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Updated Evidence in Support of Diet and Exercise Interventions in Cancer Survivors

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Abstract

Background—A growing body of evidence suggests that diet and exercise behaviors and body weight status influence health-related outcomes after a cancer diagnosis. This review synthesizes the recent progress in lifestyle interventions in light of current guidelines put forth by the American Cancer Society (ACS), the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) and the American College of Sports Medicine (ACSM).

Methods—The PubMed database was searched for terms of cancer survivor(s) or neoplasms/survivor, cross-referenced with MeSH terms of life style, health behavior, physical activity, exercise, body weight, obesity, weight loss, diet, nutrition, and intervention studies and limited to randomized controlled trials (RCTs) that had retention rates exceeding 75%.

Results—There has been an increase in the number and methodological rigor of the studies in this area, with 21 RCTs identified in the past three years. Results suggest that physical activity interventions are safe for cancer survivors and produce improvements in fitness, strength, physical function, and cancer-related psychosocial variables, whereas dietary interventions improve diet quality, nutrition-related biomarkers and body weight. Preliminary evidence also suggests that diet and exercise may positively influence biomarkers associated with progressive disease and overall survival (e.g. insulin levels, oxidative DNA damage, tumor proliferation rates).

Discussion—The evidence base regarding health-related benefits of increased physical activity, an improved diet and weight control continues to expand. Due to the large (and increasing) number of cancer survivors, more research is needed that tests the impact of lifestyle change on health-related outcomes in this population, especially research that focuses on high-reach, sustainable interventions that recruit diverse, representative samples to help increase the generalizability of findings to the population at large. Concurrent research also needs to address relative benefit in relation to various subpopulations as defined by phenotype, genotype, and/or exposures to treatment, and other lifestyle and environmental factors.

Introduction

According to the most recent 2008 compilation of cancer statistics by the International Agency for Cancer Research through the GLOBOCAN Project, there were 12.7 million new cancer cases and 7.6 million cancer deaths worldwide [1]. With continual advances in early detection and treatment, the differential between cancer incidence and mortality is ever-expanding, and with each passing year the number of cancer survivors increases dramatically. Five years ago, Parkin and colleagues reported that the number of cancer survivors in the world totaled over 24.5 million [2]; today, the number is far greater. Although these statistics are encouraging, it is important to acknowledge that the impact of

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cancer is significant and associated with several long-term health and psychosocial sequelae [3]. In addition to risk for recurrence, data clearly show that compared with general age- and race-matched populations, cancer survivors are at greater risk for developing second malignancies, cardiovascular disease, diabetes, osteoporosis, and functional decline [3]. These comorbid conditions and competing causes of death and disability are believed to result from cancer treatment, genetic predisposition, and/or common lifestyle factors [3].

Lifestyle interventions that promote improvements in diet and exercise behaviors have been proposed as a means to ameliorate the adverse effects of cancer and its treatment [3]. Various organizations, such as the American Cancer Society (ACS), the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) and most recently, the American College of Sports Medicine (ACSM) have issued guidelines for diet and/or physical activity that target cancer survivors [4–6]. These reports serve as resources for health care providers, patient advocates, and other stakeholders to improve the health and well-being of this rapidly expanding and high risk population. Table 1. features excerpts of these compiled guidelines (note that recommendations for alcohol have been omitted since this review is focused solely on diet and exercise). It should be noted, however that each of these reports points to the relative dearth of data on which their current recommendations rest – thus, the infusion of new data is exceptionally important in order to improve our knowledge of the potential benefits of lifestyle change after the diagnosis of cancer, as well as to gain an understanding of the optimal means for promoting behavioral change in this patient population. The goal of this paper is to review these recommendations in light of recent studies that have emerged within the past few years.

Methods

This article builds on a previous review of Demark-Wahnefried and Jones (2008) and provides an updated search of literature published on adult cancer survivors from November 2007 to June 2010. The PubMed database was used to perform this review and employed search terms of cancer survivor(s) or neoplasms/survivor cross-referenced with MeSH terms of life style, health behavior, physical activity, exercise, body weight, obesity, weight loss, diet, nutrition, and intervention studies. Because prospective intervention studies that employ a randomized controlled design offer the strongest evidence regarding potential benefit, we have limited our search to randomized controlled trials (RCTs) that employed health-related endpoints, and have further confined our review to trials with rates of attrition less than 25% (in an effort to remove trials that are subject to bias and results that may not be generalizable). A brief summary of these studies [7–31] is included in Table 2.

Results

Weight Management

At the forefront of both the ACS and the WCRF/AICR recommendations are guidelines for weight control [4, 5].While both organizations currently differ regarding cutpoints that distinguish a desirable weight, both advocate weight loss if individuals are overweight or obese, and also endorse avoidance of weight gain in adulthood. These guidelines emanate from a large body of epidemiologic findings that have consistently found associations between overweight and obesity and the primary risk of cancer, as well as cancer-related mortality – data which are expanding at a rapid pace as the world's population becomes increasingly overweight. Thus, in contrast to a decade ago when the maintenance of adequate nutrition was the primary concern for individuals diagnosed with cancer, as the obesity epidemic has expanded and as individuals are being diagnosed with cancer at earlier stages, overnutrition has eclipsed undernutrition in terms of prevalence in this patient population. Therefore, in their guide for informed choices, the ACS provides guidelines for

weight loss both during and after cancer treatment. While there has yet to be a trial of a weight loss intervention in relation to cancer-related death or recurrence, the number of weight loss interventions among cancer survivors appears to be increasing. During the time circumscribed for this review, there have been three trials that specifically promoted weight loss among survivor populations [10, 11, 14], and one trial that has focused on prevention of weight gain and increased adiposity post-diagnosis [9]. These trials have ranged in size from 24 [14] to 641 [10], targeted a wide range of cancers (e.g., breast, colorectal, endometrial, and prostate), utilized different modes of delivery, and ranged in duration from 6 months [9] to 2-years [10].

The diet-based pilot study by Djuric and colleagues utilized group classes to promote weight loss in obese African-American breast cancer survivors using either a Weight Watcher® based-approach or an approach that incorporated spirituality. While no differences were observed between study arms with regard to weight, participants assigned to the spirituality-based intervention reported significant improvements in fruit and vegetable consumption [14].

In contrast, the other weight management studies employed multi-component interventions that incorporated both diet and exercise elements. These interventions targeted cancer survivors across the cancer continuum, from those who were newly diagnosed and undergoing treatment [9], to those within 5-years of diagnosis [11], as well as those who were long-term survivors, i.e., five or more years beyond diagnosis [10]. The feasibility study conducted by Demark-Wahnefried et al. (2008) employed a distance medicine-based approach of mailed materials and telephone counseling to prevent gains in adiposity that commonly occur during adjuvant chemotherapy. Findings provide support that adverse changes in body composition may be mitigated with a diet-exercise intervention, but that it may be difficult to promote physical activity with home-based approaches during treatment, especially in breast cancer patients who are sedentary prior to diagnosis [9]. In contrast, von Gruenigan and colleagues (2008) found that weight status can be significantly improved with a diet and exercise intervention that utilizes mixed modes of delivery, e.g., group classes, telephone counseling, and mailed print materials, but that improvements in exercise may contribute more to improved body weight status than dietary restriction [11]. Morey et al. (2009) found significant improvements in both diet and exercise behaviors, which translated into significant weight loss, as well as reduced rates of functional decline with a year-long intervention comprised of mailed print materials and telephone counseling among elderly overweight breast, prostate and colorectal cancer survivors [10]. Thus, solid progress is being charted in trials which have used diverse interventions to promote weight loss or weight management among a wide variety of cancer survivors – work that eventually will lay the foundation for trials that explore weight loss in relation to cancer-specific endpoints.

Dietary Patterns

To reinforce the importance of weight management, many of the dietary recommendations put forth by both the ACS and the WCF/AICR advise against the consumption of energy dense foods, i.e., sugars, fats, and a variety of processed foods (Table 1). Instead, the guidelines endorse the consumption of a plant-based diet that focuses on fruits, vegetables and unrefined whole grains, with the WCRF/AICR also cautioning against moldy and salt-cured foods given their association with aerodigestive and hepatic cancers [4].

Recent dietary interventions (see Table 2) have focused on prostate cancer survivors and have monitored biomarkers associated with cancer progression (prostate specific antigen [PSA] levels and/or tumor proliferation rates). A study by Parsons et al. utilized telephone counseling to promote increased consumption of fruits and vegetables over a 6-month study period. Although the intervention elicited excellent adherence and significantly increased

consumption, which was confirmed by increases in serum carotenoids, the intervention produced a non-significant increase in PSA that countered the investigators' hypotheses [15].

Low fat diets also have been explored or tested in newly-diagnosed prostate cancer patients who elect watchful waiting [12] as well as those scheduled for prostatectomy [13]. Results from a small scale 4-week feeding trial performed by Aronson and colleagues (2010) suggested that a low fat diet may inhibit the growth rate of a hormonally-responsive prostate cancer cell line [12]. In contrast, while the low fat diet did promote changes in serum lipids, as well as cytokines and angiogenic factors associated with the NFkB pathway (unpublished data) in a full scale phase II trial by Demark-Wahnefried et al. (2008), dietary fat restriction was not associated as strongly with prostate cancer cell growth as flaxseed supplementation [13]. The mixed results of these dietary intervention trials suggest the need for more research in this area. Indeed the discrepancy in results between two of the largest dietary intervention trials, i.e., the Women's Intervention Nutrition Study (WINS) (n=2,437) and the Women's Healthy Eating and Living (WHEL) trials (n=3088), described in the forerunning review [3], as well as the numerous secondary analyses that have emanated from these trials, provides strong evidence that dietary modification may affect subgroups of patients differentially depending upon tumor receptor status, other lifestyle practices, and the specific foods that are consumed (e.g., cruciferous vegetables vs. others).

As with intervention trials aimed at weight management, dietary protocols, such as those that promote a low fat diet and/or increased fruit and vegetable consumption also have been paired with protocols to increase physical activity in multi-component interventions (see Table 2). Bloom et al. (2008) found that group classes were significantly effective in increasing physical activity among breast cancer survivors, but did not influence dietary change [7]. In contrast, Campbell and colleagues (2009) found that home-based approaches that utilize tailored print and/or motivational counseling to improve fruit and vegetable consumption and physical activity among colorectal cancer survivors, have little impact on physical activity, but do improve dietary behaviors [8].

Physical Activity

Overall, ACSM, ACS, and WCF/AICR exercise guidelines for cancer survivors mirror those for the general population by recommending at least 30 minutes of moderate-to-vigorous intensity physical activity on five or more days of the week (see Table 1). The expert panel convened by ACSM further specified that exercise programs may need to be modified for the individual survivor on the basis of his/her health status, treatment history, and anticipated disease trajectory.

Upon reviewing recent physical activity RCTs among cancer survivors (12 studies, Table 2), we observed that these interventions were conducted mostly among breast cancer survivors, with only one study among colorectal cancer survivors [28] and another two involving mixed samples [29, 31]. The interventions described in this review were generally implemented after the participants completed cancer treatments, though one study included participants actively receiving chemotherapy [31]. A combination of individual- and group-based intervention strategies [17, 21, 23, 26, 27, 30] were used in most studies. Others relied solely on individual [20, 24, 28] or group-based approaches [16, 19, 31]. Five interventions focused specifically on aerobic exercise [17, 21, 23, 24, 28], whereas others encouraged resistance training [16, 20] or a combination of aerobic and strength training [26, 29, 31]. A yoga intervention also was included [19]. Recommendations were generally focused on moderate intensity or greater aerobic exercise for at least 150 minutes per week [18, 21, 24, 28] and/or twice weekly strength training sessions for varying durations (90 min. [16, 27]; 30–45 min. [20]) and thus consistent with recent ACSM guidelines for cancer survivors.

Overall, the findings from these studies suggest that exercise is a safe and effective way to provide rehabilitation for cancer survivors and that even brief exercise interventions can be beneficial. Outcomes included improved aerobic capacity [17, 21, 24, 29, 31], strength [16, 22, 27, 31], body composition [17, 21, 26], quality of life [16, 30], as well as reduced fatigue [23, 24, 31], emotional distress [23, 31], lymphedema symptoms [27], and oxidative DNA damage [28].

In terms of progress since the last review [3], several improvements in research design and methodology were noted in these recent studies. First, this literature search uncovered more RCTs than the past review (12 vs. 4, respectively). The trend away from quasi-experimental designs is encouraging, as methodologically rigorous designs allow for more confidence in results. However, sample sizes were still relatively small, ranging from 37–269 (M=124 participants), but appear to be increasing. For example, in the current review, there were six (out of 12) studies with samples of at least 100 participants [7, 8, 13, 16, 26, 27, 29, 31], compared to the last review in which only one (of seven studies) had a sample size greater than 100. Such improvements will help increase statistical power and improve stability of findings.

There also were several differences in the recent physical activity interventions offered to cancer survivors. While the range of intervention lengths varied widely (2 weeks [28] to 2 years [20]) for the studies included in this review, four (out of 12) emphasized long-term (> 6 months) exercise interventions [16, 17, 20, 27] for cancer survivors, compared to only one study (out of the seven) from the past review. Such a shift in program duration will be more conducive to promoting and studying the enduring lifestyle changes in physical activity behavior among cancer survivors needed to beneficially impact rehabilitation and survivorship long-term.

The more recent interventions also tended to be less supervised. Strictly supervised conditions [28, 30, 31] are more easily monitored and may help alleviate participant concerns regarding safety, but any gains may be difficult to maintain once the program ends and the externally imposed structure and support is no longer available. Most studies in this review emphasized a combination of supervised and unsupervised exercise. For example, Fillion et al. (2008) provided supervised instruction with home-based exercise assignments and Rogers (2009) and colleagues attempted to gradually transition participants to home-based exercise by study completion [21, 23]. Such approaches encourage self-management of exercise behavior and favorably influence sustainability. Furthermore, mail and telephone-delivered interventions used by Pinto et al. (2008) have great potential for reaching larger numbers of cancer survivors and positively impacting public health [24].

Another interesting trend was the incorporation of mind-body approaches to wellness into physical activity interventions for cancer survivors. For example, in Adamsen et al. (2009), a high intensity 6-week physical training program was accompanied by relaxation training (progressive muscle relaxation, 30 minutes/4 times a week), body awareness and restorative training (yoga and Pilates, 90 minutes/week), and massage (30 minutes/twice a week) for cancer patients undergoing chemotherapy. Findings indicated significant improvements in vitality, physical functioning, fitness, stress and mental health, as well as reduced fatigue [31]. Another physical activity intervention was combined with nurse-led cognitive-behavioral stress management group sessions (1.5 hours/week for 4 weeks; relaxation training, practicing coping skills for fatigue, discussing connection between thoughts, emotions, and fatigue) for breast cancer survivors and improved fatigue, energy levels, and emotional distress [23].

Additionally, Carson et al. (2009) provided 8 weekly yoga classes with gentle stretching poses, breathing techniques, and meditation and was able to reduce menopausal symptoms, joint pain and sleep in early stage breast cancer patients with hot flashes [19]. Interventions incorporating relaxation training and other psychosocial/wellness components along with physical training appear to be beneficial and can help address the wide range of psychological and physical symptoms experienced by cancer survivors during and after treatment, as well as educate the participants on the nexus between the two (i.e., mind-body connection).

Finally, a few recent studies have begun to examine more than just the usual exercise capacity and quality of life outcomes. Researchers have called for well-designed studies testing the effects of physical activity upon cancer survivorship and/or surrogate/biological markers mediating the association between physical activity and survival [32]. While none of the studies identified in this review specifically examined survival outcomes, there were a few RCTs examining potential physiological mechanisms through which physical activity might impact cancer. For example, the beneficial effects of physical activity on cancer survival may be mediated through a reduction in body fat and beneficial changes in metabolic hormones (insulin), growth factors (insulin-like growth factor IGF-1 and its binding protein IGFBP-3), and adipokines (leptin, adiponectin). In this review, Irwin and c0olleagues (2008) demonstrated that a 6-month aerobic exercise intervention produced statistically significant increases in lean mass and decreases in body fat, insulin levels, IGF-1, and IGFBP-3, whereas women randomized to usual care experienced increases in these biomarkers [17]. Moreover, dose response effects were observed between exercise frequency and decreases in body fat and increases in lean body mass. Insulin levels also were examined by Ligibel and colleagues and found to be significantly reduced (28%) after a 16-week combined strength training and aerobic exercise intervention [26]. However, there were no significant changes found in body composition or adipokines (leptin, total and high molecular weight adiponectin). The authors hypothesized that longer (> 4 months) and/or more strenuous exercise programs may be required to affect these outcomes and called for more studies examining the impact of physical activity on adipokines in cancer survivors.

Another mechanism by which physical activity may exert its influence on cancer risk and prognosis could be through the modulation of oxidative DNA damage, which is implicated not only in carcinogenesis, but also may be important for relapse. Among 48 colorectal cancer patients following primary therapy, a 2-week moderate intensity exercise program reduced oxidative DNA damage as measured by pre- and post-intervention urinary 8-oxo-dG excretion concentrations (8.47±1.99 to 5.91±1.45 ng/mg creatinine, p=0.02), whereas high-intensity exercise tended to increase DNA damage (5.00+1.31 to 7.11+1.63 ng/mg creatinine, p=0.18) [28]. More research is needed to replicate these findings, but these data suggest that exercise recommendations for cancer survivors might warrant a focus on moderate-intensity, rather than vigorous, activities.

Discussion

The number of randomized trials testing lifestyle interventions in cancer survivors is growing, but the evidence base is still limited. This review uncovered more published studies on physical activity interventions for cancer survivors, than those involving dietary modification. Moreover, despite advocacy of multi-component lifestyle interventions, there still are relatively few studies of combined programs. Such approaches may be especially important in pursuing studies that target survival endpoints given that secondary analyses from the WHEL trial suggest a significant survival advantage for breast cancer survivors who exercised 30 minutes, 6 days/week and consumed at least 5 servings/day of fruits and

vegetables, which was not seen in women who adopted only one of those health behaviors (physical activity or diet) [33].

Overall, findings from this review indicate that lifestyle interventions for cancer survivors appear to still focus on outcomes related to fitness, diet, and cancer-related psychosocial factors. Physical activity interventions were shown to be safe for cancer survivors and produce improvements in fitness, strength, and quality of life (e.g., fatigue). Likewise, dietary interventions found significant improvements in diet quality, restriction of dietary fat, and increased fruit and vegetable consumption (as well as serum markers associated with these foods). Since the last review, more researchers have started examining the impact of diet and exercise on surrogate/biologic markers of survival [9, 12, 15, 17, 26, 28]. For example, results suggest that physical activity can reduce insulin levels [17, 26] and perhaps oxidative DNA damage [28] in cancer survivors. Additionally, studies are now testing the impact of interventions directly on the biology of the tumor, as in the trial which compared the effects of dietary fat restriction and/or flaxseed supplementation instituted during the presurgical period in 161 men scheduled for prostatectomy, and found lower proliferation rates in excised tumors of men assigned to flaxseed [13].

In terms of future directions, RCTs testing the effects of physical activity and diet on survival have been called for in prior reviews [32] and are still needed. Such studies would provide critical information about whether and how much lifestyle change can affect prognosis. While physicians and health care providers are still encouraged to recommend lifestyle changes to cancer survivors (consistent with the ACS, WCRF/AICR, and ACSM guidelines) on the basis of the beneficial health outcomes from studies summarized in this and past reviews [9], future research will help inform doses (or exposures) that are required and the magnitude of effects that can be expected, as well as uncover possible side effects. Furthermore, subset analyses among survivors with different phenotypes, genotypes and other lifestyle/environmental/treatment exposures may help to personalize lifestyle prescriptions over the long-term.

As this research literature grows, future directions also should focus on sustainable lifestyle interventions that are capable of reaching the large (and increasing) number of cancer survivors. For example, many of the physical activity interventions described in this review were costly and required considerable staff expertise to deliver. From the participant perspective, these programs may invoke unrealistic demands on time and travel that serve as barriers to participation. Future research should focus on developing and testing interventions with potential for sustainability and disseminability in order to serve the growing population of cancer survivors. Also, since most available studies recruited primarily White samples, including other racial/ethnic groups in future trials would help increase the generalizability of such findings to the population at large.

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Table 1

Compiled Guidelines: American Cancer Society 2006 Guidelines on Nutrition and Physical Activity for Cancer Prevention, the World Cancer Research Fund/American Institute for Cancer Research Recommendations for the Prevention of Cancer, 2007, and the American College of Sports Medicine Roundtable on Exercise Guidelines for Cancer Survivors (2010)

American Cancer Society	World Cancer Research Fund/ American Institute for Cancer Research	American College of Sports Medicine
Maintain a healthy weight throughout life • Balance caloric intake with physical activity • Avoid excessive weight gain throughout the lifecycle • Achieve and maintain a healthy weight if currently overweight or obese	**Be as lean as possible within the normal range of body weight** • Ensure that body weight through childhood and adolescent growth projects toward the lower end (<22.9) of the normal BMI range at age 21 • Maintain body weight within the normal range from age 21 • Avoid weight gain and increases in waist circumference throughout adulthood	
Adopt a physically active lifestyle • Adults: engage in at least 30 minutes of moderate-to-vigorous physical activity, above usual activities, on five or more days of the week (45–60 minutes of intentional physical activity are preferable). • Children and adolescents: engage in at least 60 minutes/ day of moderate-to-vigorous physical activity at least 5 days per week. Limit screen time (TV, computer, games) to no more than 2 hours per day.	**Be physically active as part of everyday life** • Be moderately physically active, equivalent to brisk walking, for at least 30 minutes each day • As fitness improves, aim for 60 minutes or more of moderate, or for 30 minutes or more of vigorous, physical activity every day • Limit sedentary habits such as watching television	**Avoid inactivity** • Return to normal activities as quickly as possible after surgery. Continue normal daily activities and exercise as much as possible during/ after nonsurgical treatments. Individuals with known metastatic bone disease and cardiac conditions may require modifications and greater supervision for safety. • Aerobic, resistance training and flexibility exercise recommendations are the same as age-appropriate physical activity guidelines for Americans
Consume a healthy diet, with an emphasis on plant sources • Choose foods and beverages in amounts that achieve and maintain a healthy weight. • Eat five or more servings of a variety of vegetables and fruits each day. • Choose whole grains in preference to processed (refined) grains. • Limit consumption of processed and red meats.	**Limit consumption of energy-dense foods; avoid sugary drinks** • Consume energy-dense foods sparingly • Avoid sugary drinks • Consume fast foods sparingly, if at all **Eat mostly foods of plant origin** • Eat at least five portions/servings (at least 400 g or 14 oz) of a variety of non-starchy vegetables and of fruits every day • Eat relatively unprocessed cereals (grains) and/or pulses (legumes) with every meal • Limit refined starchy foods • People who consume starchy roots or tubers as staples also to ensure intake of sufficient non-starchy vegetables, fruits, and pulses (legumes)	

American Cancer Society	World Cancer Research Fund/ American Institute for Cancer Research	American College of Sports Medicine
	Limit consumption of salt; avoid moldy cereals (grains) or pulses (legumes) • Avoid salt-preserved, salted, or salty foods; preserve foods without using salt • Limit consumption of processed foods with added salt to ensure an intake of less than 6 g (2.4 g sodium) a day • Do not eat moldy cereals (grains) or pulses (legumes)	

Table 2

Randomized Controlled Trials (RCTs) of lifestyle interventions for cancer survivors

Authors	Sample	Design	Intervention	Frequency/intensity/ duration	Results
Diet-Related RCTs					
Aronson et al. 2010	18 men diagnosed with prostate cancer within the past 2 years and on active surveillance. Mean age= 64. 67% Caucasian and 33% African American.	Evenly randomized to a low fat diet and a Western diet.	Feeding study with the low fat diet defined as <15% of total energy from fat and the Western diet defined ~40% of energy coming from fat.	4-weeks	No differences noted between study arms in PSA, serum lipids or IGF-1/-2 or binding protein change scores. LNCaP cells exposed to sera of men on the low fat diet grew significantly less rapidly (p=.03) than cells exposed to sera of men assigned to the Western diet.
Demark-Wahnefried et al. 2008	161 men with operable prostate cancer scheduled for prostatectomy. Age range 36–73 (M = 59.2). 70% Caucasian, 26% African American, 4% Other.	Phase II trial testing the comparative effects of flaxseed supplemen- tation +/− a low fat diet. Controls continued usual diet.	Flaxseed arms received 30 grams/day of ground flaxseed. Low fat arms received instruction on diet of <20% of kcal from fat. Fat gram budgets given and men recorded fat grams.	Upon randomization men received appropriate instruction and supplies. Weekly telephone calls fielded questions/problems and reviewed dietary intakes. Urine analyzed for presence of lignans to confirm flaxseed consumption. Mean study period was 30 days.	Proliferation rates were significantly lower (p<.002) among men assigned to the flaxseed arms. Median Ki- 67 positive cells/total nuclei ratios (×100) were 1.66 (flaxseed alone) and 1.50 (flaxseed + low fat) vs. 3.23 (control) and 2.56 (low fat). Men assigned to the low fat arms experienced significant decreases in serum cholesterol (p=.048). Intention to treat analysis with 7.5% attrition.
Djuric, et al. 2009	24 African American breast cancer (Stages I–IIIA) survivors. BMI 30–45. Mean age=55.	Feasibility study of diet counseling vs. diet + spirituality counseling.	Weight loss intervention based on Weight Watchers approach. Diet-spirituality counseling based on 12-step approach.	Weekly sessions for the 1st three months, biweekly sessions 3–6 months and monthly sessions for remainder of 18 month program.	Significantly greater improvements in vegetable consumption (p=.013) and spirituality (p=.024) in the Diet + Spirituality arm, but no arm differences in other dietary parameters, or body weight status. 8% attrition.
Parsons et al. 2008	43 Prostate cancer survivors on active surveillance. Mean age = 64. 88% Caucasian.	Telephone counseling vs. standardized written materials.	Experimental arm counseled to consume at least 7 servings of vegetables/day (2 cruciferous, 2 tomato products and 3 others), 2 servings/day of whole grains and 1 serving/day of beans/legumes.	Theory based, telephone counseling based intervention comprised of 13 (25–50 minute) sessions scheduled over a 6- month period.	Change in mean levels of PSA were +2.28 in the experimental arm vs. −0.06 among controls (p=0.29). Men in the experimental arm consumed significantly more vegetables and had significantly higher serum levels of carotenoids. 2% attrition.
Physical Activity RCTs					
Adamsen et al. 2009	269 patients with mixed cancers (73% female) undergoing chemotherapy. No brain or bone metastases. Mean age=47. Median days since diagnosis=84.	Supervised exercise + massage vs. usual care control.	Supervised exercise involving high intensity cardiovascular and resistance training, relaxation and body awareness training, and massage vs. usual care.	9 hours weekly for 6 weeks including resistance training 45 minutes/3x week (goal= 3 continuous series of 5–8 repetitions (rep.) at 70–100% of the 1 rep. maximum test) and cardiovascular exercise 15 minutes/ 3x week (85–95% of maximum heart rate).	At 6 weeks, the intervention had significantly reduced fatigue and improved vitality, aerobic capacity, muscular strength, physical and functional activity, and emotional well-being, but not quality of life. 13% attrition.

Authors	Sample	Design	Intervention	Frequency/intensity/ duration	Results
Allgayer et al. 2008	48 colorectal cancer patients following primary therapy. Mean age=59.	Moderate vs. high intensity exercise	Hospital based exercise programs.	2 weeks of exercise for 30–40 minutes/day at moderate intensity (0.3– 0.4 × maximal exercise capacity) vs. high intensity (0.5–0.6 × maximal exercise capacity).	Short term moderate intensity exercise significantly reduced (29%) urinary 8-oxo-dG excretion levels, suggesting decreased oxidative DNA damage. High intensity exercise resulted in a non-significant increase (42%). 10% attrition.
Carson et al. 2009	37 disease-free breast cancer (Stage IA-IIB) survivors experiencing hot flashes Mean age=54.4. Mean years since diagnosis = 4.9. 81% White, 19% African American.	Yoga vs. wait-list control.	Gentle yoga poses, meditation, breathing exercises.	8 weekly, 120 minute yoga classes.	Significantly greater post-treatment increased vigor and reductions in joint pain, fatigue, sleep disturbance, symptom-related bother, and hot-flash frequency and severity for yoga group. 19% attrition.
Fillion et al. 2008	87 French breast cancer (Stages 0–III) survivors who recently completed radiotherapy. Mean age=52.5	Walking and psychosocial management vs. usual care control	Supervised walking training (1 hour) and psycho-educational fatigue management sessions (1.5 hours).	4 weekly, 2.5-hour group meetings and 5–15 minute telephone booster sessions, with individualized goals for frequency and intensity.	Intervention arm showed significantly greater improvements in energy level, and reductions in fatigue and emotional distress 3 months post-intervention, relative to controls. 7% attrition.
Irwin et al. 2009a and 2009b	75 sedentary post-menopausal breast cancer (Stages 0–III) survivors. Completed adjuvant treatment ≥ 6 months before study. Mean age =56. Mean years since diagnosis=3.3. 84% Non-Hispanic White.	Exercise vs. usual care control.	Supervised gym- and home- based aerobic exercise.	Goal=150 minute/week of moderate-intensity exercise (60– 80% of predicted maximal heart rate) for 6 months.	Significantly greater post-treatment improvements in exercise, % body fat and lean mass for intervention group. Intervention arm experienced stable bone mineral density and decreased insulin, and IGF-1, and increased IGFBP-3, unlike control group. 9% attrition.
Ligibel et al. 2008, 20009	101 sedentary, overweight breast cancer (Stage I–III) survivors who completed chemotherapy and/or radiation therapy 3 months before study. Mean age=53. Mean months since diagnosis= 21.2 (intervention arm) and 28.6 (control arm).	Exercise vs. usual care control	Supervised strength training and home-based aerobic training	16 week moderate intensity program with 50 minutes, 2x/ week strength training and 90 minutes/week of aerobic exercise.	Significant post-treatment decreases in insulin levels and hip circumference for exercise group (not control group). No significant changes in total or high molecular weight adiponectin, or leptin for either arm. 18% attrition.
May et al. 2008, 2009	147 mixed cancer survivors. Medical treatment completed ≥ 3 months. Mean age=48.8.	Physical Training (PT) + cognitive-behavioral therapy (CBT) vs. PT alone.	Supervised PT with individual aerobic and resistance exercise sessions and group sports.	PT 2x/week for 12 weeks with 30 minutes aerobic bicycle training at intensity of HR_{rest} +70% to 80% of (HR_{peak} –HR_{rest}); 30 minutes strength training at intensity of 50%–60% of 1- repetition maximum; 60 minutes group sports.	Improved physical activity and quality of life found post-intervention and also at 3- and 9-months post-intervention for both arms ($p<.001$). 17% attrition.
Pinto et al. 2008	86 sedentary, post-treatment breast cancer (Stages 0–II) survivors.	Exercise vs. attention control	In-person exercise instruction, self monitoring with logs and pedometers,	12 weekly phone calls. Goal= moderate intensity exercise (55– 65% maximum heart rate) 30 minutes/day, 5 days/week.	Significantly greater improvements in minutes/week of moderate intensity physical activity, fitness, and reduced

Authors	Sample	Design	Intervention	Frequency/intensity/ duration	Results
	Mean age=53.14. Mean years since diagnosis= 2. 95% White.		motivation- matched telephone counseling, tip sheets.		fatigue post-treatment for intervention group. Gains were maintained at 9 months follow up. 8% attrition.
Rogers et al. 2009a, 2009b	41 sedentary breast cancer (Stages I–III) survivors receiving hormone therapy. Mean age=53. 93% White.	Exercise vs. usual care control.	Theory-based physical activity behavior change intervention including group discussions with a psychologist, and individual exercise and counseling sessions with an exercise specialist.	12 week program with 6 group sessions and 15 individual sessions. Goal=150 minutes/ week of moderate intensity activity.	Significantly greater improvements in minutes/week of moderate intensity or greater physical activity, and strength, and reduced central adiposity and lower extremity joint dysfunction at 3 months post-intervention for the intervention arm. 7% attrition.
Schmitz et al. 2009	141 breast-cancer (Stages I– III) survivors with stable lymphedema of the arm. Mean age=57. Mean months since cancer diagnosis =79 (intervention) and 88 (control). White (58%) African American (38%).	Progressive weight lifting vs. wait-list control.	Progressive weight lifting program with 1- year membership at a community fitness center.	90 minute supervised group sessions 2x/ week for first 13 weeks, then 2x/week unsupervised exercise at a self- directed intensity for 39 weeks. Exercises performed with compression garment.	Greater reductions in self-reported severity of lymphedema symptoms and exacerbations, and improvements in upper- and lower-body strength in weight lifting group (p-values<.05). No significant effect on limb-swelling. 8% attrition.
Speck et al. 2009	234 breast cancer (Stages 0– III) survivors (112 with lymphedema). Currently cancer-free. Mean age = 56.5. Diagnosis ≥ 1 year before study entry. Primarily White.	Progressive strength training vs. wait-list control.	Progressive strength training.	13 weeks of supervised instruction (90 minutes, 2x per week) then unsupervised strength training at a self- directed intensity to 1 year.	Significantly greater post-treatment improvements in strength (bench and leg press) and quality of life (perceived appearance, health, physical strength, sexuality, relationship, social functioning) for intervention group. 7.7% attrition.
Waltman et al. 2009	223 post-menopausal breast cancer survivors with bone loss who completed cancer treatment ≥ 6 months before study. Mean age=58.6. 98.7% Caucasian.	Exercise + risedronate, calcium, and vitamin D vs. risedronate, calcium, and vitamin D, alone	Progressive strength/ weight training at home for first 9 months and then with weight machines at local fitness center.	Exercise 30–45 minutes 2x weekly for 24 months at self- directed intensity.	No significant post-treatment improvements in bone mineral density over oral agents alone. Participants who were > 50% adherent to exercise (81 of 110) were significantly less likely to lose bone mineral density at the total hip and femoral neck. 10% attrition.
Dietary and Physical Activity RCTs					
Bloom et al. 2008	404 female breast cancer (Stage 0–IV) survivors who were 5 years from diagnosis and cancer-free. ≤50 y.o. at diagnosis. 76% Euro-American, 5% African American, 7% Latina, 10% Asian, 2% other.	Multi- component intervention vs. wait list control.	Sessions included supervised 30 minute resistance exercise and yoga sessions, group walks, exercise prescription, progress reports, healthy diet handouts (on low fat cooking, eating more fruits and vegetables).	Three 6-hour workshops over 3 months.	At post-test, intervention group was more likely than control to report increased physical activity (p=.036) but not diet changes. 4% attrition.
Campbell et al. 2009	266 colorectal cancer survivors and 469 controls. M=66.5 yrs.	2×2 design testing tailored print, telephone motivational	Intervention aimed at promoting physical activity and fruit and vegetable consumption.	The tailored print intervention consisted of 4 newsletters delivered over 9 months; the telephone motivational interviewing	The combined intervention produced the greatest changes in fruit and vegetable consumption, though this effect was only consistently seen

Authors	Sample	Design	Intervention	Frequency/intensity/ duration	Results
		interviewing or both vs. control of standardized print materials.		consisted of 4–20 minute calls over 9 months.	among controls, not colorectal cancer survivors. No changes in weight or physical activity were observed.
Demark-Wahnefried et al. 2008	90 newly diagnosed premenopausal women with Stage I–IIIA breast cancer scheduled for adjuvant chemotherapy. Mean age = 41.8.	Three-armed trial calcium- rich with diet (attention control) vs. exercise vs. exercise + low fat, plant- based diet.	All study arms were provided counseling and written materials on 1,200–1,500 mg of calcium/day. Exercise counseling promoted both aerobic exercise (≥30 minutes/day at least 3 days/week) and resistance training (exercise bands and water-filled weights in legs and lower body region). Additional diet counseling emphasized <20% of kcal from fat and at least 5 daily servings of fruits and vegetables.	All study participants received written mailed materials and telephone counseling (14 sessions over the 6 month study period).	Targeted accrual was achieved with 8.8% drop-out. Fat and fruit and vegetable change scores differed significantly in the diet + exercise arm; though no differences in change scores were observed for physical activity. Measures of adiposity were generally lower in the study arm that received all intervention elements (diet + exercise), though the only significant difference was in extremity adiposity, i.e., 0.7% vs. 1.2% vs. 0.1%, in control vs. exercise alone vs. exercise + diet arms, respectively (p=.047). No differences between study arms were observed for quality of life, anxiety and depression, serum lipids, sex hormone binding globulin, insulin, proinsulin, C-reactive protein, interleukin-1B, and tumor necrosis factor receptor- II.
Morey et al. 2009	641 older, overweight, long-term (colorectal, breast, prostate) cancer survivors. Mean age=73. Mean years since diagnosis=9. 89% White.	Diet-exercise intervention vs. wait list control.	Theory-based, telephone counseling and mailed print material-based diet and exercise intervention, with pedometers, exercise bands, table guide for portion control, and diet/exercise logs.	12 month program with 1 mailing of a personally-tailored workbook and quarterly newsletters, 15 telephone sessions (lasting 15–30 minutes) and 8 prompts. Goals= 15 minutes strength training every other day, 30 minutes/day endurance exercise, 7–9 servings/day fruits and vegetables, reduce fat to 10% of energy intake, 10% weight loss.	At 12 months, physical function had declined less rapidly in the intervention group (−2.15; 95% confidence interval [CI], −0.36 to −3.93), compared with the control group (−4.84; 95% CI, −3.04 to −6.63) (p=.03). Physical activity, dietary behaviors, and overall quality of life improved significantly in the intervention group, compared with control. Weight loss was also greater (2.06 kg for intervention vs. .92 kg for control, p<.001). 13% attrition.
von Gruenigen et al. 2008	45 overweight/obese early stage (I–II) endometrial cancer survivors. Mean age=55. Mean years since diagnosis=2. 98% Caucasian.	Diet-exercise intervention vs. usual care control.	Theory-based lifestyle intervention involving group and individual physical activity and nutritional counseling with behavior modification. Pedometers were provided.	6-month program with groups meeting weekly for 6 weeks, bi- weekly for 1 month, and monthly for 3 months, with calls or newsletters on weeks groups did not meet. Goal= aerobic activity 5 days/week for 45 min or more and 5% weight loss in 6 months.	At 12 months, the intervention group showed greater improvements in weight (− 3.5 kg vs. +1.4 kg) and physical activity than the control group (p-values<.05). No significant group differences in intakes of energy, vitamin C, or folate. 16% attrition.