Safety, Feasibility, and Acceptability of a Multisite Individualized Exercise Intervention for People with Multiple Myeloma

JENNIFER L. NICOL[1,2], BRENT J. CUNNINGHAM[1], CARMEL WOODROW[3], KIRSTEN N. ADLARD[1], ZOE E. PAPINCZAK[1], ROSALIND R. SPENCE[1,4], ALEXANDER N. BOYTAR[1], PETER MOLLEE[3,5], NICHOLAS WEBER[6], ANDREW J. NICOL[7], MICHELLE M. HILL[2,8], and TINA L. SKINNER[1]

[1]School of Human Movement and Nutrition Sciences, The University of Queensland, Brisbane, Queensland, AUSTRALIA; [2]QIMR Berghofer Medical Research Institute, Brisbane, Queensland, AUSTRALIA; [3]Haematology Department, Division of Cancer Services, Princess Alexandra Hospital, Brisbane, Queensland, AUSTRALIA; [4]Menzies Health Institute, Griffith University, Brisbane, Queensland, AUSTRALIA; [5]School of Medicine, The University of Queensland, Brisbane, Queensland, AUSTRALIA; [6]Haematology, Cancer Care Services, Royal Brisbane and Women's Hospital, Queensland, AUSTRALIA; [7]Brisbane Clinic for Lymphoma, Myeloma and Leukaemia, Greenslopes Private Hospital, Brisbane, Queensland, AUSTRALIA; and [8]Centre for Clinical Research, Faculty of Medicine, The University of Queensland, Brisbane, Queensland, AUSTRALIA

BASIC SCIENCES

ABSTRACT

NICOL, J. L., B. J. CUNNINGHAM, C. WOODROW, K. N. ADLARD, Z. E. PAPINCZAK, R. R. SPENCE, A. N. BOYTAR, P. MOLLEE, N. WEBER, A. J. NICOL, M. M. HILL, and T. L. SKINNER. Safety, Feasibility, and Acceptability of a Multisite Individualized Exercise Intervention for People with Multiple Myeloma. *Med. Sci. Sports Exerc.*, Vol. 55, No. 12, pp. 2214–2227, 2023. **Introduction:** High rates of disease- and treatment-related symptoms, such as bone lesions, in people with multiple myeloma (MM) create uncertainty on the safety and feasibility of exercise. This study determined the safety, feasibility, and acceptability of an individualized exercise medicine program for people with MM at any disease stage. **Methods:** A multisite, randomized waitlist-controlled trial was conducted of an individualized, high-intensity aerobic, resistance, and impact-loading exercise program. The exercise sessions were supervised twice weekly by accredited exercise physiologists, with one additional unsupervised session per week, for 12 wk. Safety was determined by number of adverse and serious adverse events. Feasibility outcome measures were study eligibility, recruitment, adherence, and attrition. Acceptability was determined by qualitative interviews and subjective levels of enjoyment. **Results:** Of 203 people with MM screened, 88% were eligible, with 34% accepting participation (60 people) and 20% attrition for the between-group analysis, meeting *a priori* criteria (≥25% and <25%, respectively). No adverse or serious adverse events attributed to testing and/or exercise training were reported. Attendance at supervised exercise sessions was 98%, with 45% completion of the home-based exercise sessions. Adherence rates were 35%, 63%, and 34% for the aerobic, resistance, and impact-loading protocols, with 55%, 80%, and 37% of participants meeting *a priori* criteria (75% of protocol). Acceptability of the exercise program was high (mean, 82%; 95% confidence interval, 78%–87%) and highly supported by qualitative responses. **Conclusions:** An individualized, high-intensity aerobic, resistance, and impact-loading exercise medicine program is safe and acceptable, and feasible by some measures for people with MM. Adherence to the prescribed exercise protocols was limited by comorbidities and disease symptoms. Strategies to improve unsupervised exercise completion are warranted in this population. **Key Words:** ADHERENCE, RANDOMIZED WAIT-LIST-CONTROLLED TRIAL, IMPACT LOADING, HIGH-INTENSITY INTERVAL TRAINING

Multiple myeloma (MM), an incurable cancer of plasma cells, is the second most common hematological malignancy and accounts for 1% of all cancers (1). In 2019, the age-standardized incidence rate worldwide was 1.92/100,000 persons (95% confidence interval (CI), 1.68–2.12), with Australasia having the highest rate in the world (5.33/100,000 (95% CI, 4.21–6.8)) (2). The median age range at diagnosis is approximately 66–70 yr, being extremely rare in those younger than 30 yr, with a slightly higher incidence in men (54.3%) (2). The incidence has increased globally by 126% from 1990 to 2016 (3). In addition, the 5-yr relative survival at diagnosis has improved significantly; for example, in the United States, it has increased from 23.7% in 1976 to 53.9% in 2016 (4). This is the result of improvements in the treatment of MM that have occurred over the same time frame, beginning with the use of autologous stem cell transplantation (ASCT) and followed by the availability of novel treatments, such as immunomodulatory drugs and proteasome inhibitors

Address for correspondence: Jennifer L. Nicol, Ph.D., School of Human Movement and Nutrition Sciences, Cnr Blair Drive and Union Road, St Lucia, QLD 4072, Australia; E-mail: j.nicol@uq.edu.au.

Submitted for publication February 2023.
Accepted for publication July 2023.
Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.acsm-msse.org).

0195-9131/23/5512-2214/0
MEDICINE & SCIENCE IN SPORTS & EXERCISE®

DOI: 10.1249/MSS.0000000000003267

(5). Hence, the number of people living with MM has increased and is predicted to rise further as the population continues to age (2).

Although people with MM are living longer, they report the most limitations in the ability to perform moderate and vigorous physical activities and tasks of daily living, with MM second only to lung cancer for the highest psychological distress and lowest quality of life of any cancer type (6). Bone disease is a frequent early manifestation of MM, with 70%–80% of patients presenting with osteolytic bone lesions and/or osteoporosis at diagnosis (7). Approximately 60% of people with MM will experience a pathological fracture (8). In addition, disease- and treatment-related peripheral neuropathy is common (9), and most patients experience some degree of steroid-induced myopathy (10). High levels of fatigue and pain are often reported (11). Cumulatively, through effects on the desire and/or ability to partake in activities of daily living, these symptoms contribute to the reduced quality of life experienced by this population (11). Overall, the symptom burden from the expanding cohort of survivors warrants investigation into interventions that can improve quality of life and maintain independence.

Exercise has been proven to be beneficial for reducing disease- and treatment-related side effects in people living with and beyond cancer, including hematological malignancies (12). However, the high rate of bone lesions in people with MM raises concerns for the safety of physical testing and exercise participation in this population. Results from a survey of hematologists showed that approximately half were concerned about recommending exercise when their patient with MM had spine fractures (52.9%) or was physically unwell (55.9%) (13).

Only six randomized controlled trials and one retrospective chart review have investigated the effects of exercise in people with MM (14). The exercise interventions were implemented with participants when MM treatment began, approximately 10 wk after the start of induction therapy, or after ASCT (14). There were no serious adverse events (SAE) reported among these studies; however, the mean age was 60 yr (range, 55–68 yr), and only one study included people who have relapsed ($n = 8/41$) (15), despite those with recurrent disease representing a significant portion of the population of people with MM (32.7%) (11). The aforementioned exercise interventions comprised aerobic and/or resistance exercises and stretching. Only one study included maximal cardiopulmonary and musculoskeletal exercise testing (16), and no exercise protocols included high-intensity aerobic and hard-intensity resistance training, which is required for the optimal measurement and time-efficient improvement of cardiorespiratory fitness (17,18) and neuromuscular strength (19,20), respectively. Furthermore, research is yet to explore the safety of bone-loading activities designed to optimize bone health.

Typically, exercise interventions in other cancer populations report high attendance in the research setting, although adherence reporting has often been poorly described (21,22). Indeed, the studies exploring the effects of exercise in people with MM all failed to report adherence to the exercise interventions (14). People with MM are, on average, older (5) and experience more symptoms and side effects that may limit their ability to attend and/or adhere to exercise than other cancer populations (23). For example, many MM treatment regimens contain corticosteroids, which cause muscle wasting and contribute to fatigue, reducing the capacity to attend and/or fully participate in exercise training (10,24). The time involved with hospital and outpatient appointments for MM treatment, particularly during the first year of diagnosis (median, 77 d; interquartile range, 55–105 d), may also restrict the opportunity to attend exercise programs (25). Collectively, this has the potential to limit the feasibility of exercise training in this population.

Findings from our survey of 126 people with MM were that around half reported that they were interested in attending an exercise program (26). However, previous exercise studies in MM have reported attrition rates of 11%–42%, with a mean attendance of 80% (range, 58%–96%) (14). Koutoukidis et al. (16) reported that 43% (38/89) of people allocated to the exercise intervention declined participation, with the most common reasons being time and travel constraints. Whether the substantial physical and mental health impairments commonly experienced by people with MM will hinder the acceptability of an exercise program is yet to be explored.

The primary aim of this study was to determine the effect of an individualized exercise intervention on health-related quality of life for people with MM across all disease stages, in addition to determining the safety, feasibility, and acceptability of the program. Here we report the outcomes for the safety, feasibility, and acceptability of the exercise intervention. Results of the efficacy of the study will be reported separately. The study aligns with recent attendance and adherence reporting recommendations for exercise oncology trials, which includes collecting data on cumulative dose (sets/repetitions/load) and tolerability (dose interruptions and modifications) (27). In addition, the safety and feasibility of common exercise physiology testing procedures were evaluated. The information obtained will guide the design of future exercise medicine programs in this understudied population.

METHODS

The study design, recruitment, and procedures have been described elsewhere (28). Written informed consent was obtained from all individual participants included in the study. All procedures involving human participants were in accordance with the ethical standards of The University of Queensland and with the 1964 Helsinki Declaration and its later amendments. The study was approved by the Human Research Ethics Committees of Greenslopes Private Hospital (No. 18/58 GREC), Metro South Hospital and Health Services (No. HREC/2019/QMS/47400), The University of Queensland (No. 2018002644/18/58 UQ HREC), and QIMR Berghofer Medical Research Institute (No. P2352). This trial was prospectively registered on March 12, 2019, with the Australian New Zealand Clinical Trial Registry (ACTRN12619000387123).

Participants

People at any stage of MM were eligible to participate. Inclusion criteria included being free of any musculoskeletal, neurological, respiratory, metabolic, or cardiovascular conditions that may prevent safe completion of the exercise demands of the study; ability to give informed consent; and ability to attend participating sites across southeast Queensland, Australia, to complete exercise training sessions and The University of Queensland for the testing sessions.

Experimental Design and Intervention

Briefly, participants underwent baseline testing (T1; Fig. 1) before they were stratified by disease stage (first-line transplant eligible, first-line transplant noneligible, relapsed, no active therapy) and randomized to exercise (EX) or waitlist control (WT) groups. Participants in the WT group were asked to maintain their current physical activity levels, whereas those in the EX group undertook a 12-wk individualized program that included twice-weekly sessions supervised one-on-one by an accredited exercise physiologist (AEP), with one additional self-guided home-based session prescribed per week. Each 60-min session consisted of high-intensity aerobic training, moderate-to-hard neuromuscular strength training, and bone-loading exercises (Supplemental Table 1, Supplemental Digital Content, Exercise intervention summarized according to TIDieR and CERT checklists, http://links.lww.com/MSS/C893). Testing was repeated after 12-wk for both groups (T2; Fig. 1), at which time, the WT group began the 12-wk exercise intervention with repeat testing at T3 (Fig. 1). Follow-up testing for both EX and WT groups was conducted at 3 and 9 months after intervention to monitor stepped-down (T4; Fig. 1) and self-guided maintenance (T5; Fig. 1) phases. During the COVID-19 pandemic, exercise sessions for existing participants were transitioned to home-based, online delivery, with a reduced testing battery conducted using COVID-safe protocols.

Adherence was enhanced during the in-person sessions through the supervision and encouragement of the AEPs. Behavior change techniques were utilized, including those known to improve adherence, such as goal setting, setting of graded tasks, and instruction of how to perform the behavior (30). For the home-based unsupervised sessions, the AEP used motivational interviewing techniques during the in-person sessions to identify and navigate barriers and challenges, while providing assistance with planning to establish habit formation.

Outcome Measures

Safety. Safety was measured through a record of any adverse event (AE) or SAE. AEs were defined as any untoward physical or medical issue that had a causal relationship with the exercise program. SAEs were events that required further medical attention, such as hospitalization. AEs and SAEs were recorded by the supervising AEP via observation (during sessions) and by questioning participants at each supervised session about any AE/SAE experienced during and/or between sessions ("How were you feeling following our last session? Has there been anything that has happened since I last saw you that has limited your ability to complete exercise, including pain, discomfort, or adverse events."). Where an AE/SAE occurred, details of the incident/injury, whether it was deemed (by both the participant and AEP) to be related to the exercise, and pertinent treatment and recovery information were recorded, including sufficient information to differentiate AEs and SAEs (e.g., requirement of medical management).

Safety of testing sessions was measured by any AE/SAE (including pain) reported or observed during the session and test completion rates on four (EX group) or five (WT group) separate occasions across a 12- or 15-month time frame.

Feasibility. ***Eligibility and uptake.*** Participation feasibility was measured by eligibility and uptake rates, with reasons for noneligibility and declining to participate recorded.

Attrition. The number of study withdrawals and reasons for withdrawal were recorded by the study investigators.

Attendance and Adherence. Exercise prescription feasibility was measured by attendance (defined as follows: $n_{\text{sessions attended}} \times n^{-1}_{\text{sessions prescribed}} \times 100$) at the 24 supervised and 12 unsupervised sessions, and adherence to the exercise prescription across 24 supervised exercise sessions as documented by the supervising AEP. Attendance for the home-based sessions was collected by the supervising AEP via the participants' self-report at each subsequent in-person session. Criteria for determining adherence to each component of the intervention protocol are described in Table 1.

Factors that may have influenced adherence (e.g., pain and fatigue) were measured by the AEP at the commencement of each exercise session using a visual analog scale of 0 to 10, where 0 corresponded to no pain/fatigue and 10 to worst pain/fatigue.

Acceptability. Enjoyment was measured during the exercise intervention at four-weekly intervals, by the completion of the Physical Activity Enjoyment Scale 8 (PACES-8) survey (37). To gain an in-depth understanding of the experiences of participants and the factors that facilitated or inhibited program feasibility and acceptability, semistructured interviews were conducted after completion of the intervention and 3-month stepped-down intervention (T4; Fig. 1). Two interviewers external to the study team with experience in qualitative interview techniques conducted the approximately 45-min face-to-face interviews using a standard script (see Supplemental Table 2 and text, Supplemental Digital Content, which includes a table of interview questions and the interview script, http://links.lww.com/MSS/C893). Interviews were audio recorded and then transcribed by an external transcription company.

Statistical Analysis. Descriptive statistics were analyzed using the Stata statistical software package (version 15.0; StataCorp, College Station, TX). The analysis was based on intention-to-treat. Medical and demographic data were collected and presented for all included participants and for each group separately (EX and WT groups). Rates of AEs, SAEs, eligibility, recruitment, attrition, attendance, adherence, and acceptability are presented in numbers and percentages, as well as completion rates of physical tests. To account for

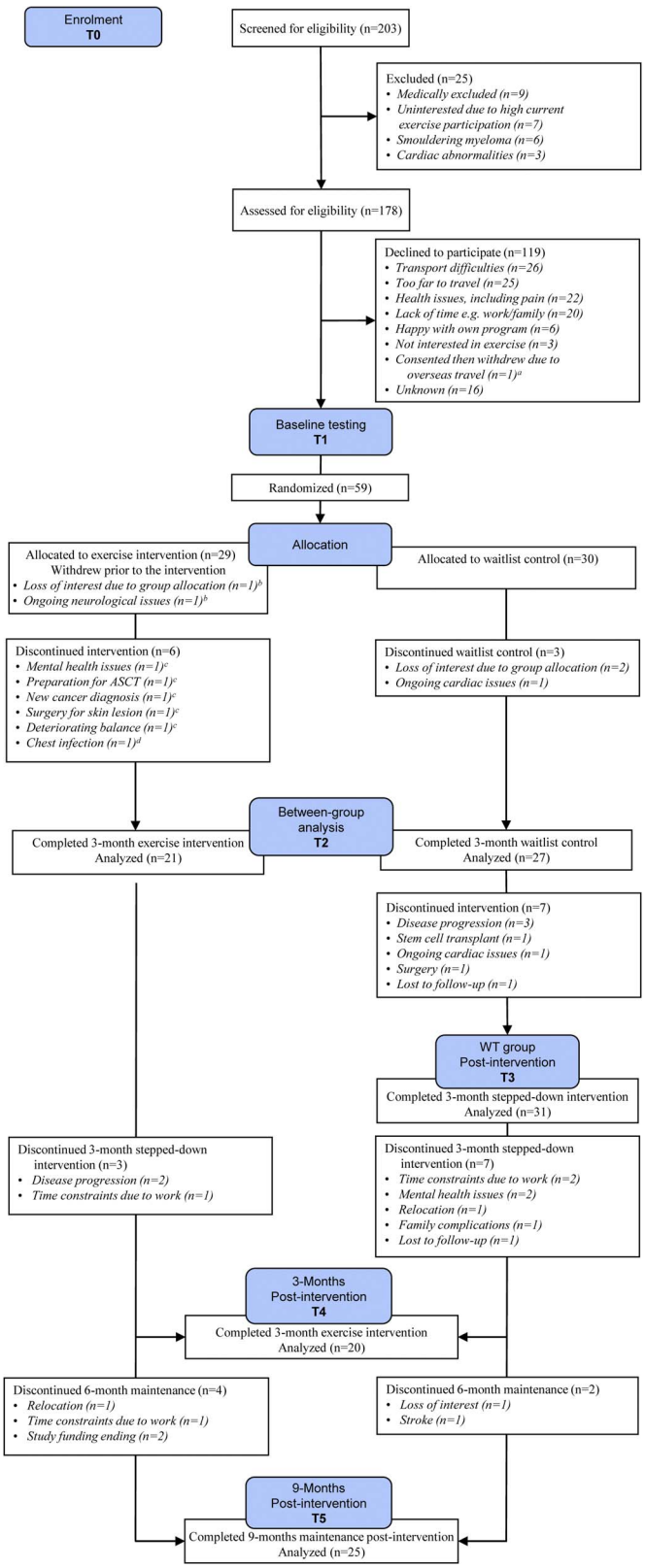

FIGURE 1—Flowchart based on the CONSORT 2010 flow diagram (29). [a] One participant withdrew before completing baseline testing. [b] Two participants completed baseline testing then withdrew. [c] Five participants discontinued the intervention at weeks 2, 4, 6, 10, and 12, respectively. [d] One participant completed the intervention but did not return for follow-up testing. T0, enrollment time point; T1, baseline prerandomization time point; T2, post–3-month time point for both EX and WT groups; T3, postintervention testing time point for WT group; T4, 3-month postintervention testing time point; T5, 9-month postintervention testing time point.

TABLE 1. Criteria for adherence to the components of the exercise intervention.

Component	Criteria for Adherence	Notes
Aerobic training	8 min high intensity (>85% HR_{peak}), +12 min moderate-to-vigorous intensity (60%–85% HR_{peak})	HR_{peak} defined as highest heart rate achieved during CPET at T1. Where a participant did not achieve his or her $\dot{V}O_{2max}$ (defined as a plateau in oxygen consumption with an increase in work rate (31)) at T1 (i.e., achieved a $\dot{V}O_{2peak}$ or invalid test result, defined as termination of the test before a reaching a plateau in oxygen consumption, or a ventilatory threshold, respectively (31)). HR_{peak} was used to inform subsequent exercise training intensities (calculated according to the following equation: peak heart rate = 208 – (0.7 × age in years) (32).
Resistance training	≥80 reps (e.g., 5 exercises × 2 sets × 8 reps) performed at an intensity of ≥5/10 on the OMNI-RES scale per session (33)	
Impact loading	≥160 impacts per session (e.g., 4 × 20 impacts per leg, which may be completed bilaterally or unilaterally) at an intensity of 1.1–5.1 × body weight GRF (i.e., marching, stomping, jumping, or drop jumping from a height) (34–36)	Where pelvic, axial skeleton (lumbar), or lower limb bone lesions were present, isometric exercises targeting the spine and pelvis in positions of support, e.g., supine, prone, or seated, were performed.

GRF, ground reaction force; HR_{peak}, peak heart rate; OMNI-RES, Omnibus Resistance Exercise Scale of Perceived Exertion (33); reps, repetitions; T1, baseline testing.

progression toward meeting the exercise protocol, data for each component of the exercise intervention were subanalyzed for the first month and the subsequent 2–3 months. Linear mixed models were used to analyze the change in reported pain and fatigue throughout the intervention, with individual participants included as a random effect. The *a priori* criterion for safety was zero SAEs attributed to exercise. Cutoff values for the feasibility criterion (an acceptance rate of ≥25% of eligible participants, an attrition rate of <25%, and attendance and adherence of ≥75%) were established *a priori* as clinically relevant based on previous studies in other advanced cancers and with bone metastases (38–40). Criterion for acceptability was a mean response of >75% for the PACES-8 survey, based on previous studies of exercise enjoyment in older adults (41).

Qualitative Analysis

Semistructured interviews were analyzed in NVivo version 12 Plus (QSR International, Chadstone, Australia) using thematic analysis (42,43). The interviews were coded independently by three coders (Z. P., A. C., and A. B. P.). First, the coders used a deductive approach to code the interview data to prespecified topics that were of key interest to the research (i.e., patient experiences with the program, beneficial aspects of the program, reasons for participation, suggestions to improve the program, and appeal of the program to the wider community). A deductive coding framework was developed by the coders *a priori* to guide this initial stage of analysis and maintain intercoder consistency. Next, the coders used an inductive approach to open-code the data within each topic area. This process involved generating initial codes that described the content of the data, then collating codes that described similar content into potential themes and subthemes. Throughout this second phase of analysis, the coders iteratively generated an inductive coding framework and met regularly to ensure these codes were consistently applied. Lastly, the coders met to discuss and agree upon the final themes and subthemes, and to identify supporting quotes. An *a priori* criterion of quotes from 10 participants was established as the threshold for a theme, and quotes from five participants as the threshold for a subtheme. Therefore, the resultant themes and subthemes are those that were most commonly cited in the data, and provided the most significant information to answer the research questions.

RESULTS

Quantitative Results

Eligibility and uptake. Of 203 people screened at T0 between April 2019 and September 2020, 178 met the inclusion criteria (88% eligibility; Fig. 1). Of the 178 eligible people, 60 agreed to participate in the study (34% recruitment rate).

Baseline characteristics of the participants are summarized in Table 2. The mean age of participants was 65.0 yr (SD, 9.0 yr; range, 45–79 yr), with 35% older than 70 yr. Eighty percent had lytic bone disease, with a further 13% experiencing other skeletal complications (e.g., osteopenia, osteoporosis, and osteoarthritis). The two groups (EX vs WT) were comparable in age, Eastern Cooperative Oncology Group (ECOG) status, fatigue, presence of skeletal fractures or osteolytic lesions and other skeletal complications, and disease stage.

Attrition. Of the 60 participants who provided written informed consent, 12 withdrew from the study for the between-group analysis at T2 (20% attrition), 8 (28%) of whom were from the EX group, 3 (10%) were from the WT group, and 1 withdrew before randomization. Two of the EX group participants withdrew after baseline testing because of loss of interest (n = 1) and an ongoing neurological issue (n = 1). Five EX group participants withdrew during the exercise intervention; one at week 2 because of mental health issues, one at week 4 because of lack of time/interest after commencement of conditioning for ASCT, one at week 5 because of investigations for a new cancer diagnosis, one at week 10 because of surgery for a skin lesion, and one at week 12 after completing 23 supervised sessions, because of a urinary tract infection causing fever, malaise, and development of deteriorating balance. One EX group participant withdrew after completing all supervised sessions but before completing follow-up testing, because of development of a chest infection. The withdrawals from the WT group before testing at T2 were due to loss of interest (n = 2) and ongoing cardiac health issues (n = 1). Seven WT group withdrawals occurred before testing

TABLE 2. Characteristics of the study participants (n = 60; n (%)).

	All (n = 60)	EX (n = 29[a])	WT (n = 30[a])
Age (yr)	65.0 (9.0)	67.1 (9.1)	62.9 (8.6)
≤49	4 (6.7)	2 (6.9)	2 (6.7)
50–59	14 (23.3)	4 (13.8)	10 (33.3)
60–69	21 (35.0)	9 (31.0)	11 (36.7)
70–79	21 (35.0)	14 (48.3)	7 (23.3)
Sex			
Male	47 (78.3)	21 (72.4)	25 (83.3)
Relationship status			
Married/partnered	46 (76.7)	22 (75.9)	24 (80.0)
Separated/divorced/widowed/single	14 (23.3)	7 (24.1)	6 (20.0)
ECOG status			
0	32 (53.3)	14 (48.3)	17 (56.7)
1	27 (45.0)	14 (48.3)	13 (43.3)
2	1 (1.7)	1 (3.4)	0
Disease stage			
First line, transplant eligible	17 (28.3)	8 (27.6)	8 (26.7)
First line, transplant noneligible	10 (16.7)	5 (17.2)	5 (16.7)
Relapsed	16 (26.7)	8 (27.6)	8 (26.7)
In remission (no active therapy)	17 (28.3)	8 (27.6)	9 (30.0)
Previous or ongoing antimyeloma therapy			
ASCT	36 (60.0)	13 (44.8)	22 (73.3)
Irradiation	10 (16.7)	4 (13.8)	6 (20.0)
Proteosome inhibitor containing	46 (76.7)	22 (75.9)	24 (80.0)
IMiD containing	33 (55.0)	17 (58.6)	16 (53.3)
Carfilzomib containing	8 (13.3)	3 (10.3)	5 (16.7)
Daratumumab containing	7 (11.7)	4 (13.8)	3 (10.0)
Current therapy with dexamethasone	34 (56.7)	19 (65.5)	14 (46.7)
Current therapy with bisphosphonates	46 (76.7)	24 (82.8)	22 (73.3)
Concurrent opioid use	15 (25.0)	7 (24.1)	7 (23.3)
Skeletal fractures or osteolytic lesions	48 (80.0)	25 (86.2)	23 (76.7)
Spine	42 (70.0)	21 (72.4)	21 (70.0)
Pelvis	18 (30.0)	11 (37.9)	7 (23.3)
Ribs	16 (26.7)	10 (34.5)	6 (20.0)
Femur	10 (16.7)	3 (10.3)	7 (23.3)
Humerus	6 (10.0)	3 (10.3)	3 (10.0)
Other	13 (21.7)	6 (20.7)	7 (23.3)
Presence of other skeletal complications	40 (66.7)	21 (72.4)	19 (63.3)
Osteoporosis (T score ≤ −2.5 at femoral neck)	4 (6.7)	2 (6.9)	2 (6.7)
Osteopenia (T score < −2.5 to <−1.0 at femoral neck)	33 (55.0)	17 (58.6)	16 (53.3)
Osteoarthritis	3 (5.0)	2 (6.9)	1 (3.3)
Low back pain	7 (11.7)	4 (13.8)	3 (10.0)
Low lean mass[b]	17 (28.3)	11 (37.9)	6 (20.0)
Clinical fatigue[c]	22 (36.7)	8 (27.6)	14 (46.7)
Moderate-vigorous physical activity, mean (SD) (range), min·wk^{-1}	100 (179) (0–960)	110 (226) (0–960)	94 (126) (0–420)
Meeting PA guidelines[d]	17 (28.3)	7 (24.1)	10 (33.3)

[a]One participant withdrew before completing baseline testing so was not randomized.
[b]Appendicular lean mass/body mass index <0.789 m^2 for men and <0.512 m^2 for women (44).
[c]Score of <34 on FACIT-Fatigue, as defined appropriate for people with cancer (45).
[d]Clinical Oncology Society of Australia physical activity guidelines for people with cancer, defined as accumulating at least 150 min of moderate-intensity or 75 min of vigorous-intensity aerobic exercise each week (46).
IMiD, immune modulatory imide drugs; PA, physical activity.

at T3, with two not commencing the intervention because of relocation for personal reasons after a stem cell transplant (n = 1) and an ongoing cardiac issue (n = 1). Four withdrawals from the WT group occurred during the exercise intervention; one at week 1 because of surgery for an unrelated medical problem and three at weeks 4, 8, and 10 because of disease progression requiring recommencement of treatment and/or investigations for the presence of new bone lesions. One WT participant completed all exercise sessions and did not return for testing at T3 because of loss to follow-up. Overall, 41 participants were assessed at T2 (EX group, n = 21) and T3 (WT group, n = 20) after the exercise intervention.

Safety. No AEs or SAEs occurred during or between sessions. A single non–exercise-related AE occurred because of a hypotensive episode while standing still during a session. The AE was clinically investigated at the hospital and found to be unexplained and unrelated to exercise. This participant returned to the study without missing any sessions. There were many AEs and SAEs that occurred during the study that were not determined to be exercise related, such as a fall on the way to an exercise session and unrelated hospital admissions. These events were determined to be unrelated to the exercise training due to the associated clinical presentations at the time of the occurrence. No SAE or AE was reported during the sessions delivered online because of the COVID-19 restrictions to face-to-face contact. Importantly, no participants experienced pathological fractures during testing or exercise training.

Attendance and adherence. In total, 41 of the 52 participants (79%) who started the exercise intervention completed postintervention testing, of which 36 (88%) attended all 24 supervised sessions. Two participants attended all exercise sessions but did not return to complete testing. The overall

TABLE 3. Adherence to the intervention protocol in the EX and WT groups over 12 wk (n = 43) or partial completion (n = 9) of the supervised component of the exercise intervention (n = 52).

	Aerobic			Resistance			Impact Loading		
FITT Adherence	**Mean**	**SD**	**95% CI**	**Mean**	**SD**	**95% CI**	**Mean**	**SD**	**95% CI**
Overall (Weeks 1–12)									
Intensity[a] per session, % prescribed	MVI: 15.0 (124.6) HI: 3.6 (44.9)	5.3 4.3	14.6–15.3 3.3–3.8	5.7 (114.0)	2.4	5.5–5.8	0.7 (63.6)	0.9	0.6–0.7
Reps or MVPA minutes per session, % prescribed	22.1 (79.0)	6.6	21.7–22.5	102.2 (127.7)	63.7	98.5–105.9	100.2 (63.6)	64.2	96.4–103.9
Protocol deviations[b], %	64.8			37.1			66.5		
Achieved *a priori* criteria[c], %	54.7			79.7			36.5		
Weeks 1–4									
Intensity[a] per session, % prescribed	MVI: 15.2 (127.0) HI: 3.1 (38.8)	5.3 4.2	14.7–15.8 2.7–3.5	5.2 (103.3)	2.6	4.9–5.4	0.5 (48.0)	0.7	0.5–0.6
Reps or MVPA minutes per session, % prescribed	21.4 (76.5)	6.6	20.8–22.1	87.9 (109.9)	51.3	82.9–93.0	84.5 (52.8)	62.6	78.3–90.6
Protocol deviations[b], %	70.3			48.9			74.1		
Achieved *a priori* criteria[c], %	48.9			70.1			28.9		
Weeks 5–12									
Intensity[a] per session, % prescribed	MVI: 14.8 (123.3) HI: 3.9 (48.3)	5.4 4.4	14.4–15.2 3.5–4.2	6.0 (119.1)	2.2	5.8–6.1	0.7 (63.6)	0.9	0.7–0.8
Reps or MVPA minutes per session, % prescribed	22.5 (80.4)	6.6	22.0–23.0	110.0 (137.6)	68.3	105.1–115.0	108.8 (68.0)	63.5	104.2–113.5
Protocol deviations[b], %	61.8			30.5			62.3		
Achieved *a priori* criteria[c], %	57.8			85.0			40.7		
Participants unable to ever achieve *a priori* criteria, *n* (%)	11 (21.2)[d]			2 (3.8)			22 (42.3)[e]		
Participants able to always achieve *a priori* criteria, *n* (%)	11 (21.2)			17 (32.7)			7 (13.5)		

[a]Intensity of aerobic exercise measured as minutes spent at the prescribed percentage of peak heart rate, intensity of resistance exercise measured using the OMNI-RES 0–10 scale (33), and intensity of impact-loading exercise measured via ground reaction force × body weight.
[b]Protocol defined as follows: 8 min of high-intensity aerobic exercise (>85% peak heart rate (HR_{peak}) and 12 min of moderate-to-vigorous intensity (60%–85% HR_{peak}); resistance training of ≥80 repetitions (e.g., 5 exercises × 2 sets × 8 repetitions) performed at an intensity of ≥5/10 on the OMNI-RES scale per session (33); impact loading of ≥160 repetitions per session (e.g., 4 × 20 impacts per leg, which may be completed bilaterally or unilaterally) at an intensity of 1.1 to 5.1 × body weight ground reaction force (34–36).
[c]*A priori* criteria = 75% of protocol.
[d]Cardiac or blood pressure issues precluded completion of high-intensity exercise, so only moderate intensity exercise was prescribed.
[e]Isometric exercises were prescribed for specific body segments where myeloma-related bone changes were considered unsuitable for impact-loading activities.
HI, high-intensity exercise (85%–95% peak heart rate); MVI, moderate-to-vigorous intensity exercise (60%–85% peak heart rate); MVPA, moderate-to-vigorous intensity physical activity, where minutes of vigorous-to-high intensity performed has a weighting factor of 2 (47); reps: repetitions.

attendance at the supervised sessions by those who started the intervention was 98%. Exercise sessions were rescheduled for 8.9% (n = 88) of sessions, with the most common reason being that the participant was feeling unwell. Because of restrictions to face-to-face contact during the COVID-19 pandemic, 3% of all exercise sessions (n = 34 sessions across six participants) were delivered via videoconferencing, using the same equipment delivered to the participants' homes. Self-reported attendance at the home-based exercise sessions was 45.4% (SD, 49.8%; 95% CI, 41.3%–49.5%).

The mean duration of aerobic exercise (combined moderate-to-vigorous and high-intensity aerobic training) was 22.1 min per session (95% CI, 21.7–22.5 min), which was 79% of the prescribed duration (Table 3). However, the number of sessions where the participant adhered to both the prescribed intensity and duration was 35.3% (Table 4). The most common reason for lack of adherence to the aerobic exercise protocol was a very low baseline exercise capacity and subsequent longer progression toward meeting the prescribed intensity and duration of the intervention (52.5% of sessions). This was evident from the higher adherence observed in weeks 5–12 (57.8%) compared with weeks 1–4 (48.9%; Table 3). Health reasons were the second most common reason for lack of adherence to the aerobic exercise protocol, for example, acute illness, head cold, and headache (3.0% of sessions).

The mean number of repetitions completed per session for resistance training was 102.2 repetitions (95% CI, 98.5–105.9; 128% of the prescribed minimum of 80 repetitions, comprising 5 exercises in 2 sets of 8 repetitions; Table 3). The mean intensity per session based on the Omnibus Resistance Exercise Scale of Perceived Exertion (33) was 5.7 (95% CI, 5.5–5.8; 114% of the prescribed minimum of 5 on the scale). However,

TABLE 4. Reasons for protocol deviations in the EX and WT groups over 12 wk (n = 43) or partial completion (n = 9) of the supervised component of the exercise intervention (n = 52).

	Aerobic Training (≥Moderate Intensity)		Resistance Training		Impact Loading	
Reasons for Not Meeting Protocol	***n***	**%**	***n***	**%**	***n***	**%**
Familiarization and/or progressing toward protocol	593	52.6	110	9.8	142	12.6
Bone lesion sites impacting ability to meet protocol	13	1.2	34	3.0	390	34.6
Time constraints	14	1.2	122	10.8	107	9.5
General pain	2	0.2	5	0.4	15	1.3
Fatigue	16	1.4	51	4.5	16	1.4
Musculoskeletal pain	27	2.4	44	3.9	45	4.0
Medication side effects (e.g., dexamethasone)	23	2.0	1	0.1	3	0.3
Neuropathy	0	0	0	0	0	0
Nausea	3	0.3	9	0.8	6	0.5
AE	0	0	0	0	0	0
Other (e.g., acute illness, head cold, headache)	38	3.4	42	3.7	26	2.3
Not applicable (no protocol deviation)	398	35.3	710	62.9	378	33.5

the number of sessions where the participant adhered to both the prescribed intensity and number of repetitions was 62.9% (Table 4). The most common reason for lack of adherence to the resistance training protocol was a very low baseline neuromuscular capacity and subsequent longer progression toward meeting the prescribed intensity and number of repetitions of the intervention (9.8%) and fatigue (4.5%). This was evident from the higher adherence to the resistance training protocol observed in weeks 5–12 (137.6% of prescribed resistance repetitions) compared with weeks 1–4 (109.9% of prescribed resistance repetitions; Table 3).

The mean number of impacts completed per session for impact loading was 100.2 repetitions (95% CI, 96.4–103.9), which was 62.6% of the prescribed minimum of 160 repetitions (80 impacts per leg; Table 3). The mean intensity of the impacts completed per session based on the peak ground reaction force was 0.7 (95% CI, 0.6–0.7) × body weight, which was 63.6% of the prescribed minimum ground reaction force of 1.1 × body weight. However, the number of sessions where the participant adhered to both the prescribed number and intensity of the impacts was 33.5% (Table 4). The most common reason for lack of adherence to the impact-loading protocol was to enhance safety for participants with bone lesions, by reducing number or intensity of impacts (34.6%) and slower progression toward meeting the prescribed intensity and number of repetitions (12.6%). This was evident from the higher adherence to the impact-loading protocol observed in weeks 5–12 (68.0% of prescribed impact repetitions) compared with weeks 1–4 (52.8% of prescribed impact repetitions; Table 3). Time constraints due to participants' schedules were also a contributing factor to both resistance training and impact-loading adherence (resistance training, 10.8%; impact loading, 9.5%; Table 4).

Self-reported pain (mean (SD), 1.0 (1.8); 95% CI, 0.9–1.1; range, 0–8) and fatigue (mean (SD), 1.7 (2.4); 95% CI, 1.5–1.8; range, 0–10) were reported on the visual analog scale 0–10 to the AEP on commencement of each exercise session. There was no significant change in the reported level of pain and fatigue across the 24 exercise sessions ($P = 0.86$ and 0.50, respectively).

Acceptability. Acceptability, as measured by responses on the PACES-8 survey, was high (mean, 82.2%; 95% CI, 77.6–86.7; $n = 46$) and remained high over the entire 12-wk intervention (at 4 wk (mean, 81.3%; 95% CI, 76.3–86.2) versus 8 wk (mean, 83.6%; 95% CI, 78.6–88.6) versus 12 wk (mean, 85.3%; 95% CI, 80.5–90.1); $P = 0.51$).

Safety and feasibility of physical function testing. No AEs or SAEs were reported during or after any of the physical tests (Table 5). Preexisting pain due to osteoarthritis, particularly of the knees, was the most common reason for partial test completion or premature test cessation for all cardiopulmonary exercise tests (CPET) at all time points. Of the 184 CPET tests possible across both groups and all time points, 148 (80.4%) of CPETs were performed, with 31 not performed because of COVID-19 lockdowns (16.8%) and 4 (2.2%) not performed for medical reasons (knee pain, atrial fibrillation) or participant request. A CPET was completed by 98% of participants at T1. At T1, a maximal oxygen uptake ($\dot{V}O_{2max}$; defined by a plateau in oxygen consumption with an increase in work rate [31]) was achieved by 12 (20.7%) participants; 33 (56.9%) participants achieved a peak oxygen uptake ($\dot{V}O_{2peak}$), whereas 14 (24.1%) could not complete a valid test (defined as termination before reaching a ventilatory threshold [31]). The proportions of WT participants who achieved a $\dot{V}O_{2max}$ or a $\dot{V}O_{2peak}$ or performed an invalid test at T1 were 4 (13.3%), 20 (66.7%), and 6 (20.0%), whereas at T2, the proportion who achieved a $\dot{V}O_{2max}$ increased to 12 (50.0%), with 7 (29.2%) $0O_{2peak}$ and 5 (20.8%) invalid tests. In comparison, the proportions of EX participants at T1 who achieved a $\dot{V}O_{2max}$, $\dot{V}O_{2peak}$ or an invalid test were 8 (28.6%), 13 (46.4%), and 8 (28.6%), whereas at T2, 6 (33.3%) $\dot{V}O_{2max}$ and 10 (55.6%) $\dot{V}O_{2peak}$ tests were achieved, with the number who could not complete a valid test decreased to 2 (11.1%). All WT participants at T2 completed the CPET, except three (12.5%) participants for whom face-to-face contact was restricted because of COVID-19.

Similarly, after intervention, all participants completed the CPET, albeit 10 (24.4%) participants for whom face-to-face contact was restricted because of COVID-19. A $\dot{V}O_{2max}$ was achieved by 9 (29.0%) participants; 16 (51.6%) participants achieved a $\dot{V}O_{2peak}$, whereas 6 (19.4%) performed an invalid test. All tests were terminated because of volitional fatigue or participant choice, with no medical reason/s for test termination for any of the CPETs. Referral for further cardiac investigations was recommended for three participants after baseline CPET (according to American College of Sports Medicine guidelines (49)), although no abnormalities were subsequently identified.

At T1, one participant in the EX group declined to attempt the 30-s sit-to-stand test because of their lack of confidence and fear regarding a lytic lesion in the left acetabulum. However, at the subsequent testing at T2, the test was safely and successfully completed. Three participants did not complete the 30-s sit-to-stand test on request at later time points because of fear of pain in the lower back and knee. After completing the midthigh pull at T1, five (12.2%) participants requested not to perform the test at subsequent testing time points because of fear of compromise to their spine lesions and aggravation of lower back symptoms. A further three participants completed reduced repetitions on at least one occasion because of fear of pain. The Y balance test was not performed or only a partial test completed by 10 (16.6%) participants at baseline because of very poor balance on both or either leg/s. The protocol was hence modified to include a single-leg balance test to provide an assessment of static balance in participants where the Y balance test was not able to be performed. A partial single-leg stance was subsequently completed by one participant at each testing time point because of reduced confidence from a lytic lesion located in the right acetabulum. At T1, only one participant (in the WT group) failed to wear the accelerometer, whereas data did not adhere to the minimum wear-time criterion of 10 waking hours on at least 4 of the 7 d for four participants (three in WT, one in EX), with two of these (in WT) unable to adhere to the wear-time criterion on any subsequent testing time point. A further nine participants (six in WT, three in EX) did not wear the accelerometer for the required

TABLE 5. Completion of physical function testing at all time points in the EX and WT groups.

	Time Point				
	Baseline	WT Baseline	Postintervention	3 mo Post	9 mo Post
Physical Tests	n = 60[a]	n = 27	n = 41	n = 31	n = 25
Cardiopulmonary exercise test, n (%)					
Number who performed the test	58 (96.7)	24 (88.9)	31 (75.6)	21 (67.7)	14 (56.0)
Achieved a $\dot{V}O_{2max}$ test[b]	12 (20.7)	12 (50.0)	9 (29.0)	13 (61.9)	6 (42.9)
Achieved a $\dot{V}O_{2peak}$ test	32 (55.2)	7 (29.2)	16 (51.6)	5 (23.8)	6 (42.9)
Completed an invalid test[c]	14 (24.1)	5 (20.8)	6 (19.4)	3 (14.3)	2 (14.3)
Medical reasons preventing completion	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (16.0)
Not performed because of COVID restrictions	1 (1.7)	3 (11.1)	10 (24.4)	10 (32.3)	7 (32.0)
30-s sit-to-stand, n (%)					
Number who performed the test	59 (98.3)	27 (100.0)	41 (100.0)	29 (93.5)	24 (96.0)
Medical reasons preventing completion	1 (1.7)	0 (0.0)	0 (0.0)	2 (6.5)	1 (4.0)
Isometric midthigh pull, n (%)					
Number who performed the test	40 (66.7)	20 (74.1)	26 (63.4)	20 (64.5)	13 (52.0)
Reduced repetitions because of fear of pain	2 (3.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (8.0)
Not performed because of fear of pain	0 (0.0)	2 (7.4)	5 (12.2)	1 (3.2)	2 (8.0)
Not performed because of unavailable equipment	16 (26.7)	2 (7.4)	1 (2.4)	0 (0.0)	0 (0.0)
Not performed because of COVID restrictions	1 (1.7)	3 (11.1)	9 (22.0)	10 (32.3)	8 (32.0)
Grip strength, n (%)					
Number who performed the test	60 (100.0)	27 (100.0)	41 (100.0)	31 (100.0)	25 (100.0)
Single-leg stance, n (%)					
Number who performed the test	43 (71.7)	24 (88.9)	40 (97.6)	31 (100.0)	24 (96.0)
Partial test because of lesion/poor balance	1 (1.7)	1 (3.7)	1 (2.4)	0 (0.0)	0 (0.0)
Protocol variation so not performed	16 (26.7)	2 (7.4)	0 (0.0)	0 (0.0)	0 (0.0)
Y-Balance test, n (%)					
Number who performed the test	50 (83.3)	21 (77.8)	27 (65.9)	21 (67.7)	18 (72.0)
Partial test because of lesion/poor balance	8 (13.3)	3 (11.1)	4 (9.8)	0 (0.0)	0 (0.0)
Not performed because of poor balance	2 (3.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Not performed because of COVID restrictions	0 (0.0)	3 (11.1)	10 (24.4)	10 (32.3)	7 (28.0)
7-d accelerometer wear, n (%)					
Number with valid data[d]	54 (90.0)	21 (77.8)	37 (90.2)	29 (93.5)	22 (88.0)
Device not worn	1 (1.7)	2 (7.4)	2 (4.9)	0 (0.0)	1 (4.0)

[a] One participant withdrew before completing all components of baseline testing.
[b] Defined by a plateau in oxygen consumption with an increase in work rate (31).
[c] Defined as termination of the test before reaching a ventilatory threshold (31).
[d] Defined as a minimum wear-time criterion of 10 waking hours on at least 4 of the 7 d, with nonwear time defined as 60 min or more of consecutive activity counts of zero (48).

BASIC SCIENCES

time frame to record valid data at various later testing time points. The grip strength test was successfully completed by all participants at all time points.

Qualitative Results

Thematic analysis of the semistructured interviews with participants (n = 30) generated 5 overarching themes and 17 subthemes relating to the acceptability and feasibility of the exercise intervention. Illustrative quotes, along with frequency counts for these themes and subthemes, are presented in Table 6.

Theme 1: Program acceptability. Participants consistently reported having positive experiences with the program and frequently used words such as "enjoyable," "beneficial," and "excellent" to describe their program experiences. The receipt of expert supervision and guidance from an AEP was the main program component underpinning program acceptability, with the majority of participants identifying this as the program component that they found most beneficial. Linked to this, several participants strongly valued how they received an individualized exercise prescription from an AEP, which was tailored to their needs and specifically targeted their physical issues associated with MM. The majority of participants believed that the program would be beneficial and appealing to the wider MM community.

Theme 2: Barriers of exercise adherence. Several participants provided insight into the factors that acted as barriers to exercise adherence throughout the different phases of the program. Disease-related symptoms and medication side effects, like bone pain and fatigue, were barriers that limited the capacity of some participants to adhere to the supervised exercise sessions. Other participants described how low motivation and a fear of injury, which were specifically linked to the lack of AEP supervision during the home-based exercise sessions, were barriers to adherence for this component of the program.

Theme 3: Facilitators of exercise adherence. The expert supervision and guidance provided by AEPs during the supervised exercise sessions was an important facilitator of exercise adherence, with participants identifying three mechanisms through which this occurred. First, the AEP supervision made participants feel safe and confident while performing the exercises and mitigated any fears of injury. Second, the motivation and encouragement that AEPs provided helped participants to achieve and maintain the prescribed intensity. Third, AEPs adjusted the exercises if/when participants experienced pain, and this then allowed them to continue with the exercise protocol.

Theme 4: Barriers to program uptake. Participants identified two potential barriers to program uptake. Of primary importance was the physical impacts of MM and its treatment/

TABLE 6. Themes, subthemes, frequency counts, and illustrative quotes from thematic analysis of semistructured interviews with participants (n = 30).

Themes and Subthemes	n	Illustrative Quotes
Theme 1: Program acceptability		
Positive program experiences	28	"It's been excellent. I really can't say how thankful I am enough that I was able to participate in the study. I really appreciated and enjoyed it." (PID 26) "The whole experience has been wonderful. I've loved every minute of it. It's the highlight of my week." (PID 38)
Beneficial and appealing to wider community	23	"I think the program is of benefit to anyone who's got myeloma." (PID 46) "The program should be received well, because you know, you're exercising, and it allows people to get healthy again. They should accept it. I don't see why not." (PID 44)
Expert supervision and guidance from AEP	20	"I'd say having an exercise physiologist guiding you was very, very beneficial within the whole program." (PID 8) "I had a supervisor there that was there just for my benefit. That for me, was impressive. I mean a one-on-one situation with somebody that's so well skilled in the make-up of your body was quite impressive for me." (PID 39)
Personalized exercise prescription	9	"The exercises are catered for yourself, it's not like a one-size-fits-all…. I think that's important." (PID 4) "I think it has been very well presented in that it has been targeting the issues that we, who have this multiple myeloma, have. It destroys your bones, and I think it has been marvelous that the exercises that have been selected have been working on bone density." (PID 27)
Theme 2: Barriers to exercise adherence		
Medication side effects	6	"I found that when I did get treatment for the bone hardener, my bones were sore. So, I couldn't do the training because my bones were sore." (PID 30)
Low motivation without AEP supervision	5	"Doing the exercises can become a bit of a chore. There can be a tendency to put it off and say, 'I'll do it tomorrow or the next day.'" (PID 7)
Fear of injury without AEP supervision	4	"The exercise you do at home, like the ones I was doing yesterday, my back was getting sore… so you think you're not doing it right and then you stop." (PID 4)
Theme 3: Facilitators of exercise adherence		
Motivation and encouragement from AEPs	7	"The trainers encourage you to keep going and to keep exercising at a certain level so that you get benefit from it. And you do your best to do that." (PID 18)
Feeling confident and safe during supervised sessions	7	"Because it was supervised, and because the exercise physiologist was so great, I felt very supported, and I think that gave me the confidence to know I was doing the right thing. That it wasn't harmful, that I wasn't going too fast." (PID 6)
AEPs adapt exercises to mitigate pain	4	"I have this guy that looked after me all the way through. Anything I had that might have a bit of soreness, or if I was doing certain things and it hurt, he straightway changed the exercise in a way that I didn't feel the pain anymore." (PID 30)
Theme 4: Barriers to program uptake		
Physical impacts of myeloma and treatment	11	"I've spoken to some other patients who elected not to do the exercise program. One of them said that because he was on a different medication regime to me, so he was going to see the specialist once a week and having medication all the time, he thought it would just be too much." (PID 11) "There's a big barrier and that is because the way 90% of patients find out about their myeloma is through getting fractures and bone problems. So everyone is trying to avoid physical activity." (PID 36)
Lack of motivation to exercise	7	"A lot of people will be hesitant because you've got to remember a lot of people are not fitness people. So they will go, 'Oh I don't want to do this. Oh I couldn't be bothered. I haven't gone to the gym for 20 years' or whatever." (PID30)
Theme 5: Facilitators of program uptake		
Wanting to improve health and fitness	14	"Because physically, it was a great opportunity to participate in something that was more structured for my health and wellbeing." (PID 17) "The motivations? Being able to do normal things, like going for a long walk instead of little, short walks." (PID 30)
Wanting to help others	11	"We might learn something from the trial to help new people coming in that have got myeloma." (PID 4) "It was 100 percent helping people with the study, that was it." (PID 21)
Educate people with MM about exercise benefits	10	"I think it's about educating the patients, you know, cancer sufferers, of the importance of exercise." (PID 14)
Program recommended by health professional	9	"I'm not the expert here and it's always been a case of, if you tell me what to do, then I'll do it because you're the experts and I'm going to listen to you." (PID 7) "The myeloma nurse or someone like that should say 'You may benefit from being involved in an exercise program.'" (PID 35)
Access to expert guidance from AEP	5	"Because you're getting all this excellent training for free from an exercise physiologist…I thought that's really valuable." (PID 36)

s. Participants commonly felt that their disease-related symptoms and medication side effects were relatively mild in comparison to other people with MM, and believed that patients with more severe disease progression and/or intensive MM treatment regimens may not be physically able to partake in the program. Participants also believed that a lack of motivation to exercise may potentially inhibit program uptake and explained how other people with MM who do not enjoy or know the benefits of exercise may not be willing to participate.

Theme 5: Facilitators of program uptake. Participants commonly identified two key motivations for their participation in the program. The first was a desire to improve their health and physical fitness through engaging in exercise. The second was an altruistic desire to help other people with MM through participating in the study. Less commonly, participants mentioned that obtaining access to free expert supervision from AEPs was their main reason for program uptake.

Participants also provided some suggestions for improving program uptake in the future. Several participants discussed the importance of educating people with MM about the mental and physical health benefits of exercise when advertising the program as a strategy to increase their motivation to participate. They also felt that it was important that this education was delivered to patients by a health professional involved in their MM treatment. Linked to this, participants often believed that people with MM would be more likely to participate if referred to the program by a trusted health professional, with several noting that this was a factor that drove their own motivation to participate.

DISCUSSION

This study examined the safety, feasibility, and acceptability of an individualized exercise intervention involving supervised and home-based exercise sessions for people diagnosed

with MM. Compared with *a priori* cut-points, the exercise intervention was deemed to be safe, acceptable, and feasible according to recruitment rates, attrition, and session attendance. However, adherence to the exercise protocols was limited by comorbidities and disease symptoms, such that the predetermined criteria were not met. Physical testing procedures were also found to be safe and feasible.

A broad cross section of people with MM across all disease stages were successfully recruited to the study. This suggests that people with MM find exercise relevant both during active treatment and while in remission. This is supported by our previous study where 57% of people with MM reported that they would like to partake in exercise during both active treatment and remission (26). The proportion of participants who had undergone an ASCT in our study was substantially higher (60% vs 7%–14%) than the two previous exercise studies in people with MM who were either off treatment or undergoing maintenance therapy (16,50). Our participants were older than previous exercise studies for people with MM (65.0 vs 59.0 yr) (14,50), with a third of our participants older than 70 yr and noneligible for ASCT, which is more representative of the general MM population in Australia (mean age, 70.2 yr). However, the representation of women within our sample (21.7%) was smaller than expected. A meta-analysis of 34 randomized controlled exercise trials for people with cancer observed that 78% of participants were female (51). The discrepancy may be partially explained by the higher proportion of men with MM in Australia than women (57.4% vs 42.6%) (52). Whether gender differences may have influenced our results requires confirmation in a larger sample.

Sixty-six percent of eligible people declined to participate in this study. The uptake of 34% was within the range reported in a systematic review of 65 randomized controlled trials of exercise interventions for people with cancer (range, 33%–80%) (53) and surpasses the *a priori* cut-point of ≥25%. Although this cut-point may be low in terms of implementation, it was conservatively chosen in this population where uptake may be affected by participants who are, on average, older, with a history of skeletal fractures or osteolytic lesions, and may be receiving concurrent therapy, including corticosteroids. In addition, study uptake may have been influenced by the large travel distances often required to attend the gym locations at the innercity treating hospitals. This is reflected in the large proportion (60%) of those eligible who reported travel, lack of time, and transport as reasons for declining to participate. Of those who declined to participate, 18% reported health issues, including pain, as the reason for their nonparticipation. Even though 80% of participants had bone disease, and a further 13% had other skeletal complications, such as osteopenia, osteoporosis, and osteoarthritis, those who agreed to participate may have been experiencing fewer complications and less severe disease than the general MM population; for example, the ECOG status was higher (98.3% vs 73.7% [11] level 0 or 1), level of clinical fatigue was lower (36.7% vs 43% [16]), and mean FACIT-Fatigue score suggested less fatigue (38.6 (SD, 9.9) vs 20.2 (SD, 12.5) (54). Findings from the semistructured interviews support this, as several participants commented that they perceived their MM to be relatively mild in comparison to other patients. Analysis of the interview data supported the suggestion that a lack of motivation to exercise may have impacted program uptake. Engaging health professionals to educate their patients with MM regarding the benefits of exercise when advertising available exercise medicine program/s may help to address this barrier in future studies. It is worthwhile noting that a limitation of these interview findings relating to uptake barriers is that they are from the perspective of program participants. Therefore, further research should be undertaken with nonparticipating people with MM to enhance knowledge of their barriers to uptake of exercise medicine programs, and to identify appropriate strategies for addressing these barriers.

Zero exercise-related AEs or SAEs occurred during or between the 1128 total hours of exercise training completed in this study, with only one non–exercise-related AE reported during a session from a hypotensive episode while standing still. Importantly, we did not observe any pathological fractures or bone complications, despite the high incidence of bone disease and the inclusion of higher-intensity and impact-loading exercises in the protocol. There were also no AEs or SAEs during 340 h of exercise sessions delivered online because of the COVID-19 restrictions to face-to-face contact, although all participants had completed in-person sessions with the AEP before the alternative delivery. Other studies in MM have concluded that exercise is safe, with no SAEs documented (14). However, no other studies have utilized high-intensity interval training or impact-loading exercise in this population. The high levels of safety reported here are likely due to the twice-weekly one-on-one supervision by experienced AEPs and highly individualized progressive exercise prescription with weekly reviews for the home-based sessions. Information on the locations of bone lesions and other medical complications was provided by treating clinicians on enrollment in the study, with AEPs regularly checking with participants to identify any changes to their health status across the duration of the study. AEPs then prescribed individualized deviations to the targeted exercise program (reduced intensity or duration, or removal/replacement of specific exercise movements) in 88.0% of sessions (64.8% for aerobic exercise, 37.1% for resistance training, and 66.5% for impact-loading activities over all sessions) to enhance the safety of the program for individuals with absolute or relative contraindications, comorbidities, injuries, or illnesses. For example, the 22 participants considered unsuitable for impact-loading exercises because of the degree of myeloma-related bone changes were prescribed isometric loading activities. The perceived importance of involving experienced AEPs to enhance safety was evidenced by several participants explaining during the interviews how the receipt of expert supervision from AEPs facilitated feelings of safety while undertaking the exercise program.

The attendance rate for supervised exercise sessions (98%) was higher than the rates previously reported by studies involving supervised exercise in people with MM (attendance

rates ranged from 71% to 92%) (14). This may be due to the flexible scheduling of exercise sessions to coincide with participants' visits to the hospital for treatment. This was also speculated by Larsen et al. (55) to contribute to high attendance to exercise in other studies of people with MM. Varied times were also offered, with early morning sessions available for those in full-time employment. Therefore, although travel, lack of time, and transport were the most commonly reported reasons for declining to participate, these factors did not seem to negatively affect recruited participants' ability to attend supervised exercise sessions.

Self-reported completion of the home-based exercise sessions was lower than the supervised sessions (45% vs 98%), which suggests that the supervised component of the program is critical to maintaining engagement. Indeed, a recent update of a Cochrane review of interventions that promote habitual exercise in those living with or beyond cancer found that the eight studies that reported adherence of ≥75% to an exercise prescription that met current guidelines all included a component of supervision (30). Corroborating this, the semistructured interviews found that the lack of AEP supervision during the home-based exercise sessions led to a lack of motivation and fear of injury, which inhibited adherence for some participants. Reasons for very low to negligible completion of home-based exercise by some participants warrant further investigation and may inform strategies to improve exercise participation in the wider MM community.

Adherence was reported according to meeting predefined protocols for exercise prescription during each exercise session. No previous studies in MM have reported adherence to the exercise prescription, and indeed it is not generally reported in such detail in any exercise oncology studies (21,22). In this study, there was high adherence to each component of the exercise prescription when rates were averaged across all participants in the intervention. However, when the number of individual sessions where the participant adhered to the predefined criteria was considered, the adherence was low and less than the *a priori* cut-points defined before commencement of the study. Indeed, there was a low proportion of participants (21.2%, 32.7%, and 13.5%) who were always able to achieve the *a priori* criteria, with some never able to achieve the *a priori* criteria (21.2%, 3.8%, and 42.3%) for aerobic exercise, resistance training, and impact-loading activities, respectively. This highlights the need to account for very low baseline exercise capacity and subsequent longer progression toward meeting the prescribed intensity and duration of the intervention as a factor that restricts program adherence, especially in the initial stages of an intervention. Indeed, this was the recorded reason for not adhering to the protocol in 53%, 10% and 13% of sessions for aerobic, resistance and impact-loading training, respectively, which improved after the first 4 wk of the intervention when motor control and learning had developed. Notably, adherence to the impact-loading protocol was low (33.5%), with one-third of sessions adjusted because of the presence of bone lesions at specific sites limiting the ability to adhere to the predefined protocol. Collectively, this suggests that, when designing an exercise medicine program in future MM studies, the prescription accounts for the, on average, very low baseline capacity, slower rate of progression, and location and stability of bone lesions, but also the demonstrated ability of a large proportion of people with MM to achieve high-intensity interval training, moderate-to-hard resistance exercise, and impact-loading activities.

The 23% attrition observed in the EX group fell within the range reported in other studies in MM (11%–42%) (14,50). The higher attrition in the EX group was not significantly greater than the WT group ($P = 0.08$) and is likely a limitation of the exercise intervention rather than randomization failure, because both EX and WT groups had similar numbers of attrition across each disease stage. Despite this, 8 of the 11 participants (72.7%) who withdrew from the study did so for medical reasons unrelated to the study (i.e., new cancer diagnosis, preparation for ASCT, deteriorating balance, chest infection, surgery, and ongoing cardiac, neurological, and mental health issues). The remaining participants (27.3%) completed baseline testing then withdrew before follow-up testing because of loss of interest. Demographic and clinical features of the participants who discontinued their participation did not differ significantly from those who remained in the study (all $P > 0.05$).

High rates of acceptability of the exercise program were reported by participants on the PACES-8 survey and were maintained across the 12-wk intervention. Further support for program acceptability was obtained from the semistructured interviews. Participants consistently described having positive experiences with the program, and no participants reported a negative review. The receipt of one-on-one supervision from AEPs and the provision of a personalized exercise program that was tailored to individual needs and health concerns were key program components that underpinned acceptability. The high levels of attendance attest to the success of the program for continuing enjoyment and acceptability over an extended period. The one-on-one supervision by AEPs experienced in working with people with cancer may have contributed to the enjoyment and acceptability of the program. In addition, the involvement of a highly individualized program that targeted different disease- and treatment-related side effects and included a wide variety and progression of exercises may have influenced the high rates of acceptability.

Despite the high number of participants with bone lesions, physical tests requiring maximal effort, including cycle ergometry CPET, were completed by the majority of participants. No SAEs or AEs occurred, demonstrating the high safety of the testing protocols. Several other studies have reported the safety and feasibility of CPET in people with hematological malignancies, including MM, with no SAEs reported (56,57). ECG monitoring throughout the CPET; supervision by two investigators, including a licensed physician (for the baseline assessment) or an exercise physiologist with certification in advanced life support (for follow-up testing); and collection of a thorough medical history and review before testing all likely contributed to the safety of the testing protocol. Although there were no protocol deviations required for grip strength, other tests of physical function required minor protocol adjustments or were

not completed by a small number of participants, often on request because of fear of pain. Valid accelerometry data were obtained for almost 90% of participants at each time point, with the exception of those in the WT group at the T3 time point when compliance with wear time was reduced to 78%. Therefore, under strict supervision, the testing battery included in this study seems to be safe and feasible in this population.

There are limitations of the study findings that are worthy of comment. Despite having a sample size that is larger than previous exercise studies in people with MM, there may be still too few participants to subanalyze and interpret the results according to disease stage, sex, or other potentially influencing characteristics. The highly supervised testing battery and twice-weekly in-person exercise protocols restrict the applicability to solely home-based or less supervised community-based exercise medicine programs. Although a majority of withdrawals from the study were due to health and medical conditions unrelated to the exercise program, withdrawal rates were on the higher side compared with other studies of exercise interventions in people with advanced cancer (38). Finally, this article focuses on safety, feasibility, and acceptability of a high/hard-intensity exercise medicine program. These outcomes were prioritized because of the novelty of the exercise intervention and to enhance the ability of researchers to replicate the study protocol but did not report on intervention efficacy.

CONCLUSIONS

An individualized exercise medicine program is safe and acceptable in an age-representative cohort of people with MM across the disease spectrum, including older individuals and those with clinical bone disease. The physical testing battery was also found to be safe and feasible. Exercise program feasibility was confirmed for recruitment and attrition, with excellent attendance and high acceptability of the program in this population, likely due to the one-on-one supervision with an experienced AEP and the individually tailored prescription. Although cumulative adherence to components of the exercise intervention was acceptable, adherence at an individual session level was low. This highlights the need to consider the very low baseline capacity and slower rate of progression toward achieving a protocol, particularly in the initial stages of an intervention, for many people with MM. This study highlights that exercise, which includes high-intensity interval training for cardiorespiratory fitness, moderate- to hard-intensity resistance exercises for muscle and bone health, and impact loading for bone health, is safe and feasible across the disease spectrum of MM with appropriate supervision and exercise individualization by exercise professionals.

The authors thank Myeloma Australia and Leukaemia Foundation of Australia for assistance with study recruitment. The authors thank Angela Cieslar for her valuable assistance with coding interview transcripts for the qualitative analysis. This research was funded by a Medical Research Futures Fund Rapid Applied Research Translation Grant, a Brisbane Diamantina Health Partners (now known as Health Translation Queensland) Cancer Theme Grant, and a Health and Behavioral Sciences–Medicine Research Collaboration Seeding Grant, The University of Queensland. The authors have no conflicts of interest.

The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The results of the present study do not constitute endorsement by American College of Sports Medicine.

Australian New Zealand Clinical Trial Registry: 12619000387123.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018;68(6):394–424.
2. Zhou L, Yu Q, Wei G, et al. Measuring the global, regional, and national burden of multiple myeloma from 1990 to 2019. *BMC Cancer*. 2021;21(1):606.
3. Cowan AJ, Allen C, Barac A, et al. Global burden of multiple myeloma: a systematic analysis for the Global Burden of Disease Study 2016. *JAMA Oncol*. 2018;4(9):1221–7.
4. Padala SA, Barsouk A, Barsouk A, et al. Epidemiology, staging, and management of multiple myeloma. *Med Sci (Basel)*. 2021;9(1):3.
5. Kazandjian D. Multiple myeloma epidemiology and survival: a unique malignancy. *Semin Oncol*. 2016;43(6):676–81.
6. Joshy G, Thandrayen J, Koczwara B, et al. Disability, psychological distress and quality of life in relation to cancer diagnosis and cancer type: population-based Australian study of 22,505 cancer survivors and 244,000 people without cancer. *BMC Med*. 2020;18(1):372.
7. Terpos E, Morgan G, Dimopoulos MA, et al. International Myeloma Working Group recommendations for the treatment of multiple myeloma-related bone disease. *J Clin Oncol*. 2013;31(18):2347–57.
8. Melton LJ 3rd, Kyle RA, Achenbach SJ, Oberg AL, Rajkumar SV. Fracture risk with multiple myeloma: a population-based study. *J Bone Miner Res*. 2005;20(3):487–93.
9. Oortgiesen BE, Kroes JA, Scholtens P, et al. High prevalence of peripheral neuropathy in multiple myeloma patients and the impact of vitamin D levels, a cross-sectional study. *Support Care Cancer*. 2022;30(1):271–8.
10. Burwick N, Sharma S. Glucocorticoids in multiple myeloma: past, present, and future. *Ann Hematol*. 2019;98(1):19–28.
11. Ramsenthaler C, Osborne TR, Gao W, et al. 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*. 2016;16:427.
12. Knips L, Bergenthal N, Streckmann F, Monsef I, Elter T, Skoetz N. Aerobic physical exercise for adult patients with haematological malignancies. *Cochrane Database Syst Rev*. 2019;1(1):CD009075.
13. Nicol JL, Hill MM, Burton NW, Skinner TL. Promoting exercise for patients with multiple myeloma: attitudes and practices of clinical haematologists. *J Cancer Surviv*. 2022;16(3):688–95.
14. Nicol JL, Chong JE, McQuilten ZK, Mollee P, Hill MM, Skinner TL. Safety, feasibility, and efficacy of exercise interventions for people with multiple myeloma: a systematic review. *Clin Lymphoma Myeloma Leuk*. 2023;23(2):86–96.
15. Shallwani S, Dalzell M-A, Sateren W, O'Brien S. Exercise compliance among patients with multiple myeloma undergoing chemotherapy: a retrospective study. *Support Care Cancer*. 2015;23(10):3081–8.
16. Koutoukidis DA, Land J, Hackshaw A, et al. 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*. 2020;123(2):187–95.
17. ERS Task Force, Palange P, Ward SA, Carlsen KH, et al. Recommendations on the use of exercise testing in clinical practice. *Eur Respir J*. 2007;29(1):185–209.
18. Kampshoff CS, Chinapaw MJ, Brug J, et al. Randomized controlled trial of the effects of high intensity and low-to-moderate intensity exercise on physical fitness and fatigue in cancer survivors: results of the Resistance and Endurance exercise After ChemoTherapy (REACT) study. *BMC Med*. 2015;13:275.

19. Levinger I, Goodman C, Hare DL, Jerums G, Toia D, Selig S. The reliability of the 1RM strength test for untrained middle-age individuals. *J Sci Med Sport*. 2009;12(2):310–6.
20. Toohey K, Pumpa K, McKune A, Cooke J, Semple S. High-intensity exercise interventions in cancer survivors: a systematic review exploring the impact on health outcomes. *J Cancer Res Clin Oncol*. 2018;144(1):1–12.
21. Neil-Sztramko SE, Winters-Stone KM, Bland KA, Campbell KL. Updated systematic review of exercise studies in breast cancer survivors: attention to the principles of exercise training. *Br J Sports Med*. 2019;53(8):504–12.
22. Neil-Sztramko SE, Medysky ME, Campbell KL, Bland KA, Winters-Stone KM. Attention to the principles of exercise training in exercise studies on prostate cancer survivors: a systematic review. *BMC Cancer*. 2019;19(1):321.
23. Ramsenthaler C, Kane P, Gao W, et al. Prevalence of symptoms in patients with multiple myeloma: a systematic review and meta-analysis. *Eur J Haematol*. 2016;97(5):416–29.
24. King T, Faiman B. Steroid-associated side effects: a symptom management update on multiple myeloma treatment. *Clin J Oncol Nurs*. 2017;21(2):240–9.
25. Mian HS, Fiala MA, Wildes TM. Burden of treatment among older adults with newly diagnosed multiple myeloma. *Clin Lymphoma Myeloma Leuk*. 2021;21(2):e152–9.
26. Nicol JL, Woodrow C, Burton NW, et al. Physical activity in people with multiple myeloma: associated factors and exercise program preferences. *J Clin Med*. 2020;9(10):3277.
27. Fairman CM, Nilsen TS, Newton RU, et al. Reporting of resistance training dose, adherence, and tolerance in exercise oncology. *Med Sci Sports Exerc*. 2020;52(2):315–22.
28. Nicol JL, Woodrow C, Cunningham BJ, et al. An individualized exercise intervention for people with multiple myeloma—study protocol of a randomized waitlist-controlled trial. *Curr Oncol*. 2022;29(2):901–23.
29. Eldridge SM, Chan CL, Campbell MJ, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *BMJ*. 2016; 355:i5239.
30. Turner RR, Steed L, Quirk H, et al. Interventions for promoting habitual exercise in people living with and beyond cancer. *Cochrane Database Syst Rev*. 2018;9(9):CD010192.
31. Balady GJ, Arena R, Sietsema K, et al. Clinician's guide to cardiopulmonary exercise testing in adults: a scientific statement from the American Heart Association. *Circulation*. 2010;122(2):191–225.
32. Tanaka H, Monahan KD, Seals DR. Age-predicted maximal heart rate revisited. *J Am Coll Cardiol*. 2001;37(1):153–6.
33. Colado JC, Pedrosa FM, Juesas A, et al. Concurrent validation of the OMNI–Resistance Exercise Scale of perceived exertion with elastic bands in the elderly. *Exp Gerontol*. 2018;103:11–6.
34. Bassey EJ, Rothwell MC, Littlewood JJ, Pye DW. Pre- and postmenopausal women have different bone mineral density responses to the same high-impact exercise. *J Bone Miner Res*. 1998;13(12):1805–13.
35. Bolam KA, Skinner TL, Jenkins DG, Galvão DA, Taaffe DR. The osteogenic effect of impact-loading and resistance exercise on bone mineral density in middle-age and older men: a pilot study. *Gerontology*. 2015;62(1):22–32.
36. Weeks BK, Beck BR. The BPAQ: a bone-specific physical activity assessment instrument. *Osteoporos Int*. 2008;19(11):1567–77.
37. Mullen SP, Olson EA, Phillips SM, et al. Measuring enjoyment of physical activity in older adults: invariance of the Physical Activity Enjoyment Scale (PACES) across groups and time. *Int J Behav Nutr Phys Act*. 2011;8:103.
38. Heywood R, McCarthy AL, Skinner TL. Safety and feasibility of exercise interventions in patients with advanced cancer: a systematic review. *Support Care Cancer*. 2017;25(10):3031–50.
39. Sheill G, Guinan E, Brady L, Hevey D, Hussey J. Exercise interventions for patients with advanced cancer: a systematic review of recruitment, attrition, and exercise adherence rates. *Palliat Support Care*. 2019;17(6):686–96.
40. Weller S, Hart NH, Bolam KA, et al. Exercise for individuals with bone metastases: a systematic review. *Crit Rev Oncol Hematol*. 2021;166:103433.
41. Huffman MK, Christ SL, Ferraro KF, Klenosky DB, Marceau K, Amireault S. Questions to measure enjoyment of and satisfaction with physical activity: are they appropriate for use in an older population? *Innov Aging*. 2021;5(4):igab041.
42. Braun V, Clarke V, Weate P. Using thematic analysis in sport and exercise research. In: Smith B, Sparkes AC, editors. *Routledge Handbook of Qualitative Research in Sport and Exercise*. London: Routledge; 2016. pp. 191–205.
43. Guest G, MacQueen KM, Namey EE. *Applied Thematic Analysis*. Thousand Oaks (CA): Sage Publications Inc; 2012.
44. Pasco JA, Holloway-Kew KL, Tembo MC, et al. Normative data for lean mass using FNIH criteria in an Australian setting. *Calcif Tissue Int*. 2019;104(4):475–9.
45. Van Belle S, Paridaens R, Evers G, et al. Comparison of proposed diagnostic criteria with FACT-F and VAS for cancer-related fatigue: proposal for use as a screening tool. *Support Care Cancer*. 2005;13(4):246–54.
46. Cormie P, Atkinson M, Bucci L, et al. Clinical Oncology Society of Australia position statement on exercise in cancer care. *Med J Aust*. 2018;209(4):184–7.
47. Australian Institute of Health and Welfare. *The Active Australia Survey: A Guide and Manual for Implementation, Analysis and Reporting*. Canberra (ACT): AIHW; 2003. Cat. no: CVD 22.
48. Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, McDowell M. Physical activity in the United States measured by accelerometer. *Med Sci Sports Exerc*. 2008;40(1):181–8.
49. American College of Sports Medicine. *ACSM's Guidelines for Exercise Testing and Prescription*. Philadelphia (PA): Lippincott Williams & Wilkins; 2014.
50. Groeneveldt L, Mein G, Garrod R, et al. A mixed exercise training programme is feasible and safe and may improve quality of life and muscle strength in multiple myeloma survivors. *BMC Cancer*. 2013;13:31.
51. Buffart LM, Kalter J, Sweegers MG, et al. Effects and moderators of exercise on quality of life and physical function in patients with cancer: an individual patient data meta-analysis of 34 RCTs. *Cancer Treat Rev*. 2017;52:91–104.
52. Australian Institute of Health and Welfare. *Cancer Data in Australia*. Canberra (ACT): Australian Government; 2022. Available from: https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/data.
53. Maddocks M, Mockett S, Wilcock A. Is exercise an acceptable and practical therapy for people with or cured of cancer? A systematic review. *Cancer Treat Rev*. 2009;35(4):383–90.
54. Jones LW, Courneya KS, Vallance JK, et al. Association between exercise and quality of life in multiple myeloma cancer survivors. *Support Care Cancer*. 2004;12(11):780–8.
55. Larsen RF, Jarden M, Minet LR, Frølund UC, Abildgaard N. Supervised and home-based physical exercise in patients newly diagnosed with multiple myeloma—a randomized controlled feasibility study. *Pilot Feasibility Stud*. 2019;5:130.
56. Tuchman SA, Lane A, Hornsby WE, et al. Quantitative measures of physical functioning after autologous hematopoietic stem cell transplantation in multiple myeloma: a feasibility study. *Clin Lymphoma Myeloma Leuk*. 2015;15(2):103–9.
57. Kenjale AA, Hornsby WE, Crowgey T, et al. Pre-exercise participation cardiovascular screening in a heterogeneous cohort of adult cancer patients. *Oncologist*. 2014;19(9):999–1005.