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## **Efficacy of home-based physical activity interventions in patients with autoimmune rheumatic diseases: a systematic review and meta-analysis**

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Short title: Home-based physical activity in autoimmune rheumatic diseases

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# **Efficacy of home-based physical activity interventions in patients with autoimmune rheumatic diseases: a systematic review and meta-analysis**

## **Abstract**

Introduction: Physical activity (PA) has been receiving increasing interest in recent years as an adjuvant therapy for autoimmune rheumatic disease (ARDs), but there is scarce information about the efficacy of home-based PA for patients with ARDs. Objective: To perform a systematic review and meta-analysis on the efficacy of home-based physical activity (PA) interventions in improving health-related quality of life, functional capacity, pain, and disease activity in patients with ARDs. Methods: Searches were performed in PubMed, Web of Science, Scopus, Cochrane, CINAHL database and Sport Discus. Trials were considered eligible if they included a home-based physical activity intervention. The population included adults with autoimmune rheumatic diseases (e.g., rheumatoid arthritis, systemic lupus erythematosus, idiopathic inflammatory myopathies, systemic sclerosis and ankylosing spondylitis), comparisons included non-physical activity control or centre-based interventions (i.e., interventions performed on a specialized exercise centre) and the outcomes were quality of life, pain, functional capacity, disease activity and inflammation. Results: Home-based physical activity improved quality of life ( $p < 0.01$ ;  $g = 0.69$ ; IC95%, 0.61 to 1.07) and functional capacity ( $p = 0.04$ ;  $g = -0.51$ ; IC95%, -0.86; -0.16), and reduced disease activity ( $p = 0.03$ ;  $g = -0.60$ ; IC95%, -1.16; -0.04) and pain ( $p = 0.01$ ;  $g = -1.62$ ; IC95%, -2.94 to -0.31) compared to the non-physical activity control condition. Additionally, home-based physical activity interventions were as effective as centre-based interventions for all investigated outcomes. Conclusions: Home-based PA is an efficacious strategy to improve disease control and alleviate symptoms in ARD.

**Keywords:** exercise, rheumatology, pain, fitness

**Trial Registration Number:** PROSPERO CRD42020183378

## **Abbreviation list:**

ARDs, autoimmune rheumatic diseases; AS, ankylosing spondylitis; BAT, before vs. after trial ; IIM, idiopathic inflammatory myopathies; non-RCT, non-randomised controlled trials PA, physical activity; QOL, quality of life; RA, rheumatoid arthritis; RCT, randomised controlled trials RT, randomized trial; SLE, systemic lupus erythematosus; SMD, standardized mean differences; SpA, spondyloarthritis; SSc, systemic sclerosis.

## 33 1. Introduction

34 Autoimmune rheumatic diseases (ARDs) are a group of systemic autoimmune disorders that  
35 mainly affect joint, bones and soft tissues and are associated with substantial morbidity and  
36 mortality [1]. These diseases are characterized by systemic inflammation and share common  
37 clinical features, including chronic pain, reduced physical fitness, and, as a consequence, poor  
38 health-related quality of life [2–5]. The most common ARDs include rheumatoid arthritis (RA),  
39 systemic lupus erythematosus (SLE), idiopathic inflammatory myopathies (IIM), systemic  
40 sclerosis (SSc), and ankylosing spondylitis (AS).

41 Physical activity (PA) has been receiving increasing interest in recent years as an adjuvant  
42 therapy for ARDs [6,7]. However, current estimates indicate that ~60% of the patients with  
43 ARDs do not achieve the recommended amount of weekly PA (i.e., 150 min/week of moderate-  
44 to-vigorous PA)[8]. Physical inactivity in ARDs may be related to generic and disease-related  
45 barriers to PA, such as lack of time and motivation, high costs and limited access to specialized  
46 facilities, pain, fatigue, fear of aggravating the disease, among others [9–12]. Also, the COVID-  
47 19 pandemic has imposed additional challenges to the adoption of PA in patients with ARDs  
48 [13,14] due to the requirements of self-isolation and home quarantine for this infection-prone  
49 population [15–17]. In conjunction, this information underscores the importance of investigating  
50 the efficacy of alternative approaches to upregulate PA in ARDs that may circumvent some of  
51 the perceived and contextual barriers to PA in this population.

52 Recently, home-based PA has emerged as a potential clinically- and cost-effective strategy to  
53 increase PA levels and improve disease control and general health across multiple clinical  
54 conditions, such as cardiometabolic diseases [18–20], women under cancer treatment [21],  
55 patients with pulmonary diseases [22], as well as in older adults [23]. Recent literature has also  
56 advocated for the use of home-based PA as a strategy to maintain PA levels during COVID-19  
57 pandemic, with a special focus in at-risk populations [13,24].

58 There is scarce information about the efficacy of home-based PA for patients with ARDs, with  
59 equivocal data about its effects on functional status, health-related quality of life and pain in this  
60 population [25–27]. Additionally, there is no summarized information about the existing home-  
61 based PA intervention protocols for ARDs. As these may differ in respect of its delivery strategy  
62 (e.g., supervised vs. unsupervised), PA protocol, and supporting tools (e.g., educational material,  
63 eHealth technology, exercise equipment), there is a need to better describe the current home-  
64 based interventions available to patients with ARDs and investigate their feasibility. Finally, as

65 safety concerns may hamper the adoption of home-based PA in ARDs [9–12], it is essential to  
66 review data on the safety of home-based PA interventions.

67 Thus, the purpose of this study was to perform a systematic review and meta-analysis on the  
68 efficacy of home-based PA interventions in improving health-related quality of life, functional  
69 capacity, pain, and disease activity in ARDs. Comparisons were performed against a non-  
70 physical activity control condition and against centre-based interventions (i.e., interventions  
71 performed on an exercise centre). As a secondary goal, this review also intended to describe the  
72 characteristics of existing home-based PA programmes for ARDs and review data on adherence  
73 and safety.

74

## 75 2. Methods

### 76 2.1 Registration

77 The present study followed the PRISMA (Preferred Reporting Items for Systematic Reviews and  
78 Meta-Analyses; see the Appendix A for a filled-in PRISMA checklist) guidelines [28] and was  
79 registered in the International Prospective Register of Systematic Reviews database  
80 (PROSPERO, CRD42020183378).

81

### 82 2.2 Search strategy and study selection

83 Searches were performed in six electronic databases (PubMed, Web of Science, Scopus,  
84 Cochrane, CINAHL database and Sport Discus via EBSCOhost) by two members of the study  
85 team (FIS and SMS), in May of 2020. There were no restrictions on date of publication or  
86 language. The descriptors used for the searches were defined using the Medical Subject Headings  
87 (whenever possible) and were related to the population (“autoimmune rheumatic diseases” OR  
88 “rheumatoid arthritis” OR “systemic lupus erythematosus” OR “Sjogren syndrome” OR gout OR  
89 “ankylosing spondylitis” OR myositis OR “systemic sclerosis” OR “idiopathic inflammatory  
90 myopathies”) and intervention (“home based program” OR “home based exercises” OR  
91 “telerehabilitation” OR "home based rehabilitation" OR “home based training” OR "tele  
92 exercise" OR " unsupervised exercise programs" OR “home based physical activity” OR “active  
93 games” OR "wii intervention" OR “wii fit” OR “exergames” OR “online exercises” OR “fitness  
94 apps” OR “physical activity apps”). To identify other relevant study data, we also screened

95 reference lists from the selected studies and review articles. The PubMed search strategy is  
96 provided in the Appendix B (Table B.1).

97 Eligibility criteria was developed using the PICO framework [28,29]. To be included, the studies  
98 needed to: (1) be conducted on adults ( $\geq 18$  years) with a clinical diagnosis of one of the following  
99 conditions: SLE, RA, spondyloarthritis (SpA), Sjögren's syndrome, SSc, AS, IIM or systemic  
100 vasculitis; (2) include an arm with a home based PA intervention, which was considered any PA  
101 intervention occurring predominantly at home (i.e.,  $> 90\%$  of the sessions being undertaken at  
102 home); and (3) include assessments of at least 1 of the following: quality of life, functional  
103 capacity, pain, inflammation (e.g., C-reactive protein), disease activity and adherence. For the  
104 study design, we included randomised controlled trials (RCTs), non-RCTs, randomised  
105 uncontrolled trials (RT), or uncontrolled trials (i.e., before vs. after trial [BAT]). For comparison,  
106 we considered both non-PA control groups and interventions involving centre-based exercise  
107 (i.e., performed on a specialized exercise centre). Studies were excluded if they were protocol  
108 studies, observational studies, acute exercise studies or studies involving pediatric rheumatic  
109 diseases.

110 On completion of the searches, two members of the study team (FIS and SMS) independently  
111 selected the manuscripts using a 2-stage strategy, namely: (1) Title and abstract screen and (2)  
112 Full text review. Any discrepancies were resolved through discussion, or third-party mediation,  
113 if required.

114

### 115 *2.3 Data extraction*

116 Data were extracted and verified by three authors (BCM, FIS and SMS) using a standardized  
117 spreadsheet and following the PICO framework [30]. Study authors were contacted to request  
118 additional or missing data, if required, and authors were given one month to respond (if  
119 necessary, an additional e-mail was sent two weeks after the first one to reinforce the request).  
120 The following characteristics were extracted from each selected study: (1) author (data); (2)  
121 participant information (e.g., number, mean age, age range, gender, disease condition); (3)  
122 characteristics of the intervention (e.g., description of the intervention, comparison, delivery of  
123 the intervention, exercise type, volume and intensity); (4) outcome data; (5) study design.

124

### 125 *2.4 Assessment of risk of bias*

126 Study quality was appraised using the Cochrane Revised Cochrane risk-of-bias tool for  
127 randomized trials [31], by two authors (SMS and FIS). This tool has 5 domain (randomization  
128 process, deviations from the intended interventions, missing outcomes, measurement of the  
129 outcome and selection of reported results) and an overall bias analysis. All studies were analyzed  
130 with this tool, even non-randomized and BAT studies, assuming that they would already be at  
131 high risk due to their design. Studies were assigned either as “high risk”, “low risk” or with “some  
132 concerns”. Risk of bias judgements were summarized across all studies for each of the domains  
133 listed. We chose to label all studies as low risk in blinding of participants and providers domain,  
134 as blinding is difficult, if not impossible, in PA trials.

135

### 136 *2.5 Data analysis: Systematic Review*

137 A narrative synthesis was performed to describe and explore the data from the studies. Studies  
138 were described in the text and tables and were organized by key details, such as study design,  
139 summary of the population (sample size, age range, gender, disease condition), intervention, and  
140 the following outcomes: (1) quality of life (through generic or disease-specific questionnaires),  
141 (2) functional capacity, (3) pain, (4) disease activity, and (5) c-reactive protein.

142 Home-based exercise interventions were described in terms of exercise type, frequency, duration  
143 and intensity. Intensity was defined based on subjective (e.g., authors’ description of the  
144 intervention) or objective (e.g., achieved heart rate or effort perception rated by the participants)  
145 information provided by the authors in the papers, and was classified as high-, moderate- or low-  
146 intensity. In the absence of sufficient information about exercise intensity, we used The 2011  
147 Compendium of Physical Activities [32] to define activity-specific metabolic equivalents  
148 (METs) and classify the exercises as low intensity (1.6–2.9 MET), moderate intensity (3–5.9  
149 MET), and high intensity (>6 MET) [33].

150 Aspects related to the delivery of the intervention, such as supervision, monitoring and use of  
151 support components were also summarized. Interventions were defined as supervised if there was  
152 a professional accompanying (either presential or online) the execution of the exercises in real  
153 time. Monitoring was defined as any attempt to monitor the execution (adherence) of the exercise  
154 sessions (e.g., emails sent to the participants; periodical telephone calls to check compliance;  
155 exercise logs; heart rate logs). The support components were any strategy employed to support  
156 and guide the home-based intervention, such as initial or periodical sessions with professionals  
157 to guide the intervention and teach the exercises, educational materials (e.g., PA booklets; DVD),  
158 eHealth tools (e.g., website, emails) and exercise equipment.

159 In addition, we also reported data on the participants' adherence to the interventions (i.e., the  
160 degree of compliance to the exercise sessions or PA interventions), and on the safety of the  
161 interventions (i.e., the occurrence of any health-related complications as a result of the  
162 intervention, such as disease relapses, acute flare-ups, cardiovascular complications; increase in  
163 disease activity or in pain; *etc*).

164

## 165 2.6 Data analysis: Meta-Analysis

166 Data analysis was performed using random-effects models. After data extraction, weighting, and  
167 missing data imputation (according to Cochrane Handbook for Systematic Reviews of  
168 Interventions) [34], the meta-analysis was performed on each of the following outcomes: (1)  
169 quality of life, (2) functional capacity, (3) pain, (4) disease activity, (5) inflammation. Quality of  
170 life was analyzed using two separate metrics: (1) by performing a weighted average of all of the  
171 Short Form Health Survey 36 (SF-36) domains (i.e., QOL\_generic) and; (2) by aggregating  
172 disease-specific questionnaires of quality of life (e.g ASQOL - Ankylosing Spondylitis Quality  
173 of Life questionnaire, RAQoL - Rheumatoid Arthritis Quality of Life Questionnaire, BAS-G -  
174 Bath Ankylosing Spondylitis Global Index). Functional capacity was extracted from the studies  
175 that presented the total value of the questionnaires Bath Ankylosing Spondylitis Functional Index  
176 (BASFI) and Health Assessment Questionnaire Disability Index (HAQ). Pain was extracted  
177 from studies that presented the values of visual analogue scale, and disease activity was extracted  
178 from disease activity specific scores (e.g., BASDAI - Bath Ankylosing Spondylitis Disease  
179 Activity Index, DAS28 - Disease Activity Score 28). Inflammation was assessed by serum C-  
180 reactive protein.

181 Meta-analyses were performed considering the following comparisons: (1) home-based  
182 interventions vs. control (i.e., usual care or no intervention) and; (2) home-based interventions  
183 vs. centre based. The uncontrolled trials (i.e., BAT) were not included in the meta-analyses, but  
184 were qualitatively described along the manuscript. Meta-analyses were only performed if there  
185 were at least 3 studies including the outcome within each comparison. For this reason, for  
186 QOL\_generic and QOL\_disease-specific, meta-analyses were performed only for the comparison  
187 between home-based PA and control. No meta analysis was conducted for C-reactive protein as  
188 only two studies provided this outcome.

189 The analyses were conducted according to Schwarzer [35]. The effects of home-based  
190 interventions on each outcome were calculated as the standardized mean differences (SMD). The



191 SMDs were calculated as the difference between the intervention and control group (absolute  
192 pre-to-post changes), divided by the pooled standard deviation for the changes. For the outcome  
193 QOL\_generic, we used only the post-intervention data due to the absence of absolute change  
194 scores in some studies [26,36–38]. Studies were combined using random-effects meta-analysis,  
195 which was conducted using Hedge's  $g$  [39]. To estimate the between-study variance, we used  
196 Restricted maximum-likelihood estimator [40]. The convention proposed by Cohen [41] was  
197 used for the interpretation of the effect magnitude: trivial  $<0.2$ , small  $\geq 0.20$ , medium  $\geq 0.50$  and  
198 large  $\geq 0.80$ . Meta-analyses were performed in RStudio version 4.02, using the 'metacont'  
199 function of the meta package.

200

### 201 **3. Results**

#### 202 *3.1 Literature search*

203 The search of the databases identified 151 studies, and we also included three studies from other  
204 sources, [42–44] totaling 154 studies. Following removal of duplicates ( $n=73$ ), 81 publications  
205 were screened for inclusion. Of these, 42 were excluded after reviewing the title and abstract.  
206 The remaining 39 papers were selected for full reading and 18 were excluded because they did  
207 not include a home-based PA intervention ( $n=8$ ) or any outcome of interest ( $n=4$ ), or were not  
208 intervention studies ( $n=6$ ). Therefore, 21 studies were included in the review and are listed in the  
209 qualitative analysis. Among these, 16 studies were suitable for meta-analysis; however, we were  
210 unable to obtain relevant data from 2 studies [45,46] (i.e., data were presented graphically only  
211 or without mean difference and standard deviation, and authors did not respond to the emails  
212 soliciting the required data). Therefore, 14 studies were included in the meta-analysis (Figure 1).

213

214 **\*Figure 1.\***

215

#### 216 *3.2 Study characteristics*

217 Among the 21 included studies, 6 were RCT, 5 were RT, 5 were non-RCT and 5 were BAT. In  
218 total, these studies enrolled 1797 patients (725 men and 1072 women), with the vast majority of  
219 studies being conducted with young to middle-aged adults (i.e., 25 and 59 years), and one study  
220 being conducted with elderly participants (age  $> 60$  years). Thirteen out of the 21 studies

221 investigated participants with AS, 5 studies included participants with RA, 2 included  
222 participants with SLE and 1 included participants with SSc (Table 1).

223

224 **\*Table 1\***

225

### 226 *3.3 Risk of bias*

227 Overall, 66.7% of the studies were classified as high risk of bias (Figure 2; Appendix C, Figure  
228 C.1). Most of the methodological issues arose from the ‘randomisation process’ (10 studies were  
229 non-RCT or BAT, and 5 of the randomised studies did not have a clear description of the  
230 randomisation process) and ‘measurement of the outcome’ (in 11 studies no information about  
231 blinding was provided or no blinding of the outcome assessors was conducted). In the domain  
232 ‘selection of the reported result’, 19 studies did not report a pre-specified analysis. In the domain  
233 ‘deviations from intended intervention’, 5 studies used ‘per-protocol’ analyses and presented  
234 >5% drop out rates. In the domain ‘missing outcome data’, few studies were judged as ‘high  
235 risk’, as they did not present reasons for the missing data.

236

237 **\*Figure 2 \***

238

### 239 *3.4 Intervention characteristics*

240 Interventions lasted an average of ~ 17 weeks (range 4 to 96 weeks). The majority of the studies  
241 (15 out of 21) employed a mixed home-based exercise routine, usually combining flexibility and  
242 strengthening exercises (n=11), occasionally added to aerobic (n=4), respiratory (n=10) and  
243 posture (n=6) exercises. One study employed only resistance exercises, [46] 1 study used  
244 calisthenic and relaxation exercises [47], and 1 study used a specific protocol of hand exercises  
245 [27]. Two studies used exergames as a PA intervention [48,49], with mixed aerobic and strength  
246 exercise routines. Interventions were performed, on average, ~ 5 (range 2 to 7) times per week,  
247 with an average duration of ~ 40 minutes (range 20 to 60 minutes) per session. Exercises were  
248 either of low (12 out of 21 studies) or moderate intensity (6 studies). Most studies (16 out of 21)  
249 did not report the number of exercises included in the protocol, with few studies reporting an

250 average of 13 exercises (range 5 to 20). Finally, one study did not provide details about the  
251 intervention [50].

252 Most PA interventions (19 out of 21) were not supervised. Two studies performed in-home  
253 supervision at the beginning of the intervention (i.e., first 2 weeks), with no supervision  
254 afterwards. Seventeen studies reported some strategy to monitor the intervention, with phone  
255 calls and exercise logs being the most used ones. Overall, studies used several support  
256 components. Fifteen studies employed face-to-face sessions with a health professional (usually  
257 a physiotherapist) for the demonstration of the exercises and provision of general health  
258 instructions. Other frequent support tools included the use of PA booklets, educational materials,  
259 and exercise equipment (e.g., elastic bands, dumbbells, cuff weights, and static bikes). Details of  
260 home-based interventions are summarized in Table 2.

261

262

### **\*Table 2\***

263

### 264 *3.5 Quality of life and functional capacity*

265 Quality of life was assessed in 12 studies, using generic (e.g., SF-36, NHP - Nottingham Health  
266 Profile)[26,27,36–38] or disease-specific questionnaires [25,47,50–53]. Six (out of 6) studies  
267 reported improvements in the QOL\_generic and 4 (out of 6) reported improvements in the  
268 QOL\_specific after home-based PA (Appendix D, Table D.1). The overall analysis revealed a  
269 medium significant improvement in quality of life measured by SF-36 in favor of the home-based  
270 intervention when compared with the control condition (Figure 3a [p =0.0004, g = 0.69; IC95%,  
271 0.61 to 1.07]). However, no differences between home-based PA and control were found for  
272 disease-specific questionnaires of quality of life (Figure 3b [p =0.09; g = -0.26; IC95%, -0.57 to  
273 0.05]).

274 Functional capacity was assessed in 16 studies using BASFI or HAQ, among which 10 reported  
275 improvements in this outcome after home-based PA [26,36,38,42–46,51] (Appendix D, Table  
276 D.1). A medium significant improvement in functional capacity was observed after home-based  
277 intervention when compared with the control condition (Figure 4 [p = 0.04; g = - 0.51; IC95%, -  
278 0.86; -0.16]). In addition, no differences in functional capacity were found between home- and  
279 centre-based PA (Figure 4 [p = 0.38 ; g = 0.12; IC95%, -0.15 to 0.40])

280

281 **\*Figure 3 \***

282 **\*Figure 4\***

283

### 284 *3.6 Disease activity*

285 Disease activity was assessed in 14 studies [25,26,52–54,36–38,43,46,47,50,51] using disease-  
286 specific questionnaires (i.e BASDAI and DAS28), among which 11 studies observed a reduction  
287 in this outcome after home-based PA [26,36–38,43,46,51–54] (Appendix D, Table D.1). In the  
288 meta-analysis, a medium significant reduction in disease activity was observed after home-based  
289 intervention when compared with the control condition (Figure 5 [p = 0.03; g = - 0.60; IC95%, -  
290 1.16; -0.04]), with no differences between home- and centre-based PA (Figure 5 [p =0.36; g =  
291 0.13; IC95%, -0.34 to 0.59])

292

293 **\*Figure 5\***

294

### 295 *3.7 Pain and C-reactive protein*

296 Pain was assessed using standardized pain scales in ten studies (11 trials), [26,27,37,45,46,49–  
297 51,53,55] among which 8 (9 trials) reported a reduction in pain after home-based PA  
298 [26,27,45,46,49,51,53] (Appendix D, Table D.1). The overall analysis revealed a large  
299 significant reduction in pain in the home-based PA compared with the control (Figure 6 [p =0.01;  
300 g = -1.62; IC95%, -2.94 to -0.31]). In addition, there were no differences in pain between home-  
301 and centre-based PA (Figure 6 [p = 0.19; g = 0.53; IC95%, -0.26 to 1.32]).

302 Only two studies assessed CRP [44,47], both comparing home based intervention to centre-based  
303 interventions, with no difference between groups in any of the studies (Appendix D, Table D.1).

304

305 **\*Figure 6\***

306

### 307 *3.8 Adherence and safety*

308 Most studies did not report data on adherence to the PA interventions. Adherence details were  
309 reported only in six studies (four with percentage of attendance of all sessions and two with mean  
310 attendance per week), with most of them presenting low to moderate rates. Berg et al.[52]  
311 reported only 34% of adherence of an individualized home-based PA programme in patients with  
312 RA. Slightly higher adherence rates were reported by Rodriguez-Lozano et al. (54.6%) [53] and  
313 Yuen et al. (63.9%) [49]. A more recent study with exergames reported 79% of attendance to the  
314 sessions in patients with SLE [48]. Two studies reported only mean attendance per week, one  
315 with an average of 2.8 times per week (~ 40%) [56] and the other with an average attendance of  
316 1.4 times per week (~70%) [46].

317 Four studies reported no adverse [27,44,48,49] or serious adverse effects [56] related to the  
318 home-based PA interventions. Importantly, the remaining studies did not report data on related  
319 adverse effects.

320

#### 321 **4. Discussion**

322 This systematic review and meta-analysis evaluated the efficacy of home-based PA interventions  
323 in patients with ARDs. Data revealed that home-based interventions are efficacious in improving  
324 quality of life and functional capacity, and reducing disease activity and pain in this population,  
325 when compared to the non-physical activity control condition. However, no benefits were found  
326 for inflammation. When comparing with centre-based interventions (the active comparison), no  
327 difference was found between groups for any outcome, suggesting that home-based interventions  
328 are as efficacious as centre-based interventions for patients with ARDs.

329 This is the first systematic review and meta-analysis to assess the efficacy of home-based PA in  
330 a collective of ARDs patients, with two previous studies being restricted to AS patients only  
331 [57,58]. The beneficial effect of home-based PA on disease activity strengthens the central role  
332 of PA in the management of ARDs [59]. With the introduction of synthetic and biologic disease-  
333 modifying drugs, the treat-to-remission strategy has become the new paradigm for the treatment  
334 of ARDs [60,61]. However, not all patients achieve complete remission with the stand-alone  
335 pharmacological treatment [62]. In this scenario, PA emerges as a potentially impactful strategy  
336 to complement the effects of pharmacological therapy upon disease control in ARDs.

337 Benefits on pain, functional capacity and quality of life underpin the broad effects of PA beyond  
338 disease control. Pain has been recognized as one of the most disabling symptoms in patients with

339 AS [63], RA [64] and SLE [65], and is one of the strongest predictors of poor quality of life in  
340 these diseases. Functional incapacity has also been shown to be associated with reduced quality  
341 of life, as it is directly linked with activities of daily living (e.g., get in/out of bed, take a bath and  
342 shopping) [66]. Therefore, it is not surprising that home-based PA was also efficacious in  
343 improving generic measures of quality of life in ARDs, reinforcing the effects of PA across  
344 multiple life domains in this population.

345 The results of the present review are in consonance with previous reviews assessing the effects  
346 of predominantly centre-based PA interventions for individuals with ARDs [67–70]. Baillet et  
347 al. [70] reported beneficial effects of aerobic exercise in quality of life, functional capacity and  
348 pain in RA patients. A later study from the same group extended these findings by showing that  
349 strength exercises were efficacious in improving functional capacity and reducing inflammation  
350 in this same population [71]. Similar results were found by Pécourneau et al.[67] that reported  
351 reduction in disease activity and improvements in functional capacity promoted by a wide range  
352 of PA programmes in AS patients. A recent review including 1286 patients with inflammatory  
353 rheumatic diseases substantiated previous findings by showing beneficial effects of PA on  
354 disease activity, pain and joint damage [68]. It is worth mentioning that most of these reviews  
355 included exercise programmes conducted in exercise centres with specialized equipment,  
356 including gym machines, exercise ergometers and swimming pools, and supervision by health  
357 professionals. While the results of these studies hold merit for showing the therapeutic effects of  
358 exercise training in ARDs, some of these settings may be difficult to implement at the community  
359 level and in low- to middle-income countries where resources are scarce. In the present study,  
360 home-based PA, which may be an easier strategy to be implemented from a public health  
361 perspective, was as efficacious as centre-based PA in promoting benefits in quality of life,  
362 functional capacity, pain and disease activity. This indicates that home-based exercises should be  
363 more often considered in the clinical practice to promote PA among patients with ARDs. That  
364 being said, adoption to home-based PA requires individuals to have both a home situation and  
365 the cognitive, emotional and health capabilities to adhere to a home-based programme. For some  
366 individuals, a centre-based or a hybrid programme (i.e., initial group introduction in an exercise  
367 center, followed by a home-based PA programme) could be the best options.

368 In the present review, the majority of home-based PA interventions employed combined exercise  
369 protocols, with a focus on stretching, strengthening and respiratory exercises. Weekly volume of  
370 PA was ~ 200 min/week and exercises were of low-to-moderate intensity. Recent PA guidelines  
371 for clinical populations [73] and for ARDs [59] recommend 150-300 min/week of moderate-to-

372 vigorous aerobic PA complemented by 2-3 days a week of strengthening, flexibility and balance  
373 exercises. Therefore, the reviewed home-based PA protocols only partially comply with existing  
374 public health recommendations of PA. The increased focus on stretching and strengthening  
375 activities may be explained by specific aspects of the investigated populations (*i.e.*, populations  
376 with severe joint impairment and loss of strength and functionality) and of the interventions (*i.e.*,  
377 a mix of rehabilitation and preventive PA). The use of lower exercise intensities may be a  
378 precautionary measure to account for the lack of supervision and monitoring during the home-  
379 based sessions. Despite recent studies reporting on the safety of high intensity exercises in ARDs  
380 [74–76], further studies are warranted to determine its feasibility, safety and efficacy when part  
381 of a home-based intervention.

382 Home-based interventions reviewed herein were mostly unsupervised, but monitoring was  
383 performed by means of periodical phone calls and PA logs. Interventions were supported by the  
384 use of PA booklets, educational materials and exercise equipment. Interestingly, even with these  
385 support components, adherence to home-based PA was moderate at its best (34-70%), raising  
386 questions on the feasibility of these interventions in their current state. The low adherence to the  
387 reviewed home-based PA programmes may be explained by the lack of a behavioural component  
388 to support the interventions, lack of supervision, superficial monitoring and excessive number of  
389 exercises [77–80]. Indeed, recent studies have advocated for the use of theory-informed  
390 behavioral interventions integrated with behavioral change techniques to support the delivery of  
391 PA interventions, with evidence that theory-informed behavioral interventions are better  
392 accepted for individuals exercising remotely [80]. In addition, home visits to supervise the first  
393 exercise sessions may enhance perception of safety and efficacy of home-based PA [36,46,55].  
394 On top of that, the use of up-to-date technologies, such as video-calling applications, PA tracking  
395 and other wearable devices, may increase the prospects of delivering and monitoring home-based  
396 PA, therefore improving the experience of home-based PA [81]. Finally, an excessive number of  
397 exercises may challenge the adoption of home-based PA, with evidence showing increased  
398 adherence when a reduced number of exercises is proposed [77]. In the present review, the vast  
399 majority of the home-based interventions were neither backed by behavioural techniques nor  
400 supported by up-to-date technologies. Additionally, although underreported, the average number  
401 of exercises was 13, which may be excessive for ARDs. Interestingly, the study that showed the  
402 highest adherence employed exergames [48], which may be seen as simple technological  
403 intervention naturally embedded with behavioural change techniques (e.g. gamification,  
404 feedback on performance and goal setting) [82,83]. Next studies should actively incorporate

405 these behavioural elements and technologies as they may increase the motivation to engage in  
406 home-based exercise programs and consequently improve the adherence to the intervention  
407 [48,49].

408

#### 409 *4.1 Risk of bias*

410 The generalisability of the present findings are limited by the quality of the included studies. In  
411 this regard, almost half of the reviewed evidence come from non-randomised studies or studies  
412 that did not present a control group or active comparison. Statistical analyses were also poorly  
413 described or followed unorthodox practices, with some studies employing separate group  
414 analysis (e.g., separate paired t-tests in the intervention and control groups) instead of more  
415 robust analyses controlling for the effects of different conditions and times. Additionally, absence  
416 of prior protocol study or clinical trial registration for the majority of the studies questions the  
417 transparency of the reported data and limits the reviewers' ability to determine if data was  
418 produced according to a pre-specified plan. Finally, the outcome assessors were not blinded to  
419 the intervention assignment in most of the reviewed studies, which may have caused the  
420 outcomes to be affected by expectations about the intervention. Notably, most of the present  
421 review outcomes were participant-reported outcomes (e.g., pain scales and questionnaires), and  
422 in these cases the participant is considered the outcome assessor, which impose an additional  
423 challenge to prevent the influence of awareness about the intervention in the measured outcomes.  
424 Overall, the high-risk of bias presented by two third of the studies included in this review points  
425 to the urgent need of well-designed RCTs, with pre-specified plan and proper statistical analysis,  
426 including ITT, and blinding of most of the personnel involved in the study.

427

#### 428 *4.2 Limitations*

429 This review is not without limitations. Firstly, this review involved only 4 ARDs (AS, RA, SLE  
430 and SSc) and most of the reviewed studies presented relatively small sample sizes and reduced  
431 follow-up periods of PA. Therefore, caution should be taken when generalizing study findings to  
432 other ARDs and to long-term PA settings. Secondly, due to the reduced number of studies, it was  
433 not possible to perform sensitivity or meta-regression analyses to test the robustness of the  
434 observed outcomes and the potential effects of moderators (e.g., PA intensity, type, duration) on  
435 the review outcomes. Thirdly, some outcomes such as adherence and adverse effects were



436 reported only by a few studies, which hampers more definite conclusions on feasibility and safety  
437 of home-based PA interventions. Finally, the description of home-based PA interventions was  
438 poor in most of the reviewed studies, challenging the summarization of the existing home-based  
439 PA protocols for ARDs.

440

#### 441 *4.3 Summary*

442 Individuals with ARDs are usually physically inactive, which has been attributed to multiple  
443 barriers to PA, such as lack of time and motivation, cost of exercise, and difficulties in accessing  
444 equipment or facilities [9,10]. The COVID-19 pandemic has also imposed an additional  
445 challenge to the adoption of physical activity in patients with ARDs given the requirements of  
446 self-isolation [13]. The results of the present review indicate that home-based PA may provide  
447 an effective platform to enable PA and improve the disease management in ARDs. The findings  
448 of the present review support the use of combined exercise protocols, including aerobic,  
449 strengthening and stretching exercises in patients with ARDs. Health professionals may use  
450 different strategies to monitor and support ARDs patients under a home-based PA programme,  
451 including regular phone calls, PA logs and booklets, educational materials, and exercise  
452 equipment. The results provided by the present review must be confirmed by larger and more  
453 rigorous RCTs. Additionally, next studies should try to incorporate sound behavioural techniques  
454 and up-to-date technologies in order to improve the delivery and monitoring of home-based PA,  
455 aimed at increasing adherence to this type of intervention.

456

### 457 **5. Conclusion**

458 The results of the present review provide novel evidence on the beneficial impact of home-based  
459 PA in ARDs. Given that physical inactivity is highly prevalent among patients with ARDs and  
460 this seems to be aggravated by the COVID-19 pandemic [14], home-based PA may provide a  
461 sensible platform to promote PA and to help improving disease control and symptoms in patients  
462 with ARDs. However, there is still need for studies with robust designs, rigorous methodological  
463 approaches and with detailed description of home-based PA interventions.

464

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475

476 **Figure legends**

477 Figure 1. Flow-chart of the systematic review

478 Figure 2. Risk of bias of the included studies. Overall percentage of ‘low risk’, ‘some concerns’  
479 and ‘high risk’ of bias in each of the bias domain.

480 Figure 3. Effects of physical activity on quality of life. Panel 3a presents the effects on generic  
481 questionnaires of quality of life (QOL\_generic), panel 3b presents the effects on disease-specific  
482 questionnaires of quality of life (QOL\_disease-specific). CI, confidence interval; SMD,  
483 standardised mean difference; SD, standard deviation.

484 Figure 4. Effects of physical activity on functional capacity. CI, confidence interval; HB, home  
485 based intervention; CB, centre based; CG, control group; SMD, standardised mean difference;  
486 SD, standard deviation.

487 Figure 5. Effects of physical activity on disease activity. CI, confidence interval; HB, home based  
488 intervention; CB, centre based; CG, control group; SMD, standardised mean difference; SD,  
489 standard deviation.

490 Figure 6. Effects of physical activity on pain. CI, confidence interval; HB, home based  
491 intervention; CB, centre based; CG, control group; SMD, standardised mean difference; SD,  
492 standard deviation.

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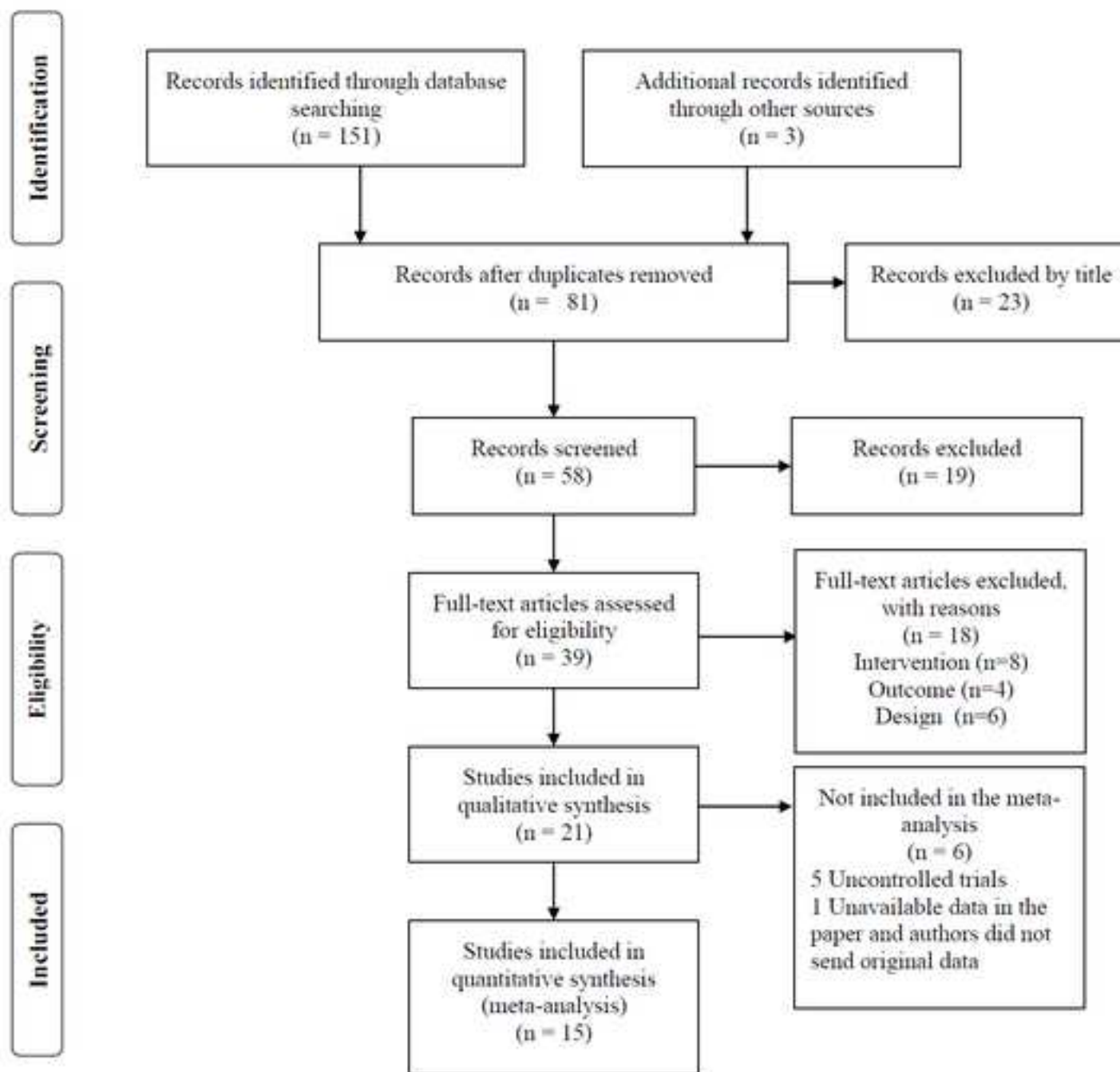
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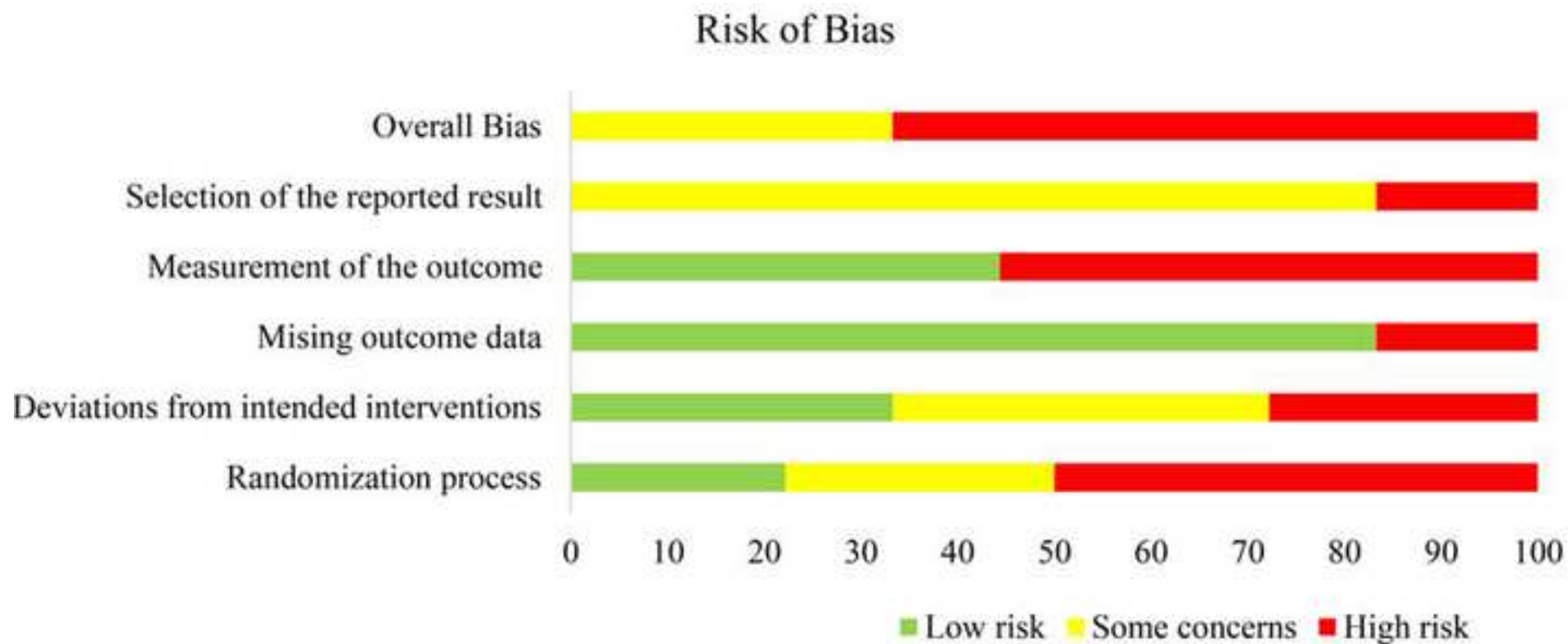
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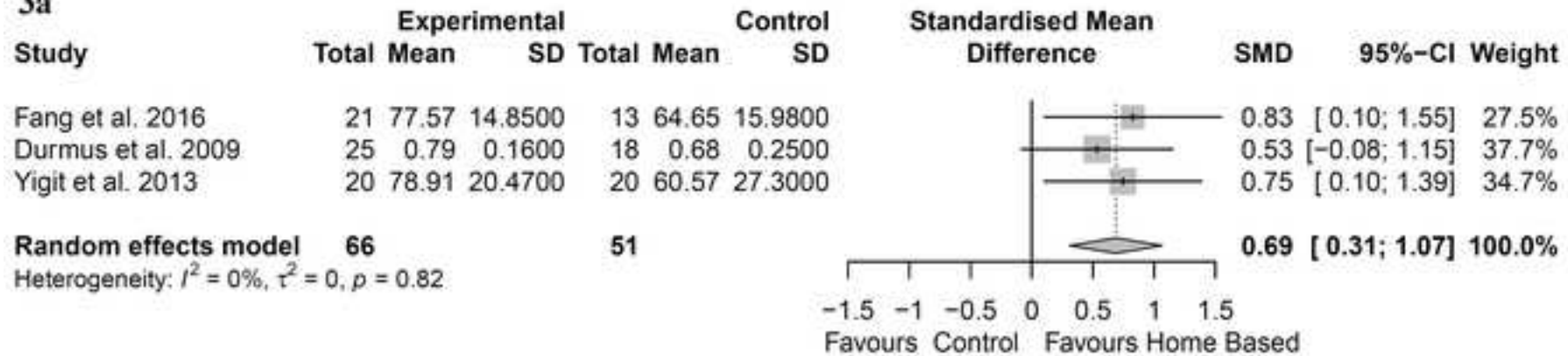
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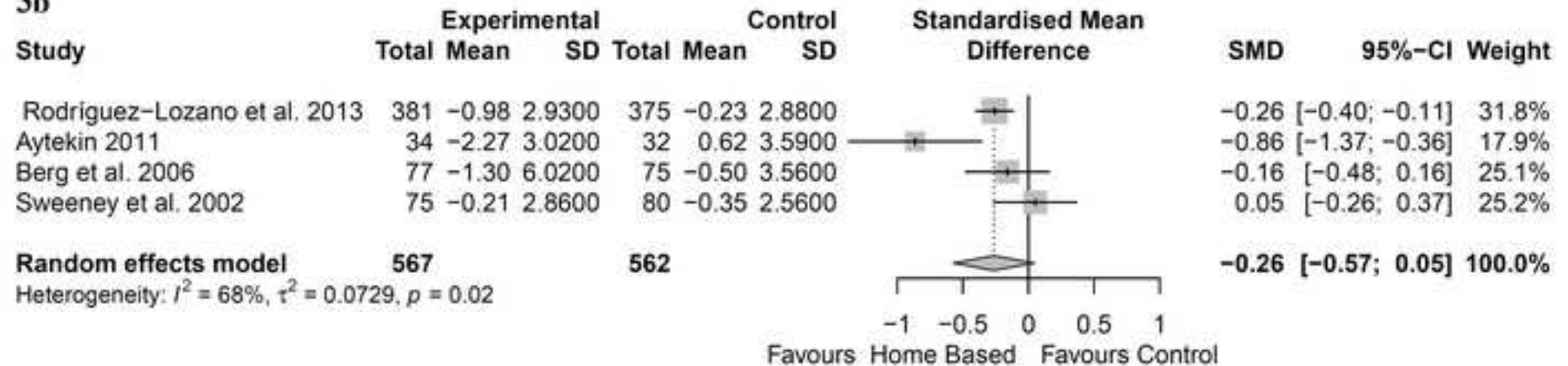




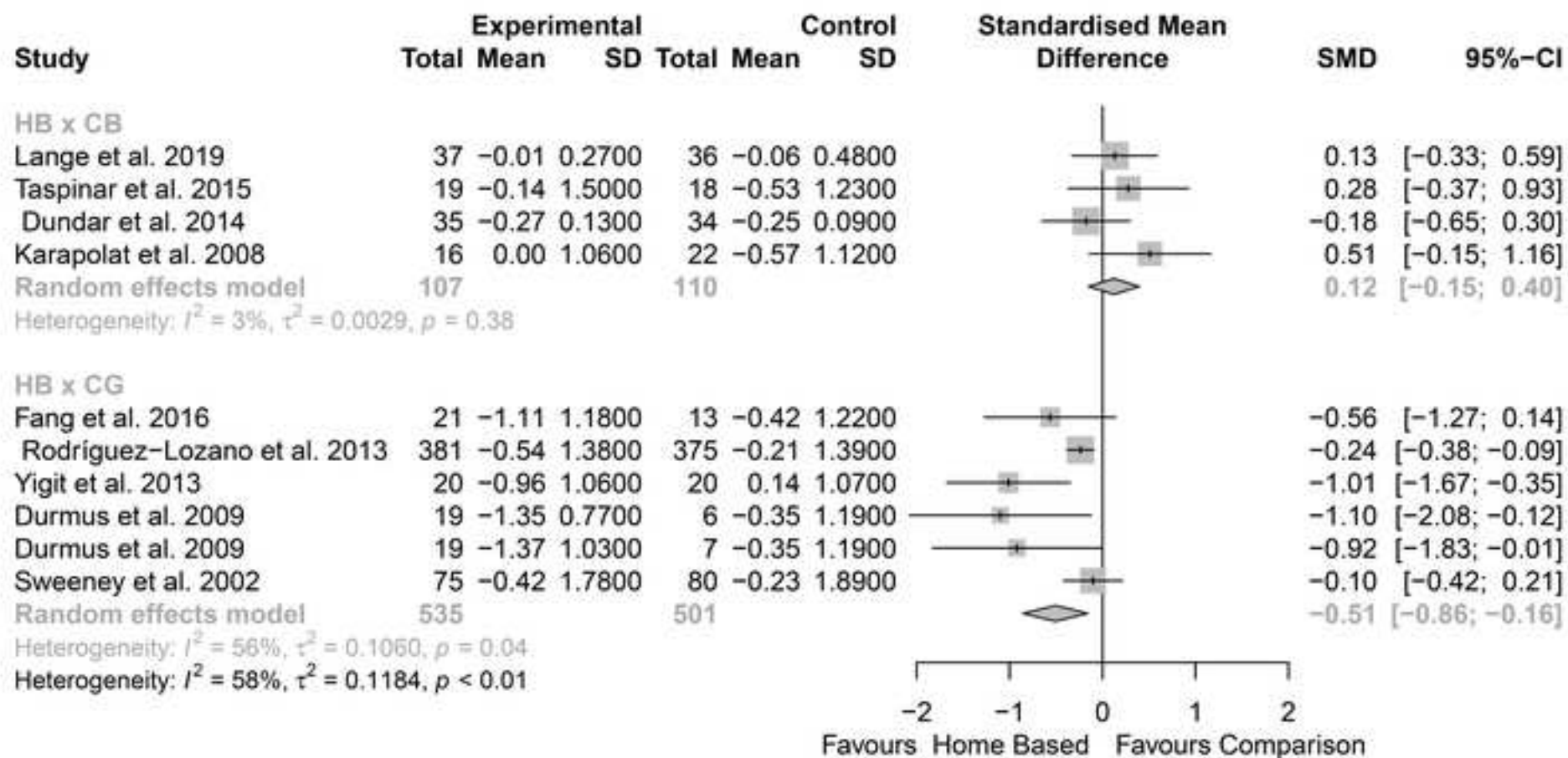
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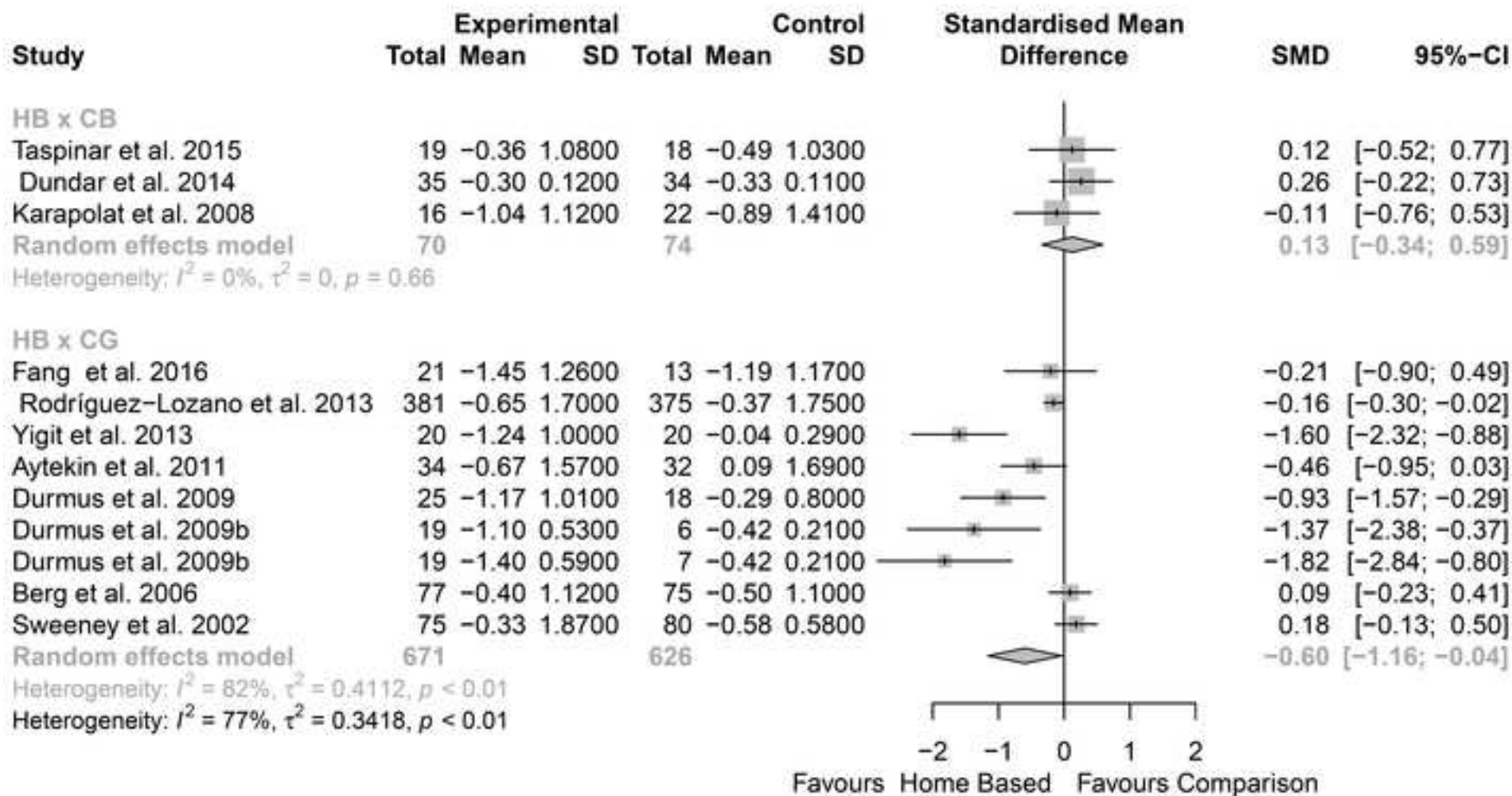


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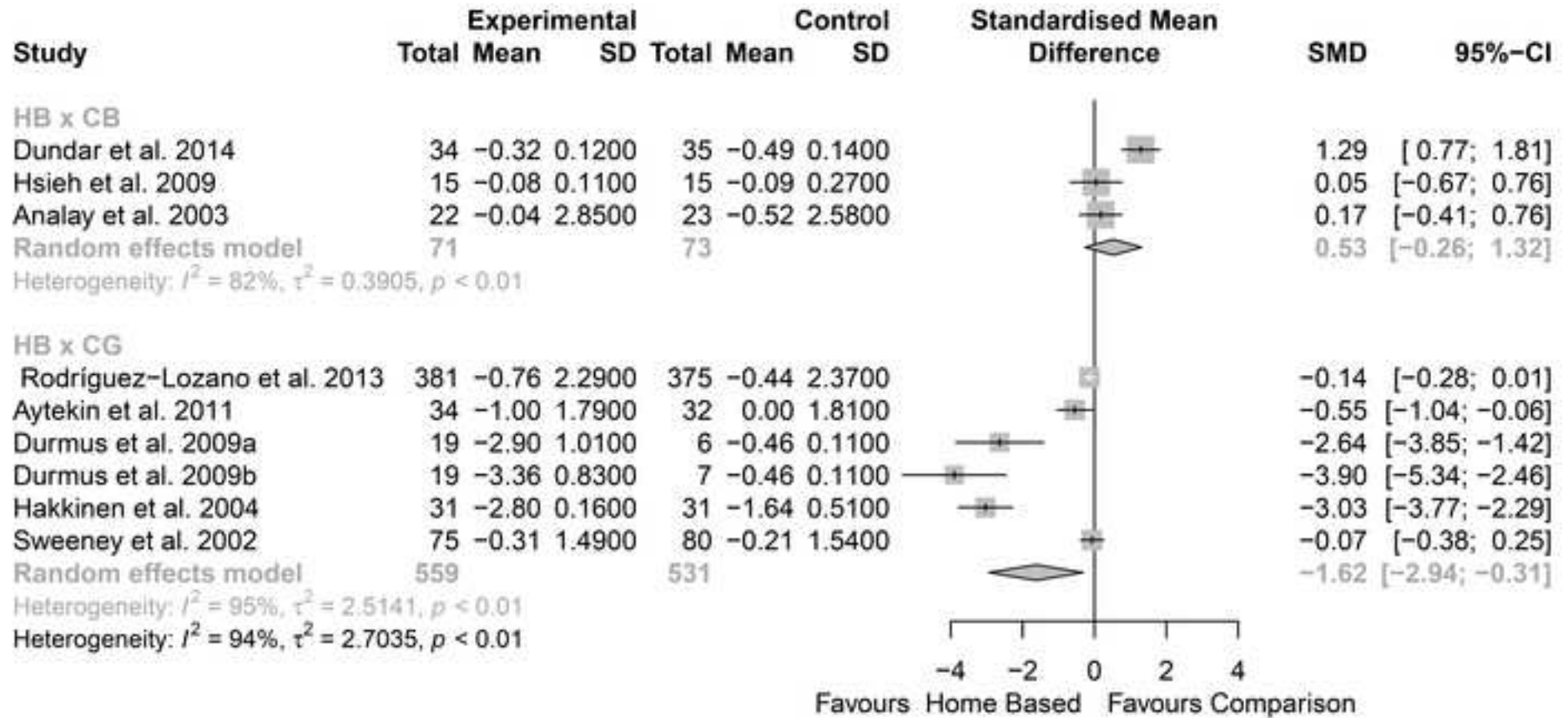


Table 01 - Methodological characteristics of studies included

Author (data)	Population				Intervention type	Comparison	Outcomes *	Study design	Adverse effects
	n	Disease	Gender	Age (weighted mean $\pm$ SD)					
Lange et al. (2019)	73	Patients with RA	♀♂	69.64 $\pm$ 2.45	Resistance training	Centre-based	HAQ	RT	None
Landim et al. (2019)	22	Patients with Ssc	♀♂	48.09 $\pm$ 11.67	Hands exercises	None	Pain (VAS), SF36, HAQ.	BAT	None
Fang et al. (2016)	34	Patients with AS	♀♂	26.56 $\pm$ 5.51	Combined exercise	Control Group	BASFI, SF36, BASDAI, BASMI?	RCT	NR
Taspinar et al. (2015)	37	Patients with AS	♀♂	35.83 $\pm$ 8.08	Combined exercise	Centre-based	ASQOL, BASFI, BASDAI, CRP	RT	NR
Dundar et al. (2014)	69	Patients with AS	♀♂	42.69 $\pm$ 11.50	Combined exercise	Centre-based	BASFI, BASDAI, SF36, Pain (VAS)	RT	NR
Yuen et al. (2013)	15	Patients with SLE	♀	46.7 $\pm$ 14.4	Wii fit	None	Adherence	BAT	None
Rodríguez-Lozano et. al. (2013)	756	Patients with AS	♀♂	45.49 $\pm$ 11.51	Combined exercise	Control Group	BASDAI, BASFI, Pain (VAS), ASQoL	RCT	NR
Yigit et. al. (2013)	40	Patients with AS	♀♂	38.38 $\pm$ 7.62	Combined exercise	Control Group	BASDAI, BASFI, SF-36	NRCT	NR
Yuen et. al. (2011)	15	Patients with SLE	♀	46.7 $\pm$ 14.4	Wii fit	None	Pain (SF-MPQ)	BAT	None
Aytekin et al. (2011)	66	Patients with AS	♀♂	36.0 $\pm$ 8.14	Combined exercise	Control Group	Pain (VAS), BASDAI, BASFI, ASQoL	NRCT	NR
Karatepe et. al. (2011)	28	Patients with RA	♀♂	52.9 $\pm$ 8.6	Combined exercise	None	HAQ, RAQoL.	BAT	NR
Durmus et. al. (2009)	43	Patients with AS	♀♂	39.42 $\pm$ 7.69	Combined exercise	Control group	BASFI, BASDAI, SF-36	NRCT	NR

Durmus et al. (2009)	51	Patients with AS	♀♂	38.66 ± 8.72	Combined exercise	Control Group	BASFI, BASDAI, pain (VAS)	NRCT	NR
Ortancil et al. (2009)	22	Patients with AS	♀♂	42.4 ± 9.9	Combined exercise	None	BASFI	BAT	NR
Hsieh et al. (2009)	30	Patients with RA	♀	52.65 ± 10.15	Combined exercise	Centre-based	HAQ, pain (VAS), CRP	RT	None
Karapolat et a. (2008)	38	Patients with AS	♀♂	47.13 ± 13.03	Combined exercise	Centre-based	BASFI; BASDAI; BASMI; NHP	NRCT	NR
Berg et al. (2006)	152	Patients with RA	♀♂	49.65 ± 13.39	Combined exercise	Control Group**	RAQol; HAQ; DAS28	RCT	NR
Lim et al. (2005)	50	Patients with AS	♀♂	28.45 ± 8.40	Combined exercise	Control group	BASFI and Pain (VAS)	RCT	NR
Hakkinen et al.(2004)	62	Patients with RA	♀♂	49.00 ± 10.49	Resistance training	Control group	DAS28, Pain (VAS), HAQ,	RCT	NR
Analay et al. (2003)	45	Patients with AS	♀♂	36.05 ± 9.70	Combined exercise	Centre-based	Pain (VAS), BASFI	RT	NR
Sweeney, Taylor and Calin (2002)	200	Patients with AS	♀♂	47.00 ± 9.89	No details	Control group	BASFI, BASDAI, BAS-G, SES	RCT	NR

Legend: ♀ - female; ♂ - male; AS - ankylosing spondylitis; ASQOL- AS Quality of Life questionnaire; BASFI- Bath ankylosing spondylitis Functional Index, BASDAI - Bath ankylosing spondylitis; Disease Activity Index; BAS-G - Bath ankylosing spondylitis Global Index; CRP - C-reactive protein; DAS28 - Disease Activity Score 28; HAQ - Health Assessment Questionnaire disability index, SF36 - Short form health survey 36 , SF-MPQ – Short Form McGill Pain Questionnaire, Ssc - systemic sclerosis ; m – months; min – minutes; n – number of subjects; NHP - Nottingham Health Profile; NR- not reported; RA - rheumatoid arthritis; SES - Stanford Self-Efficacy Scale, SLE- systemic lupus erythematosus; VAS – visual analogue scale. \*Outcomes analyzed by the review team; \*\* In the Berg et al. [52] study, we considered as “control group”, the group that received general information about home-based exercises. ‘Combined exercise’ usually involved a mix of flexibility and strengthening exercises (for more information about the interventions, see Table 2).

Table 2 – Characteristics of the home-based exercise interventions

Study	Type of exercise	Frequency (session/w)	Time (min)	Intensity	Supervision	Monitoring	Support components
Lange et al. (2019)	Flexibility, strength and balance exercises	7	NR	LI*	NS	- PA logs	- One session with a physiotherapist to set goals and receive exercise instructions
Landim et al. (2019)	Hand exercises	7	NR	LI**	NS	None	- Educational and PA booklet - DVD with exercises
Fang et al. (2016)	Flexibility exercises	≥3	60	LI**	NS	- Biweekly phone calls	- Monthly sessions with a physiotherapist to receive exercise instructions
Taspinar et al. (2015)	Calisthenic and relaxation exercises	5	20-60	MI**	NS	- Daily phone calls	None
Dundar et al. (2014)	Muscle relaxation, flexibility, respiratory and strength exercises	7	60	LI**	NS	- Weekly phone calls	- One session with a physiotherapist to receive exercise instructions -PA booklet
Yuen et al. (2013)	Exergames	≥3	30	MI (11-13 RPE_1)	PS	- Weekly phone calls - Wii Fit PA logs	- In-home training on the Wii Fit system - Wii Fit - Wii Fit user guide and list of exercises
Rodríguez-Lozano et al. (2013)	Flexibility and respiratory exercises	NR	NR	LI**	NS	- Monthly phone calls - PA logs	- One educational session with the healthcare team - One session with a physiotherapist to receive exercise instructions - Educational and PA booklet - DVD with exercises
Yigit et al. (2013)	Muscle relaxation, flexibility, strength, posture and respiratory exercises	5	30	LI**	NS	None	- One educational session with a practical demonstration of the exercises -PA booklet - CD with exercises
Yuen et al. (2011)	Exergames	≥3	30	MI (11-13 RPE_1)	PS	- Weekly phone calls - Wii Fit PA logs	- In-home training on the Wii Fit system - Wii Fit - Wii Fit user guide and list of exercises
Aytekin et al. (2012)	Flexibility, strength, posture and respiratory exercises	5	30	LI**	NS	- PA logs	- One session with a physiotherapist to receive exercise instructions -PA booklet
Karatepe et al. (2011)	Strength and flexibility exercises	10 (2 per day)	NR	NR	NS	- PA logs - Weekly phone calls	- One session with one of the researchers to receive exercise instructions -PA booklet with daily exercise chart
Durmus et al. (2009)	Muscle relaxation, flexibility, strength, posture and respiratory exercises	7	NR	LI**	NS	- Weekly phone calls	- One session with a physiotherapist to receive exercise instructions
Durmus et al. (2009)	1- Flexibility and respiratory exercises 2- Strength, flexibility, posture and respiratory exercises	7	NR	LI**	NS	- Weekly phone calls	- One session with a physiotherapist to receive exercise instructions -PA booklet
Ortancil et al. (2009)	Respiratory and flexibility exercises	21 (3 per day)	10	LI**	NS	- Weekly phone calls	- One instruction session - Incentive spirometer
Hsieh et al. (2009)	Flexibility and aerobic exercises	3	60	MI (50-80% VO <sub>2peak</sub> )	NS	- PA logs - Biweekly phone calls	- One session with a physiotherapist to receive exercise instructions

Karapolat et al. (2008)	Strength, flexibility and respiratory exercises, and walking	3	45	MI**	NS	None	- Educational sessions and individual counselling with a physiatrist - Demonstration of the exercises by a physiotherapist - PA booklet - Dumbbells and ankle cuff weights
Berg et al. (2006)	Strength and flexibility exercises, and cycling on a bicycle ergometer	5	NR	MI (60-80% HR <sub>max</sub> ; 4-5 RPE_2)	NS	- Weekly emails - PA logs - Web site logging	- Personalized exercise information in a personal Web page, - Elastic band, wooden exercise stick, cycle ergometer, HR monitor.
Lim et al. (2005)	Muscle relaxation, flexibility, strength, posture and respiratory exercises	7	30	LI**	NS	- Daily phone calls	- Demonstration of the exercises by an expert - PA booklet
Hakkinen et al. (2004)	Strength exercises	2	NR	MI (50-70% 1RM)	NS	- PA logs	- Three face-to-face sessions with a physiotherapist to receive exercise instructions - Rubber bands, dumbbells.
Analay et al. (2003)	Flexibility, strength, posture and respiratory exercises, and cycling on a bicycle ergometer	3	50	LI*	NS	- Weekly phone calls	- One educational session about the disease and purposes of the exercises - One face-to-face session with a physiotherapist to receive exercise instructions - Cycle ergometer
Sweeney, Taylor and Calin (2002)	NR	NR	NR	NR	NS	None	- Exercise and educational video - Educational booklet - Exercise progress wall chart - Exercise reminder stickers

1RM = one repetition maximum load; HR = heart rate; HR<sub>max</sub> = maximal heart rate; LI = low-intensity;; MI = moderate intensity; NR = non-reported; NS = non-supervised; PA = physical activity; PS = partially supervised; RPE\_1 = Rating of Perceived Exertion 6-20 scale; RPE\_2 = Rating of Perceived Exertion 0-10 scale; w= week . \* reported by the authors; \*\* based in The 2011 Compendium of Physical Activities [32]