Resistance exercise interventions during and following cancer treatment: a systematic review

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Findings from prior systematic reviews suggest that exercise results in meaningful improvements in many clinically relevant physiologic and quality of life (QOL) outcomes during and following cancer treatment. However, the majority of exercise-cancer studies have focused upon the benefits of aerobic exercise (AE) and knowledge of the efficacy of resistance exercise (RE) alone as a supportive care intervention for cancer patients and survivors remains limited. Consequently, the purpose of this review was to provide the first systematic evaluation of the effects of RE alone upon clinically relevant physiologic and QOL outcomes during and following cancer treatment. Literature searches were conducted to identify studies examining RE interventions in cancer patients and survivors. Data were extracted on physiologic (fitness, physical function, and body composition) and QOL (fatigue, psychological well-being, and cancer-specific and global QOL outcomes. Cohen's *d* effect sizes were calculated for each outcome. A total of 15 studies (6 in samples undergoing active cancer treatment and 9 in samples having completed cancer treatment) involving 1,077 participants met the inclusion criteria. Findings revealed that, on average, RE resulted in large effect-size improvements in muscular strength ($d = 0.86$), moderate effect-size improvements in physical function ($d = 0.66$), and small effect-size improvements in body composition ($d = 0.28$) and QOL ($d = 0.25$) outcomes. The effect sizes observed following RE are comparable in magnitude to the effects of exercise interventions reported in prior comprehensive reviews of the exercise-cancer literature which primarily focused upon AE. Additionally, the methodologic quality of the studies was generally strong. Taken collectively, results of this systematic review suggest that RE is a promising supportive care intervention that results in meaningful improvements in clinically relevant physiologic and QOL outcomes during and following cancer treatment.

Improvements in detection and treatment strategies have resulted in dramatic increases in survival rates across a variety of different types of cancer. It is well established; however, that many cancer treatments are accompanied by negative side effects such as fatigue, pain, unfavorable changes in body weight/composition, and reduced physical functioning and quality of life (QOL). These adverse effects can persist for a considerable amount of time following the cessation of treatment. Thus, many cancer patients and survivors endure lingering adverse effects of commonly employed treatment strategies as a trade-off for more effective cancer control and increased longevity.[1] Emerging evidence also suggests that cancer survivors are at increased risk for developing chronic diseases such as heart disease, diabetes, and osteoporosis.[2] Consequently, developing effective disease prevention and health promotion strategies for cancer survivors is an important clinical and public health consideration.

There is mounting empirical evidence that exercise is an efficacious lifestyle intervention that results in meaningful improvements in a variety of health and QOL outcomes during and following cancer treatment.[1,3-5] Although recent exercise training guidelines[6] propose that aerobic-, resistance-, and flexibility-exercise are safe modes of physical activity for cancer survivors, a majority of the existing exercise-cancer research has focused upon the effects of aerobic forms of exercise.[4,7] Despite the prevailing focus upon the efficacy of AE, there is

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emerging evidence of the benefits of other forms of exercise interventions. For example, resistance exercise (RE) can be particularly effective for offsetting the deleterious effects that common cancer treatments, such as chemotherapy and hormone therapy, have upon clinically relevant physiologic (muscle mass, muscle strength, bone density, and body composition) and QOL outcomes (fatigue, pain) in cancer patients and survivors.

Nonetheless, when compared with AE, considerably less empirical evidence addressing the benefits of RE is evident in the extant literature. The limited available evidence suggests that RE represents a particularly promising adjuvant exercise intervention that may yield a myriad of benefits across the cancer control continuum.[1,8,9] Therefore, the purpose of the present article is to provide a systematic review of the efficacy of RE as a supportive care intervention for improving clinically relevant physiologic and QOL outcomes during and following cancer treatment. Given that prior reviews addressing the RE-cancer relationship have focused on select cancer populations (ie, breast cancer [BRCA][10]) and phases of the cancer continuum (ie, survivorship[11]), knowledge of the potential efficacy of RE interventions across the cancer continuum for patients and survivors of various forms of cancer remains limited. It is also important to acknowledge that prior reviews included studies that combined RE with AE thereby limiting the ability to adequately isolate the benefits of RE alone from the potentially synergistic effects of resistance and AE for cancer patients and survivors. Thus, the present review represents the first attempt to systematically evaluate the effects of RE alone. The primary objectives of this review are to: systematically review the effects of RE interventions upon clinically relevant physiologic and QOL outcomes during and following cancer treatment; calculate the magnitude of the change (Cohen's *d* effect sizes) in these outcomes following RE; summarize the recruitment, retention, and adherence rates to the RE interventions; and provide a quantitative evaluation of the overall methodologic quality of the RE studies.

Methods

Inclusion criteria

The only studies included in the review were those that examined a RE intervention, in isolation, among cancer patients or survivors. For the purposes of this review, RE was defined as regular participation in a structured, repetitive strength training program over an extended period of time with the goal of improving health or fitness outcomes. Studies targeting individuals diagnosed with cancer that were actively undergoing cancer treatment or had successful cancer treatment with curative intent were included irrespective of gender, tumor type, or type of cancer treatment. All study designs were included. However, in order to isolate the independent effects of RE, studies that used RE in combination with other exercise (ie, AE or yoga), lifestyle, or behavioral interventions (ie, diet or psychosocial counseling) were excluded from the review.

Study selection and data abstraction

Studies included in the systematic review were obtained through computer and manual searches following the Preferred Reporting Items for Systematic Reviews (PRISMA).[12] We conducted an original search in September 2011 of titles and abstracts in the PubMed and MEDLINE databases. We conducted this search again in August 2012, during a revision of the manuscript, to ensure inclusion of any additional articles that were published in the interim. Searches were conducted of English language articles that addressed human participants only. Search terms including resistance exercise (resistance exercise, strength training, weight training, and rehabilitation) and cancer (cancer, oncology, tumor, malignancy, neoplasm) were entered in different combinations. Consistent with PRISMA guidelines[12] the flow diagram shown in the Figure summarizes the results of the computerized database search. Manual searches were also conducted using the reference lists of other narrative and meta-analytic reviews of the exercise-cancer literature[5-7,13-15] as well as the reference lists of each study included in the present review. Data extraction were performed by 2 reviewers (BCF, MJG) and any instances of disagreement regarding a study's inclusion or exclusion criteria was resolved by consensus of all authors.

Data synthesis

Results from the RE studies included in the present review are synthesized using both qualitative summary and quantitative effect-size calculation. Qualitative synthesis was conducted via narrative review of each study's design, RE intervention characteristics, and primary outcome findings. Quantitative synthesis was conducted using Cohen's *d* effect sizes[16] which were obtained directly from the studies themselves when reported or calculated using statistical information provided in the study. Cohen's *d* effect sizes are classified as: small, 0.20; moderate, 0.50; and large, 0.80. Because 4 of the 15 studies were uncontrolled trials that did not include a control or comparison group in the experimental design, we focused upon the magnitude of pre- to post-intervention change in the outcomes observed following participation in the RE intervention. Therefore, effect sizes were calculated by taking the difference of the mean values obtained at baseline and postintervention follow-up assess-

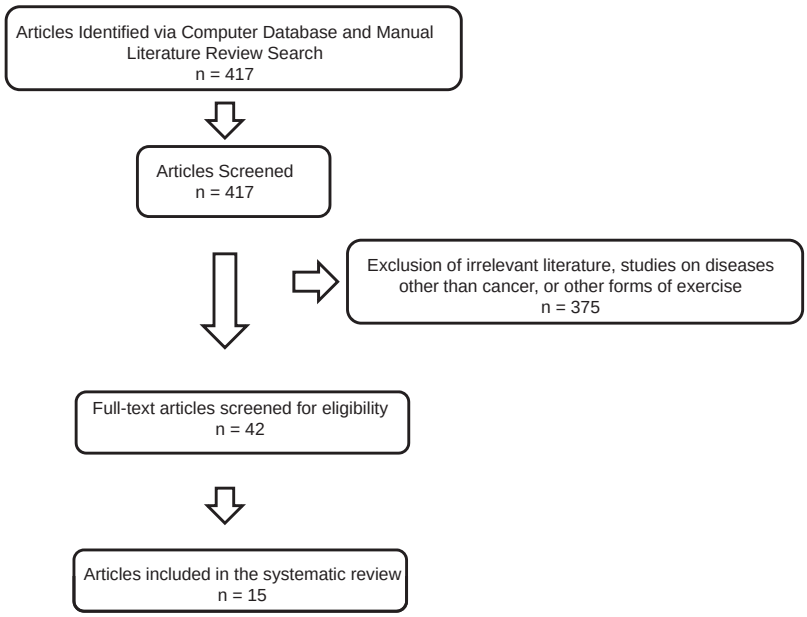

FIGURE Study search flow diagram.

ments and dividing by the pooled standard deviation. It should be noted that negative effect-size values can reflect favorable changes in select outcomes (eg, declines in ratings of fatigue or decreases in duration needed to complete timed functional performance tasks). However, the sign of effect sizes was set so that only positive values indicate improvement in that respective outcome. Thus, positive effect-size values indicate that RE resulted in improvement in an outcome whereas negative effect sizes reflect unfavorable changes in an outcome.

Methodologic quality assessment

The methodologic quality of each study was assessed by 2 independent reviewers (BCF, ARL) using 7 quality indicators from The Delphi List, a consensus criteria list for quality assessment in randomized control trials.[17] The following quality indicators were used to assess each study's methodology:

- Was randomization performed?
- Was treatment allocation concealed?
- Were groups similar at baseline on key outcome measures?
- Were participant eligibility criteria specified?
- Were outcome assessments obtained by blinded evaluators?
- Were descriptive statistics for primary outcome measures reported?
- Were intention-to-treat analyses conducted?

Each item was rated as "yes" or "no" based upon the methods reported in each study. Studies that did not provide methodological information directly addressing a particular quality indicator were recorded as not having met that indicator in the evaluation. Given there is presently no validated summary scoring system for the Delphi list, the number of indicators met by each of the studies included in the systematic review was tabulated. In addition to the tabulation, comparisons of percentages of quality indicators met by studies examining RE during and following treatment and comparisons of percentages of quality indicators met between randomized trials and non-randomized studies were also evaluated.

Results

Study characteristics

A summary of the study design as well as the participant and intervention characteristics is provided in Table 1. A total of 15 studies involving 1,077 participants met the inclusion criteria. Of these, 6 studies addressed RE interventions during treatment.[18-23] Of the studies examining the effects of RE during active cancer treatment, 4 were conducted during androgen deprivation therapy,[19-22] 1 during chemotherapy,[18] and 2 during radiation therapy.[21,23] The remaining 9 studies focused on RE in participants following the completion of active cancer treatment with curative intent. Studies examined samples of individuals diagnosed with BRCA (n = 6),[18,24-28] prostate cancer (PC; n = 4),[19-22] head and neck cancer (HNC; n = 3),[23,29,30] lung cancer (LC; n = 1),[31] and 1 study examined a mixed sample comprised of individuals

TABLE 1 Study characteristics

Study	Design	Sample size	Diagnosis, phase	Intervention characteristics (duration, supervision; sets, reps, load)	Overall findings
Schmitz[24,33]	CORCT	85	BRCA, survivors	6 mo of supervised RE; 3 sets of 8-10 reps at 70%-80% 1 RM	Improvements in muscular strength and endurance, body composition, and quality of life following RE
Courneya[18]	MCRCT	242	BRCA, patients	Supervised RE for duration of chemotherapy; 2 sets of 8-12 reps at 60%-70% 1 RM	Improvements in muscular strength, body composition, and select patient-reported outcomes following RE
Schmitz[25]	RCT	155	BRCA, survivors	12 mo of supervised and unsupervised RE; 3 sets of 10 reps at a symptom limited load	Improvements in muscular strength. Small non-significant changes in body composition
Winters-Stone[26,34]	RCT	106	BRCA, survivors	12 mo of supervised and unsupervised RE; 3 sets of 8-12 reps at 60%-80% 1 RM	Improvements in muscular strength and physical function. Small, non-significant changes in body composition, bone mineral density, and fatigue
Musanti[28]	RCT	42	BRCA, survivors	12 wk of unsupervised RE; 1 set of 12 reps at an RPE 4-8	Improvements in muscular strength and self-esteem. Small, non-significant changes in aerobic fitness, body composition, fatigue, and de pression
Schmidt[27]	RCT	38	BRCA, patients	6 mo of supervised RE; 1 set of 20 reps at 50% 1 RM	Improvements in fatigue and quality of life
Segal[19]	MCRCT	155	PC, patients	12 wk of supervised RE; 3 sets of 8-12 reps at 70%-80% 1 RM	Improvements in muscular endurance, fatigue, and quality of life
Galvao[20]	NRT	10	PC, patients	20 wk of supervised RE; 3 sets of 8-12 reps at 80% 1 RM	Improvements in muscular strength, Muscular endurance, and physical function. Small, non-significant changes in body composition and bone mineral density
Segal[21]	RCT	121	PC, patients	24 wk of supervised RE; 2 sets of 8-12 reps at 60%-70% 1 RM	Improvements in muscular strength. Small, non-significant changes in body composition, disability, and quality of life
Hansen[22]	NRT	10	PC, patients	12 wk of supervised RE; 3 sets of eccentric RE at	Improvements in muscular strength and physical self-determined RPE function. Small, non-significant changes in body composition and fatigue
McNeely[29]	RCT	20	HNC, survivors	12 wk of supervised RE; 2 sets of 15-20 reps at self-determined RPE	Improvements in patient-reported pain, function, and disability
McNeely[30]	RCT	52	HNC, survivors	12 wk of supervised RE; 2 sets of 10-15 reps at 60%-70% 1 RM	Improvements in muscular strength, muscular endurance, and patient-reported pain and disability
Rogers[23]	RCT	15	HNC, patients	12 wk of supervised and unsupervised RE; 1 set of 10 reps with light, moderate, heavy resistance bands	Small improvements in muscular strength, physical function, body composition, and patient-reported outcomes
Peddle-McIntyre[31]	RCT	17	LC, survivors	10 wk of supervised RE 3 sets of 12 reps at 60%-85% 1 RM	Improvements in muscular strength, muscular endurance, physical function, and quality of life. Small change in body compos ition
Katz[32]	NRT	10	Mixed, survivors	20 wk of supervised and unsupervised RE; 2-3 sets of 10 reps at symptom limited load	Improvements in muscular strength, physical function. Small, non-significant change in body composition and quality of life

Abbreviations: BRCA, breast cancer; CORCT, cross-over randomized controlled trial; HNC, head and neck cancer; LC, lung cancer; MCRCT, multicenter randomized controlled trial; NRT, non-randomized trial; PC, prostate cancer; RCT, randomized controlled trial; RE, resistance exercise; RPE, rating of perceived exertion.

TABLE 2 Description of the feasibility outcomes from the resistance exercise interventions

Study	Recruitment rate	Retention rate	Adherence % rate	Adverse events
Schmitz[24,33]	64%	86%[a]	80%	4 mild/moderate events involving muscle/joint strains
Courneya[18]	33%	92%[b]	68%	No events reported
Schmitz[25]	9%	86%	79%	No events reported
Winters-Stone[26,34]	43%	67%[a]	76%	No events reported
Musanti[28]	13%	88%	91%	No events reported
Schmidt[27]	63%	86%	NA	No events reported
Segal[19]	31%	86%	79%	No events reported
Galvao[20]	79%	91%	NA	No events reported
Segal[21]	37%	83%	88%	1 mild/moderate event involving chest pain after a RE session
Hansen[22]	NA	63%	100%	No events reported
McNeely[29]	80%	85%	93%	1 mild/moderate event involving nausea after a RE session
McNeely[30]	47%	88%	95%	1 mild/moderate event involving a back injury during RE
Rogers[23]	16%	87%	59%[c]	No events reported
Peddle-McIntyre[31]	43%	79%	77%	3 mild/moderate events involving joint/muscle strains
Katz[32]	83%	100%	91%	2 mild/moderate events involving development of cellulitic infection

NA, not available.
[a] average retention reported at 6-month and 12-month follow-up; [b] average retention reported at midpoint and posttreatment follow-up; [c] value represents average adherence reported during supervised and unsupervised phases of the intervention.

diagnosed with various types of cancer (ie, bladder, cervical, endometrial, uterine, melanoma).[32] Sample sizes in the studies ranged from 10 to 242 participants. Eleven studies implemented center-based, supervised, progressive RE interventions. Four studies implemented RE interventions involving a combination of supervised and unsupervised RE.[23,25,26,32] The RE intervention characteristics included training loads ranging from 25% to 80% of 1 repetition maximum (1RM), sets ranging from 1-3/exercise, and the intervention duration ranged from 12 weeks to 12 months.

Recruitment, retention, and adherence rates

A summary of the recruitment, retention, and adherence rates is provided in Table 2. With regard to participant recruitment, an average of 44% (range, 9%-83%) of individuals that were either determined eligible or screened for inclusion participated in the studies. Calculation of retention values revealed that 85% (range, 67%-100%) of participants that initiated the study completed postintervention follow-up assessments. Adherence to supervised RE sessions was 84% (range, 68%-100%).

Methodologic quality assessment

Overall, the studies met an average of 74% of the Delphi study quality indicators (range, 43%-100%) included in the methodologic assessment. A summary of the Delphi methodologic quality indicators met in each study is provided in Table 3. Notable methodological strengths were that all studies specified eligibility criteria and provided descriptive statistics for key outcomes variables and 73% of the studies implemented random assignment of participants. Areas of methodological weakness were only 47% of the studies implemented intention-to-treat analyses or conducted blinded-outcome assessments. On average, studies examining RE during active cancer treatment met 76% of the quality indicators while studies focusing on participants following treatment met 72% of the indicators. Finally, randomized studies met 83% of the quality indicators while nonrandomized studies met 47% of the indicators.

Summary of the exercise interventions

A brief summary of each study's sample, outcome assessments, and select feasibility measures (recruitment, reten-

TABLE 3 Methodologic quality indicators from the Delphi consensus criteria list[17]

Study/Authors	Randomized	Allocation concealed	Key outcomes similar at baseline	Eligibility criteria specified	Single blind	Key descriptive statistics provided	Intent to treat analysis
Schmitz[24,33]	Yes	Yes	Yes	Yes	Yes	Yes	No
Courneya[18]	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Schmitz[25]	Yes	Yes	Yes	Yes	Yes	Yes	No
Winters-Stone[26,34]	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Musanti[28]	Yes	Yes	No	Yes	No	Yes	Yes
Schmidt[27]	Yes	No	No	Yes	No	Yes	No
Segal[19]	Yes	No	Yes	Yes	Yes	Yes	Yes
Galvao[20]	No	No	Yes	Yes	No	Yes	No
Segal[21]	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Hansen[22]	No	Yes	No	Yes	No	Yes	No
McNeely[29]	Yes	No	Yes	Yes	No	Yes	No
McNeely[30]	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Rogers[23]	Yes	Yes	Yes	Yes	No	Yes	Yes
Peddle-McIntyre[31]	No	No	Yes	Yes	No	Yes	Yes
Katz[32]	No	No	Yes	Yes	No	Yes	No

tion, and adherence rates), and the effect sizes accompanying changes in the physiologic and QOL outcomes, organized by cancer site, is provided in the following section of the review. A summary of the effect size changes accompanying the outcomes in each trial is provided in Table 4.

RE interventions in BRCA patients and survivors. In a randomized, controlled cross-over design trial, Schmitz et al compared the effects of a 6-month progressive RE intervention with those of a delayed treatment control group in a sample of 85 BRCA survivors.[24] Assessments of body composition were obtained at baseline as well as at the 6- and 12-month follow-ups. Muscular strength and QOL were assessed at baseline and at the 6-month follow-up. The QOL outcomes were reported in a separate publication.[33] Of the 132 eligible participants for the study, 85 women (64%) were recruited into the study and completed the baseline assessments. Approximately 91% of the women randomized into the RE intervention completed the 6-month follow-up assessment and 80% completed the 12-month follow-up assessment. Average participant adherence, measured via attendance at the supervised RE sessions, was 80% across the 6-month RE intervention. There were 4 mild to moderate adverse events related to the RE intervention involving muscle and/or joint strains to the back, legs, and wrist. No serious adverse events related to the RE intervention were reported. The RE intervention yielded improvements in muscular strength (leg press, $d = 1.70$ at 6 months and chest press, $d = 2.45$ at 6 months), body fat percentage ($d = 0.87$ at 6 months; $d = 1.69$ at 12 months), lean body mass ($d = 1.14$ at 6 months; $d = 1.78$ at 12 months), and global ($d = 0.34$), physical ($d = 0.34$), and psychosocial ($d = 0.31$) indices of QOL. Additionally, RE was not associated with an increase in arm swelling or self-reported lymphedema symptoms.

Courneya et al[18] conducted a multicenter randomized controlled trial comparing the effects of RE, AE, and usual care treatment approaches in a sample of 242 BRCA patients undergoing adjuvant chemotherapy. Assessments of muscular strength, aerobic capacity, and multiple indices of body composition (ie, body fat percentage, lean body mass, and fat mass) were obtained at baseline and within 4 weeks following the completion of chemotherapy. Assessments of self-reported outcomes including cancer-specific QOL (FACT-Anemia), fatigue, self-esteem, depression, and anxiety were obtained at baseline, midpoint of chemotherapy, and within 4 weeks of chemotherapy completion. A total of 242 of 736 eligible participants (33%) were recruited into the trial. Of the 82 participants randomly assigned to the RE intervention, approximately 92% completed both the midpoint and posttreatment follow-up assessments. Additionally, women in the RE intervention completed 68% of their assigned supervised RE sessions during the trial. No adverse events related to the RE intervention were reported. Results revealed that RE resulted in moderate to large statistically significant improvements

in leg press strength ($d = 0.69$) and chest press strength ($d = 0.98$). Small improvements in lean body mass ($d = 0.21$) and fat mass ($d = 0.06$) were observed and no change in body fat percentage ($d = 0.06$) was documented. Small changes in self-esteem (midpoint, $d = -0.06$; posttreatment, $d = 0.30$), FACT-Anemia (midpoint, $d = 0.02$; posttreatment, $d = 0.36$), fatigue (midpoint, $d = 0.11$ and posttreatment, $d = 0.20$) depression (midpoint, $d = 0.12$; posttreatment, $d = 0.33$), and anxiety (midpoint, $d = 0.41$; posttreatment, $d = 0.45$) emerged with exposure to the RE intervention. It is also important to acknowledge that women randomized to the RE intervention demonstrated superior chemotherapy completion rates relative to both the AE and usual care treatment groups. Furthermore, RE was not associated with an increase in arm swelling or self-reported lymphedema symptoms.

In a randomized controlled trial, Schmitz et al[25] compared the effects of a 1-year RE intervention with those of a no-exercise control group in 154 BRCA survivors at risk for lymphedema. Assessments of muscular strength and multiple measures of body composition (body fat percentage, lean body mass, and fat mass) were obtained at baseline and 1-year follow-up assessments. A total of 154 of 1802 screened, eligible participants (9%) were randomized into the trial. Of the 77 participants randomly assigned to the RE intervention, approximately 86% completed the 1-year follow-up assessment. Adherence, calculated as attendance at prescribed sessions, was 79% in the RE intervention. No adverse events related to the RE intervention were reported. Results revealed that RE resulted in large, statistically significant improvements in leg press strength ($d = 0.88$) and chest press strength ($d = 1.04$). Conversely, small to negligible improvements in lean body mass ($d = 0.08$), fat mass ($d = 0.11$), and body fat percentage ($d = 0.06$) were observed following RE. Importantly, women participating in the progressive RE intervention did not experience an increase in risk of onset of lymphedema or self-reported lymphedema symptoms relative to the no-exercise control group.

In a single-blinded, randomized controlled trial, Winters-Stone et al[26] examined the effects of a 12-month RE intervention with those of a placebo exercise intervention involving stretching and relaxation techniques within a sample of 106 older, postmenopausal BRCA survivors. Assessments of muscular strength, grip strength, physical function, and QOL were obtained at baseline as well as at 6- and 12-month follow-up. Body composition and bone mineral density were assessed at baseline and 6- and 12-month follow-up. However, descriptive statistics for all outcomes were only provided for the baseline and 12-month assessments. The effects of the RE intervention on the body composition and bone mineral density outcomes were reported in a separate publication.[34] Of the 246 eligible participants, 106 women (43%) were recruited into the study and completed the baseline assessments. A total of 64% of the women randomized into the RE intervention completed the 6-month follow-up assessment and 69% completed the 12-month follow-up assessment. Average participant adherence to the supervised RE sessions was 76% across the 12-month RE intervention while adherence to the unsupervised, home-based RE sessions was 23%. No serious adverse events related to the RE intervention were reported. The RE intervention resulted in improvements in muscular strength (leg press, $d = 0.68$ and bench press, $d = 0.50$). Although not statistically significant, improvements in performance (chair stand, $d = 0.68$) and self-reported physical function ($d = 0.25$) emerged following RE. No improvements in fatigue ($d = -0.04$) accompanied RE. Furthermore, no significant differences emerged for the body composition (lean body mass, $d = 0.09$; body fat percentage, $d = 0.00$) and bone mineral density measures (hip, $d = -0.03$; spine, $d = 0.03$; trochanter, $d = -0.03$). However, analyses of these outcomes did reveal that women in the RE demonstrated superior preservation of bone mineral density and lean body mass relative to the stretching control group across the 12-month trial. Additionally, RE was not associated with an increase in arm swelling or self-reported lymphedema symptoms.

Musanti[28] conducted a 4-arm randomized controlled trial comparing the effects of RE alone with AE alone, flexibility training, and a combination of RE and AE in a sample of 42 BRCA survivors. Assessments of muscular strength and endurance, aerobic capacity, body composition, physical self-esteem, and select psychological and QOL outcomes were assessed prior to and following the 12-week home-based exercise interventions. A total of 314 BRCA survivors were screened for participation and 42 women (13%) were recruited into the study and completed the baseline assessments. A total of 88% of the women randomized into the study completed the follow-up assessments. Average participant adherence within the RE intervention was 91%. No serious adverse events related to the RE intervention were reported. The RE intervention resulted in large improvements in muscular strength (chest press, $d = 1.06$; bicep curl, $d = 1.08$). Small effect-size improvements were observed for aerobic fitness ($d = 0.23$) and fat mass ($d = 0.23$). The RE intervention also yielded moderate to large effect-size improvements in the various physical self-esteem domains ($d = 0.70$-1.90). No significant improvements in fatigue, depression, or anxiety were observed following the RE.

TABLE 4 Effect sizes for the physiologic and quality of life outcomes

Study	Design, diagnosis, phase	Effect sizes, physiologic outcomes	Effect sizes, quality of life outcomes
Schmitz[24,33]	RCCT, BRCA, survivors	Leg press strength, 1.70 Chest press strength, 2.45 Body fat percentage: 6 mo, .87; 12 mo, 1.78	CARES SF Global, .34 Physical, .34 Psychosocial, .31
Courneya[18]	MCRCT, BRCA, patients	Leg press strength, .69 Chest press strength, .98 Lean body mass, .21 Fat mass, .06 Body fat percentage, .06	FACT-A: mid, .02 ; post, .36 Self-esteem: mid, –.06; post, .30 Fatigue: mid, .11; post, .20 Depression: mid, .12; post, .33 Anxiety: mid, .41; post, .45
Schmitz[25]	RCT, BRCA, survivors	Leg press strength, .88 Chest press strength, 1.04 Lean body mass, .08 Fat mass, .11 Body fat percentage, .06	NA
Winters-Stone[26,34]	RCT, BRCA, survivors	Leg press strength, .68 Chest press strength, .50 Chair stand, .68 Lean body mass, .09 Body fat percentage, .00 Bone mineral density: Hip, –.03 Spine, .03 Trochanter, –.03	Physical function, .25 Fatigue, –.04
Musanti[28]	RCT, BRCA, survivors	Chest press strength, 1.06 Bicep curl strength, 1.08 Aerobic capacity, .23 Fat mass, .23	Physical self-esteem: PCS, 1.90; PSS, 1.60; ABS, 2.20; PSE, 1.60; GSE, .70
Schmidt[27]	RCT, BRCA, patients	NA	QOL: 3 mo, .44; 6 mo, 1.14 Fatigue: 3 mo, .82; 6 mo, .98
Segal[19]	MCRCT, PC, patients	NA	QOL: FACT-F, .52; FACT-P, .55
Galvao[20]	SANRT, PC, patients	Lower body strength, 1.56 Upper body strength, 1.82 Lower body endurance, 2.90 Upper body endurance, 2.80 Lean body Mass, –.03 Fat Mass, .09 Body fat percentage, .01 Bone mineral Density, .03 Physical function performance: 6-min walk, .82 400 m walk, .29 Stair climb, .21 Chair stand, 1.29 Balance, 1.08	NA
Segal[21]	RCT, PC, patients	Upper body strength, .90 Lower body strength, .74 Aerobic capacity, .13 Body fat percentage, .06	FACT-F: 3 mo, .17; 12 mo, –.26 FACT-P: 3 mo, –.29; 12 mo, .04 FACT-G: 3 mo, .17; 12 mo, .32
Hansen[22]	SANRT, PC, patients	Muscular strength, .57 Physical function performance: 6-min walk, .41 Up and go, .45 Muscle volume, .11	Fatigue, .15
McNeely[29]	RCT, HNC, survivors	NA	SPADI Pain, .79 Self-reported ROM, 1.43; Overall function, .62

TABLE 4 Effect sizes for the physiologic and quality of life outcomes (*continued*)

Study	Design, diagnosis, phase	Effect sizes, physiologic outcomes	Effect sizes, quality of life outcomes
Rogers[23]	RCT, HNC, patients	Muscular strength: 6 wk, .11; 12 wk, .15 Grip strength: 6 wk, –.17; 12 wk, –.10 Physical function: 6 wk, .51; 12 wk, .51 Lean body mass: 6 wk, –.01; 12 wk, –.58 Body mass index: 6 wk, .71; 12 wk, .21	FACT-G: 6 wk, –.41; 12 wk, –.19 FACT HNC: 6 wk, –.84; 12 wk, –.35 Fatigue: 6 wk; –.72, 12 wk, –.25
Peddle-McIntyre[31]	RCT, LC, survivors	Leg press strength, 1.00 Chest press strength, .96 Leg press endurance, 1.49 Chest press endurance, 1.55 Arm curl endurance, 1.49 Physical function performance: 6 min walk, .90 Chair stand, 1.21 Up and go, .58 Lean body mass, –.01 Body fat percentage, .00	SF-36 PF, .25 RP, .44 BP, .37 GH, .20 VT, .28 SF, .13 RE, .22 MH, .01 PHC, .36 MHC, –.10 FACT-G, .12 FACT-L, .07 Fatigue, .08
Katz[32]	SANRT, mixed, survivors	Chest press strength: 2 mo, .28; 6 mo, .64 Leg press strength: 2 mo, .24; 6 mo, .58 Physical function performance 6 min walk: 2 mo, .21; 6 mo, .64 50 foot walk: 2 mo, .47; 6 mo, .73 Single leg stand: 2 mo, .33; 6 mo, .00 Lean body mass: 2 mo, .07; 6 mo, .05 Body fat percentage: 2 mo, –.13; 6 mo, .02	NA

Abbreviations: ABS, attractive body subdomain; BP, bodily pain; BRCA, breast cancer; CARES SF, cancer rehabilitation evaluation system-short form; FACT-A, functional assessment of cancer therapy-anemia; FACT-F, functional assessment of cancer treatment-fatigue; FACT-G, functional assessment of cancer treatment-general; FACT-HNC, functional assessment of cancer treatment-head and neck cancer; FACT-L, functional assessment of cancer treatment-lung; FACT-P, functional assessment of cancer treatment-prostate; GH, general health; GSE, global self-esteem; HNC, head and neck cancer; LC, lung cancer; MCRCT, multicenter randomized controlled trial; MH, mental health; MHC, mental health composite; NA, not available; PC, prostate cancer; PCS, physical condition subdomain; PF, physical functioning; PHC, physical health composite; PSE, physical self-esteem; PSS, physical strength subdomain; QOL, quality of life; RCCT, randomized controlled crossover trial; RCT, randomized controlled trial; RE, role-emotional; ROM, range of motion; RP, role-physical; SANRT, single arm nonrandomized trial; SF, social functioning; SPADI, shoulder pain and disability index; VT, vitality.

However, those participants reporting clinically significant elevations at baseline demonstrated large improvements in fatigue (d = 1.50) and depression (d = 0.87) following the RE intervention.

In a 2-arm randomized trial, Schmidt et al[27] compared the effects of a 6-month gentle supervised RE intervention (low intensity, volume, and load) with those of an exercise intervention involving chair or floor-based exercise in a sample of 38 BRCA survivors. Assessments of muscular strength, aerobic endurance, and QOL were obtained at baseline, 3- and 6-month follow-up. Of 60 participants screened for the study, 38 women (63%) were enrolled and completed the baseline assessments. Approximately 86% of the women randomized into the RE intervention completed the 6-month follow-up assessment. Adherence to the RE intervention was not reported. No adverse events related to the RE intervention were reported. No descriptive statistics were provided for the changes in muscular strength or aerobic capacity. However, the RE intervention did yield improvements in QOL (3 months, d = 0.44; 6 months, d = 1.14) and fatigue (3 months, d = 0.82; 6 months, d = 0.98).

Taken collectively, results from these 6 randomized controlled trials provide strong evidence of the feasibility

and efficacy of RE exercise interventions for BRCA patients receiving chemotherapy and BRCA survivors who have completed active cancer treatment. Findings revealed that RE results in moderate to large improvements in muscular strength and small to moderate improvements in select dimensions of QOL. The effects of RE on body composition measures in BRCA patients/survivors was quite heterogeneous ranging from essentially negligible changes[6,18] to large effect-size improvements[4] across studies. It is very important to acknowledge, however, that each of the trials demonstrated that RE is a safe, well-tolerated exercise intervention. Most notably, RE did not increase the risk of lymphedema onset nor exacerbate arm swelling or self-reported lymphedema symptoms. Therefore, although the number of trials examining RE in BRCA patients/survivors still remains relatively limited, the present findings provide empirical support for the position that RE is a safe form of exercise for BRCA patients and survivors that results in statistically significant and clinically meaningful improvements in relevant physiologic and QOL outcomes.

RE interventions in prostate cancer patients undergoing active treatment. To date, 4 studies have examined the effects of RE alone in PC patients. Each study was conducted on men undergoing active treatment with 3 studies focusing on men undergoing androgen deprivation therapy (ADT)[19,20,22] and one trial examining men undergoing radiation therapy.[21]

In a 2-center randomized controlled trial, Segal et al[19] compared the effects of a 12-week center-based, supervised resistance exercise intervention with those of a wait-list control group in a sample of 155 PC patients on ADT. Assessments of muscular endurance and body composition, fatigue (FACT-F), and cancer-specific QOL (FACT-P) were obtained at baseline and 12-week follow-up. A total of 155 of 507 eligible patients (31%) were randomized into the trial. Approximately 90% of the participants in the RE intervention completed the 12-week follow-up assessment and average attendance to the prescribed RE sessions was 79% during the 12-week intervention. No adverse events related to the RE intervention were reported. RE resulted in significant increases in upper and lower body muscular endurance. However, information necessary to calculate effect sizes for improvements in muscular endurance were not provided. No significant changes in body composition were observed. The descriptive statistics necessary to calculate the effect sizes for body composition were not provided. However, RE resulted in statistically significant, moderate-in-magnitude improvements in fatigue (d = 0.52) and cancer-specific QOL (d = 0.55).

Galvao et al[20] conducted a single-arm, uncontrolled trial examining the effects of a center-based, supervised 20-week progressive RE intervention in a sample of 10 men undergoing ADT. Assessments of muscular strength, muscular endurance, body composition, bone mineral density, and physical function (6 min walk, 400m walk, balance, stair climb, and chair stand) were obtained at baseline and 20-week follow-up. A total of 11 of 14 eligible men (79%) participated in the study. Ten participants (91%) completed the 20-week follow-up assessment. Adherence to the prescribed RE sessions was not reported. No adverse events related to the RE intervention were reported. The RE intervention yielded improvements in upper body (d = 1.82) and lower body muscular strength (d = 1.56) and upper body (d = 2.80) and lower body muscular endurance (d = 2.90). Conversely, the RE intervention had negligible effects upon lean body mass (d = 0.03), fat mass (d = 0.09), body fat percentage (d = 0.01), and bone mineral density (d = 0.03). RE also resulted in improvements in the 6-min walk (d = 0.82), 400 m walk (d = 0.29), stair climb (d = 0.21), chair stand (d = 1.29), and balance (d = 1.08) performance. It is also important to acknowledge that ancillary analyses of endocrine and immune responses during the trial demonstrated that serum testosterone and prostate specific antigen levels did not increase following the progressive RE intervention. Thus, these findings indicate that a progressive, intensive RE intervention does not undermine the therapeutic androgen ablation effect of ADT.

Segal et al[21] conducted a randomized controlled trial comparing the effects of 24-week, center-based, supervised RE, AE, and usual care interventions in a sample of 121 PC patients receiving radiation therapy and ADT (approximately 60% of the sample). Assessments of muscular strength, aerobic capacity, and body composition (body fat percentage) were obtained at baseline and 6-month follow-up. Assessments of cancer-specific QOL (FACT-P) and fatigue (FACT-F) were obtained at baseline and 3-month and 6-month follow-up. A total of 121 of 325 eligible patients (37%) participated in the study. Approximately 83% of men randomized into the RE intervention completed the 3- and 6-month follow-up assessments and average adherence to the RE intervention was 88%. There was one mild to moderate adverse event related to the RE intervention involving chest pain following exercise. However, no serious adverse events related to the RE intervention were reported. The RE intervention produced increases in upper body (d = 0.90) and lower body (d = 0.74) muscular strength. However, resistance exercise resulted in negligible changes in aerobic capacity (d = 0.13), body fat percentage (d = 0.06), or physical disability (3 months, d = 0.16; 12 months, d = 0.26). Resistance exercise also resulted in small effect-size

changes in cancer-specific (3 months, $d = -0.29$; 12 months, $d = 0.04$) and general QOL (3 months, $d = 0.17$; 12 months, $d = 0.32$).

Hansen et al[22] conducted a single-arm uncontrolled trial examining the effects of a center-based, supervised 12-week RE intervention in a sample of 10 men on (n = 5) or off (n = 5) ADT. Assessments of muscular strength, body composition (muscle volume), physical function (6 min walk and timed up and go performance), and fatigue (FACT-F) were obtained at baseline and 12-week follow-up. The total number of eligible men prescreened for inclusion in the study was not reported. Of the 16 men included in the study, 10 (63%) completed the 12-week follow-up assessment. Adherence to the supervised exercise sessions among the 10 participants that completed the study was 100%. No adverse events related to the RE intervention were reported. The RE intervention resulted in statistically significant improvements in muscular strength ($d = 0.57$), 6-min walk performance ($d = 0.41$), and timed up and go performance ($d = 0.45$). However, only negligible changes in muscle volume ($d = 0.11$) and fatigue ($d = 0.15$) were observed following RE.

In summary, findings from the 4 studies examining RE interventions in PC patients undergoing ADT and/or radiation therapy suggest that RE is a safe, feasible adjuvant lifestyle intervention approach that results in significant, clinically meaningful improvements in physiologic and QOL outcomes. Given the well-established adverse effects that accompanying ADT (declines in muscular strength, lean body mass, physical function) and radiation therapy (fatigue), the beneficial effects of RE upon these outcomes provides support for the efficacy of RE as a complementary therapy to offset the considerable morbidity associated with these common therapeutic approaches for PC patients.

RE in head and neck cancer survivors. A total of 3 studies have examined the effects of RE interventions during and following treatment for HNC. Of these, 2 studies were conducted on men diagnosed with squamous cell carcinoma of the head or neck who had undergone surgical resection and were experiencing medically documented shoulder dysfunction resulting from the surgical procedure[29,30] and one study addressed a sample of men and women undergoing radiation therapy for HNC.[23]

McNeely et al[29] conducted a 2-arm, randomized controlled pilot trial comparing the effects of a progressive RE intervention with those of a usual-care range of motion (ROM) exercise/stretching therapy program in 20 HNC patients. Assessments of self-reported shoulder function, pain, and disability (SPADI),[35] cancer-specific QOL (FACT-H&N), and shoulder joint ROM were obtained at baseline and 12-week follow-up assessments during the pilot trial. In all, 20 of 25 (80%) eligible patients were randomized into the study. Of these, 8 of the 10 participants (80%) randomized to the RE intervention completed the 12-week follow-up assessment and adherence to prescribed RE sessions was 93%. There was one mild to moderate adverse event related to the RE intervention involving nausea following exercise. However, no serious adverse events related to the RE intervention were reported. Results revealed significant improvements in the SPADI total score ($d = 0.62$), SPADI pain score ($d = 0.79$), and external rotation ROM ($d = 1.43$) of the shoulder joint following RE. The RE intervention also resulted in a nonsignificant, moderate-in-magnitude decrease in the SPADI disability score ($d = 0.47$).

In a single-blind, 2-arm randomized controlled trial, McNeely et al[30] compared a 12-week progressive RE with a standard-of-care physical therapy regimen in a sample of 52 HNC patients. Assessments of muscular strength, SPADI, shoulder joint range of motion, and cancer-specific QOL (FACT-Anemia and the Neck Dissection Impairment Index) were assessed at baseline and 12-week follow-up. A total of 52 of 110 eligible patients (47%) were randomized into the trial. Twenty-two of the 25 patients (88%) randomized into the RE intervention completed the 12-week follow-up assessment and adherence to prescribed RE sessions was 95%. There was one mild to moderate adverse event related to the RE intervention involving a soft tissue injury to the back during exercise. However, no serious adverse events related to the RE intervention were reported. Results revealed the RE intervention resulted in significant improvements in muscular strength (chest press, $d = 0.37$; seated row, $d = 0.42$), muscular endurance ($d = 0.66$), pain ($d = 0.84$), and disability ($d = 0.77$).

Rogers, et al[23] conducted a 2-arm, randomized controlled pilot trial examining the preliminary efficacy of a progressive 12-week RE intervention (6 weeks supervised and 6 weeks of home-based RE) with those of a usual-care approach among 15 HNC patients undergoing radiation therapy. Assessments of muscular strength, grip strength, body composition, physical function, and QOL were obtained at baseline, 6-week and 12-week follow-up assessments. In all, 15 of 238 (16%) patients that were assessed for eligibility were randomized into the trial. Approximately 87% of patients randomized to the RE intervention completed the 12-week follow-up assessment. Adherence to prescribed RE sessions was 83% during the supervised phase and 53% during the home-based phase of the RE intervention. No adverse events related to the RE intervention were reported. RE resulted in small to moderate effect-size improvements in muscular strength ($d = 0.15$) and physical function ($d = 0.51$)

at 12-week follow-up. Examination of the effect sizes (d = −0.58-0.21) accompanying changes in the body composition and QOL revealed no meaningful improvement in any of these outcomes relative to baseline at 12-week follow-up. Indeed, select outcomes such as lean body mass and general and disease-specific QOL exhibited unfavorable changes from baseline. However, it should be noted that moderate to large between-group effect sizes favoring the RE intervention were observed for physical function, fatigue, and QOL. Thus, unfavorable changes in these outcomes were significantly attenuated in participants assigned to the RE intervention relative to those which emerged in the usual-care control group.

Collectively, the findings of these 3 randomized controlled trials demonstrate that progressive RE is a safe, tolerable, feasible intervention for postoperative HNC patients. Results of these studies also support preliminary efficacy of RE as a therapeutic intervention that results in significant improvements in pain, disability, QOL, muscular fitness, and ROM outcomes relative to standard-of-care physical therapy interventions.

RE in lung cancer survivors. To date, only one study has investigated the effects of RE in LC survivors. Peddle-McIntyre et al[31] conducted a single-arm, feasibility and preliminary efficacy study of RE in 17 LC survivors. Assessments of muscular strength and endurance, physical function, body composition, and QOL were obtained prior to the start and following 10 weeks of RE. A total of 17 of 389 (13%) LC survivors that were assessed for eligibility were randomized into the pilot trial and 87% of participants completed the postintervention follow-up assessment. Adherence during the RE intervention was 87%. A total of 3 adverse events involving minor musculoskeletal injuries related to the RE intervention were reported. Findings revealed that RE resulted in large effect-size improvements in muscular strength (chest press, d = 0.96; leg press, d = 1.00) and muscular endurance (chest press, d = 1.55; leg press, d = 1.49; arm curls, d = 1.49). Moderate to large effect-size improvements were also observed in performance measures of physical function including 6-minute walk distance (d = 0.90), chair stand time (d = 1.21), and up and go task time (d = 0.58). Modest improvements in lean body mass (d = −0.01), body fat percentage (d = 0.00), or QOL (d = −0.28-0.44) were observed following the RE intervention. These findings provide support for the feasibility and preliminary efficacy of RE for LC survivors.

RE in mixed cancer sample. In the final RE study included in the review, Katz et al[32] conducted a single-arm, uncontrolled trial examining the effects of a 5-month progressive RE intervention in a sample of 10 survivors of various cancer types (bladder, cervical, endometrial, melanoma, uterine). The RE intervention involved 2 months of supervised RE and 3 months of unsupervised RE. Assessments of muscular strength, body composition (body fat percentage and lean body mass), physical function (6-minute walk, 50-feet walk, and single leg stand) and global QOL (SF-36) were obtained at baseline and 2-month and 5-month follow-up assessments. A total of 10 of 12 eligible survivors (83%) participated in the study. All 10 participants completed the 2- and 5-month follow-up assessments and average adherence to the supervised RE sessions was 91%. There were 2 mild to moderate adverse events possibly related to the RE intervention involving the development of cellulitic infections. Results revealed the RE intervention resulted in small to moderate improvements in muscular strength (chest press: 2 months, d = 0.28; 6 months, d = 0.64; leg press: 2 months, d = 0.24; 6 months, d = 0.58), 6-minute walk (2 months, d = 0.21; 6 months, d = 0.64), 50-feet walk (2 months, d = 0.47; 6 months, d = 0.73), single leg stand (2 months, d = 0.33; 6 months, d = 0.00) but negligible changes in body fat percentage (2 months, d = −0.13; 6 months, d = 0.02) and lean body mass (2 months, d = 0.07; 6 months, d = 0.05). There were no changes in QOL following RE but the effect sizes and descriptive statistics of this measure were not reported. Although RE yielded moderate effect-size improvements in muscular strength and physical function, the observation of cellulitic infections in 2 of the participants suggests the safety and efficacy of RE in cancer survivors with lower limb lymphedema is unclear and requires further investigation.

Synthesis of overall RE intervention effects on physiologic and QOL outcomes. Evidence from the present systematic review suggests that RE interventions result in meaningful improvements in a variety of relevant physiologic and QOL outcomes during and following cancer treatment. However, the magnitude of the improvement accompanying RE varied considerably across outcomes. For example, whereas RE yielded large average effect-size increases in muscular strength (d = 0.86; range, 0.11-2.45) and muscular endurance (d = 1.88; range, 0.66-2.90) and moderate effect-size improvements in physical function (d = 0.66; range, 0.21-1.29). RE was associated with small effect-size improvements in body composition (d = 0.28; range, −0.51-1.78) and QOL (d = 0.25; range, −0.72-1.14). Overall, findings in this systematic review support the efficacy of RE as an efficacious supportive care intervention during and following cancer treatment.

Discussion

Findings from the present systematic review of the effects of RE during and following cancer treatment demon-

strates that RE interventions consistently yielded statistically significant, clinically meaningful improvements in a variety of relevant physiologic and QOL outcomes for cancer patients and survivors. Notably, RE produced important physiologic training adaptations including large effect-size improvements in muscular strength, moderate effect-size improvements in physical function, and small effect-size improvements in body composition. RE has also produced moderate effect-size improvements in fatigue and small to moderate effect size improvements in various measures of QOL. These effect sizes are comparable in magnitude to the effects of exercise interventions reported in prior comprehensive reviews of the exercise-cancer literature primarily focusing upon AE. Speck et al[5] reported large effect-size improvements in muscular strength, moderate effect-size improvements in fatigue, and small to moderate effect-size improvements in aerobic capacity, QOL, anxiety, and self-esteem. Similarly, results from a recent meta-analytic review of exercise and QOL in cancer survivors reported small to moderate effects across various measures of QOL.[36] Thus, RE interventions in isolation, are associated with improvements in physiologic and QOL outcomes that are comparable in magnitude as those observed in prior quantitative reviews addressing the effects of AE interventions or interventions involving combinations of aerobic and resistance exercise among cancer patients and survivors. With regard to safety and feasibility of RE interventions, few adverse events were reported across the 15 studies and the 44% recruitment rate, 86% retention rate, and 84% adherence rate suggests that RE is a safe, well-tolerated behavioral intervention strategy that is feasible to implement during and after treatment for a variety of cancer populations. Collectively, these findings provide strong initial evidence of the safety, feasibility, and efficacy of RE as a supportive care intervention during and following cancer treatment.

RE elicited large effect-size improvements in muscular strength and endurance and moderate effect-size improvements in physical function. These findings provide strong support for the beneficial effects of RE on relevant fitness and physiologic outcomes for cancer patients and survivors. Conversely, RE yielded small effect-size improvements in indices of body composition. Close inspection of the 9 studies examining changes in body composition reveals a pattern of heterogeneity in the effect sizes changes accompanying RE that warrants careful interpretation. That is, whereas the overall effect size for improvement in body composition measures was 0.28, this averaged effect resulted from small effect sizes (range, −0.09-0.21) in 8 studies[18,20-22,25,26,31,32] and large effect-size changes (range, 0.87-1.78) that were obtained in one study.[24] Indeed, when excluding the one randomized controlled trial reporting the large effect-sizes improvements, the average effect-size change in body composition is essentially negligible ($d = 0.05$). Given that excess body weight and body fat are linked with increased risk for chronic disease, metabolic syndrome, and cancer recurrence, the potentially beneficial effect of exercise upon body composition is arguably one key factor in the emerging interest in integrating exercise as part of the treatment of cancer patients and survivors. The pattern of change in measures of lean body mass, fat mass, and body fat percentage observed following RE in this review may raise concerns for some researchers and/or clinicians regarding the efficacy of RE for producing meaningful improvements in body composition during or following cancer treatment.

However, before questioning the utility of implementing RE to ameliorate body composition in cancer patients and survivors, several considerations must be taken into account when interpreting the body composition findings observed in the present review. For example, weight gain, increases in fat mass, and decreases in muscle mass are frequently documented during hormone therapy,[37] chemotherapy[38] and in cancer survivors following the completion of active treatment.[39] However, findings from our review demonstrated that patients undergoing hormone therapy,[19-22] chemotherapy,[18] and cancer survivors who had completed active treatment[24,29,30,32] that received RE interventions did not experience the unfavorable shifts in body composition that have been documented previously. Thus, although the present findings suggest RE consistently elicited small effect-size improvements in body composition, it also appears to have a meaningful protective effect whereby it significantly attenuates the adverse changes in body fat percentage, lean body mass, and fat mass that are reliably documented during cancer treatment and survivorship. It is also important to recognize several of the studies reviewed implemented RE interventions that may have been of insufficient duration and/or intensity to produce meaningful improvements in body composition. Schmitz et al's[34] study is associated with the greatest improvement in body composition and demonstrates that 6 months of progressive RE performed at 70-80% 1RM produced large effect-size improvements in lean body mass and body fat among BRCA survivors. Thus, we believe the findings from the present review indicate that while RE of sufficient intensity, frequency, and duration can elicit improvements in body composition, one of the most prominent benefits of RE for body composition appears to be the attenuation of unfavorable shifts in body composition that are observed during and following cancer treatment. Collectively, these results

suggest that RE is an efficacious supportive care intervention that yields clinically meaningful benefit for body composition in cancer patients and survivors.

The present review did not focus on determining the comparable efficacy of RE to attention control or comparison treatments. Nonetheless, it should be recognized that findings from 2 randomized controlled trials directly comparing the effects of RE to AE in BRCA[18] and PC patients[21] demonstrated that RE resulted in more favorable long-term improvements in fatigue and superior chemotherapy completion rates. These are meaningful benefits with the potential of having a particularly significant impact on morbidity and mortality risk in cancer treatment and survivorship. Given the preliminary evidence suggesting that RE may be linked with unique benefits relative to AE among individuals undergoing treatment for BRCA and PC, delineating the independent and potentially synergistic benefits of RE and AE could be a critical aspect of advancing knowledge of appropriate exercise prescription approaches during cancer treatment. Consequently, as interest in the value of integrating exercise into the clinical management of cancer increases, future investigations that address the unique and additive benefits of RE and AE for cancer patients is warranted.

The present review was also the first to evaluate the methodologic quality of RE intervention studies in cancer patients and survivors. Based on the relatively high percentage of quality indicators met across all studies (74%) observed in the Delphi List methodologic assessment,[17] we believe the quality of the RE intervention studies conducted during and following cancer treatment can be reasonably classified as strong. The proportion of methodologic quality indicators met was similar between studies implementing RE interventions during treatment (76%) and those implementing the intervention following treatment (72%). With regard to methodological limitations, it is important to note that fewer than half of the studies reviewed conducted blinded assessments or intention-to-treat analyses. Given these are critical design considerations for randomized controlled exercise intervention trials; this is one area in which the methodology of RE intervention studies could improve. We recommend that future RE trials address these important design features. Thus, while there is relatively little research examining the efficacy of RE interventions alone, the present evaluation suggests the extant studies are of good overall methodologic quality.

Limitations

Although we believe that conducting one of the first systematic reviews of the efficacy of RE alone during and following cancer treatment could yield important conceptual and clinical implications for cancer patients and survivors, there are several limitations of the present review that should be acknowledged. First, because our present approach incorporated procedures from both narrative and systematic reviews, the average effect sizes calculated in the present review do not account for the potential influence of divergence in sample size or variability in outcomes measures observed across studies. This is particularly important given that several studies addressed small sample size of 20 or fewer participants.[20,22,23,29,31,32] Nonetheless, given the limited amount of extant research, we believe our approach represents an important initial step in synthesizing the findings in this area. As data addressing independent effects of RE accumulates, future reviews utilizing standardized systematic and meta-analytic procedures will allow for a more thorough evaluation of the extent to which such issues may influence the magnitude of RE on clinically relevant outcomes for cancer patients and survivors.

Another relevant limitation to consider when interpreting the results of this review is the relatively narrow breadth of both the types of cancer studied and the phase of the cancer experience within which the effects of RE interventions have been examined. For example, with the exception of 2 studies involving LC survivors and a mixed sample of survivors of various types of cancer,[32] the RE interventions studies in this review primarily targeted individuals during or following treatment of 3 cancer diagnoses: BRCA, PC, and HNC. Consequently, the feasibility and preliminary efficacy of RE as a supportive care intervention for other presently understudied cancer groups (ie, hematological, endometrial) has yet to be determined. Consistent with the findings of other recent reviews of the exercise-cancer literature,[1,4] all of the RE interventions included in the present review focused upon the time period during or shortly following active cancer therapy. Due to the relatively restricted timeframe focused upon in these studies, knowledge of the effects of RE during understudied phases (ie, prevention, buffering, and palliation) of the cancer continuum identified in Courneya and Friedenreich's PEACE framework[8] remains limited. Therefore, future studies examining the effects of RE within samples of patients with different cancer diagnoses and at different phases of the cancer experience are necessary to develop a more comprehensive understanding of the feasibility and efficacy of RE as a supportive care intervention.

Table 1 reveals the characteristics of the RE interventions such as the frequency, load (amount of weight), and volume (sets and repetitions per set) varied considerably across studies. Due to the variability in intervention characteristics used in prior studies and the absence of studies

directly comparing different doses of RE, the minimum frequency, load, and volume of RE that yields favorable changes in physiologic and QOL outcomes during and following cancer treatment has yet to be adequately delineated. Given the challenges faced by individuals during and following cancer treatment, developing an estimate of the minimum amount of RE necessary to produce clinically meaningful improvements would be valuable in guiding exercise prescription for cancer patients and survivors. To date, accepted national exercise guidelines forwarded by the American College of Sports Medicine have been proposed to be both safe and efficacious to guide exercise prescription to cancer patients and survivors.[6] Nonetheless, defining the minimal or optimal amount of RE participation necessary to improve relevant outcomes among cancer patients and survivors remains unknown and is an important topic that warrants study in future randomized, controlled RE trials. However, in exploring the dose-response effects of RE, it is important to acknowledge that any single RE prescription is unlikely to be the optimal stimulus for all patients or yield a uniform magnitude of improvement in all relevant outcomes of interest. Participants' tolerance for, and adaptation to any dose of RE will be influenced by individual differences that shape their interpretation of the exercise prescription.[40,41] Therefore, while it is of considerable importance to augment knowledge of the dose-response effects of RE during and following cancer treatment, flexible prescription strategies that personalize the characteristics of the RE intervention to one's fitness level, exercise tolerance, and preferences should also be viewed as an important consideration in the design of future investigations attempting to define the dose-response relationship of RE interventions.

Successfully promoting adherence to exercise prescriptions is a critical determinant of the efficacy of exercise interventions.[40,42-44] The 84% average adherence rate observed in the present review is an impressive level of participation that underscores the feasibility of delivering RE interventions during and following cancer treatment. Despite the promising adherence results, it should be recognized that attendance alone is a relatively simplistic index of adherence that does not directly address the participants' compliance with all facets of the RE prescription (eg, sets, repetitions, load, volume, and volume load completed). Additionally, some investigations did not report adherence rates. It should also be recognized that few studies have examined the extent to which the beneficial effects of RE are sustained following the cessation of the supervised phase of the intervention. Expanding assessment of adherence to the RE prescription characteristics (sets, reps, load, volume, volume load) and exploring the relationship between RE adherence and sustained improvement in relevant physiologic and QOL outcomes is integral in defining the amount of RE participation that yields therapeutic benefits for cancer patients and survivors.

Conclusion

In summary, findings from the studies included in the present review suggest that RE is a safe, feasible supportive care intervention that results in significant, clinically meaningful improvements in both physiologic and psychosocial outcomes in individuals during and following cancer treatment. This is the first systematic review to focus upon RE. Although these preliminary findings are promising, additional randomized controlled trials are needed to firmly establish the benefits of RE for cancer patients and survivors.

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