Exercise as Synergistic Medicine for Cancer

Daniel A. Galvão, PhD
Co-Director, Exercise Medicine Research Institute
Cancer Council Western Australia Research Fellow

NHMRC Centre for Research Excellence
PROSTATE CANCER SURVIVORSHIP

Exercise Medicine Research Institute

AUSTRALIA ECU EDITH COWAN UNIVERSITY

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Overview

- Developments in *Exercise Oncology*
- Clinical questions in *Exercise Oncology*
- Implications for disease outcome
- Pre-clinical studies/ biological mechanisms
- Exercise guideline/recommendations

Winningham, MacVicar, and Burke 1986
The Physician and Sports Medicine

Exercise for Cancer Patients: Guidelines and Precautions

Maryl L. Winningham, PhD
Mary G. MacVicar, RN, PhD
Carol A. Burke, BS

Photos: Shadowlight © 1986

In brief: With more cancer patients recovering or surviving for long periods, techniques are needed to help them overcome the disabling effects of the disease, the therapies, and prolonged immobilization. Previous research and clinical observations indicate that exercise is a promising restorative technique for cancer patients, but it is a fairly new concept; no guidelines exist for objectively measuring the functional capacity of such patients or designing safe programs for them. Medical teams that devise such exercise programs should consider the fitness, age, and current medical and psychological status of the patient, the type and stage of cancer, the possibility of coronary artery disease, side effects of therapy, and the timing of blood tests and chemotherapy.

Exercise as a restorative technique for cancer patients is a relatively novel concept. Forty years ago, people were amazed by the idea of cardiac patients exercising, but rehabilitation programs for cardiac patients now are commonplace. Fear of cancer has prevented widespread understanding of the potential for the recovery, long-term survival, and rehabilitation of cancer patients. It is time to develop concepts of exercise for those suffering from cancer, which is second only to heart disease as a cause of death.[1]

Advances in treatment methods have led to increased survival and cure rates for individuals with a variety of malignant neoplasms. Expectation of increased survival rates has focused attention on the need for rehabilitative techniques to mitigate the disabling consequences of disease and therapy. Progressive loss of function is commonly reported in cancer patients; however, it is unclear whether this deterioration is due to cancer and its therapy or to the debilitating effects of inactivity and bed rest. The immobilization syndrome in itself can lead to life-threatening conditions.[2,3] Decreased muscle strength and endurance, negative nitrogen balance, phlebothromboses, pneumonitis, renal calculi, increased diuresis, orthostatic hypotension, and skin breakdown are but a few of the

continued

Patients exercise under the supervision of an interdisciplinary team at the Ohio State University Comprehensive Cancer Center.

Dr Winningham is an exercise physiologist and director of the Health Promotion and Restorative Training Laboratory, College of Nursing, Ohio State University; Dr MacVicar is an associate professor in the College of Nursing and the Comprehensive Cancer Center, Ohio State University; and Ms Burke is a student in the College of Medicine, Ohio State University. Dr Winningham and Dr MacVicar are members of the American College of Sports Medicine.

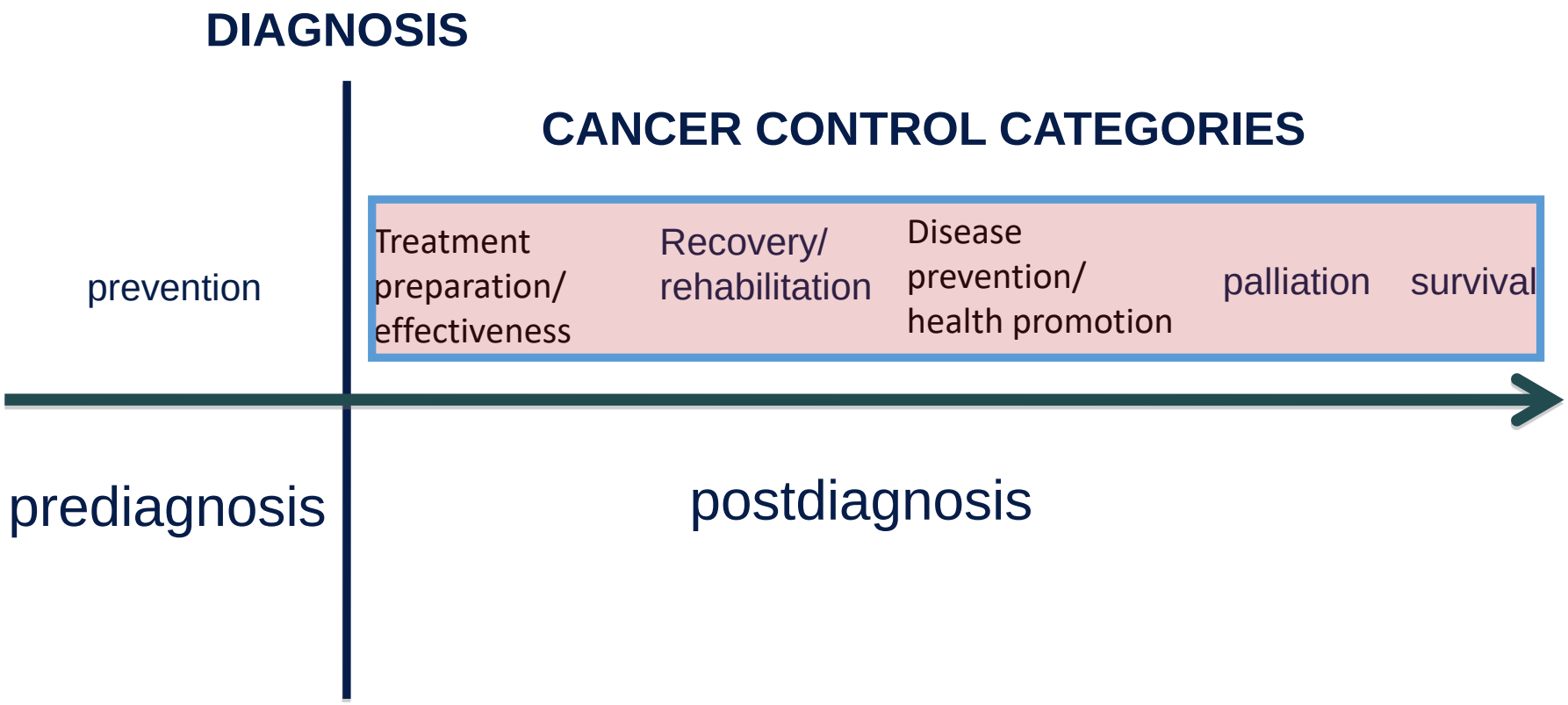
"Historically clinicians advised cancer patients to rest and avoid activity given the rigors of undertaking treatment"

"Three decades of research is showing that exercise plays a vital role in cancer prevention and control"

Schmitz et al. American College of Sports Medicine. *Med Sci Sports Exerc.* 2010;42(7):1409-

Physical Activity & Cancer Control Framework

Specific phases along the cancer continuum



Courneya and Friedenreich *Sem Onco Nurs* 2007;23:242-52

Exercise Oncology in *Journal of Clinical Oncology* - 2001-2016

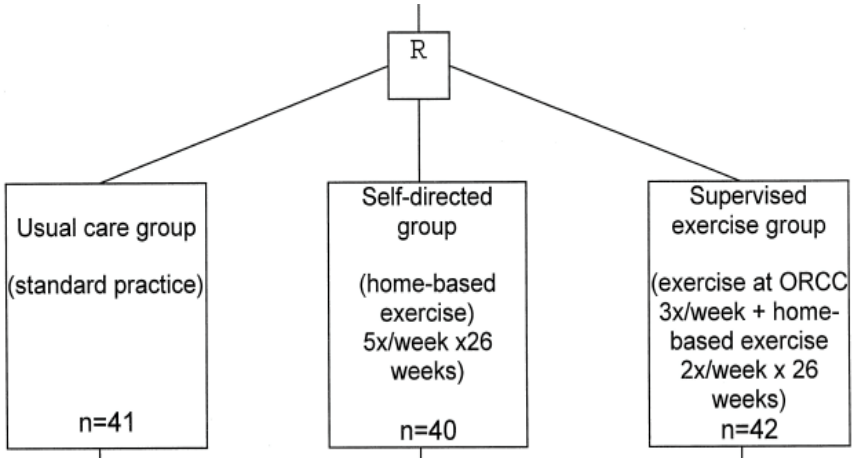
First RCTs in
Journal of Clinical Oncology (JCO)

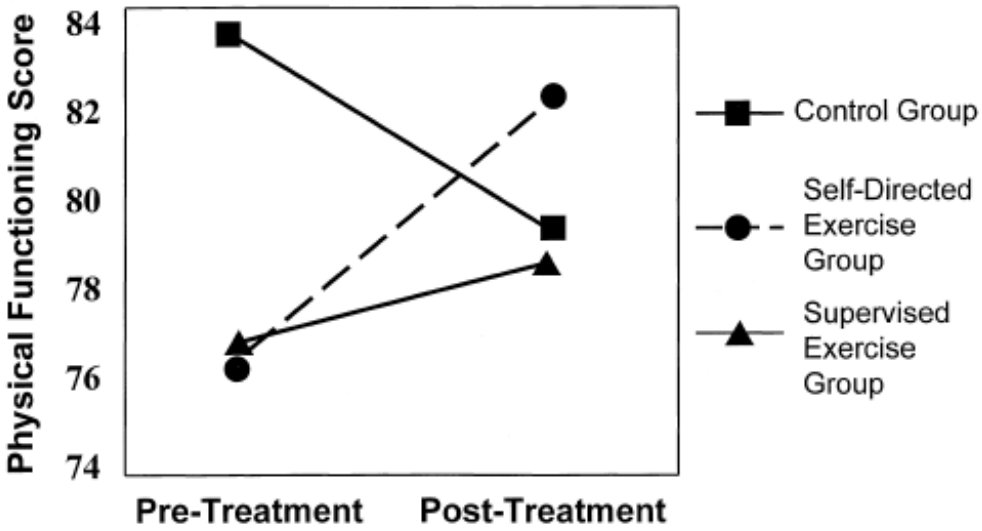
Courneya et al.
Galvão and Newton
Segal et al.
Meyerhardt et al.
Segal et al.
Courneya et al.
Courneya et al.
Segal et al.
Rudden et al.
Kenfield et al.
Galvão et al.
Irwin et al.
ASCO - Obesity
ASCO - PCa
Jones
Waart et al.
ASCO - Breast

2001 **2005** **2009** **2013** **2016**

Structured Exercise Improves Physical Functioning in Women With Stages I and II Breast Cancer: Results of a Randomized Controlled Trial

By Roanne Segal, William Evans, Darren Johnson, Julie Smith, Sal Colletta, Jane Gayton, Stephanie Woodard, George Wells, and Robert Reid





EX can blunt reduced physical functioning

EX improved aerobic capacity (3.5 mL/kg/min; P= .01) - not receiving chemotherapy

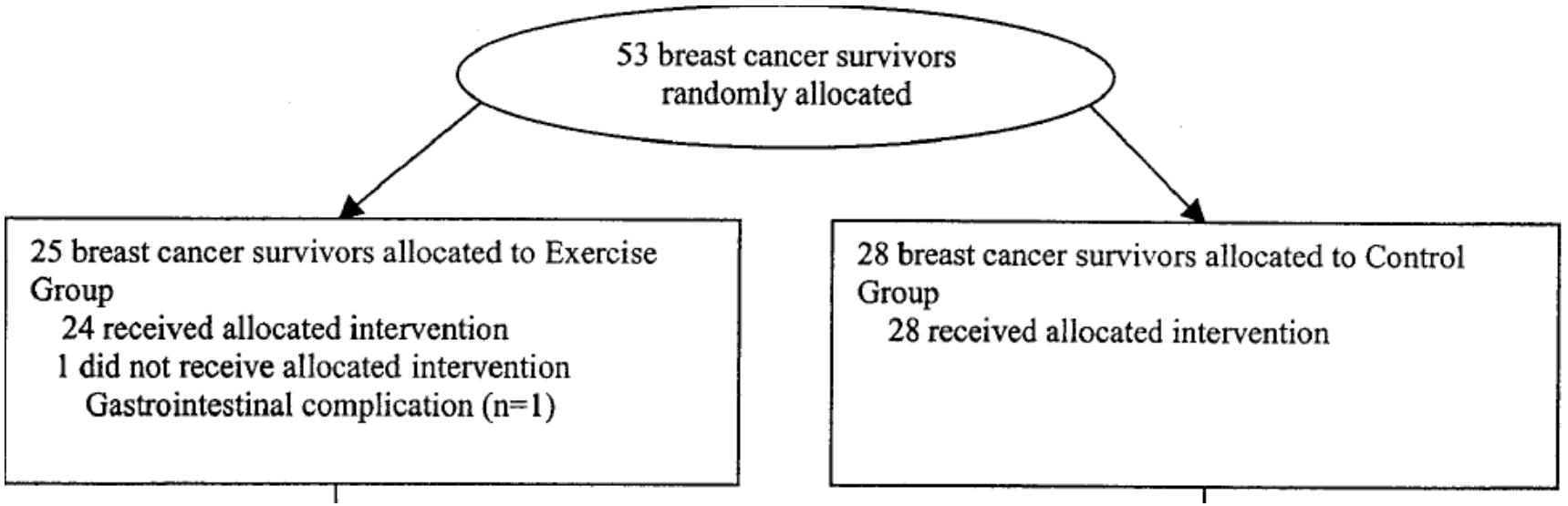
EX reduced body weight (24.8 kg; P < .05) - participants not receiving chemotherapy

No major adverse events

J Clin Oncol 19:657-665.

Randomized Controlled Trial of Exercise Training in Postmenopausal Breast Cancer Survivors: Cardiopulmonary and Quality of Life Outcomes

By Kerry S. Courneya, John R. Mackey, Gordon J. Bell, Lee W. Jones, Catherine J. Field, and Adrian S. Fairey

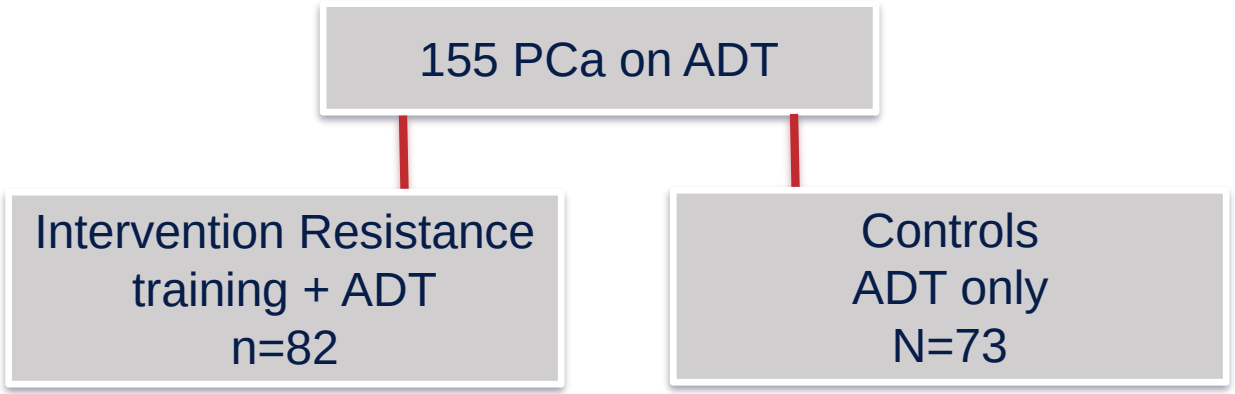


Peak oxygen consumption increased EX vs CON (0.29 L/min; 95% CI, 0.18 to 0.40; P <.001)
Overall QOL increased EX vs CON (8.8 points; 95% CI, 3.6 to 14.0; P=.001)
Change in peak oxygen consumption ***correlated with change in QOL*** (r =0.45; P < .01)
No major adverse events

J Clin Oncol 21:1660-1668.

Resistance Exercise in Men Receiving Androgen Deprivation Therapy for Prostate Cancer

By Roanne J. Segal, Robert D. Reid, Kerry S. Courneya, Shawn C. Malone, Matthew B. Parliament, Chris G. Scott, Peter M. Venner, H. Arthur Quinney, Lee W. Jones, Monika E. Slovinec D'Angelo, and George A. Wells



	Pretest		Posttest		Change†		
	Mean	SD	Mean	SD	Mean change	SD	P‡
All patients							
Intervention (n = 82)	118.2	16.7	120.2	15.9	2.0	9.1	.001
Control (n = 73)	120.9	13.6	117.6	14.9	−3.3	10.2	

EX had ***less interference from fatigue on activities of daily living*** (P=.002) than CON
Ex had ***higher quality of life*** (P=.001) than CON

J Clin Oncol 21:1653-1659.

Journal of Clinical Oncology

The Official Journal of the American Society of Clinical Oncology

Vol 21, No 9 **May 1, 2003**

Exercise and Cancer: No Pain, Some Gain?

Leonard Reyno
QEII Cancer Care Program
Halifax, Nova Scotia, Canada

EDITORIAL

As clinicians, we are often asked: ***"what more can I do to improve my overall health"?***

*"They respond directly to concerns identified by patients and families and do so in the context of randomized controlled trials…****importance of studies of this type will only increase****."*

Journal of Clinical Oncology, Vol 21, No 9 (May 1), 2003: pp 1651-1652
DOI: 10.1200/JCO.2003.12.066

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

Review of Exercise Intervention Studies in Cancer Patients

Daniel A. Galvão and Robert U. Newton

By June 2004 – 20+ studies; majority of studies with breast cancer using cardiovascular exercise

"Evidence underlines the preliminary positive physiological and psychological benefits from exercise when undertaken during or after cancer treatment."

Table 3. Guidelines and Possible Physiological Outcomes from Exercise in Cancer Patients

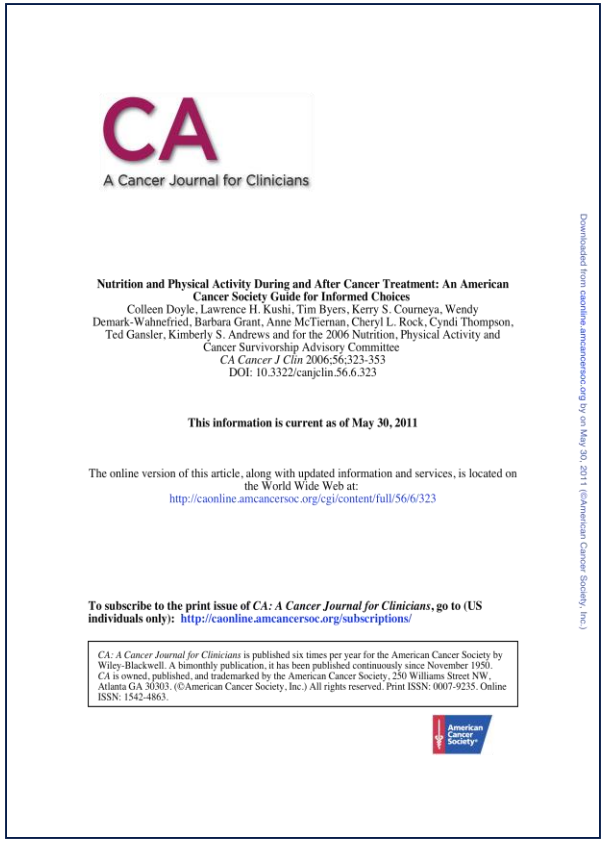
Exercise Modality	Intensity	Frequency (/week)	Volume	Dosage	Cancer Relevant Expected Outcomes
Cardiovascular exercises	55-90% MHR 40-85% MHRR	3-5	20-60 minutes	Continuous or intermittent	↑ Cardiopulmonary function ↑ Insulin sensitivity*, ↑ HDL*, ↓ LDL* ↓ Fat mass, ↓ Fatigue
Anabolic/resistance exercises	50-80% 1-RM 6-12 RM	1-3	1-4 sets per muscle group		↑ Muscle mass*, ↑ Muscle strength ↑ Muscle power*, ↑ Muscle endurance ↑ BMD*, ↑ FP, ↓ Fatigue ↑ Resting metabolic rate*, ↓ Fat mass*
Flexibility exercises	?	2-3	2-4 sets per muscle group	10-30 seconds	↑ ↔ Range of motion

Abbreviations: ↑, increase; ↓, decrease; ↔, no change; MHR, maximum heart rate; MHRR, maximum heart rate reserve; HDL, high-density lipoprotein; LDL, low-density lipoprotein; BMD, bone mineral density; FP, functional performance; RM, repetition maximum.
*Data not available with cancer population, recommendation based from studies undertaken with noncancer population.

J Clin Oncol 23:899-909. © 2005 by American Society of Clinical Oncology

Major Developments ACSM 2010

American Cancer Society



CA
A Cancer Journal for Clinicians

Nutrition and Physical Activity During and After Cancer Treatment: An American Cancer Society Guide for Informed Choices

Colleen Doyle, Lawrence H. Kushi, Tim Byers, Kerry S. Courneya, Wendy Demark-Wahnefried, Barbara Grant, Anne McTiernan, Cheryl L. Rock, Cyndi Thompson, Ted Gansler, Kimberly S. Andrews and for the 2006 Nutrition, Physical Activity and Cancer Survivorship Advisory Committee

CA Cancer J Clin 2006;56;323-353
DOI: 10.3322/canjclin.56.6.323

Exercise & Sports Science Australia

ELSEVIER

Available online at www.sciencedirect.com
ScienceDirect
Journal of Science and Medicine in Sport 12 (2009) 428–434

Journal of Science and Medicine in Sport
www.elsevier.com/locate/jsams

Position stand

Australian Association for Exercise and Sport Science position stand: Optimising cancer outcomes through exercise

Sandra C. Hayes [a,*], Rosalind R. Spence [b], Daniel A. Galvão [c], Robert U. Newton [c]

[a] *Institute of Health and Biomedical Innovation, School of Public Health, Queensland University of Technology, Australia*
[b] *School of Human Movement Studies, University of Queensland, Australia*
[c] *Vario Health Institute, Edith Cowan University, Western Australia, Australia*

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Abstract

Cancer represents a major public health concern in Australia. Causes of cancer are multifactorial with lack of physical activity being considered one of the known risk factors, particularly for breast and colorectal cancers. Participating in exercise has also been associated with benefits during and following treatment for cancer, including improvements in psychosocial and physical outcomes, as well as better compliance with treatment regimens, reduced impact of disease symptoms and treatment-related side-effects, and survival benefits for particular cancers. The general exercise prescription for people undertaking or having completed cancer treatment is of low to moderate intensity, regular frequency (3–5 times/week) for at least 20 min per session, involving aerobic, resistance or mixed exercise types. Future work needs to push the boundaries of this exercise prescription, so that we can better understand what constitutes optimal, desirable and necessary frequency, duration, intensity and type, and how specific characteristics of the individual (e.g., age, cancer type, treatment, presence of specific symptoms) influence this prescription. What follows is a summary of the cancer and exercise literature, in particular the purpose of exercise following diagnosis of cancer, the potential benefits derived by cancer patients and survivors from participating in exercise programs, and exercise prescription guidelines and contraindications or considerations for exercise prescription with this special population. This report represents the position stand of the Australian Association of Exercise and Sport Science on exercise and cancer recovery and has the purpose of guiding exercise practitioners in their work with cancer patients.

Keywords: Exercise; Neoplasms; Rehabilitation; Survival; Quality of life; Cancer

1. Exercise and cancer prevention

One in three Australian men and one in four women will be directly affected by cancer before the age of 75, with melanoma, prostate, colorectal, breast and lung cancers comprising the most common types.[1] There are an estimated 108,000 new cancer cases and 41,000 registered cancer deaths each year in Australia, and consequently cancer represents a major public health concern.[2] While the causes for many cancers remain unknown, lifestyle factors including physical activity levels are considered contributory and modifiable for some.[3,4] Since the first report linking physical activity and cancer risk was published in 1922, more than 190 reports from epidemiological studies and over 10 reviews have examined this relationship.[5] The scientific evidence supporting physical activity as a means of cancer prevention is now considered 'strong' and 'convincing' for particular cancers including colon/colorectal and breast, 'probable' for prostate and 'possible' for lung and endometrial cancers, with risk ratios or odds ratios reported for the physically active groups ranging from 0.3 to 0.8 (representing risk reductions of 25% to more than three-fold).[5] Evidence to date is considered preliminary and insufficient to make any causal inferences for melanoma, testicular, ovarian, kidney, pancreatic and thyroid cancers.[5] A review and analysis of the potential biological mechanisms underlying the possible anti-carcinogenic effects of physical activity has recently been published and gives the relationship more credibility.[6] The precise exercise prescription, in relation to type, intensity, duration and frequency, needed for cancer protection remains unknown.[7] However, since exercise prescription in this set-

* Corresponding author.
E-mail address: sc.hayes@qut.edu.au (S.C. Hayes).

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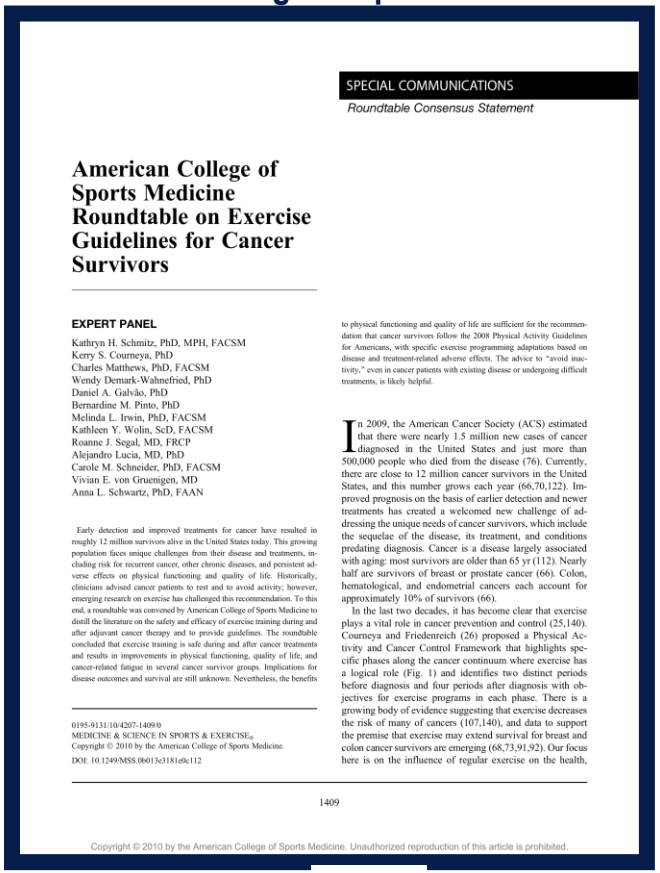
American College of Sports Medicine



SPECIAL COMMUNICATIONS
Roundtable Consensus Statement

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

EXPERT PANEL

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

Early detection and improved treatments for cancer have resulted in roughly 12 million survivors alive in the United States today. This growing population faces unique challenges from their disease and treatments, including risk for recurrent cancer, other chronic diseases, and persistent adverse effects on physical functioning and quality of life. Historically, clinicians advised cancer patients to rest and to avoid activity; however, emerging research on exercise has challenged this recommendation. To this end, a roundtable was convened by American College of Sports Medicine to distill the literature on the safety and efficacy of exercise training during and after adjuvant cancer therapy and to provide guidelines. The roundtable concluded that exercise training is safe during and after cancer treatments and results in improvements in physical functioning, quality of life, and cancer-related fatigue in several cancer survivor groups. Implications for disease outcomes and survival are still unknown. Nevertheless, the benefits to physical functioning and quality of life are sufficient for the recommendation that cancer survivors follow the 2008 Physical Activity Guidelines for Americans, with specific exercise programming adaptations based on disease and treatment-related adverse effects. The advice to "avoid inactivity," even in cancer patients with existing disease or undergoing difficult treatments, is likely helpful.

0195-9131/10/4207-1409/0
MEDICINE & SCIENCE IN SPORTS & EXERCISE®

DOI: 10.1249/MSS.0b013e3181e0c112

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

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

2001-2003-2006-2012 — 2009 — 2010

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

SPECIAL COMMUNICATIONS

Roundtable Consensus Statement

AMERICAN COLLEGE of SPORTS MEDICINE

EXPERT PANEL

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Focus on adult cancers and sites with the most evidence

Evaluation of Evidence A-D

Breast, Prostate, Colon, Hematological, Gynecological

85 studies

A - overwhelming data from RCTs
B - few RCTs exist
C - uncontrolled, nonrandomized and/or observational studies
D - insufficient for categories A-C

American College of Sports Medicine. *Med Sci Sports Exerc.* 2010;42(7):1409-1426

Breast Cancer

During chemotherapy or radiation

Results from 22 RCTs

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AMERICAN COLLEGE of SPORTS MEDICINE

- Evidence category **A** – Safety
- Evidence category **A** – Aerobic Fitness
- Evidence category **A** – Muscle Strength
- Evidence category **A** – Fatigue
- Evidence category **B** – Body Size/Composition
- Evidence category **B** – Quality of Life
- Evidence category **B** – Physical Function
- Evidence category **B** – Anxiety

American College of Sports Medicine. *Med Sci Sports Exerc.* 2010;42(7):1409-1426

Prostate Cancer

During and after treatment

Effects of exercise on key endpoints

Exercise Medicine Research Institute

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Results from 12 RCTs

- Evidence category **A** – Safety
- Evidence category **A** – Aerobic Fitness
- Evidence category **A** – Muscle Strength
- Evidence category **A** – Fatigue
- Evidence category **B** – Body Size/Composition
- Evidence category **B** – Quality of Life
- Evidence category **B** – Physical Function

American College of Sports Medicine. *Med Sci Sports Exerc.* 2010;42(7):1409-1426

Exercise Oncology
Research/clinical questions

- can exercise help manage treatment side effects/reduce treatment toxicities (e.g. muscle loss, fatigue)?
- will exercise interfere with treatment or response?
- can exercise lower the risk of cancer recurrence, delay progression and improve survival?
- what are the potential biological mechanisms?
- what is the optimal exercise program for benefit?

BJUI
BJU INTERNATIONAL

Changes in muscle, fat and bone mass after 36 weeks of maximal androgen blockade for prostate cancer

Daniel A. Galvão[1,2], Nigel A. Spry[3,4], Dennis R. Taaffe[5], Robert U. Newton[1,2], John Stanley[6], Tom Shannon[6], Chris Rowling[7] and Richard Prince[3,4]

Variables	Baseline	36 weeks	% change
PSA	22.6 (3.1)	0.23 (0.05)	-98.2 (0.5)*
Testosterone	15.1 (0.6)	0.80 (0.03)	-93.3 (0.3)*
Whole body LM (kg)	55.8 (0.8)	54.4 (0.8)	-2.4 (0.4)*
ASM (kg)	23.4 (0.3)	22.4 (0.3)	-4.2 (0.5)*
Whole body FM (kg)	20.8 (0.7)	23.1 (0.7)	+13.8 (2.3)*
Trunk FM (kg)	12.1 (0.4)	13.1 (0.4)	+12.0 (2.5)*

Galvão et al. *BJU International* 2008;102:44-47

ORIGINAL ARTICLE

Reduced muscle strength and functional performance in men with prostate cancer undergoing androgen suppression: a comprehensive cross-sectional investigation

DA Galvão[1], DR Taaffe[2], N Spry[3,4], D Joseph[3,4], D Turner[1] and RU Newton[1]

Variable	*AST (n = 48)*	*Controls (n = 70)*	P
Functional performance			
6-m usual walk (s)	4.8 ± 0.6	4.5 ± 0.6	0.042
6-m fast walk (s)	3.7 ± 0.5	3.5 ± 0.3	0.013
400-m walk (s)	274.3 ± 32.7	256.1 ± 34.0	0.005
6 m backward walk (s)	23.8 ± 13.8	19.9 ± 6.3	0.035
Chair rise (s)	13.5 ± 2.8	12.0 ± 2.6	0.004
Muscle strength			
Chest press (kg)	32.4 ± 10.5	37.5 ± 9.1	0.006
Seated row (kg)	38.7 ± 6.6	42.4 ± 8.4	0.014
Leg press (kg)	91.0 ± 41.4	86.8 ± 37.4	0.567
Leg extension (kg)	36.3 ± 13.0	44.9 ± 12.4	<0.001
Muscle endurance			
Chest press (rep)	11.6 ± 4.1	11.4 ± 5.0	0.819
Leg press (rep)	18.0 ± 6.7	17.7 ± 7.5	0.867

Abbreviations: AST, androgen suppression therapy; rep, repetitions performed at 70% of 1 repetition maximum (1-RM).

Galvão et al. Prostate Cancer Prostatic Dis. 2009;12(2):198-203.

Resistance Training and Reduction of Treatment Side Effects in Prostate Cancer Patients

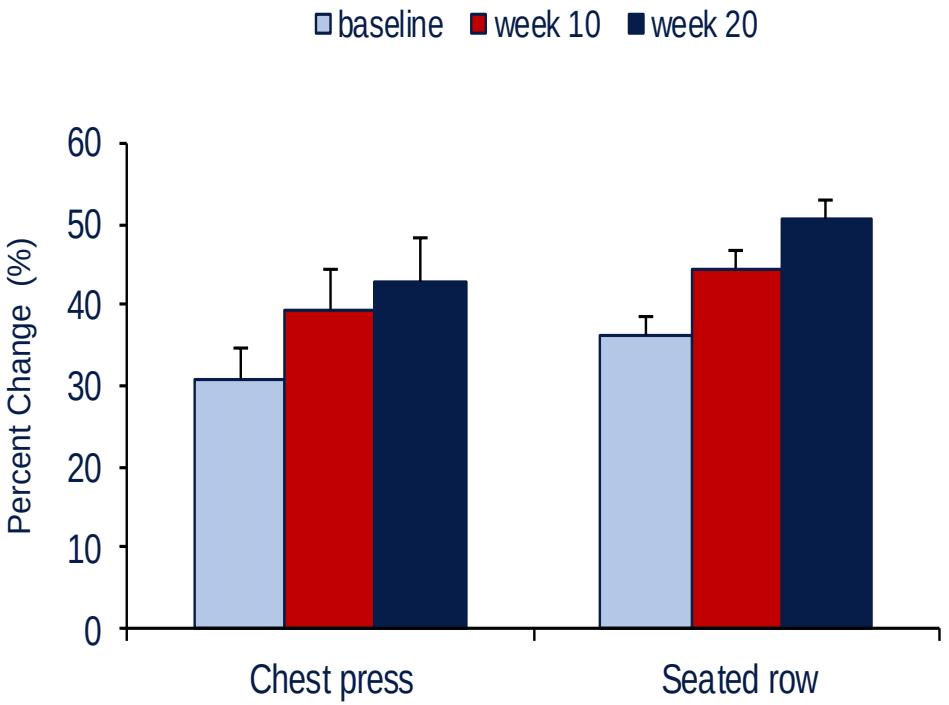
MEDICINE & SCIENCE IN SPORTS & EXERCISE®

DOI: 10.1249/01.mss.0000233803.48691.8b

DANIEL A. GALVÃO[1], KAZUNORI NOSAKA[1], DENNIS R. TAAFFE[2], NIGEL SPRY[3,4], LINDA J. KRISTJANSON[5], MICHAEL R. MCGUIGAN[1], KATSUHIKO SUZUKI[6], KANEMITSU YAMAYA[7], and ROBERT U. NEWTON[1]

Muscle Strength and Function

Subject	Age (yr)	Diagnosis (d)	ADT (d)
1	79	336	65*
2	65	92	88*
3	72	184	120*
4	66	363	210*
5	59	365	300*
6	72	732	420†
7	62	2520	720†
8	82	1821	1622†
9	63	3605	3240†
10	73	3960	3955†
Min	59	92	65
Max	82	3960	3955
Mean	70.3	1397.8	1135.6
SD	8.3	1481.8	1360.4

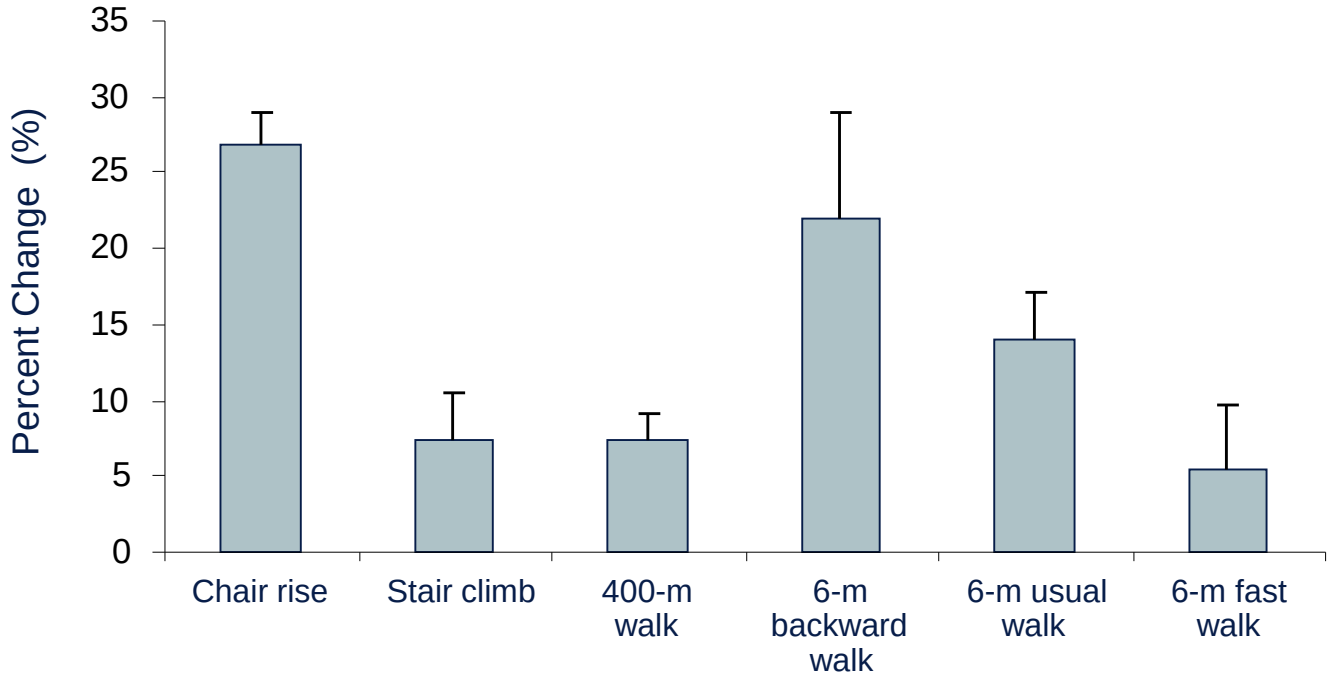


Galvão DA et al. *Med Sci Sports Exerc.* 2006;38(12):2045-2052.

The Effect of Resistance Exercise on Physical Function/Muscle Thickness

	Baseline	Week 10	Week 20	*P* Value*
PSA ($ng \cdot mL^{-1}$)	3.09 ± 6.58	1.28 ± 1.58	0.90 ± 1.13	0.374
Free testosterone ($pg \cdot mL^{-1}$)	2.13 ± 3.64	2.15 ± 3.61	1.56 ± 3.68	0.532
GH ($ng \cdot mL^{-1}$)	0.72 ± 0.75	0.83 ± 0.78	0.48 ± 0.37	0.239
Cortisol ($ng \cdot mL^{-1}$)	10.63 ± 3.54	10.35 ± 3.32	10.42 ± 2.67	0.979
Hemoglobin ($g \cdot L^{-1}$)	141.3 ± 13.1	142.3 ± 14.4	141.2 ± 13.5	0.913

- **Quadriceps Muscle Thickness Increase by 15% *P*=.050 B-Mode Ultrasound**



Galvão DA et al. *Med Sci Sports Exerc.* 2006;38(12):2045-2052.

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Combined Resistance and Aerobic Exercise Program Reverses Muscle Loss in Men Undergoing Androgen Suppression Therapy for Prostate Cancer Without Bone Metastases: A Randomized Controlled Trial

Daniel A. Galvão, Dennis R. Taaffe, Nigel Spry, David Joseph, and Robert U. Newton

Design	RCT
Sample	57
Intervention	12-week (2x) resistance & aerobic
Protocol	2-4 sets 6-12 RM 15-20 min 60%-85% HRmax 10-13 RPE
Primary endpoint	Lean mass

RPE, repetitions per event

Galvão DA et al. *J Clin Oncol.* 2010;28(2):340-347.

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Table 2. Total and Regional Body Composition Absolute Values and Change Over 12 Weeks Exercise Training

	Baseline				12 Weeks				Adjusted Group Difference in Mean Change Over 12 Weeks		
	Exercise		Control		Exercise		Control				
Measure	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	95% CI	*P**
Lean mass, kg											
Total body	56.1	6.7	57.8	8.3	56.8	6.8	57.8	8.7	0.76	0.01 to 1.5	.047
Upper limb	6.3	0.9	6.5	0.9	6.5	0.9	6.4	1.0	0.26	0.11 to 0.42	< .001
Lower limb	17.2	2.5	18.0	3.1	17.4	2.5	17.9	3.6	0.54	0.09 to 1.0	.019
ASM	23.5	3.4	24.6	4.0	24.0	3.4	24.4	4.6	0.80	0.29 to 1.3	.003
Fat mass, kg											
Total body	22.5	5.6	23.2	7.2	22.3	6.9	23.5	6.9	−0.01	−0.82 to 0.79	.964
Trunk	12.2	3.3	12.4	4.2	11.9	3.5	12.2	4.0	0.03	−0.56 to 0.57	.991
Body fat, %	27.5	4.5	27.3	4.8	27.2	4.4	27.5	4.7	−0.34	−1.0 to 0.41	.366
Whole body mass, kg											
Total body weight	80.7	10.3	83.2	14.4	81.4	10.7	83.2	14.4	0.76	−0.32 to 1.8	.163

Abbreviations: SD, standard deviation; ASM, appendicular skeletal muscle.
*Between group change by analysis of covariance (adjusted for baseline, androgen suppression treatment time, use of antiandrogen, number of medications, and education).

Galvão DA et al. *J Clin Oncol.* 2010;28(2):340-347.

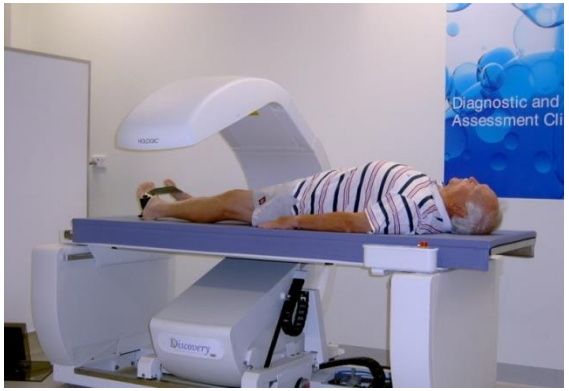
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Combined Resistance and Aerobic Exercise Program Reverses Muscle Loss in Men Undergoing Androgen Suppression Therapy for Prostate Cancer Without Bone Metastases: A Randomized Controlled Trial

Daniel A. Galvão, Dennis R. Taaffe, Nigel Spry, David Joseph, and Robert U. Newton

Lean Mass	~1 kg	EX>CO
Muscle Strength	3-31 kg	EX>CO
Aerobic Capacity	-7 sec	EX>CO
Dynamic Balance	-4 sec	EX>CO
Vitality	+13	EX>CO
Fatigue	-11	EX>CO
CRP	-3.5 mg/L	EX>CO



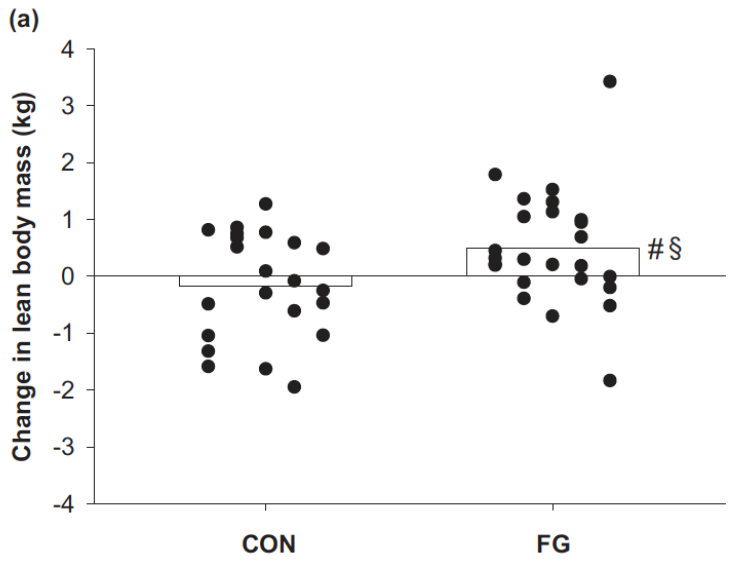
CO, usual care control; CRP, C-reactive protein; EX, exercise.

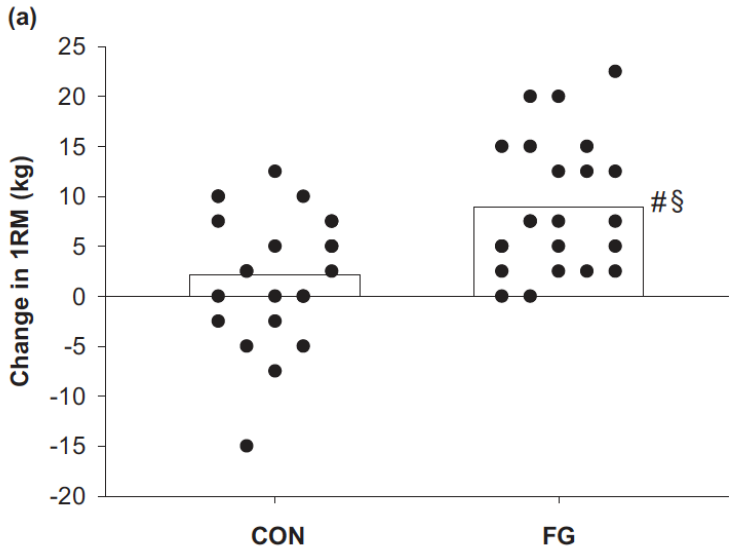
Galvão DA et al. *J Clin Oncol.* 2010;28(2):340-347.

Football training improves lean body mass in men with prostate cancer undergoing androgen deprivation therapy

J. Uth[1], T. Hornstrup[2], J. F. Schmidt[2], J. F. Christensen[1], C. Frandsen[1], K. B. Christensen[3], E. W. Helge[2], K. Brasso[4], M. Rørth[5], J. Midtgaard[1,6], P. Krustrup[2,7]

SCANDINAVIAN JOURNAL OF MEDICINE & SCIENCE IN SPORTS





Scand J Med Sci Sports 2014: 24 (Suppl. 1): 105–112
doi: 10.1111/sms.12260

BMC Cancer

BioMed Central

Study protocol

Open Access

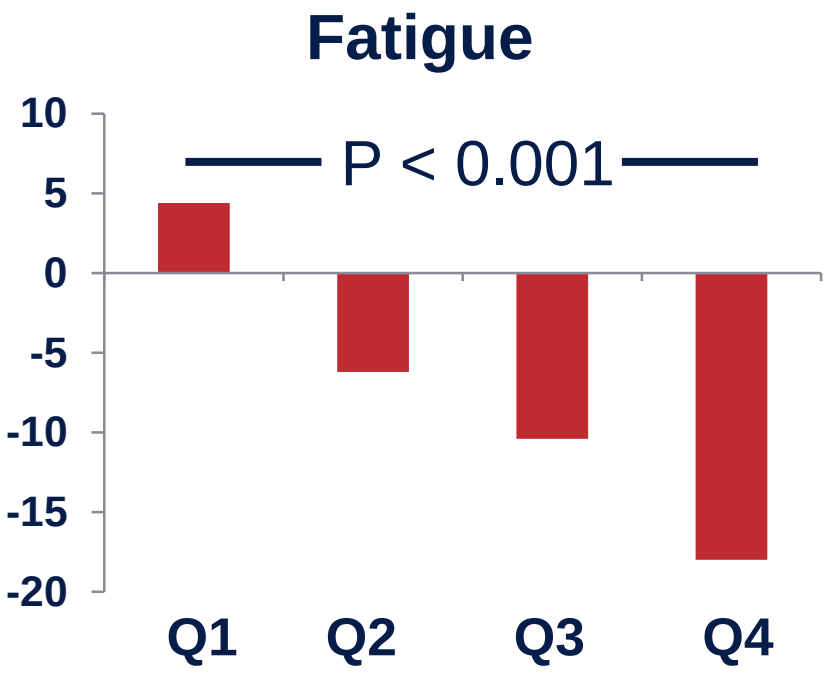
A phase III clinical trial of exercise modalities on treatment side-effects in men receiving therapy for prostate cancer

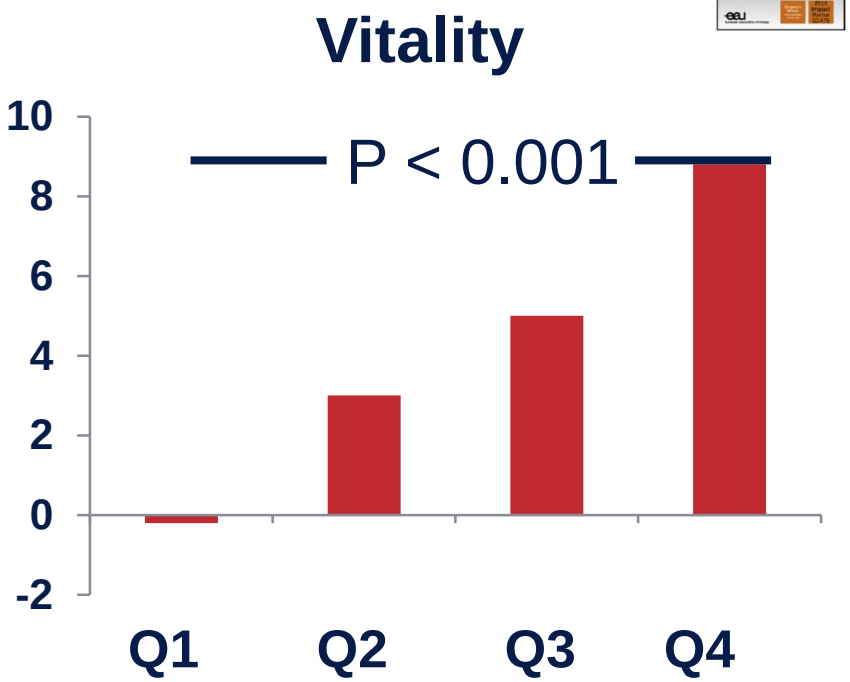
Robert U Newton*[1], Dennis R Taaffe[2], Nigel Spry[3,4], Robert A Gardiner[5], Gregory Levin[1], Bradley Wall[1], David Joseph[3,4], Suzanne K Chambers[6] and Daniel A Galvão[1]

Treatment	ADT (~5 months)	**Design**	RCT (3-arm)
Intervention	12 months	**Sample**	164
Protocol	(1) Supervised resistance/impact vs. (2) Supervised resistance/aerobic vs. (3) Usual care		
Primary endpoint	Bone mass (lumbar spine & hip BMD); lean mass; VO2, fatigue		

Newton et al. BMC Cancer. 2009 Jun 29;9:210.
Wall et al. in review MSSE.
Taaffe et al. European Urology 10 Feb 2017

Quartiles of Fatigue and Vitality





- EORTC QLQ-C30 – fatigue is a 3-item subscale
- Vitality scale of the SF-36 – a 4-item domain with scores from 0-100

Taaffe, Newton et al. European Urology 2017

Exercise After Treatment

A Multicentre Year-long Randomised Controlled Trial of Exercise Training Targeting Physical Functioning in Men with Prostate Cancer Previously Treated with Androgen Suppression and Radiation from TROG 03.04 RADAR

Daniel A. Galvão [a,], Nigel Spry [a,b,c], James Denham [d,e], Dennis R. Taaffe [a,f], Prue Cormie [a], David Joseph [a,b,c], David S. Lamb [g], Suzanne K. Chambers [a,h,i], Robert U. Newton [a]*

European Association of Urology

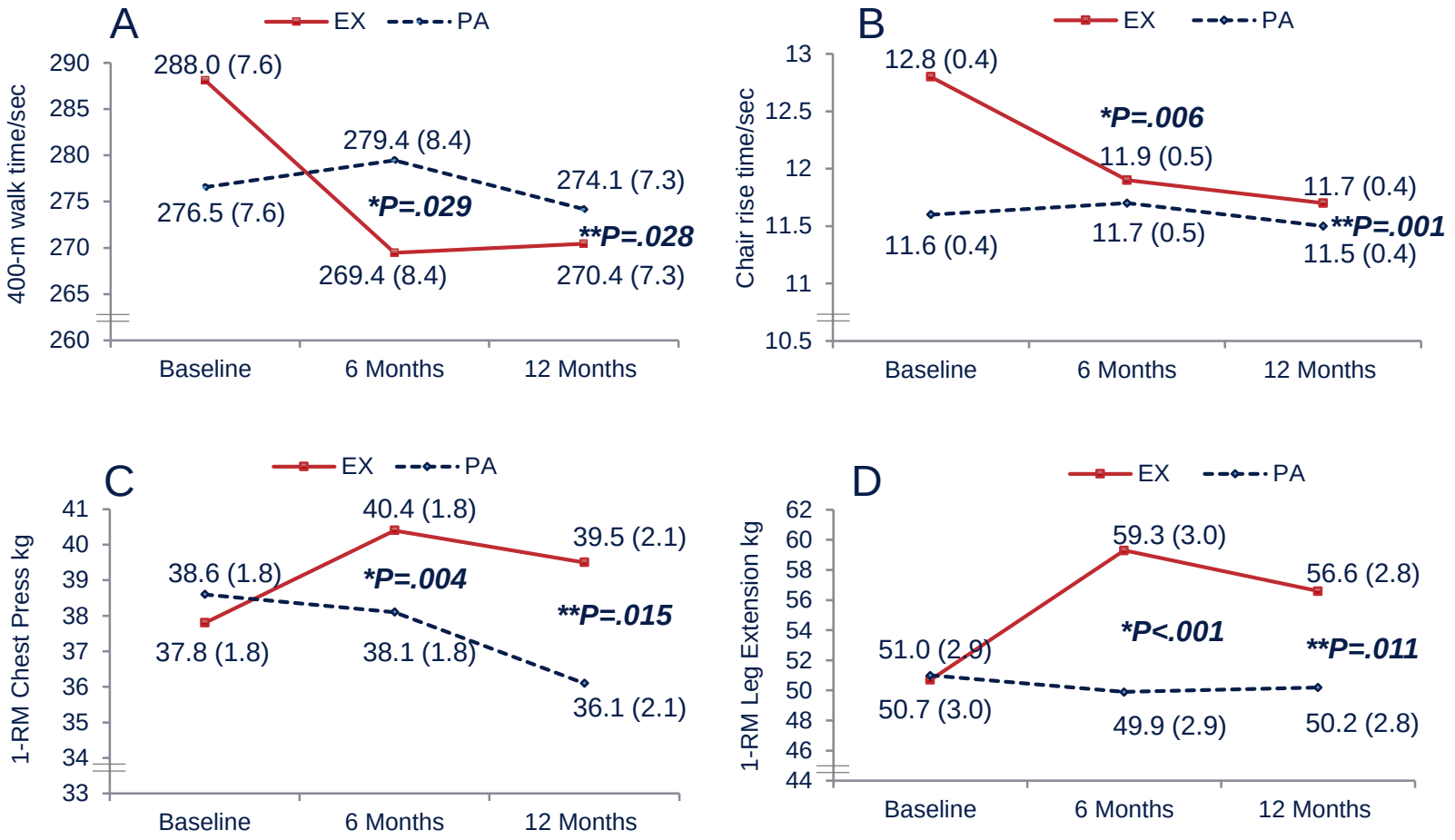
Platinum Priority – Prostate Cancer

Editorial by Michael R. Harrison and Lee W. Jones on pp. 873–874 of this issue

Diagnosis	(>5 yr post diagnosis)		
Design	RCT (2-arm)		
Sample	100	**Intervention**	12 months
Protocol	Resistance & aerobic exercise (6 months supervised + 6 months home based) vs. physical activity education material		
Primary endpoint	Cardiorespiratory fitness		

Galvão DA et al. *Eur Urol.* 2014;65(5):856-864.

Exercise vs Physical Activity Recommendations After Treatment



PA, physical activity.

Galvão DA et al. *Eur Urol.* 2014;65(5):856-864.

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European Association of Urology

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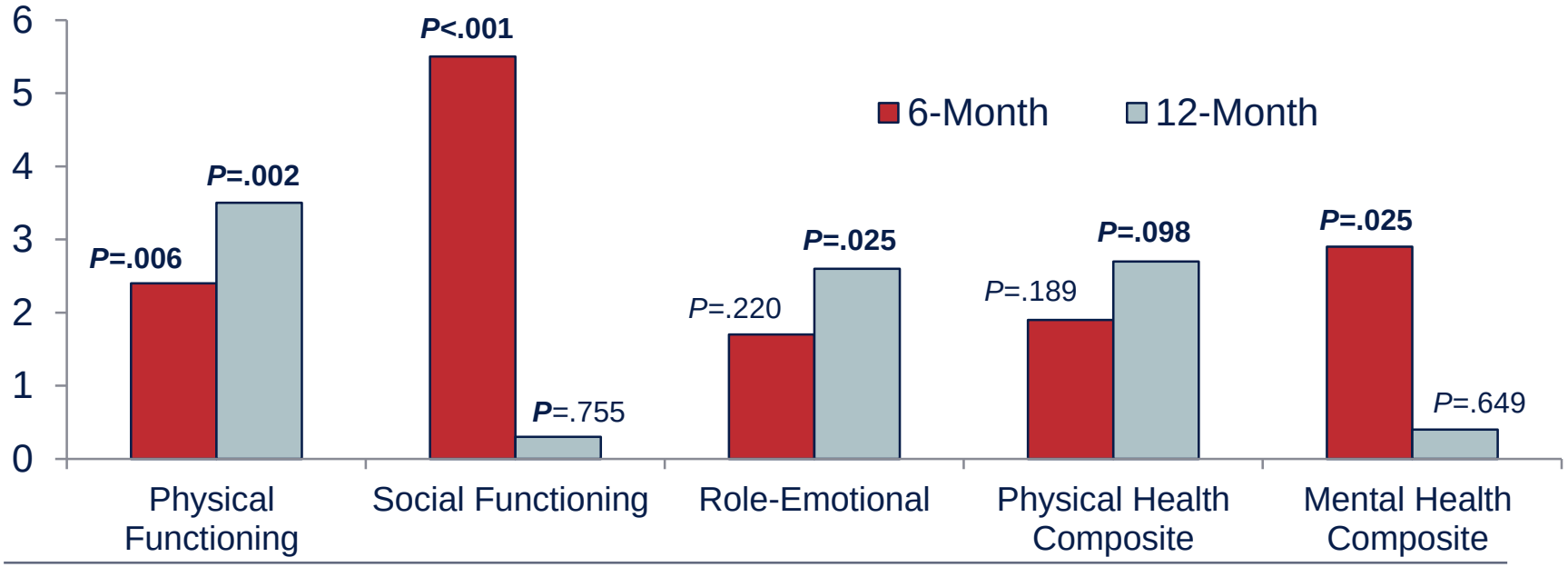
Adjusted Group Difference in Mean Change Over 6- and 12-Months*



Galvão DA et al. *Eur Urol.* 2014;65(5):856-864.

Exercise Oncology
Research/clinical questions

- can exercise help manage treatment side effects/reduce treatment toxicities (e.g. muscle loss, fatigue)?
- will exercise interfere with treatment or response?
- can exercise lower the risk of cancer recurrence, delay progression and improve survival?
- what are the potential biological mechanisms?
- what is the optimal exercise program for benefit?

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Effects of Aerobic and Resistance Exercise in Breast Cancer Patients Receiving Adjuvant Chemotherapy: A Multicenter Randomized Controlled Trial

Kerry S. Courneya, Roanne J. Segal, John R. Mackey, Karen Gelmon, Robert D. Reid, Christine M. Friedenreich, Aliya B. Ladha, Caroline Proulx, Jeffrey K.H. Vallance, Kirstin Lane, Yutaka Yasui, and Donald C. McKenzie

START trial - Multicenter

RCT 24 weeks exercise intervention (different modes)

n=242 breast cancer patients initiating ***chemotherapy*** (median 17 weeks)

78 (71) assigned to aerobic exercise	82 (73) assigned to resistance exercise	82 (75) assigned to usual care
56 received intervention	56 received intervention	82 received intervention
22 did not complete ≥ 66% of supervised exercise	26 did not complete ≥ 66% of supervised exercise	

Courneya et al. *JCO* 2007;25:4396-4404

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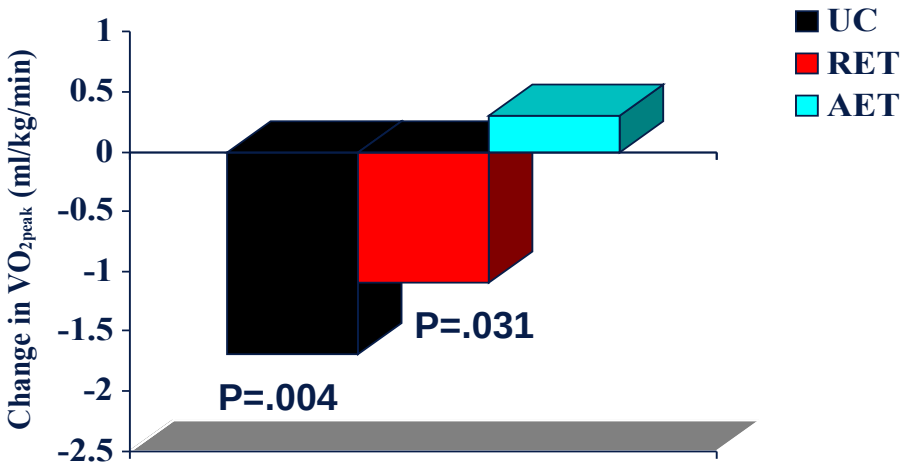
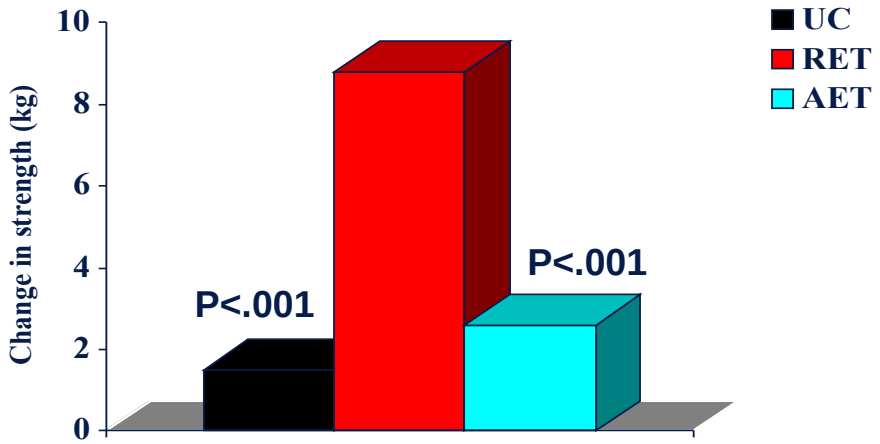
Change in VO2max



Change in Muscle Strength



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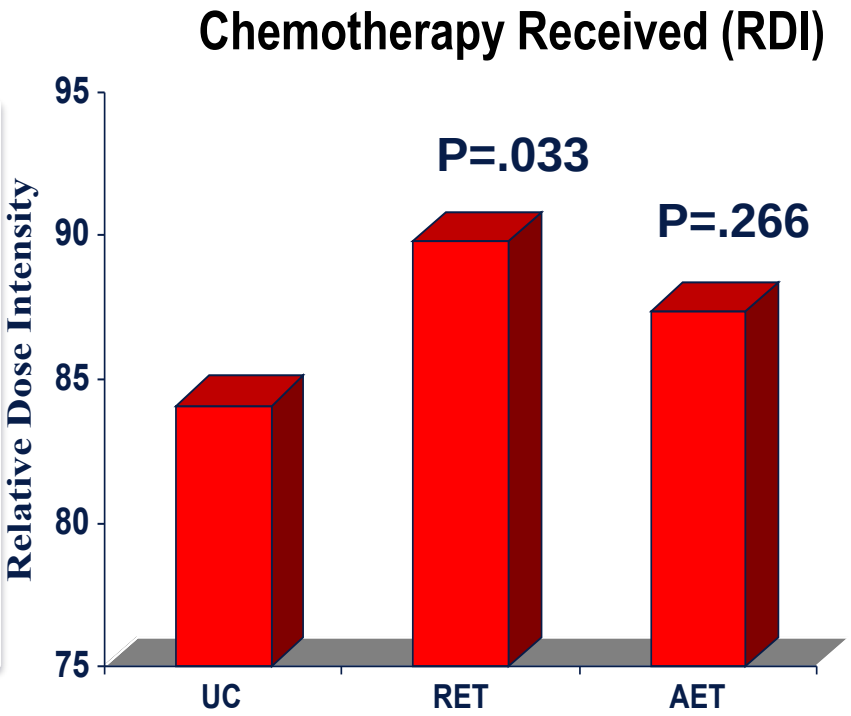
Percentage of participants who received ***85% of their planned RDI*** was:

- 65.9% UC group
- **78.0% RET group**
- 74.4% AET group



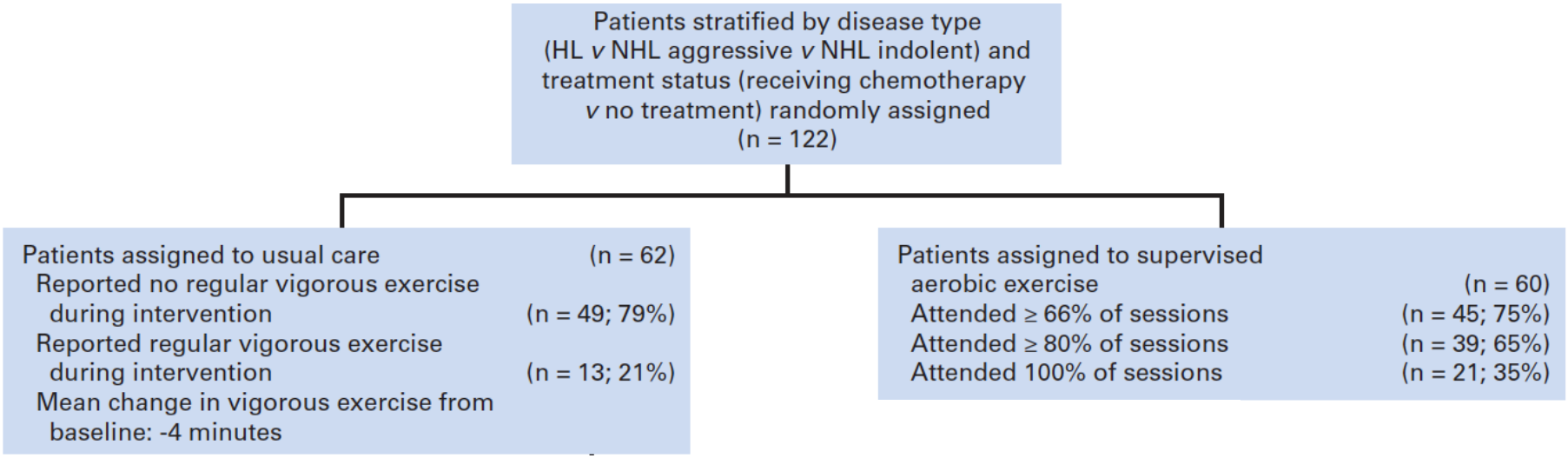
Courneya et al. *JCO* 2007;25:4396-4404

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Randomized Controlled Trial of the Effects of Aerobic Exercise on Physical Functioning and Quality of Life in Lymphoma Patients

Kerry S. Courneya, Christopher M. Sellar, Clare Stevinson, Margaret L. McNeely, Carolyn J. Peddle, Christine M. Friedenreich, Keith Tankel, Sanraj Basi, Neil Chua, Alex Mazurek, and Tony Reiman



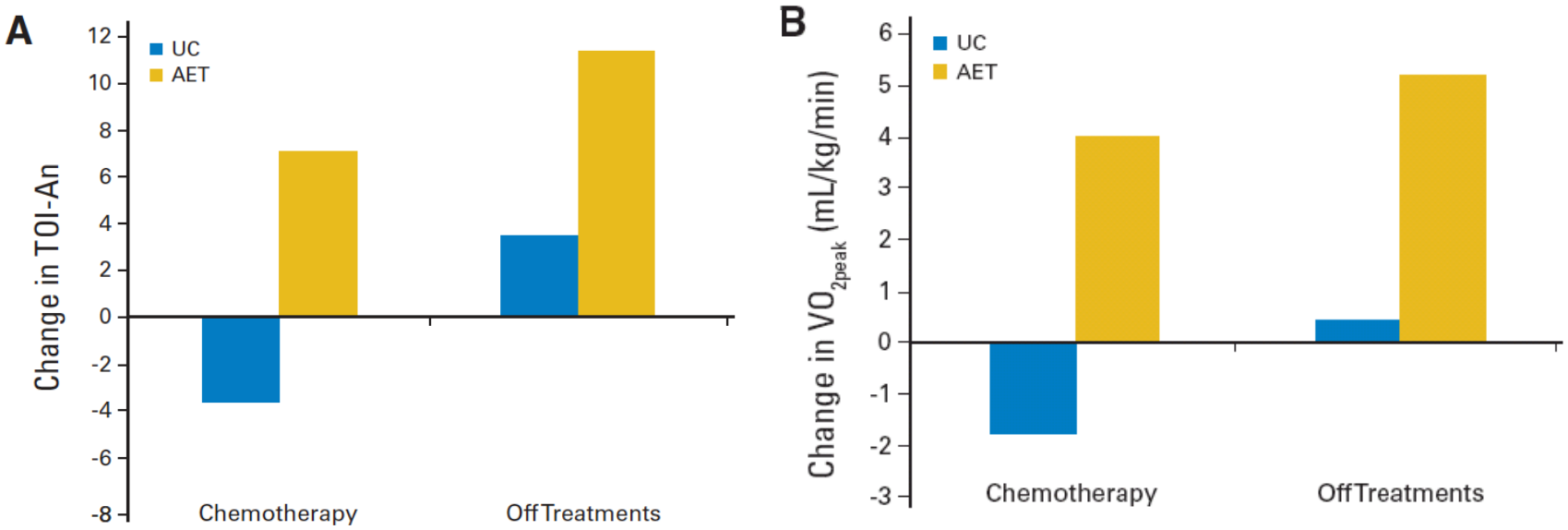
J Clin Oncol 27:4605-4612. © 2009 by American Society of Clinical Oncology

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Randomized Controlled Trial of the Effects of Aerobic Exercise on Physical Functioning and Quality of Life in Lymphoma Patients

Patients stratified by disease type (HL *v* NHL aggressive *v* NHL indolent) and treatment status (receiving chemotherapy *v* no treatment) randomly assigned (n = 122)

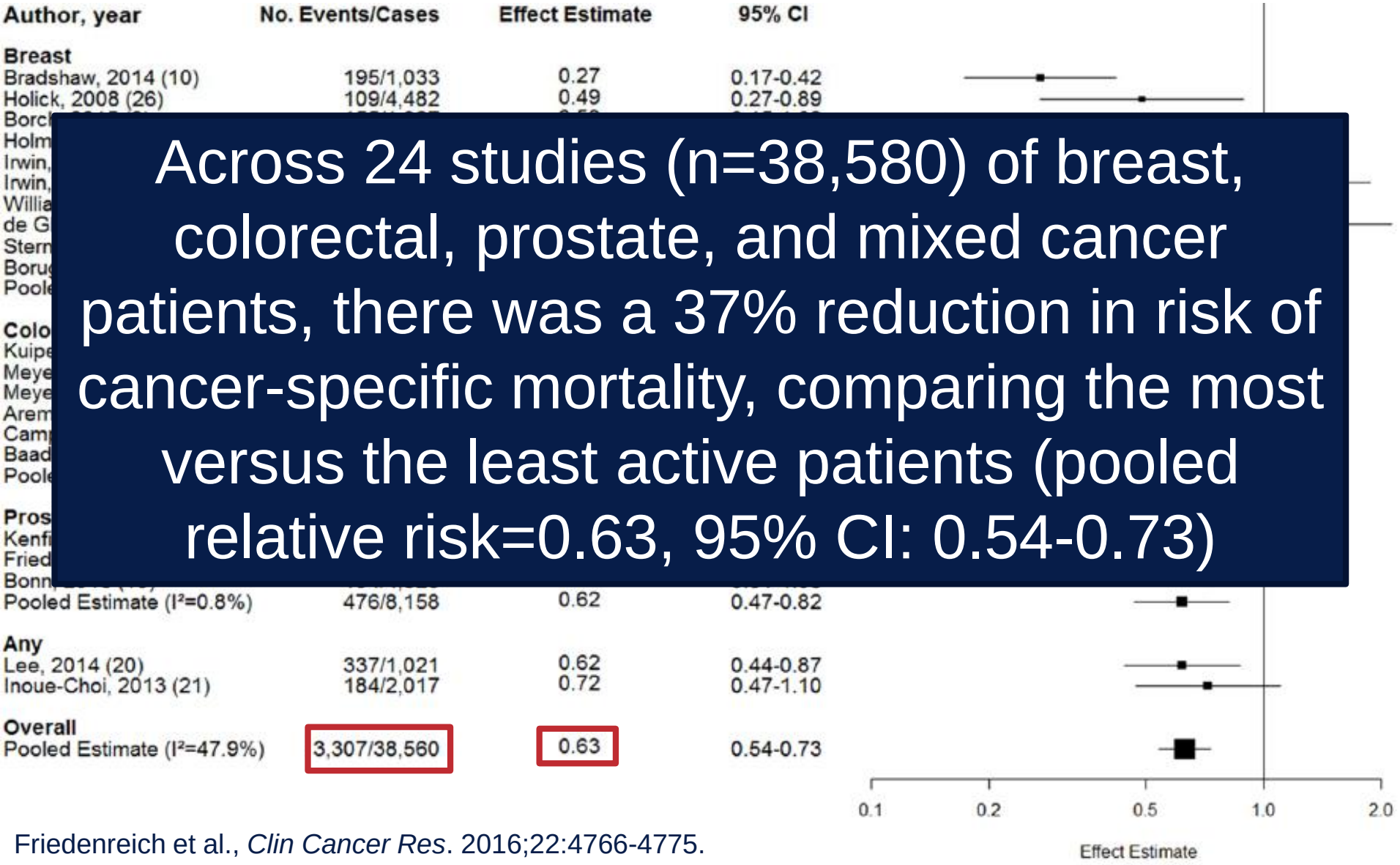


J Clin Oncol 27:4605-4612. © 2009 by American Society of Clinical Oncology

Exercise Oncology
Research/clinical questions

- can exercise help manage treatment side effects/reduce treatment toxicities (e.g. muscle loss, fatigue)?
- will exercise interfere with treatment or response?
- can exercise lower the risk of cancer recurrence, delay progression and improve survival?
- what are the potential biological mechanisms?
- what is the optimal exercise program for benefit?

Prospective Cohort Studies of Post Diagnosis Exercise and Cancer-Specific Mortality



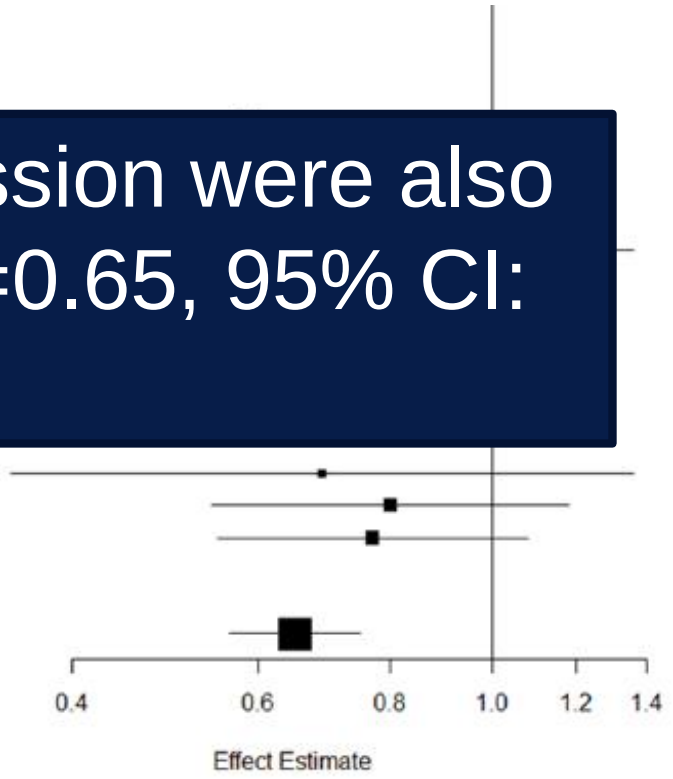
Across 24 studies (n=38,580) of breast, colorectal, prostate, and mixed cancer patients, there was a 37% reduction in risk of cancer-specific mortality, comparing the most versus the least active patients (pooled relative risk=0.63, 95% CI: 0.54-0.73)

Friedenreich et al., *Clin Cancer Res*. 2016;22:4766-4775.

Prospective Cohort Studies of Post Diagnosis Exercise and Cancer Recurrence and Progression

Author, year	No. Events/Cases	Effect Estimate	95% CI
Breast			
Richman, 2011* (23)	117/1,455	0.69	0.35-1.36
Friedenreich, 2016 (18)	239/830	0.80	0.54-1.18
Pooled estimate (I^2=0%)	356/2,285	0.77	0.55-1.08
Overall			
Pooled estimate (I^2=10%)	1,892/15,298	0.65	0.56-0.75

Risks of recurrence or progression were also reduced (pooled relative risk=0.65, 95% CI: 0.56-0.75)



Friedenreich et al., *Clin Cancer Res*. 2016;22:4766-4775.

Physical activity and survival among long-term cancer survivor and non-cancer cohorts

Anthony Gunnell[1, 2], Sarah Joyce[3], Stephania Tomlin[3], Dennis R. Taaffe[1, 4, 5], Prue Cormie[6], Robert U. Newton[1, 7, 4], David Joseph[1, 8], Nigel Spry[1, 9], Kristjana Einarsdóttir[10], Daniel A. Galvao[1, 4*]

frontiers in Public Health

N=1589 Western Australian Cancer Survivors; 8.8 years follow-up
Cox proportional hazards regression

	Cancer Specific Death
<150 minutes	HR 0.62 (0.36-1.06)
150-359 minutes	HR 0.55 (0.28-1.08)
360+ minutes	**HR 0.30** (0.13-0.70)

	All-Cause Death
<150 minutes	HR 0.70 (0.46-1.08)
150-359 minutes	**HR 0.55 (0.31-0.97)**
360+ minutes	**HR 0.30 (0.21-0.79)**

Gunnell et al. Frontiers Public Health 2017

Enhancing active surveillance of prostate cancer: the potential of exercise medicine

NATURE REVIEWS | UROLOGY

Daniel A. Galvão[1], Dennis R. Taaffe[1,2], Nigel Spry[1,3], Robert A. Gardiner[1,4,5], Renea Taylor[6], Gail P. Risbridger[7], Mark Frydenberg[8], Michelle Hill[9], Suzanne K. Chambers[1,10], Phillip Stricker[11], Tom Shannon[12], Dickon Hayne[13], Eva Zopf[1,14] and Robert U. Newton[1,4]

No established recommendations exist for delaying (or preventing) the progression of low-risk PCa cancer

Preliminary evidence suggests that lifestyle and/or exercise interventions might have therapeutic potential:

Delay disease progression
Transition to active therapy

Galvão et al. Nature Reviews Urology 2016

Lifestyle interventions during active surveillance

0022-5347/05/1743-1065/0
THE JOURNAL OF UROLOGY®
Vol. 174, 1065–1070, September 2005
Printed in U.S.A.
DOI: 10.1097/01.ju.0000169487.49018.73

INTENSIVE LIFESTYLE CHANGES MAY AFFECT THE PROGRESSION OF PROSTATE CANCER

DEAN ORNISH,*,† GERDI WEIDNER, WILLIAM R. FAIR, RUTH MARLIN, ELAINE B. PETTENGILL, CAREN J. RAISIN, STACEY DUNN-EMKE, LILA CRUTCHFIELD, F. NICHOLAS JACOBS, R. JAMES BARNARD, WILLIAM J. ARONSON, PATRICIA MCCORMAC, DAMIEN J. MCKNIGHT, JORDAN D. FEIN, ANN M. DNISTRIAN, JEANMAIRE WEINSTEIN, TUNG H. NGO, NANCY R. MENDELL AND PETER R. CARROLL‡

- PSA decreased 4% in the experimental group but increased 6% in the control group (p=0.016)
- n=6 controls undertook active treatment before 12 months (3x prostatectomy; 1 external beam radiation; 1 brachytherapy; 1 ADT) due to increased PSA (n=4) and MRI (n=2)
- The growth of LNCaP prostate cancer cells was inhibited ~8 times more by the serum from the experimental than control group (70% vs 9%, p<0.001)

Ornish D. et al. *Journal of Urology*. 2005 Sep;174(3):1065-9

Lifestyle interventions during active surveillance

Clinical Events in Prostate Cancer Lifestyle Trial: Results From Two Years of Follow-Up

Joanne Frattaroli, Gerdi Weidner, Ann M. Dnistrian, Colleen Kemp, Jennifer J. Daubenmier, Ruth O. Marlin, Lila Crutchfield, Loren Yglecias, Peter R. Carroll, and Dean Ornish

UROLOGY 72: 1319–1323, 2008.

- Prostate Cancer Lifestyle Trial (PCLT)
- 2 years of follow-up, 13 of 49 **(27%)** control patients and 2 of 43 **(5%)** experimental patients had undergone conventional prostate cancer treatment (radical prostatectomy, radiotherapy, or ADT, P<0.05)
  - 4 due to PSA increase; 4 due to PSA increase + unfavorable biopsy; 5 due to MRI compared with earlier findings (controls)
  - 1 due to PSA increase; 1 due to cancer-related anxiety (intervention)
- No differences were found between the untreated experimental and untreated control patients in PSA change or velocity at the end of 2 years

Frattaroli J. et al. *Urology*. 2008 Dec;72(6):1319-23

Effect of comprehensive lifestyle changes on telomerase activity and telomere length in men with biopsy-proven low-risk prostate cancer: 5-year follow-up of a descriptive pilot study

www.thelancet.com/oncology

Dean Ornish, Jue Lin, June M Chan, Elissa Epel, Colleen Kemp, Gerdi Weidner, Ruth Marlin, Steven J Frenda, Mark Jesus M Magbanua, Jennifer Daubenmier, Ivette Estay, Nancy K Hills, Nita Chainani-Wu, Peter R Carroll, Elizabeth H Blackburn

Telomere shortness in humans is a prognostic marker of ageing, disease, and premature morbidity

- Intervention associated with increases in relative telomere length after 5 years.

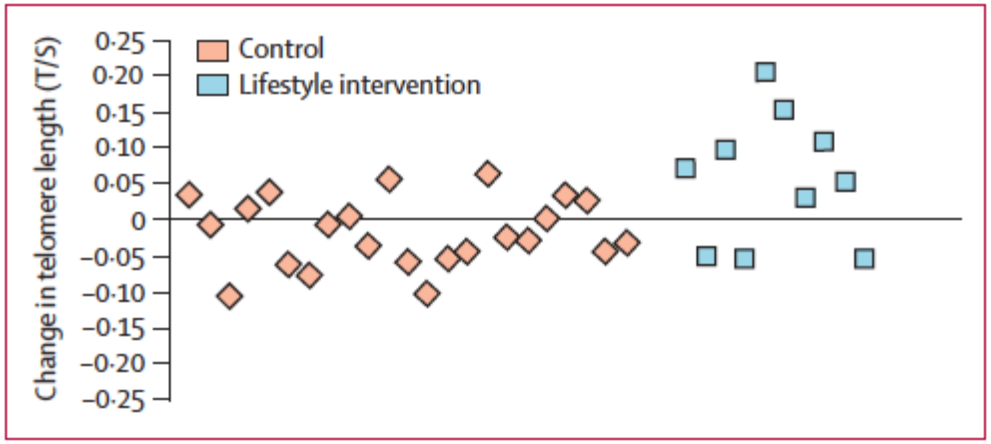


***Figure 2*: Changes in telomere length for individual participants in the lifestyle intervention and control groups**
T/S=telomere to single-copy gene ratio units.

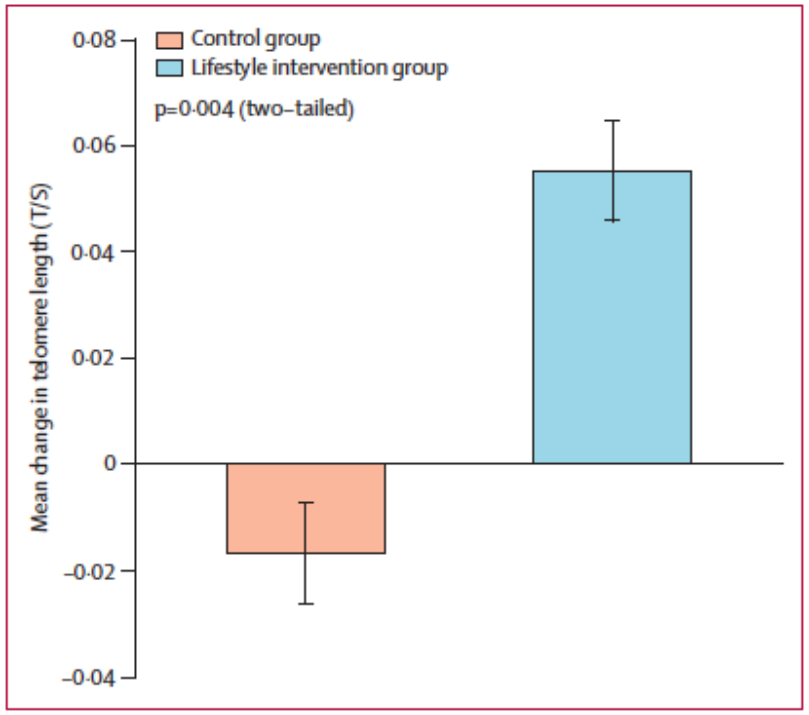


***Figure 1*: Mean change in relative telomere length over 5 years with lifestyle intervention compared with control**
Vertical lines represent 1 SEM. T/S=telomere to single-copy gene ratio units.

Ornish D. et al. Lancet Oncol. 2013 Oct;14(11):1112-20.

Exercise Oncology
Research/clinical questions

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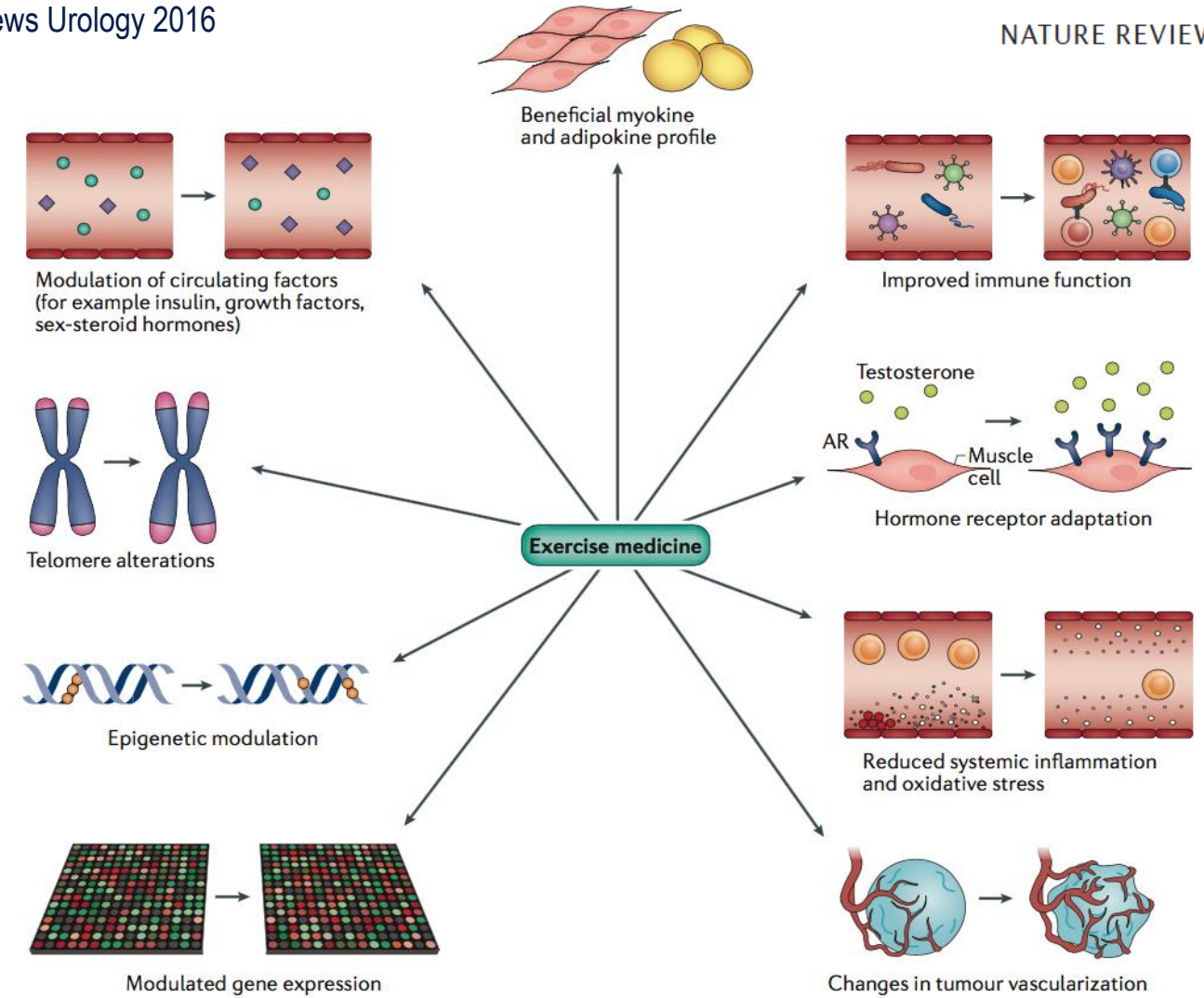
- will exercise interfere with treatment or response?
- can exercise lower the risk of cancer recurrence, delay progression and improve survival?
- what are the potential biological mechanisms?
- what is the optimal exercise program for benefit?

Potential Mechanisms

Research in *Exercise Oncology* still lacks a mechanistic understanding of how exercise directly *influences tumor biology and growth*

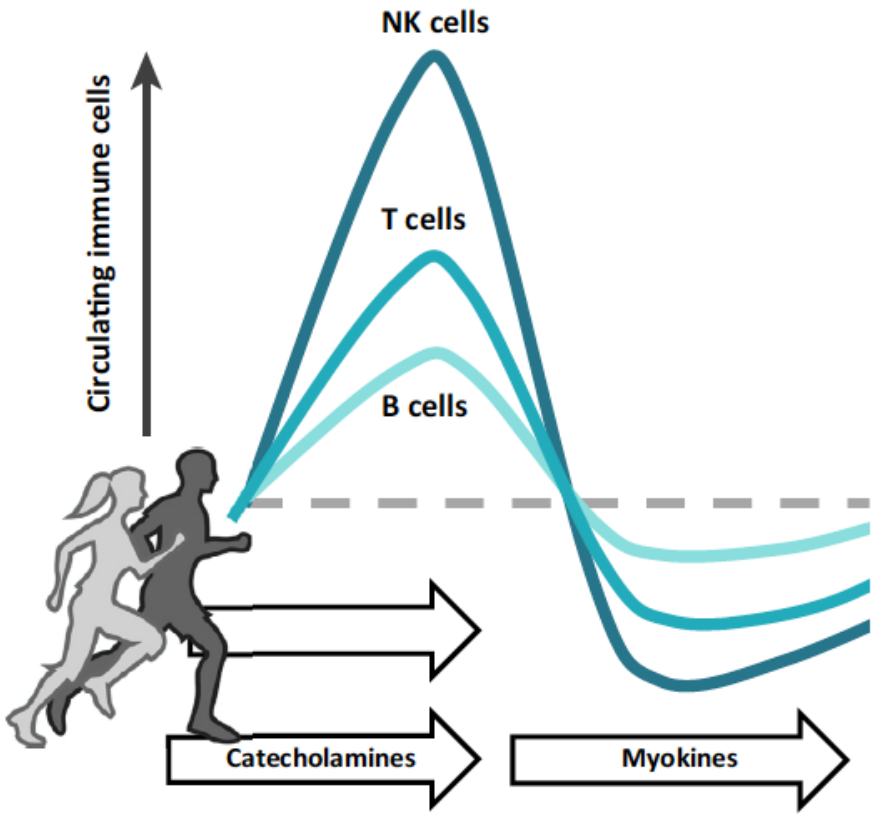
Galvão et al. Nature Reviews Urology 2016



Exercise-Dependent Regulation of NK Cells in Cancer Protection

Manja Idorn[1] and Pernille Hojman[2,*]

CellPress



Trends in Molecular Medicine

- During a bout of exercise, circulation of immune cells increase
- Increase in NK cells frequency is more pronounced than the increase in T and B cells
- Catecholamine levels which also rise during exercise are thought to drive the mobilization of immune cells into circulation
- At exercise cessation, the induced levels of myokines are proposed to affect immune cells redistribution and activation

Exercise-Dependent Regulation of NK Cells in Cancer Protection

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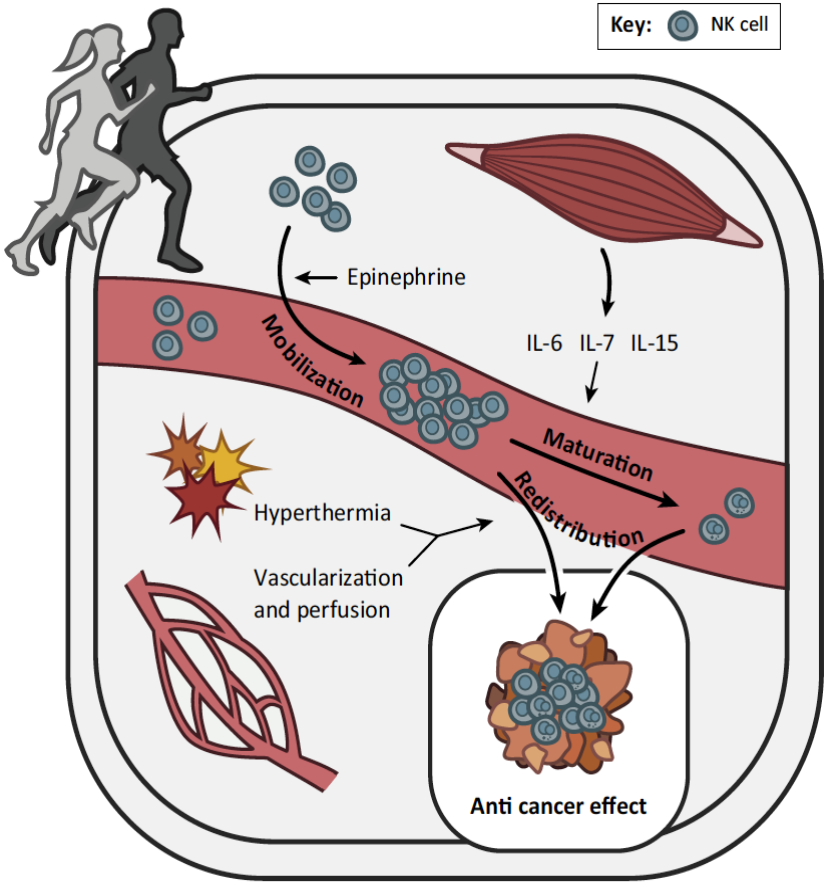
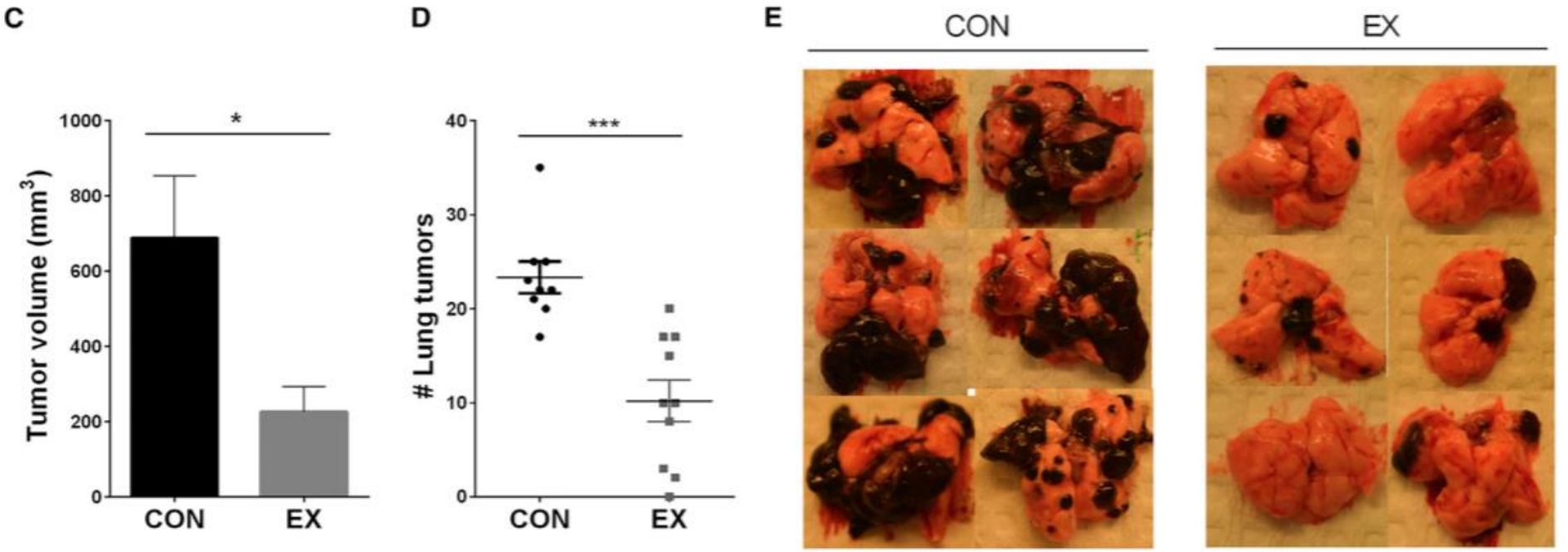


- Mobilization of NK cells are affected by:
  - muscle derived myokines
  - exercise-dependent hyperthermia
  - intratumoral vascularization and perfusion
- subsequently inducing the regulation, redistribution, and activation of mobilized NK cells

Voluntary Running Suppresses Tumor Growth through Epinephrine- and IL-6-Dependent NK Cell Mobilization and Redistribution

Line Pedersen,[1] Manja Idorn,[2] Gitte H. Olofsson,[2] Britt Lauenborg,[1] Intawat Nookaew,[3,4] Rasmus Hvass Hansen,[5] Helle Hjorth Johannesen,[5] Jürgen C. Becker,[6] Katrine S. Pedersen,[1] Christine Dethlefsen,[1] Jens Nielsen,[3] Julie Gehl,[7] Bente K. Pedersen,[1] Per thor Straten,[2,8] and Pernille Hojman[1,7,*]



Pedersen et al. Cell Metabolism 2016

Voluntary Running Suppresses Tumor Growth through Epinephrine- and IL-6-Dependent NK Cell Mobilization and Redistribution

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- Exercise reduces tumor incidence and growth in several mouse models
- Exercise increases NK cell infiltration, thereby controlling tumor growth
- Epinephrine mobilizes NK cells and β-blockade blunts the tumor suppression
- Exercise-induced muscle-derived IL-6 is involved in NK cell redistribution

Pedersen et al. Cell Metabolism 2016

Modulation of Murine Breast Tumor Vascularity, Hypoxia and Chemotherapeutic Response by Exercise

Allison S. Betof, Christopher D. Lascola, Douglas Weitzel, Chelsea Landon, Peter M. Scarbrough, Gayathri R. Devi, Gregory Palmer, Lee W. Jones*, Mark W. Dewhirst*

JNCI J Natl Cancer Inst (2015) 107(5): djv040

Orthotopic injection
(4T1 / 10 x 6)

BALB/C

RANDOMIZATION

- Arm A: Exercise
  Voluntary Wheel Running
  (n=12)
- Arm B: Chemotherapy
  Cyclophosphamide
  (n=12)
- Arm C: EX + CT
  Vol Running + Cyclo
  (n=12)
- Arm D: Control
  No Treatment Control
  (n=12)

End points

- Tumor outcomes
  - Volume
  - Metastasis
  - Signaling

Hypoxia and poor blood supply promote an aggressive phenotype

Can exercise increase blood perfusion and sensitivity to chemotherapy?

Cardio-Oncology
Research Program

Modulation of Murine Breast Tumor Vascularity, Hypoxia and Chemotherapeutic Response by Exercise

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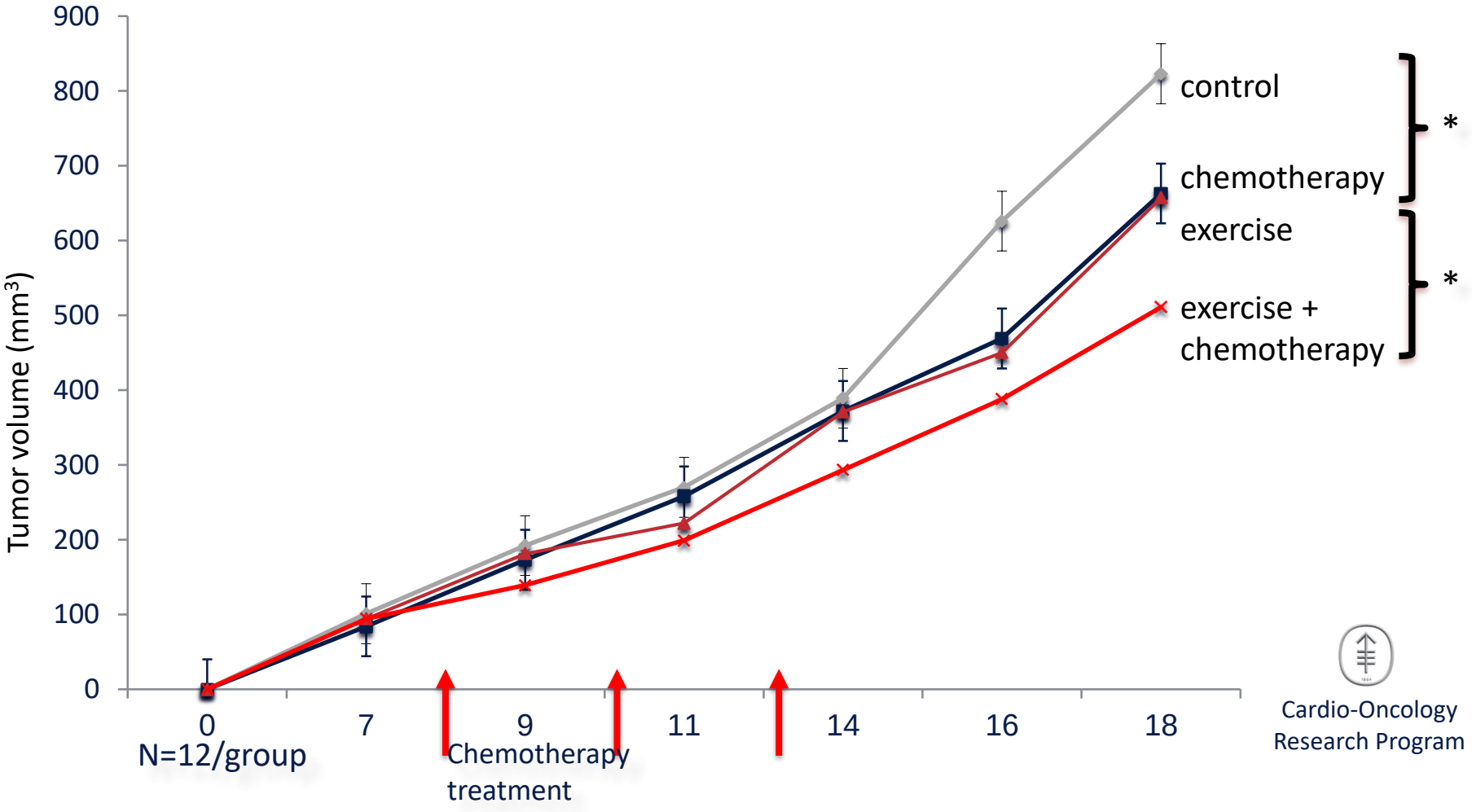
JNCI J Natl Cancer Inst (2015) 107(5): djv040



Cardio-Oncology Research Program

Modulation of Murine Breast Tumor Vascularity, Hypoxia and Chemotherapeutic Response by Exercise

Allison S. Betof, Christopher D. Lascola, Douglas Weitzel, Chelsea Landon, Peter M. Scarbrough, Gayathri R. Devi, Gregory Palmer, Lee W. Jones*, Mark W. Dewhirst*

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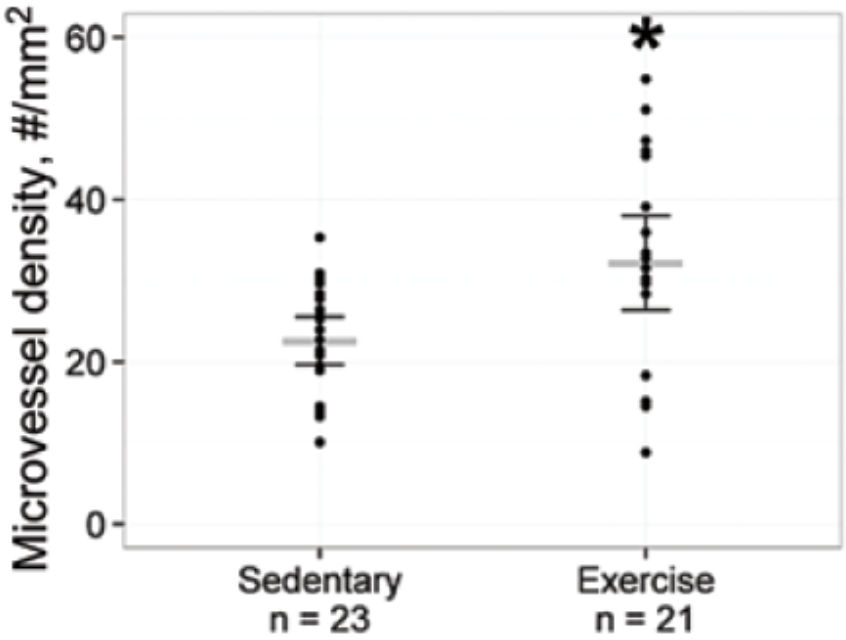
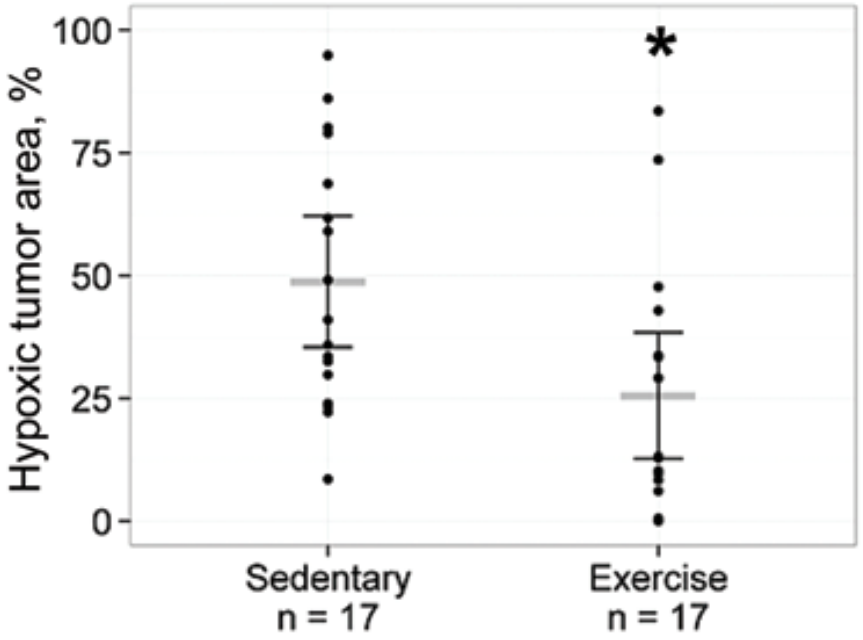




exercise stimulates “productive” or “physiologic” angiogenesis and vascular normalization, leading to a substantial reduction in intratumoral hypoxia

Effect of Acute Exercise on Prostate Cancer Cell Growth

Helene Rundqvist[1]*, Martin Augsten[1], Anna Strömberg[2], Eric Rullman[2], Sara Mijwel[1], Pedram Kharaziha[1], Theocharis Panaretakis[1], Thomas Gustafsson[2], Arne Östman[1]

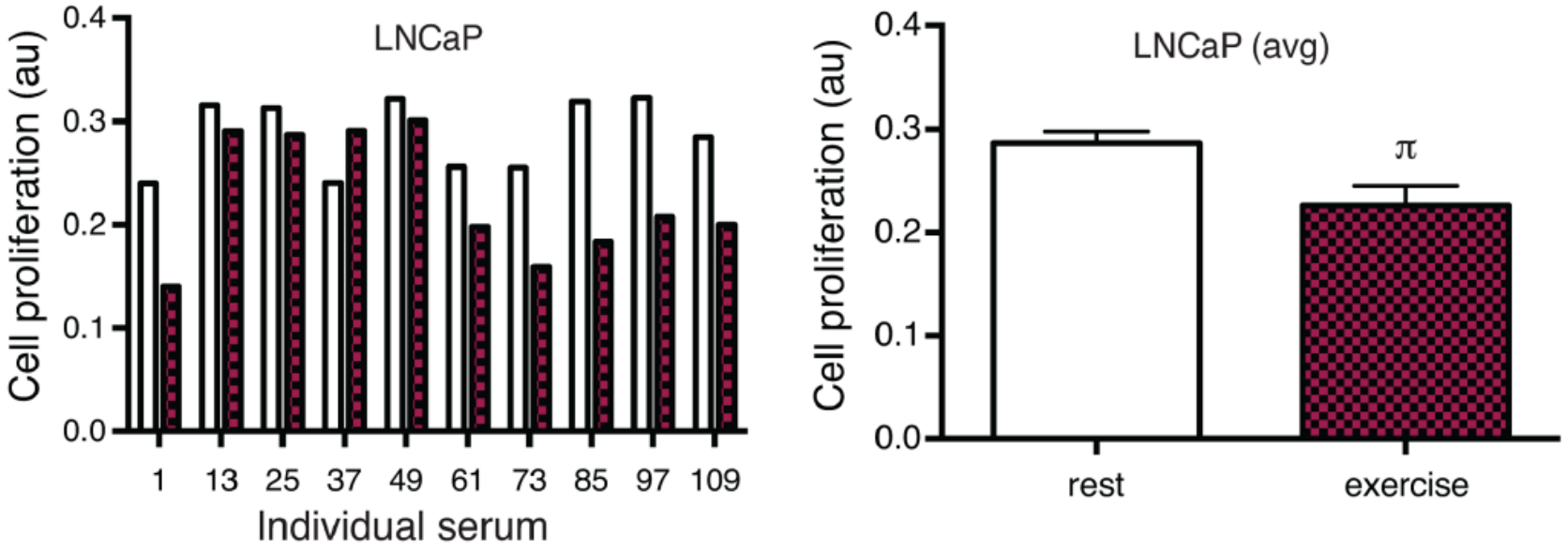


Figure 1. Growth of prostate cancer cells is reduced when exposed to exercise serum from 9 out of 10 individuals. A) Effect on LNCaP cells incubated for 48 hours with resting (rest) and exercise serum (exercise) from 10 individuals separately. B) Effect of the 10 individual serums on NIH3T3 cells. Data show all individuals separately (left panel) and as mean ± SEM. au (arbitrary units). π denotes a significant ($p \leq 0.05$) difference between incubation with rest and exercise serum.

Rundqvist H et al. *PLoS One*. 2013;8(7):e67579.

JOURNAL OF CLINICAL ONCOLOGY | COMMENTS AND CONTROVERSIES

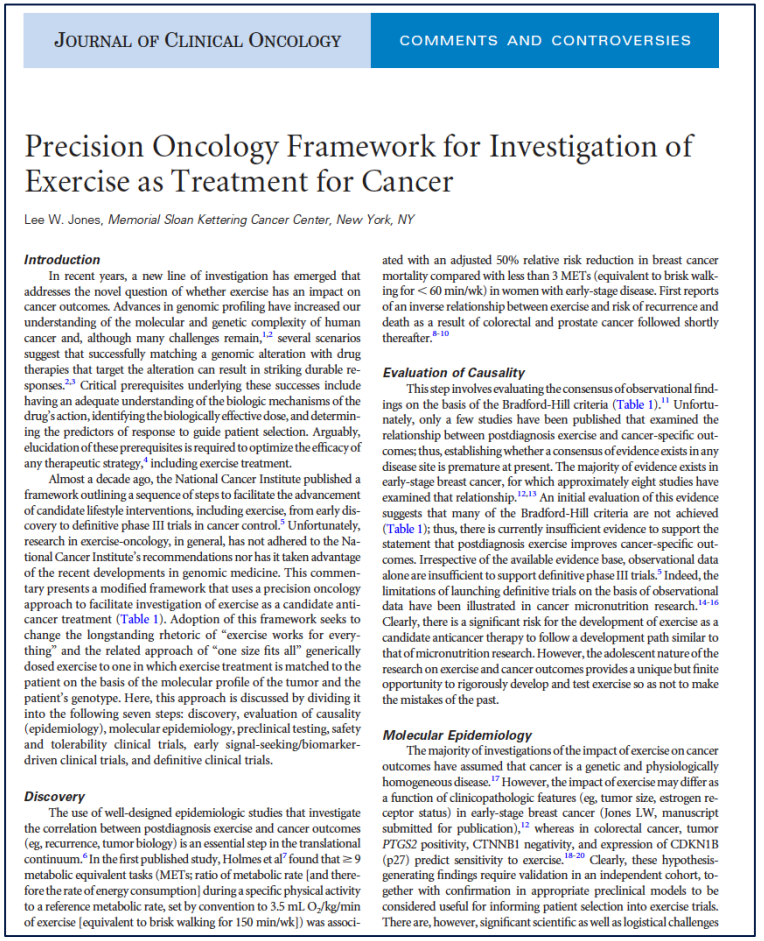
Precision Oncology Framework for Investigation of Exercise as Treatment for Cancer

Lee W. Jones, *Memorial Sloan Kettering Cancer Center, New York, NY*

Can exercise impact cancer outcomes?

Phase III Definitive trials
Colon - CHALLENGE
Prostate INTERVAL GAP-4

Disease and Overall Survival



JOURNAL OF CLINICAL ONCOLOGY COMMENTS AND CONTROVERSIES

Precision Oncology Framework for Investigation of Exercise as Treatment for Cancer

Lee W. Jones, *Memorial Sloan Kettering Cancer Center, New York, NY*

Introduction

In recent years, a new line of investigation has emerged that addresses the novel question of whether exercise has an impact on cancer outcomes. Advances in genomic profiling have increased our understanding of the molecular and genetic complexity of human cancer and, although many challenges remain,[1,2] several scenarios suggest that successfully matching a genomic alteration with drug therapies that target the alteration can result in striking durable responses.[2,3] Critical prerequisites underlying these successes include having an adequate understanding of the biologic mechanisms of the drug's action, identifying the biologically effective dose, and determining the predictors of response to guide patient selection. Arguably, elucidation of these prerequisites is required to optimize the efficacy of any therapeutic strategy,[4] including exercise treatment.

Almost a decade ago, the National Cancer Institute published a framework outlining a sequence of steps to facilitate the advancement of candidate lifestyle interventions, including exercise, from early discovery to definitive phase III trials in cancer control.[5] Unfortunately, research in exercise-oncology, in general, has not adhered to the National Cancer Institute's recommendations nor has it taken advantage of the recent developments in genomic medicine. This commentary presents a modified framework that uses a precision oncology approach to facilitate investigation of exercise as a candidate anticancer treatment (Table 1). Adoption of this framework seeks to change the longstanding rhetoric of "exercise works for everything" and the related approach of "one size fits all" generically dosed exercise to one in which exercise treatment is matched to the patient on the basis of the molecular profile of the tumor and the patient's genotype. Here, this approach is discussed by dividing it into the following seven steps: discovery, evaluation of causality (epidemiology), molecular epidemiology, preclinical testing, safety and tolerability clinical trials, early signal-seeking/biomarker-driven clinical trials, and definitive clinical trials.

Discovery

The use of well-designed epidemiologic studies that investigate the correlation between postdiagnosis exercise and cancer outcomes (eg, recurrence, tumor biology) is an essential step in the translational continuum.[6] In the first published study, Holmes et al[7] found that ≥ 9 metabolic equivalent tasks (METs; ratio of metabolic rate [and therefore the rate of energy consumption] during a specific physical activity to a reference metabolic rate, set by convention to 3.5 mL O_2/kg/min of exercise [equivalent to brisk walking for 150 min/wk]) was associated with an adjusted 50% relative risk reduction in breast cancer mortality compared with less than 3 METs (equivalent to brisk walking for < 60 min/wk) in women with early-stage disease. First reports of an inverse relationship between exercise and risk of recurrence and death as a result of colorectal and prostate cancer followed shortly thereafter.[8-10]

Evaluation of Causality

This step involves evaluating the consensus of observational findings on the basis of the Bradford-Hill criteria (Table 1).[11] Unfortunately, only a few studies have been published that examined the relationship between postdiagnosis exercise and cancer-specific outcomes; thus, establishing whether a consensus of evidence exists in any disease site is premature at present. The majority of evidence exists in early-stage breast cancer, for which approximately eight studies have examined that relationship.[12,13] An initial evaluation of this evidence suggests that many of the Bradford-Hill criteria are not achieved (Table 1); thus, there is currently insufficient evidence to support the statement that postdiagnosis exercise improves cancer-specific outcomes. Irrespective of the available evidence base, observational data alone are insufficient to support definitive phase III trials.[5] Indeed, the limitations of launching definitive trials on the basis of observational data have been illustrated in cancer micronutrition research.[14-16] Clearly, there is a significant risk for the development of exercise as a candidate anticancer therapy to follow a development path similar to that of micronutrition research. However, the adolescent nature of the research on exercise and cancer outcomes provides a unique but finite opportunity to rigorously develop and test exercise so as not to make the mistakes of the past.

Molecular Epidemiology

The majority of investigations of the impact of exercise on cancer outcomes have assumed that cancer is a genetic and physiologically homogeneous disease.[17] However, the impact of exercise may differ as a function of clinicopathologic features (eg, tumor size, estrogen receptor status) in early-stage breast cancer (Jones LW, manuscript submitted for publication),[12] whereas in colorectal cancer, tumor *PTGS2* positivity, CTNNB1 negativity, and expression of CDKN1B (p27) predict sensitivity to exercise.[18-20] Clearly, these hypothesis-generating findings require validation in an independent cohort, together with confirmation in appropriate preclinical models to be considered useful for informing patient selection into exercise trials. There are, however, significant scientific as well as logistical challenges

Jones LW. J Clin Oncol. 2015 Dec 10;33(35):4134-7.

Exercise Oncology
Research/clinical questions

- can exercise help manage treatment side effects/reduce treatment toxicities (e.g. muscle loss, fatigue)?
- will exercise interfere with treatment or response?
- can exercise lower the risk of cancer recurrence, delay progression and improve survival?
- what are the potential biological mechanisms?
- what is the optimal exercise program for benefit?

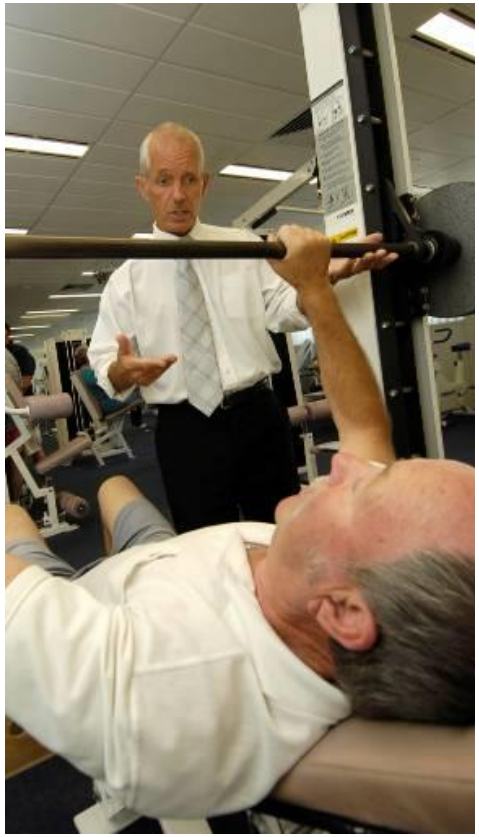
ACS/ACSM/ASCO/ESSA/NCCN Recommendations

- Engage in regular physical activity
- Avoid inactivity and return to normal daily activities as soon as possible
- Aim to exercise at least 150 min per week (aerobic) or 75 min (HI)
- **<u>Include strength training exercises at least 2 days per week</u>**

ACS, American Cancer Society; ACSM, American College of Sports Medicine.
Doyle , et al. ***CA Cancer*** *J Clin.* **2006**;56(6):323-353.
Schmitz KH et al. *Med Sci Sports Exerc.* 2010;42(7):1409-1426.

Considerations

- Long way since early studies from Winninghan (followed by RCTs in JCO)
- Exercise improves recovery/QoL after cancer
- Exercise manages symptoms during therapy (especially for symptomatic patients)
- Potential effects of exercise beyond symptoms/toxicities (cancer outcomes)
- Phase III Definitive trials (impact on disease endpoints)
- Biological mechanism



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Prostate Cancer Foundation of Australia

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Department of Innovation, Industry, Science and Research

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NHMRC Centre for Research Excellence
PROSTATE CANCER SURVIVORSHIP

Exercise Medicine Research Institute

vario health clinic

AUSTRALIA ECU EDITH COWAN UNIVERSITY

Thank You!

Daniel A. Galvão
d.galvao@ecu.edu.au

Griffith UNIVERSITY

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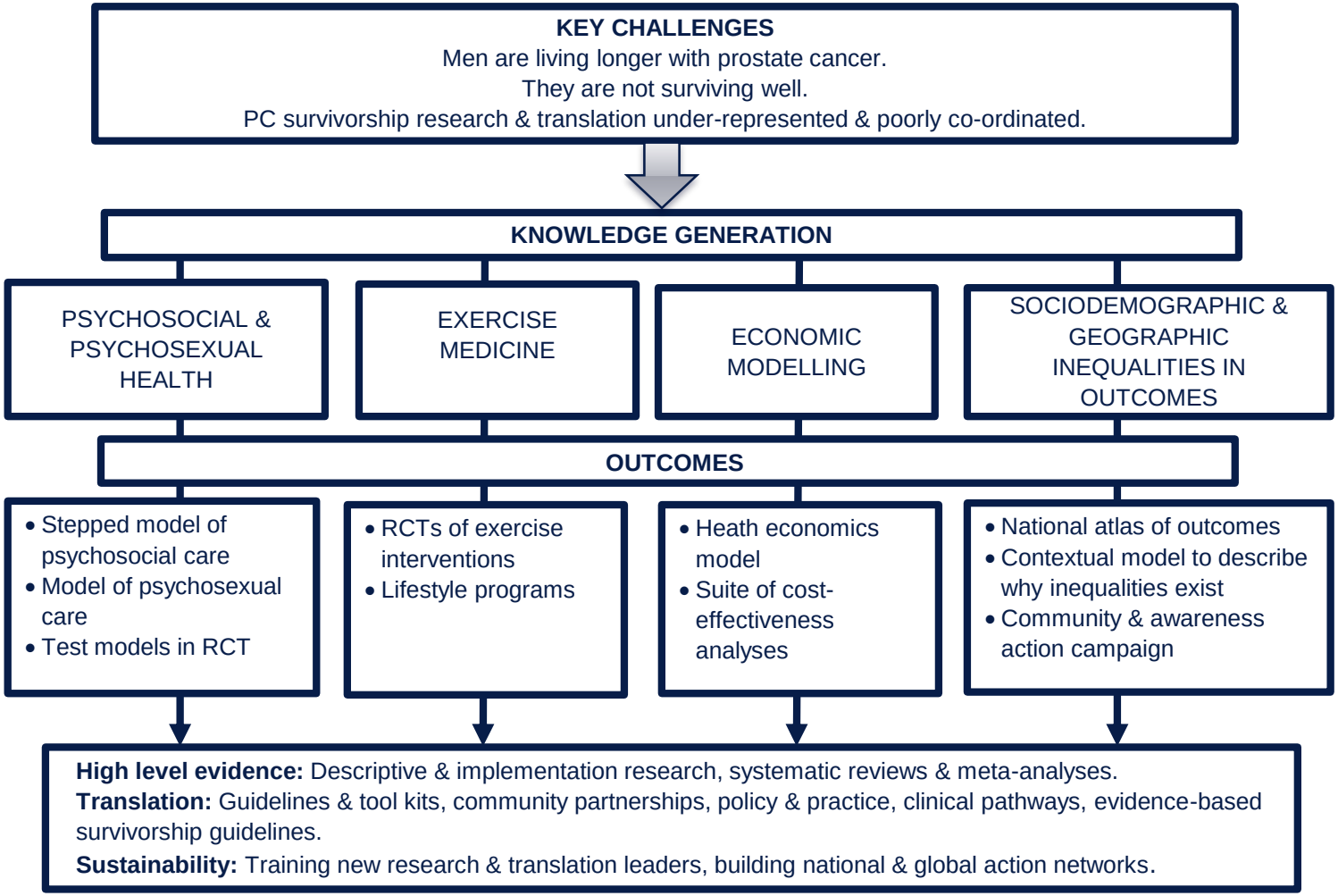

Exercise is Medicine Australia

Vision

To make physical activity a standard component of chronic disease prevention and management

Resources

Your Prescription for Health
ExeRcise is Medicine® Australia
www.exerciseismedicine.org.au

Visit www.exerciseismedicine.com.au for:

Factsheet library exercising safely for 30 health conditions including diabetes, cancer, heart disease, arthritis, depression

Screening tools identify patient risk levels and determine an appropriate action plan

Action Guides and referral templates for Healthcare Providers

Education RACGP, ACRRM and APNA approved workshops to build confidence, knowledge and skills

Practice Support Medical Software, waiting room materials, on the spot resources

Position Statements Written in collaboration with leading medical researchers