PHYSICAL ACTIVITY, EXERCISE AND CANCER

REVIEW ARTICLE

Impact of the therapeutic exercise in people with multiple myeloma on biomarkers of physical, psychological, and biological health status: A systematic review

Diego Fernández-Lázaro . *Histology Area and Neurobiology Research Group. Faculty of Health Sciences. University of Valladolid. Valladolid, Spain.*
Marina Seco-Casares. *Nursing Department. León University Assistance Complex (CAULE). Hospital of León. León, Spain.*
Álvaro López-Llorente. *Faculty of Health Sciences. Campus of Soria. University of Valladolid. Soria, Spain.*
Nuria Hernández-Burgos. *Nursing Department. University Hospital of Elda. Elda, Spain.*
Gema Santamaría Gómez. *Department of Anatomy and Radiology. Faculty of Health Sciences. Campus of Soria. University of Valladolid. Soria, Spain.*

ABSTRACT

Multiple myeloma (MM) is an incurable B-cell cancer characterized by periods of relapse and treatment-related toxicity, which often deteriorates patients' health-related quality of life (HRQL). Exercise, as a non-pharmacological adjuvant therapy, may help mitigate these effects. This systematic review aimed to offer updated, evidence-based guidance on the effect of exercise in people with MM. Controlled trials or pre-post intervention studies published up to 30 May 2025 were identified through SciELO, Cochrane and PubMed. The review, registered in PRSPERO (CRD42023458213), followed PRISMA guidelines. Of 137 articles screened, eight met inclusion criteria. Overall, the studies reported beneficial effects of exercise on physical and mental health, HRQL, sleep disorders, and anthropometric measurements, though trends tended not to reach statistical significance. No severe adverse effects were reported. Exercise appears feasible and safe for people with MM, offering potential improvements in fatigue, HOQL, and mental well-being, likely linked to enhanced physical capacity. Despite promising findings, further research is needed to confirm the role of exercise in MM management. The implementation of therapeutic exercise programs, combining aerobic and strength training, may improve the maintenance of physical capacity and subsequent health outcomes MM's people.

Keywords: Physical activity, Multiple Myeloma, Exercise, Health-related quality of life, Health benefits, Physical capacity.

Cite this article as:
Fernández-Lázaro, D., Seco-Casares, M., López Llorente, A., Hernández-Burgos, N., & Santamaría Gómez, G. (2025). Impact of the therapeutic exercise in people with multiple myeloma on biomarkers of physical, psychological, and biological health status: A systematic review. *Physical Activity, Exercise and Cancer*, *2*(2), 63-84. https://doi.org/10.55860/YYTN8138

Corresponding author. *Faculty of Health Sciences, University of Valladolid, Campus of Soria, 42003 Soria, Spain.*
E-mail: diego.fernandez.lazaro@uva.es
Submitted for publication August 18, 2025.
Accepted for publication September 30, 2025.
Published October 02, 2025.
Physical Activity, Exercise and Cancer.

Identifier: https://doi.org/10.55860/YYTN8138

INTRODUCTION

Multiple myeloma (MM) is a currently incurable clonal B-cell malignancy, characterized by an accumulation of malignant plasma cells in the bone marrow (BM). It accounts for 1% of all cancers and approximately 10% of malignant blood cancers (Fernández-Lázaro, 2011). Worldwide, more than 138,000 new cases of MM are diagnosed each year (Cancer Stat Facts: Myeloma (https://seer.cancer.gov/statfacts/html/mulmy.html)). In Spain, the incidence of this disease is between four and five cases per 100,000 per year, which translates to 2,000 to 3,000 new diagnoses of MM (150 to 200 in our region) (Castilian-Leonese Society of Haematology and Hemotherapy, 2023). Globally, these figures make this condition the second leading blood cancer, after lymphoma. It is mainly diagnosed in over-65-year-olds, although it can also develop at younger ages, with 15% of cases occurring in under-50-year-olds (Spanish Society of Haematology and Hemotherapy, 2021). In recent decades, significant advances in our understanding of the biology of the disease have enabled the development of new classes of drugs, the recognition of new prognostic factors, and the personalization of therapies including optimization of the treatment sequence (Fernández-Lázaro et al., 2018). All of this has helped to increase the mean overall survival from 3-5 years to 7-10 years (Rajkumar, 2022). This substantial increase in survival means that people with MM face a double challenge, on the one hand, regaining their psychosocial and physical well-being, and on the other, dealing with the symptoms of the disease and the adverse effects of treatment (Cormican & Dowling, 2018). Treatment systems used, especially high-dose steroids, may lead to osteolysis, in nearly 90% of cases (Fernández-Lázaro, 2019), as well as long-term toxicity, and autologous stem cell transplantation causes muscle atrophy and fatigue (Jordan et al., 2014). This bone damage, muscle wasting and fatigue tend to persist beyond the end of treatment and during stable phases of the disease (Ramsenthaler et al., 2016). Therefore, although people with MM are now living longer, the burden of the disease and cumulative toxicity of the therapy have a notable impact on their quality of life and well-being (Cormican & Dowling, 2018). The aforementioned physical deterioration means that exercise tends to be seen as an aggressive activity that increases the risk of injury, and hence, it is rarely promoted in people with MM (Nicol et al., 2022).

Therapeutic exercise programmes may help reduce fatigue and muscle wasting related to MM (Jeevanantham et al., 2021), as in other chronic conditions (Fernández-Lázaro et al., 2022a). In cancer, therapeutic exercise as an adjuvant non-pharmacological treatment has been reported to improve physical and mental state and alleviate both symptoms associated with the disease and those caused by drug therapies (Fernández-Lázaro et al., 2020a). For these reasons, safe, structured interventions for people with MM before, during and after blood cancer treatment may enhance patient health-related quality of life (HRQL) through biological and physical improvements (Gan et al., 2016). Nonetheless, there is a paucity of specific information to guide the planning and monitoring of physical training in people with MM, ensuring that it is as safe as possible and also achieves the desired results.

Two recent systematic reviews (Goodhew & Edwards, 2023; Nicol et al., 2022) did not clarify whether therapeutic exercise affects symptoms related to the disease and treatment. These studies showed a limited clinical trials (n = 7 and n = 5) that make up these systematic reviews with varied and contradictory results. Nicol et al. (2022) reported adverse events and prescription compliance and argued for the need to report the effects of therapeutic exercise on persons' physical function, and quality of life in this population of people with MM. Goodhew & Edwards (2023), stated that the included studies had a high risk of bias and low certainty of evidence so the conclusion of their review should be interpreted with caution. They proposed that future high-quality studies are required to determine the role of exercise in MM care.

In this context, the main objective of this study was to carry out a systematic review of the current evidence on the effect of therapeutic exercise programmes in patients with MM in terms of physical condition, anthropometric parameters, mental health, HRQL, sleep disorders, and blood biomarkers, as well as any adverse effects. Additionally, we sought to identify the optimal types of exercise.

In line with evidence-based medicine guidelines, we developed a research question using the Population, Intervention, Comparison, and Outcome (PICO) framework (Straus et al., 2018) as follows: P, adults with a diagnosis of multiple myeloma; I, exercise programme; C, patients with a similar health status with/without physical activity; and O, physical condition (strength, aerobic capacity, fatigue, fitness, sports performance, and exercise self-efficacy); anthropometric parameters (fat-free body mass, and body fat); mental health (mood, anxiety, depression, and mental wellbeing); HRQL; sleep disorders (nighttime sleep, daytime sleep, daytime sleepiness), blood biomarkers (haemoglobin [Hb]); and any adverse effects. The aforementioned variables were selected as outcomes given their routine use in studies assessing the efficacy of therapeutic exercise interventions. Hence, our research question was: in adults with MM, is participation in an exercise programme compared to no physical activity intervention associated with improvements in physical and mental health, HRQL, sleep, haemoglobin levels, and/or adverse effects as assessed through the aforementioned outcome measures?

MATERIAL AND METHODS

Search strategy

The study is reported following the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Page et al., 2021). A structured literature search was carried out by two researchers independently in the following electronic databases: Medline (via PubMed), SciELO and Cochrane Collection Plus. For this, Boolean operators "*OR*" and "*AND*" were used to join various combinations of Medical Subject Heading (MeSH) terms related to exercise and MM: physical activity, multiple myeloma, exercise, physical condition, anthropometric parameters, mental health, health-related quality of life, sleep disorders, blood biomarkers, and adverse effects (Appendix A). The search included randomised and non-randomised studies, specifically, before-and-after (pre-post), pilot, longitudinal and retrospective studies, as well as clinical trials (RCTs), published in English or Spanish in the last 25 years (January 2000 to May 2025).

In addition, a manual search was performed, by checking the reference lists of publications retrieved in the database search that were deemed eligible for full-text review and using ResearchGate (www.researchgate.net) to identify other papers of interest not in the aforementioned three databases. Lastly, we generated a map of the literature using Connected Papers (www.connectedpapers.com, accessed on 23 May 2025) to ensure the inclusion of recent publications and visually identify relevant publications.

Data extraction and synthesis

Through the search, we retrieved potentially relevant publications in the field of exercise in blood cancer people diagnosed with MM. All the titles and abstracts of the publications retrieved were read and compared to identify and exclude duplicates and any studies that did not meet all the selection criteria. The remaining papers underwent full-text review.

Two researchers independently performed the search and entered data collected into an Excel spreadsheet (Microsoft Inc., Seattle, WA, USA). Disagreements were resolved by consensus with a third author, in line with the Consolidated Standards of Reporting Trials (CONSORT) guidelines (Butcher et al., 2022). For each study, we extracted the following data: authors, year of publication, country where the research had been carried out, study design, characteristics of people with MM (sample size, sex and age), disease stage using the Revised International Staging System (RISS) and treatment, design of the exercise intervention, primary and secondary outcome variables, and results.

Selection criteria

To select the most relevant studies among those found in the literature search, we applied the following inclusion criteria: i) conducted in adults diagnosed with MM; ii) assessed the effects of exercise in people with MM; iii) designed as a randomised or non-randomised study (including longitudinal or retrospective and pre-post or pilot studies as well as clinical trials, but excluding editorials, narrative or systematic reviews, notes, or any other articles not reporting original research); iv) evaluated measures related to physical condition, mental health, quality of life, anthropometric characteristics, sleep disorders, blood disorders (oncohematological parameters), and/or adverse effects as outcome variables (primary or secondary); v) provided clear information on the intervention and duration of the exercise; vi) published in the last 25 years; vii) had good methodological quality based on a modified version of the critical review form of the McMaster University Occupational Therapy Evidence-Based Practice Research Group (Law et al., 1998) for quantitative studies; and viii) had a low risk of bias based on the Cochrane collaboration tool (Higgins et al., 2011). Records that did not meet all these criteria were excluded from the review. We did not apply any restrictions on baseline level of physical condition or capacity for exercise. Two review authors independently screened the remaining sample of potential studies. Where a review author was unable to reach a decision, consensus was reached through discussion with a third review author.

Study quality

The critical review form of the McMaster University Occupational Therapy Evidence-Based Practice Research Group (Law et al., 1998) is a comprehensive reliable tool for assessing the methodological quality of quantitative evidence from randomized and non-randomized studies. For critical appraisal of the studies in this review, we used a modified 16-item version of this form and assigned one point for each criterion met, as described in Gómez Afonso et al. (2023). The points were summed to yield a total quality score, and this was categorized as "*poor*" (≤ 8 points), "*fair*" (9–10 points), "*good*" (11–12 points), "*very good*" (13–14 points), or "*excellent*" (≥ 15 points) and a score ≥10 was set as the threshold for inclusion in the review (Gómez Afonso et al., 2023).

Risk of bias assessment

The risk of bias in the studies selected was assessed using the Cochrane tool (Higgins et al., 2011). The number of domains classified as low risk was summed to generate a risk-of-bias score and a score superior to four was set as the threshold for inclusion in the review.

Study registration

This systematic review met the eligibility criteria for registration in PROSPERO. It was registered to facilitate public access and avoid unnecessary duplication (#CRD42023458213).

RESULTS

Selection of studies

The literature search identified a total of 143 studies, of which 137 were found through Medline (PubMed), SciELO, or Cochrane Collection Plus and six through other sources such as ResearchGate or reference lists of relevant studies. Having first excluded 52 duplicates, we examined a total of 85 articles identified in the databases. Based on title and abstract screening, 16 articles were considered potentially eligible. After a full review of these articles and assessing the potentially relevant records from other sources, we included eight studies (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015) in the systematic review that met the selection criteria, five RCTs (Coleman et al., 2003; Coleman et al., 2008; Koutoukidis et al., 2020; Larsen et al., 2019; McCourt et al., 2023), and three pre-post studies (Groeneveldt et al., 2013; Mawson et al., 2021; Shallwani et al., 2015) in which a single group was exposed to an exercise intervention, one being a feasibility study (Mawson et al., 2021), one a pilot study (Groeneveldt et al., 2013) and one a retrospective study (Shallwani et al., 2015). The date of publication ranged from 2003 (Coleman et al., 2003) to 2023 (McCourt et al., 2023), and the research was carried out in the United States (Coleman et al., 2003; Coleman et al., 2008), the UK (Groeneveldt et al., 2013; Koutoukidis et al., 2020; Mawson et al., 2021; McCourt et al., 2023), Denmark (Larsen et al., 2019), or Canada (Shallwani et al., 2015). Figure 1 is a flow diagram illustrating the search and study selection process.

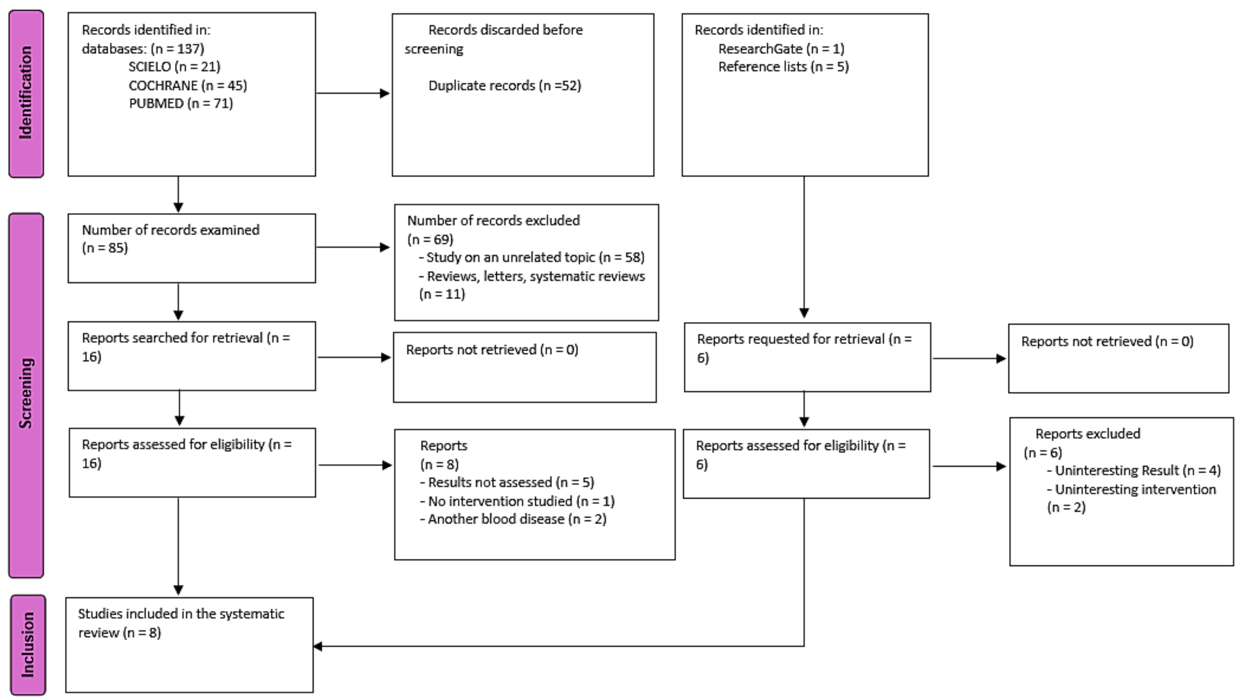

Figure 1. Flow chart of study selection for the literature review (PRISMA) (Page et al., 2021)

As shown in Figure 2, the studies on the effect of therapeutic exercise in patients with MM were mapped, following the approach used by Groeneveldt et al. (2013). Nonetheless, all eight studies finally included in the systematic review (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015) were found in databases.

Study quality assessment

The studies selected (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015) obtained methodological quality scores between 12 and 16, meaning that they met between 75% and 100% of the criteria set (Table 1). Hence, none had to be excluded for not reaching the minimum quality threshold. Their methodological quality was classified as "*excellent*" in four studies (Coleman et al., 2003; Koutoukidis et al., 2020; Larsen et al., 2019; McCourt et al., 2023), "*very good*" in one (Coleman et al., 2008) and "*good*" in three (Groeneveldt et al., 2013; Mawson et al., 2021; Shallwani et al., 2015). The main weaknesses detected were related to whether authors identified limitations of the study methodology and results (Law et al., 1998).

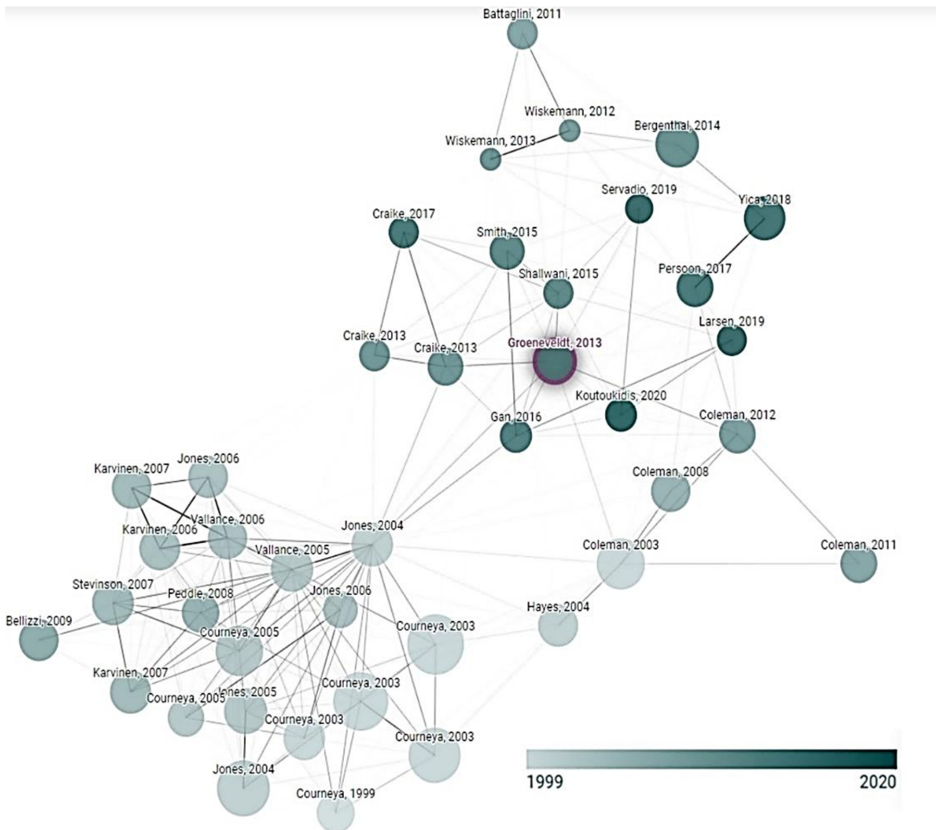

Figure 2. Map of the literature on the impact of physical exercise on patients with multiple myeloma. This graph was constructed with www.connectedpapers.com, created 23 May 2025.

Table 1. Results of the evaluation of the methodological quality of the studies included — modified version of the McMaster Critical Review Form for Quantitative Studies (Law et al., 1998).

Study	**Item**																**Total Quality score**	**%**	**Quality rating**
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**			
Coleman et al. (2003)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	15	93.8	E
Coleman et al. (2008)	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	1	14	87.5	VG
Groeneveldt et al. (2013)	1	1	0	1	1	0	1	1	1	0	1	1	1	1	1	0	12	75	G
Koutoukidis et al. (2020)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	16	100	E
Larsen et al. (2019)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	15	93.8	E
Mawson et al. (2021)	1	1	0	1	1	0	1	1	1	0	1	1	1	1	1	0	12	75	G
McCourt et al (2023)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	16	100	E
Shallwani et al. (2015)	1	1	0	1	1	0	1	1	1	0	1	1	1	1	1	0	12	75	G

Abbreviations: (1) criterion met; (0) criterion not met; Total: Total number of criteria met; %: percentage of criteria met; G: Good, 11-12 points; VG: Very good, 13-14 points; E: Excellent, ≥15 points. The modified form consists of criteria concerning the following: item 1 -Study purpose; item 2 - Literature review; item 3 - Study design; item - 4 Blinding; item 5 - Sample description; item 6 - Sample size; item 7 - Ethics and consent; item 8 - Validity of outcomes; item 9 - Reliability of outcomes; item 10 - Intervention description; item 11 - Statistical significance; item 12 - Statistical analysis; item 13 - Clinical importance; item 14 - Conclusions; item 15 - Clinical implications; and item 16 - Study limitations.

Risk of bias assessment

Analysing the risk-of-bias scores based on the Cochrane tool (Higgins et al., 2011), only one study scored six (Koutoukidis et al., 2020), five scored five (Coleman et al., 2008; Groeneveldt et al., 2013; Larsen et al., 2019; Mawson et al., 2021; Shallwani et al., 2015), and two scored four (Coleman et al., 2003; McCourt et al., 2023). The main sources of bias were found in relation to group allocation and blinding (items 2, 3 and 4) as shown in Table 2 and Figure 3.

Table 2. Bias scores of the studies included based on the Cochrane tool (Higgins et al., 2011).

Study	Item								Total
	1	2	3	4	5	6	7	8	
Coleman et al. (2003)	+	-	-	-	+	+	+	-	4
Coleman et al. (2008)	+	-	-	-	+	+	+	+	5
Groeneveldt et al. (2013)	+	-	-	-	+	+	+	+	5
Koutoukidis et al. (2020)	+	-	-	+	+	+	+	+	6
Larsen et al. (2019)	+	-	-	+	+	+	+	-	5
Mawson et al. (2021)	+	-	-	-	+	+	+	+	5
McCourt et al. (2023)	+	-	-	-	+	+	+	-	4
Shallwani et al. (2015)	+	-	-	-	+	+	+	+	5

Abbreviations = 1: random sequence generation; 2: allocation concealment; 3: blinding of participants and personnel; 4: blinding of outcome assessment; 5: incomplete outcome data; 6: selective reporting; 7: publication bias; 8: observer bias; the score for each item includes the answer to a question, where "+" indicates low risk of bias, "-" high risk of bias and "?" a lack of information or uncertainty about the potential risk; the higher the score, the greater the risk of bias.

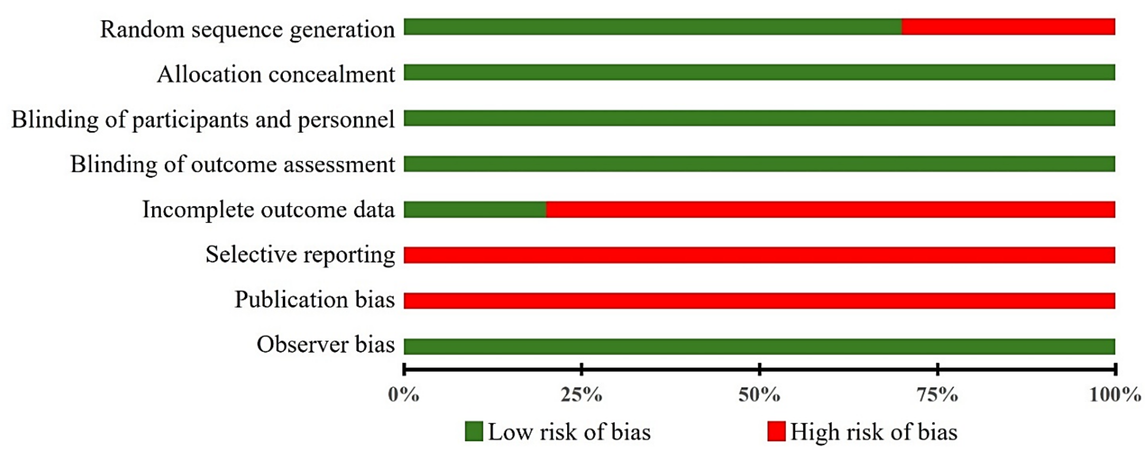

Figure 3. Risk of bias assessment based on the Cochrane Tool (Higgins et al., 2011).

Characteristics of the participants

The general characteristics of the eight studies analysed (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015) are summarised in Table 3. Overall, they initially included a total of 471 people with MM of whom 369 participants completed the studies, given that 102 were withdrawn due to disease progression or lost to follow-up, and the sample exposed to an exercise intervention was composed of 214 persons with MM. There was a higher percentage of men than women in all the studies (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015).

Table 3. Characteristics of the studies included in this systematic review on the effect of the therapeutic exercise on physical, mental and biological markers of adult MM patients.

First author, year of publication and country	Study design	Participants	Multiple myeloma/ Treatment	Physical exercise intervention, outcomes and results
Coleman et al. (2003), United States	Randomized clinical trial. Exclusion: people with physical or mental conditions reducing tolerance to exercise programme or a high risk of bone fracture	n = 24 (14♂; 10♀) Age (range; mean): 42-74; 55 years CG: n= 10 (60% ♂; 40%♀) EG: n = 14 (71%♂; 31%♀) Indirect supervision: weekly interview Exercise adherence: 58% 11 withdrawn/lost to follow-up 13 participants completed the study 5 in the CG 8 in the EG	Aggressive stage of MM Various chemotherapy cycles: - VAD - DCEP - CAD - DCEP (after ASCT)	24 weeks, 3 sessions/week. 72 sessions. 60 min/session 10 min of walking (warm-up) and stretching. A score of 9-10 on Borg Rating of Perceived Exertion AE: 18 min of moderate aerobic exercise (brisk walking). A score of 12-15 on Borg Rating of Perceived Exertion Strength: resistance bands with different levels of resistance. 1 series per exercise with one type of band + 1 series per exercises with higher resistance band. Intensity of 40-60% - Upper limbs: biceps and triceps workout, upright row - Lower limbs: chair stand, knee flexion and extension Cool down, 5 min walk. 9-10 Borg Rating of Perceived Exertion After the first chemotherapy cycle (VAD + DCEP)
Coleman et al. (2008), United States	Randomized clinical trial. Exclusion: High risk of bone fracture or spinal cord compression, severe psychiatric illnesses, anaemia, uncontrolled hypertension, blood transfusion in the previous 2 weeks or treatment with EPO in the previous 8 weeks	n= 135 EG = 69 CG = 66 15 withdrawn/lost to follow-up 120 participants completed the study (70♂; 50♀) <u>ST n= 51</u> Age (range; mean): 32-74; 55 years CG ST: n= 28 (39% ♂;61% ♀) EG ST: n=23 (52% ♂;48% ♀) Age (range; mean): 32-74; 55 years <u>LT n= 69</u> Age (range; mean): 25-76; 55 years CG LT: n=34 (71% ♂;29% ♀) EG LT: n =35 (66% ♂;34% ♀) Exercise adherence: 84.89% Indirect supervision: weekly interviews	Aggressive stage of MM Various chemotherapy cycles: ST: chemotherapy = VAD+DCEP +CAD Without EPO LT: Chemotherapy = VAD+DCEP+CAD+DCEP+ASCT With EPO	ST: no administration of EPO – 15 weeks LT: administration of EPO – 30 weeks Initial warm-up with stretching of upper and lower limbs AE: walk until tolerance-fatigue (minimum 20 min/day) Strength: every other day Biceps workout with resistance bands Triceps workout (chair push-ups) Quadriceps strengthening with chair stand Hamstring strengthening (sitting or standing)
Groeneveldt et al. (2013), United Kingdom	Pre-post study - single arm Exclusion: Spinal instability, high fracture risk, treatment with EPO, unstable angina, disabling musculoskeletal disease	n= 37 Age (range; mean): 46-74; 61 years EG = 37 9 withdrawn/lost to follow-up 28 people completed the study EG n=28 (58% ♂;42% ♀) Exercise adherence: 73 % Gradual supervision	Stable MM without treatment or under maintenance treatment - Lenalidomide - Interferon - Thalidomide	24 weeks, 3 sessions/week. 72 sessions AE: 15 min. Walk or cycle ergometer at 50% of HR reserve. ↑5min/ week ↑5% HR/week up to 30 min and 60% of HR Strength: 60 min. In large muscle groups. Progressive increase of repetitions at the discretion of the physiotherapist; increase of weight or resistance according to Borg scale. - Resistance bands, weightlifting equipment and body weight training. 1st. 3 series, 10 repetitions 2nd. 3 series, 15 repetitions
Koutoukidis, et al. (2020), United Kingdom	Randomized clinical trial. Exclusion: spinal instability or recent spinal surgery, abnormal resting ECG, risk of pathological fractures (Mirel's classification); current participation in another research study with exercise, unstable angina, disabling musculoskeletal disorder, cognitive deterioration.	n= 131 Age (range; mean): 35-86; 64 years CG: n= 42 (57% ♂; 43%♀) EG: n = 89 (54%♂; 46%♀) Exercise adherence: 64.5% 48 withdrawn/lost to follow-up 83 participants completed the study 42 in CG (57% ♂; 43%♀) 41 in EG (51% ♂; 49%♀) Complete supervision	Survivors of MM with maintenance treatment or initial stage of treatment completed, with a ECOG performance status 0-2, able to participate in regular exercise programme	24 weeks, 3 sessions/week. 72 sessions - 3 first months: 1 session/week in gym + 2 sessions/week at home. - Following 3 months: 3 sessions/week + 1 session/month in the gym AE: 10-30 min. Walk in treadmill, cycle ergometer, stationary bike or stepper, at 50-75% of maximum HR. ↑5min/4 weeks ↑5% HR/4 week up to 30 min. Strength: in large muscle groups (core, upper and lower body training) Progressive increase in repetitions. Weightlifting, body mass exercises, resistance bands. Tailored for individual participants with 10-repetition maximum assessment.
Larsen et al. (2019), Denmark	Randomized clinical trial. Exclusion: spinal cord compression, unstable vertebral fracture, untreated heart disease, comorbidities preventing physical activity, psychological or psychiatric problems, difficulties understanding the Danish language.	n= 30 Age (range; mean): 38-90; 68 years CG: n= 13 (69% ♂; 31%♀) EG: n = 17 (82%♂; 18%♀) 6 withdrawn/lost to follow-up 24 participants completed the study CG: n= 12 EG: n = 12 Exercise adherence: 94% Complete supervision + diary of home exercises carried out	People over 18 years old, with a recent diagnosis of MM or who are going to be given HCT or less invasive treatment	10 weeks, 2 sessions/week supervised – 3 sessions/week at home. 8 sessions. Supervised session 1h + 15min Programmed exercise (3 sessions/week) 1. Warm-up: 5 min (10-11 repetitions) 2. Supervised AE: 20 min in stationary bike or progression up to 20 min (12-13 repetitions increasing to 14-16 repetitions) 3. AE at home: 10- 30 min 4. Strength: in large muscle groups, 3 series of 12-15 repetitions. 5 lower-limb exercises, 3 upper-limb exercises, 1 core exercise. 30-45 min 5. Static stretching: 5 min Non-programmed exercise (4 days/week) Keeping active the remaining 4 days at least 30 min (14-16 repetitions)

Mawson et al. (2021), United Kingdom	Prospective feasibility study - two groups (assessed using different sets of PROMs) Exclusion: people with a history of unstable angina or heart attack in the previous month	n= 23 Age (range; mean): 53-78; 65 years EG: n = 23 (70%♂; 30%♀) - PROM1 - PROM2 9 withdrawn/lost to follow-up 14 participants completed the study Exercise adherence: 94% Complete supervision	People with a diagnosis of MM in waiting list for autologous stem cell transplantation (first or second transplantation)	6 weeks 136 sessions. Up to 6 sessions/week of 1 h Warm up Circuit training: 1. AE: treadmill, stationary bike, rowing machine, 2. Strength: upper and lower-limb training with own body mass, weights or resistance band training equipment. 3. Balance exercises and core stability Cool down.
McCourt et al. (2023), United Kingdom	Randomized trial. Exclusion: clinical decision or patient declined ASCT, or admission for treatment in less than 1 month, patient not understanding English, travel difficulties, significant neurological deficits.	n= 50 Age (range; mean): 34-72; 60 years old CG: n= 27 (69% ♂; 31%♀) EG: n = 23 (73.2%♂; 26.8%♀) 17 withdrawn/lost to follow-up 33 participants completed the study CG: n= 18 EG: n = 15 Exercise adherence: 66% Partial supervision	People with a diagnosis of MM referred to a specialized cancer centre who are candidates for ASCT	Phase 1 Prehabilitation: 6 weeks, 3 sessions/week. 18 sessions. - AE: treadmill or stationary bike. 15 min increasing 5 min/week up to 40 min, and intensity 5% of maximum HR/ week up to 60-80% of maximum HR - Strength: multi-joint exercises including upper- and lower-limb exercises. Patient-tailored by the physiotherapist with 10-repetition maximum assessment. Phase 2 Admission for transplantation: exercise supervised by physiotherapist 3 times/week - AE: stationary bike in 10 min rounds up to 30 min Phase 3 rehabilitation: 12 weeks, 3 sessions/week. 36 sessions. Independent exercise
Shallwani et al. (2015), Canada	Retrospective review - single arm Exclusion: referred after chemotherapy, not followed-up during chemotherapy or lack of follow-up information in the heath records	n= 41 Age (range; mean): 49-70; 63 years old EG: n = 41 (73.2%♂; 26.8%♀) 12 withdrawn/lost to follow-up 29 participants completed the study EG: n = 29 (75.9% ♂; 24.1 %♀) Exercise adherence: 71% Complete supervision	People over 18 years of age, with a diagnosis of MM confirmed by histopathology, under chemotherapy and at least one follow-up since disease diagnosis	6 weeks. 2-3 sessions/week.18 sessions of up to 1 h of duration. AE: low impact and intensity 15-60 min daily Strength: exercises of low-to-moderate intensity 3 times /week

Abbreviations: n: total number of participants; ♂: men; ♀: women; CG: control group; EG: exercise group; MM: multiple myeloma; VAD: vincristine - Adriamycin – dexamethasone; DCEP: dexamethasone – cyclophosphamide – etoposide – cisplatin; CAD: cyclophosphamide – Adriamycin – dexamethasone ; ASCT: autologous stem cell transplantation; min: minutes; AE: aerobic exercise; EPO: epoetin; ST: short term; LT: long term; HR: heart rate; ECG: electrocardiogram; Max: maximum; ↑: increase; HCT: hematopoietic cell transplantation; h: hour; PROM: patient-reported outcome measure.

Table 4. Results and conclusions of the studies on the effects of therapeutic exercise on physical, mental and biological markers in adult patients with multiple myeloma.

First author, year of publication and country	**Participants (sample size and characteristics of the initial sample)**	**Parameters assessed**	**Results EG vs. CG**	**Conclusions**
Coleman et al. (2003), United States	n= 24 (14♂; 10♀) Age (range; mean): 42-74; 55 years old CG: n= 10 (60% ♂; 40%♀) EG: n = 14 (71%♂; 31%♀)	Physical changes Fat-free body mass STR (% change) AC (minutes on treadmill) Fatigue Mood disorder Sleep Nighttime sleep Daytime sleep Daytime sleepiness (Epworth)	↑Physical changes ↑ Fat-free body mass ↑ STR (% change) ↑ AC (min in treadmill) ↑ Fatigue ↓ Mood disorder ↑ Sleep/wake ↑ Nighttime sleep ↓ Daytime sleep ↓ Daytime sleepiness (Epworth)	The beneficial trends suggest that a personalised exercise programme for participants under aggressive treatment for MM is suitable and can be effective in reducing fatigue and mood disorder and increasing AE capacity, strength and sleep.
Coleman et al. (2008), United States	n= 135 CG = 66 EG = 69	Physical changes AC (6-min walk distance) Haematology Hb level Number Transfusions Adverse events Incidence of adverse events DVT	Physical changes ↑ AC ST ↑ AC LT Haematology Hb before ASCT ↑ ST ↑ LT Hb during ASCT ↑ ST ↔ LT Hb after ASCT ↔ ST ↑ LT Number of transfusions (red cells and platelets) ↓ ST ↓ LT Adverse effects Incidence of adverse events 1 ↑ ST ↑ LT DVT +1 ↑ ST ↓ LT	Aerobic exercise and strength/resistance training combined with prophylaxis with EPO benefit people with MM by reducing the number of red blood cell and platelet transfusions and substantially improving AC with beneficial effects on Hb levels.

Groeneveldt et al. (2013), United Kingdom	n= 37 Age (range; mean): 46-74; 61 years EG= 37	Physical changes Fatigue (FACIT-F) Grip STR (upper limb) Leg muscle STR (lower limb) AC (VO2max) Fat-free body mass Perceived state HRQL (FACT-G) Anxiety (HADS) Depression (HADS)	Physical changes ↓ Fatigue ↑ Grip STR ↑ Leg muscle STR ↔ AC ↔ Fat-free body mass Perceived state ↑ HRQL ↓ Anxiety ↓ Depression	An exercise programme prescribed for pharmacologically-treated patients with MM is safe, with proven results. It is necessary to consider the long-term benefits of exercise in the lifestyles of these patients. With the appropriate precautions and tailored treatment, regular exercise can be recommended to patients living with MM
Koutoukidis, et al. (2020), United Kingdom	n= 131 Age (range; mean): 35-86; 64 years CG: n= 42 (57% ♂; 43%♀) EG: n = 89 (54%♂; 46%♀)	Physical changes Fatigue (FACIT-F) Grip STR (upper limb) Leg muscle STR (lower limb) AC (VO2peak) Fat-free body mass Body fat (%) Perceived state Mood (FACT-G) Anxiety (HADS + FACT emotional scale) Depression (HADS)	Physical changes ↓ Fatigue ↑ Grip strength ↑ Leg muscle strength ↑ AC ↑ Fat-free body mass ↓ Body fat (%) Perceived state ↑ Mood ↔Anxiety ↔ Depression	A structured programme of exercise, combining AE and strength/resistance is safe for patients diagnosed with MM, improving patients' physical capacity and possibly also reducing fatigue
Larsen et al. (2019), Denmark	n= 30 Age (range; mean): 38-90; 68 years CG: n= 13 (69% ♂; 31%♀) EG: n = 17 (82%♂; 18%♀)	Physical changes Grip STR (upper limb) Knee extensor STR (lower limb) AC (accelerometer)	Physical changes ↑ Upper limb strength ↑ Lower limb strength ↑ AC	Early personalised exercise in MM patients of any age with no bone involvement improves physical function
Mawson et al. (2021), United Kingdom	n= 23 Age (range; mean): 53-78; 65 years EG: n = 23 (70%♂; 30%♀)	On recruitment, participants were allocated alternately to one of two sets of PROMS (1 and 2 indicate measures used only in PROMs 1 or PROMs 2 respectively) Physical changes Physical capacity (6MWTD) Fitness (International Physical Activity Questionnaire1/Godin Leisure-Time Exercise Questionnaire2) Self-efficacy with exercise (SCI Exercise Self-Efficacy Scale) Perceived state Mental wellbeing (Warwick-Edinburgh Mental Wellbeing Scale) HRQL (FACT-MM1/EORTC QLQ C30 MY202)	Physical changes ↑ Physical capacity ↑ Fitness ↑ Exercise self-efficacy Perceived state ↑ Mental wellbeing ↑ HRQL	Improvements in people with MM who perform exercise during the deconditioning associated with cancer treatment, with both objective and subjective benefits from physical and psychological perspectives.
McCourt et al. (2023), United Kingdom	n= 50 Age (range; mean): 34-72; 60 years CG: n= 27 (69% ♂; 31%♀) EG: n = 23 (73.2%♂; 26.8%♀)	Physical changes Fatigue (FACIT-F) Physical capacity (6MWTD) Sports performance Exercise self-efficacy Perceived state HRQL (EORTC-QLQ-C30)	Physical changes ↓ Fatigue ↑ Physical capacity ↑ Sports performance ↑ Exercise self-efficacy Perceived state ↑ HRQL	The improvement in terms of fatigue, HRQL, functional capacity and capacity for carrying out the exercise itself, both before the transplant procedure, and during maintenance and hospital admission is a key factor that optimises physical and mental wellbeing, facilitating hospital discharge and early, post-treatment rehabilitation.
Shallwani et al. (2015), Canada	n= 41 Age (range; mean): 49-70; 63 years EG: n = 41 (73.2%♂; 26.8%♀)	Physical changes Knee extensor strength Grip strength Exercise level reached Perceived state HRQL	Physical changes ↑Physical performance ↓Fatigue Perceived state ↑ HRQL	People with MM have a good adherence to programmes and recommendations on exercise, despite the problems related to bone weakness associated with this condition. On the other hand, patients with a high risk of pathological fracture, spinal cord compression or radiation are more prone to withdraw and require greater supervision to complete these programmes. Patients who followed the programmes as instructed experienced improvements in physical capacity, reductions in fatigue and increases in HRQL.

Abbreviations: n: total number of participants; ♂: men; ♀: women; CG: control group; EG: exercise group ; AC: aerobic capacity; STR: strength; Hb: haemoglobin; DVT: deep vein thrombosis; ST: short term; LT: long term; ASCT: autologous stem cell transplantation; EPO: epoetin; FACIT-F: Functional Assessment of Chronic Illness Therapy – Fatigue; VO2max: maximum consumption of oxygen; FACT-G: Functional Assessment of Cancer Therapy – General; HADS: Hospital Anxiety and Depression Scale; HRQL: health-related quality of life; MM: multiple myeloma; PROM: patient-reported outcome measure; FACT-MM: Functional Assessment of Cancer Therapy – Multiple Myeloma; EORTC QLQ C30 MY20: 30-item questionnaire to assess quality of life in MM patients; 6MWTD: 6-min walk test distance; EORTC QLQ C30: 30-item questionnaire to assess quality of life in cancer patients.

All the studies (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015) included people with MM who did not have comorbidities impeding the exercise proposed, for example, they were not at high risk of pathological bone fracture as assessed by diagnostic imaging, in aggressive phase MM (Coleman et al., 2003; Coleman et al., 2008), had MM that was stable without treatment (Groeneveldt et al., 2013), had completed their initial therapy for MM (Koutoukidis et al., 2020), and were on maintenance therapy (Groeneveldt et al., 2013; Koutoukidis et al., 2020) or conventional (Shallwani et al., 2015) or low-intensity (Larsen et al., 2019) therapy, prior to bone marrow transplantation (Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023) (Table 3).

Characteristics of the physical activity interventions

Physical activity interventions lasted between six (Mawson et al., 2021; Shallwani et al., 2015) and 30 (Coleman et al., 2008) weeks, with two (Larsen et al., 2019; Shallwani et al., 2015), three (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; McCourt et al., 2023; Shallwani et al., 2015) or six (Mawson et al., 2021) sessions of exercise per week. In all eight studies (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015), the type of exercise carried out consisted of concurrent training that included aerobic and strength exercises. Three studies included an initial warm-up (Coleman et al., 2003; Larsen et al., 2019; Mawson et al., 2021) and two a cool-down period after each exercise session (Coleman et al., 2003; Mawson et al., 2021). The exercise was under full supervision in four of the studies (Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; Shallwani et al., 2015), under tapered supervision by researchers in two (Groeneveldt et al., 2013; McCourt et al., 2023) and indirectly supervised through interviews in two (Coleman et al., 2003; Coleman et al., 2008). Patient adherence to the exercise interventions ranged from 58% (Coleman et al., 2003) to 94% (Larsen et al., 2019; Mawson et al., 2021) (Table 3).

Assessment of results

Physical parameters

All eight studies (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015) included measures to assess the physical state of people with MM (Table 4). Comparing the exercise group with controls, results were non-significantly better ($p > .05$) in all the parameters related to persons' physical condition such as strength (Koutoukidis et al., 2020; Larsen et al., 2019), aerobic capacity (Coleman et al., 2003; Coleman et al., 2008; Koutoukidis et al., 2020; Larsen et al., 2019; McCourt et al., 2023), sports performance (McCourt et al., 2023), and exercise self-efficacy (McCourt et al., 2023). In the intervention group, non-significant improvements ($p > .05$) in strength (Groeneveldt et al., 2013), physical condition (Mawson et al., 2021), and sports performance (Mawson et al., 2021; Shallwani et al., 2015) at the end of the study after the exercise interventions. Coleman et al. (2003) observed a non-significant increase in fatigue in the intervention group compared to the control group ($p > .05$); however, four other studies (Groeneveldt et al., 2013; Koutoukidis et al., 2020; McCourt et al., 2023; Shallwani et al., 2015) reported non-significant reductions in fatigue ($p > .05$) in patients in the intervention group compared to controls (Koutoukidis et al., 2020; McCourt et al., 2023) or their own baseline state (Groeneveldt et al., 2013; Shallwani et al., 2015) (Table 4).

Anthropometric parameters

Three studies (Coleman et al., 2003; Groeneveldt et al., 2013; Koutoukidis et al., 2020) analysed anthropometric parameters. They observed non-significant increases in fat-free body mass ($p > .05$) in patients in the intervention group compared controls in two studies (Coleman et al., 2003; Koutoukidis et al., 2020) and compared to baseline in the third (Groeneveldt et al., 2013). One study reported a non-significant decrease ($p > .05$) in body fat percentage in the intervention group compared to the control group (Koutoukidis et al., 2020).

Mental health

Mental health was assessed in four studies (Coleman et al., 2003; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Mawson et al., 2021) (Table 4). Two studies reported non-significant improvements in mood (Coleman et al., 2003; Koutoukidis et al., 2020) in the intervention group compared to the control group, while others observed non-significant improvements in anxiety (Groeneveldt et al., 2013), depression (Groeneveldt et al., 2013) or mental wellbeing (Mawson et al., 2021) after the exercise intervention compared to baseline ($p > .05$) (Table 4).

Health-related quality of life

Four studies assessed HRQL (Groeneveldt et al., 2013; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015). Though in all cases the differences failed to reach significance, one reported improvements in the intervention group compared to the control group (McCourt et al., 2023), and the other three improvements ($p > .05$) between before and after the intervention (Groeneveldt et al., 2013; Mawson et al., 2021; Shallwani et al., 2015).

Sleep disorders

Sleep/wake patterns were analysed by Coleman et al. (2003). These authors reported a non-significant increase ($p > .05$) in nighttime sleep and non-significant reductions ($p > .05$) in daytime sleep and daytime sleepiness.

Blood biomarkers

Blood haemoglobin levels increased substantially ($p > .05$) after 15 weeks of exercise before and during peripheral blood stem cell transplantation without the exogenous administration of erythropoietin, and at 30 weeks after the exercise intervention after peripheral stem cell transplantation compared to levels in the control group (Coleman et al., 2008) combined with erythropoietin therapy (Table 4).

Adverse effects

In the study by Coleman et al. (2008), the percentage of participants who experienced at least one serious adverse event was slightly higher ($p > .05$) in the intervention than the control group. Two other studies reported mild adverse events (Koutoukidis et al., 2020; Larsen et al., 2019). Specifically, Koutoukidis et al. (2020) reported hip and lumbar pain in five participants and Larsen et al. (2019) reported dizziness and non-specific pain symptoms in two participants. Nonetheless, none of the adverse effects were found to be related to the exercise intervention (Coleman et al., 2008; Koutoukidis et al., 2020; Larsen et al., 2019) (Table 4).

DISCUSSION

This systematic review assessed the effects of therapeutic exercise in people with MM on physical and perceived mental state, sleep/wake patterns, blood parameters and adverse events. A total of eight studies (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015) met the pre-set selection criteria, of which five were RCTs (Coleman et al., 2003; Coleman et al., 2008; Koutoukidis et al., 2020; Larsen et al., 2019; McCourt et al., 2023), and three were pre-post studies based on a single group exposed to exercise

(Groeneveldt et al., 2013; Mawson et al., 2021; Shallwani et al., 2015). In general, the exercise interventions were followed by non-significant (p > .05) improvements in physical and mental state, HRQL and body composition. In addition, the rate of adverse events was similar in experimental (exercise) and control groups.

Multiple myeloma is a currently incurable malignant bone marrow disease, with repeated periods of relapse and remission, followed by potential treatment resistance (Fernández-Lázaro, 2019). New therapies based on proteasome inhibitors, tyrosine kinase inhibitors and immunomodulatory drugs, in combination with chemotherapy, have changed the management of MM and improved patient survival (Ocio et al., 2015). That is, people with MM survive for longer, and this means greater disease burden, levels of immune compromise, and cumulative toxicity, leading to a worsening in quality of life and well-being (Fernández-Lázaro, 2019). In this situation, there is clear role for non-pharmacological strategies for the management of this population, as in other diseases such as breast cancer (Fernández-Lázaro, 2020a), chronic renal disease (Fernández-Lázaro et al., 2020b), and inflammatory bowel disease (Fernández-Lázaro et al., 2022a), for which therapeutic exercise can be a good strategy for improving person's quality of life, physical functioning and mobility (Gan et al., 2016). Haematologists have identified that exercise is suitable for the management of people with MM, with proven benefits for quality of life, activities of daily living, mental health and fatigue (Nicol et al., 2022). Nevertheless, there are no specific protocols of therapeutic exercise for people with MM, and there are doubts regarding exercise modality and duration, as well as when it should be recommended and its safety (Hayes et al., 2019).

All the studies reviewed (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015) included participants who did not have muscle weakness, bone pain or a high risk of bone fractures, which tend to persist for a long time after the end of the treatment and during periods of disease stability, and hence, would compromise exercise capacity. Further, the studies used concurrent training (aerobic + strength exercises) over long periods of time of up to 30 weeks (Coleman et al., 2008) and six sessions a week (Mawson et al., 2021) of moderate-to-vigorous intensity (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015), similar to studies focusing on exercise in other chronic conditions (Fernández-Lázaro et al., 2020b; Fernández-Lázaro et al., 2022a). The condition of participants undertaking therapeutic exercise was very varied, some studies including people in the aggressive phase of the MM (Coleman et al., 2003; Coleman et al., 2008), while others focused on those with MM that was stable without treatment (Groeneveldt et al., 2013), who had completed initial therapy (Koutoukidis et al., 2020), were on maintenance (Groeneveldt et al., 2013; Koutoukidis et al., 2020), conventional (Shallwani et al., 2015) or low intensity (Larsen et al., 2019) therapy, prior to bone marrow transplantation (Larsen et al., 2019; McCourt et al., 2023; Mawson et al., 2021). This suggests that exercise may appropriate, safe and feasible during any period of the disease and/or its treatment; as is the case in other specific types of cancer (Campbell et al., 2019). This view is supported by none of the studies included in this review (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015) having reported increases in adverse effects associated with the exercise interventions compared to those observed in control groups, as in other studies (Gan et al., 2016; Purdy et al., 2022; Rasch et al., 2020).

The rate of person's adherence to exercise ranged from 58% (Coleman et al., 2003) to 94% (Larsen et al., 2019; Mawson et al., 2021), contrasting with poor adherence found in other studies assessing exercise interventions (Hacker et al., 2022; Purdy et al., 2022). Supervised exercise programmes of the sort used in the studies reviewed are more effective at achieving adherence than non-supervised programmes (Goodhew

& Edwards, 2023), in people with MM (Groeneveldt et al., 2013) as in those with malignant solid tumours (Baguley et al., 2017; Fernández-Lázaro et al., 2020a). In a previous systematic review (Goodhew & Edwards, 2023) has been reported that poor adherence may be attributable to factors other than the exercise itself such as the symptom burden, and the effects of the treatment (Goodhew & Edwards, 2023), while exercise may actually have a certain role in modifying both disease symptoms and harmful effects of anti-MM therapies.

Given all this, it is essential to identify the optimum modality, frequency, intensity, timing and duration of exercise interventions as well as the level of supervision required to achieve the potential benefits of therapeutic exercise in people with MM (Nicol et al., 2023). Combined training programmes (including both aerobic and muscle strength exercises) were associated with notably better aerobic capacity (Coleman et al., 2003; Coleman et al., 2008; Koutoukidis et al., 2020; Larsen et al., 2019; McCourt et al., 2023) and general muscle strength (Coleman et al., 2003) or upper and lower limb strength (Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019) than observed with usual care. Further, as would be expected, participants doing exercise obtained higher scores for physical state (Mawson et al., 2021), sports performance (Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015) and exercise self-efficacy (Mawson et al., 2021; McCourt et al., 2023). These findings are promising as a key part of coping with symptoms and treatment of MM is the regaining of physical function, as people with MM need strength and aerobic capacity for keeping up with all activities of daily living and maintaining their clinical parameters within normal ranges (Jeevanantham et al., 2021). Nonetheless, more research is required to optimise exercise programs for this population.

People with MM require life-long outpatient monitoring of clinical biomarkers, which are key for their survival (Fernández-Lázaro, 2019). As myelomatous plasma cells interfere with bone marrow blood cell production, anaemia is present in at least 60-70% of people with MM at diagnosis and the majority at some point during the course of the disease, and this condition results in exhaustion, insufficient oxygenation and an inability to perform activities of daily living (Fernández-Lázaro, 2019). In relation to this, Coleman et al. (Coleman et al., 2008) reported a substantial increase in haemoglobin levels after 15 weeks of exercise without exogenous administration of erythropoietin. Such an increase in haemoglobin could be due exercise stimulating erythropoiesis in the short term, inducing the secretion of erythropoietin from three hours to 30 hours after exercise (Schwandt et al., 1991). In addition, the long-term response to exercise, that is, due to continuous and regular training, increases circulating red blood cell count and haemoglobin levels (Fernández-Lázaro et al., 2022b).

Improvements in participants' general physical functioning (Bartels et al., 2015; Oechsle et al., 2014) could explain the results described regarding absolute (in minutes) and percentage increases in night-time sleep (Coleman et al., 2003), decreases in fatigue (Coleman et al., 2003; Groeneveldt et al., 2013; Koutoukidis et al., 2020; McCourt et al., 2023; Shallwani et al., 2015), improvements in HRQL (Groeneveldt et al., 2013; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015) and benefits in relation to mental status (mood (Coleman et al., 2003; Koutoukidis et al., 2020); anxiety (Groeneveldt et al., 2013; Koutoukidis et al., 2020); depression (Groeneveldt et al., 2013; Koutoukidis et al., 2020); and mental wellbeing (Mawson et al., 2021)). Reductions in fatigue would enable increases in the duration and intensity of exercise, in turn, resulting in greater benefits related to better physical state in MM people (Jeevanantham et al., 2021). Further, during the course of MM, the disease has negative psychological effects related to the disease itself, treatments and bodily changes (Hulin et al., 2017). Increases in fat-free body mass (Coleman et al., 2003; Groeneveldt et al., 2013; Koutoukidis et al., 2020) and reductions in body fat percentage (Koutoukidis et al.,

2020) would help improve the perceived body image in people with MM, which would be able to counteract some of the psychological sequelae.

Regarding HRQL, exercise may have benefits for people with MM and their families (O'Donnell et al., 2022), and the potential of exercise in cancer patients should be assessed in terms of whether it is likely to help achieve a life worth living, both in social, psychological and physical terms (Fernández-Lázaro, 2020a). The notable improvements observed in HRQL (Groeneveldt et al., 2013; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015) are in line with findings in other studies (Oechsle et al., 2014; Persoon et al., 2013). HRQL in people with MM may influenced by improvements in physical and mental status, sleep-wake patterns and perceived body image (O'Donnell et al., 2022). Moreover, given the high rates of adherence to therapeutic exercise observed in the eight studies included in this review (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015) and the observation that exercise has a positive influence on HRQL, continuous programmes of therapeutic exercise should be developed and tested in these population to incorporate this type of therapy as part of the adjuvant therapy regimen for the management of this type of cancer.

Overall, the results of this systematic review are compatible with the development and prescribing of supervised therapeutic multimodal exercise programmes, including aerobic capacity and strength training, tailored to the characteristics of people with MM. Although only five (Coleman et al., 2003; Coleman et al., 2008; Koutoukidis et al., 2020; Larsen et al., 2019; McCourt et al., 2023) out of the eight studies included (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015) were RCTs, the results were consistent in suggesting that patients with MM who adhere to exercise tend to have less fatigue, and a better quality of life and mental state, likely related to improvements in physical parameters. Nonetheless, our ability to draw definitive conclusions is hindered by results not reaching statistical significance and there is a clear need for more research in this field with larger sample sizes. Once data become available from more RCTs, meta-analyses should be conducted to confirm the trends observed and accurately determine the effects of exercise interventions in people with MM. Future research should also include cost-benefit analysis to determine whether exercise interventions are cost-effective.

We recognise that this study has certain limitations. First, few studies met the inclusion criteria, and hence, the sample of people with MM included was relatively small. Second, the considerable heterogeneity of studies, both in the outcomes measured and exercise intervention itself, means that a meta-analysis could not be performed. Therefore, caution should be exercised in interpreting the results. Nonetheless, our promising results are consistent with other studies and reviews in this field that have found moderate to strong evidence of health benefits of therapeutic exercise in people with MM (Nicol et al., 2023; Purdy et al., 2022; Smith et al., 2015).

Despite the aforementioned limitations, our review has strengths related to the search being based on three databases (Medline, SciELO and Cochrane Collection Plus), complemented by other sources such as ResearchGate, and reference lists of relevant studies, and its reporting in accordance with the PRISMA guidelines (Page et al., 2021). Further, to check the robustness of the studies selected, we used the McMaster critical appraisal tool to assess study quality (Law et al., 1998) and the Cochrane tool to assess the risk of bias (Higgins et al., 2011). On the other hand, the review was duly registered in the international prospective register of systematic reviews, PROSPERO (#CRD42023458213).

Reflections, practical implications and recommendations concerning exercise in multiple myeloma

Overall, the eight studies (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015) selected had different study designs and sample sizes, included people with a range of characteristics, MM stages, and blood cancer treatments, and considered different exercise regimens and outcome measures, and it is difficult to suggest a single type of exercise intervention or therapeutic exercise programme that would be suitable for all individuals with MM, though concurrent aerobic and strength training may be considered widely suitable.

Despite the aforementioned differences, all the studies (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015) included in this systematic review observed potential relationships between therapeutic exercise and notable improvements in various aspects of the state of people with MM: physical condition (Coleman et al., 2003; Coleman et al., 2008; Koutoukidis et al., 2020; Larsen et al., 2019; McCourt et al., 2023), anthropometric parameters (Coleman et al., 2003; Koutoukidis et al., 2020), mental health (Coleman et al., 2003; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Mawson et al., 2021), HRQL (Groeneveldt et al., 2013; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015), sleep disorders (Coleman et al., 2003) and haemoglobin levels (Coleman et al., 2008). Such beneficial effects may be intertwined as well as linked to therapeutic exercise. Hence, health professionals should not limit their view to physical gains as the only goal during the process of rehabilitation of people with MM; rather, they should also consider other potential physiological and psychological benefits.

A key factor is to ensure that any therapeutic exercise programme is safe, given the clinical characteristics of people with MM, including high rates of bone damage (70%), anaemia (59%), and general malaise (46%) (Fernández-Lázaro, 2019), and the nature of the pharmacological treatments used (Fernández-Lázaro et al., 2018). For these reasons, therapeutic exercise programmes for MM should be planned with great care, taking into account the contraindications to exercise and precautions that should be taken in this high-risk population (Nicol et al., 2023; Purdy et al., 2022). Concerning this, none of the studies included in our review reported any adverse events linked to the performance of therapeutic exercise (Coleman et al., 2003; Coleman et al., 2008; Groeneveldt et al., 2013; Koutoukidis et al., 2020; Larsen et al., 2019; Mawson et al., 2021; McCourt et al., 2023; Shallwani et al., 2015).

Though there is a need for robust cost-effectiveness analysis, therapeutic exercise can be considered readily available and inexpensive, and it seems to be safe, suggesting that it would be a good use of resources and it would be appropriate to prescribe it from a sports medicine perspective (Gao & Trinh, 2023). In particular, physiotherapists would be the appropriate professionals to promote exercise for therapeutic and/or preventative purposes, and not only as a recreational or professional activity. Nonetheless, we should consider three factors: i) therapeutic exercise is not an etiological treatment, that is, it cannot cure MM but rather may mitigate its effects; ii) good adherence is essential and this is often difficult to achieve (Smith et al., 2015); and iii) the use of drugs makes us feel that the disease is under control. In MM, fatigue and/or disability should not be a barrier to therapeutic exercise rather they should be seen as reasons for doing it. Indeed, physical deterioration and HRQL impairment in MM may be due to rest or inactivity and there is a need for more than traditional blood cancer therapies to address this situation. Therefore, it is necessary to provide stressful stimuli that can achieve positive physiological adaptations in each component of physical fitness, that is, the practice of therapeutic exercise (Giráldez García, 2018).

Based on the findings of this review, we can state that prescribing exercise for people with MM requires thorough evaluation of biomedical, physical and psychosocial factors, to determine the elements (frequency, intensity, type and duration) of an exercise programme for different phases of MM, meaning that the prescribing of therapeutic exercise should be specific and person-based, and not only involve suggesting in a general and imprecise way "*it would be good to do some exercise*", supporting the view that relevant specialists, for example, a sport and exercise physician, should be in charge of prescribing this activity. The responses and adaptations are dose-dependent, with associated benefits and risks or adverse effects, and individuals may respond differently, and hence, the exercise prescribed must be adapted to the specific requirements of individual people with MM, and especially to periods of inactivity in the course of the disease. This situation means therapeutic exercise should be supervised and implemented by a physiotherapist, to allow progressive changes in the exercise frequency, duration and intensity, tailoring it to the specific condition of people with MM. Moreover, supervision contributes to persons' motivation and it is likely to be indispensable for encouraging full participation in a therapeutic exercise programme throughout their personalised care and treatment programme.

CONCLUSION

Exercise interventions have been found to be feasible in people with MM, with no important safety issues identified. Further, results are compatible with exercise having health benefits for this population, reducing fatigue, and improving HRQL, mental state, and body composition, changes which could be due to notable increases in physical capacity after structured supervised training programmes that include aerobic and strength exercises. The implications are very important as we must identify ways to help people with MM who are surviving for longer also achieve a life worth living. Nonetheless, more research is urgently needed to confirm and extend these findings, as current evidence is promising but not conclusive.

AUTHOR CONTRIBUTIONS

Diego Fernández Lázaro: conceptualization, methodology, validation, resources, writing-original draft, writing – review & editing, supervision, project administration, funding acquisition. Marina Seco Casares, Álvaro López Llorente and Nuria Hernández Burgos: software, formal analysis, investigation, data curation, writing – original draft and visualization. Gema Santamaría Gómez: conceptualization, methodology, validation, resources, writing – original draft, writing – review & editing, supervision and project administration.

SUPPORTING AGENCIES

This research was founded by the "*Department of Education of the Regional Government of Castile and León*" and the European Regional Development Fund (ERDF) through the TCUE Plan 2023-2027; (grant nº. 067/230003).

DISCLOSURE STATEMENT

No potential conflict of interest was reported by the authors.

REFERENCES

Baguley, B. J., Bolam, K. A., Wright, O. R. L., & Skinner, T. L. (2017). The Effect of Nutrition Therapy and Exercise on Cancer-Related Fatigue and Quality of Life in Men with Prostate Cancer: A Systematic Review. Nutrients, 9(9), 1003. https://doi.org/10.3390/nu9091003

Bartels, F. R., Smith, N. S., Gørløv, J. S., Grufstedt, H. K., Nexø, C., Kehlet, H., Sjøgren, P., Kjeldsen, L., & Høgdal, N. (2015). Optimized patient-trajectory for patients undergoing treatment with high-dose chemotherapy and autologous stem cell transplantation. Acta. Oncol., 54(5), 750-758. https://doi.org/10.3109/0284186X.2014.999872

Butcher, N., Monsour, A., Mew, E., Chan, A. W., Moher, D., Mayo-Wilson, E., Terwee, C. B., Chee-A-Tow, A., Baba, A., Gavin, F., Grimshaw, J. M., Kelly, L. E., Saeed, L., Thabane, L., Askie, L., Smith, M., Farid-Kapadia, M., Williamson, P. R., Szatmari, P., Tugwell, P., Golub, R. M., Monga, S., Vohra, S., Marlin, S., Ungar, W. J., & Offringa, M. (2022). Guidelines for Reporting Outcomes in Trial Reports: The CONSORT-Outcomes 2022 Extension. JAMA, 328(22), 2252-2264. https://doi.org/10.1001/jama.2022.21022

Campbell, K. L., Winters-Stone, K. M., Wiskemann, J., May, A. M., Schwartz, A. L., Courneya, K. S., Zucker, D. S., Matthews, C. E., Ligibel, J. A., Gerber, L. H., Morris, G. S., Patel, A. V., Hue, T. F., Perna, F. M., & Schmitz, K. H. (2019). Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable. Med. Sci. Sports Exerc., 51(11), 2375-2390. https://doi.org/10.1249/MSS.0000000000002116

Castilian-Leonese Society of Hematology and Hemotherapy. (2023). 2023 Myeloma Hematoguide. GAMMCYL. Retrived from [Accessed 2025, 30 September]: http://www.sclhh.org/docs/pdf/consenso/guia%20mieloma%202023.pdf

Coleman, E. A., Coon, S. K., Hall-Barrow, J., Richards, K., Gaylor, D., & Stewart, B. (2003). Feasibility of exercise during treatment for multiple myeloma. Cancer Nurs., 26(5), 410-419. https://doi.org/10.1097/00002820-200310000-00012

Coleman, E. A., Coon, S. K., Kennedy, R. L., Lockhart, K. D., Stewart, C. B., Anaissie, E. J., & Barlogie, B. (2008). Effects of exercise in combination with epoetin alfa during high-dose chemotherapy and autologous peripheral blood stem cell transplantation for multiple myeloma. Oncol. Nurs. Forum., 35(3), e53-61. https://doi.org/10.1188/08.ONF.E53-E61

Cormican, O., & Dowling, M. (2018). Living with relapsed myeloma: Symptoms and self-care strategies. J. Clin. Nurs., 27(7-8), 1713-1721. https://doi.org/10.1111/jocn.14232

Fernández-Lázaro, D. (2011). Pre-clinical comparative analysis of the efficacy, mechanism of action and resistance mechanisms of two immunomodulatory drugs (IMIDS), lenalidomide and pomalidomide, in multiple myeloma [Salamanca University]. https://doi.org/10.14201/gredos.110661

Fernández-Lázaro, D., Fernández-Lázaro, C. I., Caballero García, A., & Córdoba Martínez, A. (2018). Immunomodulator drugs for the treatment of multiple myeloma. Rev. méd. Chile, 146(12), 1444-1451. https://doi.org/10.4067/s0034-98872018001201444

Fernández-Lázaro, D. (2019). Biological and molecular bases in the development of the pathogenic of the disease of multiple myeloma. Investigación clínica, 60(3), 247-264. https://doi.org/10.22209/IC.v60n3a07

Fernández-Lázaro, D., Mielgo-Ayuso, J., Caballero-García, A., Córdoba Martínez, A., Lázaro Asensio, M. P., & Férnandez-Lázaro, C. I. (2020a). Physical activity in oncological breast cancer patients: non-pharmacological sports medical therapy? Systematic review. Arch. med. deporte, 37(198), 266-274. https://doi.org/10.18176/archmeddeporte.00017

Fernández-Lázaro, D., Mielgo-Ayuso, J., Lázaro Asensio, M. P., Martínez, A. C., Caballero-García, A., & Fernández-Lázaro, C. I. (2020b). Intradialytic physical exercise in chronic kidnewy disease: a systematic review of health outcomes. Arch. Med. Deporte, 37(6), 419-429. https://doi.org/10.18176/archmeddeporte.00017

Fernández-Lázaro, D., Hernández-Burgos, N., Mielgo, R. C., & García-Lázaro, S. (2022a). Evaluation of physical activity as a therapeutic adjuvant for patients with inflammatory bowel disease: A systematic review. Investigación Clínica, 63(3), 304-322. https://doi.org/10.54817/IC.v63n3a08

Fernández-Lázaro, D., Mielgo-Ayuso, J., Santamaría, G., Gutiérrez-Abejón, E., Domínguez-Ortega, C., García-Lázaro, S. M., & Seco-Calvo, J. (2022b). Adequacy of an Altitude Fitness Program (Living and Training) plus Intermittent Exposure to Hypoxia for Improving Hematological Biomarkers and Sports Performance of Elite Athletes: A Single-Blind Randomized Clinical Trial. Int. J. Environ. Res. Public Health, 19(15), 9095. https://doi.org/10.3390/ijerph19159095

Gan, J. H., Sim, C. Y. L., & Santorelli, L. A. (2016). The effectiveness of exercise programmes in patients with multiple myeloma: A literature review. Crit. Rev. Oncol. Hematol., 98, 275-289. https://doi.org/10.1016/j.critrevonc.2015.11.005

Gao, Z., & Trinh, L. (2023). Exercise and oncology: The role of physical activity in disease prevention and health promotion. J. Sport Health Sci., 12(6), 651-652. https://doi.org/10.1016/j.jshs.2023.09.003

Giráldez García, M. A. (2018). Exercise is a scientifically-proven and valuable therapeutic and preventive tool, that everyone should take part in. Arch. Med. Deporte, 35(6), 354-356.

Gómez Afonso, A., Fernandez-Lazaro, D., Adams, D. P., Monserdà-Vilaró, A., & Fernandez-Lazaro, C. I. (2023). Effects of Withania somnifera (Ashwagandha) on Hematological and Biochemical Markers, Hormonal Behavior, and Oxidant Response in Healthy Adults: A Systematic Review. Curr. Nutr. Rep., 12(3), 465-477. https://doi.org/10.1007/s13668-023-00481-0

Goodhew, R. E., & Edwards, B. A. (2023). The effect of exercise interventions on quality of life in patients with multiple myeloma: a systematic review and meta-analysis of randomised controlled trials. Clin. Exp. Med., 23(7), 3217-3230. https://doi.org/10.1007/s10238-023-01058-5

Groeneveldt, L., Mein, G., Garrod, R., Jewell, A. P., Van Someren, K., Stephens, R., D'Sa, S. P., & Yong, K. L. (2013). A mixed exercise training programme is feasible and safe and may improve quality of life and muscle strength in multiple myeloma survivors. BMC Cancer, 13, 31. https://doi.org/10.1186/1471-2407-13-31

Hacker, E. D., Richards, R. L., Abu Zaid, M., Chung, S. Y., Perkins, S., & Farag, S. S. (2022). STEPS to Enhance Physical Activity After Hematopoietic Cell Transplantation for Multiple Myeloma. Cancer Nurs., 45(3), 211-223. https://doi.org/10.1097/NCC.0000000000001006

Hayes, S. C., Newton, R. U., Spence, R. R., & Galvão, D. A. (2019). The Exercise and Sports Science Australia position statement: Exercise medicine in cancer management. J. Sci. Med. Sport, 22(11), 1175-1199. https://doi.org/10.1016/j.jsams.2019.05.003

Higgins, J. P. T., Altman, D. G., Gøtzsche, P. C., Jüni, P., Moher, D., Oxman, A. D., Savović, J., Schulz, K. F., Weeks, L., & Sterne, J. A. C. (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ, 343, d5928. https://doi.org/10.1136/bmj.d5928

Hulin, C., Hansen, T., Heron, L., Pughe, R., Streetly, M., Plate, A., Perkins, S., Morgan, K., Tinel, A., Rodrigues, F., & Ramasamy, K. (2017). Living with the burden of relapse in multiple myeloma from the patient and physician perspective. Leuk. Res., 59, 75-84. https://doi.org/10.1016/j.leukres.2017.05.019

Jeevanantham, D., Rajendran, V., McGillis, Z., Tremblay, L., Larivière, C., & Knight, A. (2021). Mobilization and Exercise Intervention for Patients With Multiple Myeloma: Clinical Practice Guidelines Endorsed by the Canadian Physiotherapy Association. Phys. Ther., 101(1), 1-10. https://doi.org/10.1093/ptj/pzaa180

Jordan, K., Proskorovsky, I., Lewis, P., Ishak, J., Payne, K., Lordan, N., Kyriakou, C., Williams, C. D., Peters, S., & Davies, F. E. (2014). Effect of general symptom level, specific adverse events, treatment patterns, and patient characteristics on health-related quality of life in patients with multiple myeloma: results of a European, multicenter cohort study. Support. Care Cancer, 22(2), 417-426. https://doi.org/10.1007/s00520-013-1991-4

Koutoukidis, D. A., Land, J., Hackshaw, A., Heinrich, M., McCourt, O., Beeken, R. J., Philpott, S., DeSilva, D., Rismani, A., Rabin, N., Popat, R., Kyriakou, C., Papanikolaou, X., Mehta, A., Paton, B., Fisher, A., & Yong, K. L. (2020). Fatigue, quality of life and physical fitness following an exercise intervention in multiple myeloma survivors (MASCOT): an exploratory randomised Phase 2 trial utilising a modified Zelen design. Br. J. Cancer, 123(2), 187-195. https://doi.org/10.1038/s41416-020-0866-y

Larsen, R. F., Jarden, M., Minet, L. R., Frølund, U. C., & Abildgaard, N. (2019). Supervised and home-based physical exercise in patients newly diagnosed with multiple myeloma-a randomized controlled feasibility study. Pilot Feasibility Stud., 5(1). https://doi.org/10.1186/s40814-019-0518-2

Law, M., Stewart, D., Pollock, N., Letts, L., Bosch, J., & Westmorland, M. (1998). Critical Review Form Quantitative Studies. Ontatio: McMaster University. Retrived from [Accessed 2025, 30 September]: https://www.mcgill.ca/cpengine/files/cpengine/quanreview_form1.doc

Mawson, S., Keen, C., Skilbeck, J., Ross, H., Smith, L., Dixey, J., Walters, S. J., Simpson, R., Greenfield, D. M., & Snowden, J. A. (2021). Feasibility and benefits of a structured prehabilitation programme prior to autologous stem cell transplantation (ASCT) in patients with myeloma; a prospective feasibility study. Physiotherapy, 113, 88-99. https://doi.org/10.1016/j.physio.2021.08.001

McCourt, O., Fisher, A., Ramdharry, G., Land, J., Roberts, A. L., Rabin, N., & Yong, K. (2023). Exercise prehabilitation for people with myeloma undergoing autologous stem cell transplantation: results from PERCEPT pilot randomised controlled trial. Acta oncol., 62(7), 696-705. https://doi.org/10.1080/0284186X.2023.2178326

National Cancer Institute (23 February 2024). Cancer Stat Facts: Myeloma. Retrived from [Accessed 2025, 30 September]:https://seer.cancer.gov/statfacts/html/mulmy.html

Nicol, J. L., Chong, J. E., McQuilten, Z. K., Mollee, P., Hill, M. M., & Skinner, T. L. (2023). Safety, Feasibility, and Efficacy of Exercise Interventions for People With Multiple Myeloma: A Systematic Review. Clin. Lymphoma Myeloma Leuk., 23(2), 86-96. https://doi.org/10.1016/j.clml.2022.10.003

Nicol, J. L., Hill, M. M., Burton, N. W., & Skinner, T. L. (2022). Promoting exercise for patients with multiple myeloma: attitudes and practices of clinical haematologists. J.Cancer Surviv., 16(3), 688-695. https://doi.org/10.1007/s11764-021-01062-2

O'Donnell, E. K., Shapiro, Y. N., Yee, A. J., Nadeem, O., Laubach, J. P., Branagan, A. R., Anderson, K. C., Mo, C. C., Munshi, N. C., Ghobrial, I. M., Sperling, A. S., Agyemang, E. A., Burke, J. N., Harrington, C. C., Hu, B. Y., Richardson, P. G., Raje, N. S., & El-Jawahri, A. (2022). Quality of life, psychological distress, and prognostic perceptions in caregivers of patients with multiple myeloma. Blood Adv., 6(17), 4967-4974. https://doi.org/10.1182/bloodadvances.2022007127

Ocio, E. M., Fernández-Lázaro, D., San-Segundo, L., López-Corral, L., Corchete, L. A., Gutiérrez, N. C., Garayoa, M., Paíno, T., García-Gómez, A., Delgado, M., Montero, J. C., Díaz-Rodríguez, E., Mateos, M. V., Pandiella, A., Couto, S., Wang, M., Bjorklund, C. C., & San-Miguel, J. F. (2015). In vivo murine model of acquired resistance in myeloma reveals differential mechanisms for lenalidomide and pomalidomide in combination with dexamethasone. Leukemia, 29(3), 705-714. https://doi.org/10.1038/leu.2014.238

Oechsle, K., Aslan, Z., Suesse, Y., Jensen, W., Bokemeyer, C., & De Wit, M. (2014). Multimodal exercise training during myeloablative chemotherapy: a prospective randomized pilot trial. Support. Care Cancer, 22(1), 63-69. https://doi.org/10.1007/s00520-013-1927-z

Page, M. J., Moher, D., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., Mcdonald, S., McGuinness, L. A., Stewart, L. A., Thomas, J., Tricco, A. C., Welch, V. A., Whiting, P., Mckenzie, J. E. (2021). PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ, 372, n160. https://doi.org/10.1136/bmj.n160

Persoon, S., Kersten, M. J., van der Weiden, K., Buffart, L. M., Nollet, F., Brug, J., & Chinapaw, M. J. M. (2013). Effects of exercise in patients treated with stem cell transplantation for a hematologic malignancy: a systematic review and meta-analysis. Cancer Treat. Rev., 39(6), 682-690. https://doi.org/10.1016/j.ctrv.2013.01.001

Purdy, G. M., Venner, C. P., Tandon, P., & McNeely, M. L. (2022). Feasibility of a tailored and virtually supported home exercise program for people with multiple myeloma using a novel eHealth application. Digit. Health, 8. https://doi.org/10.1177/20552076221129066

Rajkumar, S. V. (2022). Multiple Myeloma: 2022 update on Diagnosis, Risk-stratification and Management. Am. J. Hematol., 97(8), 1086-1107. https://doi.org/10.1002/ajh.26590

Ramsenthaler, C., Osborne, T. R., Gao, W., Siegert, R. J., Edmonds, P. M., Schey, S. A., & Higginson, I. J. (2016). The impact of disease-related symptoms and palliative care concerns on health-related quality of life in multiple myeloma: a multi-centre study. BMC Cancer, 16(1), 427. https://doi.org/10.1186/s12885-016-2410-2

Rasch, S., Lund, T., Asmussen, J. T., Nielsen, A. L., Larsen, R. F., Andersen, M. Ø., & Abildgaard, N. (2020). Multiple Myeloma Associated Bone Disease. Cancers (Basel), 12(8), Article 2113. https://doi.org/10.3390/cancers12082113

Schwandt, H. J., Heyduck, B., Gunga, H. C., & Röcker, L. (1991). Influence of prolonged physical exercise on the erythropoietin concentration in blood. Eur. J. Appl. Physiol. Occup. Physiol., 63(6), 463-466. https://doi.org/10.1007/BF00868079

Shallwani, S., Dalzell, M. A., Sateren, W., & O'Brien, S. (2015). Exercise compliance among patients with multiple myeloma undergoing chemotherapy: a retrospective study. Support. Care Cancer, 23(10), 3081-3088. https://doi.org/10.1007/s00520-015-2680-2

Smith, L., McCourt, O., Henrich, M., Paton, B., Yong, K., Wardle, J., & Fisher, A. (2015). Multiple myeloma and physical activity: a scoping review. BMJ Open, 5(11), e009576. https://doi.org/10.1136/bmjopen-2015-009576

Spanish Society of Hematology and Hemotherapy. (2021). Multiple Myeloma Guide. Retrived from [Accessed 2025, 30 September]: https://www.sehh.es/publicaciones/guias-recomendaciones

Straus, S.E., Glasziou, P., Richardson, W.S., & Haynes, R. B. (2018). Evidence-based medicine: How to practice and teach it (4th ed.). Churchill Livingstone. ISBN: 9780702062964.

APPENDIX A

(multiple myeloma) AND (physical activity) OR (multiple myeloma) AND (exercise), (multiple myeloma) AND (Physical state), (multiple myeloma) AND (Strength), (multiple myeloma) AND (Aerobic capacity), (multiple myeloma) AND (Physical condition), (multiple myeloma) AND (Fatigue), (multiple myeloma) AND (Sports performance), OR (multiple myeloma) AND (anthropometric parameters), (multiple myeloma) AND (Lean weight), (multiple myeloma) AND (body fat), OR (multiple myeloma) AND (sleep disturbances), (multiple myeloma) AND (Sleep/wake), OR (multiple myeloma) AND (perception), (multiple myeloma) AND (HRQOL), (multiple myeloma) AND (Anxiety), (multiple myeloma) AND (Mental well-being), (multiple myeloma) AND (Depression), OR (multiple myeloma) AND (haematological), OR (blood) AND (physical activity), OR (multiple myeloma) AND (Adverse Effects) AND (physical activity).