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REVIEW

Non-pharmacological interventions to promote work participation in people with rheumatic and musculoskeletal diseases: a systematic review and meta-analysis from the EULAR taskforce on healthy and sustainable work participation

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ABSTRACT

Objective To summarise the evidence on effectiveness of non-pharmacological (ie, non-drug, non-surgical) interventions on work participation (sick leave, work status and presenteeism) in people with rheumatic and musculoskeletal diseases (RMDs). Methods A systematic review of randomised controlled

trials (RCTs) and longitudinal observational studies (LOS) was performed. Qualitative (RCTs/LOS) and quantitative (RCTs) evidence syntheses were conducted. Mixedeffects restricted maximum likelihood models were used to combine effect estimates, using standardised mean differences (SMDs) as the summary measure for each outcome domain separately, with a negative SMD favouring the intervention over comparator. Subgroup analyses were performed for type of RMD, risk status at baseline regarding adverse work outcomes and intervention characteristics.

Results Of 10153 records, 64 studies (37 RCTs and 27 LOS; corresponding to k=71 treatment comparisons) were included. Interventions were mostly conducted in clinical settings (44 of 71, 62%). Qualitative synthesis suggested clear beneficial effects of 7 of 64 (11%) interventions for sick leave, 1 of 18 (6%) for work status and 1 of 17 (6%) for presenteeism. Quantitative synthesis (37 RCTs; k=43 treatment comparisons) suggested statistically significant but only small clinical effects on each outcome (SMD_{sick})

 $_{\text{leave}}$ (95% Cl)=-0.23 (-0.33 to -0.13; *k*=42); SMD_{work} _{status}=-0.38 (-0.63 to -0.12; *k*=9); SMD_{presenteeism}=-0.25 (-0.39 to -0.12; *k*=13)).

Conclusion In people with RMDs, empirical evidence shows that non-pharmacological interventions have small effects on work participation. Effectiveness depends on contextual factors such as disease, population risk status, intervention characteristics and outcome of interest, highlighting the importance of tailoring interventions.

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Despite substantial advances in disease management, work participation of people with rheumatic and musculoskeletal diseases (RMDs) remains decreased compared with the general population.
- ⇒ The effect of various non-pharmacological interventions on work outcomes has been studied in people with RMDs, but no evidence synthesis exists of their effectiveness across RMDs and interventions.

WHAT THIS STUDY ADDS

⇒ Across RMDs, non-pharmacological interventions seem to have small but significant beneficial effects on sick leave, work status and presenteeism, but effects varied from non-important to moderate depending on type of RMD, baseline risk status and intervention characteristics.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Non-pharmacological interventions can improve work participation in people with RMDs, but need to be tailored to the individual to be effective.

INTRODUCTION

Work participation contributes to physical and mental health, social inclusion and economic independence of an individual, and is essential to society's wealth and health.¹ In Europe, work participation among people with rheumatic and musculoskeletal diseases (RMDs) remains decreased compared with the general population.^{2 3} Disease control by pharmacological interventions—especially in inflammatory

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arthritis-has shown to be effective in improving work participation outcome domains, including presenteeism, sick leave and work status (the latter specifically when the intervention is started early in the course of disease).⁴⁻⁷ Notwithstanding, the work participation gap persists. Residual disease burden despite pharmacological treatment, such as limitations in physical function, as well as personal and environmental contextual factors, are predictors of adverse work outcomes.⁸⁹ On this line, nonpharmacological (ie, non-drug, non-surgical) interventions could further improve work participation, as they can address aspects of a person's physical and mental health relevant for work, or can adjust the work environment to the person's needs. Previous reviews of nonpharmacological interventions focused on a specific type of non-pharmacological intervention or a specific RMD, such as inflammatory arthritis, and did not address all domains of work participation (presenteeism, sick leave and work status).¹⁰⁻¹² A summary of the effectiveness of all types of non-pharmacological interventions, across the whole spectrum of RMDs and for all work outcome domains, could be worthwhile. Subgroup analyses would allow quantifying effectiveness of non-pharmacological interventions by type of RMDs, intervention characteristics and outcomes.

The aim of this evidence synthesis was to summarise the effectiveness of non-pharmacological interventions on work participation—assessed using the following outcome domains: (1) sick leave, (2) work status and (3) presenteeism in people across RMDs. This evidence summary was conducted to inform a taskforce of European Alliance of Associations for Rheumatology (EULAR) responsible for developing 2021 Points to Consider to support healthy and sustainable work participation of people with RMDs.¹³

METHODS

Protocol and registration

The protocol was registered in PROSPERO.¹⁴ The Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist was used as framework for reporting.¹⁵

Patient and public involvement

A patient research partner participated in the EULAR steering group that designed the research objective and outlined the protocol. 16

Eligibility criteria

Population, Intervention, Comparator and Outcome were specified to identify eligible randomised controlled trials (RCTs) and longitudinal observational studies (LOS) with any follow-up duration evaluating non-pharmacological interventions (ie, non-drug, non-surgical) in people with any RMD (except studies that considered only or a majority (\geq 50%) of people with low back pain or work-related musculoskeletal injuries).¹⁷ Active treatment, usual care, waiting list and no

intervention were eligible comparators. Work outcome domains included sick leave, work status (eg, being (un) employed/work disabled/retired for any reason) and presenteeism (eg, loss of work ability/productivity while at work due to ill health). There were no restrictions in language, publication year or country (online supplemental table 1).

Information sources and search strategy

Search strings were formulated by a librarian (LF) to cover all relevant search terms up to August 2020 in MEDLINE, EMBASE, CENTRAL and CINAHL (online supplemental text 1). Additionally, relevant records were identified using reference lists and were added manually. Search records were de-duplicated.

Study selection and data extraction

A random subset of 1000 records ($\approx 10\%$) was screened by two reviewers independently (MHPB, CW). Inter-rater reliability between both reviewers was good (kappa=0.86), and the remainder of records was screened by a single reviewer (MHPB). Both reviewers assessed full texts of selected records independently for inclusion and extracted the data. A predefined data extraction form was used, including general article information, study objective (ie, was work a primary objective or not), methodological information (design, blinding/randomisation, follow-up duration), population characteristics (number of participants, type of RMD, baseline risk status for adverse work outcomes), intervention characteristics (setting, components, features, duration), comparator type (if applicable) and outcome (work outcome domain addressed, measurement instrument used and magnitude of the effect). Two reviewers each extracted 50%of the included studies; one of these reviewers checked all extracted data. Disagreement between researchers on study eligibility/inclusion and data extraction was discussed and, if necessary, adjudicated by a third reviewer (AB).

Risk of bias assessment

For pragmatic reasons, formalised assessments of risk of bias (RoB) were limited to RCTs, as LOS often have a high(er) RoB by design.¹⁸ Two reviewers (MHPB, CW) assessed RoB per study and for each work outcome domain separately, using the Cochrane RoB tool 2.0.¹⁹ Across outcome domains, each RCT was assigned an overall risk of bias in terms of low risk (low for all key domains), some concerns (concerns for \geq 1 key domain) and high risk (high for \geq 1 key domain). Disagreement between the reviewers on RoB assessment was discussed and, if necessary, adjudicated by a third reviewer (AB).

Data synthesis

Both RCT and LOS designs were eligible for the qualitative evidence synthesis. To minimise confounding bias in the combined effect estimates, the quantitative synthesis was limited to RCTs. Qualitative and quantitative evidence syntheses were performed separately for each of the three work outcome domains.

For *qualitative evidence synthesis*, the reviewers (MHPB, CW) collaboratively conducted an assessment for each treatment comparison by outcome domains, judging it as effective, possibly effective or ineffective. This assessment was based on methodological aspects (eg, design, number of participants, timing of follow-up duration, sources of bias, whether work participation was the primary study objective), intervention and comparator aspects (eg, content, duration or frequency), and magnitude of the reported effects (including variation between different measures of the same outcome within a study).

For *quantitative evidence synthesis*, treatment comparisons for each reported outcome measurement instrument in RCTs were used to assess the effects of the intervention versus comparator. The standardised mean difference (SMD) was used as the summary measure corresponding to Cohen's effect size. If the selected result was on a continuous scale, the SMD was calculated directly, while outcome measures collected on a binary scale were first analysed using the OR, which was then subsequently converted to an SMD.^{20 21} A negative SMD indicates a beneficial effect in improving the work outcome by the intervention compared with the comparator (SMD: <-0.2=non-important; \geq -0.2 to <-0.5=small; \geq -0.5 to <-0.8=moderate; \geq -0.8=large effect).²²

If a study reported multiple results on the same outcome domain (different outcome measurements or alternative reporting), one result was chosen based on a prespecified hierarchy of outcome measurement approaches (online supplemental table 2). For example, days of sick leave during a certain period of time was given preference over a percentage of people with any sick leave in a certain period (if both were reported).

For each outcome domain, forest plots were generated. Treatment comparisons were included in Mixed Effects Meta-Regression Analyses (Restricted Maximum Likelihood Models), with random-effects for treatment comparisons (k), while accounting for correlation between comparisons from the same study as a fixed-effect factor. In the overall model per work outcome domain, heterogeneity was examined across all treatment comparisons, by estimating tau square (T^2) , reflecting between-study variance. In case of k>10 comparisons and a T^2 of ≥ 0 , the prediction interval was additionally calculated.^{23,24} Funnel plots and tests for funnel plot asymmetry were occasion-ally used to examine bias in the results of meta-analyses. Funnel plots examine possible publication bias.²⁵

To facilitate interpretation of results, predefined and clinically relevant subgroups were distinguished by including them as extra fixed factors in separate models (online supplemental table 3): *type of RMD*, based on diagnosis (and not symptoms) as reported in the original study and further dichotomised into (1) pain syndromes, or (2) inflammatory and degenerative RMDs (i/dRMDs) including mixed populations with RMDs; participants' *baseline risk for adverse work outcomes*, described by four subgroups: (1) at risk (on sick leave or at risk of adverse work outcomes), (2) not at risk (not on sick leave nor other risk of adverse work outcome), (3) mixed risk (on sick leave/at risk or not on sick leave), or (4) not described or specified; intervention setting, classified into: (1) clinical setting, (2) workplace setting, (3) combination of clinical and workplace setting, or (4) other setting²⁶; and finally number of *intervention components*, dichotomised into: (1) single or (2) multiple.²⁶ Interpretation of stratified analyses focused on subgroups with more than five comparisons. To further explore the role of specific intervention features-defined as: (1) vocational or work support, (2) physical training or physiotherapy, (3) psychological feature, or (4) organisational or system change-post-hoc analyses assessed these in a total model, including all work outcome domains. Analyses were performed in SAS V.9.4.

RESULTS

Study selection

The search yielded 10154 records. After removing duplicates and screening of title/abstracts, 175 reports remained for full-text review, of which 71 articles were included. In addition, two studies were added manually, based on reference lists of included studies, thus bringing the total number of included studies to 73. As some studies included multiple intervention arms, and some of the articles reported on the same study (usually reporting on different follow-up times), these 73 articles comprised 64 studies were included in the qualitative analysis.^{27–95} Thirty-seven RCTs (*k*=43 treatment comparisons, based on 19926 patients in total) were eligible for the quantitative evidence synthesis (figure 1).

Study and intervention characteristics

An overview of study characteristics of included RCTs is presented in table 1 (and an extended overview in online supplemental table 4, and of LOS in online supplemental table 5). A total of 117024 participants (ranging from 20 to 72131 per study) were included. The gender distribution varied substantially between studies (percentage of women ranging from 0% to 97%). The majority of studies were performed in Scandinavian countries (37 of 64, 58%). Thirty out of 64 studies (47%) were published after 2010. Most studies addressed people with mixed/ not specified RMDs (26 of 64, 41%) or musculoskeletal pain (24 of 64, 38%) Mean disease duration was 9.1 years (reported in 10 of 64 studies, 16%). Most frequently, participants were on sick leave at time of inclusion (19 of 64, 30%) or their risk status for adverse work outcomes at inclusion was not reported (16 of 64, 25%). Sick leave was the most frequently reported outcome domain (56 of 64, 88%), followed by work status (14 of 64, 22%) and finally presenteeism (16 of 64, 25%). In 56% of studies (36 of 64), work participation was the primary outcome, 6% (4) of 64) the secondary outcome and in 38% a statement on

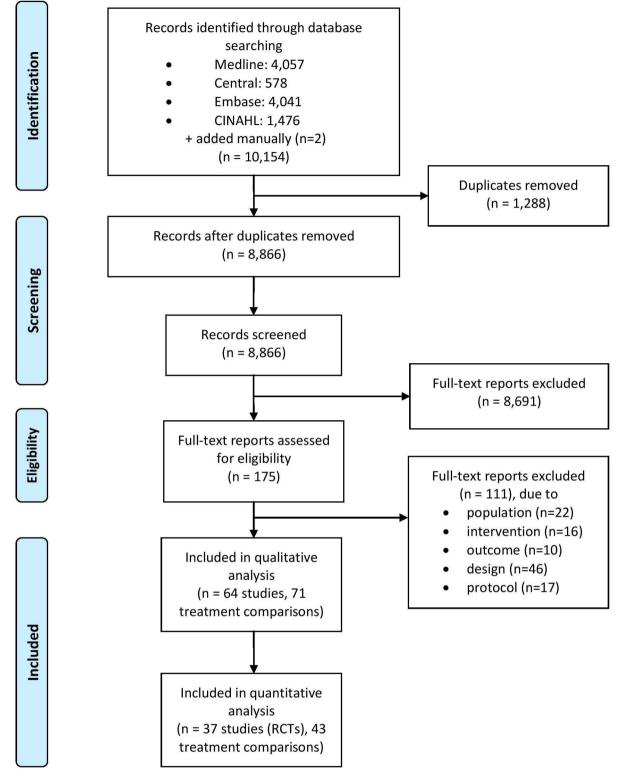


Figure 1 PRISMA flow chart of selection and inclusion process. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCTs, randomised controlled trials.

this was absent (24 of 64). Fifty-one of 64 studies (80%) had a comparator, being either an active comparator (31%) or usual care/waiting list (69%). Only 15 LOS had a comparator (out of 27, 56%). On the intervention level (n=71), interventions were mostly initiated in clinical settings (44 of 71, 62%) and often had multiple

components (57 of 71, 80%). Physical training and/or physiotherapy (43 of 71, 61%) was the most frequently studied intervention feature, for example, a 3months' physical training or rehabilitation with interactive telere-habilitation. Vocational or work support (33 of 71, 46%) was also frequently part of the intervention, for example,

Author (country, year)	Disease	Employment status and baseline risk for adverse work outcome	Intervention (setting) ((components)) (feature)	Comparator	Randomised, N	Outcome measure	Time point measurement (months)	Reported effect (intervention vs comparator*†)
Inflammatory RM	D							
De Buck <i>et al⁵⁰</i> (The Netherlands, 2005)	RA, AS, PsA, reactive arthritis, SLE or scleroderma	Working full time or part time or on sick leave, either with or without a partial disability pension	Multidisciplinary job-retention vocational rehabilitation programme (CLI) ((multiple)) (VWS, ORG)	Usual care	l: 74 C: 66	Work status: job loss (work disability or unemployment); n/ total (%)	24	14/59 (24%) vs 12/53 (23%) p=0.89
Van Vilsteren <i>et al⁹²</i> (The Netherlands, 2017)	RA	Employed, not on sick leave or on sick leave for maximum 3 months	Workplace integrated care intervention and participatory workplace intervention, with clinical occupational physician, patients' rheumatologist and occupational therapist (combined) ((multiple)) (VWS, ORG)	Usual care	l: 75 C: 75	Presenteeism: work instability (range 0–23, a high score indicated more instability); mean score (SD)	12	9.3 (5.2) vs 7.7 (6.0)
Baldwin <i>et al³⁸</i> (USA, 2012)	RA/OA	Full-time or part-time employment; not on sick leave	Ergonomic intervention and assessment, work plan and follow- up (WPLACE) ((multiple)) (VWS)	Brochures/educational material	l: 48 C: 41	Presenteeism: degree of work impairment (range 0–5); mean score (SD)	24	1.49 (1.35) vs 2.16 (1.93) p=0.03
Hammond et al ⁵⁴ (UK, 2017)	IA, RA, PsA	Employed, not on extended (>3 months) sick leave	Job retention vocational rehabilitation: work assessment, activity diaries, action planning, broad individualised programme and self-help information (OTHER) ((multiple)) (VWS)	Usual care (self-help work information)	l: 29 C: 26	Sick leave (arthritis): mean % of working days lost (SD) Work status: stopped working; n (%) Presenteeism: workplace limitations (range -100 to 0); mean change from baseline (SD)	9	Sick leave: 8.0% (13.8) vs 15.0% (25.0) Work status: 0 (0%) vs 2 (9%) Presenteeism: -12.4 (SD 13.2) vs -2.5 (SD 15.9)
Macedo et al ⁷⁴ (UK, 2009)	RA	Employed, medium or high risk of work disability	Occupational therapy: medical assessment, work assessment, education, discussion with employer on work accommodations, stress management (OTHER) ((multiple)) (VWS)	Usual care	l: 16 C: 16	Sick leave: days missed from work due to illness per month; mean change from baseline (SD) Presenteeism: impact of RA on work performance (range n.d.); mean change from baseline (SD)	6	Sick leave: -2.80 (6.18) vs 0.63 (4.86) p=0.10 Presenteeism: -43.20 (35.01) vs -4.69 (43.91) p=0.01
Allaire <i>et al³⁴</i> (USA, 2005)	RA, knee OA, SLE, AS, PsA	Employed, at risk of job loss	Work barrier identification, counselling and education (OTHER) ((multiple)) (VWS)	Pamphlets with information on how to sustain work	l: 122 C: 120	Work status: remaining employed; n/ total (%)	12	118/122 (97%) vs 108/120 (90%)
Van Tubergen <i>et al⁹¹</i> (The Netherlands, 2002)	AS	n.d.	Combined spa–exercise therapy (OTHER) ((multiple)) (PHY) at two locations: (1) Austria (including Heilstollen), (2) the Netherlands	Usual care	1: 38 2: 36 C: 37	Sick leave: workday lost because of illness; mean (SD)	9	1: 2.5 (6.5) vs 6.1 (15.8) 2: 6.4 (26.4) vs 6.1 (15.8)
Degenerative RM	ID							
Chopp-Hurley <i>et al⁴⁸ (</i> USA, 2017)	Hip and/or knee OA	Employed, not on sick leave	Exercise programme: supervised exercise classes, at workplace sport facility (WPLACE) ((single)) (PHY)	Usual care (no exercise programme)	l: 12 C: 12	Presenteeism: work ability score (range 7–49); mean (SD)	3	20 (6) vs 40 (5) p=0.049
Eichler <i>et al⁵¹</i> (Germany, 2019)	Hip or knee OA	Mixed (not) employed, n.d.	Rehabilitation with interactive telerehabilitation aftercare (OTHER) ((multiple)) (PHY)	Usual care	l: 56 C: 55	Work status: gainfully employed; n (%)	3	31 (64.6%) vs 18 (46.2%) p=0.01

Treatments

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Table 1 Continued

Author (country, year)	Disease	Employment status and baseline risk for adverse work outcome	Intervention (setting) ((components)) (feature)	Comparator	Randomised, N	Outcome measure	Time point measurement (months)	Reported effect (intervention vs comparator*†)
Eshøj <i>et al⁵³</i> (Denmark, 2001)	Non-inflammatory disorder of locomotor system		Early vocational intervention: sociomedical examination, multidisciplinary assessment and sociomedical rehabilitation plan (OTHER) ((multiple)) (VWS, ORG)	Usual care	l: 108 C: 93	Work status: employed; n (%), RR (95% Cl)	12	65 (60.2%) vs 52 (55.9%); RR 1.1 (0.8 to 1.4)
Mixed or not spe	cified RMD							
Skagseth <i>et al⁸⁶</i> (Norway, 2020)	Musculoskeletal, psychological or general and unspecified diseases	Employed, on (partial) sick leave	Workplace intervention added to an inpatient multimodal occupational rehabilitation programme (I-MORE) (CLI) ((multiple))(VWS, PHY, PSYCH)	Usual care	l: 88 C: 87	Sick leave: cumulated sickness absence days; n (IQR)	12	130 (81–212) vs 115 days (53–183) p=0.084
Briest and Bethge ⁴³ (Germany, 2016)/Knapp <i>et</i> <i>al</i> ²⁹ (Germany, 2015)	MSD	Employed, on sick leave, previous sick leave or poor return to work prognosis	Intensive work-related rehabilitation aftercare: work-related training, job-specific psychosocial training, social support, relaxation training (CLI)((multiple)) (VWS, PHY, PSYCH)	Usual care	l: 157 C: 150	Sick leave: length of sick leave in weeks during last 3 months; mean (SD) Presenteeism: work ability index (range 7–49); mean score (SD)	12	Sick leave: 1.6 (3.7) vs 1.7 (4.1) p=0.786 Presenteeism: 31.3 (9.1) vs 30.8 (10.9)
Streibelt and Bethge ⁸⁹ (Germany, 2014)	Chronic musculoskeletal disorders	Mixed (not) employed, mixed (not) on sick leave	Functional capacity evaluation on work demands and abilities (CLI) ((multiple)) (VWS, PHY, PSYCH)	Multidisciplinary rehabilitation (a less intense programme)	l: 109 C: 113	Sick leave: duration of sick leave (in weeks); mean differences, estimated marginal means (range)	12	5.2 vs 13.2; -8.0 (-17.4 to 1.4) p=0.09
Carlsson <i>et al⁴⁶</i> (Sweden, 2013)	Psychiatric disease or MSD	Mixed (not) employed, currently sick-listed with maximum period of 28 days	Early multidisciplinary assessment at primary healthcare centre (CLI) ((single)) (ORG)	Usual care	l: 18 C: 15	Sick leave; mean net days during last 9 months (SD)	12	77 (109) vs 37 (62) p=0.580
Bethge e <i>t al⁴⁰</i> (Germany, 2011)	MSD	Mixed (not) employed; at least 12 weeks of sick leave in the year before	Multimodal work hardening: motivation, counselling, coping behaviour, exercises, functional capacity training and relaxation techniques (CLI) ((multiple)) (VWS, PHY)	Conventional musculoskeletal rehabilitation	l: 118 C: 118	Sick leave: working and ≤6 weeks of sick leave; %; OR (95% Cl)	12	Intervention (pre/pos 39.2%–59.5%; Comparator (pre/ post): 48.6%–51.4%; OR: 2.363 (1.266 to 4.410) p=0.007)
Heinrich <i>et al⁶⁰</i> (The Netherlands, 2009), first arm	Non-specific MSD	Self-employed with new work disability claim (duration 1 day–8 weeks)	1. Physical training (CLI) ((multiple)) (PHY)	Usual care	l: 53 C: 50	Sick leave: gross claim duration; median days (IQR)	12	228 (122–365) vs 165 (48–365) p=0.18
Heinrich e <i>t al⁶⁰</i> (The Netherlands, 2009), second arm	Non-specific MSD	Self-employed with new work disability claim (duration 1 day–8 weeks)	2. Physical training with cognitive- behavioural component and workplace-specific exercises (CLI) ((multiple)) (PHY, PSYCH)	Usual care	l: 76 C: 75	Sick leave: gross claim duration; median days (IQR)	12	148 (75–343) vs 137 (48–365) p=0.95
Meijer <i>et</i> al ⁷⁷ (The Netherlands, 2006)	Non-specific upper extremity musculoskeletal disorders	Employed, on sick leave	Psychological and physical sessions aiming to reconditioning, 'de-medicalising', unrestrained moving and return to work (CLI) ((multiple)) (VWS, PHY, PSYCH)	Usual care: supervision by occupational health services		Sick leave <u>:</u> return to work; % of original number of hours (95% Cl)	12	86.0% (68.5% to 103.4%) vs 72.8% (52.5% to 93.2%) p=0.840

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Author (country, year)	Disease	Employment status and baseline risk for adverse work outcome	Intervention (setting) ((components)) (feature)	Comparator	Randomised, N	Outcome measure	Time point measurement (months)	Reported effect (intervention vs comparator*†)
Abasolo <i>et al²⁷</i> (Spain, 2005)	MSD	Employed, temporary work disability	Education, protocol-based clinical management and administrative duties (CLI) ((multiple)) (ORG) at three locations	Usual care	11: 1845 C1: 3045 12: 1474 C2: 1557 13: 1953 C3: 3203	Sick leave: return to work; relative rate (95% CI)	12	1: 1.26 (1.19 to 1.33) 2: 1.27 (1.20 to 1.35) 3: 1.31 (1.24 to 1.36)
Shiri <i>et al</i> ⁸⁴ (Finland, 2011)/ Martimo <i>et al</i> ³¹ (Sweden, 2010)	Upper extremity symptoms	Employed, not on sick leave	Early ergonomic intervention: contact with employer, work visit on work accommodations (combined) ((multiple)) (VWS)	Usual care	l: 89 C: 84	Sick leave: sick leave days: mean (SD) Presenteeism: productivity loss; % (proportion of patients with any loss) and magnitude (SD)	12	Sick leave: 4.07 (11.2) vs 5.12 (13.2) Presenteeism: 25%, 6.8 (17.4) vs 51.3%, 18.4 (25.7)
Bultmann et al ⁴⁴ (Denmark, 2009)	LBP and MSD	Employed, on sick leave	Coordinated and tailored work rehabilitation, including a work disability screening and work rehabilitation plan by an interdisciplinary team (OTHER) ((multiple)) (VWS, ORG)	Conventional case management	l: 68 C: 51	Sick leave: cumulative sickness absence hours; mean (SD)	12	656.6 (565.2) vs 997. (668.8) p=0.006
Fleten and Johnsen ⁵⁶ (Norway, 2006)	LBP, rheumatic disorder/arthritis, other MSK	Employed, newly sick- listed, longer than 14 days	Postal package to participants with information on work-related measures (OTHER) ((single)) (other)	Usual care (no postal package)	l: 495 C: 495	Sick leave: mean difference (95% CI) in number of sick leave days	12	Per disease group: LBP: 17.2 (-12.5 to 46.9) RMD: -68.3 (-123.3 to -13.3) Other MSK: 0.5 (-18. to 19.1)
Keysor <i>et al⁶³</i> (USA, 2018)	Rheumatic/MSK disorder	Employed, at risk of unemployment according to patient	Modified vocational rehabilitation approach: assessment, written materials, action plan, follow-up (OTHER) ((single)) (VWS)	Written materials only	l: 143 C: 144	Sick leave: sick leave due to health complaints; mean days in last 3 months Work status: permanent job loss due to retirement/laid off/work disability; occurrence; n (%), HR (95% Cl) Presenteeism: work limitations; mean change from baseline (SD)	24	Sick leave: 1.4 vs 3.6 p<0.001 Work status: 11 (8%) vs 25 (17%); 0.47 (0.23 to 0.95) p=0.03 Presenteeism: -8.60 (1.92) vs -8.33 (2.22) p=0.93
MSKP								
Sennehed <i>et</i> a/ ⁸³ (Sweden, 2018)/ Forsbrand <i>et</i> a/ ⁸³ (Sweden, 2020)	Acute/subacute neck and back pain	Mixed (not) employed, at risk of sick leave	Structured physiotherapy and convergence dialogue meeting to support work ability and return to work (CLI) ((multiple)) (VWS, PHY)	Structured physiotherapy	l: 146 C: 206	Sick leave: no sick leave or disability pension for 4 consecutive weeks; n/total (%) Presenteeism: work ability score; mean difference (95% CI)	12	Sick leave: 108/127 (85%) vs 127/171 (75%) p=0.002 Presenteeism: -0.05 (-0.63 to 0.53)

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Table 1 Cor	ntinued							
Author (country, year)	Disease	Employment status and baseline risk for adverse work outcome	Intervention (setting) ((components)) (feature)	Comparator	Randomised, N	Outcome measure	Time point measurement (months)	Reported effect (intervention vs comparator*†)
Wynne-Jones <i>et</i> al ⁹⁴ (UK, 2018)	Musculoskeletal pain	Employed, on sick leave	Vocational advice service on psychological beliefs, work perceptions and contextual factors (CLI) ((multiple)) (VWS, PSYCH)	Education to general and nurse practitioners	l: 158 C: 180	Sick leave: days off work; mean (SD) Presenteeism: presenteeism score (range 6–30); mean (SD)	12	Sick leave: 20.3 (40.6) vs 24.3 (50.7) p=0.198 Presenteeism: 22.0 (5.6) vs 20.1 (5.7) p=0.082
Åsenlöf <i>et al³⁷</i> (Sweden, 2009)/ Emilson <i>et al³²</i> (Sweden, 2017)	Musculoskeletal pain	Mixed (not) employed; n.d.	Tailored behavioural medicine treatment in a physiotherapy context (CLI) ((single)) (PSYCH)	Exercise-based physiotherapy	l: 57 C: 65	Sick leave: on sick leave; n/total (%)	24	2/28 (7%) vs 10/37 (27%) p=0.06
Brendbekken <i>et al⁴²</i> (Norway, 2017)	MSKP	Employed, on sick leave in last 12 months for 50%–100%	Multidisciplinary intervention by social worker, physician, physiotherapist: visual educational tool, self-management and focus on working conditions (CLI) ((multiple)) (VWS)	Brief intervention of 2 sessions with only a physician or physiotherapist	l: 141 C: 143	Sick leave: full return to work; n/total	24	60/141 vs 52/142
Andersen <i>et</i> <i>al</i> ³⁵ (Denmark, 2015), first arm	Back or neck pain	Employed, maximum 9 weeks sick- listed	Tailored physical activity programme+health guidance in dialogue meeting (CLI) ((multiple)) (PHY)	Health guidance in dialogue meeting	l: 47 C: 47	Sick leave: return to work; n/total (%) Presenteeism: work ability (range 0–10); mean score (SD)	11	Sick leave: 23/46 (50%) vs 17/47 (36%) Presenteeism (pre vs post): I: 3.1 (2.7) vs 5.0 (3.1) C: 2.9 (2.8) vs 4.8 (2.9)
Myhre e <i>t al⁸⁰</i> (Norway, 2014)	Neck and back pain	Employed, on sick leave between 4 weeks and 12 months	Work-focused rehabilitation: clinical examination, education, physical therapy, enhance coping, return to work planning (CLI) ((multiple)) (VWS) at two locations	Usual care	l1: 109 C1: 107 l2: 100 C2: 97	Sick leave: returned to work (5-week period without benefits); n (%)	12	1: 69 (65%) vs 80 (75%) 2: 73 (75%) vs 72 (75%)
Lindell <i>et al⁷¹</i> (Sweden, 2008)	Non-specific back and neck pain	Mixed (not) employed, sick-listed	Cognitive–behavioural rehabilitation: graded activity, manual therapy, applied relaxation, ognitive–behavioural therapy (CLI) ((multiple)) (VWS, PHY, PSYCH)	Usual care	l: 63 C: 62	Sick leave: mean net days of sick leave (95% Cl)	18	397 (354 to 440) vs 391 (345 to 436)
Zaproudina <i>et</i> <i>al⁹⁵</i> (Finland, 2007), first arm	Chronic non-specific neck pain	Employed, not on sick leave	Traditional bone setting (CLI) ((single)) (PHY)	Conventional physiotherapy	l: 35 C: 34	Sick leave: days sick-listed; number per person	12	0.61 vs 2.6
Zaproudina <i>et</i> <i>al⁹⁵</i> (Finland, 2007), second arm	Chronic non-specific neck pain	Employed, not on sick leave	Traditional bone setting (CLI) ((single)) (PHY)	Massage therapy	l: 35 C: 33	Sick leave: days sick-listed; number per person	12	0.61 vs 3.9
Chiu <i>et al⁴⁷</i> (China, 2005)	Neck pain	Mixed (not) employed, n.d.	Exercise programme: activation and dynamic strengthening of neck muscles+infrared irradiation (CLI) ((single)) (PHY)	Usual care (infrared irradiation)	l: 67 C: 78	Sick leave: n (%) of cases with sick leave during last 3 weeks	6	2 (3.0%) vs 7 (9.0%) p=0.22
Linton <i>et al⁷²</i> (Sweden, 2005), first arm	Non-specific neck or back pain	Employed, maximum of 4 months' sick leave in last year	Minimal treatment+cognitive- behavioural treatment (CLI) ((multiple)) (PSYCH)	Minimal treatment (information, check for red flags)	l: 69 C: 47	Sick leave: occurrence of long-term sick leave (≥15 days); n (%)	12	4 (7.4%) vs 4 (16.4%) (extracted from figure)

Author (country, year)	Disease	Employment status and baseline risk for adverse work outcome	Intervention (setting) ((components)) (feature)	Comparator	Randomised, N	Outcome measure	Time point measurement (months)	Reported effect (intervention vs comparator*†)
Linton <i>et al⁷²</i> Sweden, 2005), second arm	Non-specific neck or back pain	Employed, maximum of 4 months' sick leave in last year	Minimal treatment+cognitive- behavioural treatment+preventive physical therapy (CLI)((multiple)) (PHY, PSYCH)	Minimal treatment (information, check for red flags)	l: 69 C: 47	Sick leave: occurrence of long-term sick leave (≥15 days); n (%)	12	4 (6.6%) vs 4 (16.4%) (extracted from figure)
Jensen <i>et al⁶⁴</i> Sweden, 2001)/ Bergström <i>et</i> al ³⁰ (Sweden, 2012), first arm	Non-specific back or neck pain	Mixed (not) employed, on sick leave	1. Behavioural medicine rehabilitation (CLI)((multiple)) (PHY, PSYCH)	Usual care	l: 63 C: 48	Sick leave: sick leave (any) during last month; % Work status: full-time early retirement; OR (95% CI)	18	Sick leave: Males: 52% vs 70% Females: 50% vs 54% Work status: Males: 0.4 (0.1 to 1.9); Females: 0.4 (0.1 to 1.4)
Jensen <i>et al⁶⁴</i> Sweden, 2001)/ Bergström <i>et</i> al ⁶⁰ (Sweden, 2012), second arm	Non-specific back or neck pain	Mixed (not) employed, on sick leave	2. Behaviour-oriented physical therapy (CLI)((multiple)) (PHY)	Usual care	l: 54 C: 48	Sick leave: sick leave (any) during last month; % Work status: full-time early retirement; OR (95% CI)	18	Sick leave: Males: 65% vs 70% Females: 54% vs 54% Work status: Males: 0.6 (0.1 to 2.9); Females: 0.1 (0.0 to 0.6)
Jensen <i>et al⁶⁴</i> Sweden, 2001)/ Bergström <i>et</i> al ³⁰ (Sweden, 2012), third arm	Non-specific back or neck pain	Mixed (not) employed, on sick leave	3. Cognitive–behavioural therapy (CLI) ((multiple)) (PSYCH)	Usual care	l: 49 C: 48	Sick leave: sick leave (any) during last month; % Work status: full-time early retirement; OR (95% CI)	18	Sick leave: Males: 59% vs 70% Females: 54% vs 54% Work status: Males: 0.5 (0.1 to 2.3); Females: 0.1 (0.0 to 0.8)
Johansson <i>et</i> a ^{/66} (Sweden, 1998)	Chronic musculoskeletal pain	Mixed (not) employed, n.d.	Cognitive-behavioural multidisciplinary pain management programme: education, goal setting, physical training, relaxation, planning of return to work (CLI) ((multiple)) (VWS, PHY, PSYCH)	Waiting list	l: 21 C: 21	Sick leave: level of sick leave (range 0–100%); mean % (SD)	1	80.4% (34.8) vs 59.6% (42.5)
Viikari-Juntura e <i>t al⁹³</i> (Finland, 2012)/Shiri e <i>t</i> al ²⁸ (Finland, 2013)	Musculoskeletal pain	Employed, not on sick leave or only short-term sick leave	Part-time sick leave (WPLACE) ((single)) (ORG)	Full-time sick leave	l: 31 C: 30	Sick leave: time to return to work (≥4 weeks without recurrent sick leave); median days (IQR), HR (95% CI) Presenteeism: productivity loss; mean % (SD)	12	Sick leave: 12 (6–33) vs 20 (8–35) HR 1.60 (0.98 to 2.63) p=0.10 Presenteeism: 22.6% (26.7) vs 23.9% (24.2) p=0.52
Andersen <i>et</i> a ^{/35} (Denmark, 2015), second arm	Back or neck pain	Employed, maximum 9 weeks sick- listed	Chronic pain self-management programme+health guidance in dialogue meeting (OTHER) ((multiple)) (PSYCH)	Health guidance in dialogue meeting	l: 47 C: 47	Sick leave: return to work; n, total n (%) Presenteeism: work ability (range 0–10); mean score (SD)	11	Sick leave: 22/47 (46.8%) vs 17/47 (36.2%) Presenteeism (pre vs post): l: 2.5 (3.4) vs 4.8 (3.4) C: 2.9 (2.8) vs 4.8 (2.9

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Table 1 Continued	ntinued							
Author (country, year) Disease	Disease	Employment status and baseline risk for adverse work outcome	Intervention (setting) ((components)) (feature)	Comparator	Randomised, N	Randomised, N Outcome measure	Time point measurement (months)	Reported effect (intervention vs comparator*†)
Linton and Ryberg ⁷³ (Sweden, 2001)	Persistent neck and back pain	Mixed (not) employed, maximum of 30 days' sick leave in last year	Cognitive-behavioural programme, Usual care pain management, adaptation to work, skill building (OTHER) ((multiple)) (PSYCH)	Usual care	l: 84 C: 91	Sick leave: sickness absence ≥14 days; n (%)	Q	4 (5%) vs 14 (15%)
Other								
Granviken and Vasseljen ⁵⁸ (Norway, 2015)	Subacromial impingement	n.d.	Supervised exercises and home exercises (CLI) ((single)) (PHV)	Home exercises	l: 23 C: 23	Sick leave: on sick leave; n/total (%) Work status: unemployed or disability pension; n	Q	Sick leave: 3/21 (14.3%) vs 4/18 (22.2%) Work status: 1 unemployed, 1 disability pension
Studies sorted bas *At endpoint or for †Direction of report AS, arthritis psoriat N, number; n.d., nc randomised contro	sed on (1) disease (inflamm: follow-up period unless oft ted effect follows the outco tica; C, control; CLI, clinical tt described/reported; OA, i lied trials; RMD, rheumatic	Studies sorted based on (1) disease (inflammatory RMD, degenerative RMD, mixed or not spe "At endpoint or for follow-up period unless otherwise indicated in column "Outcome measure" TDirection of reported effect follows the outcome measure's description (eg, work limitation: h AS, arthritis psoriatica; C, control; CLI, clinical setting; combined, clinical and workplace settir N, number; n.d., not described/reported; OA, osteoarthritis; OR, odds ratio; ORG, organisatior randomised controlled trials; RMD, rheumatic and musculoskeletal disease; RR, relative risk; candomised controlled trials; RMD, rheumatic and musculoskeletal disease; RR, relative risk;	Studies sorted based on (1) disease (inflammatory RMD, degenerative RMD, mixed or not specified RMD; MSKP; othen), (2) setting (clinical, combined, workplace, other) and (3) publication year (descending). "At endpoint or for follow-up period unless otherwise indicated in column "Outcome measure". Therection of reported effect follows the outcome measure's description (eg, work limitation: higher score indicates more limitations; work ability: higher score indicates better ability). As, arthritis psoriatica; C, control; CLI, clinical setting; combined, clinical, intervention; A, inflammatory arthritis; LBP, low back pain; MSD, musculoskeletal disease; MSK, musculoskeletal; MSKP, musculoskeletal pain; N, number; n.d., not described/reported; OA, osteoarthritis; OR, organisational or system change feature; PHY, physical training and therapy; PsA, psoriatic arthritis; PSYCH, psychological feature; RA, rheumatoid arthritis; RCIs, randomised controlled trials; RMD, rheumatic and musculoskeletal disease; RR, relative risk; SLE, systemic lupus erythematosus; VWS, vocational or work support; WPLACE, workplace.	stip (2) setting (clinical, comb. re limitations; work ability: h ammatory arthritis; LBP, low ture; PHY, physical training i nematosus; VWS, vocational	ined, workplace, other, igher score indicates t back pain; MSD, musk and therapy; PsA, psor or work support, WPL) and (3) publication year (descend) better ability). culoskeletal disease; MSK, muscul tatic arthritis; PSYCH, psychologic ACE, workplace.	ing). loskeletal; MSKP, m :al feature; RA, rheu	usculoskeletal pain; ımatoid arthritis; RCTs,

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two ergonomic advice sessions comprising an assessment, work plan and follow-up. Examples of interventions with psychological features (29 of 71, 41%) were 4 weeks of cognitive-behavioural therapy, or a 3months' tailored behavioural treatment. Organisational and/or system change (15 of 71, 21%) included the option to take partial sick leave (as opposed to full-time sick leave), or a nursing care model within the scope of a nurse's abilities. Follow-up duration of RCTs varied from 1 month to 2 years and for LOS 4 months to 7 years. Details on study and intervention characteristics are presented in table 1, and online supplemental tables 4 and 5.

Risk of bias

Results of the RoB assessment of RCTs are shown in online supplemental table 6. On the study level, the majority (63%) showed 'some concerns', and to a lesser extent 'high risk' (33%) or 'low risk' (3%).⁷¹ RoB domain 5, 'Selective reporting', was the most frequently (77%)source of 'some concerns' or 'high risk', mainly due to lack of protocol registration/analysis plan.

Synthesis of results

Qualitative evidence synthesis

Sixty-four studies (71 treatment comparisons) in the qualitative analysis reported a total of 99 work outcome results: 64 of 99 (65%) for sick leave, 18 of 99 for work status (18%) and 17 of 99 for presenteeism (17%). These 99 work outcome results were qualitatively assessed and across outcomes the treatment comparisons were judged as ineffective (66 of 99, 67%), possibly effective (24 of 99, 24%) or clearly effective (9 of 99, 9%). For sick leave, 7 of 64 (11%) interventions were judged effective and 12 of 64 (19%) possibly effective; for work status 1 of 18 (6%) and 8 of 18 (44%); and for presenteeism 1 of 17 (6%) and 4 of 17 (24%) (online supplemental table 7). Between RCTs and LOS, a higher percentage of comparisons in RCTs was judged to demonstrate an (at least possible) effect (24 of 65, 37%) compared with LOS (9 of 34, 26%).

Quantitative evidence synthesis

Thirty-seven RCTs (k=43 treatment comparisons) were included in the quantitative analyses, measuring sick leave (k=42), work status (k=9) and presenteeism (k=13)(online supplemental table 4). Based on visual assessment of the funnel for sick leave, non-reporting of RCTs with lower sample size and unfavourable effects could not be excluded (online supplemental figure 1). For studies reporting work status and presenteeism, the funnel plots did not suggest publication bias.

Sick leave

Based on data from 18784 patients, SMDs of the 42 treatment comparisons for sick leave ranged from -0.87 to 0.54. 27 35 37 40 42-44 46 47 54 56 58 60 64 66 871-74 77 80 83 84 86 89 91 93-95 Nine (9 of 42, 21%) showed a moderate or even large effect, 11 (11 of 42, 26%) a small effect and 22 a nonimportant or even unfavourable effect (22 of 42, 52%).

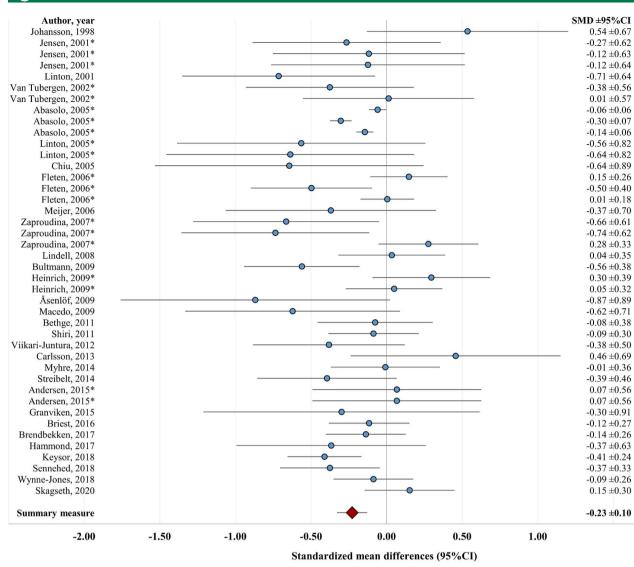


Figure 2 Forest plot of treatment comparisons (n=42) for sick leave. A negative standardised mean difference (SMD) indicates beneficial effect of intervention versus comparator in improving the work outcome; a positive SMD indicates unfavourable effect of intervention versus comparator in improving the work outcome. An asterisk (*) indicates that a study has multiple treatment comparisons and was therefore included multiple times in the forest plot (this was accounted for in the analysis).

The meta-analysis revealed an overall small but significant effect (SMD_{combined}: -0.23, 95% CI: -0.33 to -0.13; figure 2), with limited heterogeneity (T²=0.014, prediction interval –0.49 to 0.02). $SMDs_{combined}$ varied substantially between subgroups. When concentrating subgroups with more than five comparisons, the effect was numerically higher than the main estimate for interventions in i/dRMDs but was non-important (and not significant) for people with pain syndromes. Also, the effect was moderate for populations with mixed baseline risk status (ie, with or without sick leave), but non-important (although statistically significant) for populations on sick leave at baseline. Interventions in a clinical setting and receiving single-component interventions seemed to have a non-important, but still significant effects (table 2). In exploratory analysis of intervention features, all effects were consistently favourable, but non-important (online supplemental table 8).

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Work status

Based on data from 1241 patients, SMDs of the nine treatment comparisons for work status ranged from -0.66 to 0.03.^{34 50 51 53 58 64 68} Five (5 of 9, 56%) showed a moderate effect on work status, two (2 of 9, 22%) a small effect, and two (2 of 9, 22%) a non-important or even unfavourable effect.

The meta-analysis revealed an overall small effect $(SMD_{combined}: -0.38, 95\% CI: -0.63 to -0.12; figure 3)$, with limited heterogeneity $(T^2=0)$. SMDs_{combined} varied substantially between subgroups. When concentrating on subgroups with more than five comparisons, effects were moderate in the subgroup with pain syndromes and receiving multiple component interventions (table 2). In exploratory analysis of intervention features, generally small effects were observed, except for a larger effect on work status in interventions not including an

	Sick leave		Work status		Presenteeism	
	Treatment comparisons (N)	SMD (95% CI)	Treatment comparisons (N)	SMD (95% CI)	Treatment comparisons (N)	SMD (95% CI)
Overall	42	-0.23 (-0.33 to -0.13)	9	-0.38 (-0.63 to -0.12)	13	-0.25 (-0.39 to -0.12)
Disease						
Pain syndromes	19	-0.07 (-0.33 to 0.19)	3	-0.50 (-0.93 to -0.08)	3	-0.19 (-0.50 to 0.12)
i/dRMDs	23	–0.35 (–0.57 to –0.14)	6	-0.28 (-0.49 to -0.07)	9	-0.20 (-0.39 to 0.00)
Baseline risk for adverse work outcomes						
At risk (on sick leave or other risk)	28	-0.11 (-0.19 to -0.02)	6	0.03 (-0.52 to 0.59)	7	0.01 (-0.27 to 0.29)
Not at risk (not on sick leave, no other risk)	3	-0.35 (-0.67 to -0.03)	0	NA	3	-0.44 (-0.73 to -0.15)
Mixed risk (on sick leave/not on sick leave)	5	–0.51 (–0.83 to –0.18)	1	-0.38 (-0.62 to -0.14)	3	-0.17 (-0.31 to -0.02)
Risk not described/specified	6	-0.19 (-0.51 to 0.12)	2	-0.43 (-0.94 to 0.08)	0	NA
Setting						
Clinical	29	-0.12 (-0.21 to -0.02)	5	-0.31 (-0.65 to 0.03)	4	-0.14 (-0.44 to 0.16)
Workplace	1	-0.38 (-0.98 to 0.22)	0	NA	3	-0.19 -0.63 to 0.25)
Combined (clinical+workplace)	1	-0.09 (-0.53 to 0.36)	0	NA	2	-0.13 (-0.56 to 0.30)
Other	11	-0.24 (-0.40 to -0.08)	4	-0.35 (-0.61 to -0.09)	4	-0.34 (-0.70 to 0.01)
Components						
Single	11	-0.12 (-0.22 to -0.33)	2	-0.28 (-0.49 to -0.07)	3	-0.22 (-0.41 to -0.04)
Multiple	31	-0.25 (-0.42 to -0.08)	7	-0.51 (-0.93 to -0.08)	10	-0.09 (-0.44 to 0.27)

A negative SMD suggested a beneficial effect in improving the work outcome by the intervention over the control. i/dRMD, inflammatory or degenerative or mixed rheumatic and musculoskeletal disease; NA, no studies included the specified contextual factor for this work outcome domain; SMD, standardised mean difference.

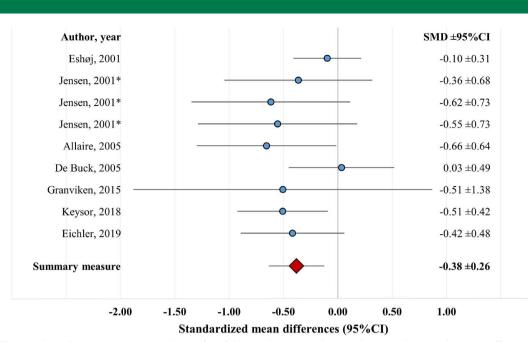
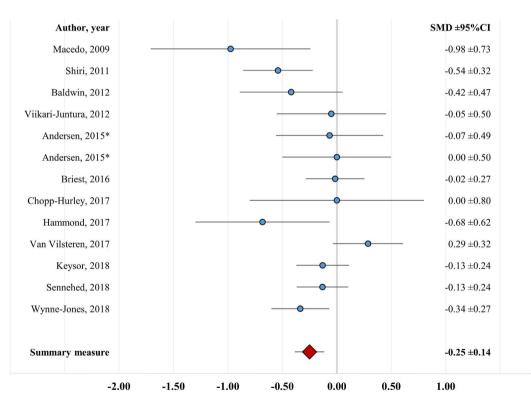


Figure 3 Forest plot of treatment comparisons (n=9) for work status. A negative standardised mean difference (SMD) indicates beneficial effect of intervention versus comparator in improving the work outcome; a positive SMD indicates unfavourable effect of intervention versus comparator in improving the work outcome. An asterisk (*) indicates that a study has multiple treatment comparisons and was therefore included multiple times in the forest plot (this was accounted for in the analysis).



Standardized mean differences (95%CI)

Figure 4 Forest plot of treatment comparisons (n=13) for presenteeism. A negative standardised mean difference (SMD) indicates beneficial effect of intervention versus comparator in improving the work outcome; a positive SMD indicates unfavourable effect of intervention versus comparator in improving the work outcome. An asterisk (*) indicates that a study has multiple treatment comparisons and was therefore included multiple times in the forest plot (this was accounted for in the analysis).

Presenteeism

Based on data from 2015 patients, SMDs of the 13 treatment comparisons for presenteeism ranged from -0.98to 0.29.³⁵ ³⁸ ⁴³ ⁴⁸ ⁵⁴ ⁶⁸ ⁷⁴ ⁸³ ⁸⁴ ⁹²⁻⁹⁴ Three (3 of 13, 23%) showed a moderate to large effect on presenteeism, two (2 of 13, 15%) a small effect and eight (8 of 13, 62%) a non-important or even unfavourable effect.

The meta-analysis revealed an overall small effect $(SMDs_{combined}: -0.25, 95\% \text{ CI: } -0.39 \text{ to } -0.12; \text{ figure 4})$, with limited heterogeneity $(T^2=0)$. $SMD_{combined}$ varied substantially between subgroups. When concentrating on subgroups with more than five comparisons, effects were non-important (and non-significant) in people with a baseline risk for adverse outcome (on sick leave or other risk) and for multicomponent interventions (table 2). In exploratory analysis of intervention features, effects were blurred and showed non-important to small effects (online supplemental table 8).

DISCUSSION

In people with RMDs, both qualitative and quantitative evidence syntheses of non-pharmacological interventions showed overall favourable effects on work participation outcomes. Qualitative synthesis of 64 interventions in RCTs and LOS indicated that 33% had a clear or possible beneficial effect on work participation, while there were no signs for an important detrimental effect on work participation. Further quantitative synthesis of 37 RCTs demonstrated an overall small and significant effect size. Within each work outcome domain, effect size could vary substantially between subgroups, ranging from non-important to moderate and at times even large.

Qualitative and quantitative syntheses provided complementary information. LOS were considered in addition to RCTs, ensuring a more complete view of nonpharmacological interventions with work as an outcome. On the other hand, the qualitative synthesis distinguished only three categories of effectiveness and considered absolute effects, while the quantitative synthesis was based on precision of the relative effect on a continuous scale in studies with lower risk of bias by design.

Although we originally aimed to also understand whether interventions differed in effects between work outcomes of interest, the number and type of interventions per outcome domain differed substantially, limiting comparison of combined SMDs between domains. Nonetheless, the largest overall effects were observed on work status, while effects on sick leave and presenteeism were generally similar.

Clearly, overall effect sizes were small for each work outcome domain. Notwithstanding, within domains, substantial variation in effect size was observed, with some interventions having even a large effect. This suggests the effects of interventions could be substantial when tailored to specific groups. Subgroup analyses in the quantitative synthesis provided some further insight, although robust patterns by subgroup were not seen. Despite our best efforts, we could not formulate a clear statement about which (type of) non-pharmacological interventions work best. Likely, sample sizes (ie, the number of included studies) were often insufficient to interpret subgroup differences or to address meta-confounding (eg, the effect of country).⁹⁶ In addition, misclassification of subgroup factors (due to poor reporting, for example, of intervention features or disease) could also explain why no robust patterns were observed.

Overall, interventions had a stronger effect on sick leave in people with i/dRMD compared with those with pain syndromes. A previous Cochrane review on the effects on work-related interventions in inflammatory arthritis found these interventions are possibly effective for work participation, although quality of evidence was very low. Considering also other non-pharmacological interventions and studies published afterwards, our results indicated a positive effect on sick leave in people with i/dRMD.¹¹ The needs of people with i/dRMDs might be easier to address, compared with the more complex needs of those with pain syndromes. Confounding of the effect of type of RMD by intervention or other population/study characteristics could not be addressed in our analyses.

Although we expected that individuals at risk for adverse work outcome at baseline (eg, already on sick leave) would benefit more from non-pharmacological interventions for each work outcome, this was not confirmed by our analyses. Possibly, an intensive nonpharmacological intervention in those on sick leave (and likely experiencing more active disease) results in short-term physical and/or mental overload for patients without benefits for sick leave and presenteeism. In contrast, those without risk for adverse work outcome seemed to benefit more, suggesting preventative interventions are more successful. Alternatively, individuals at higher risk might receive less intensive treatments or had worse disease that was insufficiently treated.

Clinical as well as combined clinical and workplace intervention settings had non-important (but statistically significant) effects on various work-related outcome domains. A recent scoping review of 22 studies in clinical care among people with musculoskeletal conditions including back pain concluded 61% of included interventions achieved the 'desired effect'. These interventions had a specific focus on work, while in our meta-analyses only 37% (n=15 of 41) had a 'vocational or work-related support' feature in clinical settings or combined settings (clinical and workplace).¹⁰ As the number of workplace interventions in our meta-analyses was very low (n=4), this precluded any firm conclusions regarding their effect. A previous meta-analysis on workplace interventions in various diseases including among which eight RCTs in people with RMDs found improvements in sick leave, but half of the studies included back pain or work-related musculoskeletal disorders (which were outside the scope of our review). $^{12} \,$

In the conduct of this review, a first limitation could be found in design and reporting of the underlying studies: inclusion criteria in terms of work status and risk for adverse work outcome were often unclear; follow-up duration was inappropriate for some work outcome domains; loss to follow-up was substantial for several studies and not always dealt with adequately; the power to detect meaningful effects on work outcomes was often insufficient; definitions for work participation outcomes unclear and varying; reporting of work outcome results was extremely heterogeneous; information on contextual factors that would have facilitated subgroup analyses (job type, healthcare, social security and labour market systems⁹⁷) was limited. As an example on reporting, we noted 20 different outcome measurement and reporting approaches for sick leave across studies.⁵⁶⁹⁸⁹⁹ Suboptimal reporting and methodology could be partly explained by work participation outcomes being not always a primary study objective. Of note, including these studies was a conscious choice, as we wanted to evaluate also the effect on work outcomes of non-pharmacological interventions without a specific focus on work outcomes. Also, as healthcare systems differ in access to non-pharmacological interventions, generalisability of results is an issue. On this line, it is notable that the majority of studies in this review was conducted in Scandinavian countries. To foster better designing, analysing and reporting of future studies with work as primary or secondary outcome, EULAR Points to Consider on designing and reporting this type of studies as well as reporting guidelines for non-pharmacological interventions should provide guidance.^{100–102} Another limitation is the pragmatic choice to limit the RoB assessment and quantitative synthesis to RCTs, in an effort to minimise bias. Several LOS did not have a comparator group (eg, pre/post-design). LOS do not necessarily have a high RoB (for example, if they have adequate control of confounders). We did not identify a framework or recommendations to perform a qualitative synthesis of studies in a systematic review that includes a meta-analysis. Therefore, the reported effect, as well as aspects related to the design and judgement on quality of the development and implementation of the intervention, were considered by reviewers. Due to the complexity of our review (heterogeneity in designs, disease, intervention features, outcomes), we decided to use our own format for the qualitative synthesis. The major strength of the current review is the broad approach by including all non-pharmacological interventions in all RMDs, thus making maximum use of all available evidence in this area and inter/extrapolating between RMDs were considered appropriate. Second, both qualitative and quantitative evidence syntheses were conducted, as described above. Third, the broad expertise of the authors and steering group, which included clinicians, researchers and a patient research partner, allowed for extensive deliberation on the study methodology, while ensuring that all

relevant perspectives were taken into account. Finally, validated tools and checklists were used for risk of bias and quantitative synthesis in this review.^{15 103}

The aim of this review was to inform the task force involved with the 2021 EULAR Points to Consider to support people with RMDs to participate in healthy and sustainable paid work.¹³ This is why only studies published up to August 2020 were considered, which could be considered a limitation.

For (clinical) practice, our findings suggest tailoring non-pharmacological interventions to the individual person and their context. However, this requires identification of people's work situation and the factors potentially threatening their participation in healthy and sustainable work. In this regard, work deserves adequate attention as part of disease management in clinical practice, as already stated in the self-management recommendations for inflammatory arthritis, but lacking in many other management recommendations.¹⁰⁴

CONCLUSIONS

Non-pharmacological interventions can improve sick leave, work status and presenteeism in people with RMDs. Overall effects are small, but these vary in size across disease, risk status and intervention setting. This suggests that these interventions need to be tailored to the individual if we want to optimise work participation. Going forward, homogeneous design, analysis and report of studies are essential to arrive at a more unified synthesis, and to ultimately best promote work participation for people with RMDs.

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