

American College of Sports Medicine Roundtable on Exercise Guidelines for Cancer Survivors

EXPERT PANEL

Kathryn H. Schmitz, PhD, MPH, FACSM
Kerry S. Courneya, PhD
Charles Matthews, PhD, FACSM
Wendy Demark-Wahnefried, PhD
Daniel A. Galvão, PhD
Bernardine M. Pinto, PhD
Melinda L. Irwin, PhD, FACSM
Kathleen Y. Wolin, ScD, FACSM
Roanne J. Segal, MD, FRCP
Alejandro Lucia, MD, PhD
Carole M. Schneider, PhD, FACSM
Vivian E. von Gruenigen, MD
Anna L. Schwartz, PhD, FAAN

Early detection and improved treatments for cancer have resulted in roughly 12 million survivors alive in the United States today. This growing population faces unique challenges from their disease and treatments, including risk for recurrent cancer, other chronic diseases, and persistent adverse effects on physical functioning and quality of life. Historically, clinicians advised cancer patients to rest and to avoid activity; however, emerging research on exercise has challenged this recommendation. To this end, a roundtable was convened by American College of Sports Medicine to distill the literature on the safety and efficacy of exercise training during and after adjuvant cancer therapy and to provide guidelines. The roundtable concluded that exercise training is safe during and after cancer treatments and results in improvements in physical functioning, quality of life, and cancer-related fatigue in several cancer survivor groups. Implications for disease outcomes and survival are still unknown. Nevertheless, the benefits

to physical functioning and quality of life are sufficient for the recommendation that cancer survivors follow the 2008 Physical Activity Guidelines for Americans, with specific exercise programming adaptations based on disease and treatment-related adverse effects. The advice to “avoid inactivity,” even in cancer patients with existing disease or undergoing difficult treatments, is likely helpful.

In 2009, the American Cancer Society (ACS) estimated that there were nearly 1.5 million new cases of cancer diagnosed in the United States and just more than 500,000 people who died from the disease (76). Currently, there are close to 12 million cancer survivors in the United States, and this number grows each year (66,70,122). Improved prognosis on the basis of earlier detection and newer treatments has created a welcomed new challenge of addressing the unique needs of cancer survivors, which include the sequelae of the disease, its treatment, and conditions predating diagnosis. Cancer is a disease largely associated with aging: most survivors are older than 65 yr (112). Nearly half are survivors of breast or prostate cancer (66). Colon, hematological, and endometrial cancers each account for approximately 10% of survivors (66).

In the last two decades, it has become clear that exercise plays a vital role in cancer prevention and control (25,140). Courneya and Friedenreich (26) proposed a Physical Activity and Cancer Control Framework that highlights specific phases along the cancer continuum where exercise has a logical role (Fig. 1) and identifies two distinct periods before diagnosis and four periods after diagnosis with objectives for exercise programs in each phase. There is a growing body of evidence suggesting that exercise decreases the risk of many of cancers (107,140), and data to support the premise that exercise may extend survival for breast and colon cancer survivors are emerging (68,73,91,92). Our focus here is on the influence of regular exercise on the health,

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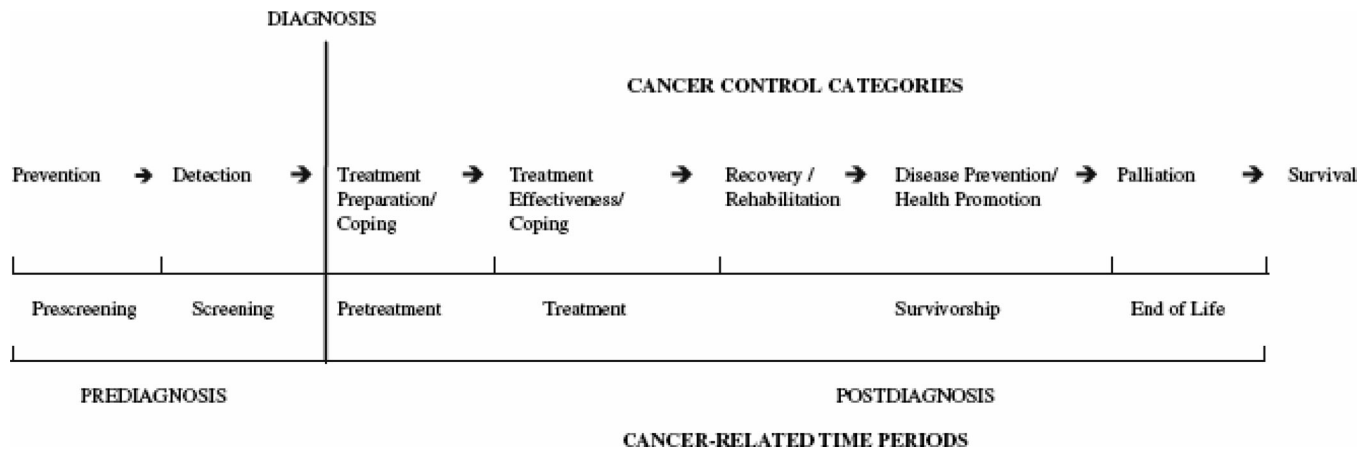


FIGURE 1—Physical activity and cancer control framework. (Reprinted from Courneya KS, Friedenreich CM. Physical activity and cancer control. *Semin Oncol Nurs.* 2007;23(4):242–52. Copyright © 2007 Elsevier. Used with permission.)

quality of life (QOL), and psychosocial well-being of cancer survivors after diagnosis. Studies reviewed herein have hypothesized that some of the psychological and physiological challenges faced by cancer survivors can be prevented, attenuated, treated, or rehabilitated through exercise.

Given the proliferation of exercise programs for cancer survivors worldwide, an emergent evidence base for the efficacy of exercise among cancer survivors, and the relative lack of guidelines for health and fitness professionals to draw upon in working with this special population, a team of clinical and research experts in the field of cancer and exercise gathered in June 2009. A roundtable was convened by American College of Sports Medicine (ACSM) and sponsored by the Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine in St. Louis (St. Louis, MO) and the Oncology Nursing Foundation to review the evidence leading to the guidance provided herein. For these guidelines, we adopt the definition of “cancer survivor” purported by the National Coalition for Cancer Survivorship, i.e., from the time of diagnosis until the end of life (<http://www.canceradvocacy.org> (Accessed April 13, 2009)).

These guidelines are developed against the backdrop of existing recommendations for exercise from the ACSM and the American Heart Association (60), the ACS (50), and the recent 2008 US Department of Health and Human Services (US DHHS) Physical Activity Guidelines for Americans (107). All of these guidelines are similar, with minor variations. The recent US DHHS guidelines indicate that, when individuals with chronic conditions such as cancer are unable to meet the stated recommendation on the basis of their health status, they “should be as physically active as their abilities and conditions allow.” An explicit recommendation was made to “avoid inactivity,” and it was clearly stated that “Some physical activity is better than none.” The key US DHHS guideline for aerobic activity focused on an overall volume of weekly activity of 150 min of moderate-intensity exercise or 75 min of vigorous-intensity exercise or an equivalent combination. Guidance for strength training is to

perform two to three weekly sessions that include exercises for major muscle groups (60,107). Flexibility guidelines are to stretch major muscle groups and tendons on days that other exercises are performed (60,100).

Given that the recent guidelines accommodate chronic conditions and the health status of the individual (50,100,107), there was consensus that the exercise objectives noted above are generally appropriate for cancer survivors. However, it is recognized that exercise programs may need to be adapted for the individual survivor on the basis of their health status, treatments received, and anticipated disease trajectory.

For the 2009 ACSM Roundtable, we focused on adult cancers and sites where most evidence had been assembled and reviewed the literature for multiple health outcomes. The diversity of cancer types and related treatment and sequelae and the lack of data for some presented challenges for our review. Extrapolation was required for rare cancers and some end points.

Evaluation of the evidence was based on the categories outlined by the National Heart, Lung, and Blood Institute (99) as follows: A (overwhelming data from randomized controlled trials (RCTs)), B (few RCTs exist or they are small and results are inconsistent), C (results stem from uncontrolled, nonrandomized, and/or observational studies), and D (evidence insufficient for categories A to C). It is acknowledged that these evaluation criteria do not incorporate information on the strength of effects but focus instead on the quantity of studies that have shown any statistically significant effect regardless of how large that effect may be. Research on the safety and efficacy of exercise in cancer survivors is an emerging field; consequently, it is expected that regular updates of these guidelines will be needed.

The review provided herein is intended to highlight the important role that exercise plays in cancer control and survivorship and to provide a broad outline to health and fitness professionals interested in implementing physical activity programs for cancer survivors both during and after cancer treatment. It should be noted that the important issue of the efficacy of behavioral interventions to increase

physical activity among cancer survivors was not directly addressed at the Roundtable, and readers interested in this topic are referred to existing publications for general information on this topic (109).

EFFECTS OF CANCER TREATMENT AND ADVERSE EFFECTS RELEVANT TO PHYSICAL ACTIVITY

To provide optimal guidance to survivors, fitness professionals need to understand common therapeutic approaches to cancer. Most cancer patients will receive surgery. This surgery could be minor (e.g., removal of a mole) or major (e.g., removal of a large section of the colon). About half of cancer patients undergo ionizing radiation treatments. Radiotherapy may be delivered before or after surgery, alone or with concomitant chemotherapy. The mode of delivery, schedule, and frequency are unique to a particular cancer but often includes frequent appointments during a defined period (e.g., five appointments per week for 6 wk). The majority of cancer patients also receive chemotherapy, which is prescribed orally or delivered intravenously on defined schedules that are cyclical in nature. The type and duration of treatment are individualized but can last for a few months or for a much more protracted period, depending on the type and severity of both the cancer and the specific chemotherapeutic agents used. Hormonal therapies are used when indicated, most notably in certain types of breast and prostate cancers. Therapeutically, this can be approached by drug therapy or surgery (e.g., removal of the ovaries (oophorectomy) or testicles (orchiectomy)). Finally, there are a growing number of targeted therapies that are being developed for cancer that are tumor-specific (e.g., trastuzumab (herceptin), a monoclonal antibody given to breast cancer survivors who overexpress the HER-2 receptor [15]). Moreover, it is important for fitness professionals to be aware

that cancer therapies are constantly changing. To best evaluate a cancer survivor's exercise tolerance and prescribe a safe and effective exercise program, it is necessary to understand the specifics of a cancer survivor's diagnosis and treatments received. Further, these effects will need to be understood in the context of existing health (premorbid conditions) and fitness level before cancer diagnosis. By understanding the treatments received, it may be possible to review the body systems adversely affected and that may have positive or negative implications for exercise tolerance and training.

The adverse effects of cancer treatments may be immediate, resolving during a period of days or weeks, or may be persistent, lasting years after treatment is completed. For the purpose of this review, we use the term "persistent effects," an umbrella term that includes both long-term and late effects (6). Long-term effects are side effects or complications that begin during or very shortly after treatment and persist afterward and for which the cancer survivor must compensate. Late effects are distinct from long-term effects in that they appear months or years after treatment completion (e.g., arrhythmias or cardiomyopathies after exposure to cardiotoxic agents) (67). See Table 1 for a listing of persistent effects of cancer treatments, including effects on multiple body systems relevant to exercise training: cardiovascular, musculoskeletal, nervous, endocrine, and immune. It should be noted that, for persistent adverse effects of cancer treatment, there may be predisposing host factors, including age, gender, and other comorbid health conditions, which synergize to influence incidence and severity of adverse treatment effects (66). The reader is referred to a recent Institute of Medicine report on adult cancer survivorship (66) for an in-depth review of persistent effects of treatment.

In the following paragraphs, we present the consensus guidelines for exercise testing and prescription for cancer survivors, followed by a review of the research evidence for

TABLE 1. Persistent changes resulting from the most commonly used curative therapies.

	Surgery	Chemotherapy	Radiation	Hormonal Therapy, Oophorectomy or Orchiectomy	Targeted Therapies
Second cancers		✓	✓		
Fatigue	✓	✓	✓		✓
Pain	✓	✓	✓	✓	✓
Cardiovascular changes: damage or increased CVD risk	✓	✓	✓	✓	✓
Pulmonary changes	✓	✓	✓		
Neurological changes:					
Peripheral neuropathy		✓			
Cognitive changes	✓	✓	✓	✓	✓
Endocrine changes					
Reproductive changes (e.g., infertility, early menopause, impaired sexual function)	✓	✓	✓	✓	✓
Body weight changes (increases or decreases)	✓	✓		✓	
Fat mass increases	✓	✓		✓	
Lean mass losses	✓	✓		✓	
Worsened bone health		✓	✓	✓	
Musculoskeletal soft tissues: changes or damage	✓		✓	✓	
Immune system					
Impaired immune function and/or anemia		✓	✓	✓	✓
Lymphedema	✓		✓		
Gastrointestinal system: changes or impaired function	✓	✓	✓	✓	✓
Organ function changes	✓				
Skin changes			✓	✓	✓

the safety and efficacy of exercise interventions over a wide spectrum of common cancer sites.

GUIDELINES FOR PHYSICAL ACTIVITY TESTING AND PRESCRIPTION IN CANCER SURVIVORS

Panel members were charged with reviewing the evidence for the following adult cancer survivor populations: breast, prostate, colon, hematologic, and gynecologic cancers. Breast was further divided into during and after treatment because there was adequate research evidence available for both periods. The resulting reviews were presented and discussed at the roundtable, and consensus for the guidelines presented in Tables 2 to 4 was reached either during the meeting or in subsequent discussions.

Overall, these guidelines fall into evidence level B. The relative contribution of empirical published scientific evidence and RCTs for these recommendations varies. Ideally, we will eventually have levels of evidence specific to a given exercise intervention (e.g., mode, frequency, intensity, duration) for a given cancer site at a particular phase of the cancer trajectory (e.g., during chemotherapy, survivorship, end of life) and for specific end points (e.g., fatigue, physical function, QOL, survival).

Exercise testing. The expert reviewing a specific cancer site was asked to comment on recommendations for medical assessments and exercise testing before starting an exercise program on the basis of published empirical evidence and their own clinical and/or research experience.

All exercise testing recommendations are made against the backdrop of existing guidelines (5). Table 2 presents guidance for preexercise medical assessments and exercise testing for cancer survivors resulting from this consensus process. Fitness professionals should understand the most common toxicities associated with cancer treatments, including increased risk for fractures and cardiovascular events with hormonal therapies, neuropathies related to certain types of chemotherapy, musculoskeletal morbidities secondary to treatment, and treatment-related cardiotoxicity. Survivors with metastatic disease to the bone will require modification of their exercise program (e.g., reduced impact, intensity, volume) given the increased risk of bone fragility and fractures.

Exercise prescription. Panel members were also asked to review research for evidence that exercise was safe and feasible during and after treatment, whether exercise affected treatment efficacy, symptoms, toxicities, ability to withstand treatment, or persistent adverse effects of treatment, and recurrence or survival. As with the testing guidelines, development of exercise prescription guidelines occurred against the background of other published exercise guidelines (50,60,100,107). Exercise prescriptions should be individualized according to a cancer survivor's pretreatment aerobic fitness, medical comorbidities, response to treatment, and the immediate or persistent negative effects of treatment that are experienced at any given time. Table 3 reviews the objectives for exercise among cancer survivors, as well as general and cancer site-specific contraindications for starting an exercise program, reasons for stopping exercise, and injury risk guidelines. One of the goals noted in Table 3 was

TABLE 2. Preexercise medical assessments and exercise testing.

Cancer Site	Breast	Prostate	Colon	Adult Hematologic (No HSCT)	Adult HSCT	Gynecologic
General medical assessments recommended before exercise	Recommend evaluation for peripheral neuropathies and musculoskeletal morbidities secondary to treatment regardless of time since treatment. If there has been hormonal therapy, recommend evaluation of fracture risk. Individuals with known metastatic disease to the bone will require evaluation to discern what is safe before starting exercise. Individuals with known cardiac conditions (secondary to cancer or not) require medical assessment of the safety of exercise before starting. There is always a risk that metastasis to the bone or cardiac toxicity secondary to cancer treatments will be undetected. This risk will vary widely across the population of survivors. Fitness professionals may want to consult with the patient's medical team to discern this likelihood. However, requiring medical assessment for metastatic disease and cardiotoxicity for all survivors before exercise is not recommended because this would create an unnecessary barrier to obtaining the well-established health benefits of exercise for the majority of survivors, for whom metastasis and cardiotoxicity are unlikely to occur.					
Cancer site-specific medical assessments recommended before starting an exercise program	Recommend evaluation for arm/shoulder morbidity before upper body exercise.	Evaluation of muscle strength and wasting.	Patient should be evaluated as having established consistent and proactive infection prevention behaviors for an existing ostomy before engaging in exercise training more vigorous than a walking program.	None	None	Morbidly obese patients may require additional medical assessment for the safety of activity beyond cancer-specific risk. Recommend evaluation for lower extremity lymphedema before vigorous aerobic exercise or resistance training.
Exercise testing recommended	No exercise testing required before walking, flexibility, or resistance training. Follow ACSM guidelines for exercise testing before moderate to vigorous aerobic exercise training. One-repetition maximum testing has been demonstrated to be safe in breast cancer survivors with and at risk for lymphedema.					
Exercise testing mode and intensity considerations	As per outcome of medical assessments and following ACSM guidelines for exercise testing.					
Contraindications to exercise testing and reasons to stop exercise testing	Follow ACSM guidelines for exercise testing.					

TABLE 3. Exercise prescription for cancer survivors.

	Breast	Prostate	Colon	Adult Hematologic (No HSCT)	Adult HSCT	Gynecologic
Objectives/goals of exercise prescription	<ol style="list-style-type: none"> To regain and improve physical function, aerobic capacity, strength and flexibility. To improve body image and QOL. To improve body composition. To improve cardiorespiratory, endocrine, neurological, muscular, cognitive, and psychosocial outcomes. Potentially, to reduce or delay recurrence or a second primary cancer. To improve the ability to physically and psychologically withstand the ongoing anxiety regarding recurrence or a second primary cancer. To reduce, attenuate, and prevent long-term and late effects of cancer treatment. To improve the physiologic and psychological ability to withstand any current or future cancer treatments. These goals will vary according to where the survivor is in the continuum of cancer experience, as depicted in Figure 1. 					
General contraindications for starting an exercise program common across all cancer sites	Allow adequate time to heal after surgery. The number of weeks required for surgical recovery may be as high as 8. Do not exercise individuals who are experiencing extreme fatigue, anemia, or ataxia. Follow ACSM guidelines for exercise prescription concerning cardiovascular and pulmonary contraindications for starting an exercise program. However, the potential for an adverse cardiopulmonary event might be higher among cancer survivors than age-matched comparisons given the toxicity of radiotherapy and chemotherapy and long-term/late effects of cancer surgery.					
Cancer-specific contraindications for starting an exercise program	Women with immediate arm or shoulder problems secondary to breast cancer treatment should seek medical care to resolve those issues before exercise training with the upper body.	None	Physician permission recommended for patients with an ostomy before participation in contact sports (risk of blow) and weight training (risk of hernia).	None	None	Women with swelling or inflammation in the abdomen, groin, or lower extremity should seek medical care to resolve these issues before exercise training with the lower body.
Cancer-specific reasons for stopping an exercise program. (Note: General ACSM guidelines for stopping exercise remain in place for this population.)	Changes in arm/shoulder symptoms or swelling should result in reductions or avoidance of upper body exercise until after appropriate medical evaluation and treatment resolves the issue.	None	Hernia, ostomy-related systemic infection.	None	None	Changes in swelling or inflammation of the abdomen, groin, or lower extremities should result in reductions or avoidance of lower body exercise until after appropriate medical evaluation and treatment resolves the issue.
General injury risk issues in common across cancer sites	Patients with bone metastases may need to alter their exercise program concerning intensity, duration, and mode given increased risk for skeletal fractures. Infection risk is higher for patients who are currently undergoing chemotherapy or radiation treatment or have compromised immune function after treatment. Care should be taken to reduce infection risk in fitness centers frequented by cancer survivors. Exercise tolerance of patients currently in treatment and immediately after treatment may vary from exercise session-to-exercise session about exercise tolerance, depending on their treatment schedule. Individuals with known metastatic disease to the bone will require modifications and increased supervision to avoid fractures. Individuals with cardiac conditions (secondary to cancer or not) will require modifications and may require increased supervision for safety.					
Cancer-specific risk of injury and emergency procedures	The arms/shoulders should be exercised, but proactive injury prevention approaches are encouraged, given the high incidence of arm/shoulder morbidity in breast cancer survivors. Women with lymphedema should wear a well-fitting compression garment during exercise. Be aware of risk for fracture among those treated with hormonal therapy, a diagnosis of osteoporosis, or bony metastases.	Be aware of risk for fracture among patients treated with ADT, a diagnosis of osteoporosis or bony metastases	Advisable to avoid excessive intra-abdominal pressures for patients with an ostomy.	Multiple myeloma patients should be treated as if they have osteoporosis.	None	The lower body should be exercised, but proactive injury prevention approaches are encouraged, given the potential for lower extremity swelling or inflammation in this population. Women with lymphedema should wear a well-fitting compression garment during exercise. Be aware of risk for fractures among those treated with hormonal therapies, with diagnosed osteoporosis, or with bony metastases.

TABLE 4. Review of US DHHS Physical Activity Guidelines (PAG) for Americans and alterations needed for cancer survivors.

	Breast	Prostate	Colon	Adult Hematologic (No HSCT)	Adult HSCT	Gynecologic
General statement	Avoid inactivity; return to normal daily activities as quickly as possible after surgery. Continue normal daily activities and exercise as much as possible during and after nonsurgical treatments. Individuals with known metastatic bone disease will require modifications to avoid fractures. Individuals with cardiac conditions (secondary to cancer or not) may require modifications and may require greater supervision for safety. Recommendations are the same as age-appropriate guidelines from the PAG for Americans.					
Aerobic exercise training (volume, intensity, and progression)	Be aware of fracture risk. Recommendations are the same as age-appropriate guidelines from the PAG for Americans.	Be aware of increased potential for fracture. Recommendations are the same as age-appropriate PAG.	Physician permission recommended for patients with an ostomy before participation in contact sports (risk of blow). Altered recommendations. See below.	None	Ok to exercise everyday; lighter intensity, and lower progression of intensity recommended. Care should be taken to avoid overtraining given immune effects of vigorous exercise. Recommendations are the same as age-appropriate PAG.	Recommendations are the same as age-appropriate guidelines from the PAG for Americans. Morbidly obese women may require additional supervision and altered programming. If peripheral neuropathy is present, a stationary bike might be preferable over weight bearing exercise. Altered recommendations. See below.
Cancer site-specific comments on aerobic exercise training prescriptions	Altered recommendations. See below.	Recommendations are the same as age-appropriate PAG.	Altered recommendations. See below.	None	Recommendations are the same as age-appropriate PAG.	Altered recommendations. See below.
Resistance training (volume, intensity, and progression)	Altered recommendations. See below.	Recommendations are the same as age-appropriate PAG.	Altered recommendations. See below.	None	Recommendations are the same as age-appropriate PAG.	Altered recommendations. See below.
Cancer site-specific comments on resistance training prescription	Start with a supervised program of at least 16 sessions and very low resistance; progress resistance at small increments. No upper limit on the amount of weight to which survivors can progress. Watch for arm/shoulder symptoms, including lymphedema, and reduce resistance or stop specific exercises according to symptom response. If a break is taken, back off the level of resistance by 2 wk worth for every week of no exercise (e.g., a 2-wk exercise vacation = back off to resistance used 4 wk ago). Be aware of risk for fracture in this population. Recommendations are the same as age-appropriate PAG for Americans.	Add pelvic floor exercises for those who undergo radical prostatectomy. Be aware of risk for fracture.	Recommendations are the same as age-appropriate PAG. For patients with a stoma, start with low resistance and progress resistance slowly to avoid herniation at the stoma.	None	Resistance training might be more important than aerobic exercise in bone marrow transplant patients. See text for further discussion on this point.	There are no data on the safety of resistance training in women with lower limb lymphedema secondary to gynecologic cancer. This condition is very complex to manage. It may not be possible to extrapolate from the findings on upper limb lymphedema. Proceed with caution if the patient has had lymph node removal and/or radiation to lymph nodes in the groin.
Flexibility training (volume, intensity, and progression)	Recommendations are the same as age-appropriate PAG for Americans.	Recommendations are the same as age-appropriate PAG for Americans.	Recommendations are the same as age-appropriate PAG, with care to avoid excessive intra-abdominal pressure for patients with ostomies. If an ostomy is present, modifications will be needed for swimming or contact sports. Research gap.	Recommendations are the same as age-appropriate PAG for Americans.	Recommendations are the same as age-appropriate PAG for Americans.	Recommendations are the same as age-appropriate PAG for Americans.
Exercises with special considerations (e.g., yoga, organized sports, and Pilates)	Yoga seems safe as long as arm and shoulder morbidities are taken into consideration. Dragon boat racing not empirically tested, but the volume of participants provides face validity of safety for this activity. No evidence on organized sport or Pilates.	Research gap	Research gap	Research gap	Research gap	Research gap

to improve body composition. Maintaining and increasing muscle mass are recommended for all cancer survivors during and after treatment. However, the need to decrease body fat varies by cancer site. For example, survivors with esophageal, head and neck, or gastric cancers may be underweight at the time of diagnosis and may lose more weight as a result of treatment, whereas many early stage breast and prostate cancer survivors are overweight or obese at the time of diagnosis and may increase weight (and body fat) during treatment. The goal to improve body composition through fat loss is directed at survivors who are overweight or obese. Specific risks of exercise training by cancer site should be understood by fitness professionals, such as elevated fracture risk among breast or prostate cancer survivors who have undergone certain types of hormonal therapy and lymphedema risk more commonly seen among breast and urogynecologic cancer survivors. Table 4 presents guidelines for exercise prescription in cancer survivors. The panel compared its recommendations with the US DHHS Physical Activity Guidelines for Americans (107). Overall, the panel agreed with the previously published ACS and US DHHS guidance to “avoid inactivity” and to return to normal daily activities as soon as possible after surgery and during adjuvant cancer treatments. The age-appropriate guidelines for aerobic activity are seen by the panel to be appropriate for cancer survivors as well, with a few cancer site-specific comments regarding the potential for elevated risk of skeletal fractures and infection among specific survivors who receive particular types of treatments. The comments on safety of exercise during and after treatment from the studies reviewed (see the following section) can generally be summarized as follows: exercise is safe both during and after

most types of cancer treatment, including intensive life-threatening treatments such as bone marrow transplant. Resistance and flexibility exercises are also recommended for cancer survivors, with alterations suggested for those with and at risk for lymphedema, and care about fracture risk among some survivor populations (e.g., those with osteoporosis or bony metastases) and infection risk among those who are immune-compromised because of treatment (e.g., care is needed to avoid spread of infection through use of equipment at public gyms). It is acknowledged that specific research examining the safety of strengthening and flexibility activities is limited presently. The safety and efficacy of alternate types of exercise such as yoga, Pilates, Curves™, or organized sport activities have not been well studied, so recommendations are not possible for most survivor populations for these activities. A discussion of the research gaps regarding the safety and efficacy of exercise among cancer survivors is provided at the end of this document. In the next paragraphs, we review results regarding the effects of exercise on specific outcomes for which there is published empirical evidence.

EVIDENCE OF THE SAFETY AND EFFICACY OF EXERCISE TRAINING BY CANCER SITE

Overview

Table 5 presents an overview of the evidence available to support both the safety and efficacy of exercise training in survivors of common cancers and for a variety of outcomes. In the next paragraphs, we review the evidence by cancer site. For cancers with more limited evidence, the text includes results from nonrandomized and/or uncontrolled intervention trials and observational studies. Studies that

TABLE 5. Overview of evidence regarding the efficacy of exercise interventions for specific outcomes in cancer survivors.^a

Outcome	Breast (during Chemotherapy and Radiotherapy)	Breast (after Chemotherapy and Radiotherapy)	Prostate	Colon	Adult Hematologic (No HSCT)	Adult HSCT	Gynecologic
No. studies reviewed ^b	21	32	12	4	4	11	1
Safety (no exercise-related adverse events reported)	13	15	6		1	6	
Physical function	2	4	4			1	
Physical fitness							
Aerobic fitness	10	10	5	1	3	5	
Muscular strength	5	6	4			2	
Flexibility		5	1				
Physical activity level	5	8	4	1		1	1
Body size (weight, BMI, body composition, muscle mass)	4	8	6		1	2	1
Bone health	2	1					
Safety about lymphedema-related outcomes	2	7					
QOL	4	12	6		1	3	
Energy level or vigor/vitality		3	1				
Fatigue	4	4	5		3	3	
Sleep	1				1		
Depression		3			1		
Anxiety	3	3					
Physiological outcomes (e.g., hemoglobin, blood lipids, IGF pathway hormones, oxidative stress, inflammation, or immune parameters; includes PSA for prostate cancer)	3	6	2	2			
Symptoms/adverse effects (including pain)	3	3	1		1		

IGF, insulin-like growth factor.

^a Numbers in the table reflect the number of studies with a significant positive effect on the outcomes listed.

^b For breast, only RCTs meeting criteria for high internal validity were reviewed. See text for description of criteria of internal validity criteria. For other sites, all intervention studies were included.

included patients with various cancer diagnoses are included within site-specific reviews if 40% of the sample or ≥ 50 survivors of a specific site are represented.

Breast

Because of the large number of studies in the area of exercise and breast cancer, only RCT data from studies that met at least four of the following seven common RCT internal validity criteria are included: 1) concealment—those assessing eligibility cannot influence treatment assignment, 2) similarity of groups at baseline on prognostic and outcome measures, 3) standardization of interventions—all participants in a given group received the same intervention, 4) $>70\%$ exercise adherence, 5) $\leq 20\%$ attrition, 6) blinding outcome assessors to randomization outcome, and 7) comparable timing of outcome assessment in all groups. Studies on exercise during versus after chemotherapy or radiation are presented separately.

During chemotherapy or radiation therapy. There have been 22 RCTs with high internal validity that have assessed the safety and efficacy of exercise training among breast cancer survivors during chemotherapy or radiation treatment (1,7,9,10,17,18,29,32,42,47,48,51,64,77,82,93,94,98,115–117,127). Not all of these RCTs focused exclusively on breast cancer; some included other cancer types. Study sample sizes ranged from 20 to 450, with a mean of 88 women.

Evidence Category A: Safety. Of the 22 reviewed RCTs of exercise training among breast cancer survivors during treatment, 13 specifically reported adverse events (1,9,17,18,29,32,42,47,51,64,115–117), and all surmised that exercise was safe during breast cancer treatment.

Evidence Category A: Aerobic Fitness. All 10 RCTs that have examined exercise training during chemotherapy and/or radiation have reported significant aerobic capacity improvements (1,18,29,32,47,51,93,115–117). The interventions ranged from home-based walking programs to structured, supervised fitness sessions that included aerobic, resistance, and flexibility activities.

Evidence Category A: Muscular Strength. All five RCTs that have examined the effects of exercise training on muscular strength during treatment for breast cancer have shown statistically significant improvements (1,9,32,115,116). All of these interventions included both aerobic and strength training activities.

Evidence Category B: Body Size and Body Composition. Six RCTs have examined the effect of exercise to improve body size (e.g., weight, body mass index (BMI)) or body composition (e.g., fat mass, lean mass) during treatment of breast cancer (9,10,32,42,116,117). Two of these studies showed no effect of exercise on body size or composition end points (10,42). Percent body fat was improved in three interventions (9,32,116), body weight was reduced in exercisers more than that in usual-care participants in two interventions (116,117), lean mass was improved among

women who did supervised resistance training during chemotherapy (32).

Evidence Category B: QOL. Four RCTs have shown that supervised exercise (aerobic, resistance, and stretching interventions) improves QOL in breast cancer survivors during chemotherapy or radiotherapy (1,18,64,98). Three RCTs observed no such effect (17,32,42).

Evidence Category B: Fatigue. There have been seven RCTs that have examined the efficacy of exercise to mitigate fatigue during chemotherapy: four showed a significant positive effect (48,64,93,115) and three showed no effect or failed to achieve statistical significance (10,32,94). The largest of these seven studies ($n = 242$) was the Supervised Trial of Aerobic versus Resistance Training trial, which showed that aerobic exercise or resistance training had no effect on fatigue during chemotherapy for breast cancer survivors (32).

Evidence Category B: Anxiety. Five RCTs have explored whether exercise during breast cancer treatment could reduce anxiety. Three demonstrated statistically positive effects (7,48,93), and two were suggestive but did not reach statistical significance (32,42). Interventions included home-based walking programs (93), some were telephone counseling interventions (7,42), whereas others were hospital- or facility-based (32,48).

Other Outcomes. In addition to the above-reviewed outcomes, there is evidence that exercise training may improve physical function, bone mineral density, shoulder range of motion, sleep, hemoglobin levels, and several psychological outcomes (e.g., self-esteem and mood) during the time of treatment. Exercise may also mitigate symptoms and adverse effects associated with chemotherapy or radiotherapy, including reduced duration of thrombopenia, in-hospital care stay, visits to a general practitioner for symptom management, duration of diarrhea, and pain (47,48,98). Two studies showed no evidence of increased onset of lymphedema among breast cancer survivors who did either aerobic exercise or resistance training during chemotherapy (32,115).

Finally, there have been two RCTs that have examined the effect of exercise on bone during treatment (115,127). One observed that aerobic exercise, but not exercise with resistance bands, was associated with significant protection from loss of lumbar spine bone mineral density (115). The other compared a pedometer-based walking program with treatment with intravenous zoledronic acid for bone density changes for 1 yr and observed that the group prescribed a pedometer-based walking program of 10,000 steps per day lost considerably more bone than the drug treatment group among premenopausal and perimenopausal women undergoing chemotherapy (127).

After chemotherapy or radiation. There have been 32 RCTs with high internal validity that assessed the safety and efficacy of exercise training in breast cancer survivors who have completed surgery, chemotherapy, and radiation therapy (2,8,11,12,16,22,28,31,39,43,45,53,63,65,74,80,85–87,89,96,97,103,104,110,111,113,114,120,128–130). For many of these studies, women still undergoing hormonal

therapy alone, or in combination with targeted therapies, may have been included. Study sample sizes ranged from 14 to 306, with an average of 86.

Evidence Category A: Safety. Of the 32 reviewed RCTs of exercise training among breast cancer survivors after treatment, 15 specifically commented on safety and/or adverse events (2,8,31,43,45,63,65,74,80,87,96,104,113,114,129), and all concluded that exercise was safe after treatment. The reported adverse events were rare, mild, and expected on the basis of the activity prescribed (e.g., plantar fasciitis from walking, other musculoskeletal injuries). One particular set of adverse events worth noting is that 25% of participants in a home-based intervention for shoulder rehabilitation in the 2 wk after breast cancer surgery had to discontinue the exercises because of symptoms or swelling (80). The estimated prevalence of long-term arm and shoulder morbidity is 35%–58% in breast cancer survivors (84,101). There are two reasons to point this out: 1) practitioners should be aware of the need for particular care with arms and shoulders of breast cancer survivors in designing exercise testing and prescriptions and 2) further research on timing, mode, and level of exercise supervision is needed to prevent or reduce these common adverse outcomes of breast cancer treatment.

Evidence Category A: Aerobic Fitness. Timed distance tests and maximal oxygen consumption have been evaluated in 12 exercise interventions for breast cancer survivors after treatment to determine improvement in aerobic capacity (8,11,16,31,39,53,65,103,104,110,111,128). All but two of these studies (11,53) observed statistically significant improvements in aerobic capacity in the treatment compared with control participants.

Evidence Category A: Muscular Strength. All six resistance and aerobic-based exercise trials for posttreatment breast cancer survivors that have assessed changes in both upper and lower body muscle strength have observed significant positive effects (2,12,65,97,114,129).

Evidence Category A: Flexibility. All six RCTs that have tested whether an exercise intervention would improve flexibility in breast cancer survivors after treatment have shown a positive effect (16,22,28,80,97,113); the effect was statistically significant in all but one of the studies (28).

Evidence Category B: Body Size and Body Composition. Changes in body weight, BMI, fat mass, lean mass, body fat percentage, and waist circumference were assessed in 16 exercise interventions for breast cancer survivors after treatment (2,8,16,28,31,39,43,45,65,74,85,86,89,96,111,114). The effects vary widely, with half of the studies showing statistically significant positive effects on one or more variables related to body size or body composition (2,16,28,43,65,74,89,96). A complete review of the effects of each type of intervention on specific body composition variables is beyond the scope of this document but can be found elsewhere (71,81,123).

Evidence Category B: QOL. The QOL outcomes have been assessed using a wide variety of instruments in 18

exercise interventions for breast cancer survivors after treatment (8,12,16,22,28,31,39,43,45,53,65,74,87,96,105,113,128,130). Of these, 12 noted statistically significant improvements (8,16,22,28,31,39,53,65,96,105,113,130), and 6 did not (12,43,45,74,87,128). Consistent improvements have been noted in studies using the Breast Cancer Subscale of the Functional Assessment of Cancer Therapy—Breast (14). Specific reviews about the effects of exercise training on QOL in cancer survivors are available (88).

Evidence Category B: Fatigue or “Energy” or Vigor/Vitality. There have been nine RCTs that have assessed the effects of exercise training on fatigue after breast cancer treatment (11,12,28,31,39,53,110,111,128). Of these, four observed that exercise improved fatigue (28,31,53,111), four observed no significant effect of exercise compared with no exercise (11,12,39,110), and one observed worse fatigue after an exercise intervention than with exercise (128). There have also been four studies that have examined whether exercise improves “energy level” or “vigor/vitality” (16,53,96,111). Of these, only one showed no effect (96). For more on this topic, readers are referred to literature reviews and meta-analyses focusing specifically on activity-based interventions for cancer-related fatigue (75,78).

Evidence Category A: Physical Function. There have been six RCTs that have objectively or subjectively assessed physical function improvements resulting from an exercise intervention (8,28,39,45,65,96). All observed a positive effect of exercise, which was statistically significant in all but two studies (8,45). Two of these studies objectively assessed physical function using the “sit-to-stand” measure (8,65), the other four studies used self-reported measures such as physical function subscales of the SF-36 or the Functional Assessment of Cancer Therapy. Results of the recently published Reach out to Enhance Wellness in Older Survivors trial indicate that a diet and exercise intervention significantly improved SF-36 physical function scores among 641 older long-term cancer survivors (45% breast cancer survivors) (96).

Evidence Category B: Depression and Anxiety. There have been seven high-quality RCTs that have tested the effects of exercise on symptoms of depression and/or anxiety among breast cancer survivors who have completed primary treatment (12,16,39,45,110,120,128). Results are mixed. Three (39,120,128) reported significant improvements in depressive symptoms, whereas four others did not (12,16,45,110). Of the four studies that have examined the effects of exercise on symptoms of anxiety (12,16,120,128), all but one (12) reported significant improvements due to exercise interventions compared with control.

Evidence Category A: Safety Regarding Lymphedema Onset or Worsening. Lymphedema is a common and feared adverse effect of breast cancer treatment. Upper body exercise has been historically discouraged for women who have had axillary lymph nodes removed and/or radiation to the axilla. In light of this, it is notable that there have been seven RCTs that have all shown that upper body exercise (aerobic

and/or resistance training) does not contribute to the onset or worsening of lymphedema among survivors at risk (2,8,63,80,87,113,114). The largest of these trials was the Physical Activity and Lymphedema Trial, which demonstrated that slowly progressive resistance training undertaken with a compression garment is actually protective against lymphedema flare-ups (114). In general, these studies have included women who had both axillary node dissection and sentinel node biopsy. In all of the completed trials that have specifically focused on the safety of upper body exercise among women with or at risk for lymphedema, the protocols all started with 8 wk or more of supervised training with a certified fitness professional.

Evidence Category B: Body Image. Six studies have examined the effect of exercise training on body image among breast cancer survivors who have completed primary treatment (12,39,110,111,113,124). One found no effect (113), one observed a positive effect that was not statistically significant (39), and the other four observed significant improvements in body image as a result of an exercise intervention (12,110,111,124). The largest of these (124) used a body image instrument designed specifically for use on breast cancer survivors (69).

Evidence Category C: Symptoms/Adverse Effects and Pain. There have been six studies that have examined the effects of exercise on symptoms/adverse effects (12,114) and/or pain (8,12,80,87,96). The evidence for both outcomes is mixed. One study observed improved symptoms (114), another did not (12). Five studies examined effects on bodily pain, two showed positive effects of exercise training (8,12), and the other three showed no improvement but no worsening either (80,87,96).

Other Outcomes. The effects of exercise on other outcomes, such as bone health or immune function, have been tested in very few studies. There have been two RCTs that have examined the effects of an exercise intervention on bone health in breast cancer survivors who had completed treatment. The Yale Exercise and Survivorship trial observed improvement in bone mineral density from dual-energy X-ray absorptiometry scans after a 12-month intervention (74). Twiss et al. (129) observed no improvement on balance or falls in breast cancer survivors with bone loss.

Two RCTs tested the effects of exercise training on immune factors after breast cancer treatment. Nieman et al. (103) did not find that exercise training resulted in significant increases in natural killer (NK) cells or NK cell cytotoxic activity after 8 wk of aerobic exercise training. Fahey et al. (52) observed significant improvements in immune parameters, including NK cell cytotoxic activity, after 15 wk of thrice-weekly aerobic exercise.

Finally, exercise before and after breast cancer diagnosis has been shown to be associated with a decreased risk of recurrence and/or death from breast cancer in observational studies (54,68,73). A more complete review on the topic of exercise, diet, body weight, and breast cancer recurrence/survival is available elsewhere (72).

The vast majority of the literature on exercise in cancer focuses on breast cancer. Research evidence for all other cancer sites is much more limited.

Prostate

The leading cause of death in men with prostate cancer is cardiovascular disease, for which the protective effects of exercise are clear (79,107). Prostate cancer generally occurs in older men, in whom cardiovascular disease and mortality are relatively common; thus, the usual cardiac screening approaches already suggested and endorsed by the ACSM and American Heart Association are recommended (5).

There have been 12 intervention studies on exercise in prostate cancer survivors, ranging in sample sizes from 10 to 261 men (20,35,36,43,45,55,56,58,95,96,118,119,137). There have also been three observational studies (13,38,44). The following review focuses primarily on results from the intervention studies. The outcomes with the greatest amount of evidence are reviewed first.

Evidence Category A: Safety. Of the 12 intervention studies, 6 specifically reported on safety (lack of harm in comparison to control participants) of exercise interventions in this population (20,43,45,58,96,119). All studies that reported on safety concluded that exercise is safe in prostate cancer survivors. The potential for exercise to negatively alter prostate-specific antigen (PSA) levels has also been investigated. Resistance and aerobic exercise have been shown not to adversely affect PSA after 12–24 wk of training in five studies (36,56,58,118,119). PSA was also not negatively affected immediately after high-intensity resistance exercise (55).

Evidence Category A: Aerobic Fitness. Five studies demonstrated that aerobic and/or resistance training improves aerobic capacity in prostate cancer survivors undergoing androgen deprivation therapy (ADT), radiation therapy, or both (35,56,58,95,119). Two other home-based studies that prescribed lower-intensity lifestyle activity demonstrated no effect (20,36).

Evidence Category A: Muscular Strength. All four resistance exercise trials for prostate cancer survivors undergoing ADT and radiation have reported improvements in both upper and lower body muscle strength (56,58,118,119).

Evidence Category B: Body Size and Body Composition. Six intervention studies have observed improvements in at least one body composition variable after an exercise intervention (36,43,56,58,96,119), including weight control and/or prevention of fat mass gain or maintenance/increases in lean mass during ADT. Five other intervention studies have shown no such benefit (20,35,45,118,137).

Evidence Category B: QOL. Six intervention trials have shown a significant positive effect of exercise training on QOL (35,58,95,96,118,119), and four have not (20,36,43,45). One study found improved QOL with resistance but not aerobic exercise training (119).

Evidence Category A: Fatigue. Five RCTs demonstrated the efficacy of aerobic or resistance exercise training to reduce fatigue among prostate cancer survivors (58,95, 118,119,137). The reduction in fatigue was reported among survivors undergoing ADT (56,58,118), radiation therapy (95), or both (119). Home-based aerobic and/or low-intensity resistance exercise also has been shown to reduce fatigue in survivors undergoing ADT or radiation (35,137). There is one low-intensity home-based RCT that did not show a significant effect of exercise on fatigue (36).

Evidence Category B: Physical Function. There are four intervention trials that have observed positive effects of aerobic or resistance exercise on self-reported or objectively assessed physical function (56,58,95,96). One of these studies was the previously mentioned Reach out to Enhance Wellness in Older Survivors trial in which 41% of the 641 long-term cancer survivors had prostate cancer and where the telephone counseling and tailored mailed material intervention produced a reduction in the rate of physical function decline compared with a wait-list control. (96). Two studies have shown that resistance or combined aerobic and resistance exercise improves physical performance in prostate cancer survivors undergoing ADT (56,58).

Other Outcomes. Beyond the outcomes reviewed above, the limited data currently available on the effects of exercise training on persistent cancer treatment toxicities in prostate cancer survivors, such as sexual functioning, incontinence, and balance, preclude placing the results in a specific evidence category. For example, a cross-sectional study indicates that, for men who received external beam radiation therapy within the past 18 months, levels of physical activity are positively associated with sexual functioning (38). An observational study found lower incontinence in prostate cancer survivors who were normal weight and physically active compared with survivors who were obese and sedentary (138). Two small intervention studies ($n = 10$ and $n = 57$, respectively) have shown improvements in dynamic balance after resistance or combined resistance and aerobic exercise in prostate cancer survivors (56,58). Ongoing large RCTs are examining the effects of exercise on other persistent prostate cancer toxicities including skeletal health (57,102).

Colon

There have been four RCTs that assessed the efficacy of exercise training in cancer survivors, which have included colon cancer survivors. Three of these focused specifically on colon cancer survivors in studies with sample sizes of 23, 48, and 102, respectively (3,4,27), the fourth included 42 individuals with lung and colon cancers (49). There is also a pre-post pilot study that examined the feasibility of a telephone-based exercise intervention among 20 colon cancer survivors (61). Because there have been so few RCTs on the efficacy of exercise training in this survivor population, there is limited ability to generate any evidence statements. Several ongoing trials promise to expand knowledge in this

area (108,125). One report commented that there were no significant ECG abnormalities noted during maximal aerobic fitness testing (3); however, none of the other studies commented on safety or adverse events. There have been individual RCTs that included colon cancer survivors and demonstrated significant improvements in aerobic fitness, oxidative stress, physical functioning, and inflammation. No data have been reported on interactions with pharmacological agents. Effects of exercise training on symptoms, toxicities, and ability to complete treatment as prescribed are largely unknown among colon cancer survivors. Given that most colon cancer survivors are older adults, comorbidity is an issue that must be taken into account in considering exercise testing and prescription. For example, most participants in one study had hypertension, hypercholesterolemia, and/or arthritis (61).

Finally, there have been two reported observational studies that suggest that recreational exercise after a colon cancer diagnosis may reduce the risk of colon cancer-specific and overall mortality (91,92).

Hematologic Cancers

Among adults, hematologic malignancies usually develop in the second half of life. In the following paragraphs, we review the evidence regarding the safety and efficacy of exercise in survivors of hematologic cancers for two distinct subgroups: adults who did not receive hematopoietic stem cell transplantation (HSCT) and adults who received HSCT. (Note: HSCT includes both bone marrow and peripheral blood stem cell transplantations.) We limit our review here to adults. For a review on the effects of exercise on childhood hematologic survivors, see Wolin et al. (139).

No HSCT. There have been three exercise RCTs in adult hematologic cancer survivors (21,23,33) and one pre-post intervention study (106). The sample sizes of these studies are generally small, ranging from 9 to 35 survivors, with one exception: one aerobic exercise trial in lymphoma patients had a sample size of 122 (33). The only trial that commented on safety (33) reported three injuries (hip, back, and knee) but no negative effect on treatment efficacy or completion rate.

Evidence Category B: Aerobic Fitness. Two RCTs (21,33) and one pre-post intervention trial (106) have observed an improvement in cardiorespiratory fitness after exercise training among adult hematologic cancer patients during and after chemotherapy.

Evidence Category B: Fatigue. Two RCTs (21,33) and one pre-post intervention trial (106) observed reductions in fatigue among adult patients with hematologic cancer during and after chemotherapy, whereas another RCT (23) observed no improvements with exercise training.

Other Outcomes. Among four completed exercise trials in adult hematologic cancer survivors who had not undergone HSCT, multiple end points were explored. Two studies examined changes in body composition (33,106), with one showing a positive effect on body composition and

QOL (33). Three RCTs examined effects on depression (21,23,33), with only one (the largest, $n = 122$) showing a positive effect (33). None of the three RCTs that examined the effect of exercise training on anxiety (21,23,33) found benefit, and no benefit was observed for sleep in another study (23). The largest study (33) showed that aerobic training improved physical function, QOL, fatigue, happiness, depression, aerobic fitness, and body composition in 122 lymphoma survivors both on and off treatment. The study also noted that exercise did not interfere with chemotherapy completion rate or treatment efficacy, although it was not powered to examine these outcomes.

Adults during or after HSCT. There have been 11 exercise interventions conducted among adults during and/or after HSCT (19,24,37,40,41,46,62,83,90,121,136). Of these, six were RCTs (24,37,41,83,90,121), one included concurrent controls but was not randomized (62), and four were uncontrolled pre-post studies (19,40,46,136). Although the study by Shelton et al. (121) was an RCT, both groups were prescribed exercise; therefore, only pre-post results are reported herein. The sample sizes for these trials ranged from 12 to 35, with one exception: there was one RCT that examined effects of a walking program in 100 allogeneic donor HSCT patients (41).

Evidence Category A: Safety. A total of six studies commented specifically on the safety of exercise during and after HSCT in adults (24,37,40,46,62,136). All six studies unanimously report a lack of harm from aerobic exercise or strength training in this population.

Evidence Category C: Aerobic Fitness. Seven studies examined whether exercise training would improve or prevent declines in aerobic fitness parameters during or after HSCT in adults (19,24,40,46,62,121,136). Five studies demonstrated a treatment effect on fitness; however, all but one (62) were pre-post intervention studies without a control group. Two other studies showed no effect of training (24,40).

Evidence Category C: Muscular Strength. Two of the three studies that have examined strength as an end point in exercise trials among adults receiving HSCT have shown significant improvement (24,62,90); both of these studies were RCTs (62,90).

Evidence Category C: QOL. All three studies that examined whether exercise would improve QOL among adults undergoing HSCT indicated significant improvements with training (41,62,136), including two controlled trials (41,62).

Evidence Category C: Fatigue. Of the five studies that examined whether exercise during or after HSCT in adults would improve fatigue, three showed significant benefit (19,41,136) and two did not (24,121). In the one RCTs included (41), the effect of a walking program on fatigue was only significant in a subset of participants who received nonmyeloablative conditioning.

Other Outcomes. In addition, positive effects have been demonstrated in one or two studies for exercise among adults receiving HSCT for a few other end points, including

body composition (24,62) and physical function (121). Two RCTs have shown improved immune function during HSCT among adults with in-hospital exercise regimens (37,83). The single studies that examined the effects of exercise on depression and anxiety (46) or sleep (24) in this population observed no effect.

Gynecologic

There is only one completed RCTs that focused exclusively on gynecologic survivors. This trial included exercise as part of a weight loss intervention among 45 endometrial cancer survivors (132). Five other RCTs with mixed populations included small numbers of gynecologic cancer survivors among the participants ($n = 5-15$ patients) (12,28,59,128,131). The limited data on the safety and efficacy of exercise interventions among gynecologic cancer survivors preclude any statements regarding the level of evidence for any specific outcomes.

A cross-sectional study of ovarian cancer survivors in Canada observed that those who reported meeting the public health exercise recommendations for exercise reported significantly less fatigue, peripheral neuropathy, depression, anxiety, and sleep dysfunction (126). QOL has been observed to be compromised in ovarian cancer survivors and is a prognostic indicator for overall survival in this population (134,135). QOL has also been shown to be compromised among endometrial cancer survivors (133). A survey of 386 Canadian endometrial cancer survivors found that lack of exercise and excess body weight were associated with poorer QOL (30).

A multisite trial has been designed to occur within the Gynecologic Oncology Group to examine the effects of exercise on disease outcomes in ovarian cancer survivors. This planned trial would be particularly helpful in providing data regarding progression-free and, ultimately, overall survival. Fatigue, anxiety, and sleep disturbances are common in gynecologic cancer survivors. It should be noted that there is no research on the safety of exercise in women with lower limb lymphedema secondary to gynecologic cancer and its treatment. Given that this condition is complex to manage, it may not be appropriate to extrapolate safety from the findings on upper limb lymphedema.

RESEARCH GAPS/NEEDS

The overarching goal of this area of research is to discern the specifics of how exercise training can reduce the burden of cancer among survivors. It is possible that exercise training may constitute a potent-enough treatment to warrant third-party payer coverage for cancer rehabilitation among specific populations of survivors and for specific end points, analogous to cardiac rehabilitation after a myocardial infarction. Examples of end points for which research is needed to discern whether exercise might be equal, superior,

or more cost-effective than currently available approaches include bone health among survivors treated with hormonal therapies, metabolic, and cardiovascular outcomes among survivors exposed to specific curative therapies (e.g., some types of chemotherapy, biologic therapies, and chest wall radiation) and recurrence and survival among breast and colon cancer survivors. To enhance the probability of third-party payer coverage for “cancer rehabilitation” in the United States, research needs to focus on the effects of exercise on end points that are common and costly to treat and manage and within commonly diagnosed cancers with high survival rates. Regardless of whether third-party payer coverage ever occurs, for exercise to become widely prescribed by oncologists and adopted as a common intervention for recovery of full function after cancer treatment (as it is after cardiac events), it is vital that studies approach the issues of safety, cost effectiveness, and cost savings for health care utilization for persistent late effects.

As the body of research on exercise in cancer survivors continues to emerge, questions of generalizability and methodological quality can be addressed further. In the currently published literature, the proportion of available cancer survivors who opt to participate in exercise trials is often low enough to force the question of whether the interventions are truly effective and generalizable in the overall population of survivors. This is reflective of the developmental stage of the research in this area: studies have been trying to establish feasibility, safety, and efficacy rather than effectiveness or generalizability. The methodological quality of studies on exercise in cancer survivors has improved considerably during the past two decades. However, the published research can still be viewed critically, and this may deter oncologists from prescribing exercise to their patients who are survivors. Few exercise interventions have been rigorously tested against an attention control, and too few of the published studies actively comment on whether there were any adverse effects of exercise during or after cancer treatment. The moderating effects of cancer stage, treatment types, and prediagnosis factors (e.g., age, gender, weight, comorbidity, fitness) on exercise effects require further explication. Interaction with age is of interest given comorbidities and health care costs in this population. Most cancer survivors are older than 65 yr, yet most research has been conducted with middle-aged survivors younger than 65 yr. Additional limitations have included lack of accurate measures and, for some cancers, small sample sizes.

Studies are also needed to examine the relationship between exercise and a wide variety of end points in other segments of the cancer survivor population who have been largely absent from previous research. These survivors include racial and ethnic minorities and those with low educational attainment and/or low socioeconomic status. There is also a need to assess the safety and efficacy of alternate types of exercise, such as Pilates, various forms of yoga, martial arts, Curves™, and organized sport activities. These types of studies will contribute important information about

the generalizability of the effects of exercise on the outcomes reviewed herein.

Colon cancer is the third most common cancer with fairly good prognosis, yet few trials have examined the potential contributions of exercise toward attenuating treatment adverse effects and improving recovery. There is scant literature on the potential effects of exercise on common problems experienced by gynecologic cancer survivors, including poor QOL, fatigue, peripheral neuropathy, and obesity. Research on hematologic malignancies is, in general, at a feasibility stage, with a lack of control groups, incomplete randomization, or failure to conduct intent-to-treat analyses. There are limited studies that have explored the safety and efficacy of exercise in survivors of types of cancer not mentioned in this review. The potential to expand the research described herein to new cancer sites is tremendous and deeply needed, although it is acknowledged that RCTs may be difficult for rare cancers.

There are also numerous end points that require further study to specify the dose–response effects of exercise training among cancer survivors during and after treatment including prevention, attenuation, or reversal of treatment-related adverse effects (e.g., dyspnea, nausea, ataxia, dizziness, peripheral neuropathy), specific psychosocial outcomes, hormonal treatment effects, sleep, bone health, metabolic health, and cardiovascular health.

Finally, greater specificity is needed to assist fitness professionals who will provide exercise testing and prescription for cancer survivors as to the accommodations and specific tailoring needed on the basis of interactions of precancer health and fitness with cancer diagnosis and treatment types. For example, there is a need to evaluate exercise programs that accommodate or adapt to the individual physiological changes survivors experience from treatment (e.g., dyspnea, ataxia, peripheral neuropathy). The level of supervision needed for exercise training varies widely according to these characteristics, as well as the timing within the cancer experience (during vs after treatment). The extant literature is insufficient to assist fitness professionals with the specifics required to ensure that cancer survivors receive safe and effective fitness evaluations and exercise prescriptions.

CONCLUSIONS AND SUMMARY

An expert panel reviewed the published empirical evidence and came to consensus regarding the safety and efficacy of exercise testing and prescription in cancer survivors. Although there are specific risks associated with cancer treatments that need to be considered when survivors exercise, there seems to be consistent evidence that exercise is safe during and after cancer treatment. Exercise training–induced improvements can be expected concerning aerobic fitness, muscular strength, QOL, and fatigue in breast, prostate, and hematologic cancer survivors. Resistance training can be performed safely by breast cancer survivors with and at risk for lymphedema. The extent to which these findings may generalize to other cancer

survivor groups is unknown. Multiple research gaps remain in this field, including the need for greater specificity about the dose–response effects of specific modes of exercise training on specific end points and within a broader range of populations, such as survivors of colon and gynecologic cancers.

Fitness trainers who work with cancer survivors are urged to learn as much as possible about the specifics of the cancer diagnosis and treatment of a client to make informed, safe choices about exercise testing and prescription. Cancer diagnosis and treatment affect numerous body systems that are required for and affected by exercise training, including the neurologic, musculoskeletal, immune, endocrine, metabolic, cardiopulmonary, and gastrointestinal systems. Because cancer treatments are increasingly customized according to specific tumor characteristics, fitness professionals may benefit from contacting the medical treatment team for more precise information regarding the treatments received. Cancer survivors may not know the level of specificity required for a fitness professional to best discern the expected persistent effects on the above-noted body systems.

Multiple efforts are underway to increase the capacity of fitness professionals to serve the unique needs of cancer survivors, including the newly released ACSM Cancer Exercise Trainer certificationSM, a set of webinars intended to prepare fitness professionals for the certification examination, a book to help study for the certification examination (expected in 2010), and these guidelines. The LiveSTRONG at the Young Men's Christian Association (YMCA) initiative, a collaboration of the Lance Armstrong Foundation and the National YMCA (http://www.livestrong.org/site/c.khLXK1PxHmF/b.5119497/k.5FD9/LIVESTRONG_at_the_YMCA.htm), seeks to make the YMCA a destination of choice for cancer survivors seeking wellness activities, and there are capacity-building training activities for fitness professionals included in this effort. Multiple training programs already exist to assist fitness professionals with deepening their knowledge of the effects of cancer diagnosis and treatment on both the tolerance of and the need for exercise training, including the Rocky Mountain Cancer Rehabilitation Institute program

(<http://www.unco.edu/rmcri/cestc.html>) and Rehabilitation Systems (<http://rehabsys.com>). Exercise is effective in reducing the burden of several specific cancers, including demonstrated benefits related to physical function, QOL, and cancer-related fatigue. A sizeable percentage of the population of cancer survivors, nearly 12 million strong and growing, stand to benefit from well-designed exercise programming led by increasingly well-educated and well-informed fitness professionals.

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