


Aerobic and Resistance Exercise in Cancer Patients: Methods and Benefits


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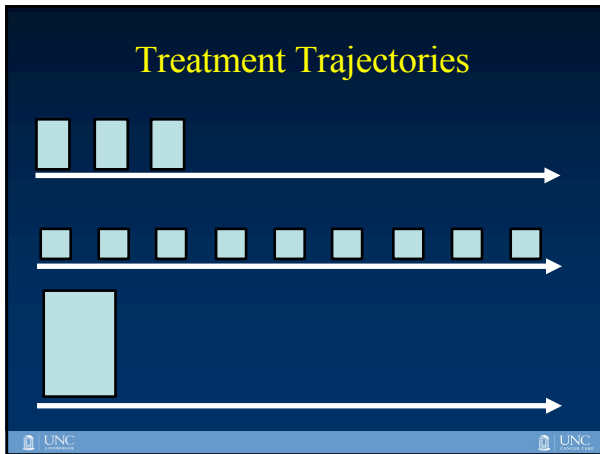
Overview

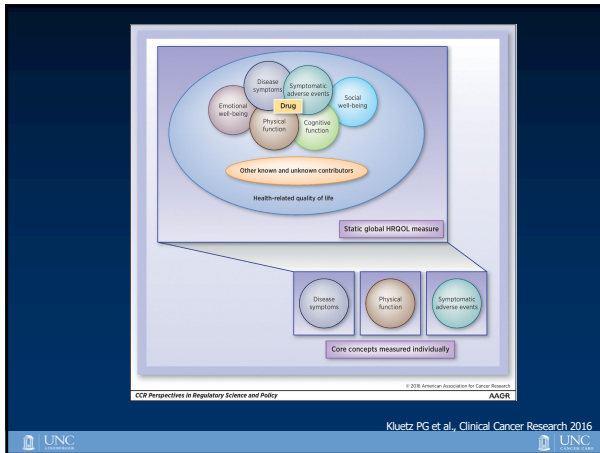
- Physical Performance in Cancer
- Exercise Oncology: Overview
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- Future Directions

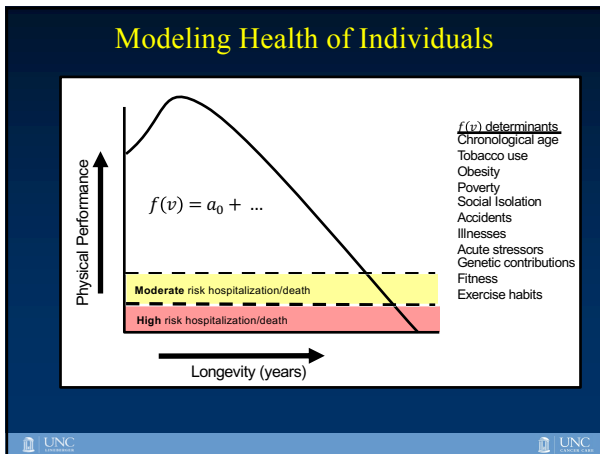


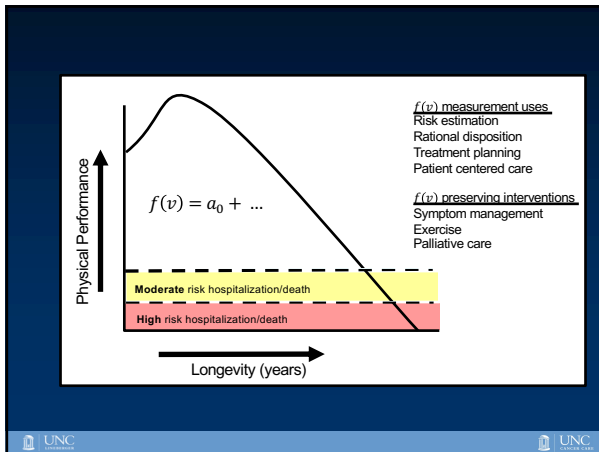
Physical Performance in Cancer





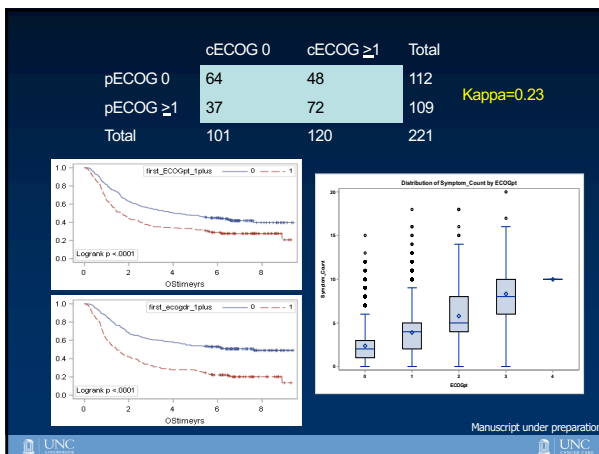


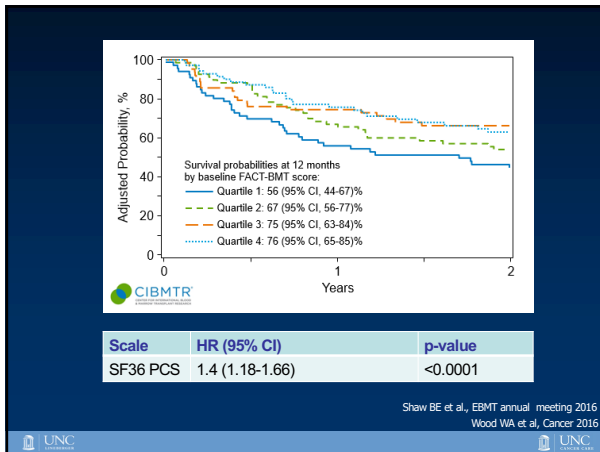


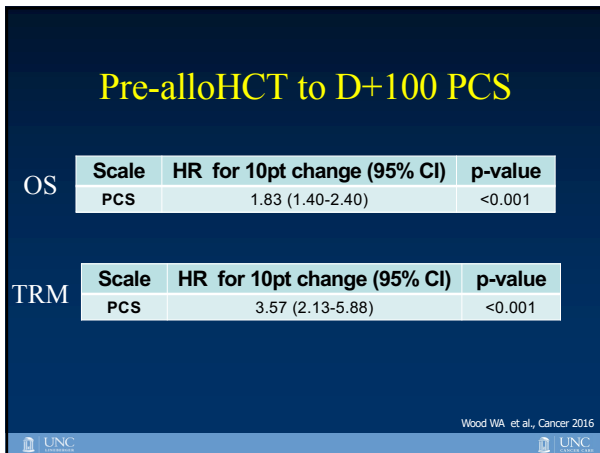


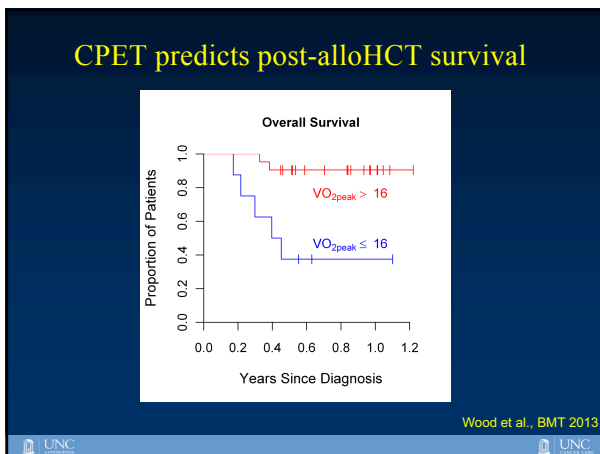
ECOG Performance Status

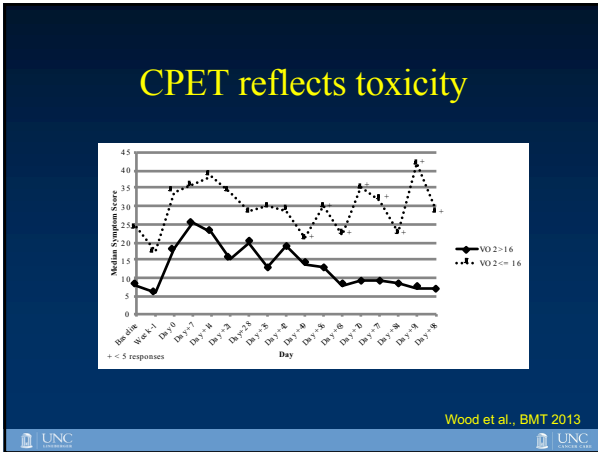
Performance Status	Definition
0	Fully active; no performance restrictions
1	Strenuous physical activity restricted; fully ambulatory and able to carry out light work
2	Capable of all selfcare but unable to carry out any work activities. Up and about > 50 percent of waking hours
3	Capable of only limited selfcare; confined to bed or chair > 50 percent of waking hours
4	Completely disabled; cannot carry out any selfcare; totally confined to bed or chair

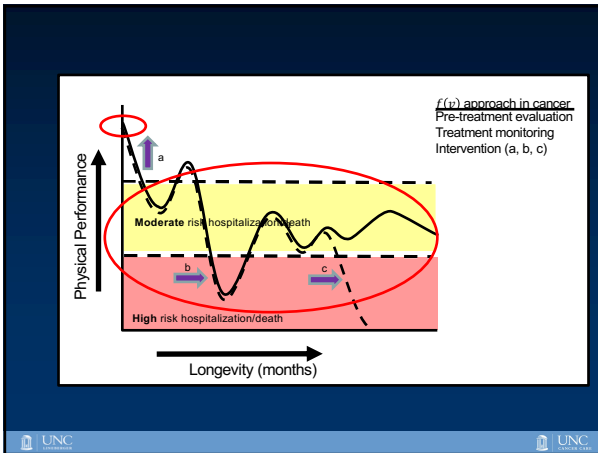




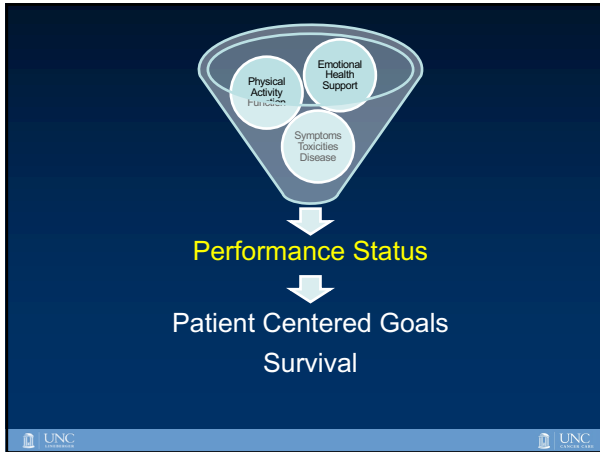






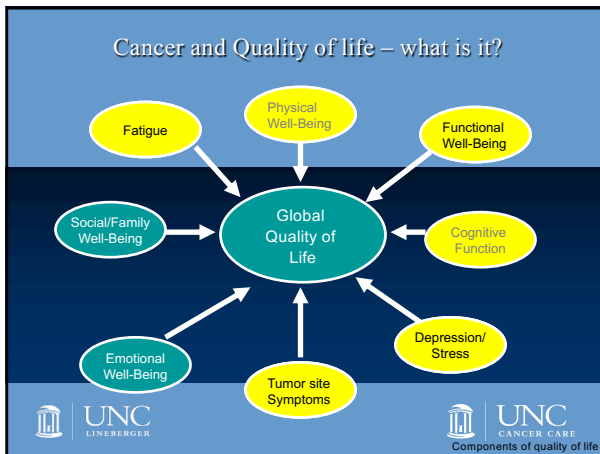


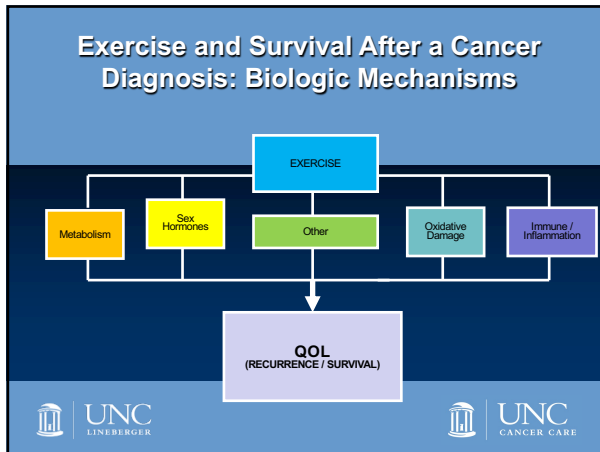




Exercise Oncology: Overview







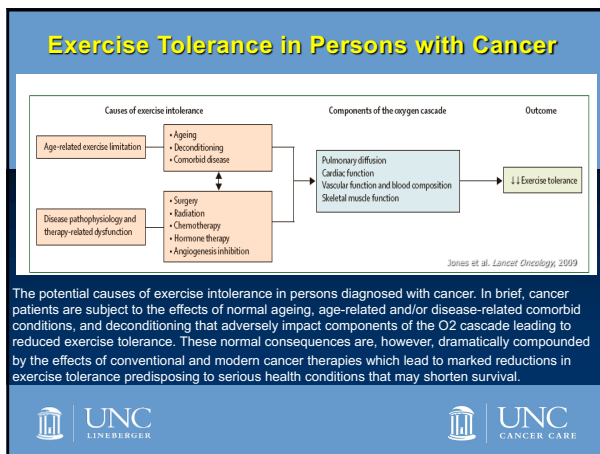
Biological Mechanisms

(Possible mechanisms involved in the relationship between exercise and cancer prevention)

Friedenreich & Orenstein J Nutr 2002

Cancer Site	Possible Mechanisms	Rationale
Colon	↓ gastrointestinal transit time; ↓ ratio of prostanoids, etc.	PA ↑ gut motility and reduces mucosal exposure to carcinogens
Breast	↓ lifetime exposure to estrogen, etc.	PA delays menarche, ↓ ovarian estrogen production; ↓ %BF (↓ fat produced estrogens)
Prostate	↓ exposure to testosterone, etc.	↑ production of sex hormone-binding globulin
All Cancers	↑ anti-tumor immune defenses; decrease IGFs, etc.	May ↑ # and activity of macrophages, lymphokine-activated killer cells (regulating cytokines)

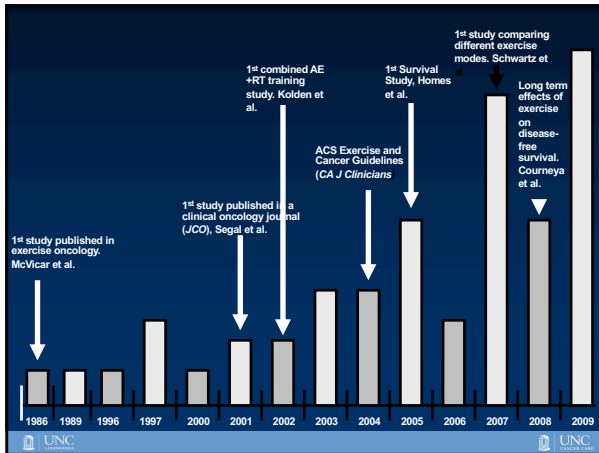
UNC UNC



Exercise Oncology Overview

- Approximately 200 plus studies to date have examined the effects of exercise in oncology patients
- From 2008 to 2013 approximate 35 exercise intervention studies that included some objective measurement of physical or mental function and used traditional exercise interventions were published







"An ever-growing number of studies in the area of exercise oncology, especially those examining the effects of exercise training in breast cancer survivors, speak loudly to the increased interest by the medical community in exploring complementary interventions that can alleviate treatment-related side effects and improve quality of life of cancer patients".

Battaglini et al, 2014



RESULTS OF STUDIES 2000-2006

- 11 studies met the review inclusion criteria with 6 of them being randomized controlled trials
- 54.5% (n=6) of the studies were conducted in patients who had completed chemotherapy and/or radiation therapy, (45.5%) were conducted with patients undergoing treatment (n=4), and 1 study including patients in and off-treatment as part of the study design
- 68.8% of the studies combined aerobic with resistance training with only 31.2% of the studies using aerobic training only
- Exercise prescription, 8-14 weeks, 2-4 days per week for approximately 30 minutes of aerobic and 40 minutes of resistance training, with intensities varying from 50-80% of peak heart rate, 50-75% of heart rate reserve, rate of perceived exertion (RPE) between 11-15.
- The resistance training consisted of exercises targeting major muscles groups performed for 2-3 sets, with approximately 10-12 repetitions using weight training machines, dumbbells, and rubber bands.

1989-1999 Study Results Summary

Measure	No. of studies	N	Baseline		Post-Intervention		Change		P
			Mean	SD	Mean	SD	Mean	95% CI	
Cardiorespiratory Function									
Resting $\dot{V}O_{2max}$, mL.kg ⁻¹ .min ⁻¹	0								
Exercise	0								
Control	0								
Bike $\dot{V}O_{2max}$, mL.kg ⁻¹ .min ⁻¹	5	81	23.26	2.95	25.40	2.75	2.14	-2.69-1.59	.000
Exercise	2	36	23.10	6.08	21.95	5.30	-1.15	-5.84-8.14	.261
Control	2	36	23.10	6.08	21.95	5.30	-1.15	-5.84-8.14	.261
Bike $\dot{V}O_{2max}$, L.min	1	22	1.67	.35	1.81	.37	0.14	-	-
Exercise	1	19	1.60	.36	1.63	.35	.03	-	-
Control	1	19	1.60	.36	1.63	.35	.03	-	-
Est. Treadmill $\dot{V}O_{2max}$, mL.kg ⁻¹ .min ⁻¹	1	40	30.56	-	35.2	-	4.62	-	-
Exercise	0								
Control	0								
Est. Bike $\dot{V}O_{2max}$, mL.kg ⁻¹ .min ⁻¹	1	19	1.60	-	1.63	-	0.03	-	-
Exercise	0								
Control	0								
$\dot{V}O_{2max}$, L.min ⁻¹	1	22	1.67	-	1.81	-	0.14	-	-
Exercise	1	19	1.60	-	1.63	-	0.03	-	-
Control	1	19	1.60	-	1.63	-	0.03	-	-
mCAFT $\dot{V}O_{2max}$, mL.kg ⁻¹ .min ⁻¹	1	82	25.7	.28	26.45	.49	-0.75	-	-
Exercise	1	41	25.1	6.1	25.1	6.1	0.0	-	-
Control	1	41	25.1	6.1	25.1	6.1	0.0	-	-
12-min walk test, m	2	56	1032.35	8.98	1264.80	126.15	232.45	-1446.53- 981.63	.248
Exercise	2	37	1045.20	59.11	944.80	194.03	-100.4	-1111.77- 1312.57	.484
Control	2	37	1045.20	59.11	944.80	194.03	-100.4	-1111.77- 1312.57	.484
6min walk test, m	1	9	672.9	-	776.03	-	103.13	-	-
Exercise	0								
Control	0								
2hr walk test, min	0								
Exercise	0								
Control	0								
1 mile walk test, min	1	43	17.45	-	16.34	-	-1.11	-	-
Exercise	1	43	17.45	-	17.85	-	0.2	-	-
Control	1	43	17.45	-	17.85	-	0.2	-	-

Body Composition

Measure	No. of studies	N	Baseline		Post-Intervention		Change		P
			Mean	SD	Mean	SD	Mean	95% CI	
Body mass, kg									
Exercise	9	248	69.47	10.36	68.43	9.54	-1.04	-0.38-2.45	.131
Control	7	183	75.8	6.46	76.64	6.31	0.84	-2.15-0.47	.166
Fat mass, kg									
Exercise	4	75	25.95	9.73	23.93	8.57	-2.03	-1.76-5.81	.187
Control	3	73	32.90	8.18	33.20	6.52	-0.30	-4.52-3.92	.789
Lean mass, kg									
Exercise	0								
Control	0								
Body fat, %									
Exercise	8	218	33.82	8.25	32.31	8.03	1.51	0.37-2.66	.017
Control	6	165	36.48	9.29	36.66	8.96	0.18	-1.19-0.84	.873
Lean body mass, %									
Exercise	0								
Control	0								
Strength									
Measure	No. of studies	N	Baseline		Post-Intervention		Change		P
			Mean	SD	Mean	SD	Mean	95% CI	
Strength									
1RM UB Composite, kg									
Exercise	1	21	9.1	1.93	10.16	2.08	0.96	-	-
Control	1	15	8.77	1.75	8.59	1.29	-0.18	-	-
1RM LB Composite, kg									
Exercise	0								
Control	0								
1RM UB, kg									
Exercise	2	67	22.63	10.15	30.23	13.39	7.61	-36.77-21.56	.187
Control	0								
1RM LB, kg									
Exercise	3	76	99.87	31.29	133.19	57.10	33.32	-104.03-37.39	.180
Control	0								

Cardiorespiratory Function

Measure	No. of studies	N	Baseline		Post-Intervention		Mean Change	95% CI	P
			Mean	SD	Mean	SD			
Cardiorespiratory Function									
Treadmill $\dot{V}O_{2max}$, mL.kg ⁻¹ .min ⁻¹									
Exercise	1	71	25.2	-	25.7	-	+0.5	-	-
Control	1	73	24.6	-	23.5	-	-1.3	-	-
Treadmill $\dot{V}O_{2max}$, L.min ⁻¹									
Exercise	1	71	1.72	-	1.77	-	+0.05	-	-
Control	1	73	1.76	-	1.66	-	-0.08	-	-
Est. Treadmill $\dot{V}O_{2max}$, mL.kg ⁻¹ .min ⁻¹									
Exercise	9	285	23.51	4.56	27.05	5.12	+3.54	-4.84 to -2.26	<.0001
Control	5	88	24.45	6.08	25.02	6.80	+0.57	-2.00 to 0.85	.328
Bike $\dot{V}O_{2max}$, mL.kg ⁻¹ .min ⁻¹									
Exercise	2	37	22.11	3.68	24.49	3.38	+2.38	-5.12 to 0.35	.057
Control	2	33	21.98	6.34	20.83	6.82	-1.15	-3.23 to 5.54	.165
Bike $\dot{V}O_{2max}$, L.min ⁻¹									
Exercise	1	10	1.41	-	1.59	-	+0.18	-	-
Control	1	10	1.34	-	1.2	-	-0.14	-	-
Est. Bike $\dot{V}O_{2max}$, mL.kg ⁻¹ .min ⁻¹									
Exercise	1	18	21.07	-	23.88	-	+2.81	-	-
Control	0	0	-	-	-	-	-	-	-
6-min Walk Test, m									
Exercise	2	30	483.23	56.37	482.57	49.84	+19.34	-78.04 to 39.36	.146
Control	2	32	450.14	33.57	440.62	33.40	-9.52	8.05 to 10.98	.003
12-min Walk Test, m									
Exercise	3	129	931	102.93	1093	160.18	+162	-344.35 to 20.35	.062
Control	3	124	921.03	148.50	898.13	132.92	-32.9	-96.10 to 161.90	.387
2 km Walk Test, min									
Exercise	3	313	18.05	0.44	17.38	0.42	-0.67	-0.13 to 1.47	.016
Control	3	290	17.94	0.33	17.33	0.23	-0.61	0.34 to 0.98	.010

Abbreviations: $\dot{V}O_{2max}$, peak oxygen uptake; Treadmill $\dot{V}O_{2max}$, $\dot{V}O_{2max}$ obtained directly through CPET with gas exchange; Est. Treadmill $\dot{V}O_{2max}$, $\dot{V}O_{2max}$ estimated via submaximal CPET; Est., Estimated.

Body Composition

Measure	No. of studies	N	Baseline		Post-Intervention		Mean Change	95% CI	P
			Mean	SD	Mean	SD			
Body Composition									
Body Mass, kg									
Exercise	10	550	74.66	3.94	74.25	3.84	-0.41	-0.38 to 1.20	.268
Control	9	527	73.59	4.63	74.72	4.69	+1.13	-2.35 to 0.09	.065
Fat Mass, kg									
Exercise	1	262	25.73	-	26.43	-	+0.70	-	-
Control	1	236	24.45	-	25.12	-	+0.67	-	-
Body Fat, %									
Exercise	13	609	38.0	5.03	37.15	5.80	-0.85	0.06 to 1.64	.037
Control	11	536	38.50	4.41	39.0	4.12	+0.50	-0.84 to -0.16	.009
Lean Body Mass, kg									
Exercise	3	330	43.91	0.32	44.29	0.31	+0.38	-0.45 to -0.31	.012
Control	3	308	43.45	0.37	43.27	0.56	-0.18	-0.49 to 0.87	.358
Lean Body Mass, %									
Exercise	1	10	71.0	-	74.1	-	+3.1	-	-
Control	1	10	69.1	-	68.9	-	-0.2	-	-

Psychosocial Measurements



Measure	No. of studies	N	Baseline		Post-Intervention		Mean Change	95% CI	P
			Mean	SD	Mean	SD			
Quality of Life									
EORTC, 0 - 100									
Exercise	2	296	74.05	13.36	79.95	7.71	+5.90	-56.72 to 44.92	.379
Control	1	236	80.9	-	84.3	-	+3.4	-	-
FACT-G, 0 - 104									
Exercise	4	165	78.98	3.30	85.88	4.22	+6.90	-11.93 to -1.88	.022
Control	4	178	79.74	6.89	79.63	10.88	-0.11	-10.50 to 10.72	.976
FACT-B, 0 - 104									
Exercise	5	99	103.92	6.75	110.32	4.25	+6.40	-15.12 to 2.32	.111
Control	5	82	106.76	5.72	106.53	9.98	-2.23	-9.18 to 13.64	.616
SF-36 Physical Function, 0 - 100									
Exercise	1	25	47.41	-	50.80	-	+3.39	-	-
Control	0	0	-	-	-	-	-	-	-
Fatigue*									
Exercise	3	140	3.88	1.05	3.08	0.41	-0.80	-1.37 to 2.97	.250
Control	2	45	3.78	0.17	3.91	0.35	+0.13	-1.78 to 1.52	.500
FSL, 1 - 10									
Exercise	1	11	3.4	-	3.4	-	0	-	-
Control	1	9	3.25	-	3.3	-	+0.05	-	-
FACT-F									
Exercise	4	373	37.85	2.95	39.58	5.87	+1.73	-6.97 to 3.52	.372
Control	4	351	40.11	4.07	40.08	3.73	-0.03	-3.03 to 3.09	.975
Depression**									
BDI, 0 - 83									
Exercise	2	83	11.75	0.07	8.35	0.35	-3.40	0.86 to 5.94	.087
Control	2	102	10.96	2.89	11.21	0.42	+0.25	-22.49 to 21.99	.910
R-Beck Inventory									
Exercise	2	295	8.53	7.11	4.60	1.98	-3.93	-42.19 to 50.05	.425
Control	2	271	7.15	5.15	6.67	5.18	-0.48	0.23 to 0.73	.027
CES-D, 0 - 24									
Exercise	1	71	12.8	-	9.7	-	-3.1	-	-
Control	1	73	13.9	-	10.8	-	-3.1	-	-
HADS, 0 - 21									
Exercise	1	30	4.17	-	2.7	-	-1.47	-	-
Control	1	28	4.79	-	4.64	-	-0.15	-	-

*Lower scores reflect lower fatigue; **Lower scores reflect lower depression; BDI, Beck Depression Inventory

2007-2013 Study Results Summary



- Significant improvement in cardiorespiratory function was observed for the exercise group (improvement from baseline of $3.54 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, $p < .0005$) using estimated $\text{VO}_{2\text{peak}}$
- When measured directly using a cycle ergometer test protocol with gas exchange, improvement from baseline of $2.38 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, $p = .057$)
- Most notorious changes in in body composition were significant decrease in body fat % ($p = .037$) and increase in lean body mass ($p = .002$)
- Quality of life significantly improved in the exercise group (FACT-G; improvement of +6.90 points, $p = .022$)
- The effects of exercise training significantly reduced depression levels in the exercise group (reduction of -3.40 points, $p = .037$)
- Minimal adverse events due to exercise were reported; when reported, events such as lightheaded, hypotension, nausea, and weakness during exercise testing

During the period between 2007-2013, noticeable improvements in study designs and testing of different exercise training protocol were observed.




RESULTS OF RESISTANCE TRAINING STUDIES 2007-2013

- Only 4 studies used resistance training as the main mode of exercise training and 3 used resistance training as an arm part of the study design
- The intensity for resistance training ranged from 55-85% of 1-RM
- For studies that used resistance training as their major mode of exercise or as the mode of a study arm used weight machines, free weights, elastic bands, tubing, therapeutic balls, and resistance-training circuits
- The average frequency of training was 3 days per week ranging from 2-5 training sessions per week, with overall training duration average of 23 weeks (range of 3-48 weeks)



2007-2013 Strength Training Study Results Summary

- No significant changes in cardiorespiratory function observed
- Significant increase in body mass and lean body mass was observed in the exercise group (increase of 1.20 and 0.65 kg, $p = .016$ and $p = .049$, respectively)
- Upper body strength significantly increased in the exercise group (increase of +5.31 kg, $p = .005$) while for lower body, strength significantly increased in both, exercise and control groups ($p = 0.25$, $p = .008$ respectively) with a greater increase observed in the exercise group (increase of +17.82 kg vs. +5.42 kg, respectively)
- No significant changes in quality of life were observed in either the exercise and control groups.



SUMMARY OF OVERALL RESULTS OF THE STUDIES CONDUCTED DURING THE PAST 25 YEARS

- From 1989 – 1999: only aerobic studies, with very heterogeneous samples of patients, small sample sizes, and poorly described exercise interventions.
- From 2000-2006: beginning of the exploration of different modes of exercise including resistance training; improvement on study designs including larger sample sizes and randomized controlled trials, and better description of exercise training prescriptions. However, heterogeneity of exercise prescriptions make it nearly impossible to evaluate the effects of exercise training
- From 2007-2013: a larger number of studies were conducted; emphasis on issues associated with body composition; more pronounced improvements observed in many studies outcomes; better designed studies accounting for limitations of previous studies.





The past 25 years of research on the effects of exercise in cancer survivors are promising !

- Since this is a relatively new area of research and until larger randomized trials are completed (controlling for many variables that can confound study results such as type, frequency, intensity of exercise, different types of cancer treatments, age of patients, previous fitness levels, and other co-morbidities that can further diminish the tolerability for exercise participation) definite conclusions and more precise exercise summary guidelines can be presented
- Despite these methodological limitations and our inability to currently provide specific exercise guidelines for breast cancer patients, general-generic exercise set forth by the American College of Sports Medicine are available
- Based on current research, patients should engage, whenever possible, in 150 minutes per week of moderate-intensity exercise spread throughout the week, that the exercise prescription should include aerobic and resistance modes of exercise, and that the prescription should be individualized taking into consideration the limitations of each patients





Take Home Messages





Physical performance is important in cancer

- Predicts outcomes
- Associated with symptoms
- Tied to patients' experiences with cancer and life goals





There are several ways to measure and model physical performance in cancer

- Patient report
- Testing (e.g. CPET)
- Wearable sensors



Exercise maintains physical performance



- Aerobic
- Strength
- Combined



Future Directions



Our challenge is to make physical performance measurement and physical activity prescription a regular part of cancer care to improve cancer outcomes and patients' lives





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THANK YOU

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