

The comparative efficacy of supervised- versus home-based exercise programs in patients with ankylosing spondylitis

A meta-analysis

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Abstract

Objectives: The aim of this meta-analysis is to investigate the comparative efficacy between supervised- and home-based programs in patients with ankylosing spondylitis (AS).

Method: A systematic search in PubMed, Web of Science, EMBASE, and the Cochrane Library was electronically performed by 2 independent investigators in order to capture all potential studies comparing supervised- with home-based in patients with AS from inception to April 2018. After extracted essential information, appraised risk of bias, statistical analysis was performed with Review Manager (RevMan) software (version 5.3.0). The protocol was registered at PROSPERO platform with an identifier of CRD42018097046.

Results: A total of 7 studies comprising 271 patients were included finally. Meta-analyses showed that, compared to home-based program, supervised-based program was associated with reduced bath ankylosing spondylitis metrology index (BASMI) scores (mean difference [MD], -0.45; 95% confidence interval [CI], -0.73, -0.17), bath ankylosing spondylitis disease activity index (BASDAI) scores (MD, -0.48; 95% CI, -0.88, -0.08), and bath ankylosing spondylitis functional index (BASFI) scores (MD, -0.78; 95% CI, -1.19, -0.37). However, depression scores (standard mean difference, -0.22; 95% CI, -0.58, 0.14) between the 2 groups showed no significant difference.

Conclusions: Both supervised- and home-based programs can benefit to reduce BASMI, BASDAI, and BASFI scores in AS patients. However, short-term, supervised exercise program may be more effective than home-based exercises at decreasing disease activity with AS.

Abbreviations: AS = ankylosing spondylitis, ASAS = assessments of SpondyloArthritis International Society, BASDAI = bath ankylosing spondylitis disease activity index, BASFI = bath ankylosing spondylitis functional index, BASMI = bath ankylosing spondylitis metrology index, BDI = beck depression inventory, CI = confidence interval, DMARDs = disease-modified anti-rheumatic drugs, EULAR = European league against rheumatism, HADS-D = hospital anxiety and depression scale-depression, MD = mean difference, NSAIDs = non-steroidal anti-inflammatory drugs, PRISMA = preferred reporting items for systematic reviews and meta-analyses, RCTs = randomized controlled trials, SMD = standard mean difference, TNF = tumor necrosis factor.

Keywords: ankylosing spondylitis, home-based exercise, meta-analysis, supervised-based exercise, systematic review

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1. Introduction

Ankylosing spondylitis (AS) is 1 of the chronic and progressive rheumatic condition, which was mainly characterized by the pain, fatigue, joint destruction, deformity, disability, joint dysfunction.^[1] Issued data suggested that the prevalence of AS ranges from 0.1% to 1.4%.^[2] To date, the etiologies of AS is still not completely detected; however, published evidences unfolded several potential factors contributing to occurrence of AS such as heredity, environmental factors including micro-organisms and intestinal micro-biomes. Among patients with radiographic AS, the ratio of male to female is approximately 2:1; whereas this ratio is 1:2 among patients with non-radiographic AS.^[3] The progression of AS often cause limited motion and deformity of the spine, dysfunction, and even poor quality of life.^[4] Moreover, evidences also suggested an increased cardiovascular morbidity and mortality among patients with inflammatory arthritis.^[5] Therefore, AS has been regarded as an important factor to not only lead to work disability, but also result in serious social economic burden.^[6] And thus, it is critical to relieve pain and morning stiffness experienced by AS patients so that deformity can be delayed or even prevented.

To date, several therapeutic options including pharmacological and non-pharmacological regimes have been developed to relieve symptoms experienced by AS patients. Although several promising alternative pharmacological options have been developed, the lasted recommendations issued by the Assessments of SpondyloArthritis International Society and the European League Against Rheumatism (ASAS/EULAR) remains emphasizing the role of the combination of pharmacological and non-pharmacological regimes.^[7–9] It is noted that exercise, which is 1 of the most common non-pharmacological treatments, positively interferes in all kinds of physical and psychological sides. Several studies revealed that even low intensity physical exercise also obtained considerable reductions in mortality and improved health outcomes among patients when compared with subjects receiving controls.^[10,11]

At present, 2 exercise programs including home-based and supervised-based exercise has been used extensively to treat AS patients. Several studies have established the effects of home-based exercise regime in improving health-related quality of life and reducing fatigue in AS patients.^[12–14] Moreover, supervised-based exercise program was also established to have positive effects on pain, mobility, function, and disease activity in AS patients.^[15,16] More importantly, the 2 exercise programmes are all detected to be superior to the route interventions. So it is difficult to make decision in clinical practice because promising results are found in the 2 regimes.^[17] We therefore performed this systematic review and meta-analysis to investigate the comparative efficacy and safety between supervised- and home-based exercise programs in patients with AS.

2. Materials and methods

This study was conducted in accordance with the framework recommended by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement^[18] (Supplementary PRISMA checklist, S1). The study protocol was registered in PROSPERO (CRD42018097046)^[19] and has been published in *Medicine*.^[20] The design does not require ethical approval because no patient was involved.

2.1. Eligibility criteria

Studies enrolling adult patients with AS who were diagnosed by a rheumatologist were considered. Randomized controlled trials (RCTs) or clinical trials, in which at least 1 of the groups received the supervised-based exercises or home-based exercises, were included. The outcomes were the scores reported in Bath AS Metrology Index (BASMI), the Bath AS Functional Index (BASFI), the Bath AS Disease Activity Index (BASDAI), and depression score which was assessed with the beck depression inventory (BDI) and hospital anxiety and depression scale-depression. Studies with insufficient data were excluded. The studies conducted by the same research team, the 1 with insufficient data and poor methodology was eliminated.

2.2. Search strategy

Four electronic databases including PubMed, Web of Science, EMBASE, and the Cochrane Library were electronically searched using the following terms home-based exercise, supervise* exercise, supervised-based exercise and AS. Search algorithm was adjusted according to the unique requirements of each database. All databases were searched from their inception until to April 2018. In the present meta-analysis, we only considered the study published in English language. Moreover, we checked the bibliographies of eligible studies and topic-related review to capture any potential study. If disagreement on citation search was identified, a third senior investigator was consulted to solve it.

2.3. Study selection

Two authors independently screened titles and abstracts in order to identify studies that meet the inclusion criteria. And then, we retrieved the full-text of potential studies, and 2 independent investigators checked the eligibility of each study. Any divergence about study selection was addressed through consulting a third senior investigator.

2.4. Data extraction

All captured citations were imported into Endnote literature management software V.X7. We then assigned 2 reviewers to abstract the basic information and data for the specific outcomes from the eligible studies, such as first author, publication year, age of participants, sample size, details of interventions and outcomes of interesting using the standard data extraction form. We contacted the corresponding author when sufficient data of an eligible study cannot be abstracted from the full text.

2.5. Quality assessment

We assigned 2 independent reviewers to appraise the risk of bias from following 7 domains: randomization sequence generation, allocation concealment, blinding of participants, blinding of study personnel, blinding of outcome assessors, incomplete outcome data, selective reporting and other bias with the Cochrane risk of bias assessment tool.^[21,22] A study was assigned a risk level of 'high risk of bias', 'unclear risk of bias' or 'low risk of bias' according to the match level between the actual information and the evaluation criteria.^[22]

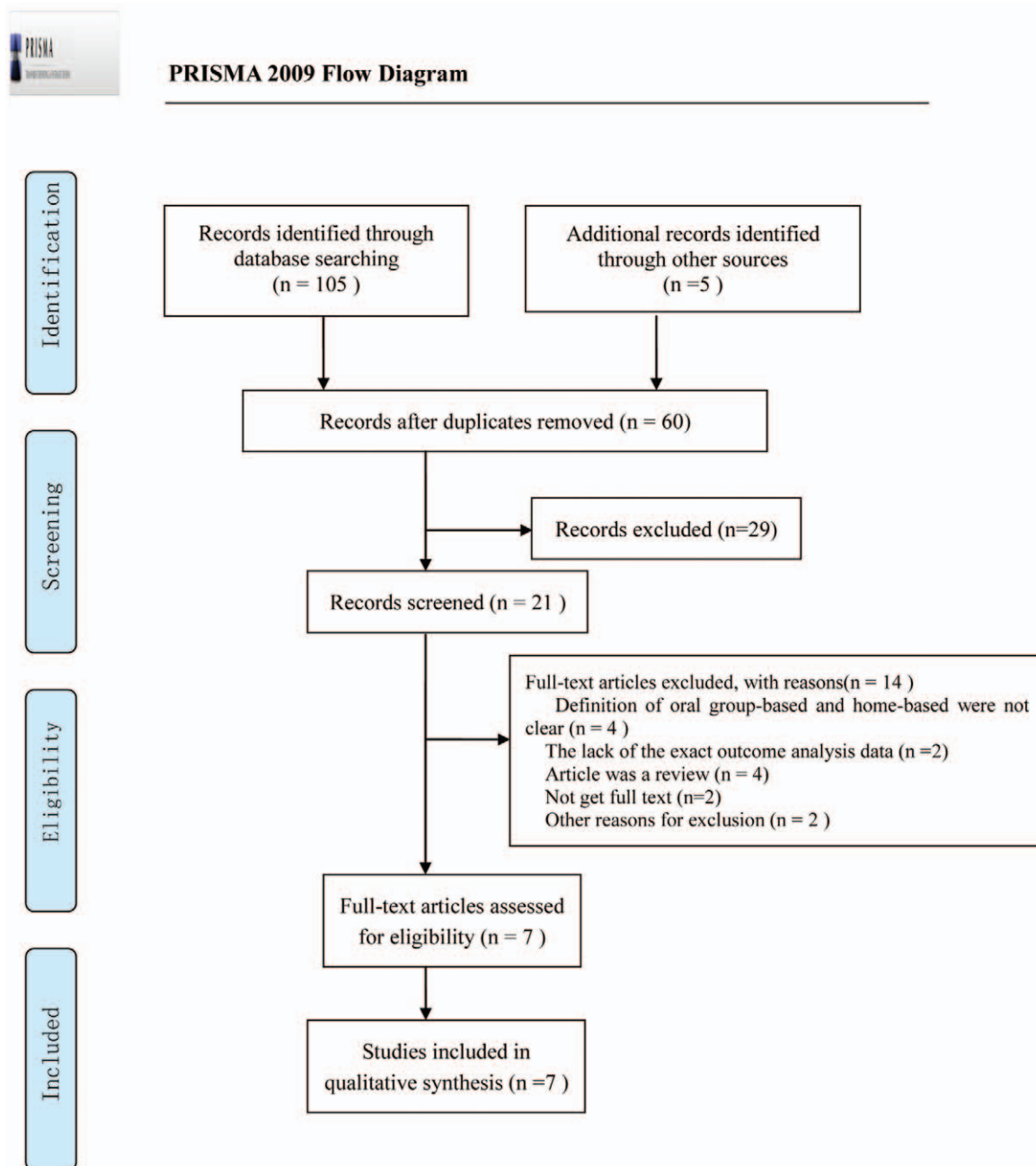


Figure 1. Flow diagram of the article selection procedure.

2.6. Statistical analysis

Continuous data were expressed as the mean difference (MD) or standard mean difference (SMD) with 95% confidence interval (CI). The heterogeneity among included trials was qualitatively tested using P value, and quantitatively estimated using I^2 statistic. A fixed-effects model was adopted if all included studies were considered to be homogeneous ($I^2 < 50\%$). In contrast, a random-effects model was used. A 2-tailed P value of less than .05 indicates statistical significance. All statistical analyses were performed using Review Manager (RevMan) software, version 5.3.0 (Cochrane Collaboration, Copenhagen, Denmark).

2.7. Outcome measures

The outcomes of interesting was the scores of BASMI, BASFI, BASDAI, and depression. All were reported in individual study.

3. Results

3.1. Study selection and characteristics

A total of 120 trials were identified after initially literature searched (Fig. 1). After checking the eligibility of all potential studies, 7 trials including 271 participants were deemed eligible for meeting inclusion criteria (Table 1) because ineligible studies were all excluded as following reasons: outcomes were reported

Table 1
Basic characteristics of all eligible studies.

Studies	Country	Sample Size (SG/HBG)	Age (SG/HBG)	Gender (M:F) (SG/HBG)	Disease duration (SG/HBG) (months/years)	Intervention time	Evaluated time	Intervention Regime		
								SG	HBG	Outcomes
Analay 2003	Turkey	23/22	(37.6 ± 11.3)/(34.3 ± 7.9)	(20:3)/(18:4)	NA	6 wk/3 mo	6 wk/3 mo	SP	HEP	BASFI, BDI
Karapolat 2008	Turkey	22/16	(47.5 ± 11.8)/(46.60 ± 14.8)	(15:7)/(11:5)	(19.3 ± 11.7)/(19.3 ± 10.6)	6 wk	6 wk	SP	HEP	BASMI, BASDAI, BASFI, Pain, BDI
Widberg 2009	Sweden	16/16	36.5 (29-60)/35 (23-53)	M	2.5 (0-20)/3.5 (0-20)	8 wk	8 wk	SP	HEP	BASDAI, BASFI, BASMI
Gunendi 2010	Turkey	16/16	(45.6 ± 12.4)/(43.4 ± 12.0)	(13:3)/(11:5)	(156.4 ± 146.4)/(127.3 ± 103.3)	3 wk	3 wk	SP	HEP	BASDAI, BASFI
Altan 2012	Turkey	29/24	(46.5 ± 11.2)/(43.6 ± 10.1)	NA	NA	12 wk/24 wk	12 wk/24 wk	SP	HEP	BASDAI, BASFI, BASMI
Aydin 2016	Turkey	18/19	(35.83 ± 8.08)/(33.52 ± 7.72)	(11:8)/(9:9)	(7.22 ± 2.19)/(7.10 ± 2.79)	8 wk	8 wk	HP	HEP	BASDAI, BASFI, BASMI, HADS-D
Fang 2016	China	21/13	(26.62 ± 4.72)/(26.4 ± 6.78)	(17:4)/(13:0)	(4.56 ± 3.92)/(4.88 ± 3.50)	6 mo	6 mo	SP	HEP	BASDAI, BASFI, BASMI

BASDAI = bath ankylosing spondylitis disease activity index, BASFI = bath ankylosing spondylitis functional index, BASMI = bath ankylosing spondylitis metrology index, BDI = beck depression scale, HADS-D = hospital anxiety and depression scale-depression, HBG = home-based group, HEP = home exercise program, HP = hospital program, NA = not applicable, SG = supervised group, SP = supervised program.

as to be interquartile range,^[23] inadequate sample size,^[24] 1 without full text,^[25] ineligible study design^[24,25] and lack of essential data,^[16] and ineligible outcomes.^[26] Five of the eligible studies were conducted in the Turkey,^[15,17,27-29] 1 in Sweden^[30] and 1 in China.^[31] The duration of the interventional programs ranged from 3 weeks to 6 months.

3.2. BASMI

Five studies^[17,28-31] which involving 194 AS patients reported the BASMI after the interventions were initiated. There was no significant heterogeneity between the supervised-based training groups and home-based exercise groups in BASMI ($P = .36$, $I^2 = 8\%$). Pooled result revealed significant difference in terms of this given outcome when supervised-based training program compared to home-based program (MD, -0.45; 95% CI, -0.73, -0.17), which indicated that the supervised-based training were superior to the home-based exercises in reducing the BASMI scores (Fig. 2A).

3.3. BASDAI

Six studies^[17,27-31] which involving 226 AS patients reported the BASDAI after the interventions were initiated. A fixed-effects model was applied because of no significant heterogeneity was detected ($P = .19$, $I^2 = 33\%$). Pooled result revealed that significant difference between supervised-based training program and home-based program (MD, -0.48; 95% CI, -0.88, -0.08), which indicated that the supervised-based training groups were superior to the home-based exercises on reducing the BASDAI scores (Fig. 2B).

3.4. BASFI

Seven studies^[15,17,27-31] which enrolled 271 AS patients reported BASFI. A fixed-effects model was applied because of no significant heterogeneity was found ($P = .78$, $I^2 = 0\%$). Meta-analysis suggested significant difference when supervised-based training program compared to home-based program (MD, -0.78; 95% CI, -1.19, -0.37), which indicated that the supervised-based training groups were superior to the home-based exercises groups on reducing the BASFI scores (Fig. 2C).

3.5. BDI scores

Three studies^[15,17,28] which involving 120 AS patients reported BDI scores. A fixed-effects model was applied because of no

significant heterogeneity was identified ($P = .74$, $I^2 = 0\%$). Summarized analysis obtained no significant difference in terms of this given outcome when supervised-based training program compared to home-based program (SMD, -0.22; 95% CI, -0.58, 0.14), which indicated that the supervised-based training groups were not-superior to the home-based exercises groups on reducing the depression scores (Fig. 2D).

3.6. Quality assessment

Five studies^[15,28-31] included in this study could be identified as having adequate sequence generation, allocation concealment and blinding, 2 studies non-RCT;^[17,27] the 6 studies addressed incomplete outcome data.^[15,17,28-31] Furthermore, the baselines were comparable in all the studies. The quality assessment outcome was summarized in Figures 3 and 4.

4. Discussion

This meta-analysis found that both the supervised- and home-based exercise programs were all benefit to reduce BASMI, BASDAI, and BASFI in AS patients; however, we also found the short-term, supervised exercise program may be more effective than home-based exercises at decreasing disease activity. Summarized result based on 6 eligible studies suggested that the supervised-based exercises applied in hospital may be more effective than home-based exercises in reducing disease activity related to AS.^[15,27-31] The results of most of included study were all consistent with the finding in our study. However, 1 eligible study reported conflicting result.^[17] Meanwhile, we found that the advantageous to carry out home-based exercise programs than the absence of any exercise program in 1 previous systematic review, noteworthy is our study used meta-analysis, but, Lopes et al only used systematic review.^[32] At the same time, we found significant improvement in BASFI, BASDAI, HAQ, BASMI measurements at the end of the treatment because all patients have a good compliance with exercise programs, which suggest that supervision exercise program is more effective than home-based program.^[33] For example, Fang et al^[31] found that the home-based exercises and supervised training can improve physical function and quality of life in patients with AS for 6 months in Mainland China. A study also suggested that a structured educational and exercise program had a positive effect on the functional status, disease activity, and general well-being

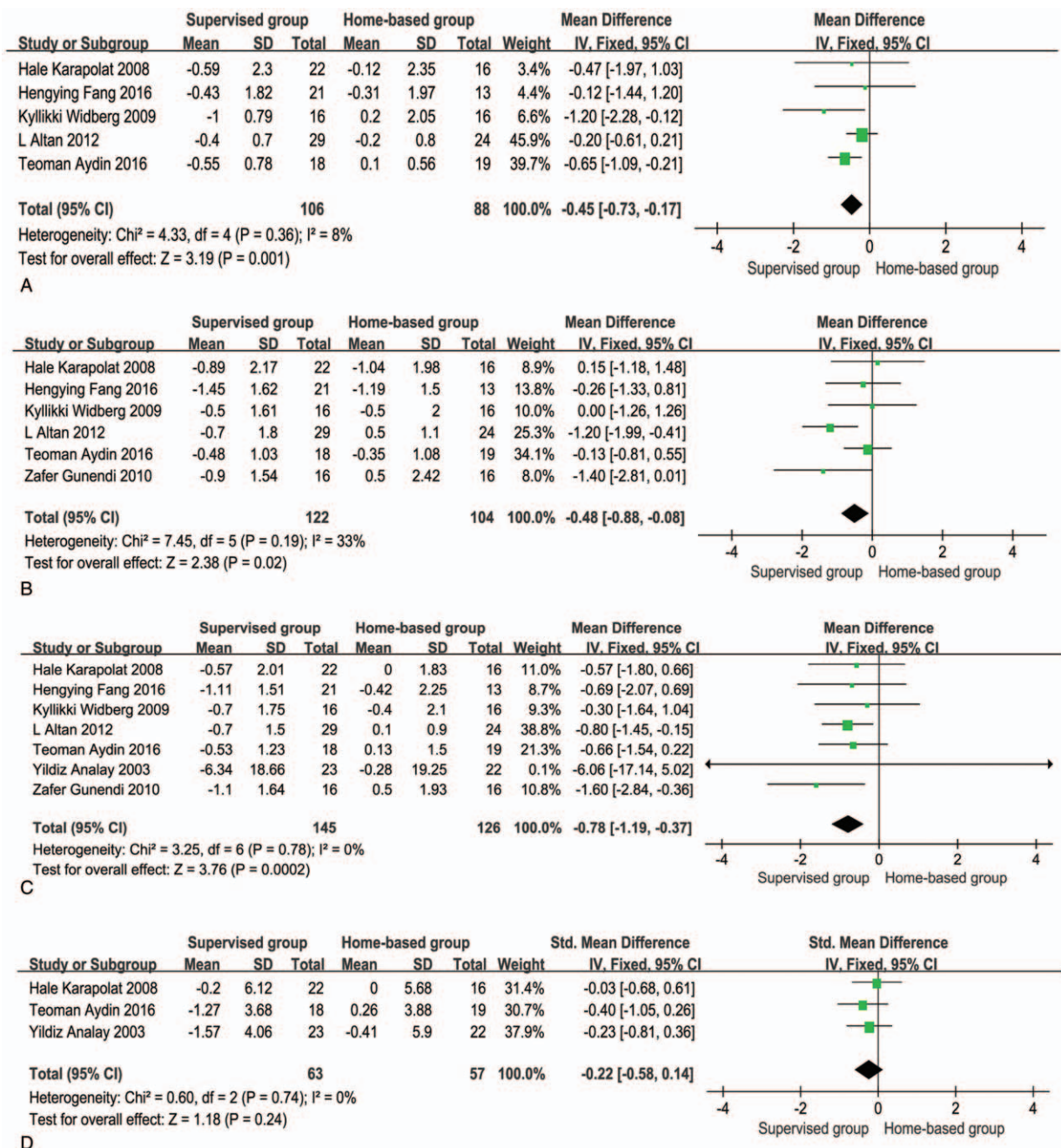


Figure 2. Meta-analyses of outcomes scores between group-based exercises and home-based exercises. A) BASMI Scores. B) BASDAI Scores. C) BASFI Scores. D) BDI scores. BASDAI=bath ankylosing spondylitis disease activity index, BASFI=bath ankylosing spondylitis functional index, BASMI=bath ankylosing spondylitis metrology index, BDI=beck depression scale.

and quality of life.^[34] In addition to this, we found that ultrasound treatment increased the effect of exercise in patients with AS patients,^[35,36] but the interventional time was different, vary 2 weeks from 8 weeks. Therefore, ultrasound treatment may be an important assistant treatment method in future for AS patients.

Six studies designed the supervised or group-based exercises in the intervention group and home-based exercise in the control group, however the exercise interventions were still to have a little bit different. For example, 3 studies adopted group-based

exercises in intervention group, of which 1 organized an 6 weeks intensive exercise program supervised by physiotherapist,^[15] 1 applied a 3 weeks supervised exercise program that consisted of aerobic, strengthening, and stretching exercises,^[17] 1 designed a 6 weeks group-exercise program composed of respiratory exercises, stretching, mobilization and strengthening exercises for lower, upper extremity and back muscles supervised by physiotherapist.^[27] One 5-day exercise program consisted of calisthenic exercises for 3 days and relaxation exercises for 2 days.^[28] The exercise program of 1 study followed the basic

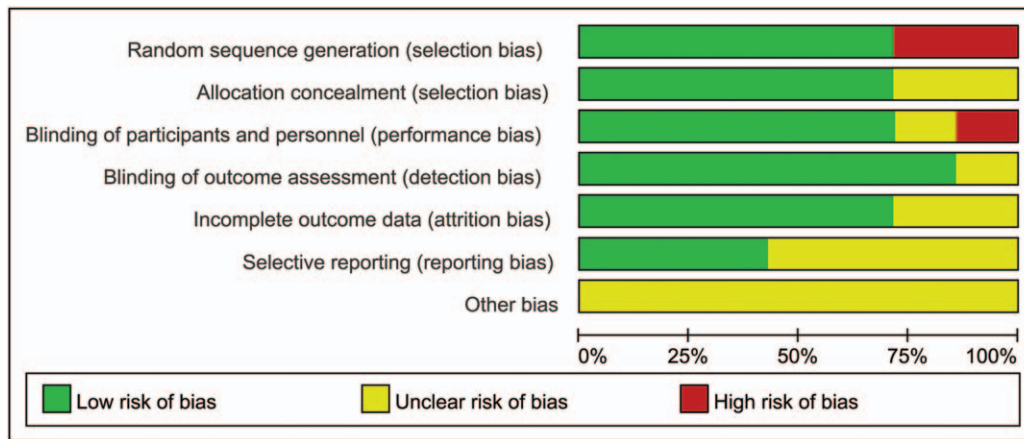


Figure 3. Percentage of risk of bias: authors' judgments about percentages of each risk of bias item in all included studies.

principles of Pilates method that 1 hour was given by a certified trainer to 3 times a week for 12 weeks.^[29] One study were given individualized self- and manual mobilization for 1 hour twice a week for 8 weeks.^[30] For remaining 1,^[31] the intervention group adopted 6 months home-base flexibility exercises and exercise

therapy which was supervised by a physiotherapist, and the control group were instructed to receive the guidance on conventional drugs and disease education including the guidance of home-based exercise training from doctors on the basis of drug treatment. Therefore, further studies with comparable exercise regime were warranted.

According to the ASAS/EULAR, drugs treatments also play an important role in AS patients' management, and the drugs include non-steroidal anti-inflammatory drugs (NSAIDs), disease-modified anti-rheumatic drugs (DMARDs) and tumor necrosis factor (TNF) inhibitor for AS patients now. However, we found that the drugs used in all included studies were variation. All articles illustrate the medical conditions in our included studies, which the patients be included or excluded, such as patients receiving disease-modifying drugs were also excluded in Analay, Y et al,^[15] in Gunendi, Z et al's study that all patients were on NSAIDs drugs only,^[27] in Aydin T et al's study have been given anti-TNF treatment would be excluded,^[28] however, in Fang, H et al's study that all patients treated with drugs, including NSAIDs, Biologics and others, therefore, there were no restrictions with regard to type of non-pharmacological intervention, or to dose, duration or route of administration.^[31] However, 2 of the included studies did not report the drugs condition about AS patients in materials and methods.^[17,29] One study suggested that patients had stable pharmacological treatment with NSAIDs and DMARDs be included.^[30] Therefore, drugs therapy may be also important for AS patients, future studies should focus on the same drugs treatment condition.

To our knowledge, we found 4 articles^[12,32,37,38] had systematically examined the effect exercises in AS patients, but there were only 2 systematic reviews for comparison group-based with home-based exercise^[32,37] and the results were not pooled. Therefore, we first used a meta-analysis to systematically investigate the effect of supervised-based exercises and home-based exercises, although exercise is frequently advised as part of their managements. However, there are still some limitations to this meta-analysis that should be acknowledged. First, perhaps the most notably, only a small number of studies met the inclusion criteria, thus reducing the power of the analyses. Second, the inclusion of only English-language literature may also have restricted the number of available relevant articles. Finally, the exercise intervention forms and time are different. Therefore, we hope future studies with a multi-centered and large-scale sample, adequate interventional time, similar exercise

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Hale Karapolat 2008	⊖	?	?	?	+	?	?
Hengying Fang 2016	+	+	+	+	+	+	?
Kyllikki Widberg 2009	+	+	+	+	+	?	?
L Altan 2012	+	+	+	+	?	?	?
Teoman Aydin 2016	+	+	+	+	+	+	?
Yildiz Analay 2003	+	+	+	+	+	+	?
Zafer Gunendi 2010	⊖	?	⊖	+	?	?	?

Figure 4. Risk of bias summary: authors' judgments about each risk of bias item for each included study.

forms, frequency and methods, and randomized methodology to draw conclusions about the exercise in AS patients.

The findings do suggest that both the group-based or supervised and home-based exercises may be effective on reducing BASMI, BASDAL, BASFI and depression in AS patients. Hence, the short-term, supervised exercise program may be more effective than home-based exercises at decreasing disease activity with AS.

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Writing – original draft: Hui Liang, Xu Tian.

Writing – review & editing: Xu Tian.

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