Australian Association for Exercise and Sport Science position stand: Optimising cancer outcomes through exercise

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Abstract

Cancer represents a major public health concern in Australia. Causes of cancer are multifactorial with lack of physical activity being considered one of the known risk factors, particularly for breast and colorectal cancers. Participating in exercise has also been associated with benefits during and following treatment for cancer, including improvements in psychosocial and physical outcomes, as well as better compliance with treatment regimens, reduced impact of disease symptoms and treatment-related side-effects, and survival benefits for particular cancers. The general exercise prescription for people undertaking or having completed cancer treatment is of low to moderate intensity, regular frequency (3–5 times/week) for at least 20 min per session, involving aerobic, resistance or mixed exercise types. Future work needs to push the boundaries of this exercise prescription, so that we can better understand what constitutes optimal, desirable and necessary frequency, duration, intensity and type, and how specific characteristics of the individual (e.g., age, cancer type, treatment, presence of specific symptoms) influence this prescription. What follows is a summary of the cancer and exercise literature, in particular the purpose of exercise following diagnosis of cancer, the potential benefits derived by cancer patients and survivors from participating in exercise programs, and exercise prescription guidelines and contraindications or considerations for exercise prescription with this special population. This report represents the position stand of the Australian Association of Exercise and Sport Science on exercise and cancer recovery and has the purpose of guiding exercise practitioners in their work with cancer patients.

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1. Exercise and cancer prevention

One in three Australian men and one in four women will be directly affected by cancer before the age of 75, with melanoma, prostate, colorectal, breast and lung cancers comprising the most common types.1 There are an estimated 108,000 new cancer cases and 41,000 registered cancer deaths each year in Australia, and consequently cancer represents a major public health concern.2 While the causes for many cancers remain unknown, lifestyle factors including physical activity levels are considered contributory and modifiable for some.3,4 Since the first report linking physical activity and cancer risk was published in 1922, more than 190 reports from epidemiological studies and over 10 reviews have examined this relationship.5 The scientific evidence supporting physical activity as a means of cancer prevention is now considered ‘strong’ and ‘convincing’ for particular cancers including colon/colorectal and breast, ‘probable’ for prostate and ‘possible’ for lung and endometrial cancers, with risk ratios or odds ratios reported for the physically active groups ranging from 0.3 to 0.8 (representing risk reductions of 25% to more than three-fold).5 Evidence to date is considered preliminary and insufficient to make any causal inferences for melanoma, testicular, ovarian, kidney, pancreatic and thyroid cancers.5 A review and analysis of the potential biological mechanisms underlying the possible anti-carcinogenic effects of physical activity has recently been published and gives the relationship more credibility.6 The precise exercise prescription, in relation to type, intensity, duration and frequency, needed for cancer protection remains unknown.7 However, since exercise prescription in this set-
ting is not only about the prevention of cancer, but more broadly encompasses prevention of chronic disease and optimising health, quality of life and function, it seems relevant for the application of national physical activity guidelines as well. Of note, published evidence supports a dose–response relationship between physical activity levels and some cancers including colorectal, breast and prostate, showing that cancer risk decreases as activity levels increase. Therefore, the notion that some activity is better than none, and more activity is generally better than less (at least up to levels meeting national guidelines), should be considered when prescribing exercise to healthy populations.

2. Exercise and cancer recovery

Survival prospects following cancer diagnosis are increasing, with females experiencing higher survival probabilities than males (five-yr relative survival rates are 64% and 58%, respectively).1 For some of the more common forms of cancer, five-yr survival prospects are even higher: melanoma, 92%; breast, 88%; prostate, 85%. Whether treatment modality, five-yr survival prospects are even higher: melanoma, 92%; breast, 88%; prostate, 85%. Whether treatment intention is curative or palliative, the disease and treatment-related side-effects may create numerous problems for the patient. Alone or in combination, cancer treatments including chemotherapy, radiation and systemic chemo- or hormone therapy can lead to a range of complications including loss of function (musculoskeletal, cardiovascular, cardiopulmonary), infections, diarrhoea, pain, numbness, lymphoedema, nausea, fatigue, reduction in bone mass, and body composition changes, to name a few.8 While the presence of side-effects tends to peak during treatment, symptoms may persist for many mths or even years following treatment9 and some complications, such as lymphoedema, may not present until several years following treatment.10 Furthermore, cancer and its associated treatment may increase risk of other common chronic conditions, such as cardiovascular disease, diabetes and osteoporosis.11 Of all the potential side-effects during and following cancer treatment, fatigue is regarded as one of the most common and disabling.12

The potential and expected benefits derived from participation in exercise will vary according to timing of cancer treatment, as well as whether treatment was considered successful (that is, patient no longer has evidence of disease).11 Courneya and Friedenreich13 developed the Physical activity and cancer control framework (PACC), which suggests researchers and clinicians consider the following periods and clinical outcomes from the point of diagnosis, with respect to exercise prescription: treatment preparation/coping before treatment, treatment effectiveness/coping during treatment, recovery/rehabilitation, disease prevention/health promotion and survival during ‘survivorship’ (the period between diagnosis and recurrence or death) and palliation for those approaching the end of life. In the Australian context, the treatment preparation period before treatment is limited to select cases (e.g. ‘watchful waiting’ following a diagnosis of lymphoma) as the time between cancer diagnosis and surgical or adjuvant treatment is typically minimal for most cancers (usually 1–2 weeks). Therefore, clinicians are more likely to play a significant role during and following cancer treatment, in the prevention of treatment-related concerns, reducing the impact of these when they exist, overcoming side-effects and generally assisting this population to ‘bridge the gap’ between treatment cessation and effectively returning to ‘normal’ daily lives. Further, the potential role of exercise prescription extends to improvement of long-term health through optimising function, as well as prevention of cancer recurrence and other chronic disease.

Over 70 exercise intervention trials have been conducted, mostly involving women with breast cancer in North America (i.e. USA and Canada). This literature is examined in several qualitative, narrative reviews,8,9,14–20 which together indicate that exercise during and/or following treatment prevents decline and/or improves cardiorespiratory and cardiovascular function, improves body composition (preservation or increase in muscle mass, loss of fat mass), improves immune function, improves strength and flexibility, improves body image, self-esteem and mood, reduces the number and severity of side-effects including nausea, fatigue and pain, reduces hospitalisation duration, improves chemotherapy completion rates, allows for better adjustment to illness, and reduces stress, depression and anxiety, all of which contribute to improvements in quality of life (Table 1).

While impressive findings, conclusions from such narrative reviews emphasise consistency and direction of findings but do not consider the magnitude of the observed effects.11 Hence the potential clinical relevance of the ‘exercise effect’ cannot be derived from these reviews and the potential public health impact remains unknown. More recently, the results from several meta-analyses, conducted on the exercise and cancer recovery literature, have been published.11,21–23 The results demonstrate persuasive findings for a small (weighted mean effect size \( [WMES] = 0.2–0.5 \)) to moderate (\( [WMES] = 0.5–0.8 \)) effect of physical activity interventions on specific outcomes, in particular cardiorespiratory and cardiopulmonary fitness (\( [WMES] = 0.5, p < 0.01 \)), activity levels (\( [WMES] = 0.3, p = 0.01 \)), physiologic outcomes such as blood pressure or increase in muscle mass, loss of fat mass), improves immune function, improves strength and flexibility, improves body image, self-esteem and mood, reduces the number and severity of side-effects including nausea, fatigue and pain, reduces hospitalisation duration, improves chemotherapy completion rates, allows for better adjustment to illness, and reduces stress, depression and anxiety, all of which contribute to improvements in quality of life (Table 1).

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### Table 1

**Summary of potential benefits of exercise during and/or following cancer treatment**.

<table>
<thead>
<tr>
<th>Preserved or Improved</th>
<th>Reduced</th>
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</thead>
<tbody>
<tr>
<td><strong>Muscle mass, strength, power</strong></td>
<td><strong>Number of symptoms and side-effects reported, such as nausea, fatigue and pain</strong></td>
</tr>
<tr>
<td><strong>Cardiorespiratory fitness</strong></td>
<td><strong>Intensity of symptoms reported</strong></td>
</tr>
<tr>
<td><strong>Physical function</strong></td>
<td><strong>Duration of hospitalisation</strong></td>
</tr>
<tr>
<td><strong>Physical activity levels</strong></td>
<td><strong>Psychological and emotional stress</strong></td>
</tr>
<tr>
<td><strong>Range of motion</strong></td>
<td><strong>Depression and anxiety</strong></td>
</tr>
<tr>
<td><strong>Immune function</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Chemotherapy completion rates</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Body image, self-esteem and mood</strong></td>
<td></td>
</tr>
</tbody>
</table>

*Benefits reported in qualitative, narrative reviews of the literature.*
transfusions, blood counts, days in hospital (WMES = 0.3, $p < 0.01$) and symptoms/side-effects (WMES = 0.4, $p < 0.01$) during treatment, as well as fitness (WMES = 0.7, $p < 0.01$) and vitality (WMES = 0.8, $p < 0.04$) following treatment.\(^{1,21}\) The results for fatigue were less compelling (WMES = 0.1, $p = 0.12$). While exercise does not exacerbate fatigue, the reductions reported in the literature may not be of sufficient magnitude to be meaningful for the patient.\(^{11}\) However, anecdotaly, patients do report reductions in fatigue and it is therefore plausible that the lower mean effect size is attributable to the sensitivity of the tools used to capture fatigue. Nonetheless, it is important to remember that the implementation of appropriate exercise prescription (that is, individualised with respect to starting point and speed of progression) minimises risk of injury and optimises the potential for individual gain. Exercise under these circumstances, at worst, does no harm, but more likely leads to a range of benefits during and following treatment (Table 1) that in turn positively influence quality of life. Furthermore, lack of physical activity during and/or following cancer treatment has the potential to exacerbate symptoms (e.g. fatigue) and contribute to loss of function (musculoskeletal and cardiovascular health), hence contributing to reductions in quality of life.\(^{24}\)

While the literature examining the role of physical activity on quality of life following cancer diagnosis is vast (with over 70 exercise trials being conducted), only more recently have results from observational studies of colon/colorectal and breast cancer patients examined the relationship between exercise and survival.\(^{25–30}\) Since 2005, several papers have reported positive associations between participation in physical activity following breast\(^{28–31}\) or colorectal\(^{25–27}\) cancer diagnosis with improved survival and reduced risk of recurrence. The findings indicate that participation in physical activity reduces the risk of recurrence and death by up to half, when compared with those who are sedentary (engaging in less than 3 metabolic equivalent-task hours per week of activity). A change in activity level from pre- to post-diagnosis was also important, with those who increased their activity levels following cancer diagnosis reducing their risk of death,\(^{25,31}\) while those who decreased their activity levels increasing their risk four-fold.\(^{31}\) There is also evidence suggesting a dose–response relationship exists, with some exercise being better than none and more better than less.\(^{26}\) Unfortunately, the lower threshold for attaining survival benefits, as well as the upper threshold beyond which no further survival benefit is accrued, remain unknown. While there is much to be learned with respect to physical activity and survival following cancer, particularly for cancers other than breast and colorectal, these findings are promising and exciting. Further investigations through randomised, controlled trials are currently underway.

### Table 2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Aerobic-based exercise prescription recommendations during and following cancer treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type</strong></td>
<td>Recommendations and comment</td>
</tr>
<tr>
<td></td>
<td>Most exercises involving large muscle groups are appropriate. Cancer survivors do not need to be restricted to walking and stationary cycling. Below are examples of when to avoid specific types of activity:</td>
</tr>
<tr>
<td></td>
<td>When to avoid:</td>
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<tr>
<td></td>
<td>During periods of increased risk of infection (e.g., low absolute neutrophil counts, when catheters are being used, during wound recovery from surgery)</td>
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<tr>
<td></td>
<td>Primary or metastatic bone cancer patients, when platelet counts are low, presence of bone pain</td>
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<tr>
<td></td>
<td>Activities requiring balance and coordination (e.g., treadmill exercise, cycling)</td>
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<tr>
<td></td>
<td>Ataxia, dizziness or peripheral sensory neuropathy</td>
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<tr>
<td></td>
<td>Use of public facilities (e.g. local gymnasium)</td>
</tr>
<tr>
<td></td>
<td>During periods of increased risk of infection</td>
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<tr>
<td><strong>Frequency</strong></td>
<td>At least 3–5 times/week, but daily exercise may be preferable for deconditioned patients who do lower intensity and shorter duration exercise sessions</td>
</tr>
<tr>
<td><strong>Intensity</strong></td>
<td>Moderate, depending on current fitness level and medical treatments. Guidelines recommend 50–75% VO(<em>2) max or HR(</em>{\text{reserve}}), 60–80% HR(<em>{\text{max}}), or an RPE of 11–14 (original Borg scale). HR(</em>{\text{reserve}}) is the best guideline if HR(_{\text{max}}) is estimated rather than measured. Examples of when to avoid high intensities include low haemoglobin levels, immunosuppressed states or the presence of fever. When nausea, dyspnea, fatigue and/or muscle weakness exist, exercise intensity and duration should be prescribed to tolerance.</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>At least 20–30 min continuous exercise; however, deconditioned patients or those experiencing severe side-effects of treatment may need to combine short bouts (e.g., 3–5 min) with rest intervals.</td>
</tr>
<tr>
<td><strong>Progression</strong></td>
<td>Progression should be slower and more gradual for deconditioned patients or those who are experiencing severe side-effects of treatment. Patients should meet frequency and duration goals before they increase intensity. Of note, progression for some could actually mean maintenance of weekly activity levels or slower declines in total physical activity levels. That is, declines in activity may be inevitable during certain treatment periods, but an exercise program can assist in minimising these declines.</td>
</tr>
</tbody>
</table>

Table has been reproduced and modified, with permission, from [37].
Exercise interventions have focused predominantly on women with breast cancer, although effects have been investigated with other patients, including those with head and neck, lung, ovarian, testicular, stomach, colorectal and prostate cancers, melanoma, cancer during childhood and adolescence, as well as those undertaking bone marrow transplant treatment. The effects of aerobic-based exercise, in particular walking and stationary cycling, have received the greatest attention, either alone or in combination with resistance training. Fewer studies have assessed exercise protocols comprised solely of resistance training. Tested interventions usually included at least three exercise sessions per week of at least 15 min duration, at moderate intensities. However, these prescriptive characteristics vary across studies: aerobic-based exercise—frequency ranged from 1–6 days/week; duration ranged from 10–60 min per session; and intensity ranged from low to moderately-high (50–85% of maximal effort/heart rate); resistance-based exercise, frequency ranged from 2–3 times/week; exercising both large muscle groups (e.g., leg press, chest press) and smaller muscle groups (e.g., bicep curls) by doing 1–4 sets of 6–20 repetitions at intensities of 50–80% of one-repetition maximum (1-RM) or to tolerance or failure. This information is presented to highlight the limits of our exercise prescription knowledge and what follows are recommendations based on what can be derived from current research.

Recommendations for aerobic-based exercise prescription for cancer patients and survivors are provided in Table 2.

Recommendations for resistance-based exercise prescription for cancer patients and survivors are provided in Table 3.

The current literature does not allow inferences to be made about the lower and upper thresholds of exercise required to achieve benefits, nor which types of exercise or modes of delivery are optimal. Exercise adherence, when reported, is similar irrespective of whether the exercise prescribed was aerobic-only, resistance-only or mixed. While future work is required to better understand what constitutes optimal exercise prescription and how specific characteristics of individuals (e.g., age, cancer type, treatment, presence of specific symptoms) influence this prescription, we know enough to positively influence the lives of those undergoing and recovering from cancer treatment. On current knowledge, it is recommended that both aerobic and resistance exercise be prescribed, unless specific problems dictate otherwise. Exercise, starting at appropriate levels and progressing at a pace that reflects the individual’s personal circumstances, is an important component of cancer recovery.

Individuals with a cancer diagnosis are considered a special population in terms of exercise prescription. A range of factors, beyond those usually encountered when providing exercise advice, must be taken into account, particularly when individuals are undergoing treatment or experiencing cancer-related side-effects or complications.

- Communication with treating specialists is necessary. Working in collaboration with the treating specialist/s ensures all necessary contraindications and clinical concerns are known and appropriately taken into account, and the treating specialist/s are aware and involved with the complementary therapies being prescribed. Further, acknowledgement and support by the treating specialist is crucial for compliance and adherence to the exercise program.

- Exercise programs need to be flexible, particularly during periods of cancer treatment. Programs need to be adjusted according to changes in treatment, presence of side-effects, functional and physical status of the patient, and presence of contraindications and clinical concerns. Practically, this may involve prescribing or helping an individual to develop two exercise goals: one that can be accomplished when the presence of side-effects are intense (sometimes referred to by patients as ‘I’m having a bad day’) and another that is relevant for when side-effects are better tolerated (‘good day’). Additionally, steady progress in relation to this population may mean regular participation in exercise compared with continual progression of intensity/duration/frequency.

- The potential for psychosocial benefits should not be overlooked and is an important consideration during exercise prescription. Practitioners need to prescribe exercise that takes into account the wants as well as the needs of the cancer survivor, and at the same time, to ensure the exercise program is enjoyable and builds confidence. Practitioners should also take the time to identify and educate cancer survivors of the specific cancer-related benefits of exercise (as

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### Table 3

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Recommendation and comment</th>
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<tr>
<td>Type</td>
<td>• Resistance exercises should be dynamic in nature using both concentric (lifting and pushing/pulling phase) and eccentric (controlled lowering/returning phase) muscle contractions.</td>
</tr>
<tr>
<td>Frequency</td>
<td>1–3 times/week, with rest days between sessions</td>
</tr>
<tr>
<td>Intensity</td>
<td>50–80% 1-repetition maximum or 6–12 repetition maximum</td>
</tr>
<tr>
<td>Duration</td>
<td>6–10 exercises, 1–4 sets per muscle group</td>
</tr>
<tr>
<td>Progression</td>
<td>Progression as per described for aerobic exercise.</td>
</tr>
</tbody>
</table>

Table has been reproduced and modified, with permission, from [38].
It is important to not lose sight of the individual with whom you are working. A diagnosis of cancer and its associated treatment bring with it unique barriers to regular participation in exercise. However, these are not the only factors to be considered when prescribing exercise to this population. Overcoming ‘typical’ exercise barriers, such as affordability, time constraints, lack of interest/motivation, etc, which may be exacerbated or reduced as a consequence of the cancer experience, should also be considered, discussed and resolved.

In the past, when dealing with cancer patients, vigorous exercise has been avoided, as have high-impact types of activity. Furthermore, cancer survivors with particular side-effects such as lymphoedema have until recently been excluded from participating in exercise intervention studies, for fear of exacerbating this condition. As more evidence accumulates, it appears that this rest strategy has actually exacerbated problems facing cancer patients. We must continue to be cautious when prescribing exercise to special populations. However, at the same time, we must ensure that cancer survivors are provided with exercise programs with appropriate type, intensity and duration, to ensure beneficial outcomes. For example, it makes sense that patients with bony metastasis avoid high-impact activities and/or activities that increase risk of falls. However, this same advice may not be appropriate for a woman who has completed treatment for breast cancer and enjoys the social and physical aspect of a game of netball. We must overcome the perception that cancer patients should pursue rest or only ‘gentle exercise’. Such a strategy is ineffective at stimulating the neuromuscular, endocrine, immune and skeletal systems for symptom reduction and health enhancement.

Fatigue and lymphoedema merit special attention, as they represent cancer symptoms that have previously been treated with rest. It is now understood that exercise participation during and/or after cancer treatment at worst does not exacerbate fatigue. It is also known that failure to participate in a progressive exercise program could potentially exacerbate fatigue rather than prevent or minimise it. With rest, or when physical activity levels are down-regulated, a detrimental cycle of diminished activity which leads to reduced function and subsequent fatigue is initiated. As for lymphoedema, evidence is accumulating to demonstrate that participation in an exercise program does not increase lymphoedema risk or exacerbate the condition if already present. Restricting the involvement in exercise of cancer survivors with fatigue or secondary lymphoedema may limit their opportunity to participate in a potential rehabilitative strategy that could lead to significant benefits for their physical and psychosocial wellbeing, as well as adversely influence their prognosis (risk of recurrence or survival). Nevertheless, our exercise prescription knowledge for this population remains somewhat limited.

While the literature supports the view that exercise should be incorporated during and following cancer treatment, this philosophy is not held by all. Resistance may be encountered from clinicians, other allied health professionals, as well as family and friends of cancer patients. Often the resistance is a
Diagnosis. While the optimal exercise prescription remains unknown, and may depend on the type of cancer, the cancer treatment undertaken and the characteristics of the patient, it is clear that participation in some activity is better than none, and that more is generally better than less, at least up to levels meeting national physical activity guidelines. There are now well-defined physical and psychological problems associated with cancer and its treatment that respond well to appropriate exercise. Therefore, exercise prescription with this population should be seen as vital adjuvant therapy aimed at maintaining or improving structure and function, alleviating symptoms, and assisting recovery of survivors or slowing decline of palliative patients. Regardless, the overarching goal should be to enhance quality of life, and the social and interpersonal interactions derived from exercise are critical components of this process.

4. Conclusions

Appropriately qualified exercise professionals can influence public health through the prescription of exercise for the prevention of cancer, supporting the medical management of cancer, as well as optimising recovery following cancer diagnosis. While the optimal exercise prescription remains a whole-body approach. Therefore, there exists a significant role for exercise professionals in the care of people with cancer.

Additionally, the quality of research in the exercise and cancer domain varies. More rigorous, randomised, controlled trials that are well described, involving larger sample sizes and population-based samples are required to advance our understanding regarding the impact of physical activity on cancer-related outcomes, for prevention and treatment. Furthermore, the potential benefits of exercise in relation to cancer is a focus of growing concern, with expanded opportunities for postgraduate education, including training to work with the special population of cancer patients and survivors as well as training to conduct research on exercise prescription in relation to cancer prevention.

Conflict of interest

There are no potential conflicts of interest to disclose.

Acknowledgements

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References