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## Review

## Exercise for managing cancer- and treatment-related side effects in older adults

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## ABSTRACT

The incidence of cancer in adults aged 60 years and older is expected to rise, and because cancer is associated with aging, the overall prevalence of cancer will rise as well. With advances in cancer treatment, more older adults will receive treatment but they will also suffer the biopsychosocial consequences of cancer and cancer treatment. In this review, we describe the importance of assessing biopsychosocial needs in this vulnerable population and highlight studies supporting the use of exercise in addressing these needs. We discuss challenges and research gaps in several areas including 1) Identifying the exercise doses and modes for specific outcomes, 2) Understanding risks and safety of exercise, and 3) Implementing exercise programs into clinical practice at the individual, health care team, and organizational levels, including strategies to increase adherence.

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## 1. Introduction

The world's population is expected to increase from 7.2 billion in 2015 to 9.7 billion in 2050, and adults aged >60 years constitute the

group with the highest projected growth rate [1]. As cancer is associated with aging, the overall prevalence of cancer will increase as well. With improved availability and tolerability of cancer treatments, more older adults are able to receive treatment and derive benefits, thereby increasing the number of older cancer survivors [2,3]. This group, however, is more vulnerable to short- and long-term treatment-related physical and psychological side effects due to underlying age-related comorbidities, polypharmacy, and both cognitive and physical impairments [4–8].

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Increasing emphasis has been placed on assessing and addressing the biopsychosocial needs of older adults [9,10]. The biopsychosocial model stresses the importance of understanding and treating the patient's illness and assessing physical health and emotional well-being as well as social and environmental factors, many of which are inter-related and may influence one another [11]. In the context of cancer and aging, cancer itself and its treatments may lead to functional and cognitive decline or diminished emotional health by contributing to depression and anxiety [4,12–14]. This in turn may result in treatment delay or non-adherence, affecting disease outcomes [15]. Acknowledging the complex needs of older patients, a cancer-specific geriatric assessment tool was developed to uncover these important biopsychosocial needs in older patients [16]. Once these needs have been identified, behavioral interventions such as exercise can be helpful in addressing these needs. For example, exercise may prevent or improve side effects including functional and cognitive decline associated with cancer and cancer treatment, as well as ameliorate psychological and behavioral needs such as depression, anxiety, distress, and low self-esteem. These benefits could lead to improvement in treatment adherence, treatment outcomes, and quality of life (QoL) [17–25]. However, exercise is not routinely incorporated into cancer care due to multiple barriers, and studies have shown that <50% of physicians recommend exercise in routine clinical care and <20% of patients recalled being instructed to exercise by their oncologist [26–29].

In this narrative review, we discuss the common biopsychosocial consequences of cancer and cancer treatment in older patients with cancer. We also review published studies evaluating the effects of exercise on various outcomes and associated challenges faced delivering exercise interventions in this population.

## 2. Biopsychosocial Consequences of Cancer and Cancer Treatment

Aging is associated with deterioration in multiple organs [30], often accompanied by morbidity, disability and frailty, with a gradual decline in physical fitness and functional reserve [31]. With a diagnosis of cancer and the addition of cancer treatment, a seemingly fit older individual can decompensate quickly. Many studies have demonstrated that older patients experience a multitude of physical issues as they navigate the management of their cancer, including functional decline, fatigue, bone loss, cardiovascular toxicity, sarcopenia, and cachexia [5,32–37]. The prevalence of some of these problems is higher in the older population with cancer than in their younger counterparts and in those of the same age without cancer [32,34]. In a study by Abbema and colleagues, functional status decline at twelve months post-surgery was higher in patients with cancer aged >70 years (43.6%) than in patients with cancer aged 50–69 years (24.6%) and in persons without cancer aged >70 years (28.1%) [34]. Similarly, in a study by Butt and colleagues, patients with cancer reported more fatigue (36.9%) than those without cancer (46.6%), and fatigue was found to increase with age [32]. Detecting and addressing these issues are important, as they are associated with poor outcomes such as increased healthcare utilization and decreased treatment tolerance, QoL, and survival in patients with cancer [38–41].

In addition to physical issues, older patients with cancer experience a variety of psychological and social effects from cancer and cancer treatments including sleep disorders, anxiety, depression, distress, fear, and cognitive impairment [5,7,42]. The prevalence of these symptoms range from 10 to 72% in studies of the geriatric oncology population [5,7,42,43]. Over the last few decades, patients with cancer have described their socio-psychological side effects as severe and long-lasting [44]. In addition, socio-psychological side effects are perceived to be less tolerable than physical side effects [45]. These side-effects are associated with poor outcomes including lower performance status, diminished QoL, and decreased survival [14,46].

## 3. Exercise Recommendations and Studies in Older Adults With Cancer

The American College of Sports Medicine (ACSM) recommends that patients with cancer and cancer survivors adhere to the United States Department of Health and Human Services 2008 Physical Activity Guidelines for Americans: 1) Weekly accumulated 150 min of moderate-intensity or 75 min of vigorous-intensity or an equivalent combination of moderate and vigorous aerobic activity (for older cancer survivors whose physical conditions preclude participation in 150 min of moderate-intensity physical activity, they are encouraged to be as active as they are able); 2) Two to three sessions of strength training that engages major muscle groups per week; and 3) Major muscle group stretching on exercise days [47]. Although this physical activity guideline is generally appropriate for patients with cancer and cancer survivors, 38% of cancer survivors do not adhere to the guideline after the completion of primary cancer treatment [48]. Among these individuals, almost half are older adults (over 65 years) [49]. Despite the publication of numerous studies showing the benefits of exercise for managing cancer-related toxicities, inclusion of geriatric oncology patients in this research is uncommon.

Table 1 illustrates examples of randomized controlled trials that investigated the effects of exercise intervention (either alone or with another intervention such as diet) on biopsychosocial health in at least 100 patients with cancer with a mean or median age of 60 years or above. The exercise interventions are diverse in terms of mode (e.g. aerobic exercise [50,51], resistance training [50–54], the combination of aerobic and resistance training [52,55,56]), intensity, frequency, duration, and delivery methods (e.g. home-based exercise program [57,58]). These studies demonstrate that exercise may improve various biopsychosocial outcomes including physical function, muscle strength, cardiovascular fitness, body composition, weight loss, fatigue, QoL, depression, and cognitive and social function.

### 3.1. Challenges and Research Gaps

#### 3.1.1. Identifying the Exercise Doses and Modes for Specific Outcome

An interesting question is whether various intended outcomes require different exercise doses and modes. In non-cancer populations such as patients with osteoarthritis of the knee, the benefit of aerobic exercise on pain was greater with quadriceps-specific exercises than with lower limb exercise, particularly if performed at least three times a week [59]. Patient characteristics as well as the intensity and duration of exercise did not affect pain reduction [59]. In the cancer population, a meta-analysis of 42 trials of adult patients with cancer demonstrates that combined aerobic and resistance training provides the largest treatment effect on cancer-related fatigue. Moderate-intensity aerobic exercise has a greater effect on walking endurance than high-intensity exercise. It is unclear, however, if low-intensity exercise is sufficient to improve outcomes, since studies comparing moderate- and low-intensity exercise are scarce (see Table 1) [60]. One study in patients with breast cancer receiving chemotherapy and/or radiation therapy shows a negative association between exercise intensity and fatigue and QoL [61]. Low- to moderate-intensity resistance training either alone or with aerobic exercise appears to be effective in improving muscle strength, although studies suggest the combination is better [62,63]. On the other hand, the relationships reported between exercise dose and anxiety and depression in the cancer population have been generally inconsistent [61,64].

#### 3.1.2. Understanding Risks and Safety of Exercise in Older Adults

A concern when considering an exercise prescription is the risk of exercise specifically among older adults with cancer. In 2010, ACSM published its exercise guideline in cancer survivors [47]. The expert panel reviewed over 80 studies and concluded that exercise is safe

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