Exercise Behaviors and Fatigue in Patients Receiving Immunotherapy for Advanced Melanoma: A Cross-Sectional Survey via Social Media

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Abstract

Objective: Treatment with immunotherapy has positively changed the long-term outlook of many patients with advanced melanoma; however, fatigue is a common and debilitating side effect. Evidence indicates exercise can improve treatment-related fatigue for patients receiving chemotherapy and radiotherapy. However, currently little is known about exercise behaviors and preferences of patients receiving immunotherapy. This project aimed to describe self-reported levels of fatigue related to immunotherapy; patient perspectives of exercise behaviors; and barriers and facilitators to engagement in exercise for patients receiving, or recently completed immunotherapy for unresectable stage III and stage IV melanoma. **Method:** A cross-sectional purpose-built survey was distributed to members of the Melanoma Patients Australia closed Facebook group via an online survey platform. The survey remained active for I month, with 3 posts during this time inviting members to participate. **Results:** A total of 55 responses were collected. Just over half the participants (n = 31; 56%) described exercising while receiving immunotherapy, with walking as the most common activity (n = 24; 77%). Participants described a range of physical and emotional benefits of exercise, the most predominant being fatigue reduction. Barriers to exercise also included fatigue and competing physical demands at home or work. Patient understanding of what constitutes exercise appeared to differ from clinical classifications. **Conclusions:** Results from this study indicate that patients are engaging in exercise activities and barriers will assist in developing tailored exercise interventions for this cohort.

Keywords

cancer, exercise, immunotherapy, patient experience, fatigue

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Introduction

Advanced Melanoma and Immunotherapy

Currently, Australia has the second highest rate of melanoma in the world, with a total of 15 229 new cases diagnosed, and 2040 deaths in the 2019 alone.¹ Melanoma affects people of all ages, and previously, prognosis for advanced diagnoses was very poor.¹ However, immune checkpoint inhibitors that target programmed death (PD)-1 and cytotoxic T lymphocyte antigen-4 (CTLA-4) ligands immunotherapy have resulted in clinically significant survival improvement for people diagnosed with stage IV melanoma.²⁻⁶ Importantly, for approximately 30% of patients, immunotherapy drugs such as ipilimumab, nivolumab, and pembrolizumab have delivered 5-year survival responses, even for those who had received previous treatment.^{2,7,8}

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Immunotherapy-Related Fatigue

Improved survival is often accompanied by treatment toxicities or immune-related side effects due to the novel mechanisms of action of these drugs.⁹ Side effects include rash, endocrinopathies, and fatigue, and less frequently severe toxicities such as pneumonitis, hepatitis, colitis, and myocarditis.¹⁰⁻¹³ Fatigue significantly affects all domains of quality of life (QoL) including overall health and wellbeing, comfort, function, and economic factors.¹⁴ In the cancer literature, fatigue has been reported as a difficult symptom to cope with,¹⁵ as its impact is often compounded by limiting participation in social activities, hobbies, and interests that previously provided happiness and comfort.¹⁶

Cancer Treatment–Related Fatigue and Exercise

Exercise research has demonstrated that combined aerobic and strength training may be effective in reducing fatigue during treatment across a range of cancer types and treatments.¹⁷⁻²¹ Exercise has also been found to improve cancerrelated outcomes such as immune response, mortality, and recurrence of cancer; and health outcomes such as maintaining a healthy body weight and physical fitness.^{22,23} Importantly, generic prescription of exercise therapy is safe, tolerable, and efficacious for improving symptom control for patients with cancer, both during and after anticancer therapy.^{19,24} The Clinical Oncology Society of Australia (COSA) has also recently issued a position statement regarding the prescription of exercise for oncology patients.²⁵ However, few exercise studies have included patients with melanoma, nor to the best of our knowledge, have studies investigated the role of exercise in mitigating immunotherapy-related fatigue.

Consumer-Led Research

Melanoma Patients Australia (MPA) was established in 2006 and provides professional counselling, support, and information for those with melanoma, their families, friends, and carers through a national network. As part of this, MPA facilitates a moderated closed Facebook group.

Throughout 2017 and early 2018, MPA received multiple calls and emails from consumers asking about exercise and its potential to improve cancer-related fatigue for people diagnosed with advanced melanoma receiving immunotherapy. In order to address these queries, MPA proposed this study to formally collect data on this population's experience of fatigue and exercise.

The aim of this project was to understand the experience of fatigue and exercise behaviors in patients currently receiving, or recently completed immunotherapy for unresectable stage III or stage IV melanoma. Exercise was not formally defined as we were interested in understanding patients' perspectives of what constituted exercise behavior for them.

Objectives

- 1. To describe participants' levels of fatigue
- 2. To describe participants' exercise behaviors
- To identify barriers and facilitators to participants engaging in exercise

This study received approval from the Peter MacCallum Cancer Centre Human Research Ethics Committee (Project Number 17/192L) and was endorsed by members of the Melanoma and Skin Cancer Trials group (formally known as Australia and New Zealand Melanoma Trials Group) (Study Number ANZMTG 06.17).

Method

Design

This study utilized a purpose-built 21-item survey, which included 15 closed response items and 5 open-text questions. Eligible members of the MPA Facebook group were invited to participate. While the MPA Facebook group comprises ~500 members, this group includes people diagnosed with melanoma of all stages (I-IV), their family, and other interested parties. The exact proportion of eligible members was unknown but estimated to be more than 200.

Study Conceptualization

The study was conceptualized in response to inquiries from members of MPA asking for advice and information about the amount and type of exercise that can be safely undertaken during and after treatment with immunotherapy. The survey questions were designed to collect data on current exercise practices, as well as barriers to exercise as experienced by people who were receiving, or had received immunotherapy. The intention is to use these data to inform the development of a personalised, semisupervised exercise intervention for people about to commence immunotherapy that will be tested in a randomised pilot study to determine feasibility, acceptability, and adherence.

Participants

The members of MPA were eligible to participate if they had a diagnosis of unresectable stage III or stage IV melanoma and were currently receiving immunotherapy or had received immunotherapy as their last treatment.

Recruitment

Recruitment methods adhered to the ethical guidelines for social media recruitment proposed by Gelinas et al.²⁶ The MPA Facebook Group moderator posted a link to the survey on the Facebook page. The link contained a lay description of the study aims, eligibility criteria, and methods. Participants were provided with information regarding acknowledgement of informed consent through survey completion, in adherence with national human research guidelines.²⁷ The survey was posted on January 8, 2018, and was reposted twice more on January 15, 2018, and February 5, 2018.

Measures

The survey was created specifically to address study objectives (see Supplementary Material). Preexisting validated measures were used where available. Additional items were custom-designed by the study team comprising cancer researchers, melanoma nurse specialists, medical oncologists, and consumer advocates. Face validity was assessed by clinical staff and consumer advocates, with feedback used to refine questions where necessary.

Demographic and Exercise Behavior Questions. This survey was designed for the study and collected data on age, sex, postcode, and treatment- and cancer-related symptoms.

Exercise behavior questions comprised 4 items designed to collect participant self-reported data on current level of activity, exercise behaviors (if any), and barriers and facilitators to exercise while receiving immunotherapy. As describing "barriers" or "facilitators" is not the norm in communication with patients, questions were developed using more appropriate and consumer-approved language. Responses were then analyzed to identify barriers and facilitators to exercise. Both closed and open questions (free-text responses) were used to collect breadth and depth of information.

PROMIS Fatigue–Short Form 7a. The PROMIS Fatigue instrument consists of 7 items and was included to collect data on self-reported subjective fatigue over the previous seven days.²⁸

Analysis

Quantitative Data. Quantitative data generated through the demographic and exercise behaviors questions were exported into Microsoft Excel Version: 14.0.7212.5000 (Excel) for analysis.

The PROMIS Fatigue–Short Form 7a was scored as per PROMIS guidelines. The final score is represented by the *t* score, a standardized score with a mean of 50 and a standard

deviation (SD) of 10. Data were analyzed using SPSS version 24.

Qualitative Data. Qualitative data were generated from the free-text components of the survey. Written responses were exported from SurveyMonkey into Excel, with identifying information removed. Qualitative content analysis was employed to analyze the data, as it allows for exploration of phenomenon such as motivation, experiences, and views of participants in order to answer clinical relevant health questions.²⁹ Data were classified into codes, categories, and (where relevant) themes using an iterative process—initially deductively by survey question, and then inductively by frequency of novel information. Codes, categories, and themes were developed. The coding framework was reviewed, and any discrepancies resolved.

Activity Guidelines. Self-report data generated through the exercise behaviors survey comprised specific activities undertaken weekly, for example, walking, jogging/running, swimming, and so on. In order to ascertain the proportion of participants who completed both resistance and aerobic exercise as recommended by the COSA guidelines, activities were classified according to type (cardio/ resistance), using the exercise definitions provided by the guidelines. Responses from participants were reviewed to determine whether resistance and/or aerobic activities were reported. Participants who reported completing both aerobic and resistance activities were scored as having the potential to meet the COSA guidelines. Those who completed only aerobic or only resistance exercise were scored as not having the potential to meet the COSA guidelines.

Results

Demographics and Clinical Characteristics

A total of 55 responses were collected. The demographic and clinical characteristics of participants are reported in Table 1.

Most participants were female (n = 34; 62%), had a diagnosis of stage IV melanoma (n = 46; 84%), and were currently receiving treatment (n = 43; 78%). Of the 12 not receiving treatment, most had received single-agent pembrolizumab or ipilimumab (67%). Participants represented every state or territory of Australia, and every category of the Accessibility and Remoteness Index,³⁰ including remote (n = 1; 2%) and very remote Australia (n = 1; 2%). As noted, some participants were not receiving treatment at the time of completing the survey, so some data are retrospective, given it was based on remembering back to when on treatment.

| Age (years) Mean (standard deviation) Range | 54 (10) 34-78 | | |
|---|------------------|----|--|
| | n | % | |
| Sex | | | |
| Male | 20 | 36 | |
| Female | 34 | 62 | |
| Missing | I | 2 | |
| Location | | | |
| Queensland | 19 | 35 | |
| Victoria | 12 | 22 | |
| New South Wales | 10 | 18 | |
| Western Australia | 5 | 9 | |
| South Australia | 4 | 7 | |
| Australian Capital Territory | 3 | 5 | |
| Tasmania | 1 | 2 | |
| Northern Territory | I | 2 | |
| Geographic location | | | |
| Major city | 34 | 62 | |
| Inner regional | 14 | 25 | |
| Outer regional | 5 | 9 | |
| Remote | 1 | 2 | |
| Very remote | I | 2 | |
| Melanoma stage | | | |
| Stage III | 9 | 16 | |
| Stage IV | 46 | 84 | |
| Immunotherapy type | | | |
| Currently receiving | 43 | 78 | |
| Single agent | 31 | 72 | |
| Combination | 11 | 26 | |
| Unknown | I | 2 | |
| Previously received | 12 | 22 | |
| Single agent | 8 | 67 | |
| Combination | 4 | 33 | |
| Experienced side effects | | | |
| Yes | 46 | 84 | |
| No | 8 | 15 | |
| Missing | | 2 | |
| If yes, number of side effects (n = 46) | - | - | |
| Mean (standard deviation) | 4 (| 2) | |
| Range | - | | |

Table 1. Sample Demographic and Clinical Characteristics (N = 55).

Participant-Reported Side Effects

Table 2 details the side effects described by the participants. Almost all participants reported experiencing side effects from their immunotherapy (n = 46; 84%). Those participants were invited to describe side effects experienced in an open-text response. Participants often listed multiple side effects; therefore, percentages listed in Table 2 refer to both the total number of side effects reported and the proportion of participants reporting each type of side effect. Responses were categorized by physiological system, except for fatigue, as the etiology of fatigue can be multifaceted. Fatigue was most commonly reported (n = 34, 62%), followed by dermatological side effects (n = 33, 60%), such as rash or itch. Side effects mediated by immune activity within the endocrine, gastrointestinal, respiratory, musculoskeletal, and neurological systems were also reported. Participants' description of side effects varied, therefore, commonly used terms have been included in Table 2.

The PROMIS Fatigue mean score for the sample was 54.8 (SD = 9.0), which is slightly higher than the standardized mean of 50.

Participant-Reported Exercise Behaviors

Participants' exercise behaviors are described in Table 3. Just over half (n = 31; 56%) described exercising while receiving immunotherapy, even though 64% (n = 35) also reported that immunotherapy affected their ability to exercise. The specific kinds of activities performed are detailed in Table 4. Of the participants who reported exercising while on treatment, walking was the most common activity (n = 24; 77%) followed by swimming (n = 13; 42%).

Most participants spent less than 60 minutes at a time doing an activity. However, playing golf, gardening, or walking were activities which commonly lasted more than 60 minutes. Most activities were conducted between one and four times per week, and walking was the only activity respondents participated in five or more times a week. Over half the participants who reported exercising during treatment completed both resistance and aerobic activities over the course of a typical week (n = 18, 58%).

Qualitative Analysis

Participants were invited to provide perspectives of exercise behaviors undertaken in open-ended questions. Some wrote detailed explanations, others brief notes or comments to elaborate on their response to closed questions.

Effects of Immunotherapy on Exercise (Potential Barriers Related to Immunotherapy). Participants who responded "yes" to the closed text question asking whether immunotherapy affected their ability to exercise were invited to elaborate: "Can you tell us how it [immunotherapy] affected your usual exercise behaviors?" A total of 35 participants responded. Of these, a large proportion (n = 24, 69%) mentioned fatigue.

I'm not as active and it was due to the fatigue. [Patient ID: 22] (Female, 46 years)

I was too exhausted to exercise. [Patient ID: 47] (Female, 54 years)

| Side Effect Category (Sample of Patient Descriptors Used) | No. of Unique Side Effects Reported per Category | % of Participants | % of Total Side Effects Reported |
|---|---|----------------------|-------------------------------------|
| Fatigue (exhaustion, tiredness, lethargy) | 34 | 62 | 25 |
| Dermatological (itchy skin, rashes, psoriasis, changes in skin and hair pigment, vitiligo, sun sensitivity, blisters, hair thinning, lichen sclerosis, lichen planus) | 33 | 60 | 24 |
| Gastrointestinal (bowel issues, colitis, dry mouth, mouth ulcers, nausea, loss of appetite, reflux, hepatitis, liver inflammation) | 24 | 43 | 18 |
| Endocrine (thyroid issues, pituitary gland problems, low blood pressure, pancreatitis, Addison's disease) | 15 | 24 | 11 |
| Respiratory (chest irritation, cough, shortness of breath, asthma, inflamed sinus, pneumonitis, sarcoidosis) | 9 | 16 | 7 |
| Musculoskeletal (aching joints, muscle soreness) | 8 | 15 | 6 |
| Neurological (cognitive issues, dizziness, headaches, swelling of the brain) | 8 | 15 | 6 |
| Other (sleep problems, swelling, high temperature, uveitis) | 4 | 7 | 3 |

Table 2. Summary of Participants' Self-Reported Side Effects From Immunotherapy (Participants, N = 55; Side Effects Reported, N = 135)^a.

^aNumerous side effects were reported per person; therefore, side effects are listed as both the proportion of participants who experienced them and as a proportion of the total number for each category.

I am exercising now, I didn't during treatment [because of] fatigue nausea and bone pain. [Patient ID: 24] (Female, 54 years)

Participants also described a lack of motivation as well as a range of other side effects including dizziness, dry mouth, sun sensitivity, and pain as being factors that contributed to their inability to exercise.

Lost the will to train. [Patient ID: 49] (Male, 55 years)

Weakness, instability, dizziness . . . prevented me having confidence to move around, fearing falls. [Patient ID: 21] (Female, 67 years)

Furthermore, two participants described fear as the primary reason for not exercising, as they were frightened about how exercise might affect their body while receiving treatment.

I haven't pushed my body at all. I played high intensity team sports prior to diagnosis and treatment but I haven't started that again because I'm too scared of how it might affect my body and I'm too fatigued to start the training. [Patient ID: 38] (Female, 35 years)

Despite describing immunotherapy-related barriers to exercise, participants often elaborated on how they overcame these barriers, or adjusted their exercise behaviors as a result of listening to their body.

After my last treatment (number 14), I have had some flank pain and have been lethargic and more tired. I've done less than I normally would. I have been doing gentle swimming rather than lapping. [Patient ID: 12] (Female, 59 years) For a couple of days after my infusion, I feel incredibly tired but I push through it, exercising anyway and feeling better for it. Occasionally I can't and end up going to bed; I just listen to my body. [Patient ID: 20] (Female, 53 years)

Participants also described feeling "too unwell" at times, and this affected on their ability to exercise.

I plan on walking now that I'm feeling better but up until now, I've been too unwell to exercise. [Patient ID: 46] (Female, 43 years)

I just walked the dog twice per day but my walks have gradually reduced in length due to illness and fatigue. [Patient ID: 1] (Female, 59 years).

Reasons for Not Exercising (General Barriers). There were 24 participants who reported having never exercised. Of these, 19 provided some explanation in response to the question, "Can you tell us more about why you are not currently exercising, or have never exercised, or why you did not exercise during treatment?" Interestingly, a proportion (n = 6, 32%) still described undertaking activities such as housework, walking pets. and gardening. The "no-exercise" participants stated that as a result of undertaking these activities they did not have time or energy to exercise. A small number said they preferred to avoid "formal exercise" or did not do any specific exercise.

I don't generally exercise other than normal activities like gardening. [Patient ID: 3] (Male, 57 years)

I feel that I do a lot of exercise by doing my housework and all of my son and daughter-in-law's housework along with all our 6

| | | 0/ |
|---|-----------------|----|
| | n | % |
| Immunotherapy affected ability to exercise ($n = 55$) | | |
| Yes | 35 | 64 |
| No | 14 | 25 |
| Missing | 6 | 11 |
| Exercise behaviors (n = 55) | | |
| Exercised during treatment | 31 | 56 |
| Usually exercise but did not exercise during treatment | 15 | 27 |
| Never exercise (prior or during treatment) | 6 | 11 |
| Missing | 3 | 5 |
| Of the $n = 31$ who did exercise during treatment: | | |
| Number of exercise activities engaged in weekly: | | |
| l activity a week | 6 | 19 |
| 2 activities a week | 11 | 35 |
| 3 activities a week | 8 | 26 |
| 4 activities a week | 2 | 6 |
| 5 activities a week | I | 3 |
| 6 activities a week | 2 | 6 |
| Missing | I | 3 |
| Met COSA exercise requirements (n = 31) | | |
| Met both aerobic and resistance | 18 ^a | 58 |
| Only met aerobic | 12 | 39 |
| Missing | I | 3 |

 Table 3. Participants' Self-Reported Exercise Behaviors While

 Receiving Immunotherapy.

Abbreviation: COSA, Clinical Oncology Society of Australia.

^aMet guideline requirements in relation to type of exercise undertaken, but intensity was not recorded.

washing and all of their washing and ironing. [Patient ID: 15] (Female, 66 years)

Reasons for Exercising (Facilitators). Participants who reported exercising while receiving immunotherapy were given an opportunity to provide additional information via an opentext question, "Can you describe in your own words why you choose to exercise during immunotherapy treatment?" A total of 42 participants responded. Predominantly, participants described exercise as something they enjoyed and wished to continue to preserve routine in their lives.

I have always exercised as it makes me relaxed and keeps me fit. [Patient ID: 26] (Female, 50 years)

I began Pilates for my back and have continued during treatment. I have a pool and swimming has always been a favorite. There's plenty of gardening that needs doing on five acres with a large yard and vegetable garden. I have just tried to continue my usual activities. [Patient ID: 12] (Female, 59 years)

I do gardening because it gets me outside into nature, provides pleasure to see the results, and simply because it is necessary. [Patient ID: 27] (Female, 71 years) Some participants described exercise as a way to maintain a healthy weight. Others felt exercise provided a means by which they could contribute to "fighting" their cancer, and ensure their body was in the best condition to receive treatment. One participant described a show on television about the benefits of exercise for patients receiving chemotherapy, and thought it might help with immunotherapy too.

Want to be as healthy as possible to fight the disease. [Patient ID: 42] (Female, 63 years)

I tried to keep a healthy mind and a healthy body. Even though I was stage 4 and given 12 months, I wanted to fight at all levels including fitness. [Patient ID: 50] (Male, 57 years)

Many participants felt that exercise benefited their mental health and helped them feel "normal" during treatment. Other benefits included improved sleep, increased energy and reduced fatigue, and improved well-being. Furthermore, participants talked about how exercise provided social opportunities to discuss worries with friends.

Mentally and physically, I see it's important. I have always exercised often so important I have a small amount to focus on. [Patient ID: 29] (Male, 47 years)

Friends walked with me and it was a good way to catch up and sometimes talk about issues that were worrying me. [Patient ID: 23] (Female, 55 years)

How Exercise Made Participants Feel. Forty-two participants responded to the open-ended question asking, "How does exercise make you feel?" Exercise sometimes caused tiredness and some described "overdoing it," or pushing themselves too far, and feeling exhausted as a consequence. Despite this, participants were often glad they exercised as it also made them feel good.

Tired but good. [Patient ID: 47] (Female, 54 years)

Good afterwards. [Patient ID: 42] (Female, 63 years)

I feel better but if I over exert myself I am very tired later. [Patient ID: 26] (Female, 50 years)

Others described feeling energized, happier, and more healthy and alive. One man stated it even made him feel better than before he was diagnosed.

Good. Refreshed. Energized. In pain for the gain. [Patient ID: 35] (Female, 46 years)

Makes me feel happy in myself. [Patient ID: 43] (Male, 48 years)

| Activity Type (n = 31) | _ | Time Spent Exercising (Minutes), n (%) | | | How Many Times per Week, n (%) | | | | |
|---|---------|--|--------|--------|--------------------------------|--------|--------|--------|---------|
| | n (%) | ≤30 | 31-60 | ≥60 | Missing | 1-2 | 3-4 | ≥5 | Missing |
| Walking | 24 (77) | 5 (21) | 3 (13) | 4 (17) | 12 (50) | 3 (13) | 3 (13) | 6 (25) | 12 (50) |
| Swimming | 13 (42) | 3 (23) | 2 (15) | 0 (0) | 8 (62) | 3 (23) | 2 (15) | 0 (0) | 8 (62) |
| Weights | 8 (26) | I (I3) | 2 (25) | 0 (0) | 6 (63) | 2 (25) | I (I3) | 0 (0) | 6 (63) |
| Exercise classes | 8 (26) | 0 (0) | 2 (25) | 0 (0) | 6 (75) | 2 (25) | 0 (0) | 0 (0) | 6 (75) |
| Yoga | 8 (26) | 0 (0) | 4 (50) | 0 (0) | 4 (50) | 4 (50) | 0 (0) | 0 (0) | 4 (50) |
| Jogging/running | 5 (16) | I (20) | 0 (0) | I (20) | 3 (60) | I (20) | I (20) | 0 (0) | 3 (60) |
| Golf | 4 (13) | 0 (0) | I (25) | 2 (50) | I (25) | 3 (75) | 0 (0) | 0 (0) | l (25) |
| Gardening | 3 (10) | I (33) | I (33) | 0 (0) | 2 (33) | I (33) | I (33) | 0 (0) | I (33) |
| Pilates | 2 (6) | 0 (0) | l (50) | 0 (0) | I (50) | I (50) | 0 (0) | 0 (0) | l (50) |
| Group sport (like netball or football) | 2 (6) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 2 (100) |

Table 4. Participant Reported Types, Duration, and Frequency of Exercise Behaviors During Immunotherapy.

Other benefits of exercise included reduced stress levels, relaxation, ability to cope, increased motivation, and provided a sense of achievement.

Alive. Able to sleep well at night. [Patient ID: 14] (Male, 65 years)

Exercise makes me feel positive and in control. I feel more energetic in the afternoon and can get through the post 3 PM slump. [Patient ID: 23] (Female, 55 years)

Discussion

Recent literature suggests a high proportion of patients receiving immunotherapy experience a level of fatigue that affects their QoL.¹¹ Importantly, exercise has been shown to improve fatigue in patients who have received chemotherapy or radiotherapy.¹⁸ The aim of this project was to explore and understand the experience of fatigue and exercise behaviors in patients currently receiving, or having recently completed immunotherapy for stage III and IV melanoma.

Participants readily described a range of physical and emotional benefits of exercise, with the most predominant being a reduction in fatigue. Using exercise primarily to combat side effects of treatment was mentioned; however, most people discussed exercise in terms of maintaining daily activities and routines, and assisting with feeling "normal" and social. This in turn promoted well-being and improved QoL. Participants particularly felt that they were contributing to their own health care by undertaking exercise. These findings support existing literature demonstrating the benefits of exercise in the oncology setting.^{31,32}

Fatigue was the most common barrier to exercise, even for those who engaged regularly, yet a reduction in levels of fatigue was cited as a major benefit of exercise. This is in keeping with literature regarding barriers to exercise interventions for other cancer types and forms of treatment.^{33,34} Other barriers reported by participants included being afraid to engage in exercise due to uncertainty about how it might affect them while receiving treatment. This supports previous qualitative work by Crandall and colleagues³² where patients who had surgery for lung cancer also described fear and lack of confidence in exercising. These barriers could be overcome with formal exercise guidance.³² Supervised, personalized exercise interventions, prescribed by exercise physiologists to address treatment-related fatigue, would be helpful in this population.^{19,21,24} Participants in this study did not mention time or cost when asked about reasons for not exercising, as observed in other cancer cohorts.^{32,35,36}

Interestingly, patient understanding of what constitutes exercise may differ from what is formally defined as exercise by health professionals. A number of participants reported not engaging in exercise, yet free-text responses indicated that they participated in activities such as walking, gardening, and physically demanding jobs. These activities were considered barriers to "formal" exercise because they resulted in tiredness. These data suggest that participants' work or home activities need to be considered when prescribing exercise so people are not overloaded, resulting in fatigue. Additionally, lack of time for and adherence to programs are often cited as barriers in cancer exercise trials.^{21,36,37} Furthermore, a recent meta-analysis of exercise and nonpharmaceutical interventions found support for a wide range of exercise behaviors reduced cancerrelated fatigue,¹⁷ indicating people could self-select from a variety of exercise activities and still experience benefits in fatigue reduction.

The COSA exercise guidelines recommend people with cancer should work toward completing at least 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity aerobic exercise and 2 to 3 resistance exercise sessions each week.²⁵ While we did not collect adequate data on intensity or time spent exercising to map accurately to the guidelines, activities listed in the exercise behaviors questionnaire

could be classified into aerobic or resistance-type exercises. Participants who completed both resistance and aerobic activity were therefore viewed as having the potential to meet the COSA guidelines. Participants reported completing a range of different physical activities; however, only 58% completed both resistance and aerobic activities. The rest completed only aerobic-type activities. Further education and formal guidance would be useful in assisting these patients meet current exercise recommendations.

Conclusion

Findings demonstrate that some patients receiving immunotherapy are able to undertake exercise during treatment, and that they perceived that exercise was able to reduce their treatment-related fatigue. However, education and guidance is required to assist patients engage in optimal exercise behaviors. Barriers to exercising while receiving immunotherapy were also identified, with fatigue noted as a major impediment to participation. Importantly, participants were independently engaging in a wide range of exercise behaviors, indicating that prescribed exercise interventions may be well received in this population.

Limitations

The following limitations of the study are acknowledged. Response bias is possible as participants interested or engaged in exercise were more likely to respond. Furthermore, individuals who volunteer to complete surveys are known to be different to the general population.³⁸ A response rate could not be calculated as it was not possible to identify how many members of the Facebook group were eligible but did not participate. However, using social media to advertise the study allowed people from all states and territories of Australia, including remote areas to participate. Other limitations included the absence of data on exercise intensity and missing data from the frequency and length of exercise activity questions. While missing data are common when using self-report measures, we do acknowledge that it also limits our ability to fully describe exercise behaviors of this sample.

Clinical Implications

Even within this small sample, a wide range of immunotherapy-related side effects were identified. These data support the premise of the study that side effects, particularly fatigue, are problematic for patients treated with immunotherapy. Importantly, for some participants, exercise is something they are willing to engage in to reduce fatigue. These data have informed and supported plans to develop and test an exercise intervention for this population.

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Declaration of Conflicting Interests

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Supplemental Material

Supplemental material for this article is available online.

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