

**Effectiveness of education programs on axSpA patients: a systematic review of randomized controlled trials**

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## Abstract

**Introduction:** The current standard of care of patients with spondyloarthritis (SpA), in addition to pharmacological treatment, includes regular exercise and patient education.(1) The primary goal of this systematic literature review (SLR) is to update the evidence of the effectiveness of education programs for patients with axial SpA (axSpA).

**Methods:** We systematically searched three databases, PubMed, Embase and Web of Science Core Collection, from January 2000 to June 2023, using the following terms: “patient education”, “patient counselling”, “patient teaching”, “patient engaging”, “patient empowerment”, “health education”, “spondyloarthritis”, “spondyloarthropathies”, “spondylitis” and “ankylosing spondylitis”. The “Population (P)”, “Intervention (I)”, “Comparator (C)”, “Outcome (O)”, PICO criteria were used. “P”, defined as axSpA, “I” as education, “C” as standard of care or physical exercise and “O” as disease activity, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score (ASDAS); disease functional repercussion, Bath Ankylosing Spondylitis Functional Index (BASFI); disease metrological repercussion, Bath Ankylosing Spondylitis Metrological Index (BASMI); disease quality of life Ankylosing Spondylitis Quality of Life (ASQoL), EuroQoI-5D (EQ-5D) and Short Form 36 Health Survey (SF36); disease economic impact, cost-utility, cost-benefit and incremental cost-effectiveness ratio (ICER). Only randomized clinical trials were included. Two reviewers independently assessed the identified papers according to the established criteria and extracted the data.

**Results:** From the initial 494 studies identified, 6 were selected for data extraction and qualitative analysis. The study sample sizes ranged between 41-65 individuals, all diagnosed with ankylosing spondylitis. The leaders of the programs varied, the intervention period ranged between 4-12 weeks and the follow up ranged between 3-12 months. In three studies, the comparator was standard of care, and in the other three was physical exercise. Overall, there was an improvement in BASDAI, BASFI, BASMI, ASQoL and SF-36, after the application of educational programs. No studies evaluated the economic impact of educational programs.

**Conclusion:** Education appears to be an important adjuvant as non-pharmacological treatment for patients with axSpA, enhancing various disease outcomes, particularly when delivered by Health Professionals using physical materials such as pamphlets. However, there is an ongoing need for additional research to obtain more robust conclusions.

**Keywords:** Axial Spondyloarthropathy; Education (patients); Systematic Literature Review; Medical education; Clinical trials and methods.

## Introduction

Spondyloarthritis (SpA) is a heterogeneous group of diseases that significantly impact patients' daily activities, making the formulation of an effective therapeutic approach challenging. The current standard of care, along with pharmacological treatment, include regular exercise and patient education<sup>1</sup>.

Patient education is a crucial component in the management of rheumatic and musculoskeletal diseases (RMDs). It can be defined as "any set of planned educational activities designed to improve patients' health behaviors, and through this, their health status and ultimately long-term outcomes"<sup>2</sup>. Education programs are useful for providing patients with the skills to manage their rheumatic disease and could potentially play a role in improving patients' related outcomes, including disease activity, functional capacity and quality of life<sup>3,4</sup>. In recent years, European Alliance of Associations for Rheumatology (EULAR) has provided guidelines to help healthcare professionals (HPs) integrate education into patients' management<sup>4-6</sup>. Patient education should be provided at the time of diagnosis, during the initiation or modification of pharmacological treatment and whenever required by the patient's physical or psychological condition<sup>6</sup>. To maximize effectiveness, education should include information about the disease process (diagnosis, symptoms, prognosis), its management (risks and benefits of each treatment option, self-management, comorbidities) and function-social aspects (daily activities, ergonomic advice, community involvement, lifestyle changes)<sup>4,5,7,8</sup>. Delivery formats for education can include verbal communication (face-to-face, online interactions or phone calls), written materials or multimedia formats<sup>5,6</sup>. Providers delivering education may include HPs, a multidisciplinary team or trained patients<sup>6</sup>. Importantly, education should be tailored to each patient. While several studies, primarily in rheumatoid arthritis (RA) patients<sup>9-12</sup>, have reported the effectiveness of patient education, the available evidence remains inconclusive. Group-based education programs appears to be more effective than individual ones<sup>9</sup>. Shorter courses (defined as < 8 weeks) and those led by HPs also show better results<sup>9</sup>. However, there is currently no evidence of long term benefits<sup>12</sup>.

Moreover, there is a gap in information regarding education for patients with axial spondyloarthritis (axSpA). A recent systematic literature review about efficacy and safety of non-pharmacological and non-biological pharmacological treatment demonstrated a favorable efficacy of non-pharmacological interventions<sup>13</sup>. However, only two studies about education were included and it is difficult to reach a conclusion. The primary goal of this systematic literature review (SLR) is to update the evidence of the effectiveness of education programs for

patients with axSpA. Additionally, this SLR aims to provide valuable insights for the task force responsible for formulating the Portuguese recommendations for the non-pharmacological treatment of axSpA.

## Methods

### Search methodology and study selection

A systematic literature search was performed using databases such as Pubmed, Embase and Web of Science, from January 2000 to June 2023. The following search terms were used: “patient education” [OR synonyms] AND “spondyloarthritis” [OR synonyms]. Articles were limited to English, French, Portuguese and Spanish language. Eligible study types included randomized controlled trials (RCTs) and clinical controlled trials (CCTs). SLR were only considered to identify references from original studies. The “Population (P)”, “Intervention (I)”, “Comparator (C)”, “Outcome (O)” (PICO) method was used:

- P: adult patients (age $\geq$ 18 years) with a diagnosis of axSpA (including both radiographic (r-axSpA) and non-radiographic (nr-axSpA) stages) according to ASAS criteria;
- I: education programs (without specification);
- C: standard care (routine follow-ups) or physical exercise;
- O: disease activity and/or functional status and/or quality of life. For disease activity the outcomes considered were Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)<sup>14</sup>, Ankylosing Spondylitis Disease Activity Score (ASDAS)<sup>15</sup>; for functional status, Bath Ankylosing Spondylitis Functional Index (BASFI)<sup>16</sup>; for mobility repercussion, Bath Ankylosing Spondylitis Metrological Index (BASMI)<sup>17</sup>. Health Assessment Questionnaire (HAQ)<sup>18</sup>, Ankylosing Spondylitis Quality of Life (ASQoL)<sup>19</sup>, Short Form Health Survey 36 (SF-36)<sup>20</sup> and EuroQol five-dimension scale (EQ5D)<sup>21</sup> were considered to evaluate the quality of life. The economic impact of the disease was evaluated by cost-utility, cost benefit and ICER. Patient response to treatment was assessed using the ASAS response criteria<sup>22</sup>, BASDAI response (improvement of  $\geq$ 50% and/or  $\geq$ 2 units) or according to ASDAS cut-offs<sup>19</sup>. Additionally, pain levels (visual analogue scale from 0 to 100), fatigue, radiographic progression [modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS)<sup>23</sup>] and inflammation on magnetic resonance imaging [Spondyloarthritis Research Consortium of Canada (SPARCC) score<sup>24</sup>] were assessed if available.

Studies that exclusively involved physical or psychosocial therapies were not included in this analysis.

### **Data extraction and assessment of risk of bias (RoB)**

All articles obtained through the search strategy were uploaded into an EndNote library and the duplicates removed. Titles and abstracts were independently assessed by two reviewers (LB and RC), with a third reviewer involved in case of disagreement (HS), to determine whether they met the inclusion/exclusion criteria. The included articles were then reviewed in full-text. Relevant data identified in advance, were extracted from each study. We extracted data on country, year and sample size. Demographic data included age and gender, while clinical data included diagnosis (nr-axSpA and r-axSpA), disease duration (years), current therapy and positivity for HLA-B27 when available. Characteristics of the education program included the number and duration of each education session, delivery mode (group or individual sessions), session leaders (HPs, patients, multidisciplinary team), and supplementary material (e.g., written, multimedia). Additionally, the two reviewers, LB and RC, independently evaluated the risk of bias (RoB) for each study using the “Cochrane tool” for RCTs(25). Disagreements regarding RoB assessment were resolved through discussion and consensus. An overall assessment of the quality of the evidence for each outcome was performed using the Grading of Recommendations, Assessment, Development and Evaluation (high, moderate, low, very low)<sup>26</sup> and Summary of Findings (SoF) tables were produced with the GRADEPro GDT software. The authors preferred a narrative SoF due to the differences in metrics used by the included studies.

### **RESULTS**

Due to the considerable heterogeneity among the studies, it was not feasible to pool the data, and the results are presented descriptively. Out of 494 references initially identified, 12 were chosen for a thorough full-text review. After excluding studies that did not meet the specified inclusion/exclusion criteria, 6 were ultimately included in this SLR (Figure 1). All selected studies were RCTs. Notably, 6 RCTs have been added since the last review on non-pharmacological and non-biological treatment<sup>27-32</sup>. The study protocols and characteristics of each study are presented in Table I and Table II. Overall, the included studies were heterogeneous due to differences in:

- Types of intervention: group sessions<sup>27,28,30-32</sup>, individual sessions<sup>29</sup>, sessions given by a multidisciplinary team<sup>27,28,30,31</sup>, sessions given by trained patients<sup>32</sup>, sessions given by a health physician<sup>29</sup>;
- Content of the intervention: information about the disease process and treatment<sup>27,28,30-32</sup>, function-social aspects<sup>27,28,30-32</sup>) and physical exercise<sup>27,29-31</sup>;

- Duration of the intervention: range between 1 week and 3 months;
- Outcome parameters.

Notably, all studies had small group sizes ( $n < 30$ ). Although all studies enrolled patients with established axSpA (with 2 studies not specifying the classification criteria), the specific subtypes (r-axSpA and/or nr-axSpA) were not clearly delineated. Information regarding HLA-B27 positivity was unavailable. The effects of interventions per outcome are described in the online supplemental material (Tables II-IV) and the SoF is presented in Table III.

### **Risk of Bias of Studies**

Two studies were identified as having a high RoB, four studies classified as “some concerns” and none met the criteria for a low RoB (Supplementary Table I). The reviewers collectively agreed to include all appraised studies. Despite the lack of quality of evidence, the reviewers decided to include all of them due to the lack of available studies and to get as much information as possible about this topic.

## **DISCUSSION**

Arthritis undeniably exerts a significant impact on patients’ daily lives, prompting an exploration into whether patient education could offer additional and complementary benefits to address their challenges. Thus, educational programs tailored to the specific needs of individuals with inflammatory arthritis are crucial. However, the comparative analysis of the different available interventions poses challenges.

This SLR aims to summarize the latest evidence on the effectiveness of educational programs for patients with axSpA. The studies assessing educational interventions in axSpA patients are limited in number and display heterogeneity, attributed to variations in the types of educational programs, their content, intervention durations, evaluations periods, providers, and individual patient characteristics. This heterogeneity yields unsatisfactory results<sup>27–32</sup> and present challenges in conducting a meta-analysis complicating the evaluation of the impact of educational programs. The evidence supporting the approach of educational programs for axSpA patients lacks high certainty. While this SLR emphasizes the potential positive impact of educational programs on disease activity, functionality, and general mobility, the influence on quality of life is less clear. Unfortunately, there is a lack of available data regarding the impact on therapeutic response, fatigue, or radiographic progression. Furthermore, information

regarding the economic impact of these interventions was unavailable. Compared to the previous SLR<sup>13</sup>, no new findings on the effectiveness of education were obtained.

Beyond the overall impact of educational programs, it is also relevant to assess the content delivered, the individuals/teams delivering the programs, and the methods used. Our SLR reveals that well-structured programs are still lacking, leading to a significant information gap in this context. The efficacy of these programs is widely recognized to depend on various factors such as sociodemographic characteristics, accessibility to health services, and disease status. The content delivered was not consistent across programs. It ranged from information about the disease process and treatment<sup>27,28,30-32</sup>, function-social aspects<sup>27,28,30-32</sup> and physical exercise<sup>27,29-31</sup>. The absence of standardized content makes direct comparison difficult. In the clinical trials included, the interventions were delivered by HP<sup>28</sup>, trained patients<sup>31</sup>, or multidisciplinary teams<sup>26,27,29,30</sup>. Interestingly, interventions delivered by trained patients yielded less favorable outcomes. Despite the greater connection that patients might feel with their peers, it appears that interventions led by HP's or multidisciplinary teams have a more substantial impact on the efficacy of education. All studies provided patients with supplementary materials, such as pamphlets, which seemed to reinforce educational sessions or serve as reminders, contributing positively to the overall intervention. Exploring different approaches, specifically comparing the use of physical materials versus digital information, would be of interest in future research.

There are still other relevant aspects, notably the duration of the programs, follow up period and whether they are conducted individually or in group settings. In previous studies, group-based education programs were found to be more effective than individual ones<sup>9</sup>. According to the authors, the influence of group dynamics could serve as motivation for patients. However, in this review, only one study included individual sessions<sup>29</sup>. This particular clinical trial aimed to motivate and support individuals with ankylosing spondylitis in engaging in physical activity (primary outcome) through individually-tailored appointments. Following the intervention, the experimental group exhibited higher compliance with physical exercise and a significant decrease in BASMI and ASQoL scores. While there were statistically significant improvements in BASMI and ASQoL results, a direct comparison with group sessions was not conducted. Therefore, establishing robust conclusions is challenging. Regarding the duration of the intervention, and contrary to Carnes D. *et al*<sup>9</sup>, who suggest better attendance in shorter courses, we found evidence supporting both long-term and short-term programs, depending on the outcomes considered. The follow up period may also influence the results. All studies except one<sup>27</sup> had a follow up period longer than 6 months. The authors believe that the longer the time since the first session, the greater the possibility of forgetting what was learned. Worse results

in studies with longer follow-up periods may reflect this premise. From a financial perspective, opting for shorter programs may be more attractive.

AxSpA is a chronic disease, and like other RMDs, education should be integrated throughout the entire course of the disease. It is crucial for patients to learn how to coexist with the disease, manage their disease treatment effectively, and adapt their lifestyle to optimize outcomes<sup>3,33</sup>. These aspects are instrumental in enhancing patients' ability to actively participate in the decision-making process. Education could serve as the key to addressing these unmet needs. Engaging patients in the decision-making process has the potential to boost their motivation, which is essential for effective patient education.

#### **STRENGTHS & LIMITATIONS OF THE SLR**

Overall, this SLR highlights the effectiveness of educational programs in enhancing various outcomes of the disease, particularly when delivered by HPs using physical materials such as pamphlets. However, due to the lack of studies and the heterogeneity of the existing ones, it is difficult to establish direct comparisons and robust conclusions.

There is an ongoing need for additional research to establish strong recommendations and assess the long-term effects of these educational initiatives. Questions persist regarding the most effective programs in terms of content, suitable providers, delivery formats, optimal duration, the necessity for repetition, and specific moments to enhance efficacy.



Tables and Figures

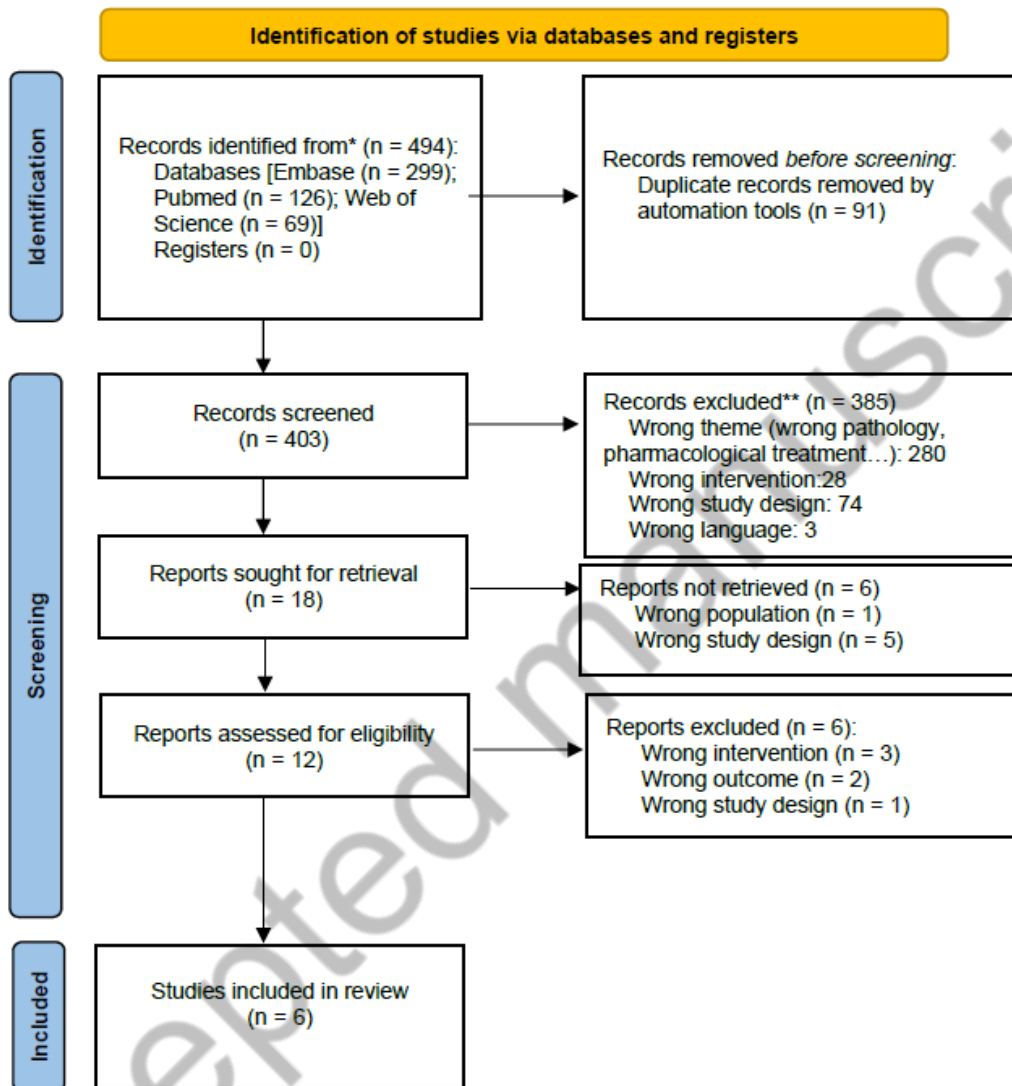


Figure 1. Flow chart of the study selection and inclusion process

**Table I.** Characterization of the protocols used in each study included in the systematic literature review

Study ID	Intervention	n	Protocol	Leader	Frequency	Duration of intervention	Follow up	Supplementary information
Aksoy [2017]	Educational sessions	20	Group sessions Supervised exercises	Multidisciplinary team	Group exercises 40 minutes/day and home exercises 4 times a week	1 week	3 months	Pamphlet
	Control Group	21	Routine follow-ups with general information about the disease Home exercises		Home exercises 4 times a week			
Kaya [2013]	Educational sessions	27	Group sessions Educational pamphlet	Trained patient	1hour/week	1 month	6 months	Pamphlet
	Control group	29	Routine follow-ups Educational pamphlet					Pamphlet
Masiero [2014]	Educational sessions	21	Two group sessions	Multidisciplinary team	Two-week interval sessions lasting 3 hours each	2 weeks	12 months	Pamphlet
	Control group	22	Routine follow-ups					Pamphlet
O'Dwyer [2017]	Educational sessions	20	Individual sessions	Health physician	30minutes/session with variable frequency	3 months	6 months	Pamphlet
	Control group	20	Routine follow-ups					
Demontis [2015]	Educational sessions	22	Two group sessions	Multidisciplinary team	Two-week interval	8 weeks	7 months	Pamphlet
	Educational sessions+physical exercise	20	Two group sessions Supervised exercises	Multidisciplinary team	Twelve twice-weekly sessions lasting 60 minutes each	8 weeks	7 months	Pamphlet
Masiero [2011]	Educational sessions	20	Two group sessions	Multidisciplinary team	Two-week interval sessions lasting 3 hours each	2 weeks	6 months	Pamphlet CD
	Control group	22	Routine follow-ups					Pamphlet

**Table II.** Study characteristics

Study ID	Intervention	n	Classification criteria	Males (%)	Age (years)	Disease duration (years)	Primary endpoint	Secondary endpoint
Aksoy [2017]	Educational sessions	20	mNY	75	37.95 ± 9.84	9.42 ± 7.10	BASDAI, BASFI, BASMI, BAS-G, ASQoL, SF-36, chest expansion, laboratory parameters	
	Standard of care	21	mNY	81	37.47± 11.09	8.64 ± 6.71		
Kaya [2013]	Educational sessions	27	NI	77.8	43.1 ± 9.1	9 (1-31)	ASQoL	Depressive symptoms
	Control group	29	NI	86.2	40.9 ± 9.3	5 (1-25)		
Masiero [2014]	Educational sessions	21	mNY	85.0	43.85 ± 8.1	7.41±4.7	Cervical and lumbar pain intensity, chest expansion, BASMI, BASDAI, BASFI, fatigue, spinal active range of motion	
	Control group	22	mNY	80.9	46.15 ± 10.3	9.15±4.23		
O'Dwyer [2017]	Educational sessions	20	NI	65	39 ± 8	8 (5-13)	Physical activity	Physical fitness, BASMI, BAS-G, BASDAI, BASFI, ASQoL, ASES-AS, EBBS
	Control group	20	NI	65	45 ± 10	10 (5-22)		
Demontis [2015]	Educational sessions	22	mNY	77.3	45.0±8.45	8.12±4.5	Sway density improvement	BASDAI, BASFI, BASMI
	Educational sessions+physical exercise	20	mNY	75	49.3±11.3	9.1±7.51		
Masiero [2011]	Educational sessions	20	mNY	80	44.0 (38.2-52.5)	6.5 (4.0-10.0)	Cervical and lumbar pain intensity, chest expansion, BASMI, BASDAI, BASFI, fatigue, spinal active range of motion	
	Control group	22	mNY	81.8	47.5 (40.7-52.5)	9.0 (3.2-13.7)		

mNY - Modified New York criteria, NI – not indicated

No given information about HLA-B27 positivity

**Table III.** GRADE Summary of Findings

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)
BASDAI	Effective**	208 (5 RCTs)	⊕○○○ Very low
BASFI	Effective **	208 (5 RCTs)	⊕○○○ Very low
BASMI	Effective **	208 (5 RCTs)	⊕○○○ Very low
ASQoL	Effective **	137 (3 RCTs)	⊕○○○ Very low
SF-36, Physical function	Effective §	97 (2 RCTs)	⊕○○○ Very low
SF-36, Role physical	Effective §	97 (2 RCTs)	⊕○○○ Very low
SF-36, Bodily pain	Effective §	97 (2 RCTs)	⊕○○○ Very low
SF-36, Social functioning	Not effective	97 (2 RCTs)	⊕○○○ Very low
SF-36, Mental health	Effective §	97 (2 RCTs)	⊕○○○ Very low
SF-36, Role mental	Not effective §	97 (2 RCTs)	⊕○○○ Very low
SF-36, Vitality	Effective §	97 (2 RCTs)	⊕○○○ Very low
SF-36, General Health	Effective §	97 (2 RCTs)	⊕○○○ Very low

Outcomes	Impact	No of participants (studies)	Certainty of the evidence (GRADE)
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**GRADE Working Group grades of evidence**

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

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\*\*Statistically significant in 2 studies (one did not compare intervention vs control)

§ Statistically significant in only one study

ASQoL - Ankylosing Spondylitis Quality of Life; BASDAI - Bath Ankylosing Spondylitis Disease Activity Index; BASFI - Bath Ankylosing Spondylitis Functional Index Ankylosing Spondylitis; BASMI - Bath Ankylosing Spondylitis Metrological Index; SF - Short Form Health Survey 36

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**Supplementary Material**

**Supplementary Table I.** Cochrane risk of bias assessment

Study ID	Domains					
	Randomization process	Deviations from intended interventions	Mising outcome data	Measurement of the outcome	Selection of the reported result	Overall Bias
Masiero [2011]	L	S	L	L	S	S
Aksoy [2017]	L	S	L	L	S	S
Kaya [2013]	L	S	L	L	S	S
Masiero [2014]	H	S	L	L	S	H
O'Dwyer [2017]	L	S	L	L	S	S
Demontis [2015]	H	S	L	L	S	H

H – High, L – Low, S – Some concerns

**Supplementary Table II. BASDAI, BASFI, BASMI**

Study ID	Intervention	n	Time point (Weeks)	BASDAI			BASFI			BASMI		
				Baseline	Time point	<i>p</i>	Baseline	Time point	<i>p</i>	Baseline	Time point	<i>p</i>
Aksoy [2017]	Educational sessions	20	12	3.52±1.55	2.74±1.43	≤0.05	2.88±1.98	1.76±1.47	≤0.001	0.62±0.43	0.59±0.41	N.S.
	Standard of care	21		2.93±2.12	2.74±1.69	N.S.	2.17±2.37	2.12±2.26	N.S.	0.54±0.35	0.54±0.37	N.S.
Masiero [2014]	Educational sessions	21	48	2.9±1.2	2.8±2.1	>0.05*	2.7±1.6	2.4±2.4	>0.05*	3.8±1.1	3.6±2.1	>0.05*
	Standard of care	22		3.1±1.7	3.2±2.2		2.9±1.7	3.0±2.0		4.0±1.3	4.1±1.6	
O'Dwyer [2017]	Educational sessions	20	24	3.2 (2.5-4.9)	2.2 (1.6-5.0)	>0.05*	1.4 (0.5-3.3)	0.6 (0.3-2.5)	>0.05*	2.3±1.1	1.7±1.0	≤0.05*
	Control group	20		2.8 (2.2-3.9)	2.5 (1.8-4.2)		2.3 (0.7-4.0)	2.4 (0.7-4.0)		2.9±1.3	2.8±1.4	
Demontis [2015]	Educational sessions	22	28	2.6 (2.2-3.9)	2.4 (1.7-4.0)	≤0.05*	2.8 (1.8-3.5)	1.7 (1.0-4.1)	>0.05*	3.6 (2.6-5.2)	4.0 (2.8-4.9)	≤0.01*
	Educational sessions+physical exercise	20		3.0 (2.2-2.4)	2.4 (0.5-3.0)		2.4 (1.8-3.9)	1.1 (0.7-2.0)		4.3 (3.4-5.8)	3.1 (2.4-3.8)	
Masiero [2011]	Educational sessions	20	24	4.4 (2.4-7.4)	2.8 (1.3-4.1)	>0.05*	4.6 (2.5-7.0)	1.3 (0.5-2.5)	≤0.01*	4.6 (5.0-7.0)	3.6 (1.9-4.6)	>0.05*
	Control group	22		4.6 (2.3-6.4)	3.0 (1.8-5.1)		4.5 (3.0-4.8)	2.7 (1.4-4.0)		4.9 (3.2-6.2)	4.3 (2.7-5.8)	

\*Comparison between educational and control group

**Supplementary Table III. ASQoL**

Study ID	Intervention	n	Time point (Weeks)	ASQoL		
				Baseline	Time point	<i>p</i>
Aksoy [2017]	Educational sessions	20	12	8.3±14.4	5.3±3.3	≤0.001
	Standard of care	21		5.3±5.5	5.1±5.5	N.S.
Kaya [2013]	Educational sessions	27	24	7 (0-17)	11 (0-18)	>0.05
	Control group	29		5 (0-17)	5 (0-16)	>0.05
O'Dwyer [2017]	Educational sessions	20	24	5.0 (2.5-6.0)	2.5 (0.0-5.8)	≤0.05*
	Control group	20		4.5 (2.3-7.0)	4.0 (1.0-6.0)	

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**Supplementary Table IV. SF-36**

Study ID	Intervention	n	Time point (Weeks)	SF-36	Baseline	Time point	p
Aksoy [2017]	Educational sessions	20	12	PF	66.6±19.9	80.2±16.5	≤0.001
				RP	52.5±39.7	71.3±35.6	≤0.05
				BP	51.5±21.5	68.5±20.4	≤0.001
				SF	65.6±24.6	86.3±18.9	≤0.001
				MH	57.7±21.1	65.6±18.7	≤0.05
				RM	61.6±44.9	73.3±41.3	N.S.
				V	50.5±20.5	56.3±17.7	≤0.05
				GH	51.7±20.3	58.8±19.4	≤0.05
	Standard of care	21		PF	72.4±25.7	73.3±23.4	N.S.
				RP	61.9±44.5	66.7±44.9	N.S.
				BP	54.2±26.4	57.1±26.8	N.S.
				SF	77.9±20.5	77.9±22.7	N.S.
				MH	52.3±21.2	55.4±22.4	N.S.
				RM	65.0±42.8	69.8±40.6	N.S.
				V	44.2±21.7	47.1±20.4	N.S.
				GH	50.7±21.8	51.4±24.6	N.S.
Kaya [2013]	Educational sessions	27	24	PF	65 (0-100)	55 (0-100)	N.S.
				RP	75 (0-100)	50 (0-100)	N.S.
				BP	55 (0-100)	57.5 (0-90)	N.S.
				SF	63 (25-100)	50 (12.5-100)	≤0.05
				MH	60 (12-92)	56 (36-100)	N.S.
				RM	66.7 (0-100)	33 (0-100)	N.S.
				V	60 (20-95)	55 (20-100)	N.S.
				GH	45 (10-80)	35 (10-92)	N.S.
	Control group	29		PH	80 (10-100)	80 (35-100)	N.S.
				RP	50 (0-100)	75 (0-100)	N.S.
				BP	57.5 (32.5-100)	67.5 (22.5-90)	N.S.
				SF	62 (10-100)	62.5 (12.5-100)	≤0.05
				MH	68 (25-96)	60 (24.96)	N.S.
				RM	67 (0-100)	100 (0-100)	N.S.
				V	65 (15-95)	60 (20-85)	N.S.
				GH	47 (15-92)	46 (20-90)	N.S.

PF-Physical function, RP-Role physical, BP-Bodily pain, SF-Social functioning, MH-Mental health, RM-Role mental, V-Vitality, GH-General Health