Published in final edited form as:
Curr Sports Med Rep. 2009 ; 8(6): 325–330. doi:10.1249/JSR.0b013e3181c22324.

Exercise for the Management of Side Effects and Quality of Life among Cancer Survivors

Karen M. Mustian, Ph.D., M.P.H., A.C.S.M, F.S.B.M.[1], **Lisa K. Sprod, Ph.D.**[1], **Oxana G. Palesh, Ph.D., M.P.H.**[1], **Luke J. Peppone, Ph.D.**[1], **Michelle C. Janelsins, Ph.D.**[1], **Supriya G. Mohile, M.D.**[1], and **Jennifer Carroll, M.D.**[1]

[1] University of Rochester School of Medicine and Dentistry, James P. Wilmot Cancer Center

Abstract

Physical activity may play an important role in the rehabilitation of cancer survivors during and following treatment. Current research suggests numerous beneficial outcomes are experienced in cancer survivors undergoing exercise interventions during or following cancer treatment. Exercise not only plays a role in managing side effects but also improves functional capacity and quality of life. The purpose of this article is to provide an overview of the oncology literature supporting the use of exercise as an effective intervention for improving cancer-related fatigue, other side effects, functional capacity, and quality of life among cancer survivors.

INTRODUCTION

According to the American Cancer Society, nearly 1.5 million Americans will be diagnosed with cancer in 2009 (2). Despite the large number of cancer diagnoses, the five-year survival rate for *all* cancer types has increased from 50% in the 1970s to almost 70% in the first decade of the 21st century (47). While better detection and improved treatments have resulted in a growing number of cancer survivors, these survivors endure both short- and long-term side effects from cancer and its treatments. Side effects from cancer and its treatments are far-reaching and negatively impact cancer survivors during treatment and in the years following treatment completion. Exercise can play a significant role in managing some of these side effects and improving quality of life (QOL) during and following treatment. The purpose of this article is to provide an overview of the exercise oncology literature supporting the use of exercise as an effective intervention for managing cancer-related fatigue (CRF) and other side effects while improving QOL among cancer survivors. As used in this article, a cancer survivor is defined as anyone who has been diagnosed with cancer, regardless of cancer type, cancer severity, and cancer treatment status.

Correspondence author: Dr. Karen M. Mustian, University of Rochester School of Medicine, James P. Wilmot Cancer Center, Department of Radiation Oncology, 601 Elmwood Ave, Box 704, Rochester, NY 14642, Tel: 585-275-5513, Fax: 585-461-5601, Karen_Mustian@urmc.rochester.edu.
Co-authors: (all addresses are the same as above)
Lisa K. Sprod, Ph.D., Tel: 585-275-9958, Fax: 585-461-5601, Lisa_Sprod@urmc.rochester.edu
Oxana G. Palesh, Ph.D., M.P.H., Tel: 585-273-3998, Fax: 585-461-5601, Oxana_Palesh@urmc.rochester.edu
Luke J. Peppone, Ph.D., Tel: 585-275-7827, Fax: 585-461-5601, Luke_Peppone@urmc.rochester.edu
Michelle C. Janelsins, Ph.D., Tel: 585-276-4656, Fax: 585-461-5601, Michelle_Janelsins@urmc.rochester.edu
Supriya G. Mohile, M.D., Tel: 585-273-5357, Fax: 585-461-5601, Supriya_Mohile@urmc.rochester.edu
Jennifer Carroll, M.D., M.P.H., Tel: 585-506-9484, Fax: 585-473-2245, Jennifer_Carroll@urmc.rochester.edu

Funding Disclosure: Supported by NCI grants 1K07CA120025 and K07CA132916.

CANCER TREATMENT-RELATED SIDE EFFECTS

Cancer treatments such as surgery, chemotherapy, radiation therapy, and hormone therapy often result in psychological and physiological sequelae and side effects that interfere with treatment completion, the ability to function and perform essential daily activities, and QOL. Cancer-related fatigue, psychosocial side effects, and physiological dysfunction such as impaired muscle and cardiorespiratory function are common cancer treatment-related side effects and are discussed in more detail below.

Cancer-Related Fatigue

Cancer-related fatigue (CRF) is the most common and most debilitating side-effect reported by cancer survivors (20,36,40,44). CRF is frequently reported by survivors throughout the cancer continuum as more distressing and having a greater negative impact on their daily activities and QOL than other cancer-related side effects including vomiting, nausea, pain, and depression (20,36,40). Typically, CRF begins near the time of diagnosis, worsens as treatments progress, and persists in the months and years after treatment completion (20,36,40,44). Approximately 60% to 100% of cancer survivors undergoing treatment report CRF, with at least 41% indicating severe CRF (20,36,40,44). Up to 81% of cancer survivors report persistent CRF following treatment completion, with 17% to 38% indicating persistent, severe CRF at least six months after completing treatment (20,36,40,44). Additionally, undergoing a combination of treatments results in more fatigue than single treatment modalities (20,36,40, 44). CRF differs from the fatigue experienced by individuals without cancer in its severity, impact on QOL and the inability to alleviate CRF with adequate rest alone (20,36,40,44). Recovery from cancer and its treatments is more complicated when the negative effects of fatigue on QOL continue to increase daily (20,36,40,44). The lack of effective remedies to prevent or alleviate CRF adds to the distress cancer survivors endure. In addition, CRF commonly co-occurs with many additional psychophysiological side effects. While we do not know whether additional psychophysiological side effects are implicated in the development of CRF, they nevertheless impair a cancer survivor's QOL (20,36,40,44).

Psychosocial Side Effects

Psychosocial side effects are very common in cancer survivors. Nearly 10% to 25% of cancer survivors report depression (46) and 30% to 50% of cancer survivors report sleep disruption (50). Sleep dysfunction is exacerbated in survivors who spend a significant amount of time in bed as daytime activities may be interrupted by napping/rest and night sleep time may be disrupted by periods of activity (4). Pain is reported by 45% to 59% of cancer survivors (9). Nearly half of cancer survivors report anxiety, with approximately 20% meeting anxiety disorder criteria (58). Cognitive difficulties, including impaired memory and an inability to concentrate, occur in approximately 25% to 80% of cancer survivors (6). Cancer survivors also may have a difficult time working, participating in leisure and social activities and in activities with their families, sustaining meaningful relationships, and they often experience negative outcome expectancies and hopelessness during and after treatment (20,36,40,44).

Muscle Atrophy and Bone Loss

Muscle atrophy and muscle weakness commonly occur as a result of cancer and its treatment (48,60–62). Adenosine triphosphate (ATP) is a key mediator in generating muscle mass and in contractile function. Decreased ATP synthesis may play a significant role in the development of CRF and other side effects (48). Chemotherapy, radiation therapy, and hormonal therapy can lead to diminished bone mineral density. Adjuvant chemotherapy can lead to premature menopause, resulting in rapid bone loss due to the sudden cessation of production of endogenous estrogen (7). Additionally, primary or prophylactic oophorectomy in premenopausal women reduces estrogen production and subsequently reduces bone mineral

density (57). The increasing use of aromatase inhibitors to prevent breast cancer recurrence also has resulted in higher rates of bone loss due to the inhibition of estrogen production (22). This cancer treatment-induced bone loss results in increased fracture risks for breast cancer survivors.

Cardiopulmonary Toxicity

Singularly or in combination, chemotherapy can lead to impaired cardiovascular and respiratory function (20,36,40,44). Chemotherapeutic agents such as the anthracyclines, and trastuzumab, a monoclonal antibody, may lead to acute or late cardiomyopathy, manifesting during treatment or years after treatment completion (64). The administration of cardiotoxic chemotherapy drugs concurrent with chest irradiation for the treatment of breast cancer can synergistically result in greater damage to cardiac tissue than either treatment alone (44,53, 54). The acute cardiac effects of radiation include vascular tissue inflammation, vascular dilation, increased capillary permeability, and interstitial edema (44,53,54). Chemotherapy-induced cardiotoxicity may ultimately lead to systolic and/or diastolic left-ventricular dysfunction, coronary artery disease, pericarditis/myocarditis, severe congestive cardiomyopathy, valvular disease, sinus tachycardia, supraventricular arrhythmias, and conduction abnormalities (44,53,54). Side effects are dose-dependent, with the likelihood of clinically relevant cardiac damage increasing with cumulative doses (53,54). CRF is a common symptom and early preclinical indicator of cardiotoxicity in cancer survivors (44). CRF severity is worsened by diminished cardiac function, and cardiac dysfunction results in additional stress to the heart, which in turn leads to greater CRF, suggesting that CRF and cardiac damage may share a common pathophysiology (44). Treatments with the anticancer drugs methotrexate and bleomycin can lead to pulmonary toxicity and result in shortness of breath due to impaired lung function (11).

Exercise as a Promising Therapy for Cancer Side Effects

Cancer and cancer treatment-related side effects vary greatly among cancer survivors due to variations in cancer types, severity of the disease, type of treatments undergone, and underlying health conditions. Therefore, it is unlikely that researchers will develop an intervention effective for the attenuation of multiple side effects targeting a single pathopsychological or pathophysiological mechanism to provide effective relief for most cancer survivors. It is more likely that, instead, an intervention capable of influencing multiple systems and psychophysiological pathways *simultaneously* will be needed to effectively prevent and manage side effects. In addition to the side effects discussed above (CRF, psychosocial symptoms, cardiotoxicity, bone loss), other common side effects include impaired immune function, neuroendocrine dysfunction, and neurotoxicity. Exercise is a promising therapy which may help alleviate many of the aforementioned common side effects in cancer survivors. A variety of exercise interventions, including aerobic exercise, resistance exercise, and mindfulness-based exercise have been found to reduce some of the side effects commonly experienced by cancer survivors.

PHYSICAL ACTIVITY

Research consistently indicates that exercise shows great promise as a means to mitigate the acute, chronic, and late side effects stemming from cancer and its treatments (40). Eight recent reviews (19,27,28,40,43,44,52,59) summarize the evidence demonstrating outcomes from exercise interventions implemented in cancer survivors during and after treatment. The main outcomes examined included CRF, depression, anxiety, sleep disruption, cognitive function, self-esteem, nausea, cardiopulmonary function, muscular strength, flexibility, and body composition.

Aerobic Exercise

Aerobic exercise is performed at an intensity that is low enough to allow for prolonged periods of activity, utilizes large muscle groups and is rhythmic in nature. Common modes of aerobic exercise include walking, running, cycling, and swimming. Aerobic exercise has been shown to reduce many side effects stemming from cancer and its treatments, while also improving QOL. Specifically, aerobic exercise can reduce CRF, depression, anxiety, sleep disturbances, and nausea while increasing aerobic capacity.

Mock and colleagues (32–35) reported improvements in CRF, aerobic capacity, QOL, depression, anxiety, sleep disturbance, and nausea among breast cancer survivors during chemotherapy and radiation therapy with home-based walking programs of moderate intensity (*e.g.*, self-paced % of heart rate reserve; 50% to 70% maximum heart rate). Participants activity levels ranged from 4–6 days/week for 10–45 minutes over 1.5 to 6 months compared with non-exercising controls.

Dimeo and colleagues (16,17) examined the effects of two different aerobic exercise interventions in cancer survivors with mixed solid tumors (*e.g.*, breast, lung, and gastrointestinal) and participants with lymphoma receiving surgery and/or high dose conventional chemotherapy, radiation therapy and autologous peripheral blood stem cell transplantation. Participants utilized a moderately intense interval walking program (alternating between 70% of heart rate maximum and half speed for 3 minutes each) 7 days/week for a total of 33 minutes during hospitalization (16) or participated in a moderately intense interval bed cycle ergometer program (alternating between 50% of heart rate reserve and rest pauses for 1 minute each) 7 days/week for a total of 30 minutes. Participants who exercised reported less CRF, less psychological distress, better psychological well-being, better social and cognitive function, improved satisfaction with life, less dyspnea, and improved aerobic capacity and QOL compared to non-exercise usual-care controls (17).

Courneya and colleagues (12) found improvements in CRF, anxiety, depression, physical, emotional and functional well-being, satisfaction with life, QOL, aerobic capacity, and flexibility among colorectal cancer survivors undergoing chemotherapy while participating in a moderately intense (65% to 75% maximal heart rate) walking and flexibility program 3 to 5 days/week for 20 to 30 minutes when compared with survivors in a waitlist control condition. Female breast cancer survivors undergoing chemotherapy concurrent with participation in an aerobic exercise intervention showed improvements in self-esteem and peak oxygen consumption (14).

Similarly, Windsor and colleagues (63) demonstrated less CRF and improvements in aerobic capacity among prostate cancer survivors receiving radiation therapy while participating in a home-based walking program 3 times a week for 30 minutes at a moderate intensity (60% to 70% maximum heart rate) for 10 weeks compared with participants in a usual-care control condition. Additionally, Pinto and colleagues (45) reported improved CRF, vigor, mood, and body esteem among breast cancer survivors (stage 0-II) post-treatment participating in a home-based moderate intensity (55% to 65% maximum heart rate) walking program 2 to 5 days a week for 12 weeks compared with participants in a contact-monitoring control condition.

Breast cancer survivors participating in at least 1 hour of walking exercise following treatment completion had greater survival rates than breast cancer survivors who exercised less than 1 hour per week (21). Risk of breast cancer recurrence, breast cancer-specific death, as well as mortality from any cause was reduced by 26% to 40% in women who exercised using self-selected full-body aerobic activities such as outdoor walking and swimming. Exercising for at least one hour offered protection, and additional protection was gained when exercise was performed at a moderate intensity 3–5 hours per week (21). Similarly, colon cancer survivors

who participated in at least three hours of moderate intensity exercise following diagnosis, such as walking, jogging, cycling, and swimming, were at a 39% to 59% reduced risk of mortality resulting from colon cancer and a 50% to 63% reduced risk of all-cause mortality compared to sedentary colon cancer survivors (29,30).

Resistance Exercise

Resistance training involves muscle contraction against a load. Performing an arm curl with external resistance, such as therapeutic resistance bands, barbells or dumbbells, is an example of a resistance training exercise. Resistance exercise also has been shown to improve many side effects stemming from cancer and its treatments, as well as improving QOL. Resistance training also has been found to favorably impact cancer survivors during and following cancer treatment.

For example, Segal and colleagues (55) have found that prostate cancer survivors undergoing androgen deprivation therapy saw improvements in CRF, cognitive function, muscular strength and QOL when completing a supervised resistance training program 3 times a week, performing 2 sets of 8 to12 repetitions at a moderate intensity (60% to 70% 1-repetition maximum) for a total of 12 weeks, compared with non-exercising usual-care controls.

Resistance training concurrent with chemotherapeutic treatments for breast cancer has also been shown to be effective, increasing self-esteem and resulting in greater upper body and lower body strength and lean body mass compared to a usual care group (14). Schmitz and colleagues found that resistance training 2 days per week over the course of 6 to 12 months resulted in increased lean mass and decreased body fat percentage (51). More recently Ahmed and colleagues demonstrated that resistance training did not result in more cases of lymphedema in cancer survivors, contrary to popular beliefs (1).

Combined Aerobic and Resistance Exercise

Exercise programs combining both aerobic and resistance modes of physical activity positively influence many side effects stemming from cancer and its treatments. Campbell and colleagues (1,8) demonstrated improvements using aerobic and resistance training in cancer survivors. Early stage breast cancer survivors receiving chemotherapy and/or radiation therapy had improved CRF, physical function, satisfaction with life and QOL after completing a structured and supervised multi-modal (aerobic and resistance training) moderate intensity (60% to 75% age-adjusted maximum heart rate) exercise program 2 days a week for 12-weeks compared with participants in a usual care control condition.

Additional research by Milne and colleagues integrating a combined resistance training and aerobic exercise intervention showed a 12-week exercise intervention, including approximately 20 minutes of endurance training and 12 resistance training exercises (2 sets, 10–15 repetitions), resulted in improved aerobic fitness and muscular strength (31).

Courneya and colleagues also compared the outcomes of an aerobic and a resistance training exercise intervention during chemotherapy in breast cancer survivors on their ability to tolerate dosages of prescribed chemotherapy. Participants in the usual care no-exercise group were only able to receive 84.1% of their prescribed relative dose intensity (most beneficial outcomes are seen with 85% of relative dose intensity or higher) whereas participants in the aerobic and resistance training groups were able to tolerate 87.4% and 89.8% of relative dose intensity, respectively (14).

More recently, Mustian and colleagues (42) demonstrated that a 4-week home-based individually-tailored and progressively-increasing walking and resistance band exercise program improved aerobic capacity, strength, CRF, and QOL among breast and prostate cancer

survivors undergoing radiation therapy (42). Participants in this program were able to progressively increase from walking less than 5,000 steps per day to almost 12,000 steps per day. Resistance band exercising increased from zero minutes per day to more than 20 minutes per day for an average of 3.5 days per week. Cancer survivors performed this exercise at an average intensity of 3–4 on a 10 point rating of perceived exertion scale.

Mindfulness Based Exercise

Mindfulness-based exercise modes such as Yoga and Tai Chi can provide substantial benefits for cancer survivors by decreasing side effects, and improving function and QOL. For example, Joseph and colleagues (26) conducted an early study comparing yoga, support therapy, and meditation interventions among cancer survivors undergoing radiation therapy. The 8-week yoga intervention consisted of simple yoga relaxation exercises two times a week for 90 minutes, and included yoga postures, breathing, and visualization. Participants in the yoga arm of this study reported improvements in sleep, QOL, treatment tolerance, mood, appetite, and bowel function.

Mustian and colleagues (38,39,41) demonstrated that a community-based 12-week 15-move Yang Style Short-Form of Tai Chi Chuan exercise, performed 3 times a week for 60 minutes, improved aerobic capacity, strength, flexibility, body composition, self-esteem, and QOL among breast cancer survivors post-treatment.

Cohen and colleagues (10) conducted a study comparing the effectiveness of a Tibetan yoga exercise program to a wait-list control for improving sleep, fatigue and psychological adjustment among lymphoma survivors who were receiving treatment or within 12 months post-treatment. The Tibetan yoga intervention consisted of one yoga session a week for 7-weeks, with foci on yoga postures, visualization, breathing, and mindfulness. Participants in the yoga exercise program reported lower sleep disturbance.

CONCLUSIONS AND RECOMMENDATIONS FOR EXERCISE IN CANCER SURVIVORS

Unfortunately, most cancer survivors do not discuss initiating or continuing an exercise program with their treating oncologist or primary care physician (23,24,37,49). However, research shows that cancer survivors prefer that their oncologists initiate discussion about exercise prescriptions (24). Survivors who receive exercise prescriptions or referrals from their treating physician return to exercise more quickly after treatment and have better adherence (13,25,56). Oncologists need to discuss with cancer survivors how they can safely begin an exercise program during and after treatments and to inform survivors of any potential limitations (*e.g.*, orthopedic, cardiopulmonary, oncologic) that can affect their exercise tolerance. Cancer survivors can benefit from an oncology referral to a *qualified* exercise specialist, specifically an oncology-certified exercise professional. The majority of cancer survivors report preferring to receive exercise counseling from a qualified exercise professional affiliated with the cancer center in which they receive treatment (23). Qualified exercise professionals include individuals with formal education at the Bachelor's level or higher in accredited exercise science or kinesiology programs. Additional certification by the American College of Sports Medicine with the Oncology Specialty would be preferable, and this certification, which can be obtained by individuals with varied educational backgrounds, provides a very useful professional benchmark ensuring exercise professionals have the minimum competencies necessary to meet the unique needs of cancer survivors both during and after treatment (3,18).

At this point, specific evidence-based exercise guidelines have not been established for cancer survivors by professional organizations such as the American College of Sports Medicine or the American Society of Clinical Oncology. However, following the exercise guidelines established by the American Cancer Society for cancer prevention may prove beneficial for cancer survivors (18). The guidelines are aimed at adopting an active lifestyle and recommended that adults participate in at least 30 minutes of physical activity, ideally 45 to 60 minutes, at least 5 days per week, at a moderate to vigorous intensity (18).

Evidence from current research also suggests that exercise prescriptions for cancer survivors should be individualized and tailored considering the disease site and stage, planned treatments, individual's current fitness level along with past and present exercise participation and preferences. Research suggests that exercise interventions involving moderately intense [55% to 75% of heart rate maximum–corresponding to a rating of perceived exertion between 11 and 14 (5)] aerobic exercise ranging from 10 to 90 minutes in duration, 3 to 7 days/week are consistently effective at managing side effects and improving QOL among cancer survivors with an early stage diagnosis (*i.e.*, non-metastatic disease) (15,21,40,43). Stationary cycling may be a useful mode of physical exercise for survivors with impairments such as ataxia or balance difficulties (15,21,40,43). Short bouts of activity (3 to 10 minutes) accompanied by periods of rest culminating in a total of 30 minutes daily also can be effective at reducing side effects and improving QOL (15,21,40,43). Preliminary research suggests that progressive resistance exercise (*e.g.*, therapeutic resistance bands, dumbbells, fixed weight systems) performed 3 times a week at a moderate to vigorous intensity (60% to 90% of 1-repetition maximum) progressively increasing up to 2 to 4 sets ranging from 8 to 15 repetitions is effective at reducing side effects and improving QOL among cancer survivors. Research also suggests that mindfulness-based modes of exercise such as Yoga and Tai Chi Chuan performed 1 to 3 times a week for 60 to 90 minutes, at a moderate intensity level can reduce side effects and improve QOL.

Studies also have demonstrated that low intensity exercise is safe and well-tolerated by survivors with metastatic disease. To decrease the risk of lymphedema, compression sleeves should be worn when appropriate, but recent research suggests that resistance training does not result in increased incidence of lymphedema (1,15,21,40,43). It also is prudent to advise cancer survivors to avoid excessive high-intensity exercise which can potentially compromise the immune system and interfere with treatment and recovery (15,21,40,43).

SUMMARY

The current exercise and cancer control literature provides consistent support for the efficacy of exercise interventions in managing cancer- and treatment-related side effects as well as QOL. However, this body of literature is still in its infancy and limitations do exist. Small sample sizes, a lack of consistency in the type and amounts of exercise utilized and methodological concerns make it difficult to generalize the findings to the diverse cancer survivor population. Additionally, making comparisons based on dose and exercise mode is challenging due to a lack of appropriate statistical and follow-up analyses (e.g., intent-to-treat analyses in randomized controlled trials) (19,27,28,40,43,44,52,59). Despite these limitations, Preliminary evidence consistently suggests that that physical activity is not only safe but advantageous for cancer survivors in managing multiple side effects associated with cancer and cancer treatments (21,40,43). Overall, research suggests that aerobic activity, resistance training, a combination of both, and mindfulness forms of exercise such as yoga and Tai Chi are effective in reducing cancer survivors' complaints and improving QOL.

Reference List

1. Ahmed RL, Thomas W, Yee D, Schmitz KH. Randomized controlled trial of weight training and lymphedema in breast cancer survivors. J Clin Oncol 2006 June 20;24(18):2765–72. [PubMed: 16702582]
2. American Cancer Society. Cancer Facts & Figures 2009. Atlanta: American Cancer Society; 2009.
3. American College of Sports Medicine. ACSM's Guidelines for exercise testing and prescription. Baltimore: Lippincott, Williams, & Wilkins; 2006.
4. Ancoli-Israel S, Moore PJ. The relationship between fatigue and sleep in cancer patients: A review. Eur J Cancer Care (Engl) 2001 December;10:245–55. [PubMed: 11806675]
5. Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982;14(5):377–81. [PubMed: 7154893]
6. Bower JE, Bower JE. Behavioral symptoms in patients with breast cancer and survivors. [Review] [135 refs]. J Clin Oncol 2008 February 10;26(5):768–77. [PubMed: 18258985]
7. Bruning PF, Pit MJ, de Jong-Bakker M, van den EA, Hart A, van EA. Bone mineral density after adjuvant chemotherapy for premenopausal breast cancer. Br J Cancer 1990 February;61(2):308–10. [PubMed: 2310683]
8. Campbell A, Mutrie N, White F, McGuire F, Kearney N. A pilot study of a supervised group exercise program as a rehabilitation treatment for women with breast cancer receiving adjuvant treatment. European Journal of Oncology Nursing 2005;9(1):56–63. [PubMed: 15774341]
9. Chang VT, Hwang SS, Feuerman M, Kasimis BS. Symptom and quality of life survey of medical oncology patients at a veterans affairs medical center: a role for symptom assessment. Cancer 2000 March 1;88(5):1175–83. [PubMed: 10699909]
10. Cohen LW. Psychological adjustment and sleep quality in a randomized trial of the effects of a Tibetan yoga intervention in patients with lymphoma. Cancer 2004 May 15;100(10):2253–60. [PubMed: 15139072]
11. Cottin VJ. TBMPJSaJPB. Pulmonary function in patients receiving long-term low-dose methotrexate. Chest 1996;(109):933–8. [PubMed: 8635373]
12. Courneya KS, Friedenreich CM, Quinney HA, Fields AL, Jones LW, Fairey AS. A randomized trial of exercise and quality of life in colorectal cancer survivors. Eur J Cancer Care (Engl) 2003 December;12(4):347–57. [PubMed: 14982314]
13. Courneya KS, Mackey JR, Jones LW. Coping with cancer: can exercise help? Phys Sportsmed 2000;28:49–73. [PubMed: 20086640]
14. Courneya KS, Segal RJ, Gelmon K, Reid RD, Mackey JR, Friedenreich CM, Proulx C, Lane K, Ladha AB, Vallance JK, Liu Q, Yasui Y, McKenzie DC. Six-month follow-up of patient-rated outcomes in a randomized controlled trial of exercise training during breast cancer chemotherapy. Cancer Epidemiol Biomarkers Prev 2007 December;16(12):2572–8. [PubMed: 18086760]
15. Courneya KS, Segal RJ, Mackey JR, Gelmon K, Reid RD, Friedenreich CM, Ladha AB, Proulx C, Vallance JK, Lane K, Yasui Y, McKenzie DC. Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: a multicenter randomized controlled trial. J Clin Oncol 2007 October 1;25(28):4396–404. [PubMed: 17785708]
16. Dimeo F, Thomas F, Raabe_Menssen C, Propper F, Mathias M. Effect of aerobic exercise and relaxation training on fatigue and physical performance of cancer patients after surgery. A randomised controlled trial. Support Care Cancer 2004;12:774–9. [PubMed: 15338385]
17. Dimeo FC, Stieglitz RD, Novelli-Fischer U, Fetscher S, Keul J. Effects of physical activity on the fatigue and psychologic status of cancer patients during chemotherapy. Cancer 1999 May 15;85(10): 2273–7. [PubMed: 10326708]
18. Doyle C, Kushi LH, Byers T, Courneya KS, mark-Wahnefried W, Grant B, McTiernan A, Rock CL, Thompson C, Gansler T, Andrews KS. Nutrition and physical activity during and after cancer treatment: an American Cancer Society guide for informed choices. CA Cancer J Clin 2006 November;56(6):323–53. [PubMed: 17135691]
19. Galvao DA, Newton RU. Review of exercise intervention studies in cancer patients. J Clin Oncol 2005;23(4):899–909. [PubMed: 15681536]

20. Hofman M, Ryan JL, Figueroa-Moseley CD, Jean-Pierre P, Morrow GR. Cancer-related fatigue: The scale of the problem. The Oncologist 2007;12(1):4–10. [PubMed: 17573451]
21. Holmes MD, Chen WY, Feskanich D, Kroenke CH, Colditz GA. Physical activity and survival after breast cancer diagnosis. JAMA 2005;293(20):2479–86. [PubMed: 15914748]
22. Howell A, Cuzick J, Baum M, Buzdar A, Dowsett M, Forbes JF, Hoctin-Boes G, Houghton J, Locker GY, Tobias JS. Results of the ATAC (Arimidex, Tamoxifen, Alone or in Combination) trial after completion of 5 years' adjuvant treatment for breast cancer. Lancet 2005 January 1;365(9453):60–2. [PubMed: 15639680]
23. Jones LW, Courneya KS. Exercise counseling and programming preferences of cancer survivors. Cancer Pract 2002 July;10(4):208–15. [PubMed: 12100105]
24. Jones LW, Courneya KS. Exercise discussions during cancer treatment consultations. Cancer Pract 2002 March;10(2):66–74. [PubMed: 11903271]
25. Jones LW, Courneya KS, Fairey AS, Mackey JR. Effects of an oncologist's recommendation to exercise on self-reported exercise behavior in newly diagnosed breast cancer survivors: a single-blind, randomized controlled trial. Ann Behav Med 2004 October;28(2):105–13. [PubMed: 15454357]
26. Joseph CD. Psychological supportive therapy for cancer patients. Indian Journal of Cancer 1983;20:268–70. [PubMed: 6392068]
27. Knols R, Aaronson N, Uebelhart D, Fransen J, Aufdemkampe G. Physical exercise in cancer patients during and after medical treatment: A systematic review of randomized and controlled clinical trials. J Clin Oncol 2005;23(16):3830–42. [PubMed: 15923576]
28. McNeely ML, Campbell KL, Rowe BH, Klassen TP, Mackey JR, Courneya KS. Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. CMAJ Canadian Medical Association Journal 2006 July 4;175(1):34–41.
29. Meyerhardt JA, Giovannucci EL, Holmes MD, Chan AT, Chan JA, Colditz GA, Fuchs CS. Physical activity and survival after colorectal cancer diagnosis. J Clin Oncol 2006 August 1;24(22):3527–34. [PubMed: 16822844]
30. Meyerhardt JA, Heseltine D, Niedzwiecki D, Hollis D, Saltz LB, Mayer RJ, Thomas J, Nelson H, Whittom R, Hantel A, Schilsky RL, Fuchs CS. Impact of physical activity on cancer recurrence and survival in patients with stage III colon cancer: findings from CALGB 89803. J Clin Oncol 2006 August 1;24(22):3535–41. [PubMed: 16822843]
31. Milne HM, Wallman KE, Gordon S, Courneya KS. Impact of a combined resistance and aerobic exercise program on motivational variables in breast cancer survivors: a randomized controlled trial. Ann Behav Med 2008 October;36(2):158–66. [PubMed: 18795388]
32. Mock V, Burke MB, Sheehan P, Creaton EM, Winningham ML, McKenney-Tedder S, Schwager LP, Liebman M. A nursing rehabilitation program for women with breast cancer receiving adjuvant chemotherapy. Oncol Nurs Forum 1994 June;21(5):899–907. [PubMed: 7937251]
33. Mock V, Dow KH, Meares CJ, Grimm PM, Dienemann JA, Haisfield-Wolfe ME, Quitasol W, Mitchell S, Chakravarthy A, Gage I. Effects of exercise on fatigue, physical functioning, and emotional distress during radiation therapy for breast cancer. Oncol Nurs Forum 1997 July;24(6):991–1000. [PubMed: 9243585]
34. Mock V, Frangakis C, Davidson N, Ropka M, Pickett M, Poniatowski B, Stewart K, Cameron L, Zawacki K, Podewils L, Cohen G, McCorkle R. Exercise manages fatigue during breast cancer treatment: a randomized controlled trial. Psychooncology 2005;14:464–77. [PubMed: 15484202]
35. Mock V, Pickett M, Ropka ME, Muscari LE, Stewart KJ, Rhodes VA, McDaniel R, Grimm PM, Krumm S, McCorkle R. Fatigue and quality of life outcomes of exercise during cancer treatment. Cancer Pract 2001 May;9:119–27. [PubMed: 11879296]
36. Morrow GR. Cancer-related fatigue: causes, consequences, and management. The Oncologist 2007;12(1):1–3. [PubMed: 17573450]
37. Mustian KM, Griggs JJ, Morrow GR, McTiernan A, Roscoe JA, Bole CW, Atkins JN, Issell BF. Exercise and side effects among 749 patients during and after treatment for cancer: a University of Rochester Cancer Center Community Clinical Oncology Program Study. Support Care Cancer 2006 July;14(7):732–41. [PubMed: 16482444]

38. Mustian KM, Katula JA, Gill DL, Roscoe JA, Lang D, Murphy K. Tai Chi Chuan, health-related quality of life and self-esteem: A randomized trial with breast cancer survivors. Support Care Cancer 2004 December;12(12):871–6. [PubMed: 15599776]
39. Mustian KM, Katula JA, Zhao H. A pilot study to assess the influence of tai chi chuan on functional capacity among breast cancer survivors. The Journal of Supportive Oncology 2006 March;4(3):139–45. [PubMed: 16553140]
40. Mustian KM, Morrow GR, Carroll JK, Figueroa-Moseley CD, Jean-Pierre P, Williams GC. Integrative nonpharmacologic behavioral interventions for the management of cancer-related fatigue. The Oncologist 2007;12(1):52–67. [PubMed: 17573456]
41. Mustian KM, Palesh OG, Flecksteiner SA. Tai Chi Chuan for breast cancer survivors. Med Sport Sci 2008;52:209–17. [PubMed: 18487900]
42. Mustian KM, Peppone L, Darling T, Palesh O, Heckler C, Morrow GR. A 4-Week Home-Based Aerobic and Resistance Exercise Program During Radiation Therapy: A Pilot Randomized Clinical Trial. The Journal of Supportive Oncology. 2009 In press.
43. Mustian KM, Peppone L, Palesh O, Janelsins MC, Mohile S, Purnell J, Darling T. Exercise and Cancer-Related Fatigue. U S Oncology. 2009 in press.
44. Mustian, K.; Adams, MJ.; Schwartz, R.; Lipshultz, S.; Constine, L. Cardiotoxic Effects of Radiation Therapy in Hodgkin's Lymphoma and Breast Cancer Survivors and the Potential Mitigating Effects of Exercise. In: Rubin, P.; Constine, L.; Marks, L.; Okunieff, P., editors. Cancer Survivorship Research and Education: Late Effects on Normal Tissues. Berlin: Springer-Verlag; 2008. p. 103-15.
45. Pinto BM, Goldstein MG, Ashba J, Sciamanna CN, Jette A. Randomized controlled trial of physical activity counseling for older primary care patients. American Journal of Preventive Medicine 2005 November;29(4):247–55. [PubMed: 16242586]
46. Pirl WF, Roth AJ. Diagnosis and treatment of depression in cancer patients. Oncology (Williston Park) 1999 September;13(9):1293–301. [PubMed: 10509324]
47. Ries LAGMDKM. SEER Cancer Statistics Review 1975–2005. National Cancer Institute; Bethesda, MD: 2008. Available from: URL: seer.cancer.gov/csr/1975_2005/
48. Ryan JL, Carroll JK, Ryan EP, Mustian KM, Fiscella K, Morrow GR. Mechanisms of cancer-related fatigue. The Oncologist 2007;12(1):22–34. [PubMed: 17573453]
49. Sabatino SA, Coates RJ, Uhler RJ, Pollack LA, Alley LG, Zauderer LJ. Provider counseling about health behaviors among cancer survivors in the United States. J Clin Oncol 2007 May 20;25(15): 2100–6. [PubMed: 17513816]
50. Savard J, Morin CM. Insomnia in the context of cancer: A review of a neglected problem. J Clin Oncol 2001 February 1;19(3):895–908. [PubMed: 11157043]
51. Schmitz K, Ahmed R, Hannan P, Lee D. Safety and efficacy of weight training in recent breast cancer survivors to alter body composition, insulin and insulin-like growth factor axis proteins. Cancer Epidemiol Biomarkers Prev 2005;14(7):1588–95. [PubMed: 16030088]
52. Schmitz KH, Holtzman J, Courneya KS, Masse LC, Duval S, Kane R. Controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. [Review] [64 refs]. Cancer Epidemiology, Biomarkers & Prevention 2005 July;14(7):1588–95.
53. Schneider, CM.; Dennehy, CA.; Carter, SD. Exercise and Cancer Recovery. Illinois: Human Kinetics; 2003.
54. Schneider CS, Hsieh CC, Sprod LK, Carter SD, Hayward R. Exercise Training Manages Cardiopulmonary Function and Fatigue During and Following Cancer Treatment in Male Cancer Survivors. Integ Cancer Ther 2007;6(3):235–41.
55. Segal RJ, Reid RD, Courneya KS, Malone SC, Parliament MB, Scott CG, Venner PM, Quinney HA, Jones LW, D'Angelo ME, Wells GA. Resistance exercise in men receiving androgen deprivation therapy for prostate cancer.[comment]. J Clin Oncol 2003 May 1;21(9):1653–9. [PubMed: 12721238]
56. Segar ML, Katch VL, Roth RS, Weinstein AG, Portner TI, Glickman SG, Haslanger S, Wilkins EG. The effect of aerobic exercise on self-esteem and depressive and anxiety symptoms among breast cancer survivors. Oncol Nurs Forum 1998;25(1):107–13. [PubMed: 9460778]
57. Shuster LT, Gostout BS, Grossardt BR, Rocca WA. Prophylactic oophorectomy in premenopausal women and long-term health. Menopause Int 2008 September;14(3):111–6. [PubMed: 18714076]

58. Stark D, Kiely M, Smith A, Velikova G, House A, Selby P. Anxiety disorders in cancer patients: their nature, associations, and relation to quality of life. J Clin Oncol 2002 July 15;20(14):3137–48. [PubMed: 12118028]

59. Stevinson C, Lawlor D, Fox K. Exercise interventions for cancer patients: systematic review of controlled trials. Cancer Causes and Control 2004;15:1035–56. [PubMed: 15801488]

60. Tischler ME, Slentz M. Impact of weightlessness on muscle function. [Review] [37 refs]. Asgsb Bulletin 1995 October;8(2):73–81. [PubMed: 11538553]

61. Tisdale MJ, Tisdale MJ. Cachexia in cancer patients. [Review] [94 refs]. Nat Rev Cancer 2002 November;Cancer 2(11):862–71.

62. Tisdale MJ, Tisdale MJ. The 'cancer cachectic factor'. Support Care Cancer 2003 February;11(2): 73–8. [PubMed: 12560934]

63. Windsor PM, Nicol KF, Potter J. A randomized, controlled trial of aerobic exercise for treatment-related fatigue in men receiving radical external beam radiotherapy for localized prostate carcinoma. Cancer 2004 August 1;101(3):550–7. [PubMed: 15274068]

64. Yeh ETH. Cardiotoxicity Induced by Chemotherapy and Antibody Therapy. Annu Rev Med 2006 February 1;57(1):485–98. [PubMed: 16409162]