

## The Independent Effects of Strength Training in Cancer Survivors: a Systematic Review

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Hanson, E.D., Wagoner, C.W., Anderson, T., Battaglini, C.L. (2016) The Independent Effects of Strength Training in Cancer Survivors: a Systematic Review. *Current Oncology Reports* 18:31. <https://doi.org/10.1007/s11912-016-0511-3>

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### **Abstract:**

Cancer treatment is associated with adverse changes in strength, body composition, physical function, and quality of life. Exercise training reduces cancer incidence and mortality rates and may offset some of the treatment-related effects. To determine the independent effects of strength training (ST) on the effects of cancer treatment, an initial search was performed in March and then updated in November 2015. Additional articles were identified by scanning references from relevant articles. Studies using traditional ST on strength, body composition, aerobic capacity, functional assessments, and psychosocial parameters were included. Excluded studies had no objective strength measurement or combined ST with additional exercise. Mean and standard deviations from 39 studies across seven cancer types were extracted for main outcomes. ST-induced change scores with 95 % confidence intervals were calculated and were evaluated with paired *t* tests, where appropriate. Twenty to fifty percent improvements in maximal strength were observed, indicating that the ST programs were effective. Physical function was also enhanced (7–38 %), although gains were less consistent. Body composition and psychosocial changes were rare, with only a few changes in selected cancer types. As such, ST appears to promote benefits that may be specific to cancer types. Strength was the only consistent outcome that improved in all cancer survivors. However, these gains in strength are still of tremendous importance, given its impact on functionality and quality of life. Several practical considerations for exercise testing, training, and data reporting are presented for consideration to improve the overall depth of the field.

**Keywords:** Resistance training | Cancer | Exercise | Strength | Body composition | Quality of life

### **Article:**

#### **Introduction**

Cancer incidence rates in the USA rose steadily until the mid-1990s before plateauing, and available data from the most recent 5 years are showing signs of decline for certain cancers [1]. However, recent estimates suggest there are nearly 14.5 million cancer survivors and this number is expected to grow by another 4 million over the next 10 years [2] with treatment-related costs that exceed 75 billion dollars annually [3]. In 2015 alone, 1.7 million new cases were anticipated

to be diagnosed with ~600,000 cancer-related deaths, although mortality rates have started to improve [1]. The decrease in mortality may be the result of early detection and treatment, improved treatment protocols, and lower smoking rates.

Cancer treatments may include surgery, radiation, chemotherapy, immunotherapy, and hormone therapies that effectively reduce tumor burden, as 5-year survival rates have increased regularly since the 1970s [1]. However, simply living longer poses many challenges for survivors, as numerous side effects persist during and after treatment with the most common ones including debilitating fatigue and reduced quality of life (QoL) [4, 5]. Additionally, treatment-related effects that alter muscle strength and body composition (either directly or indirectly via physical inactivity) promote loss of physical function, which further exacerbates fatigue and QoL [4]. Interestingly, many of these side effects are similar to those observed during natural aging processes but appear to be accelerated in cancer populations [6, 7, 8], possibly due to the harsh nature of anti-cancer treatments [9]. As such, therapies that assist in the mitigation of common age-related declines in physical, mental, and functional capacities are excellent candidates for alleviating or even reversing the side effects of cancer treatment.

Exercise, and strength training (ST) in particular, has long been used to reduce the effects of aging and chronic disease [10] and is now becoming a focal point in cancer patients, before, during, and after treatment. Epidemiological studies have shown that physical activity levels are associated with decreased incidence rates among certain cancer types [11, 12, 13], possibly via alterations in body composition, hormones, inflammatory markers, and immune function [14]. Following diagnosis, physical activity levels appear critical in reducing the risk of cancer-related mortality [15, 16], with cancer survivors engaging in higher levels of physical activity showing improved mortality outcomes. Both scenarios create a strong overall case for exercise interventions in cancer survivors and also those at high risk for cancer. Aerobic training was the first intervention used in breast cancer survivors to help offset weight gain associated with treatment [17]. From this initial study, the field of exercise oncology was established and it grew slowly over the first decade [18]. More recently, studies have expanded to also include ST or combined training across many different types of cancer [18, 19, 20] with generally beneficial effects being reported along with minimal adverse events. While exercise interventions have gained traction as a potential complementary therapy and both types of exercise have benefits to cancer survivors, there are certain traits that change only with ST, specifically, muscle hypertrophy and strength. ST-induced musculoskeletal gains may improve physical function, decrease fatigue, and ultimately produce a higher QoL. Because aerobic and ST have the potential to interfere with the respective adaptation processes [21], examining ST in isolation in cancer patients is important in determining the effectiveness of this specific modality in reducing treatment-related side effects. In primarily the past 10 years, studies have begun to explore the effects of ST alone in hormone-dependent cancers [22, 23, 24, 25••, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39••, 40, 41, 42, 43, 44, 45, 46••, 47••, 48], colorectal [49] and lung [50, 51], which are among the most common cancer types and leading cause of cancer-related mortality [1, 2].

The main objective of this systematic review was to examine the independent effects of resistance training programs on reducing or reversing the adverse effects of cancer treatment. Specifically, studies were included only if objective measures of strength were used as a means

of assessing the efficacy of the training program as improvements in strength have been shown to be associated with improvements in physical function and QoL in both healthy and cancer populations [35, 52]. This approach expands on previous articles in this area [6, 19, 53••] by utilizing objective strength measures, the inclusion of less common cancers, and incorporates recently published studies. Results are presented by cancer type and in descending order of number of studies rather than by specific outcomes, as the latter varied widely within and also across different types of cancer.

## **Methodology**

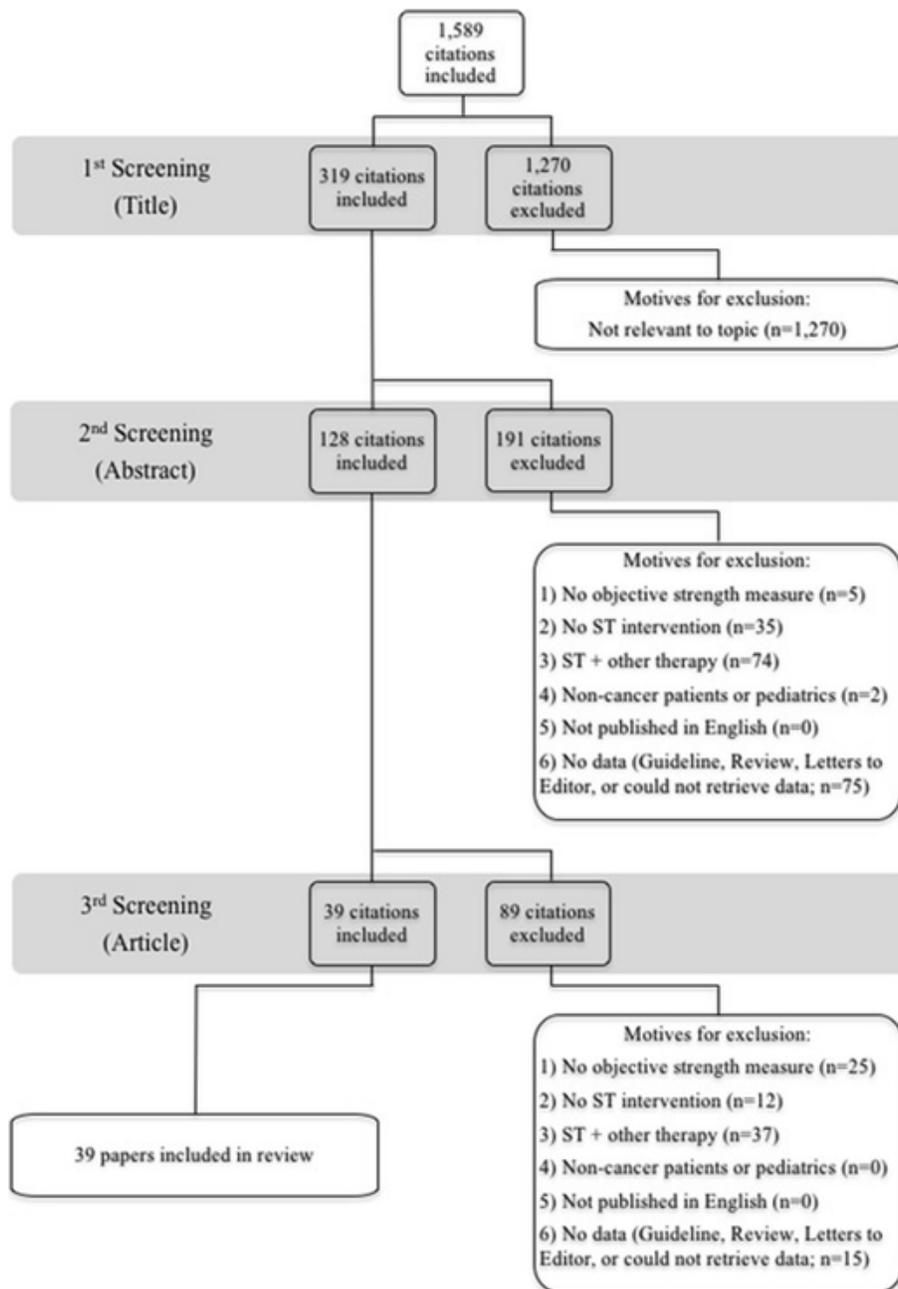
A systematic review of the literature was conducted using the search engine PubMed to identify ST publications in cancer populations. The initial search was run on March 6, 2015 with a final update on November 10, 2015 to include any recent publications that had not been captured initially. The search terms utilized were all possible combinations of the terms in list 1 (“strength training,” “resistance training,” “weight training,” and “functional overload”) and list 2 (“oncology,” “cancer,” or “neoplasm”) separated by the “AND” operator (i.e., strength training AND oncology). The search did not discriminate based on cancer type and had no date restrictions. Reference lists of relevant publications were also utilized.

### **Study Selection**

The publications included in this review were restricted to studies that evaluated the effects of ST only or studies that included an arm of ST only. The included studies objectively measured the independent effects of traditional resistance training (body weight, dumbbells, bars, and bands) on the following patient-related outcomes: isokinetic strength, isometric strength, maximal strength (1RM), multiple RM, grip strength, body composition, aerobic capacity, functional assessments, psychosocial parameters, and blood biomarkers. Studies that were ultimately excluded from the review included those that (1) had no objective measure of strength, (2) had no ST intervention, (3) combined ST with any other mode of exercise, (4) included pediatric patients or non-cancer participants, (5) were not published in English, and (6) there was no data reported. The first screening eliminated publications based on the title of the publication. The second screening eliminated studies based on a reading of abstract. The third and final screening eliminated studies based on a reading of the full text. In the case of missing data or unclear methodology, efforts were made to contact the corresponding author prior to elimination. Two reviewers (CW and TA) evaluated each study, and a consensus on inclusion was reached. In instances where consensus was not reached, a third reviewer (EH) made the final decision. Figure 1 below presents the literature review citation selection flowchart.

### **Data Extraction**

In studies that met all inclusion criteria, baseline and post-ST means and standard deviations were extracted for all main outcome variables. Values were converted to SI units, as required, and averaged for statistical analysis based on cancer type. As a wide range of strength tests were performed, upper and lower body composite strength scores were derived by combining and averaging strength values for each study within their respective cancer type. Change scores with ST were calculated and averaged by subtracting the baseline value from the post-training score.



**Fig. 1** Flowchart for inclusion or exclusion of literature within this review

### Statistical Analysis

Descriptive statistics (mean and standard deviations) were calculated on all fitness parameters, except for those parameters that were derived from a single study. For those parameters where two or more studies used the same testing procedure, paired-sample *t* tests were used to compare baseline and post-exercise training data, while 95 % confidence intervals were computed for the calculated change scores. An alpha level of 0.05 was set a priori for all procedures. For those parameters where only one study used a particular testing procedure, means, standard deviations,

and any statistical differences from baseline were reported based on information provided in the original publication and no further analyses were performed.

## Results

The cancer survivors in the current review were mostly middle-aged and older adults, with the exception of germ cell patients where survivors were much younger. The interventions tended to be of moderate length (12–16 weeks), although two trials were as short as 8–9 weeks and the longest was 2 years. The intensities of the ST programs were highly variable but were primarily moderate to high intensity (as defined in healthy older adults [54]) and were typically performed two to three times per week in early/localized cancer stages, although exceptions did exist (Table 1).

**Table 1.** Summary of study participant characteristics and training interventions

Cancer type	Study no.	Age (year)	Intervention length (week)	Training frequency (day/week)	Intensity (%1RM)	Disease stage
Breast	16	57 (49–68)	31.5 (8–104)	2 (2–4)	50–85 %	Majority early, mixed [24, 27]
Prostate	11	67 (65–73)	16 (10–24)	3 (2–3)	Variable	Majority early, mixed [37], advanced [23]
Mixed	4	59 (47–70)	24 (12–52)	3 (2–4)	Variable	Early [57], advanced [39••], unknown [58, 59]
Head and neck	4	54 (52–55)	12 (–)	2 (2–3)	60–70 %, variable	Majority mixed, early [70]
Lung	2	65 (63–67)	8 (6–10)	2.5 (2–3)	60–85 %	Early
Gastro-intestinal	1	59 (–)	12 (–)	2 (–)	60–80 %	Advanced
Germ cell	1	34 (–)	9 (–)	3 (–)	10–15RM	Mixed

Data are reported as mean (range)

*Breast Cancer.* Sixteen studies met the study inclusion criteria.

**Strength Assessment:** Overall, ST led to large increases in lower (29 %,  $P < 0.001$ ) and upper (23 %,  $P < 0.001$ ) body composite strength scores and 10RM chest press (88 %,  $P = 0.017$ ; Table 2). In the controls, strength significantly improved in lower body (5.2 %,  $P = 0.001$ ) but showed only a trend for upper body composite scores (10 %,  $P = 0.051$ ); however, the magnitude of the change was much smaller when compared to survivors in the ST groups. This suggests a slight learning effect instead of improvement derived from main physiological adaptations expected with regular strength training. Chest press and leg extension 8RM were reported to increase with ST [24], while grip strength was increased in both groups.

**Body Composition:** Absolute body composition was unaltered for fat and lean mass but ST decreased percent body fat ( $P = 0.006$ ) in the exercise group, while the controls had a significant increase ( $P = 0.004$ ). Bone mineral density did not change in either group nor did ST alter bone formation and reabsorption biomarkers [29].

**Table 2.** Effects of ST on strength, body composition, physical function, aerobic capacity, and psychosocial parameters in breast cancer survivors

	Study no.	Subject no.	Baseline mean (SD)	Post-ST mean (SD)	Mean change	95 % CI	Pvalue
<b>Strength</b>							
Lower body composite (kg)							
Exercise	15	756	79.2 (12.6)	102.0 (19.2)	22.9	72.2–86.1	<0.001
Control	10	568	96.6 (38.7)	101.6 (40.4)	5.1	68.9–124.3	0.001
8RM leg extension (kg)							
Exercise	1 <sup>a</sup>	82	24.4 (11.2)	32.8 (12.6) <sup>b</sup>	8.2	–	–
Control	1 <sup>a</sup>	82	22.8 (8.9)	24.6 (7.8) <sup>b</sup>	1.4	–	–
Upper body composite (kg)							
Exercise	17	809	26.1 (12.9)	32.2 (15.7)	6.08	19.5–32.7	<0.001
Control	11	540	22.3 (8.4)	24.6 (8.4)	2.31	16.7–27.9	0.051
8RM chest press (kg)							
Exercise	1 <sup>a</sup>	82	23.2 (7.2)	31.9 (10.8) <sup>b</sup>	8.8	–	–
Control	1 <sup>a</sup>	82	22.8 (8.9)	24.6 (7.8) <sup>b</sup>	1.5	–	–
10RM chest press (kg)							
Exercise	2	20	13.9 (2.6)	26.1 (3)	12.2	–9.3–37	0.017
Control	–	–	–	–	–	–	–
Grip strength (kg)							
Exercise	3	195	28.9 (6.6)	30.9 (6.0)	1.9	12.7–45.2	0.040
Control	2	165	25.8 (0.2)	27.0 (0.4)	1.2	23.8–27.7	0.053
<b>Body composition</b>							
Absolute FM (kg)							
Exercise	5	340	30.2 (2.5)	30.03 (1.9)	–0.2	27–33.4	0.640
Control	3	317	30.1 (1.63)	30.1 (1.67)	0.02	26.06–34.1	0.970
Absolute LM (kg)							
Exercise	4	192	43.3 (5.1)	43.5 (4.3)	0.2	35.2–51.4	0.710
Control	2	89	46.7 (3.4)	46.5 (2.8)	–0.3	16.2–77.2	0.677
BF (%)							
Exercise	7	471	38.7 (3.1)	38.3 (3.1)	–0.4	35.8–41.5	0.006
Control	4	363	39.2 (0.5)	39.5 (0.6)	0.3	38.3–40	0.004
BMD (g/cm <sup>3</sup> )							
Exercise	3	60	1.0 (0.1)	1.0 (0.1)	0.0	0.7–1.4	0.266
Control	2	42	0.9 (0.1)	0.9 (0.1)	0.0	–0.3–2.2	0.446
<b>Functional assessments</b>							
12-min walk (m)							
Exercise	1 <sup>a</sup>	21	1020 (357)	1055 (177) <sup>b</sup>	35	–	–
Control	1 <sup>a</sup>	23	1035 (257)	944 (241)	–91	–	–
DASH							
Exercise	1 <sup>a</sup>	26	11.4 (9.1)	10.2 (11)	–1.2	–	–
Tandem balance (s)							
Exercise	1 <sup>a</sup>	110	14.2	8.6 <sup>b</sup>	–5.6	–	–
Control	1 <sup>a</sup>	113	14.6	11.5 <sup>b</sup>	–3.1	–	–
Arm curl (reps in 30 s)							
Exercise	2	20	17.4 (0.3)	20.5 (0.1)	3.1	14.9–19.9	0.021
Chair stand (reps in 30 s)							

	Study no.	Subject no.	Baseline mean (SD)	Post-ST mean (SD)	Mean change	95 % CI	Pvalue
Exercise	2	20	14.3 (2.5)	17.0 (3.5)	2.7	-8.6-37.2	0.161
<u>Aerobic capacity</u>							
VO <sub>2Peak</sub> (mL/kg/min)							
Exercise	2	91	24.5 (1.5)	24.2 (0.0)	-0.3	11.8-37.2	0.442
Control	1 <sup>a</sup>	82	24.8 (6.2)	23.5 (5.4)	-1.6	-	-
<u>Psychosocial</u>							
Anxiety							
SSAS							
Exercise	1 <sup>a</sup>	82	42.0 (12)	36.4 (12.7) <sup>c</sup>	-5.7	-	-
Control	1 <sup>a</sup>	82	42.0 (13.7)	37.4 (12) <sup>c</sup>	-4.2	-	-
Depression							
ESDS							
Exercise	1 <sup>a</sup>	82	13.8 (10.1)	10.6 (9.5) <sup>c</sup>	-2.3	-	-
Control	1 <sup>a</sup>	82	13.9 (9.7)	10.8 (9.4) <sup>c</sup>	-1.9	-	-
Fatigue							
FACT-A							
Exercise	1 <sup>a</sup>	82	34.3 (10.1)	36.3 (9.4) <sup>c</sup>	0.9	-	-
Control	1 <sup>a</sup>	82	34.6 (11.1)	34.9 (12.5) <sup>c</sup>	-0.7	-	-
QOL							
FACT-A							
Exercise	1 <sup>a</sup>	82	132.2 (23.5)	140.9 (24.8) <sup>c</sup>	5.9	-	-
Control	1 <sup>a</sup>	82	135.3 (28.1)	139.9 (28.2) <sup>c</sup>	1.0	-	-
Body image and relationships scale							
Exercise	4	264	76.3 (9.4)	64.3 (9.6)	-11.9	61.2-91.3	0.051
Control	1 <sup>a</sup>	121	76.8 (17.3)	74.7 (18.2)	-	-	-
SF36							
Exercise	1 <sup>a</sup>	112	52.1 (9.4)	53.2 (9.6) <sup>c</sup>	1.7	-	-
Control	1 <sup>a</sup>	120	53.9 (7.5)	53.8 (8.7) <sup>c</sup>	2.2	-	-

Data from references [22, 24, 25<sup>••</sup>, 26, 27, 28, 29, 30, 38, 40, 41, 42, 43, 44, 48, 71]. Lower body composite includes leg extension and leg press. Upper body composite includes chest and overhead presses and seated row

*RM* repetition maximum; *FM* fat mass; *LM* lean mass; *BF* body fat; *BMD* bone mineral density; *DASH* disabilities of the arm, shoulder, and hand; *SSAS* Spielberger state anxiety scale; *ESDS* epidemiologic studies depression scale; *FACT-A* functional assessment of cancer therapy–anemia; *BIRS* body image and relationships scale

<sup>a</sup>As reported in original research article for variables with only one study

<sup>b</sup>Significantly different from baseline value, per original article

<sup>c</sup>No within-group *P* value provided in original article or supplementary data

Functional Assessment: Arm curls completed in 30 s were improved with ST (18 %, *P* = 0.021), but chair stands were not. Single studies reported that ST improved 12-min walk distance [28] and tandem balance [30] but not shoulder function [38]. Aerobic capacity did not change with ST or in controls [24].

Psychosocial Assessment: Body image and relationship scores decreased by 19 %, indicating less concern with physical appearances following ST. In the other limited data

available from single studies, ST reduced anxiety and depression and improved fatigue and QoL [24]. However, controls had similar responses with slightly smaller magnitudes except fatigue, which increased. However, no within-group comparisons were reported in this study.

**Table 3.** Effects of ST on strength, body composition, physical function, aerobic capacity, and psychosocial parameters in prostate cancer survivors

	Study no.	Subject no.	Baseline mean (SD)	Post-ST mean (SD)	Mean change	95 % CI	Pvalue
<b>Strength</b>							
<b>Lower body composite (kg)</b>							
Exercise	12	649	110.6 (56.8)	142.8 (70.8)	32.2	18.8–45.7	<0.001
Control	4	154	98.8 (56.4)	98.2 (57.6)	−0.6	−3.8–2.6	0.591
<b>Upper body composite (kg)</b>							
Exercise	13	1032	42.7 (11.2)	53.5 (13.4)	10.8	8.44–13.21	<0.001
Control	4	166	39.6 (14.6)	38.7 (14.0)	−1.0	−132.5–130.5	0.348
<b>8RM leg extension (kg)</b>							
Exercise	4	459	98.7 (13.4)	124.0 (17.1)	25.4	19.0–31.8	<0.001
Control	1 <sup>a</sup>	41	117.3 (53.5)	119.2 (55.9) <sup>c</sup>	1.9	–	–
<b>8RM chest press (kg)</b>							
Exercise	4	459	44.6 (10.7)	54.5 (13.4)	9.8	−5.8–25.5	0.005
Control	1 <sup>a</sup>	41	55.2 (13.3)	52.9 (14.6) <sup>b</sup>	−2.3	–	–
<b>Body composition</b>							
<b>Absolute FM (kg)</b>							
Exercise	4	65	27.8 (2.4)	27.6 (2.7)	−0.2	−0.9–0.4	0.337
Control	2	40	26.8 (0.6)	27.1 (0.6)	0.3	–	0.500
<b>Absolute LM (kg)</b>							
Exercise	4	95	62.0 (3.6)	62.6 (3.7)	0.6	−0.5–1.8	0.123
Control	2	40	55.6 (3.3)	55.2 (3.82)	−0.4	−4.8–4.1	0.500
<b>BF (%)</b>							
Exercise	7	145	31.0 (1.1)	30.8 (1.3)	−0.2	−0.6–0.08	0.116
Control	3	81	31.5 (1.4)	32.2 (1.7)	0.7	−1.2–2.6	0.261
<b>BMC (kg)</b>							
Exercise	2	27	3.1 (0.0)	3.0 (0.0)	−0.1	−0.4–0.36	0.626
<b>Functional assessments</b>							
<b>Up and go (s)</b>							
Exercise	6	63	6.1 (1.0)	5.6 (0.9)	−0.6	−0.8–−0.4	0.001
<b>Stair climb (s)</b>							
Exercise	3	52	5.9 (1.1)	5.4 (1.0)	−0.5	−1.0–0.05	0.060
Control	1 <sup>a</sup>	30	5.9 (1.0)	5.9 (1.0)	0.0	−0.2–0.1	–
<b>Chair stands (s)</b>							
Exercise	2	27	14.9 (0.6)	13.8 (4.7)	−1.2	−48.8–46.5	0.811
<b>Chair stand (reps)</b>							
Exercise	4	431	13.3 (2.5)	15.1 (2.5)	1.8	9.4–17.3	0.006
Control	1 <sup>a</sup>	30	16.0 (3.0)	16.0 (3.0)	0	–	–
<b>6-min walk (m)</b>							
Exercise	4	36	525.6 (58.8)	565.7 (54.8)	40.1	19.3–60.9	0.009
<b>6-m walk (s)</b>							

	Study no.	Subject no.	Baseline mean (SD)	Post-ST mean (SD)	Mean change	95 % CI	Pvalue
Exercise	4	54	4.8 (0.8)	4.3 (0.8)	-0.5	-0.8--0.2	0.019
Control	1 <sup>a</sup>	10	4.5 (0.6)	4.8 (0.4) <sup>c</sup>	0.3	-	-
<b>400-m walk (s)</b>							
Exercise	4	415	284.9 (23.7)	262.5 (15.6)	-22.5	-42.7--2.21	0.039
Control	1 <sup>a</sup>	10	280.8 (53.0)	286.5 (50.5)	5.7	-	-
<b>Aerobic capacity</b>							
<b>VO<sub>2</sub> peak (mL/kg/min)</b>							
Exercise	3	80	28.5 (2.8)	28.9 (3.7)	0.5	-1.9--2.9	0.464
Control	1 <sup>a</sup>	41	28.8 (5.1)	27.6 (5.1) <sup>b</sup>	-1.2	-	-
<b>Psychosocial</b>							
<b>Anxiety</b>							
<b>BSI-18 (1-5)</b>							
Exercise	1 <sup>a</sup>	10	1.7 (1.8)	3.3 (5.5) <sup>b</sup>	1.6	-	-
Control	1 <sup>a</sup>	10	1.5 (2.0)	2.7 (3.2) <sup>c</sup>	1.2	-	-
<b>Depression</b>							
<b>BSI-18 (1-5)</b>							
Exercise	1 <sup>a</sup>	10	2.9 (4.0)	3.7 (5.7)	0.8	-	-
Control	1 <sup>a</sup>	10	1.4 (2.1)	3.7 (6.1)	2.3	-	-
<b>Fatigue</b>							
<b>FACT-F subscale</b>							
Exercise	3	66	41.7 (2.0)	43.9 (1.6)	2.2	0.8--3.6	0.020
Control	1 <sup>a</sup>	41	44.6 (8.7)	42.1 (8.8) <sup>b</sup>	-2.5	-	-
<b>MFSI (short form)</b>							
Exercise	1 <sup>a</sup>	10	5.2 (16.8)	8.8 (24.9) <sup>c</sup>	3.6	-	-
Control	1 <sup>a</sup>	10	6.0 (12.3)	3.8 (13.7) <sup>c</sup>	-2.2	-	-
<b>BFI</b>							
Exercise	1 <sup>a</sup>	17	28.0 (21.4)	17.5 (18.1)	-10.5	-	-
<b>QOL</b>							
<b>FACT-G (0-104)</b>							
Exercise	1 <sup>a</sup>	40	88.2 (13.0)	92.4 (13.2) <sup>b</sup>	4.2	-	-
Control	1 <sup>a</sup>	41	90.0 (13.0)	89.8 (13.1) <sup>c</sup>	-0.2	-	-
<b>FACT-P</b>							
Exercise	2	98	115.7 (3.5)	120.5 (0.4)	4.8	-30.2--39.7	0.334
Control	1 <sup>a</sup>	73	120.9 (13.6)	117.6 (14.9) <sup>c</sup>	-3.3	-	-

Data from references [23, 31, 32, 33, 34, 35, 36, 37, 45, 46••, 47••]. Lower body composite includes leg extension and leg press. Upper body composite includes chest and overhead presses and seated row

*RM* repetition maximum; *FM* fat mass; *LM* lean mass; *BF* body fat; *BMD* bone mineral density; *DASH* disabilities of the arm, shoulder, and hand; *SSAS* Spielberger state anxiety scale; *ESDS* epidemiologic studies depression scale; *FACT-A* functional assessment of cancer therapy–anemia, *BIRS* body image and relationships scale

<sup>a</sup>As reported in original research article for variables with only one study

<sup>b</sup>Significantly different from baseline value, per original article

<sup>c</sup>No within-group *P* value provided in original article or supplementary data

*Prostate Cancer.* Eleven studies met the study inclusion criteria.

**Strength Assessment:** Similar to breast cancer, lower (29 %,  $P = 0.006$ ), upper (25 %,  $P < 0.001$ ), and 8RM leg extension (26 %,  $P < 0.001$ ) and 8RM chest press (22 %,  $P = 0.005$ ; Table 3) increased significantly with ST. Changes in the controls were minimal, with no change for upper or lower body strength or leg extension 8RM [37] and a decrease in chest press 8RM [37].

**Body Composition:** Body composition measures were unaltered, as ST did not significantly decrease fat mass or increase bone mineral content. There was a weak trend for increased lean mass and reduced % fat, but neither was significant (both  $P = 0.12$ ). Similarly, a lack of change was present in controls, although the small differences in the opposite direction from ST were observed. Regional body composition showed more change, with thigh muscle volume ( $\text{cm}^3$ ) being significantly increased by 6.4 % [35] and quadriceps area ( $\text{cm}^2$ ) in the right (pre 73.7 (3.5), post 75.1 (3.3); 95 % CI 72.3–75.1;  $P = 0.045$ ) but not left (pre 72.1 (3.6), post 73.5 (4.7); 95 % CI 70.7–73.5;  $P = 0.330$ ) leg increased following ST. ST increased muscle fiber cross-sectional area by 12 %, and controls decreased by  $-8.5$  % with the most pronounced changes occurring in type II fibers [46••].

**Functional Assessment:** Timed up and go ( $-8.2$  %,  $P = 0.001$ ); chair stand repetitions (14 %,  $P = 0.006$ ); and 6-m ( $-10$  %,  $P = 0.019$ ), 400-m ( $-7.9$  %,  $P = 0.039$ ), and 6-min (7.6,  $P = 0.009$ ) walk times all improved significantly with ST, along with a trend for improved stair climb time ( $-8.5$  %,  $P = 0.060$ ). There was no change in maximal oxygen uptake. Control data for functional assessments was limited to single studies for each task, but 6- and 400-m walk times were 6.7 and 2.0 % slower, respectively, with reduced maximal oxygen uptake [37]. Chair stand repetitions and stair climb time did not change.

**Psychosocial Assessment:** Like with breast cancer, ST studies in prostate cancer used many different tools to assess fatigue and QoL, making comparisons difficult. Only one questionnaire was used repeatedly and ST increased FACT-F score by 5.3 % ( $P = 0.020$ ). In other questionnaires, regardless of which particular one was used, ST appears to improve fatigue scores (indicating less fatigue), whereas controls tended to worsen. QoL was unchanged with ST when a questionnaire with prostate specific questions (FACT-P) was used but improved in a single study using the more general questionnaire (FACT-G) [37]. The QoL change scores with ST in FACT-P and FACT-G were very similar, suggesting that improvements with exercise may be influencing.

**Biomarker Assessment:** Biomarkers remained stable, as changes in prostate specific antigen (ST  $-1.3$ ,  $P = 0.184$ ; Con 2.7 ng/ml,  $P = 0.504$ ) and testosterone (ST 0.1,  $P = 0.854$ ; Con  $-0.9$  pmol/l,  $P = 0.604$ ) were absent from both groups. Hemoglobin (g/l) had a non-significant decrease of 1.8 % with ST (pre 143.2 (2.7), post 140.6 (0.9); 95 % CI 119.1–167.3;  $P = 0.488$ ) and controls from a single study decreased by  $-3.6$  % [37]. Growth hormone and cortisol levels were unchanged with ST [55].

**Table 4.** Effects of ST on strength, body composition, physical function, and psychosocial parameters in head and neck cancer survivors

	Study no.	Subject no.	Baseline mean (SD)	Post-ST mean (SD)	Mean Change	95 % CI	Pvalue
<u>Strength</u>							
Dead lift (kg)							
Exercise	1 <sup>a</sup>	5	107.9 (37.8)	115.0 (54.4) <sup>c</sup>	7.1	–	–
Control	1 <sup>a</sup>	8	94.2 (46.4)	92.1 (41.3) <sup>c</sup>	–2.1	–	–
Upper body composite (kg)							
Exercise	4	108	28.8 (13.1)	40.8 (17.8)	12.0	4.4–19.6	0.015
Control	4	100	24.4 (9.8)	29.1 (11.8)	4.7	1.3–8.2	0.022
Grip strength (kg)							
Exercise	2	18	61.5 (30.0)	62.7 (33.1)	1.2	–26.8–29.2	0.682
Control	1 <sup>a</sup>	8	39.1 (14.1)	35.5 (11.6)	–3.6	–	–
<u>Body composition</u>							
Absolute FM (kg)							
Exercise	1 <sup>a</sup>	19	17.1 (9.2)	16.9 (9.3) <sup>c</sup>	–0.2	–	–
Absolute LM (kg)							
Exercise	2	26	111.6 (5.2)	106.1 (2.0)	–5.5	–67.8–62.4	0.688
Control	1 <sup>a</sup>	8	62.8 (17.8)	60.1 (3.3)	–2.7	–	–
<u>Functional assessments</u>							
Chair rise (s)							
Exercise	1 <sup>a</sup>	5	4.4 (4.1)	2.9 (0.7)	–1.5	–	–
Control	1 <sup>a</sup>	8	3.1 (0.8)	3.1 (0.4)	0.0	–	–
Stair climb (steps/s)							
Exercise	1 <sup>a</sup>	19	2.6 (0.5)	3.0 (0.4)	0.4	–	–
6-min walk test (m)							
Exercise	1 <sup>a</sup>	11	544.0 (112.7)	593.5 (71.6)	49.5	–	–
10-m fast walk (m/s)							
Exercise	1 <sup>a</sup>	19	2.1 (0.3)	2.3 (0.4)	0.2	–	–
Arm curl (reps in 30 s)							
Exercise	1 <sup>a</sup>	19	19 (4)	24 (5)	5	–	–
Chair stand (reps in 30 s)							
Exercise	2	30	19.1 (0.1)	23.8 (1.1)	4.7	–4.2–13.6	0.094
<u>Psychosocial</u>							
Fatigue							
FACT-anemia							
Exercise	1 <sup>a</sup>	27	33.5 (9.7)	36.7 (9.0) <sup>c</sup>	3.2	–	–
Control	1 <sup>a</sup>	25	32.7 (11)	34.3 (11.1) <sup>c</sup>	1.6	–	–
FACT-F							
Exercise	1 <sup>a</sup>	7	14.4 (6.7)	19.0 (10.0) <sup>c</sup>	4.6	–	–
Control	1 <sup>a</sup>	8	10.1 (7.4)	16.5 (11.1) <sup>c</sup>	6.4	–	–
EORTC QLQ-C30 (0–100)							
Exercise	1 <sup>a</sup>	19	50 (20)	24 (14) <sup>b</sup>	–26	–	–
QOL							
FACT-anemia							
Exercise	1 <sup>a</sup>	27	133.9 (23.8)	142.4 (27.0) <sup>c</sup>	8.5	–	–
Control	1 <sup>a</sup>	25	130.6 (30.9)	134.4 (34.0) <sup>c</sup>	3.8	–	–

	Study no.	Subject no.	Baseline mean (SD)	Post-ST mean (SD)	Mean Change	95 % CI	Pvalue
FACT-General							
Exercise	1 <sup>a</sup>	7	73.8 (14.8)	70.6 (18.2) <sup>c</sup>	-3.2	-	-
Control	1 <sup>a</sup>	8	90.4 (10.8)	84.6 (13.8) <sup>c</sup>	-5.8	-	-

Data from references [56, 61, 70, 72]. Upper body composite includes chest press and seated row *FACT-anemia* functional assessment of cancer therapy–anemia, *FACT-F* functional assessment of cancer therapy–fatigue, *EORTC QLQ-C30* European Organization for Research and Treatment of Cancer Quality of Life Questionnaire

<sup>a</sup>As reported in original research article for variables with only one study

<sup>b</sup>Significantly different from baseline value, per original article

<sup>c</sup>No within-group *P* value provided in original article or supplementary data

*Head and Neck Cancer.* Four studies met the study inclusion criteria.

**Strength Assessment:** Upper body strength was improved (42 %, *P* = 0.015) with ST and also improved in controls (19 %, *P* = 0.022; Table 4). Grip strength was maintained with ST and appeared to decline slightly in controls [56]. Lower body strength from a single study showed signs of improvement, but the change was not significant [56].

**Body Composition:** Body composition was unchanged with ST, both in terms of fat and lean mass.

**Functional Assessment:** ST showed a trend to improve chair stand performance (25 %, *P* = 0.094), but other functional tasks were unchanged.

*Mixed Cancers.* Four studies met the study inclusion criteria.

**Strength Assessment:** In the studies that combined cancer types, most cases were breast cancer (53 %), followed prostate (10 %), lymphoma (6.7 %), and colorectal (4.9 %) with less common cancers making up the remaining 25 % (Table 5). Lower body strength increased with ST (24 %, *P* = 0.051), but there was only a trend for upper body improvements (21 %, *P* = 0.106) and was unchanged in controls.

**Table 5.** Effects of ST on strength, body composition, physical function, and psychosocial parameters in mixed cancer survivors

	Study no.	Subject no.	Baseline mean (SD)	Post-ST mean (SD)	Mean Change	95 % CI	Pvalue
<u>Strength</u>							
Lower body composite (kg)							
Exercise	4	251	71.7 (20.8)	89.1 (27.7)	17.4	-0.1–34.9	0.051
Control	1 <sup>a</sup>	33	73.9 (35.8)	76.2 (29.5) <sup>c</sup>	2.3	-	-
Upper body composite (kg)							
Exercise	4	265	27.2 (6.8)	33.0 (7.8)	5.8	-2.3–13.9	0.106
Control	2	66	28.2 (7.7)	27.9 (6.1)	-0.3	-14.9–14.4	0.864
<u>Body composition</u>							
Absolute FM (kg)							
Exercise	1 <sup>a</sup>	20	28.5 (6.9)	28.8 (6.5) <sup>c</sup>	0.3	-	-
Absolute LM (kg)							

	Study no.	Subject no.	Baseline mean (SD)	Post-ST mean (SD)	Mean Change	95 % CI	Pvalue
Exercise	2	30	55.0 (2.9)	55.3 (1.3)	0.3	-14.3-15	0.812
<b>BF (%)</b>							
Exercise	2	54	33.3 (1.1)	33.4 (0.3)	0.1	-6.8-7.1	0.500
Control	1 <sup>a</sup>	33	31.7 (8.6)	38.1 (8.1) <sup>b</sup>	6.4	-	-
<b>Hip BMD (g/cm<sup>2</sup>)</b>							
Exercise	1 <sup>a</sup>	20	0.8 (0.1)	0.8 (0.1)	0.0	-	-
<b>Functional assessments</b>							
<b>12-min walk (m)</b>							
Exercise	1 <sup>a</sup>	34	1022 (186)	1144 (185) <sup>b</sup>	122	-	-
Control	1 <sup>a</sup>	33	1035 (200)	983 (193)	-52	-	-
<b>6-min walk (m)</b>							
Exercise	2	87	459.8 (21.5)	492.8 (15.9)	33.0	-17.9-84	0.077
<b>6-m walk (s)</b>							
Exercise	1 <sup>a</sup>	20	4.6 (0.5)	4.3 (0.4) <sup>b</sup>	-0.3	-	-
<b>50-ft walk (s)</b>							
Exercise	1 <sup>a</sup>	10	11.9 (1.9)	10.5 (1.8) <sup>b</sup>	-1.4	-	-
<b>400-m walk (s)</b>							
Exercise	1 <sup>a</sup>	20	262.6 (43.6)	255.4 (43.4) <sup>b</sup>	-7.2	-	-
<b>Psychosocial</b>							
<b>Fatigue</b>							
<b>MFSI (short form)</b>							
Exercise	1 <sup>a</sup>	20	9.5 (20.1)	5.4 (14.2)	-4.1	-	-
<b>FSI (1-10)</b>							
Exercise	1 <sup>a</sup>	187	3.3 (1.8)	2.5 (1.5) <sup>b</sup>	-0.8	-	-
<b>Anxiety</b>							
<b>BSI-18 (1-5)</b>							
Exercise	1 <sup>a</sup>	20	2.4 (3.8)	2.1 (2.8) <sup>c</sup>	-0.3	-	-
<b>QOL</b>							
<b>MOS-36 (0-100)</b>							
Exercise	1 <sup>a</sup>	20	44.2 (9.4)	46.2 (7.8)	2.0	-	-
<b>Depression</b>							
<b>BSI-18 (1-5)</b>							
Exercise	1 <sup>a</sup>	20	3.2 (4.8)	2.9 (5.2) <sup>c</sup>	-0.3	-	-

Data from references [39••, 57, 58, 59]. Lower body composite includes leg extension and leg press. Upper body composite includes chest and overhead presses and seated row  
*MFSI* Multi-Dimensional Fatigue Symptom Inventory, *FSI* Fatigue Symptom Inventory, *BSI-18* Brief Symptom Inventory-18, *MOS-36 Item* Medical Outcome Study 36-Item Short-Form Health Survey

<sup>a</sup>As reported in original research article for variables with only one study

<sup>b</sup>Significantly different from baseline value, per original article

<sup>c</sup>No within-group *P* value provided in original article or supplementary data

Body Composition: Similar to other cancers (with the exception of reduced % fat observed in breast cancer survivors), ST did not alter body composition. Of note, controls from one study did report a large increase in %fat, from 31.7 to 38.1 % [57].

Functional Assessment: Functional tasks showed increases with ST in individual studies, whereas 6-min walk distance showed only a tendency to improve (7.2 %,  $P = 0.077$ ). Single studies also showed improvements in 12-min walk [57], 6- and 400-m walk [39••], and 50-ft walk [58] performances.

Psychosocial Assessment: Limited data for fatigue and QoL was available, with improved fatigue noted in one study [59] but not another [39••]. QoL and depression were unchanged with ST.

**Table 6.** Effects of ST on strength and body composition in germ cell cancer survivors

	Subject no.	Baseline mean (SD)	Post-ST mean (SD)	Mean change
<u>Strength</u>				
Leg press (kg)				
Exercise	15	155 (38)	194 (41) <sup>a</sup>	39
<u>Body composition</u>				
Absolute LM (kg)				
Exercise	15	60.8 (8.2)	60.1 (8.1) <sup>a</sup>	-0.7
Control	15	61.0 (5.4)	58.9 (4.2) <sup>a</sup>	-2.1
Quadriceps fiber area (um <sup>2</sup> )				
Exercise	15	4877 (812)	5190 (1108)	313
Control	15	4576 (1028)	4272 (605)	-304

Data from reference [60]

<sup>a</sup>Significantly different than baseline value per original article

**Table 7.** Effects of ST on strength and psychosocial parameters in gastro-intestinal cancer survivors

	Subject no.	Baseline mean (SD)	Post-ST mean (SD)	Mean change
<u>Strength</u>				
15RM knee flexor (kg)	11	13.7 (5.6)	16.0 (5.3) <sup>a</sup>	2.3
15RM knee extensor (kg)	11	14.5 (7.3)	15.0 (5.5)	0.5
15RM biceps (kg)	11	13.0 (4.7)	19.0 (6.8) <sup>a</sup>	6.0
15RM triceps (kg)	11	11.1 (4.0)	14.5 (5.3)	3.4
15RM back (kg)	11	11.1 (3.2)	15.7 (7.9) <sup>a</sup>	4.6
<u>Psychosocial</u>				
Fatigue	13	70.7 (21.2)	46.5 (24.3) <sup>a</sup>	-24.2
QOL	17	42.4 (29.7)	56.9 (45.6)	14.5

Data from reference [49]

QOL: EORTC QLQ-C30 European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30

<sup>a</sup>Significantly different than baseline value per original article

*Other Cancers.* Four studies met the study inclusion criteria.

For germ cell and gastro-intestinal cancers, only one study per cancer type examining the effects of ST was available [49, 60], while two studies were available for lung cancer [50, 51]. Additionally, control data was presented only for germ cell cancer [60].

Strength Assessment: ST appeared to be effective across all studies, with a 25 % improvement in leg press 1RM (Table 6) and 17–46 % in 15RM (Table 7) across the major muscle groups for germ cell and gastro-intestinal cancers, respectively. ST also increased upper (31 %,  $P = 0.182$ ) and lower (31 %,  $P = 0.280$ ) body strengths in lung cancer survivors, but these changes did not reach significance (Table 8).

Body Composition: Lean mass and % fat were unaltered with ST in lung and germ cell cancers [49, 50]. There was, however, a 6.4 % increase in quadriceps fiber area with ST in germ cell cancer survivors, while controls showed a decrease of –6.6 % (Table 6), although these differences were not significant [60]. No body composition data was reported for gastro-intestinal patients.

**Table 8.** Effects of ST on strength, physical function, and psychosocial parameters in lung cancer survivors

	Study no.	Subject no.	Baseline -mean (SD)	Post-ST mean (SD)	Mean change	CI	Pvalue
<u>Strength</u>							
Lower body composite (kg)	3	159	53.1 (24.8)	69.7 (36)	16.6	–18.8–52.0	0.182
Upper body composite (kg)	2	88	32.8 (4.9)	42.8 (11.7)	10.0	–51.0–71.0	0.280
<u>Body composition</u>							
BF%	1 <sup>a</sup>	15	34.1 (9.1)	34.1 (9.1)	0.0	–	–
Absolute LM (kg)	1 <sup>a</sup>	15	43.0 (9.7)	43.1 (9.2)	0.1	–	–
<u>Functional assessments</u>							
6-min walk test (m)	2	86	489.0 (53.3)	549.5 (16.3)	60.5	–273.1–392.8	0.285
Up and go (s)	1 <sup>a</sup>	15	6.3 (1.6)	5.5 (5.5) <sup>b</sup>	–0.8	–	–
Chair stand (reps in 30 s)	1 <sup>a</sup>	15	11.2 (3.1)	15.4 (3.8) <sup>b</sup>	4.2	–	–
Arm curl (reps in 30 s)	1 <sup>a</sup>	15	14.6 (3.1)	18.2 (3.2) <sup>b</sup>	3.6	–	–
<u>Aerobic capacity</u>							
VO <sub>2peak</sub> (mL/kg/min)	1 <sup>a</sup>	71	1.3 (0.4)	1.4 (0.5) <sup>b</sup>	0.1	–	–
<u>Psychosocial</u>							
<u>Anxiety</u>							
SSAS10	1 <sup>a</sup>	15	15.1 (3.0)	14.5 (3.0)	–0.6	–	–
HADS-A	1 <sup>a</sup>	71	7.2 (4.4)	6.3 (4.2) <sup>b</sup>	–0.9	–	–
<u>Depression</u>							
ESSD	1 <sup>a</sup>	15	3.8 (4.2)	4.4 (5.6)	0.6	–	–
HADS-A	1 <sup>a</sup>	71	5.3 (3.8)	4.7 (3.5)	–0.6	–	–
Fatigue	1 <sup>a</sup>	15	45.6 (5.2)	46.1 (7.0)	0.5	–	–
<u>QOL</u>							
SF36	1 <sup>a</sup>	15	50.3 (7.9)	53.2 (8.1)	2.9	–	–
FACT-L	1 <sup>a</sup>	71	94.4 (18.9)	96.0 (18.4)	1.6	–	–

Data from references [50, 51]

SSAS10 10-item Spielberger state anxiety scale, ESSD epidemiologic studies short depression, QOL quality of life, SF36 short-form health survey, HADS-A hospital anxiety and depression, FACT-L functional assessment of cancer therapy-lung

<sup>a</sup>As reported in original research article for variables with only one study

<sup>b</sup>Significantly different from baseline value per original article

Functional Assessment: Physical function was assessed in lung cancer survivors, and 6-min walk distance increased by 60 m but was not significantly different from baseline ( $P = 0.285$ ). Improvements were seen in other tasks (13–38 %; Table 8) as reported in a single study [50].

Psychosocial Assessment: Collectively, the improvements in strength and function (where measured) did not appear to consistently translate into improved fatigue or QoL. In gastro-intestinal cancer survivors, fatigue scores worsened during the ST intervention but there was no change in QoL (Table 7) [49]. Fatigue, depression, anxiety, and QoL were all unchanged with ST in lung cancer patients (Table 8) [50].

### Isokinetic and Isometric Maximal Strength Assessment

A few studies examined the role of ST on isokinetic and isometric maximal strength. Because the number of studies overall was low ( $N = 6$ ), the data were grouped together to provide a general overview of these studies results. ST increased isokinetic strength in seven out of eight tasks, while controls only increased in two tasks, as shown in Table 9 [30, 61]. Isometric strength showed similar findings, with eight tasks out of a possible nine being higher following ST [26, 30, 48], a single instance where it was unchanged but was decreased in controls [60], and a study which reported an increase in right leg but not left quadriceps strength [34].

**Table 9.** Isokinetic and isometric muscle strength changes following ST

	Author, year	Subject no.	Cancer type	Movement	Baseline mean (SD)	Post-ST mean (SD)	Change (+, -, and n.s.)	
Isokinetic	Twiss et al. 2009	110	Breast	Hip extension at 60°/s (Nm/kg)	27.7	35.6	+7.9	
		113	Control		27.3	28.6	n.s.	
		110	Breast	Hip flexion at 60°/s (Nm/kg)	30.5	33.4	+2.9	
		113	Control		30.3	29.4	n.s.	
		110	Breast	Knee extension at 60°/s (Nm/kg)	37.9	42.3	+4.4	
		113	Control		36.7	36.9	n.s.	
		110	Breast	Knee flexion at 60°/s (Nm/kg)	18.5	22.4	+3.9	
		113	Control		18.4	18.4	n.s.	
		110	Breast	Wrist extension at 60°/s (Nm/kg)	3.6	4.3	n.s.	
		113	Control		3.4	4.1	+0.7	
	110	Breast	Wrist flexion at 60°/s (Nm/kg)	3.8	7.5	+3.7		
	113	Control		3.8	4.6	+0.8		
		Lonbro et al. 2013	19	Head and neck	Knee extension at 60°/s (Nm)	141	156	+15
			19	Head and neck	Knee flexion at 60°/s (Nm)	80	97	+17
	Schmidt et al. 2015	21	Breast	Leg press (Nm)	85.6 (33.0)	90.1 (29.2)	n.s.	
		26	Control		79.7 (24.5)	80.0 (26.5)	n.s.	
		21	Breast	Bench press (Nm)	113.0 (54.5)	148.5 (37.5)	+35.5	
		26	Control		85.3 (36.5)	91.3 (29.0)	n.s.	
		21	Breast	Latissimus pull-down (Nm)	111.5 (48.5)	147.0 (38.0)	+35.5	
		26	Control		94.2 (42.3)	96.5 (32.8)	n.s.	

	Author, year	Subject no.	Cancer type	Movement	Baseline mean (SD)	Post-ST mean (SD)	Change (+, -, and n.s.)
Isometric	Lonbro et al. 2013	19	Head and neck	Knee extension (Nm)	168	202	+33
		19	Head and neck	Knee flexion (Nm)	95	111	+16
	Johansson et al. 2014	26	Breast	Elbow extensors (N)	141 (25)	154 (27)	+13
		26	Breast	Elbow flexors (N)	214 (33)	227 (33)	+13
		26	Breast	Shoulder adductors (N)	138 (30)	155 (27)	+17
		26	Breast	Shoulder flexors (N)	185 (37)	199 (36)	+14
	Christensen et al. 2014	15	Germ cell	Quadricep (Nm)	247 (59)	249 (66)	n.s.
		15	Control		223 (36)	195 (39)	-28
	Hansen et al. 2009	5	Prostate (ADT)	Left quadricep (Nm)	336.4 (47.7)	361.9 (84.4)	n.s.
		5	Prostate		302.1 (61.9)	298.1 (35.6)	n.s.
		5	Prostate (ADT)	Right quadricep (Nm)	323.0 (94.9)	385.9 (125.8)	+62.9
		5	Prostate		299.5 (55.5)	342.9 (50.8)	n.s.

Data from references [26, 30, 34, 48, 60, 61]

n.s. non-significant change, + significant increase from baseline per original paper, and - significant decrease from baseline per original paper

## Discussion

The primary focus of this review was to assess the independent effects of ST across different types of cancer survivors to determine its efficacy in reducing the side effects of treatment. Overall, 39 studies across seven different cancer types were identified as having completed isolated ST intervention with nearly 70 % of the data coming from studies conducted in breast (42 %) or prostate (26 %) cancers. Of the remaining cancer types, conclusions were drawn from only four studies (head and neck and mixed), two studies in lung, and a single study each in germ cell and gastro-intestinal cancers that ranged on the intensity, length, and frequency of ST and also the cancer stage of the participants. Overall, the independent effects of ST are still limited, with much that remains unclear, as studies have yet to directly compare many basic fitness principles within cancer populations. Instead, exercise interventions from healthy older adults have been the preliminary basis for studies in cancer survivors. However, the response in cancer patients may not always follow the same response as healthy individuals, perhaps due to systemic changes that occur during or following treatment or due to the disease itself; thus, there is a pressing need to examine ST in specific oncology populations. While the choice of ST interventions alone does limit the available pool of studies, it does give specific insight into what effects ST has, whereas previous approaches have permitted combined interventions (e.g., ST + aerobic and ST + impact training) and the relative contribution of each cannot be determined [19, 20, 53••]. Due to the relatively low number of studies in each cancer group that met the inclusion criteria for this systematic review of the literature, for the purpose of organization, this discussion will be separated by the different outcomes assessed. Lastly, recommendations for future research are provided.

Strength

Not surprisingly, studies routinely show robust improvements in maximal strength ranging from 20 to 50 % of the initial value, indicating that the training programs were effective. Some of the control populations also showed improvements in strength (on occasion significant), which is suggestive of a learning effect that does lessen the overall magnitude of improvement, making the results difficult to interpret. Therefore, an adequate familiarization session, where survivors are introduced and experience different modes of strength testing prior to undergoing baseline testing, is an area that should be given much more attention for the improvement of the scientific rigor necessary for more objective interpretation of study results. This issue continues to plague the field of strength research, despite being raised as a limitation several years ago [19].

The possible learning effect observed in some of the control populations during strength testing suggests that the maximal strength values at baseline were likely to be less than true maximums. Because percentages of 1RM were used to prescribe intensity, reporting lower 1RM values has two effects: (1) overestimation of the actual training response and (2) potentially fails to provide the optimal stimulus for adaptation, particularly in studies using lower-intensity training ranges. However, despite the potentially reduced training stimulus, strength adaptations are still likely to occur in untrained populations. Because gains in strength do not transfer directly to higher functional capacity or QoL [35, 52], diminished improvements in strength can occur without the corresponding changes in other areas, likely due to the multi-factorial nature of functional tasks and QoL and sub-optimal training loads.

### Body Composition

Body composition was rarely altered with ST except for the change in % fat in breast cancer, although in a few instances, body composition worsened in controls, suggesting that ST may be able to maintain current fat and lean mass levels, in general. Prostate cancer was the only other cancer with any indication of improvements, as trends were present for improved lean mass and consequently decreased % fat. Interestingly, the only potential changes in body composition were in hormone-dependent cancers, which made up the majority of studies and may have been the only types sufficiently powered to detect statistical differences. Another influential factor may have been the average length of the breast cancer interventions, which was on average at least eight weeks longer. The relatively small caloric deficits ensuing from each ST session would have had greater opportunity to influence body composition. As exercise intensity and frequency were similar across cancer types, they do not appear to play an obvious role. However, if the interventions were structured toward only two training sessions per week and used lower exercise intensity, these could also contribute to the lack of change due to reduced training volume. Finally, the impact of diet was not examined within this review, as exercise + dietary interventions were excluded. But, either caloric excesses or deficits would impact on fat and lean mass gains, respectively, and should be considered for future exploration within exercise oncology.

### Physical Function and Aerobic Capacity

Despite the lower number of studies, particularly in the less common cancers, ST primarily promotes gains in physical function that would offer benefit to the cancer survivor. Improvements in functionality were most consistent in prostate, with all tasks having multiple

studies contributing to the aggregate score and all but one task (chair stand time) was significantly improved from baseline. Other cancers, even breast, usually had a wide range of physical function assessments, so performing a formal analysis was not often possible. Alternatively, many tasks did improve but are from individual studies and only suggest possible effects of specific training protocols. It is curious as to why prostate functional outcomes were more consistent relative to others. Relatively few explanations are apparent, as the exercise training programs were similar to other cancers for duration, intensity, training frequency, disease stage, and strength improvements. While strength is associated with functional status at baseline [62], and alterations in strength may be indicative of changes in physical function, it only explains a relatively small component of the improvements [35, 52].

Despite studies showing that ST can improve aerobic capacity in older adults [63, 64], the changes in cancer survivors are minimal. This is not surprising, given that  $VO_{2peak}$  was often a secondary outcome and studies were not likely powered to detect changes. Additionally, ST is not the optimal intervention to improve oxygen uptake, and without any change in body composition or total mass, relative aerobic capacity remains stable as well. Conversely, 6- and 12-min walk tests and 400-m walk times significantly improved in several different cancer populations (prostate, mixed, and breast). These functional tasks are often used as inexpensive, quick, and safe clinical tests to estimate aerobic capacity and have been validated as a predictor of  $VO_{2peak}$  in cancer patients [65]. The exact reasons for this discrepancy are not apparent but could be related to the validity of performing cardiopulmonary testing in cancer populations.

### Psychosocial Assessment

Improved musculoskeletal function, body composition, and physical function all contribute to fatigue, QoL, and other psychological factors. Given that muscle and physical functions both improved, it is reasonable to expect that psychosocial parameters would follow suit. Previous work has shown that increased muscle endurance was linked to lower fatigue levels, and lower fatigue and greater physical function are associated with higher QoL in prostate cancer patients [35]. Surprisingly, despite consistent improvements elsewhere, psychosocial improvements were rare. Similar to physical function but to an even greater extent, the assessments used were highly variable. In fact, only breast and prostate had multiple studies that used the same questionnaire for at least one outcome. Of the ~30 psychosocial components examined, only body image and relationship improved with ST in breast cancer and fatigue in prostate improved with ST. No change in prostate QoL was found. Single studies do report improved psychosocial parameters but are subject to the limitations seen with physical function. Moreover, in several instances, within-group analysis was not performed or change scores only were reported, further reducing the number of possible outcomes to analyze. Finally, trials that include only a single arm or were pilot studies are susceptible to an attention bias rather than strictly the effects of the ST intervention. While even modest improvements in fatigue, QoL, or other variables is an important outcome, given that it is the patient's perception that is being evaluated, the lack of consistency across this area makes definite conclusions regarding the effects of ST impossible at this time.

## Exercise Interventions

There are some common themes across the different ST interventions in cancer survivors. Typically, studies focused on training the major muscle groups, which follows current recommendations to maximize benefits following ST in untrained individuals. Most participants trained two to three times per week, which corresponds to position stands on training frequency put forth by several governing bodies [66, 67] and is similar to recommendations in healthy older adults and other clinical populations [10, 54, 68]. Interestingly, exercise frequency in prostate cancer was recently investigated and found that more frequent training tended to show greater improvements in strength and functional tasks, whereas less frequent training improved psychosocial function to a greater extent [47••] and is, to our knowledge, one of the first studies to examine this within oncology patients. Exercise intensity ranged from 50 to 85 % of maximal strength, covering a spectrum from low to moderate intensity up to near maximal loads. While not consistently reported, the lack of adverse events indicates that higher-intensity ST appears safe, possibly even more effective. Strength gains in older adults showed a positive, linear relationship with intensity from 50 up to 90 % and were a strong factor in predicting improvement [54]. Current studies in cancer tend to show a similar pattern; however, while intensity may be in the optimal range, the volume of work being performed is often reduced. Thus, when these factors are combined to determine training load (sets  $\times$  repetitions  $\times$  resistance), the resulting training stimulus appears to be somewhat conservative; however, improvements in strength have been observed across the board. Given the paucity of data thus far, this cautious approach is reasonable but should be a focal point of future investigations, particularly in stable cancer survivors, where the effects of different volumes and intensity of training must be explored. Lastly, exercise adherence rates need to be reported. In recent years, this information has become more prevalent in the literature but some studies do not set attendance requirements. Conducting research with cancer survivors presents many challenges with respect to recruiting and retaining participants, so it is understandable why researchers may hesitate to do so. However, by recording voluntary rather than requiring specific adherence rates, this subtle difference may contribute significantly to the varying degree of adaptation observed with ST across studies.

## Recommendations for Future Research

To move the field forward, there are several practical considerations to consider that may improve the overall depth of the field. First, exercise adherence needs to be reported and considered during analysis if participant participation rates vary. Second, familiarization of all primary outcomes (e.g., strength testing) needs to be standard practice and must be reported. This will better reflect the impact of ST and to allow for more accurate exercise prescription. The failure to familiarize likely skews the results of the intervention and makes interpretation of the true effects difficult. Next, the use of clinical exercise and functional tests (e.g., 6-min walk, timed up and go, and 1RM) would allow for a more standardized approach, and greater comparisons between ST protocols within and across cancer types would be possible. Additionally, many clinical tests have minimal clinically important difference [69] that assist physicians in judging the effectiveness of ST interventions and could be an important factor in demonstrating the efficacy of exercise in cancer survivors. Finally, sample sizes need to expand beyond the traditional pilot studies in most cases. While exceptions always exist, multi-site

randomized control trials across multiple sites will help promote exercise oncology toward becoming an accepted and physician-recommended therapy. Until then, ST in cancer patients will continue to be an effective complementary therapy before, during, and after treatment but the impact will be limited. Exercise interventions utilizing ST have great potential to impact the lives of cancer survivors, by helping to increase both quality and duration of life, particularly if such programs can expand to include effective home and community-based protocols that can be delivered on a large scale.

## Conclusions

In summary, ST does appear to promote different benefits that might be specific to different cancer types; however, due to the low number of studies currently available in the literature, the only outcome that consistently showed significant improvements was the measurement of strength. Nevertheless, improvements in strength are of tremendous importance, since in many other clinical populations, it is associated with improved overall functionality, decreased risk of falls, and greater ability to perform activities of daily living. Similar finds could also be achieved in cancer patients, as physical function showed signs of being improved with ST. Therefore, future studies should continue to explore the effects of ST with appropriately powered methodologies examining the ST effects on many important health and QoL outcomes.

## Notes

*Acknowledgments.* There was no funding provided in support of this study.

Compliance with Ethical Standards

*Conflict of Interest.* Erik D. Hanson, Chad W. Wagoner, Travis Anderson, and Claudio L. Battaglini declare that they have no conflict of interest.

*Human and Animal Rights and Informed Consent.* This article does not contain any studies with human or animal subjects performed by any of the authors.

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