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Exercise and diet studies among patients living with multiple myeloma: current evidence and considerations of patient preferences

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Background: Multiple myeloma (MM) is the second most common blood cancer after leukemia in adults. Despite advancements in treatment that have extended survival, MM remains incurable and the cancer and its treatment result in adverse acute, long-term and latent side-effects, necessitating a focus on strategies to attenuate these side-effects and improve quality of life. This narrative review highlights MM patient preferences for exercise and/or diet interventions relative to complete and ongoing interventions to identify gaps and needs for future lifestyle interventions in MM patients aimed at improving MM survivorship care.

Methods: This updated review was completed using a comprehensive search that was conducted using PubMed and ClinicalTrials.gov databases using keywords related to MM, exercise, physical activity, diet, nutrition and patient preferences. Studies involving adults diagnosed with MM were included.

Results: Among published studies, there are five exercise interventions and four diet and nutrition observational studies. The importance of individualized exercise interventions tailored to MM patients' needs was emphasized. Supervised exercise interventions showed higher adherence and engagement compared to unsupervised interventions. Observational diet/nutrition studies demonstrated that decreased gut microbiome diversity post-transplant is linked to poorer outcomes. Additionally, nutritional status and dietary patterns, such as high-carbohydrate and plant-based diets, can significantly impact clinical outcomes in MM patients, including sustained minimal residual disease negativity. Current clinical trials are primarily focused on feasibility and adherence, with a limited emphasis on long-term outcomes. In ClinicalTrials.gov, there are six ongoing exercise interventions, with an additional seven that are completed with no published results, one suspended trial and one active but not recruiting. Additionally, there are two combined diet and exercise interventions that are currently recruiting, with one active but no longer recruiting. Among diet and nutrition ongoing trials, there are currently two

actively recruiting, two completed with no primary paper published and one study that was withdrawn.

Discussion: These findings underscore the need for more comprehensive, long-term and adequately powered studies on the impact of exercise and diet interventions in MM patients. Patient education and empowerment within these trials are crucial for enhancing engagement and adherence to these interventions.

KEYWORDS

multiple myeloma, exercise, diet and nutrition, gut microbiome, patient preferences

1 Introduction

Multiple Myeloma (MM) is categorized as a clonal plasma cell proliferative disorder that can significantly impact bones, kidneys and the body's ability to produce healthy white blood cells, red blood cells, and platelets. It is the 14th most common cancer type in the United States and the second most prevalent blood cancer after leukemia (1). While the incidence of MM has increased over time (e.g., 5.5 per 100,000 persons in 1992 versus 6.8 in 2022), survival rates have increased an additional eight years due to improved treatment options (2, 3).

Patients with MM often experience adverse cancer- and treatment-related side effects, such as severe fatigue, poor appetite, reduced enjoyment of life, increased pain, and muscle weakness (4, 5). While engagement in regular exercise and physical activity (PA) have been widely recognized for numerous benefits in individuals living with varying cancer types and stages – such as reducing fatigue, anxiety, depression, and improving quality of life and physical function – there remains a gap in the evidence specifically addressing the impact of PA on those diagnosed with MM (6). The general PA guidelines for individuals living with cancer on active treatment or upon completion of treatment includes 90 or 150 minutes per week of moderate intensity aerobic activity, respectively, and two sessions per week of resistance training, targeting every major muscle group (6).

A recent literature review highlighted the potential benefits of using lifestyle modifications, such as regular exercise and healthful dietary strategies, to improve overall health in patients with MM, including enhancements in physical functioning, fatigue, quality of life, and long-term health outcomes (7). However, the review emphasized the need for further research to explore the associations between weight management, sleep, substance use, exercise, and nutrition on disease outcomes such as overall survival, progression-free survival, and non-relapse mortality. Similarly, a second review echoed these findings, noting that seven studies have investigated PA in MM patients, with five of those studies including PA interventions (8). These intervention studies often had small sample sizes (average $n = 82$) and short intervention durations (average length of 15 weeks). Despite these

limitations, the studies consistently found that exercise is both feasible and safe for this population, including those undergoing active treatment such as autologous stem cell transplantation and maintenance therapy. Both reviews stressed the necessity for more comprehensive studies involving larger and more clinically diverse populations, such as those with bone and lytic lesions, to better understand the impact of PA on MM patients.

In addition to engagement in regular exercise, a healthy diet can play a crucial role in supporting cancer patients through treatment and recovery. It can help mitigate treatment side effects, maintain energy levels, and support immune function (9). The American Institute for Cancer Research (AICR) provides comprehensive guidelines for cancer prevention and survivorship, emphasizing the importance of a healthy diet, regular PA, and maintaining a healthy weight (10). There are currently no specific guidelines for MM patients; however, evidence supports that MM patients at higher risk of malnutrition, as measured by the Malnutrition Screening Tool, experience worse survival after stem cell transplant (11) and exacerbated effects of cytokine release syndrome in patients undergoing CAR-T cell therapy (12). Emerging research is also exploring the role of gut microbiome characteristics in MM patients. The gut microbiome, which can be influenced by exercise engagement and dietary intake, plays a significant role in immune function and inflammation (13, 14). Alterations in the gut microbiome, such as lower bacteria diversity compared to healthy controls pre- and post-treatment including transplant, have been linked to the progression of MM and the body's response to treatment (15–17). Taken together, these findings highlight the importance of consuming a healthy diet during and after MM treatment, with further research evaluating the impact of diet quality and the gut microbiome in this patient population.

Considering this evidence supporting the roles of exercise and diet in MM survivorship care, the purpose of this literature review is to build upon previous reviews by providing an updated synthesis of the latest research on exercise and/or diet for individuals with MM. Additionally, this review will present patient preferences for these types of interventions to further guide future research.

2 Methods

2.1 Search strategy

To provide an update to the previous reviews (7, 8), we conducted a comprehensive search of the electronic database PubMed. The search terms used were a combination of keywords including, but not limited to “Multiple Myeloma”, “Myeloma”, “exercise”, “physical activity”, “Diet”, “Diet Therapy”, “Nutrition”, “Gut Microbiome”, “Patient Satisfaction”, “Patience Preference”, “Motivation”. The Medical Subject Headings (MeSH) terms and expansions were applied across the terms where applicable. Additionally, clinical trials registered with ClinicalTrials.gov were found using “Multiple Myeloma” as the disease type and search terms under keywords included “Exercise”, “Diet” and “Nutrition.”

2.2 Inclusion and exclusion criteria

Studies that involved human subjects who were diagnosed with MM that were over the age of 18 years old were considered. Exercise, diet and/or nutrition and a combination of exercise and diet interventional studies, including feasibility studies, and observational studies were included in the search. Dietary and nutrition studies assessing specific diets, nutrient modifications, nutrition timing, quality, dietary patterns, adherence and supplementation were considered. Studies that only included those diagnosed with monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma (SMM) were excluded. Interventional studies that have already been included in past systematic or meta-analysis reviews were not included in the effort to present the most up to date information. Clinical trials listed on ClinicalTrials.gov were reviewed with the same inclusion and exclusion criteria.

2.3 Article screening and data extraction

All search tasks were completed by a single researcher in October and November 2024 and all returned articles were entered in a shared online resource (University of Utah Box Cloud Storage) for screening and data extraction. Two reviewers independently screened the titles, abstracts and content according to the inclusion and exclusion criteria. The full-text articles were independently reviewed and synthesized by two reviewers within Microsoft Excel. As this is a narrative review, no statistical analyses were performed.

3 Findings

The initial search on PubMed retrieved 501 publications. Despite the structured query, a majority (n=492) of the extracted papers were not relevant to the topic of interest or did not meet the inclusion criteria. This review includes nine different studies for

individuals living with MM, comprising of five exercise interventions and four observational studies on diet and/or nutrition (Table 1). Among the five exercise interventions, two were randomized controlled trials, two were single-arm trials, and one was a non-randomized, two-armed, prospective trial where participants were instructed to choose their study arm/intervention for the duration of the trial. Three of these studies implemented individual-based exercise interventions, while two incorporated both individual and group-based exercise, reflecting a mix of social and independent exercise approaches. Regarding diet, two were prospective observational studies, one was a retrospective cohort analysis, and one was a cross-sectional observational study. There were no published studies evaluating exercise and diet together. This review also includes 23 clinical trials registered on ClinicalTrials.gov focusing on exercise and/or diet interventions in individuals with MM, including 15 focused on exercise, five on diet, and three that combined exercise and diet (Table 2).

3.1 Published exercise and physical activity studies

All interventions emphasize the importance of individualized exercise programs tailored to the needs of MM patients for safety and efficacy, patient engagement, and effectiveness (18–22) (Table 1). Additionally, interventions were implemented across the care continuum for all studies, including those who were newly diagnosed (22, 23), receiving first line or other active treatments (18–22), undergoing maintenance therapy (20), and those under active monitoring (18–20). There is noted variability in exercise adherence and patient engagement, with supervised programs showing higher adherence rates; for example, attendance in all supervised session was 88% whereas attendance at home-based, unsupervised sessions was 45.4% (19). The lack of reliable monitoring in unsupervised programs, such as technical issues with syncing devices or limited data collection, was a significant point of weakness where these challenges contributed to reduced adherence and engagement (18). Among individualized programs, various modalities, including telehealth with remote supervision, were found to be effective for both transplant-eligible and transplant-ineligible patients undergoing first line therapy. This includes patients either completing active therapy or under active surveillance (19). Of the five published exercise interventions, four focused on feasibility as the primary outcome (18–21). These trials demonstrated high feasibility and acceptability, however, Jensen et al. (20), had mixed results regarding acceptability. While 50% of patients accepted at least one referral to a supportive care service (e.g., physical therapy, mental health provider, etc.), only 33% accepted a physical therapy referral, while others shared negative experiences or doubts about effectiveness of this service. Hillengass et al. (18) noted that some benefits, particularly in aerobic endurance, were not sustained post-intervention, suggesting a need for follow-up programs or ongoing support for both patients undergoing treatment and those under active surveillance receiving no treatment. Among studies looking at outcomes beyond

TABLE 1 Summary of studies examining Exercise/PA and Diet in MM.

Authors (year)	Country	Study Design	Exercise and/or Diet	Intervention Type or Measurement Tool	Primary Outcome	Key Findings	Timepoint on Cancer Care Continuum
Jensen et al. (2024) (20)	USA	Single Arm Prospective Trial	Exercise	Physical Therapy (PT) referral	Feasibility (Percentage of Referrals Completed)	<ul style="list-style-type: none">50% of patients accepted at least one referral to a supportive care servicePT referrals had 33% acceptance rateMany patients declined PT citing previous experience or doubts of effectiveness	<ul style="list-style-type: none">58% Induction Therapy33% Maintenance Therapy9% No current therapy
Hillengass et al. (2024) (18)	USA	Non-Randomized, Two-Armed, Prospective Trial (Participants were instructed to choose their study arm)	Exercise	6 months Supervised RT 2x weekly OR home-based behavior intervention via FitBit prompts	Feasibility (Proportion of enrolled patients at EOS)	<ul style="list-style-type: none">Improved physical function in supervised groupAerobic capacity improvements not sustained post-interventionUnsupervised group had lower adherence	<ul style="list-style-type: none">85.7% Received treatment (did not specify if active treatment or maintenance)14.3% No current therapy
Purdy et al. (2022) (21)	Canada	Single Arm Prospective Trial	Exercise	12 weeks Tailored exercise program through telehealth Supervised RT, unsupervised aerobic activity	Feasibility (> 21 consented participants over 7 months)	<ul style="list-style-type: none">Program found feasible, with high adherenceImprovements in aerobic capacity, leg strength, core endurance & balancePts reported high satisfaction with program	<ul style="list-style-type: none">14% Transplant ineligible first line active therapy29% Post-stem cell transplant, first line active therapy57% > 2 lines active therapy
Larsen et al. (2024) (22)	Denmark and New Zealand	RCT	Exercise	10 weeks Control arm: usual activity Intervention arm: Supervised RT & aerobic training 3x weekly	Knee Extension Strength (Manual Dynamometer)	<ul style="list-style-type: none">No significant differences in strengthIntervention group had reduced pain & insomnia, improved appetiteBoth groups saw physical function improvements & improved emotional well-being	<ul style="list-style-type: none">Received Induction Therapy
Nicol et al. (2023) (38)	Australia	RCT	Exercise	12 weeks Control arm: usual activity Intervention arm: Supervised one-on-one RT 2x weekly & home-based aerobic training 1x weekly	Feasibility & Safety (Eligibility and consent rates, recorded adverse events)	<ul style="list-style-type: none">Program deemed safe, no AEsAdherence was higher in supervised sessions compared to home-based sessionsImprovements in confidence & motivation	<ul style="list-style-type: none">28.3% Transplant eligible first line active therapy16.7% Transplant ineligible first line active therapy26.7% Active therapy28.3% No current therapy
D'Angelo et al. (2023) (23)	USA	Observation Prospective	Diet	Gut microbiome samples pre- & post-ASCT	Identify associations (Stool samples and disease outcomes defined by IWMG criteria)	<ul style="list-style-type: none">Significant reduction in gut microbiome diversity following ASCT, primarily driven by IV antibiotic exposureDiversity returned to pre-ASCT levels by day +100Higher levels of diversity were significantly associated with CR/VGPR	<ul style="list-style-type: none">Received Induction Therapy
Okamoto et al. (2020) (26)	Japan	Retrospective Cohort	Diet	CONUT scores	Identify associations (CONUT scores and disease prognosis defined by OS)	<ul style="list-style-type: none">High CONUT (>= 5) was identified as an independent prognostic factor for poor OS	<ul style="list-style-type: none">Did not specify current treatment status

(Continued)

TABLE 1 Continued

Authors (year)	Country	Study Design	Exercise and/or Diet	Intervention Type or Measurement Tool	Primary Outcome	Key Findings	Timepoint on Cancer Care Continuum
Borsi et al. (2021) (24)	Romania	Cross-Sectional Observation	Diet	Dietary intake assessment & Nutritional knowledge assessment	Assess nutritional knowledge & diet quality (Dietary intake assessment, Nutritional knowledge assessment, and Myeloma biomarkers)	<ul style="list-style-type: none">High carbohydrate diets & low carbohydrate – high saturated fat diets were associated with worse clinical indicators	<ul style="list-style-type: none">Did not specify current treatment status
Shah et al. (2022) (25)	USA	Observation Prospective	Diet	Gut microbiome samples prior to maintenance therapy	Identify associations (Stool samples and treatment response defined by IMWG criteria)	<ul style="list-style-type: none">Sustained MRD negativity was associated with higher stool butyrate concentration, & higher gut microbiome diversityDiets rich in seafood & plant proteins were correlated with higher stool butyrate concentration	<ul style="list-style-type: none">Did not specify current treatment status

PT, physical therapy; RT, resistance training; EOS, End of Study; RCT, randomized controlled trial; ASCT, Autologous Stem Cell Transplant; AEs, Adverse Events; CR/VGPR, Complete Response/Very Good Partial Response; IMWG, International Myeloma Working Group; CONUT, Controlling Nutritional Status; OS, Overall Survival; MRD, Minimal Residual Disease.

TABLE 2 Summary of studies registered in ClinicalTrials.Gov.

NCT ID#	Status of Study	Study Type	Type of Intervention	Proposed Intervention	Primary Outcome(s)	Specific to MM	Timepoint on Cancer Care Continuum
NCT05642884	Recruiting	RCT; 2 arm (Intervention & control)	Exercise	8 weeks Health coaching & 2x weekly supervised aerobic activity	Feasibility, Adherence (Participation, Completion and Adherence rate)	Yes	<ul style="list-style-type: none">Transplant EligibleUndergoing induction therapy
NCT03946332	Recruiting	RCT; 2 arm (Intervention & Control)	Exercise	Supervised exercise during hospitalization Home-based exercise equipment given at discharge	QoL (EORTC QLQ-C30, and QLQ-MY20)	Yes	<ul style="list-style-type: none">Immediately post ASCT (currently hospitalized)
NCT04484714	Completed	Single Arm (Intervention)	Exercise	12 weeks Virtual supervised group fitness or independent RT & aerobic exercises	Feasibility, Adherence (Percentage of exercise dose completed at EOS)	Yes	<ul style="list-style-type: none">Transplant ineligible – undergoing first line therapyTransplant eligible – post transplantR/R Myeloma with >1 prior lines of therapy
NCT02439112	Completed	RCT; 2 arm (Intervention & Control)	Exercise	10 weeks Supervised tailored RT & aerobic activity	Knee extension strength (Handheld dynamometer)	Yes	<ul style="list-style-type: none">Newly diagnosed – requiring active treatment

(Continued)

TABLE 2 Continued

NCT ID#	Status of Study	Study Type	Type of Intervention	Proposed Intervention	Primary Outcome(s)	Specific to MM	Timepoint on Cancer Care Continuum
NCT04300335	Suspended (COVID-19)	RCT; 2 arm (Interventions)	Exercise	Supervised RT & home-based aerobic activity	Feasibility, Adherence (Adherence rates at EOS)	Yes	<ul style="list-style-type: none"> Post-treatment (does not specify type)
NCT06145581	Recruiting	Single Arm (Intervention)	Exercise	12 weeks Virtual home-based PA sessions including flexibility, walking & breathing, wrist worn activity tracker	Fatigue (BFI and FACIT-F)	Yes	<ul style="list-style-type: none"> Receiving maintenance therapy
NCT01809717	Completed	Single Arm (Intervention)	Exercise	3 months RT with hypertrophy focus	Safety (Number of AEs)	Yes	<ul style="list-style-type: none"> 1 year post treatment (does not specify type) Transplant eligible
NCT04100044	Completed	Single Arm (Intervention)	Exercise	6 months PT tailored home-based RT & aerobic exercise	Adherence, Retention (Fitbit defined physical activity, and percentage of days wear provided Fitbit through EOS)	Yes	<ul style="list-style-type: none"> Post-planned ASCT Transplant ineligible
NCT06280924	Recruiting	RCT; 2 arm (Intervention & Control)	Exercise	10 weeks Informational handouts about exercise Exercise program delivered in-person or virtual	Feasibility, Completion rate (Percentage of participants who complete intervention and follow-up)	Yes	<ul style="list-style-type: none"> Transplant eligible Receiving induction therapy
NCT03135925	Completed	Single Arm (Intervention)	Exercise	6 weeks Weekly supervised exercise	Feasibility, Attendance rate (Number of exercise sessions attended)	Yes	<ul style="list-style-type: none"> Transplant eligible
NCT05142371	Active; Not Recruiting	RCT; 2 arm (Intervention & Control)	Exercise	8 weeks Home-based exercise 3x weekly	Physical Function (SPPB)	Yes	<ul style="list-style-type: none"> Post-transplant
NCT03793907	Completed	RCT: 2 arm (Interventions)	Exercise	6 months Unsupervised walking program tracked via FitBit Supervised RT 2x weekly	Feasibility (Proportion of enrolled participants after 6 months)	Yes	<ul style="list-style-type: none"> Does not specify
NCT04303091	Completed	Single Arm (Intervention)	Exercise	12 weeks Group based exercise 1x weekly Home based exercise recommendations	Feasibility (Proportion of participants who complete the intervention)	Yes	<ul style="list-style-type: none"> Does not specify
NCT05706766	Recruiting	RCT; 2 arm (Intervention & Control)	Exercise	8 weeks Virtually supervised RT & aerobic training 3x weekly	Muscular Strength (Leg Press)	Yes	<ul style="list-style-type: none"> Transplant eligible
NCT05763563	Recruiting	Single Arm (Intervention)	Exercise	4-6 weeks Home-based activity encouraged Optional supervised exercise	Feasibility, Adherence (> 60% eligible and approached patients consent and enroll, and >70% of exercise sessions completed)	No	<ul style="list-style-type: none"> CAR-T eligible
NCT06559709	Recruiting	Pilot; Single Arm (Intervention)	Diet	Plant-based meal delivery service	Feasibility, Tolerability (Proportion of eligible patients to consent, EOS surveys for patient tolerability opinions)	Yes	<ul style="list-style-type: none"> Transplant eligible

(Continued)

TABLE 2 Continued

NCT ID#	Status of Study	Study Type	Type of Intervention	Proposed Intervention	Primary Outcome(s)	Specific to MM	Timepoint on Cancer Care Continuum
NCT04685525	Withdrawn	Single Arm (Intervention)	Diet	Microbiome Supporting Diet	Feasibility, Adherence (Percent of participants with at least 2 out of 3 assessments)	Yes	<ul style="list-style-type: none">• Transplant eligible
NCT04530812	Completed	RCT; 2 arm (Intervention & Control)	Diet	Fermented Milk Supplementation (Kefir)	Metabolism Biomarkers, Pain, Fatigue, Gut Health, QoL (PTH, and EORTC-QLQ-C30)	Yes	<ul style="list-style-type: none">• On active or maintenance therapy
NCT04497961	Recruiting	RCT; 2 arm (Drug 1 + Diet & Drug 2 + Diet)	Diet	Prepared whole food plant-based meals & behavior coaching	Global Health Status (EORTC-QLQ-C30, EORTC QLQ-MY20, and PRO-CTCAE)	Yes	<ul style="list-style-type: none">• Post-first line therapy
NCT04629430	Completed	Single Arm (Intervention)	Diet	Pre-biotic food/drink supplementation 2x daily	Feasibility, Completion Rate (Patient reported intake of at least 2 servings on 80% of study days)	Yes	Transplant eligible
NCT04000880	Active; Not Recruiting	RCT; 3 arm (Interventions)	Diet & Exercise	6 months Web-based coaching regarding diet & exercise Diet & exercise tracking	Diet quality, body weight, PA adherence, sleep quality (Diet recall, and accelerometers for PA and sleep)	No	<ul style="list-style-type: none">• Post-first line therapy
NCT05312255	Recruiting	RCT; 4 arm (Interventions)	Diet & Exercise	6 months Supervised 2x weekly RT FitBit device with prompts Intermittent fasting Propanolol	Immune cell subsets (Flow cytometry)	No	<ul style="list-style-type: none">• Does not specify
NCT05956457	Recruiting	Single Arm (Intervention)	Diet & Exercise	Digital health coaching 1x weekly FitBit device	Feasibility (Retention rate >70%)	Yes	<ul style="list-style-type: none">• Receiving > 2nd line of active therapy

RCT, Randomized Controlled Trial; QoL, Quality of Life; RT, resistance training; EOS, End of Study; R/R, relapsed/refractory myeloma; BFI, Brief Fatigue Inventory; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; AEs, Adverse Events; CAR-T, Chimeric Antigen Receptor T-cell immunotherapy; ASCT, Autologous Stem Cell Transplant; SPPB, Short Performance Battery Test; PTH, Parathyroid Hormone.

feasibility, exercise has been shown to significantly alleviate pain and improve symptoms like insomnia and appetite loss (19, 21, 22).

3.2 Published diet and nutrition studies

Findings related to diet and nutrition studies comprised only of observational studies (Table 1). These studies evaluated dietary patterns, gut microbiome, and nutritional status, in relation to important health outcomes in MM. Dietary patterns such as high-carbohydrate diets, including adequate fat and protein intake, or low-carbohydrate and high-saturated fat diets, with adequate protein intake, have been associated with poorer clinical indicators such as hemoglobin, uric acid, albumin, beta-2 microglobulin and percentage of bone marrow plasma cells, among others (24). Furthermore, gut microbiome diversity is significantly decreased following stem cell transplantation, primarily due to the use of intravenous antibiotics. The loss of diversity is primarily driven by the depletion of species from the *Clostridia* class, *Lachnospiraceae* family, and genera such as *Blautia*, *Ruminococcus*, and *Faecalibacterium*, all of which are independently linked to better outcomes after allogeneic stem cell transplants and CAR-T therapy (23). Notably, it was also found that the presence of butyrate-producing bacteria in MM patients, following plant-based diets, is linked to sustained minimal residual disease (MRD) negativity in those receiving lenalidomide maintenance therapy (25). Additionally, the Controlling Nutritional Status (CONUT) score, a tool used to assess malnutrition risk and predict adverse outcomes, has shown to be a significant prognostic factor in patients with MM, with lower scores indicating higher risk of malnutrition, poorer survival rates and increased complications, particularly among transplant-eligible patients (26).

3.3 Not published but registered on Clinicaltrials.gov

Of the 23 clinical trials regarding exercise and/or diet for individuals diagnosed with MM, there are 15 that include exercise only interventions, five studies focused on diet, and three studies that include both an exercise and diet or nutrition component (Table 2). Nine of the listed trials have been marked “Completed”, 10 are categorized as “Recruiting”, while the remaining four are marked as “Withdrawn”, “Active; Not Recruiting”, or “Suspending – COVID-19.” All trials do not include posted results, do not overlap with previously presented material, and are exclusive to MM survivors with the exception of three trials that include other cancer types such as non-Hodgkin lymphoma, localized kidney or ovarian cancer and other hematological malignancies that are eligible for hematopoietic stem cell transplant. Primary study outcomes varied, but the majority of the trials (n=13) focused primarily on feasibility and/or adherence of the proposed intervention. Exercise interventions vary widely among those proposed, including both supervised and unsupervised individual and group exercise environments, as well as both resistance and/or

aerobic training components. Diet and nutrition interventions include plant-based meal delivery services, pre-biotic food and drink supplements including fermented milk, as well as diet tracking and health coaching. Of the nutrition-based studies, nine reported that supervised training occurs one-on-one; however, only two studies indicated that the exercise would be individually tailored to the individual, with one study considering bone involvement in its programming.

3.4 Patient preferences

Ten publications investigated patient preferences for exercise and diet interventions in MM, and of these, seven employed survey or questionnaire-based methodologies (27–33), providing quantitative insights into patient preferences. The remaining three utilized qualitative interview approaches (34–36), offering a deeper understanding of individual experiences and perspectives. This combination of methods allowed for a comprehensive examination of the current literature, highlighting both broad trends and personal insights into patient needs.

When interviewing patients with MM, Hodge et al. (28) found that only 17% of participants were aware of the American Cancer Society’s nutrition and PA guidelines. Furthermore, 56% of participants reported no direction from their oncology team regarding lifestyle recommendations. The review goes on to identify several unmet survivorship needs including access to dietitians for guidance on healthy eating as well as support and knowledge on safe PA and how to engage in PA while living with MM. An online survey of patients with plasma cell disorders, including MM, showed that the majority of respondents (90%) noted that they were interested in learning more about nutrition research and their diagnosis, with only 15% receiving detailed guidance from their oncology team (27). These themes are echoed in exercise and PA focused studies, including in a post exercise intervention qualitative study conducted by Purdy et al. (35) where participants felt safest and most confident when the exercise was tailored to their specific needs. The desire for patients to learn more about which exercises are safe to perform, how exercise can benefit their overall well-being, and accessibility concerns including conducting virtual exercise visits are all salient themes (29–34). Additionally, interest in a dual-component intervention combining both diet and exercise has been shown among those who are undergoing treatment for MM (28).

4 Discussion

The purpose of this updated review was to highlight the current and ongoing research in exercise and diet interventions among those with MM and highlight the needs and desires of MM patients regarding these interventions. This review builds on previous work highlighting the potential benefits of individualized exercise programs, and potential dietary modifications. Out of the relevant studies found, common conclusions and limitations can be elicited.

Previous reviews of the literature (7, 8, 37, 38) and most recent research regarding exercise and MM emphasized the importance of individualized exercise interventions, specific to the needs of MM patients (19, 20). Exercise programs tailored to the individual have been shown to lead to better adherence, improved safety, and improved patient confidence (18–20). Additionally, supervised exercise programs yield improved adherence compared to unsupervised home exercise programs (18). These outcomes align with patient preferences regarding interventions that will be most beneficial to them not only logistically, but also regarding their confidence in being able to perform PA safely (35).

The lack of available diet intervention research in the MM population speaks to the need of more nutrition-focused research. While current research suggests a promising relationship between diet, gut microbiome health, and MM outcomes, several significant gaps remain (39). There is limited understanding of how to actively modulate the microbiome in MM patients to support post-transplant recovery and disease control (24). Borsi et al. (24) also noted there was a return to pre-transplant microbiome diversity by 100 days post-transplant, which warrants further studies to explore targeted microbiome interventions (e.g., probiotics, dietary fiber, or prebiotics) to prevent diversity loss in the immediate post-transplant period. Although the potential benefits of plant-based diets on clinical outcomes were highlighted (25, 40), no standardized dietary guidelines exist for MM patients. Furthermore, findings on high carbohydrate intake's adverse effects suggest a need for dietary counseling, especially for patients with advanced disease (24). The role of dietary changes and microbiome composition in enhancing drug efficacy, such as with lenalidomide maintenance, is still not well understood; it was found that butyrate-producing bacteria may support sustained MRD negativity (25), yet more research is needed to clarify these interactions to guide optimized dietary recommendations. Additionally, as noted by Borsi et al. (24), MM patients often lack adequate knowledge of their nutritional needs, emphasizing the need for comprehensive dietary education programs and/or counseling that deliver clear, evidence-based guidance on nutrition and microbiome health, both during and after treatment, to help patients make informed dietary choices that may improve treatment outcomes and quality of life. This lack of knowledge correlates with patients expressed desire to learn more about how to maximize their diet to help attenuate treatment side-effects and improve quality of life during their cancer journey (27, 28).

Patient preferences can play a crucial role in the success of PA and diet interventions for MM patients. As noted, studies have shown that MM patients often prefer individualized exercise programs that are tailored to their specific needs, including knowledge regarding safe exercises to complete with bone involvement. Despite this, many ongoing studies do not fully incorporate these preferences into their design. For instance, while supervised exercise programs have been shown to improve adherence, many studies are relying on unsupervised home-based programs that may not provide the necessary support or motivation for patients. Additionally, there is strong interest among patients in understanding how dietary modifications can support them during treatment, and as part of their overall health. The apparent

disconnect between patient preferences and interventions highlights the need for more patient-centered research approaches that prioritize the specific desires and needs of MM patients to facilitate intervention adherence and sustained engagement in the promoted lifestyle behavior of the intervention.

One significant gap in the literature shared by both exercise and diet interventions, is the lack of trials with efficacy of the intervention or effectiveness of the program as the primary outcome. Most trials focused on feasibility of the diet and/or exercise intervention/program as the primary outcome. It is established that exercise and diet interventions and programs are feasible in multiple myeloma across the cancer care continuum, notably during induction and maintenance therapy. Moving forward, more work is needed evaluating the efficacy or effectiveness of such interventions and programs on relevant health outcomes for multiple myeloma patients. Moreover, longer-term interventions (i.e., > 12 weeks) are needed, especially those focusing on the impact of specific dietary patterns, such as plant-based or low-carbohydrate diets, are required to determine if these diets provide lasting benefits. Including studies exclusive to the post-HSCT peri-transplant recovery period, with interventions that explore this time in the cancer care continuum and beyond, is warranted. Additionally, there is a notable lack of studies that explore the associated physiological mechanisms that may be associated with the benefits of exercise and diet interventions on specific outcomes relevant to multiple myeloma patients.

This narrative review highlights the critical need for more comprehensive research on the impact of PA and diet interventions in patients with MM, as well as research that takes into consideration patient's desires. The scarcity of research including diet and/or nutrition interventions, particularly regarding the relationship between the gut microbiome and health outcomes in MM patients, highlights the urgent need for future studies in this area.

4.1 Limitations

Although this narrative review contributes to the field by synthesizing the most recent exercise and diet intervention studies published, as well as ongoing trials, including patient preferences, it is not without its limitations. First, the search was specific to only PubMed and ClinicalTrials.gov, potentially excluding relevant studies not indexed in the searched databases. Additionally, information regarding duration, frequency and mode of exercise was not consistently reported among studies registered in ClinicalTrials.gov.

5 Conclusion

In conclusion, significant gaps remain, including the lack of efficacy studies, dietary interventions to improve health outcomes, and interventions that consider the preferences of patients with MM. By developing integrated lifestyle interventions that align with patient preferences and needs, it is possible to improve adherence

and engagement, as well as address underlying nutritional or physical function needs that could lead to improved quality of life and survival. Through a patient-centered approach, we can better support individuals with MM in managing their condition and improving their overall health.

Author contributions

KM: Conceptualization, Data curation, Investigation, Methodology, Writing – original draft, Writing – review & editing. GS: Investigation, Methodology, Writing – original draft, Writing – review & editing. DS: Writing – review & editing. AC: Conceptualization, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing.

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