

Mobilization and Exercise Intervention for Patients With Multiple Myeloma: Clinical Practice Guidelines Endorsed by the Canadian Physiotherapy Association.

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commercial re-use, please contact journals.permissions@oup.com Abstract Objective Individuals
with multiple myeloma (MM) often have reduced functional performance due to the cancer itself or
as a direct side effect of cancer treatments. Physical therapy is a part of cancer rehabilitation;
however, no guidelines are available to provide information and direction for physical therapists
managing patients with MM. The goal of this guideline is to provide recommendations based on a
systematic review and consensus process that physical therapists can use to manage patients with
MM.

A systematic review of the literature published until August 2018 was performed in 8 databases with
2 independent reviewers assessing quality. Seventeen articles were identified as relevant, and a
draft guideline was developed in the form of action statements. A total of 10 physical therapists with
hematology experience and 10 patients with MM were recruited for consensus process. A priori
threshold of 80% agreement was used to establish a consensus for each statement. The draft

guidelines were reviewed externally by 4 methodologists using the AGREE II tool and a stakeholder representing OH (Cancer Care Ontario) Program in Evidence Based Care, McMaster University. The final guideline was reviewed and officially endorsed by the Canadian Physiotherapy Association.

A total of 30 action statements were developed that achieved consensus, indicating physical therapy recommendations based on physiological markers (ie, hemoglobin, platelet count), complete patient presentation, and the stage of medical treatment.

These clinical practice guidelines were developed to aid physical therapists in implementing evidence-based and best-practice care for patients with MM to optimize rehabilitation outcomes.

These guidelines fill an important knowledge gap and are the first to provide information specifically for physical therapist management of patients with MM.

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Many of these symptoms can potentially be targeted with individualized exercise programs, which may aid in reduced cancer-related fatigue and muscle wasting, 3 better sleep patterns, and better QOL. 4–6 Provided that patients receiving treatment typically become physically inactive, 2–3 it would be imperative to mobilize these patients before, during, and after medical therapy to target any resulting deconditioning. However, there is a lack of specific information to guide safe mobilization and safe activity levels in patients with MM. A scoping review revealed that there are no physical therapy-specific guidelines available for exercise prescription before, during, and after chemotherapy and stem cell transplantation. Thus, the objectives of this study were to (1) develop a set of consensus-based recommendations to help physical therapists make decisions on mobilization and exercise intervention of patients with MM in acute care settings, particularly based on laboratory values (hemoglobin, platelet, and white blood cell counts) and bony lesions; and (2) develop evidence-based recommendations for physical therapy management before, during, and after chemotherapy and stem cell transplantation to improve strength, endurance, functional mobility, fatigue, increased nighttime sleep, and QOL in patients with MM.

A combination of systematic review, critical appraisal, and expert opinion was used for guideline development.

The guideline development steps recommended by the American Physical Therapy Association were followed when drafting recommendations and determining levels of evidence. 33 Recommendations for research questions with inadequate evidence were developed based on a consensus process. 34 Recommendations were made in the form of action statements (AS), and levels of evidence and grades of AS were determined using the recommendations of Kaplan and colleagues. 35 Tables 1 and 2 outline the levels of evidence and grades of recommendations. Refer to the study protocol for further information about the guideline development process. 7

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Definition of Grades of Recommendation for Action Statements a

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A literature search strategy was developed and performed by 2 research assistants (M.L. and Z.M.), as outlined in the study protocol, to understand the research evidence around the physical therapy management of MM. 7 In brief, a reviewer (Z.M.) systematically searched databases and retrieved 48,060 articles with EndNote software, and 28,679 articles were recovered after removing duplicates. Two independent reviewers (Z.M. and M.L.) carefully screened abstracts for inclusion, and 124 potential articles were selected for full-text review. A total 109 articles were excluded (ie, abstracts only, correlational studies, and irrelevance to guideline), and the remaining 15 articles plus 2 additional articles (grey literature) were included for final guideline development (Figure). Each article was critically appraised (Z.M. and M.L.) using the standardized methodological assessment tool outlined in the study protocol. 7 Supplementary Table 1 shows the study characteristics and the critical appraisal scores of each included article.

Preferred Reporting Items for Systematic Reviews (PRISMA) flow diagram.

Completed in 2 parts: The initial draft AS were developed by 2 experienced oncology/hematology physical therapists after reviewing supporting articles and guidelines (AS1–6). The second set of AS (AS7–10) was based on data from the 17 included articles. Recommendations were made in the form of AS, along with levels of evidence and grades, as outlined in the study protocol. 7 An a priori threshold of 80% agreement was used to establish a consensus for each AS, and a quality cut score of greater than 70% was set for AGREE II domains for consideration of the guidelines. 8

Two groups of participants (physical therapists and patients with MM) were recruited for this study. The consensus process was conducted in 2 phases. Phase I involved feedback from physical therapists and Phase II involved feedback from patients with MM. A total of 10 registered physical therapists working in the public sector across Canada who were experienced with oncology populations and able to read, understand, and write in English were recruited for Phase I of the consensus process. Of these, 4 physical therapists were from Ontario, 2 from Winnipeg, 2 from Québec, and 1 from British Columbia and 1 from Alberta. The physical therapists' work experience ranged from 4 to 27 years with tremendous experience working with patients with MM. A total of 10 patients diagnosed with MM admitted to 1 Ontario hospital for cancer treatment and able to speak, read, write, and understand English were recruited for phase II of the consensus process. Participants (physical therapists) for phase I were recruited by 1 investigator (V.R.) through a college of physiotherapy public registry. V.R. contacted potential participants, explained the study, answered questions, and obtained consent through email. One physical therapist and 1 patient withdrew from the study after initially consenting to participate in the study. Phase I consensus process included 3 rounds of email conversation, whereas Phase II involved only 1 round of feedback from patients. Participants were asked to mark either agree or disagree to the proposed statements and to provide their comments for each statement.

A total of 32 AS including sub-statements were sent for Phase I of the consensus process to receive feedback from physical therapists. In the first round, 16 items (item nos. 4c, 4d, 4e, 5b, 7, 8,

8d, 9, 9a, 9b, 9c, 9d, 10, 10a, 10b, and 10c) received 100% consensus to include, 9 items (item nos. 1, 2, 4, 4a, 4f, 5a, 8a, 8b, and 8c) received 89% consensus to include, 3 items (item nos. 3, 5c, and 4b) received 78% consensus to include, and 1 item (item no. 6) received only 67% consensus to include. The focus group recommended rewording some sentences and including additional precautions for a few of the items. Accordingly, the statements were revised based on the feedback from the physical therapists. The research team decided to include item numbers 3, 5c, and 4b, which received 78% consensus. One item (no. 6) was completely revised that received only 67% consensus and sent for a second round of consultation. The item was revised based on feedback and was sent for a third round and received 89% consensus for inclusion in the final guideline. Our research team decided to eliminate 1 AS (acupuncture for pain relief during or after medical treatment) during the first round because the majority of the physical therapists reported that they did not have expertise in acupuncture treatment. A total of 30 AS were developed that achieved consensus (Suppl. Table 2).

The revised guideline was sent for Phase II of the consensus process to receive input from patients with MM. The participants were asked to read each statement and provide their input in the comment box beside each statement. All 10 patients “agreed” with the recommended statements and provided positive comments. None of the patients gave negative comments or recommended to modify the statements.

As per recommendation, 4 methodologists were identified to review these clinical practice guidelines to increase the reliability of the assessment. 8 These methodologists have clinical and research experience, with 3 having a physiotherapy background and 1 with a nursing background. All methodologists recommended this guideline for use (Tab. 3).

AGREE II Domain Scores and Recommendations for Use of This Guideline a

a Quality of guideline score ranges from 1 (lowest possible quality) to 7 (highest possible quality).

b Domain scores were calculated as per the scoring criteria outlined in the AGREE II tool. 8

c Domain scores of $\geq 70\%$ considered a high-quality guideline. 8

Methodological feedback on a draft document was provided by a stakeholder representing the OH (Cancer Care Ontario) Program in Evidence Based Care, McMaster University. The final guideline was reviewed and officially endorsed by the Canadian Physiotherapy Association.

Physical therapist intervention is generally contraindicated in patients with hemoglobin values less than 8 g/dL. 9 It is recommended to take precautionary measures but not to withhold physical therapy for patients with hemoglobin levels lower than 8 g/dL. 9 Evidence shows that patients with levels as low as 7 g/dL (Hgb level) can tolerate physiotherapy, but those patients with cardiac and respiratory conditions are at a higher risk of compromised cardiac output and desaturation. 10 Stiller and Phillips 11 recommend withholding mobilization for patients with levels lower than 7 g/dL. Therefore, while providing care for patients with lower hemoglobin levels (<8 g/dL), physical therapists should monitor vital signs and signs of adverse events (ie, chest pain, pallor, leg cramps, dizziness, arrhythmias, shortness of breath, respiratory distress, SBP > 200 mmHg or DBP > 110 mmHg, drop in SBP > 10 mmHg from the baseline, heart rate increases >120 bpm with activity, SpO₂ levels $<88\%$ with activity, and/or a positive orthostatic response). Lastly, it is strongly recommended that physical therapists liaise with physicians before delivering physical therapist interventions and discuss any additional signs to monitor during therapy sessions.

Patients with MM typically receive a transfusion of red blood cells (RBC) when the Hb concentration is lower than 7 g/dL in stable adults or lower than 8 g/dL in those with cardiac issues. Patients may receive a transfusion for approximately 2 to several hours depending on the number of units of RBCs. Withholding physical therapy solely on the basis of an RBC transfusion might affect patients'

mobility and functional status. It is reported that patients' receiving physical therapist intervention during RBC transfusion did not have any adverse events. 11 It is recommended that patients be monitored closely for abnormal vital signs and other events (ie, dislodging of intravenous site, syncope, and reaction to blood products). 12

Typically, platelet counts may drop following chemotherapy with the lowest count occurring 7 to 10 days post chemotherapy and take 2 to 3 weeks to recover. While bed rest is important in preventing bleeding, multiple weeks of bed rest may cause significant functional decline in older patients with MM. Therefore, it is important to consider the benefits and harms of exercise to prevent functional decline.

There is not a low limit cut-off for suspending all physical activity in patients with thrombocytopenia, particularly in patients undergoing chemotherapy. 14 The Leukemia/Bone Marrow Transplant Program of British Columbia (L/BMT program of BC) recommends limited physical activity when platelet counts are $<15,000/\mu\text{L}$; however, Sekhon and Roy 13 reported risk of bleeding with counts $<10,000/\mu\text{L}$. Interestingly, these authors also report that platelet count is an imprecise predictor of bleeding risk. Overall, given that platelets are typically transfused when the platelet count is $<10,000/\mu\text{L}$, we recommend only essential ambulation (ie, bathroom) with counts $<10,000/\mu\text{L}$. Assistance/supervision and gentle range of motion (ROM) in sitting or lying are recommended to prevent bleeding due to a fall.

The L/BMT program of BC recommends gentle exercises without resistance for patients having platelet counts between 15,000 to 20,000/ μL . The Seattle Cancer Care Alliance recommends strength training and cardiovascular exercises without resistance and strain for patients with platelet levels between 10,000 and 19,999/ μL . 15 Neal et al 16 conducted a retrospective cross-sectional study in 119 patients with cancer admitted to an acute inpatient rehabilitation facility with at least 1 with a platelet count of $<150,000/\mu\text{L}$. Of the 119 patients, 49 had hematologic cancer and there were 56 bleeding events. Interestingly, a higher number of bleeding events (35/56) occurred when the platelets were 51,000/ μL or greater, and these events were not associated with very low counts ($<11,000$ or 11,000–20,000/ μL), all of which suggest that patients with cancer can safely undergo inpatient rehabilitation even with low platelet counts. 16 Therefore, we recommend gentle ROM and strength-training exercises without resistance and without strain for patients with platelet levels between 10,000 and 20,000/ μL to avoid bleeding from high exertional blood pressure. Exercise in standing and ambulation is recommended for platelet levels between 10,000 and 20,000/ μL only if the patient is steady on his/her feet with or without assistive devices and has no signs of bleeding.

The L/BMT program of BC recommends light resistance exercises for patients with platelet levels between 20,000 and 40,000/ μL . 17 However, the Seattle Cancer Care Alliance 38 and the American College of Sports Medicine (ACSM) (exercise recommendations for persons with chronic diseases and disabilities) 14 recommend exercises using elastic bands in patients with platelet counts between 20,000 and 50,000/ μL . Given the variation of the population for which the above guidelines are recommended, we suggest light resistance exercises using elastic bands if no signs of bleeding without strain for patients with MM with platelets between 20,000 and 40,000/ μL . It is also recommended that exercises be performed without strain to avoid bleeding due to possible spikes in blood pressure.

We recommend gentle aerobic activity, including stationary cycling in patients with platelets $>40,000/\mu\text{L}$ in compliance with the L/BMT program of BC. In addition, we recommend avoiding vigorous exercises in patients with levels $<50,000/\mu\text{L}$ in compliance with ACSM and proper use of clothing and equipment to prevent bleeding from trauma.

Therefore, we recommend that physical therapists monitor for signs of bleeding and educate patients about these signs and precautions for prevention. It would be ideal to liaise with physicians as well regarding physical therapist interventions as only a slender line exists between bed rest for preventing bleeding and exercise/physical activity to prevent functional decline in adults with MM admitted in acute care settings. It is recommended physical therapists use their discretion and

clinical judgment in this decision making.

Neutropenia is often present in patients with MM and is an expected side effect following chemotherapy. Although asymptomatic neutropenia is not a medical emergency, neutropenia increases the risk of infection. 18 Febrile neutropenia is an oncologic medical emergency, and patients with febrile neutropenia are often hospitalized for treatment. There are no specific exercise recommendations for patients with leukopenia and neutropenia; therefore, we recommend the following for physical therapy in this population to prevent infection. Patients with MM with neutropenia or leukopenia are immunocompromised, and the use of face masks (barrier for microorganism entry) and regular hand hygiene can reduce their risk of infection. We recommend that patients with MM wear a face mask when ambulating in the hallways and to wash hands properly before and after sessions. Physical therapy equipment and assistive devices should be routinely sanitized before and after use by patients, and physical therapist intervention should be conducted individually in the patient's room to avoid infection and the consequences associated with it. 19

Patients with MM present with myeloma bone disease affecting any part of the skeleton, resulting in bony pain and increased risk of fractures. Bone destruction is primarily mediated by osteolytic metastasis, 20 and it is estimated that 70% to 80% of patients with MM suffer from bone pain, 50% to 60% have fractures, and 2% to 3% have spinal cord compression leading to increased morbidity, poor mobility, and decreased QOL. 21 Evidence supports that exercise improves physical function in patients with cancer, but additional precautions and modifications are necessary in developing an exercise regimen in this population. Bony lesions are not absolute contraindications to physical therapy intervention; however, components of exercise prescription should be modified and additional precautions should be followed to minimize the risk of fractures (ie, avoiding high-impact activities, end range movements, ie, hyper- and rotational movements, that increase compressive and shearing forces, follow back care principles, and use appropriate mobility aids and braces). 22 Physical therapists should be cautious in designing exercises as twisting movements, forward bending, overhead reaching, pushing, pulling, and lifting weights can cause or worsen vertebral fractures in patients with bony lesions. It is also recommended that physical therapists use their clinical judgment and expertise to modify components of programs to fit patient needs.

Exercise for patients with MM may be important and beneficial before, during, and after medical treatment given that exercise, for those with and without cancer, can reduce fatigue and muscle wasting and increase QOL. 3, 6 The first phase (peri-transplant) may be an opportunistic period before deconditioning as the benefits of increased fitness may reduce treatment-related recovery time, 23 creating a platform for better sleep, less fatigue, and better QOL. Unfortunately, limited research is available during this phase. 23, 24 The next phase of the treatment pathway is medical therapy, another critical period for patients with MM both for combating the disease symptoms as well as treatment-related symptoms (poor sleep, increased fatigue, and physical/mental health declines). 3–6 A limited number of research articles report on exercise programs for patients with MM during treatment. 5, 24–28 The last phase, or post-treatment phase, is again a different but critical recovery period. The treatment-related deconditioning, increased fatigue, and reduced QOL could all negatively impact the patient physically and mentally. Multiple studies have assessed the effects of mixed training programs during this phase. 29, 31, 32 Provided that therapy-related deconditioning may result in worsened sleep, fatigue, and QOL, it is important to implement guidelines that may reduce the psychosocial impact. Standard treatment guidelines typically call for bedrest during this phase; however, a more physical activity-based routine may be required to reduce recovery time and aid with these psychosocial aspects.

The research regarding sleep and fatigue outcomes involves strictly home-based, individualized exercise programs during medical therapy. 5, 28 The results suggest that these exercise interventions (low-intensity aerobic/strengthening exercise) during treatment can decrease fatigue and increase total minutes and percentage of sleep. This highlights that exercise may aid with deconditioning and recovery time, 5, 25, 27 which may positively impact psychosocial well-being of these patients. 26, 28

Multiple studies have explored psychosocial factors during 25 27 or after medical therapy. 30–32 The research supporting this guideline for during medical treatment periods tends to incorporate supervised, multimodal, low-intensity aerobic and/or strength/resistance-training regimens, all tailored to individual needs. Although the studies were review based 25 or had a mixed hematological cancer sample, 27 the results identify that patients undergoing medical treatment who are exercise-compliant tend to experience reduced fatigue and better QOL, particularly in physical functioning. After medical treatment, these patients embrace deconditioning and enter the recovery phase. Multiple studies met the criteria for inclusion. 30–32 These programs utilized a combination of high- or low-intensity exercise with both supervised and/or unsupervised sessions to understand the impact on psychosocial well-being. Although no significant differences were identified, all studies highlight decreased fatigue and better QOL than usual care. With little to no adverse events, it would be recommended to follow a tailored exercise program during and after treatment to aid with recovery and deconditioning by improving psychosocial aspects of the patients' lives.

The results of the studies above highlight the importance of exercise during and after medical therapy to positively influence the mental well-being of the patient. Although some of the research obtained above involves mixed MM and hematological samples, the similar treatment pathways suggest that the results may be applicable to patients with MM. Of note, study limitations (mixed and small samples, contamination of control group, etc.) must be considered prior to prescribing exercise to patients with MM during and post-medical therapy. However, given the benefits described above, along with a low risk of harm to the patient, the results suggest that clinicians may prescribe exercise to reduce sleep, fatigue, and QOL issues, pending individualized considerations are met. Further, it was identified that patients with skeletal issues can exercise safely but may ultimately require supervision and thoughtful modifications to their exercise regimen.

Exercise before, during, and after medical treatment may be difficult due to the disease process and/or the aggressive debilitating side effects. As such, a limited number of articles reported physical outcomes of mixed exercise programs for patients with MM before, 24 during, 5 , 25–30 and after medical therapy. 30–32

Before undergoing medical therapy may be the most opportune time to increase aerobic capacity and strength, thereby aiding with the impending deconditioning and recovery process. The research for patients with MM in this phase is limited, but the results suggest that it is safe and feasible as an unsupervised program; however, compliance with strength training was minimal. 23 , 24 Aerobic training in the form of walking may be the preferred modality yet may not provide enough benefit, compared with resistance and high-intensity training, for these patients. 24 More research is required in this phase to understand the impact of exercise in the later stages of the treatment pathway.

Many studies highlight the physical benefits of exercise during and after medical treatment. Functional mobility during and after deconditioning is an important aspect of recovery, as these patients need the strength and aerobic capacity to function with all activities of daily living. During treatment, these patients will typically become inpatients, and supervised exercise or rehabilitation may be implemented at this time. The evidence suggests that this is feasible as no adverse events for either aerobic or strength training exercises were reported, 24–26 with potential for functional mobility and self-care improvements to aid with repatriation to the home environment. 26

Multiple studies have reviewed more specific performance-related outcomes for exercise during the treatment phase, both with full MM samples 5 , 28 , 29 and mixed hematological cancer samples. 28 , 30 , 33 These studies incorporate home-based or supervised, tailored exercise programs on physical performance benefits (aerobic capacity, muscular strength, and physiological changes). As expected, all patients typically experienced declines in physical performance, yet the trends suggest that exercise, if adhered to, reduces this impact, allowing patients to maintain close to baseline scores. 5 , 29 , 30 Specifically, these programs may allow for an increase in aerobic

capacity and muscular strength compared with usual care 27 and, not surprisingly, support a higher rating of good overall condition, more physical activity, and better integration into daily life.

The last phase of the treatment pathway, post-therapy, incorporates 2 accepted studies. 31 , 32 Home-based, tailored programs can benefit patients in terms of strength, body composition, and physical activity. The clinically important trends highlighted that more patients had maintenance of body composition and higher rate of weekly physical activity, again with aerobic training (walking) as a preference. In terms of strength, all patients experienced a decline from baseline, but those who exercised had a less severe decline. The research for post-treatment exercise suggests benefits of early intervention for stable, mixed hematological patients to support early recovery.

The evidence for physical benefits of exercise before, during, and after treatment exists for patients with MM. These mixed, individualized exercise programs may create a stronger physical base prior to treatment and reduce the impact during the deconditioning phase, possibly reducing recovery time. With multiple articles suggesting this patient population can adhere to a tailored regimen, we recommend that physical therapists utilize these guidelines to develop physical activity-based treatment plans at all stages of the medical therapy pathway. It is clear however, that they must take into consideration all aspects of the patient's health when determining these plans in order to avoid unnecessary injury or complications during an already complex health situation. Further, those with skeletal issues can still exercise but may require supervision and motivation to follow through with any program. Overall, these studies have limitations (ie, retrospective design, small/mixed sample sizes), but the trends support both supervised/unsupervised and tailored exercise for this population during all stages of the treatment protocol, and, generally speaking, this can be inexpensive and require minimal resources while potentially providing multiple physical and mental benefits.

A quick scoping review was conducted in June 2020 by 1 of the original investigators (Z.M.) to identify any new evidence supporting or conflicting with the current views of this guideline. The review uncovered 8 articles that met the inclusion criteria set for the current guideline. Of note, these articles were not included in the current guideline development process but will be included in the 2025 guideline update.

In terms of interventional studies, the results highlight similar trends as mentioned throughout this guideline. With regards to feasibility, multiple studies deemed exercise pre-treatment and during medical treatment to be successful (excellent adherence rate, no adverse events), particularly as a positive emotional impact prior to the deconditioning. 36 , 38 , 39 , 41 Other studies assessing exercise during and post medical treatment focused highly on individualized exercise in which daily laboratory values were utilized to make exercise adjustments. With outcomes focused on fatigue, fitness, and QOL, the trends suggest that exercise can be beneficial, supporting the current guideline in that exercise may have a multimodal positive or neutral effect throughout the deconditioning process. 37 , 39–41 These recent findings further extend our understanding that this patient population requires highly individualized exercise to optimize their treatment pathway. In terms of new research, a study found that inspiratory muscle training plus conventional physical therapy may aid with reduced negative symptoms (ie, less need for oxygen therapy) compared with conventional physical therapy alone. 40 The current guideline does not explore inspiratory breathing specifically, and thus these results pose an interesting new pathway for future research.

The results of the 2 meta-analyses 42 , 43 suggest that exercise has a neutral or positive effect on most outcomes studied in the literature thus far, with more possible positive effects on muscle strength, 43 fatigue, 42 , 43 and QOL. 42 , 43 A subgroup analysis also suggests pre-transplant exercise has a favorable effect on upper/lower body muscle strength, fatigue, and QOL, but there were no effects on anything except QOL for all other treatment stages. 43 Interestingly, the results from Knips and colleagues 42 suggest no clear evidence on the majority of outcomes but indicate that the number and size of trials need to increase significantly. Unfortunately, there is still minimal literature in this field, and this limits the results of both of these meta-analyses. In addition, Mohammed et al 44 conducted a literature review and developed a protocol for patients undergoing

hematopoietic stem cell transplantation, and it supports the recommendations proposed by our group.

Since August 2018, the published studies generally support the evidence for individualized exercise throughout the treatment process in this patient population. The current guideline has evidence to suggest that exercise is important throughout the treatment process to combat deconditioning, of which the most recent research furthers our understanding. As most of the newly published research are feasibility studies, there is a need for large, randomized, and multicenter studies for strictly patients with MM. This said, the topic of individualized exercise across the treatment pathway for patients with MM is continuously moving forward, and the results suggest that it is feasible, safe, and effective for this patient population.

These guidelines included a physical therapist intervention in multiple settings, such as acute care, outpatient department, and home environment, and these variables may affect the translation of evidence into practice. Physical therapists should assess their own practice environment and use their clinical skills to implement the AS based on patients' needs. We recommend that the following strategies be implemented in practice: (1) keep a copy of these guidelines at your practice; (2) share these guidelines with your peers (physical therapists) and patients, and with the physicians, oncologists, and hematologist of your patients who are interested in learning about physical therapy for MM; and (3) build relationships with referral sources to encourage early referrals of patients with MM. We are planning to revise these guidelines in 2025 based on the feedback from physical therapists and their patients and findings from updated literature reviews.

This guideline was developed with a combination of systematic review and critical appraisal as well as with expert opinion. In this sense, the guideline may lack adequate evidence, particularly with the latter. However, to increase the merit of this guideline, a multidisciplinary team was utilized. This team consisted of researchers, physical therapists (with oncology/hematology experience), an exercise physiologist, a physician, and a direct consultation with a hematologist. The ASs were also reviewed by physical therapists with specific experience in treating patients with MM, which further strengthens the validity of the guideline. Furthermore, this guideline was reviewed and rated by methodologists with clinical and research experience in oncology.

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