also supported by the King's College Hospital Charity

#### References

- 1. Scott DL, Wolfe F, Huizinga TWJ. Rheumatoid arthritis. Lancet. 2010;374:1094–1108.
- 2. Cross M, Smith E, Hoy D, Carmona L, Wolfe F, Vos T, et al. The global burden of rheumatoid arthritis: estimates from the Global Burden of Disease 2010 study. Ann Rheum Dis. 2014;1316-1322.
- 3. Astin JA, Beckner W, Soeken K, Hochberg MC, Berman B. Psychological interventions for rheumatoid arthritis: a meta-analysis of randomized controlled trials. Arthritis Care Res. 2002;47:291-302.
- 4. Smith G. An Introduction to psychological interventions. In: Smith G, editor.

  Psychological interventions in mental health nursing. Maidenhead: Open University

  Press; 2012. p. 1-11.
- 5. Smith V, Devane D, Begley CM, Clarke M. Methodology in conducting a systematic review of systematic reviews of healthcare interventions. BMC Med Res Methodol. 2011;11:15.
- 6. Aromataris E, Fernandez R, Godfrey CM, Holly C, Khalil H, Tungpunkom P. Summarizing systematic reviews: methodological development, conduct and reporting of an umbrella review approach. J Evid Based Healthc. 2015;3:132-140.
- 7. Lefevre-Colau MM, Buchbinder R, Regnaux JP, Roren A, Poiraudeau S, Boutron I. Self-management education programmes for rheumatoid arthritis (Protocol). Cochrane Database Syst Rev. 2014: CD01133810.

- 8. Shea BJ, Hamel C, Wells GA, Bouter LM, Kristjansson E, Grimshaw J, et al. AMSTAR is a reliable and valid measurement tool to assess the methodological quality of systematic reviews. Clin Epidemiol. 2009;62:1013-20.
- 9. Monasta L, Batty GD, Cattaneo A, Lutje V, Ronfani L, van Lenthe FJ, et al. Early-life determinants of overweight and obesity: a review of systematic reviews. Obes rev. 2010;11:695-708.
- 10. Rebar AM, Stanton R, Geard D, Short C, Duncan MJ, Vandelanotte C. A meta-metaanalysis of the effect of physical activity on depression and anxiety in non-clinical adult populations. Health Psychol Rev. 2015;9:366-378.
- 11. Astin JA. Mind-body therapies for the management of pain. Clin J Pain. 2004;20:27-32.
- 12. Astin JA, Shapiro SL, Eisenberg DM, Forys KL. Mind-body medicine: state of the science, implications for practice. J Am Board Fam Pract. 2003;16:131-47.
- 13. Badamgarav E, Croft Jr JD, Hohlbauch A, Louie JS, O'Dell J, Ofman JJ, et al. Effects of disease management programs on functional status of patients with rheumatoid arthritis. Arthritis Care Res. 2003;49:377-87.
- 14. Berdal G, Smedslund G, Dagfinrud H, Hagen KB, Kjeken I. Design and effects of supportive follow-up interventions in clinical care of patients with rheumatic diseases: a systematic review with meta-analysis. Arthritis Care Res. 2015;67:240-54.
- 15. Bohlmeijer E, Prenger R, Taal E, Cuijpers P. The effects of mindfulness-based stress reduction therapy on mental health of adults with a chronic medical disease: A

- meta-analysis. J Psychosom Res. 2010;68:539-44.
- 16. Chilton R, Pires-Yfantouda R, Wylie M. A systematic review of motivational interviewing within musculoskeletal health. Psychol Health Med. 2012;17:392-407.
- 17. Christie A, Jamtvedt G, Dahm KT, Moe RH, Haavardsholm EA, Hagen KB. Effectiveness of nonpharmacological and nonsurgical interventions for patients with rheumatoid arthritis: an overview of systematic reviews. Phys Ther. 2007;87:1697-715.
- 18. de Ridder D, Schreurs K. Developing interventions for chronically ill patients: is coping a helpful concept? Clin Psychol Rev. 2001;21:205-40.
- 19. De Thurah A, Esbensen B, Roelsgaard I, Frandsen T, Primdahl J. Efficacy of embedded nurse-led versus conventional physician-led follow-up in rheumatoid arthritis: A systematic review and meta-Analysis. RMD Open: 2017;3:e000481.
- 20. Du S, Yuan C, Xiao X, Chu J, Qiu Y, Qian H. Self-management programs for chronic musculoskeletal pain conditions: A systematic review and meta-analysis. Patient Educ Couns. 2011;85:e299-e310.
- 21. Dwarswaard J, Bakker E, van Staa A, Boeije H. Self-management support from the perspective of patients with a chronic condition: a thematic synthesis of qualitative studies. Health Expect. 2016;'194-208.
- 22. Foster G, Taylor SJ, Eldridge SE, Ramsay J, Griffiths CJ. Self-management education programmes by lay leaders for people with chronic conditions. Cochrane Database Syst Rev. 2007: CD005108.

- 23. Frich LMH. Nursing interventions for patients with chronic conditions. J Adv Nurs. 2003;44:137-53.
- 24. Galo J, Mehat P, Rai S, Avina-Zubieta A, De Vera M. What are the effects of medication adherence interventions in rheumatic diseases: a systematic review. Ann Rheum Dis. 2016;75:667-673.
- 25. Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. Cochrane Database Syst Rev. 2008:CD000011.
- 26. Kripalani S, Yao X, Haynes RB. Interventions to enhance medication adherence in chronic medical conditions: A systematic review. Arch Intern Med. 2007;167:540-50.
- 27. Larkin L. Gallagher S, Cramp F, Brand C, Frazer A, Kennedy N. Behaviour change interventions to promote physical activity in rheumatoid arthritis: a systematic review. Rheumatol Int. 2015;35:1631-1640.
- 28. Macfarlane GJ, Paudyal P, Doherty M, Ernst E, Lewith G, MacPherson H, et al. A systematic review of evidence for the effectiveness of practitioner-based complementary and alternative therapies in the management of rheumatic diseases: rheumatoid arthritis. Rheumatology (Oxford). 2012;51:1707-13.
- 29. Bawa F, Mercer S, Atherton R, Clague F, Keen A, Scott N et al. Does mindfulness improve outcomes in patients with chronic pain? Systematic review and meta-analysis. Br J Gen Pract. 2015;65:e387-e400.
- 30. Mulligan K, Newman S. Psychoeducational interventions in rheumatic diseases: A review of papers published from September 2001 to August 2002. Curr Opin

- Rheumatol.2003;15:156-9.
- 31. Ndosi M, Vinall K, Hale C, Bird H, Hill J. The effectiveness of nurse-led care in people with rheumatoid arthritis: a systematic review. Int J Nurs Stud. 2011;48:642-54.
- 32. Neill J, Belan I, Ried K. Effectiveness of non-pharmacological interventions for fatigue in adults with multiple sclerosis, rheumatoid arthritis, or systemic lupus erythematosus: a systematic review. J Adv Nurs. 2006;56:617-35.
- 33. Parker JC, Smarr KL, Slaughter JR, Johnston SK, Priesmeyer ML, Hanson KD, et al. Management of depression in rheumatoid arthritis: a combined pharmacologic and cognitive-behavioral approach. Arthritis Care Res. 2003;49:766-77.
- 34. van Straten A, Geraedts A, Verdonck-de Leeuw I, Andersson G, Cuijpers P. Psychological treatment of depressive symptoms in patients with medical disorders: a meta-analysis. J Psychosom Res. 2010;69:23-32.
- 35. Varekamp I, Verbeek JH, van Dijk FJ. How can we help employees with chronic diseases to stay at work? A review of interventions aimed at job retention and based on an empowerment perspective. Int Arch Occup Environ Health. 2006;80:87-97.
- 36. Vliet Vlieland TPM, Pattison D. Non-drug therapies in early rheumatoid arthritis. Best Practi Res Clin Rheumatol. 2009;23:103-16.
- 37. Warsi A, LaValley MP, Wang PS, Avorn J, Solomon D.H. Arthritis self-management education programs: a meta-analysis of the effect on pain and disability. Arthritis Rheum. 2003;48:2207-2213
- 38. Wills CE. Review: evidence on the effectiveness of interventions to improve patient

- adherence to prescribed medications is limited. Evid Based Nurs. 2008;11:109.
- 39. Zhou B, Li G, Zhang Y, Zhao Z. Effects of Nursing Interventions on Depression of Patients With Rheumatoid Arthritis: A Meta-Analysis of Randomized Controlled Trials. Arch Psychiatr Nurs. 2016;30:717-721.
- 40. Nyssen O, Taylor S, Wong G, Steed E, Bourke L, Lord J et al. Does therapeutic writing help people with long-term conditions? Systematic review, realist synthesis and economic considerations. Health Technol Assess. 2016;20:1-367.
- 41. Beltman MW, Oude Voshaar RC, Speckens AE. Cognitive-behavioural therapy for depression in people with a somatic disease: meta-analysis of randomised controlled trials. Br J Psychiat. 2010;197:11-19.
- 42. Cramp F, Hewlett S, Almeida C, Kirwan JR, Choy EH, Chalder T, et al. Non-pharmacological interventions for fatigue in rheumatoid arthritis. Cochrane Database Syst Rev. 2013:CD008322.
- 43. Dissanayake RK, Bertouch JV. Psychosocial interventions as adjunct therapy for patients with rheumatoid arthritis: a systematic review. Int J Rheum Dis. 2010;13:324-334.
- 44. Knittle K, Maes S, De Gucht V. Psychological interventions for rheumatoid arthritis: Examining the role of self-regulation with a systematic review and meta-analysis of randomized controlled trials. Arthritis Care Res. 2010;62:1460-72.
- 45. Leverone D, Epstein BJ. Nonpharmacological interventions for the treatment of rheumatoid arthritis: a focus on mind-body medicine. J Pharm Pract. 2010;23:101-

109.

- 46. Niedermann K, Fransen J, Knols R, Uebelhart D. Gap between short- and long-term effects of patient education in rheumatoid arthritis patients: a systematic review.

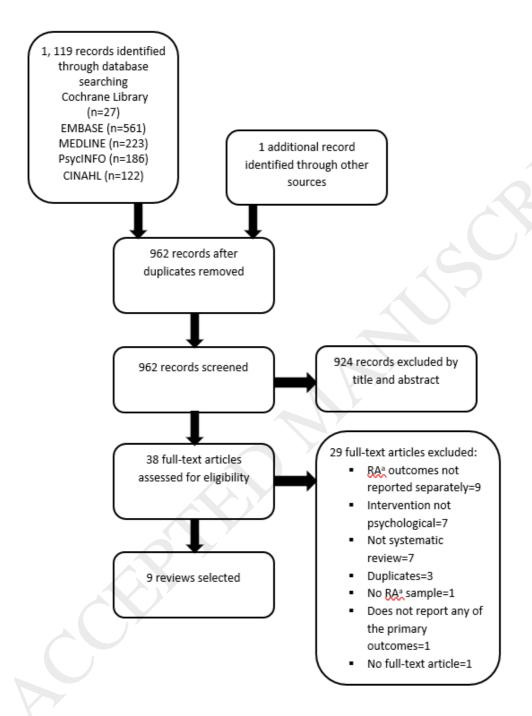
  Arthritis Care Res. 2004;51:388-98.
- 47. Riemsma RP, Kirwan JR, Taal E, Rasker JJ. Patient education for adults with rheumatoid arthritis. Cochrane Database Syst Rev. 2003: CD003688.
- **48.** Cohen, J. Statistical Power Analysis for the Behavioral Sciences. New York: Academic Press; 1977.
- **49.** Tugwell P, Boers M, Brooks P, Simon L, Strand V, Idzerda L. OMERACT: an international initiative to improve outcome measurement in rheumatology. Trials .2007;8:38–43
- 50. Mayo-Wilson E, Montgomery P, Hopewell S, Macdonald G, Moher D, Grant S.

  Developing a reporting guideline for social and psychological intervention trials. Brit J

  Psychiat. 2013; 20

#### **Figures**

Figure 1: Progress through the stages of review selection



<sup>a</sup>RA = Rheumatoid Arthritis

### **Tables**

Table 1: List of psychological components defined in the protocol and their corresponding techniques

Category	Example of techniques
Motivational interviewing	Affirmations, reflections
Cognitive behavioural therapy	Cognitive restructuring, behavioural
	activation
Supportive counselling	Reflection, supportive listening
Psychotherapy	Interpretation, confrontation
Self-regulatory techniques	Goal-setting, action planning
Mindfulness-based cognitive therapy	Focus on changing relationship to thoughts
Disclosure therapy	Sharing information, often written down

# ACCEPTED MANUSCRIPT

Table 2: Summary of characteristics of selected systematic reviews

		Total no. of	Interventions	Outcomes
	studies	participants		
	included			
To carry out a meta-analytic review of	25 RCTs <sup>c</sup>	1, 676	CBT <sup>a</sup> (13), biofeedback (5),	Pain, functional
studies that compared "psychosocial" (e.g.		patients	psychotherapeutic	disability, psychological
cognitive behavioural, psychoeducational)			interventions (5), disclosure	status, coping, self-
interventions to non-intervention controls			therapy (2).	efficacy, tender joints
(e.g. wait list, usual care, or attention				
placebo) in patients with RA <sup>b</sup>				
To conduct a meta-analysis of the	Sub-group of	194	CBT <sup>a</sup> (3)	Primary outcome
effectiveness of CBT <sup>a</sup> for depression in	3 RCTs <sup>c</sup>	patients		depressive symptoms
people with underlying somatic disease	included			
	patients with			
	RA <sup>b</sup>			
	studies that compared "psychosocial" (e.g. cognitive behavioural, psychoeducational) interventions to non-intervention controls (e.g. wait list, usual care, or attention placebo) in patients with RAb  To conduct a meta-analysis of the effectiveness of CBTa for depression in	To carry out a meta-analytic review of studies that compared "psychosocial" (e.g. cognitive behavioural, psychoeducational) interventions to non-intervention controls (e.g. wait list, usual care, or attention placebo) in patients with RAb  To conduct a meta-analysis of the Sub-group of effectiveness of CBTa for depression in 3 RCTsc people with underlying somatic disease included patients with	included  To carry out a meta-analytic review of 25 RCTs <sup>c</sup> 1, 676  studies that compared "psychosocial" (e.g. patients  cognitive behavioural, psychoeducational)  interventions to non-intervention controls  (e.g. wait list, usual care, or attention  placebo) in patients with RA <sup>b</sup> To conduct a meta-analysis of the Sub-group of 194  effectiveness of CBT <sup>a</sup> for depression in 3 RCTs <sup>c</sup> patients  people with underlying somatic disease included  patients with	included  To carry out a meta-analytic review of 25 RCTs <sup>c</sup> 1, 676 CBT <sup>a</sup> (13), biofeedback (5), studies that compared "psychosocial" (e.g. patients psychotherapeutic interventions (5), disclosure interventions to non-intervention controls (e.g. wait list, usual care, or attention placebo) in patients with RA <sup>b</sup> To conduct a meta-analysis of the Sub-group of 194 CBT <sup>a</sup> (3)  effectiveness of CBT <sup>a</sup> for depression in 3 RCTs <sup>c</sup> patients  people with underlying somatic disease included patients with

Cramp et	To evaluate the benefit and harm of non-	Sub-group of	1, 556	Self-management (3), group	Primary outcomes were
al. (2013)	pharmacological interventions for the	13 RCTs <sup>c</sup>	patients	education (3) CBT <sup>a</sup> (3),	self-reported fatigue
	management of fatigue in people with RAb	included		benefit finding (1), expressive	and adverse events.
		psychosocial		writing (2), mindfulness (1),	Secondary outcomes
		interventions		lifestyle management (1),	were pain, anxiety,
				energy conservation (1).	depression, disability,
					tender and swollen
					joints
Dissanaya	To identify individual psychological	34 RCTs <sup>c</sup>	2, 021	CBT <sup>a</sup> (16), disclosure therapy	Pain, biomedical and
ke and	interventions for which there is high		patients	(4), counselling (3),	clinical markers of
Bertouch	quality evidence			biofeedback (2), relaxation	disease, disability,
(2010)				training (2), meditation and	mood and cognition,
				mindfulness (2),	behaviour, patient
				psychotherapy (2).	satisfaction
Knittle et	To determine the overall efficacy of	27 RCTs <sup>c</sup>	1, 663	Group education (8), CBT <sup>a</sup>	Physical activity, pain,

al. (2010)	psychological interventions of increasing patien	ts	(7), Education (3), pain	disability, depressive
	physical activity, as well as of reducing		management (3), stress	symptoms and anxiety
	pain, disability, depressive symptoms, and		management (2),	
	anxiety among patients with RAb. Also, to		combination therapy CBT <sup>a</sup>	
	determine whether interventions		and occupational therapy (1),	
	including more techniques derived from		relaxation (1), mindfulness	
	Self-Regulatory Theory produce greater		(1), self-instruction (1).	
	treatment gains than those using fewer			
	such techniques			

Niederma	To systematically collect RCTs examining	Sub-group of	369	CBT <sup>a</sup> (3), stress management	Improved knowledge,
nn et al.	educational and psychoeducational	4 RCTs <sup>c</sup>	patients	(1)	health behaviour, or
(2004)	interventions for RA <sup>b</sup> patients, with focus	included			skills to influence
	on their long-term effectiveness	psychoeduca			psychological or

		tional			physical health status
		interventions			
Nyssen et	To review the clinical effectiveness and	Sub-group of	380	Therapeutic writing (4)	Studies reporting any
al. (2016)	cost-effectiveness of therapeutic writing	4 RCTs <sup>c</sup>	patients		relevant clinical
	for people with long-term conditions	included			outcomes including
	compared with no writing, or other	patients with			both disease-specific
	controls, reporting any relevant clinical	RAb			outcomes and generic
	outcomes.				outcomes.
Riemsma	To examine the effectiveness of patient	Sub-group of	5	Counselling (5), Behavioural	Pain, functional
et al.	education interventions on health status	29 RCTs <sup>c</sup>	Counselling	treatment (24).	disability, psychological
(2003)	in patients with RA <sup>b</sup>	included	RCTs <sup>c</sup> ; 800		well-being, disease
		psychological	patients		activity
		interventions	24		
			Behavioural		
			treatment		

RCTs<sup>c</sup>; 1,

747

patients

<sup>&</sup>lt;sup>a</sup>CBT = Cognitive Behavioural Therapy. <sup>b</sup>RA = Rheumatoid Arthritis. <sup>c</sup>RCTs = Randomised Controlled Trials.

Table 3: Quality of systematic reviews based on the 11-item AMSTAR<sup>a</sup> Checklist

Syste	1.	2.	3. Was	4.	5.	6.	7.	8.	9.	10.	11.	Т.
matic	Was	Was	а	Did	Was	Were	Was	Was	Were	Was	We	ot
revie	an a	ther	compr	the	a 	the	the · ·	the · ·	the	the	re	al
WS	prio	e 	ehensi	searc	list	chara	scient	scient	meth	likeli	pot	SC
	ri	dupli	ve	h	of	cterist	ific	ific	ods	hoo	enti	or
	desi	cate	literat	cover	incl	ics of	qualit	qualit	used	d of	al	е
	gn	stud	ure	unpu	ude	the	y of	y	to	publi	con	
	prov	у	search	blish	d	includ	the	used	comb	catio	flict	
	ided ?	selec	perfor	ed	and	ed	includ	appro	ine	n bins	s of	
	ŗ	tion and	med?	litera	excl	studie	ed	priate	findin	bias	inte	
				ture?	ude d	S	studie	ly in	gs of	asse	rest	
		data				provid ed?	S	formu	studi	ssed ?	list ed?	
		extra ction			stud ies	eur	assess ed	lating concl	es	ŗ	eur	
		?			prov		and	usion	appro priat			
		•			ided		docu	s?	e?			
					?		ment	3:	C:			
					:		ed?					
Astin	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No	6
et al.		. 05				. 65			. 05			
2002												
Belt	No	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	7
man												
et al.												
2010												
Cram	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	1
p et												1
al.												
2013												
Dissa	No	Yes	Yes	No	No	Yes	Yes	Yes	NA <sup>b</sup>	No	No	5
naya		<i>(</i> )				. 00	. 00	. 00				
ke &												
Berto												
uch												
2010												
Knittl	No	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	No	6
e et												
al.												
2010												
Lever	No	No	No	No	No	Yes	No	No	NA <sup>b</sup>	No	Yes	2
one												
&												
Epste												
in												
2010												
·				·								

Nied	No	Yes	Yes	No	No	Yes	Yes	Yes	$NA^b$	No	No	5
erma												
nn et												
al.												
2004												
Nyss	Yes	No	Yes	1								
en et												0
al.												
2016												
Riem	Yes	Yes	Yes	1								
sma												1
et al.												
2003												

<sup>&</sup>lt;sup>a</sup>AMSTAR = Assessment of Multiple Systematic Reviews. <sup>b</sup>NA = Not applicable.

Table 4: Summary of Effect Sizes

Outcome	Author	Measuremen t point	Effect size	95% Confidence Interval	Significance	Number of RCTs included in pooled result	Quality assess ment
Disease activity/severity	Nyssen et al.	Post intervention	-0.02	-0.37, 0.32	P=0.89, NS	3	10
	(2016)	Follow-up	-0.61	-0.96, -0.26	P<0.001	3	10
Patient global assessment	Riemsm a et al. (2003)	Post intervention	-0.30	-0.55, -0.04	P=0.02	4	11
Tender and swollen joints	Astin et al.	Post intervention	0.15	-0.09, -0.39	NS	7	6
	(2002)	Follow-up	0.30	0.04, -0.56	P=0.005	5	6
Inflammation	Nyssen et al. (2016)	Post intervention	0.10	-0.34, 0.53	P=0.67, NS	3	10
Functional disability	Astin et al.	Post intervention	0.27	0.12, -0.42	P<0.001	12	6
	(2002)	Follow-up	0.12	-0.09, -0.33	NS	7	6
	Riemsm a et al.	Post intervention	-0.23	-0.36, -0.10	P<0.001	27	11
	(2003)	Follow-up	-0.10	-0.23, 0.02	P=0.10, NS	18	11
	Knittle et al. (2010)	Post intervention	0.32	0.13, 0.51	P<0.001	17	6
Pain	Astin et al.	Post intervention	0.22	0.07, -0.37	P=0.003	13	6
	(2002)	Follow-up	0.06	-0.17, -0.29	NS	6	6
	Riemsm a et al. (2003)	Post intervention	-0.09	-0.19, 0.02	P=0.10, NS	26	11
	Knittle et al. (2010)	Post intervention	0.18	0.08, 0.29	P<0.001	22	6
Fatigue	Cramp et al. (2013)	Post intervention	-0.24	-0.40, -0.07	Significant	13	11
Depression	Astin et	Post	0.15	-0.01, -0.31	P=0.03	12	6

	al.	intervention					
	(2002)	Follow-up	0.33	-0.07, -0.59	P=0.01	5	6
	Riemsm a et al. (2003)	Post intervention	-0.14	-0.25, -0.04	P=0.009	13	11
	Riemsm a et al. (2003)	Follow-up	0.12	-0.25, 0.01	P=0.07, NS	13	11
	Knittle et al. (2010)	Post intervention	0.23	0.06, 0.39	P=0.01	19	6
Anxiety	Knittle et al. (2010)	Post intervention	0.17	0.02, 0.32	P=0.03	11	6
Self-efficacy	Astin et al. (2002)	Post intervention	0.35	0.11, 0.59	P=0.017	5	6
		Follow-up	0.20	-0.08, -0.48	NS	3	6
Coping	Astin et al. (2002)	Post intervention	0.46	0.09, 0.83	P=0.007	4	6
		Follow-up	0.52	-0.07, -1.11	P=0.04	3	6
Physical activity	Knittle et al.	Post intervention	0.47	0.12, 0.83	P=0.009	4	6
	(2010)	Follow-up	0.36	0.06, 0.67	P=0.02	4	6

<sup>&</sup>lt;sup>a</sup>NS = Non-significant. <sup>b</sup>RCTs = Randomised Controlled Trials.